



Contents lists available at ScienceDirect

Journal of Arrhythmia

journal homepage: www.elsevier.com/locate/joa

CrossMark

Guideline

2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary

Hugh Calkins, MD, Chair¹, Gerhard Hindricks, MD, Vice-Chair^{2,*},
 Riccardo Cappato, MD, Vice-Chair^{3,61,62,¶}, Young-Hoon Kim, MD, PhD, Vice-Chair^{4,§},
 Eduardo B. Saad, MD, PhD, Vice-Chair^{5,‡}, Luis Aguinaga, MD, PhD^{6,‡}, Joseph G. Akar, MD, PhD⁷,
 Vinay Badhwar, MD^{8,#}, Josep Brugada, MD, PhD^{9,*}, John Camm, MD^{10,*}, Peng-Sheng Chen, MD¹¹,
 Shih-Ann Chen, MD^{12,§}, Mina K. Chung, MD¹³, Jens Cosedis Nielsen, DMSc, PhD^{14,*},
 Anne B. Curtis, MD^{15,||}, D. Wyn Davies, MD^{16,¶}, John D. Day, MD¹⁷, André d'Avila, MD, PhD^{18,††},
 N.M.S. (Natasja) de Groot, MD, PhD^{19,*}, Luigi Di Biase, MD, PhD^{20,*}, Mattias Duytschaever, MD, PhD^{21,*},
 James R. Edgerton, MD^{22,#}, Kenneth A. Ellenbogen, MD²³, Patrick T. Ellinor, MD, PhD²⁴,
 Sabine Ernst, MD, PhD^{25,*}, Guilherme Fenelon, MD, PhD^{26,‡}, Edward P. Gerstenfeld, MS, MD²⁷,
 David E. Haines, MD²⁸, Michel Haissaguerre, MD^{29,*}, Robert H. Helm, MD³⁰, Elaine Hylek, MD, MPH³¹,
 Warren M. Jackman, MD³², Jose Jalife, MD³³, Jonathan M. Kalman, MBBS, PhD^{34,§},
 Josef Kautzner, MD, PhD^{35,*}, Hans Kottkamp, MD^{36,*}, Karl Heinz Kuck, MD, PhD^{37,*},
 Koichiro Kumagai, MD, PhD^{38,§}, Richard Lee, MD, MBA^{39,#}, Thorsten Lewalter, MD, PhD^{40,¶},
 Bruce D. Lindsay, MD⁴¹, Laurent Macle, MD^{42,*}, Moussa Mansour, MD⁴³, Francis E. Marchlinski, MD⁴⁴,
 Gregory F. Michaud, MD^{45,†}, Hiroshi Nakagawa, MD, PhD⁴⁶, Andrea Natale, MD⁴⁷, Stanley Nattel, MD⁴⁸,
 Ken Okumura, MD, PhD^{49,††}, Douglas Packer, MD⁵⁰, Evgeny Pokushalov, MD, PhD^{51,*},
 Matthew R. Reynolds, MD, MSc⁵², Prashanthan Sanders, MBBS, PhD⁵³, Mauricio Scanavacca, MD, PhD^{54,‡},
 Richard Schilling, MD^{55,*}, Claudio Tondo, MD, PhD^{56,*}, Hsuan-Ming Tsao, MD^{57,§}, Atul Verma, MD⁵⁸,
 David J. Wilber, MD⁵⁹, Teiichi Yamane, MD, PhD^{60,††}

¹ Johns Hopkins Medical Institutions, Baltimore, MD² Heart Center Leipzig, Leipzig, Germany³ Humanitas Research Hospital, Arrhythmias and Electrophysiology Research Center, Milan, Italy

Abbreviations: AAD, antiarrhythmic drug; AF, atrial fibrillation; AFL, atrial flutter; CB, cryoballoon; CFAE, complex fractionated atrial electrogram; LA, left atrial; LAA, left atrial appendage; LGE, late gadolinium-enhanced; LOE, level of evidence; MRI, magnetic resonance imaging; OAC, oral anticoagulation; RF, radiofrequency

Developed in partnership with and endorsed by the European Heart Rhythm Association (EHRA), the European Cardiac Arrhythmia Society (ECAS), the Asia Pacific Heart Rhythm Society (APHRS), and the Latin American Society of Cardiac Stimulation and Electrophysiology (Sociedad Latinoamericana de Estimulación Cardíaca y Electro-fisiología [SOLAECE]).

Developed in collaboration with and endorsed by the Society of Thoracic Surgeons (STS), the American College of Cardiology (ACC), the American Heart Association (AHA), the Canadian Heart Rhythm Society (CHRS), the Japanese Heart Rhythm Society (JHRS), and the Brazilian Society of Cardiac Arrhythmias (Sociedade Brasileira de Arritmias Cardíacas [SOBRAC]).

Chair: Hugh Calkins, MD, Johns Hopkins Medical Institutions, Baltimore, MD, USA.

Section Chairs:

Definitions, Mechanisms, and Rationale for AF Ablation: Shih-Ann Chen, MD, National Yang-Ming University, Taipei, Taiwan.

Modifiable Risk Factors for AF and Impact on Ablation: Jonathan M. Kalman, MBBS, PhD, Royal Melbourne Hospital and University of Melbourne, Melbourne, Australia.

Indications: Claudio Tondo, MD, PhD, Cardiac Arrhythmia Research Center, Centro Cardiologico Monzino, IRCCS, Department of Cardiovascular Sciences, University of Milan, Milan, Italy.

Strategies, Techniques, and Endpoints: Karl Heinz Kuck, MD, PhD, Asklepios Klinik St. Georg, Hamburg, Germany.

Technology and Tools: Andrea Natale, MD, Texas Cardiac Arrhythmia Institute, St. David's Medical Center, Austin, TX, USA.

Technical Aspects of Ablation to Maximize Safety and Anticoagulation: David E. Haines, MD, Beaumont Health System, Royal Oak, MI, USA.

Follow-up Considerations: Francis E. Marchlinski, MD, Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine, Philadelphia, PA, USA.

Outcomes and Efficacy: Matthew R. Reynolds, MD, MSc, Lahey Hospital and Medical Center, Burlington, MA, USA.

Complications: D. Wyn Davies, MD, Imperial College Healthcare NHS Trust, London, United Kingdom.

Training Requirements: Bruce D. Lindsay, MD, Cleveland Clinic, Cleveland, OH, USA.

Surgical and Hybrid AF Ablation: James R. Edgerton, MD, The Heart Hospital, Baylor Plano, Plano, TX, USA.

Clinical Trial Design: Atul Verma, MD, Southlake Regional Health Centre, University of Toronto, Toronto, Canada.

Correspondence: Heart Rhythm Society, 1325 G Street NW, Suite 400, Washington, DC 20005. E-mail address: clinicaldocs@hrsonline.org.

<http://dx.doi.org/10.1016/j.joa.2017.08.001>

1880-4276/© 2017 HRS, EHRA, a registered branch of the ESC; ECAS; JHRS and APHRS; and SOLAECE. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

- 4 Korea University, Seoul, South Korea
- 5 Hospital Pro-Cardiaco and Hospital Samaritano, Botafogo, Rio de Janeiro, Brazil
- 6 Centro Privado de Cardiología, Tucuman, Argentina
- 7 Yale University School of Medicine, New Haven, CT
- 8 West Virginia University School of Medicine, Morgantown, WV
- 9 Cardiovascular Institute, Hospital Clínic, University of Barcelona, Catalonia, Spain
- 10 St. George's University of London, London, United Kingdom
- 11 Indiana University School of Medicine, Indianapolis, IN
- 12 National Yang-Ming University, Taipei, Taiwan
- 13 Cleveland Clinic, Cleveland, OH
- 14 Aarhus University Hospital, Skejby, Denmark
- 15 University at Buffalo, Buffalo, NY
- 16 Imperial College Healthcare NHS Trust, London, United Kingdom
- 17 Intermountain Medical Center Heart Institute, Salt Lake City, UT
- 18 Hospital SOS Cardio, Florianópolis, SC, Brazil
- 19 Erasmus Medical Center, Rotterdam, the Netherlands
- 20 Albert Einstein College of Medicine, Montefiore-Einstein Center for Heart & Vascular Care, Bronx, NY
- 21 Universitair Ziekenhuis Gent (Ghent University Hospital), Ghent, Belgium
- 22 The Heart Hospital, Baylor Plano, Plano, TX
- 23 Virginia Commonwealth University School of Medicine, Richmond, VA
- 24 Massachusetts General Hospital, Boston, MA
- 25 Royal Brompton and Harefield NHS Foundation Trust, National Heart and Lung Institute, Imperial College London, London, United Kingdom
- 26 Albert Einstein Jewish Hospital, Federal University of São Paulo, São Paulo, Brazil
- 27 University of California, San Francisco, San Francisco, CA
- 28 Beaumont Health System, Royal Oak, MI
- 29 Hôpital Cardiologique du Haut-Lévêque, Pessac, France
- 30 Boston University Medical Center, Boston, MA
- 31 Boston University School of Medicine, Boston, MA
- 32 Heart Rhythm Institute, University of Oklahoma Health Sciences Center, Oklahoma City, OK
- 33 University of Michigan, Ann Arbor, MI, the National Center for Cardiovascular Research Carlos III (CNIC) and CIBERCV, Madrid, Spain
- 34 Royal Melbourne Hospital and University of Melbourne, Melbourne, Australia
- 35 Institute for Clinical and Experimental Medicine, Prague, Czech Republic
- 36 Hirslanden Hospital, Department of Electrophysiology, Zurich, Switzerland
- 37 Asklepios Klinik St. Georg, Hamburg, Germany
- 38 Heart Rhythm Center, Fukuoka Sanno Hospital, Fukuoka, Japan
- 39 Saint Louis University Medical School, St. Louis, MO
- 40 Department of Cardiology and Intensive Care, Hospital Munich-Thalkirchen, Munich, Germany
- 41 Cleveland Clinic, Cleveland, OH
- 42 Montreal Heart Institute, Department of Medicine, Université de Montréal, Montréal, Canada
- 43 Massachusetts General Hospital, Boston, MA
- 44 Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine, Philadelphia, PA
- 45 Brigham and Women's Hospital, Boston, MA
- 46 Heart Rhythm Institute, University of Oklahoma Health Sciences Center, Oklahoma City, OK
- 47 Texas Cardiac Arrhythmia Institute, St. David's Medical Center, Austin, TX
- 48 Montreal Heart Institute and Université de Montréal, Montreal, Canada, McGill University, Montreal, Canada, and University Duisburg-Essen, Essen, Germany
- 49 Division of Cardiology, Saiseikai Kumamoto Hospital, Kumamoto, Japan
- 50 Mayo Clinic, Rochester, MN
- 51 State Research Institute of Circulation Pathology, Novosibirsk, Russia
- 52 Lahey Hospital and Medical Center, Burlington, MA
- 53 Centre for Heart Rhythm Disorders, South Australian Health and Medical Research Institute, University of Adelaide and Royal Adelaide Hospital, Adelaide, Australia
- 54 Instituto do Coração (InCor), São Paulo, Brazil
- 55 Barts Heart Centre, London, United Kingdom
- 56 Cardiac Arrhythmia Research Center, Centro Cardiologico Monzino, IRCCS, Department of Cardiovascular Sciences, University of Milan, Milan, Italy
- 57 National Yang-Ming University Hospital, Yilan City, Taiwan
- 58 Southlake Regional Health Centre, University of Toronto, Toronto, Canada
- 59 Loyola University of Chicago, Chicago, IL
- 60 Jikei University School of Medicine, Tokyo, Japan
- 61 Department of Biomedical Sciences, Humanitas University, Milan, Italy
- 62 IRCCS, Humanitas Clinical and Research Center, Milan, Italy

* Representative of the European Heart Rhythm Association (EHRA)

† Representative of the American Heart Association (AHA)

‡ Representative of the Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología (SOLAECE)

§ Representative of the Asia Pacific Heart Rhythm Society (APHRS)

|| Representative of the American College of Cardiology (ACC)

¶ Representative of the European Cardiac Arrhythmia Society (ECAS)

Representative of the Society of Thoracic Surgeons (STS)

** Representative of the Canadian Heart Rhythm Society (CHRS)

†† Representative of the Japanese Heart Rhythm Society (JHRS)

‡‡ Representative of the Sociedade Brasileira de Arritmias Cardíacas (SOBRAC)

ARTICLE INFO

Available online 15 September 2017

Keywords:

Ablation
 Arrhythmia
 Atrial fibrillation
 Atrial flutter
 Atrial tachycardia
 Catheter ablation
 Surgical ablation
 Stroke
 Anticoagulation

Document Reviewers: Carina Blomström-Lundqvist, MD, PhD; Angelo A.V. De Paola, MD, PhD; Peter M. Kistler, MBBS, PhD; Gregory Y.H. Lip, MD; Nicholas S. Peters, MD; Cristiano F. Pisani, MD; Antonio Raviele, MD; Eduardo B. Saad, MD, PhD; Kazuhiro Satomi, MD, PhD; Martin K. Stiles, MB ChB, PhD; Stephan Willems, MD, PhD.

Section 1: Introduction

During the past three decades, catheter and surgical ablation of atrial fibrillation (AF) have evolved from investigational procedures to their current role as effective treatment options for patients with AF. Surgical ablation of AF, using either standard, minimally invasive, or hybrid techniques, is available in most major hospitals throughout the world. Catheter ablation of AF is even more widely available, and is now the most commonly performed catheter ablation procedure.

In 2007, an initial Consensus Statement on Catheter and Surgical AF Ablation was developed as a joint effort of the Heart Rhythm Society (HRS), the European Heart Rhythm Association (EHRA), and the European Cardiac Arrhythmia Society (ECAS).¹ The 2007 document was also developed in collaboration with the Society of Thoracic Surgeons (STS) and the American College of Cardiology (ACC). This Consensus Statement on Catheter and Surgical AF Ablation was rewritten in 2012 to reflect the many advances in AF ablation that had occurred in the interim.² The rate

of advancement in the tools, techniques, and outcomes of AF ablation continue to increase as enormous research efforts are focused on the mechanisms, outcomes, and treatment of AF. For this reason, the HRS initiated an effort to rewrite and update this Consensus Statement. Reflecting both the worldwide importance of AF, as well as the worldwide performance of AF ablation, this document is the result of a joint partnership between the HRS, EHRA, ECAS, the Asia Pacific Heart Rhythm Society (APHRS), and the Latin American Society of Cardiac Stimulation and Electrophysiology (Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología [SOLAECE]). The purpose of this 2017 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 writing group, convened by these five international societies. The writing group is charged with defining the indications, techniques, and outcomes of AF ablation procedures. Included within this document are recommendations pertinent to the design of clinical trials in the field of AF ablation and the reporting of outcomes, including definitions relevant to this topic.

The writing group is composed of 60 experts representing 11 organizations: HRS, EHRA, ECAS, APHRS, SOLAECE, STS, ACC, American Heart Association (AHA), Canadian Heart Rhythm Society (CHRS), Japanese Heart Rhythm Society (JHRS), and Brazilian Society of Cardiac Arrhythmias (Sociedade Brasileira de Arritmias Cardíacas [SOBRAC]). All the members of the writing group, as well as peer reviewers of the document, have provided disclosure statements for all relationships that might be perceived

Table 1
 Atrial fibrillation definitions

AF episode	An AF episode is defined as AF that is documented by ECG monitoring or intracardiac electrogram monitoring and has a duration of at least 30 seconds, or if less than 30 seconds, is present throughout the ECG monitoring tracing. The presence of subsequent episodes of AF requires that sinus rhythm be documented by ECG monitoring between AF episodes.
Chronic AF	Chronic AF has variable definitions and should not be used to describe populations of AF patients undergoing AF ablation.
Early persistent AF	Early persistent AF is defined as AF that is sustained beyond 7 days but is less than 3 months in duration.
Lone AF	Lone AF is a historical descriptor that is potentially confusing and should not be used to describe populations of patients with AF undergoing AF ablation.
Long-standing persistent AF	Long-standing persistent AF is defined as continuous AF of greater than 12 months' duration.
Paroxysmal AF	Paroxysmal AF is defined as AF that terminates spontaneously or with intervention within 7 days of onset.
Permanent AF	Permanent AF is defined as the presence of AF that is accepted by the patient and physician, and for which no further attempts to restore or maintain sinus rhythm will be undertaken. The term <i>permanent AF</i> represents a therapeutic attitude on the part of the patient and physician rather than an inherent pathophysiological attribute of AF. The term <i>permanent AF</i> should not be used within the context of a rhythm control strategy with antiarrhythmic drug therapy or AF ablation.
Persistent AF	Persistent AF is defined as continuous AF that is sustained beyond 7 days.
Silent AF	Silent AF is defined as asymptomatic AF diagnosed with an opportune ECG or rhythm strip.

AF = atrial fibrillation; ECG = electrocardiogram.

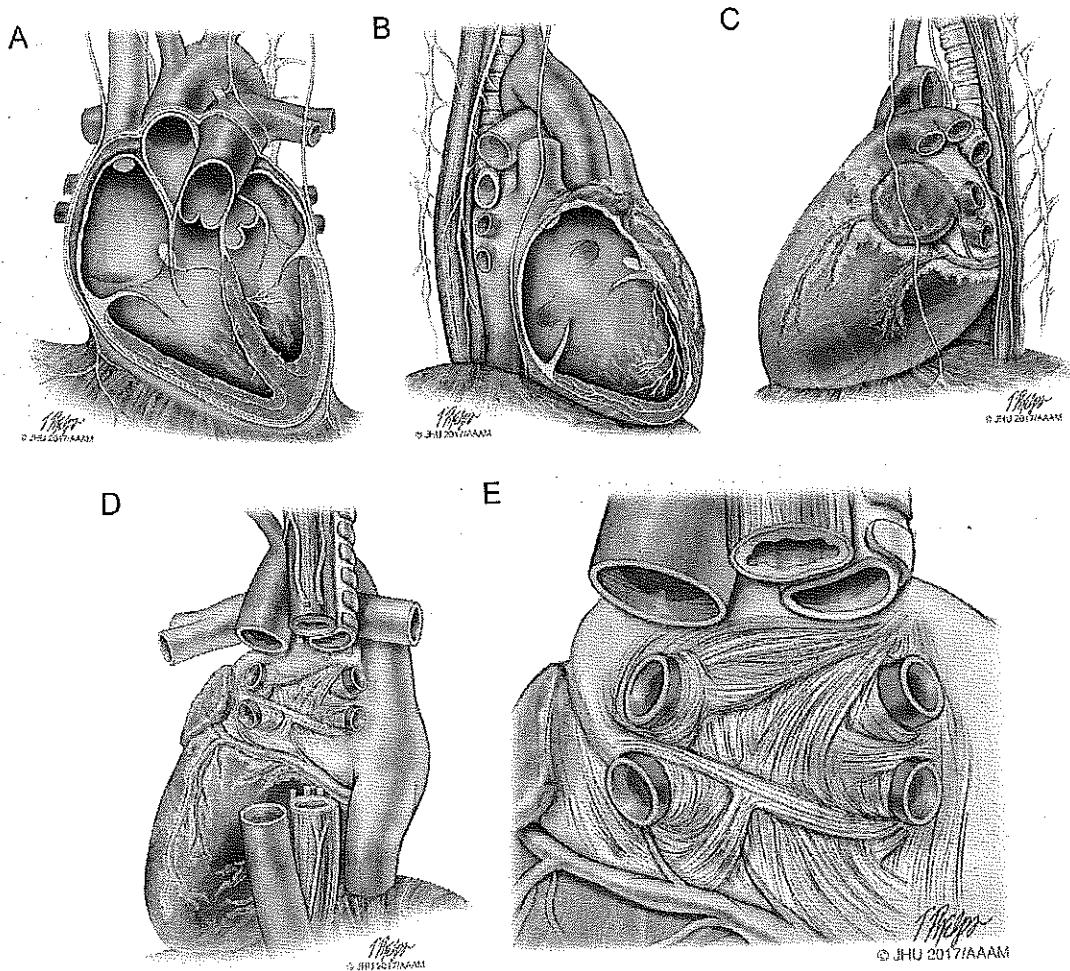


Figure 1. Anatomical drawings of the heart relevant to AF ablation. This series of drawings shows the heart and associated relevant structures from four different perspectives relevant to AF ablation. This drawing includes the phrenic nerves and the esophagus. A: The heart viewed from the anterior perspective. B: The heart viewed from the right lateral perspective. C: The heart viewed from the left lateral perspective. D: The heart viewed from the posterior perspective. E: The left atrium viewed from the posterior perspective.
Illustration: Tim Phelps © 2017 Johns Hopkins University, AAM.

as real or potential conflicts of interest. All author and peer reviewer disclosure information is provided in Table A1 and Table B1.

In writing a consensus document, it is recognized that *consensus* does not mean that there was complete agreement among all the writing group members. Surveys of the entire writing group were used to identify areas of consensus concerning performance of AF ablation procedures and to develop recommendations concerning the indications for catheter and surgical AF ablation. These recommendations were systematically balloted by the 60 writing group members and were approved by a minimum of 80% of these members. The recommendations were also subject to a 1-month public comment period. Each partnering and collaborating organization then officially reviewed, commented on, edited, and endorsed the final document and recommendations.

The grading system for indication of class of evidence level was adapted based on that used by the ACC and the AHA.^{3,4} It is important to state, however, that this document is not a guideline. The indications for catheter and surgical ablation of AF, as well as

recommendations for procedure performance, are presented with a Class and Level of Evidence (LOE) to be consistent with what the reader is familiar with 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; and a Class III recommendation means that AF ablation is of no proven benefit and is not recommended.

The writing group reviewed and ranked evidence supporting current recommendations with the weight of evidence ranked as Level A if the data were derived from high-quality evidence from more than one randomized clinical trial, meta-analyses of high-quality randomized clinical trials, or one or more randomized clinical trials corroborated by high-quality registry studies. The writing group ranked available evidence as Level B-R when there

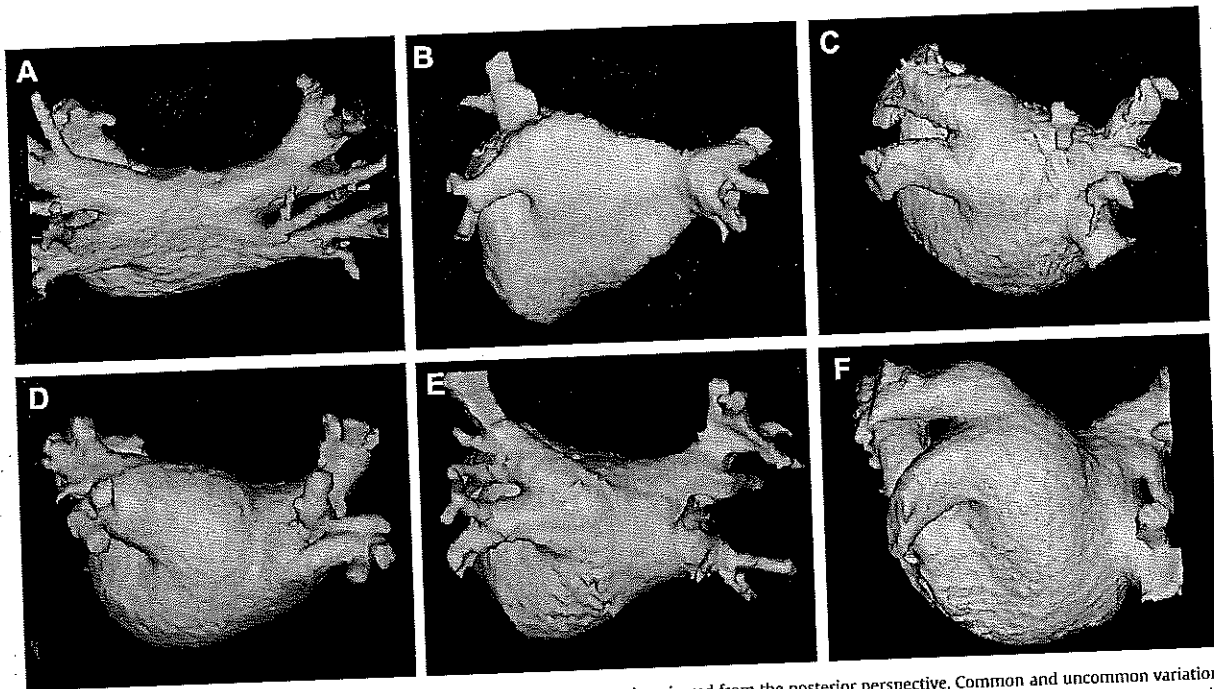


Figure 2. This figure includes six CT or MR images of the left atrium and pulmonary veins viewed from the posterior perspective. Common and uncommon variations in PV anatomy are shown. A: Standard PV anatomy with 4 distinct PV ostia. B: Variant PV anatomy with a right common and a left common PV. C: Variant PV anatomy with a left common PV with a short trunk and an anomalous PV arising from the right posterior left atrial wall. D and E: Variant PV anatomy with a common left PV with a long trunk. F: Variant PV anatomy with a massive left common PV.

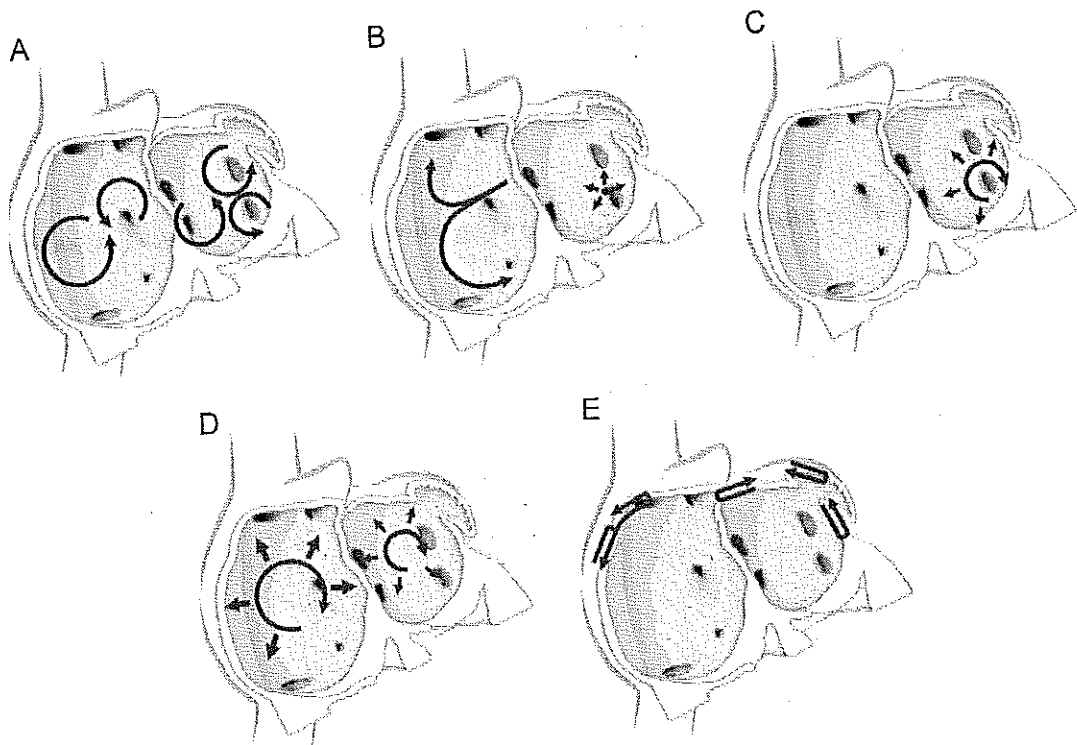


Figure 3. Schematic drawing showing various hypotheses and proposals concerning the mechanisms of atrial fibrillation. A: Multiple wavelets hypothesis. B: Rapidly discharging automatic foci. C: Single reentrant circuit with fibrillatory conduction. D: Functional reentry resulting from rotors or spiral waves. E: AF maintenance resulting from dissociation between epicardial and endocardial layers, with mutual interaction producing multiplying activity that maintains the arrhythmia.

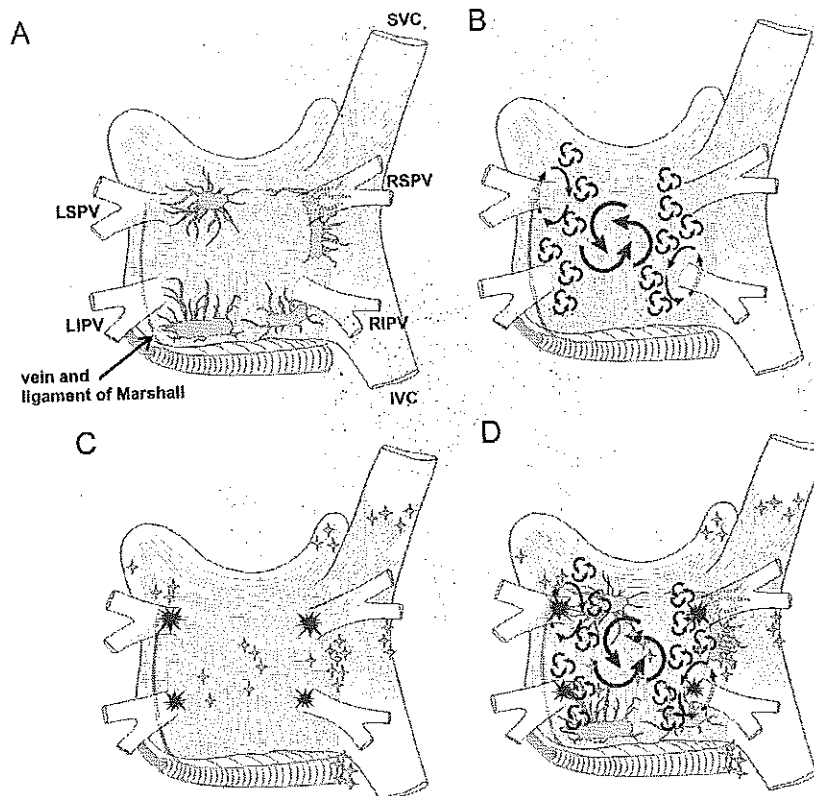


Figure 4. Structure and mechanisms of atrial fibrillation. **A:** Schematic drawing of the left and right atria as viewed from the posterior perspective. The extension of muscular fibers onto the PVs can be appreciated. Shown in yellow are the five major left atrial autonomic ganglionic plexi (GP) and 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 with permission from Calkins et al. *Heart Rhythm* 2012; 9:632–696.e21.²

was moderate-quality evidence from one or more randomized clinical trials, or meta-analyses of moderate-quality randomized clinical trials. Level B-NR was used to denote moderate-quality evidence from one or more well-designed, well-executed non-randomized studies, observational studies, or registry studies. This designation was also used to denote moderate-quality evidence from meta-analyses of such studies. Evidence was ranked as Level C-LD when the primary source of the recommendation was randomized or nonrandomized observational or registry studies with limitations of design or execution, meta-analyses of such studies, or physiological or mechanistic studies of human subjects. Level C-EO was defined as expert opinion based on the clinical experience of the writing group.

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 for the purpose of guiding overall AF management strategies.^{5,6} This consensus document is specifically focused on catheter and surgical ablation of AF, and summarizes the opinion of the writing group 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 caring for patients who are undergoing, or are being considered for, catheter or surgical ablation procedures for AF, and those involved in research in the field of AF ablation. This statement is not intended to recommend or promote catheter or

surgical ablation of AF. Rather, the ultimate judgment regarding care of a particular patient must be made by the health care provider and the patient in light of all the circumstances presented by that patient.

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. A second major objective is to provide recommendations for designing clinical trials and reporting outcomes of clinical trials of AF ablation. 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 under way.

Section 2: Definitions, Mechanisms, and Rationale for AF Ablation

This section of the document provides definitions for use in the diagnosis of AF. This section also provides an in-depth review of the mechanisms of AF and rationale for catheter and surgical AF ablation (Table 1, Figures 1–6).

Section 3: Modifiable Risk Factors for AF and Impact on Ablation

Management of patients with AF has traditionally consisted of three main components: (1) anticoagulation for stroke prevention;

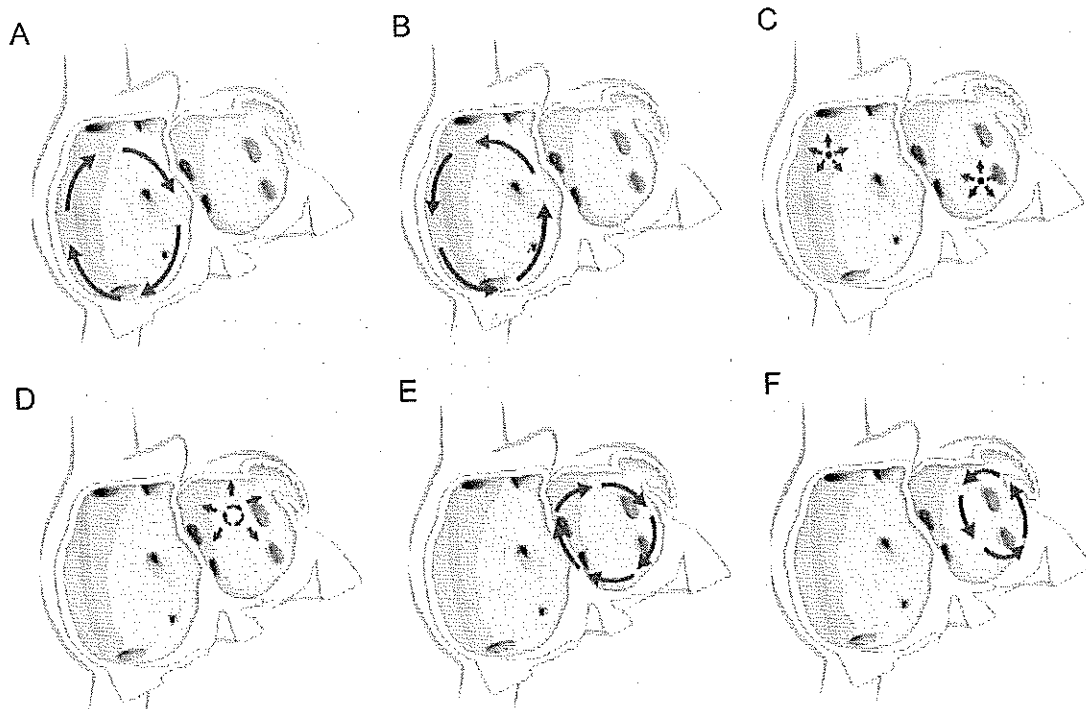


Figure 5. Schematic drawing showing mechanisms of atrial flutter and atrial tachycardia. **A:** Isthmus-dependent reverse common (clockwise) atrial flutter. **B:** Isthmus-dependent common (counter clockwise) atrial flutter. **C:** Focal atrial tachycardia with circumferential spread of activation of the atria (can arise from multiple sites within the left and right atrium). **D:** Microreentrant atrial tachycardia with circumferential spread of activation of the atria. **E:** Perimitral atrial flutter. **F:** Roof-dependent atrial flutter.

(2) rate control; and (3) rhythm control. With the emergence of large amounts of data, which have both defined and called attention to the interaction between modifiable risk factors and the development of AF and outcomes of AF management, we believe it is time to include risk factor modification as the fourth pillar of AF management. This section of the document reviews the link between modifiable risk factors and both the development of AF and their impacts on the outcomes of AF ablation.

Section 4: Indications

Shown in Table 2, and summarized in Figures 7 and 8 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 provided, as well as a selection of the key references supporting these levels of evidence. In making these recommendations, the writing group considered the body of published literature that has defined the safety and efficacy of catheter and surgical ablation of AF. Also considered in these recommendations is the personal lifetime experience in the field of each of the writing group members. Both the number of clinical trials and the quality of these trials were considered. In considering the class of indications recommended by this writing group, 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 a surgeon who has received appropriate training and/or who has a certain level of experience and is performing the procedure in an experienced center (Section 11). Catheter and surgical ablation of AF are highly complex procedures, and a careful assessment of the benefit and risk must be considered for each patient. Second, these indications

stratify patients based only on the type of AF and whether the procedure is being performed prior to or following a trial of one or more Class I or III antiarrhythmic medications. This document for the first time includes indications for catheter ablation of select asymptomatic patients. As detailed in Section 9, there are many other 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 (LA) size, patient age and frailty, as well as the duration of time the 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. In the presence of substantial risk or anticipated difficulty of ablation, it could be more appropriate to use additional antiarrhythmic drug (AAD) options, even if the patient on face value might present with a Class I or IIa indication for ablation. Third, it is important to consider patient preference and values. Some patients are reluctant to consider a major procedure or surgery and have a strong preference for a pharmacological approach. In these patients, trials of antiarrhythmic agents including amiodarone might be preferred to catheter ablation. On the other hand, some patients prefer a nonpharmacological approach. Fourth, it is important to recognize that some patients early in the course of their AF journey might have only infrequent episodes for many years and/or could have AF that is responsive to well-tolerated AAD therapy. And finally, it is important to bear in mind that a decision to perform catheter or surgical AF ablation should only be made after a patient carefully considers the risks, benefits, and alternatives to the procedure.

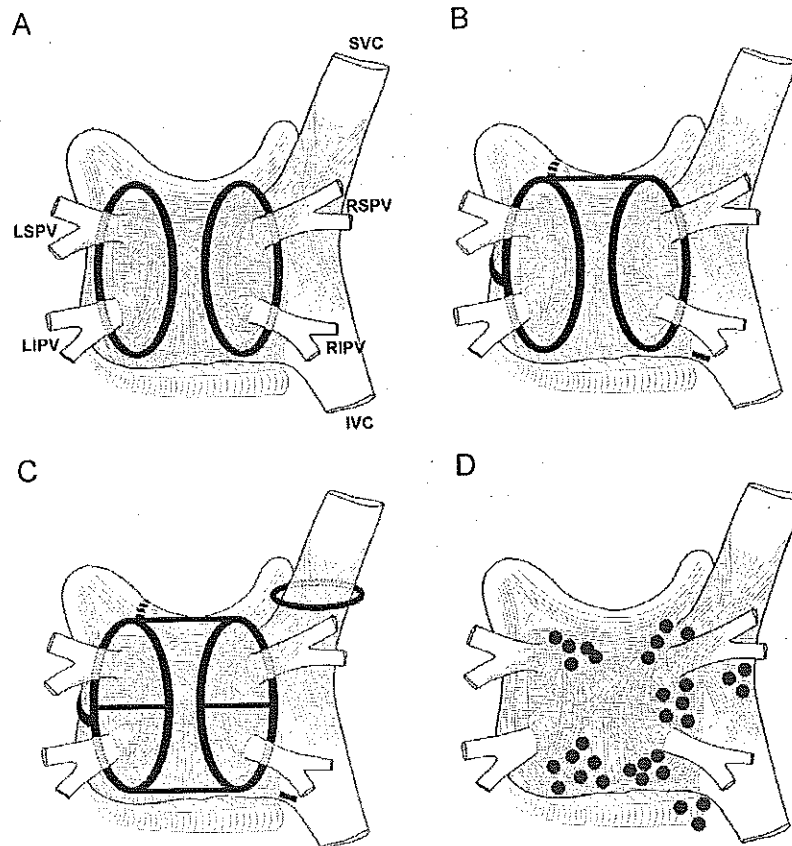


Figure 6. Schematic of common lesion sets employed in AF ablation. **A:** The circumferential ablation lesions that are created in a circumferential fashion around the right and the left PVs. The primary endpoint of this ablation strategy is the electrical isolation of the PV musculature. **B:** Some 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 end 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 shown. 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 6B, but also shows additional linear ablation lesions between the superior and inferior PVs resulting in a figure of eight lesion sets 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:** Representative sites for ablation when targeting rotational activity or CFAEs are targeted. Modified with permission from Calkins et al. *Heart Rhythm* 2012; 9:632–696.e21.³

Section 5: Strategies, Techniques, and Endpoints

The writing group recommendations for techniques to be used for ablation of persistent and long-standing persistent AF (Table 3), adjunctive ablation strategies, nonablative strategies to improve outcomes of AF ablation, and endpoints for ablation of paroxysmal, persistent, and long-standing persistent AF are covered in this section. A schematic overview of common lesion sets created during an AF ablation procedure is shown in Figure 6.

Section 6: Technology and Tools

This section of the consensus statement provides an update on many of the 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 radiofrequency (RF) energy is the dominant energy source available for ablation of typical and atypical atrial flutter (AFL).

Although cryoablation is a commonly employed tool for AF ablation, it is not well suited for ablation of typical or atypical AFL. Other energy sources and tools are available in some parts of the world and/or are in various stages of development and/or clinical investigation. Shown in Figure 9 are schematic drawings of AF ablation using point-by-point RF energy (Figure 9A) and AF ablation using the cryoballoon (CB) system (Figure 9B).

Section 7: Technical Aspects of Ablation to Maximize Safety and Anticoagulation

Anticoagulation strategies pre-, during, and postcatheter ablation of AF (Table 4); signs and symptoms of complications that can occur within the first several months following ablation (Table 5); anesthesia or sedation during ablation; and approaches to minimize risk of an atrial esophageal fistula are discussed in this section.

Table 2
Indications for catheter (A and B) and surgical (C, D, and E) ablation of atrial fibrillation

	Recommendation	Class	LOE	References
Indications for catheter ablation of atrial fibrillation				
A. Indications for catheter ablation of atrial fibrillation				
Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Catheter ablation is recommended.	I	A	7–18
	Persistent: Catheter ablation is reasonable.	IIa	B-NR	8,16–26
	Long-standing persistent: Catheter ablation may be considered.	IIb	C-LD	8,16–26
Symptomatic AF prior to initiation of antiarrhythmic therapy with a Class I or III antiarrhythmic medication	Paroxysmal: Catheter ablation is reasonable.	IIa	B-R	27–35
	Persistent: Catheter ablation is reasonable.	IIa	C-EO	
	Long-standing persistent: Catheter ablation may be considered.	IIb	C-EO	
B. Indications for catheter atrial fibrillation ablation in populations of patients not well represented in clinical trials				
Congestive heart failure	It is reasonable to use similar indications for AF ablation in selected patients with heart failure as in patients without heart failure.	IIa	B-R	36–54
Older patients (> 75 years of age)	It is reasonable to use similar indications for AF ablation in selected older patients with AF as in younger patients.	IIa	B-NR	53–59
Hypertrophic cardiomyopathy	It is reasonable to use similar indications for AF ablation in selected patients with HCM as in patients without HCM.	IIa	B-NR	60–82
Young patients (< 45 years of age)	It is reasonable to use similar indications for AF ablation in young patients with AF (< 45 years of age) as in older patients.	IIa	B-NR	63,64
Tachy-brady syndrome	It is reasonable to offer AF ablation as an alternative to pacemaker implantation in patients with tachy-brady syndrome.	IIa	B-NR	33–35
Athletes with AF	It is reasonable to offer high-level athletes AF as first-line therapy due to the negative effects of medications on athletic performance.	IIa	C-LD	27,28,65
Asymptomatic AF**	Paroxysmal: Catheter ablation may be considered in select patients.**	IIb	C-EO	66,67
	Persistent: Catheter ablation may be considered in select patients.	IIb	C-EO	68
Indications for surgical ablation of atrial fibrillation				
C. Indications for concomitant open (such as mitral valve) surgical ablation of atrial fibrillation				
Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Surgical ablation is recommended.	I	B-NR	69–82
	Persistent: Surgical ablation is recommended.	I	B-NR	69–82
	Long-standing persistent: Surgical ablation is recommended.	I	B-NR	69–82
Symptomatic AF prior to initiation of antiarrhythmic therapy with a Class I or III antiarrhythmic medication	Paroxysmal: Surgical ablation is recommended.	I	B-NR	69–82
	Persistent: Surgical ablation is recommended.	I	B-NR	69–82
	Long-standing persistent: Surgical ablation is recommended.	I	B-NR	69–82
D. Indications for concomitant closed (such as CABG and AVR) surgical ablation of atrial fibrillation				
Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Surgical ablation is recommended.	I	B-NR	83–88
	Persistent: Surgical ablation is recommended.	I	B-NR	83–88
	Long-standing persistent: Surgical ablation is recommended.	I	B-NR	83–88
Symptomatic AF prior to initiation of antiarrhythmic therapy with a Class I or III antiarrhythmic medication	Paroxysmal: Surgical ablation is reasonable.	IIa	B-NR	83–88
	Persistent: Surgical ablation is reasonable.	IIa	B-NR	83–88
	Long-standing persistent: Surgical ablation is reasonable.	IIa	B-NR	83–88
E. Indications for stand-alone and hybrid surgical ablation of atrial fibrillation				
Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Stand-alone surgical ablation can be considered for patients who have failed one or more attempts at catheter ablation and also for those who are intolerant or refractory to antiarrhythmic drug therapy and prefer a surgical approach, after review of the relative safety and efficacy of catheter ablation versus a stand-alone surgical approach.	IIb	B-NR	83–85,89–103
	Persistent: Stand-alone surgical ablation is reasonable for patients who have failed one or more attempts at catheter ablation and also for those patients who prefer a surgical approach after review of the relative safety and efficacy of catheter ablation versus a stand-alone surgical approach.	IIa	B-NR	83–85,89–103
	Long-standing persistent: Stand-alone surgical ablation is reasonable for patients who have failed one or more attempts at catheter ablation and also for those patients who prefer a surgical approach after review of the relative safety and efficacy of catheter ablation versus a stand-alone surgical approach.	IIa	B-NR	83–85,89–103
	It might be reasonable to apply the indications for stand-alone surgical ablation described above to patients being considered for hybrid surgical AF ablation.	IIb	C-EO	103–108

AF = atrial fibrillation; LOE = Level of Evidence; HCM = hypertrophic cardiomyopathy.

** A decision to perform AF ablation in an asymptomatic patient requires additional discussion with the patient because the potential benefits of the procedure for the patient without symptoms are uncertain.

Section 8: Follow-up Considerations

AF ablation is an invasive procedure that entails risks, most of which are present during the acute procedural period. However, complications can also occur in the weeks or months following ablation. Recognizing common symptoms after AF ablation and distinguishing those that require urgent evaluation and referral to an electrophysiologist is an important part of follow-up after AF ablation. The success of AF ablation is based in large part on freedom from AF recurrence based on ECG monitoring. Arrhythmia

monitoring can be performed with the use of noncontinuous or continuous ECG monitoring tools (Table 6). This section also discusses the important topics of AAD and non-AAD use prior to and following AF ablation, the role of cardioversion, as well as the indications for and timing of repeat AF ablation procedures.

Section 9: Outcomes and Efficacy

This section provides a comprehensive review of the outcomes of catheter ablation of AF. Table 7 summarizes the main findings of

Indications for Catheter Ablation of Symptomatic Atrial Fibrillation

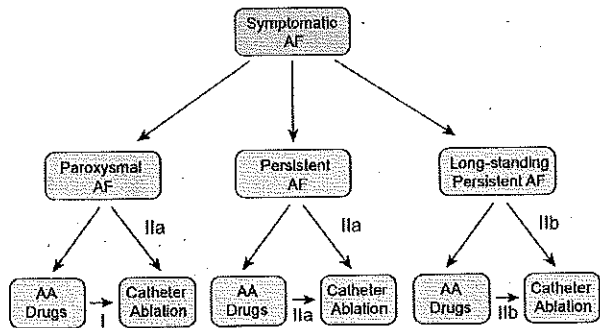


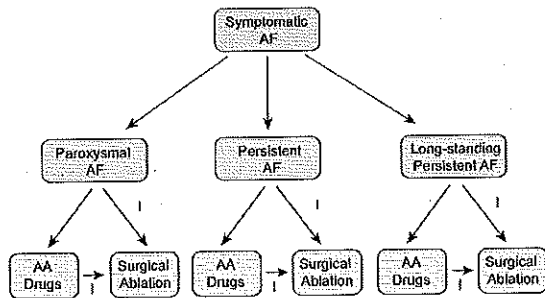
Figure 7. Indications for catheter ablation of symptomatic atrial fibrillation. Shown in this figure are the indications for catheter ablation of symptomatic paroxysmal, persistent, and long-standing persistent AF. The Class for each indication based on whether ablation is performed after failure of antiarrhythmic drug therapy or as first-line therapy is shown. Please refer to Table 2B and the text for the indications for catheter ablation of asymptomatic AF.

the most important clinical trials in this field. Outcomes of AF ablation in subsets of patients not well represented in these trials are reviewed. Outcomes for specific ablation systems and strategies (CB ablation, rotational activity ablation, and laser balloon ablation) are also reviewed.

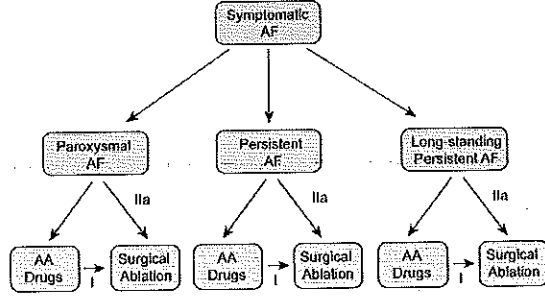
Section 10: Complications

Catheter ablation of AF is one of the most complex interventional electrophysiological procedures. AF ablation by its nature involves catheter manipulation and ablation in the delicate thin-walled atria, which are in close proximity to other important organs and structures that can be impacted through collateral damage. It is therefore not surprising that AF ablation is associated with a significant risk of complications, some of which might result in life-long disability and/or death. This section reviews the complications associated with catheter ablation procedures performed to treat AF. The types and incidence of complications are presented, their mechanisms are explored, and the optimal

Indications for Concomitant Open (Such as Mitral Valve) Surgical Ablation of AF



Indications for Concomitant Closed (Such as CABG or AVR) Surgical Ablation of AF



Indications for Stand-Alone Surgical Ablation of AF

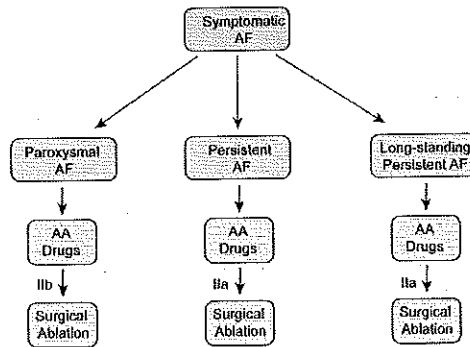


Figure 8. Indications for surgical ablation of atrial fibrillation. Shown in this figure are the indications for surgical ablation of paroxysmal, persistent, and long-standing persistent AF. The Class for each indication based on whether ablation is performed after failure of antiarrhythmic drug therapy or as first-line therapy is shown. The indications for surgical AF ablation are divided into whether the AF ablation procedure is performed concomitantly with an open surgical procedure (such as mitral valve replacement), a closed surgical procedure (such as coronary artery bypass graft surgery), or as a stand-alone surgical AF ablation procedure performed solely for treatment of atrial fibrillation.

Table 3
Atrial fibrillation ablation: strategies, techniques, and endpoints

Recommendation	Class	LOE	References
PV isolation by catheter ablation	I	A	7-18,10-26,106
	I	B-R	7-16,10-26,109
	IIa	B-R	9,10-120
	IIb	B-R	102,111-114,120-128
	IIb	B-R	128-133
	IIb	B-NR	134-139
	IIb	B-R	140-143
	I	C-LD	19,141-149
	IIa	C-LD	150-161
	IIa	C-LD	13,14,126,162-178
Ablation strategies to be considered for use in conjunction with PV isolation	IIb	C-LD	21,178-185
	IIb	C-LD	150-161
	IIb	C-LD	186-193
	IIb	B-NR	19,20,142,145-146,194-201
	IIb	C-LD	19,20,142,145-146,194-201
	IIb	B-R	175,202-211
	IIb	B-R	19,20,195-197,212-220
	IIb	B-NR	223-241
	IIb	B-NR	19,69,242-259
	IIa	B-R	260-268
Nonablation strategies to improve outcomes	IIa	B-R	260-268
	IIa	B-R	260-268
	IIa	B-R	270,276-278,285-307
	IIa	B-R	270,276-278,285-307
	IIb	C-LD	308-312
	IIb	C-LD	308-312
	I	B-NR	313-235
	I	C-LD	68,336-365
	IIa	C-EO	68,336,345,365
	IIa	C-EO	68,336,345,365

AF = atrial fibrillation; LOE = Level of Evidence; PV = pulmonary vein; RF = radiofrequency; MRI = magnetic resonance imaging; BMI = body mass index.

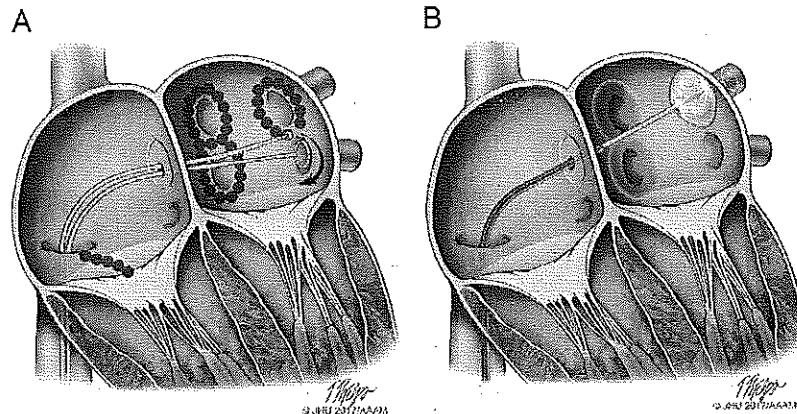


Figure 9. Schematic drawing showing catheter ablation of atrial fibrillation using either RF energy or cryoballoon AF ablation. **A:** Shows a typical wide area lesion set created using RF energy. Ablation lesions are delivered in a figure of eight pattern around the left and right PV veins. Also shown is a linear cavotricuspid isthmus lesion created for ablation of typical atrial flutter in a patient with a prior history of typical atrial flutter or inducible isthmus-dependent typical atrial flutter at the time of ablation. A multielectrode circular mapping catheter is positioned in the left inferior PV. **B:** Shows an ablation procedure using the cryoballoon system. Ablation lesions have been created surrounding the right PVs, and the cryoballoon ablation catheter is positioned in the left superior PV. A through the lumen multielectrode circular mapping catheter is positioned in the left superior PV.

Illustration: Tim Phelps © 2017 Johns Hopkins University, AAM.

Table 4
Anticoagulation strategies: pre-, during, and postcatheter ablation of AF

Recommendation	Class	LOE	References	
Preablation	I	A	366–373	
		B-R	374	
	IIa	B-NR	375	
	I	B-NR	5,6	
	IIa	B-NR	372,376–380	
	IIa	C-EO	5,6	
	IIa	C-EO	5,6	
	IIb	C-EO	381–386	
	During ablation	I	B-NR	369,380–382,387–393
		IIa	B-NR	394
Postablation	I	C-EO		
	I	C-EO	1,2	
	I	C-EO	5,6	
	I	C-EO	5,6	
	IIa	C-EO	372,376–380	
	IIb	C-EO		

AF = atrial fibrillation; LOE = Level of Evidence; NOAC = novel oral anticoagulant; TEE = transesophageal electrocardiogram; ACT = activated clotting time.

* Time in therapeutic range (TTR) should be > 65%–70% on warfarin.

Table 5
Signs and symptoms following AF ablation

	Differential	Suggested evaluation
Signs and symptoms of complications within a month postablation		
Back pain	Musculoskeletal, retroperitoneal hematoma	Physical exam, CT imaging
Chest pain	Pericarditis, pericardial effusion, coronary stenosis (ablation related), pulmonary vein stenosis, musculoskeletal (after cardioversion), worsening reflux	Physical exam, chest X-ray, ECG, echocardiogram, stress test, cardiac catheterization, chest CT
Cough	Infectious process, bronchial irritation (mechanical, cryoballoon), pulmonary vein stenosis	Physical exam, chest X-ray, chest CT
Dysphagia	Esophageal irritation (related to transesophageal echocardiography), atrioesophageal fistula	Physical exam, chest CT or MRI
Early satiety, nausea	Gastric denervation	Physical exam, gastric emptying study
Fever	Infectious process, pericarditis, atrioesophageal fistula	Physical exam, chest X-ray, chest CT, urinalysis, laboratory blood work
Fever, dysphagia, neurological symptoms	Atrial esophageal fistula	Physical exam, laboratory blood work, chest CT or MRI; avoid endoscopy with air insufflation
Groin pain at site of access	Pseudoaneurysm, AV fistula, hematoma	Ultrasound of the groin, laboratory blood work; consider CT scan if ultrasound negative
Headache	Migraine (related to anesthesia or transeptal access, hemorrhagic stroke), effect of general anesthetic	Physical exam, brain imaging (MRI)
Hypotension	Pericardial effusion/tamponade, bleeding, sepsis, persistent vagal reaction	Echocardiography, laboratory blood work
Hemoptysis	PV stenosis or occlusion, pneumonia	Chest X-ray, chest CT or MR scan, VQ scan
Neurological symptoms	Cerebral embolic event, atrial esophageal fistula	Physical exam, brain imaging, chest CT or MRI
Shortness of breath	Volume overload, pneumonia, pulmonary vein stenosis, phrenic nerve injury	Physical exam, chest X-ray, chest CT, laboratory blood work
Signs and symptoms of complications more than a month postablation		
Fever, dysphagia, neurological symptoms	Atrial esophageal fistula	Physical exam, laboratory blood work, chest CT or MRI; avoid endoscopy with air insufflation
Persistent cough, atypical chest pain	Infectious process, pulmonary vein stenosis	Physical exam, laboratory blood work, chest X-ray, chest CT or MRI
Neurological symptoms	Cerebral embolic event, atrial esophageal fistula	Physical exam, brain imaging, chest CT or MRI
Hemoptysis	PV stenosis or occlusion, pneumonia	CT scan, VQ scan

AF = atrial fibrillation; ECG = electrocardiogram; CT = computed tomography; MRI = magnetic resonance imaging; VQ = ventilation-perfusion.

approach to prevention and treatment is discussed (Tables 8 and 9).

Section 11: Training Requirements

This section of the document outlines the training requirements for those who wish to perform catheter ablation of AF.

Section 12: Surgical and Hybrid AF Ablation

Please refer to Table 2 and Figure 8 presented earlier in this Executive Summary.

Section 13: Clinical Trial Design

Although there have been many advances made in the field of catheter and surgical ablation of AF, there is still much to be learned about the mechanisms of initiation and maintenance of AF and how to apply this knowledge to the still-evolving techniques of AF ablation. Although single-center, observational reports have dominated the early days of this field, we are quickly moving into an era in which hypotheses are put through the rigor of testing in well-designed, randomized, multicenter clinical trials. It is as a result of these trials that conventional thinking about the best techniques, success rates, complication rates, and long-term outcomes beyond AF recurrence—such as thromboembolism and mortality—is being put to the test. The ablation literature has also

seen a proliferation of meta-analyses and other aggregate analyses, which reinforce the need for consistency in the approach to reporting the results of clinical trials. This section reviews the minimum requirements for reporting on AF ablation trials. It also acknowledges the potential limitations of using specific primary outcomes and emphasizes the need for broad and consistent reporting of secondary outcomes to assist the end-user in determining not only the scientific, but also the clinical relevance of the results (Tables 10–13).

Unanswered Questions in AF Ablation

There is still much to be learned about the mechanisms of AF, techniques of AF ablation, and long-term outcomes. The following are unanswered questions for future investigation:

1. AF ablation and modification of stroke risk and need for ongoing oral anticoagulation (OAC): The CHA₂DS₂-VASc score was developed for patients with clinical AF. If a patient has received a successful ablation such that he/she no longer has clinical AF (subclinical, or no AF), then what is the need for ongoing OAC? Are there any patients in whom successful ablation could lead to discontinuation of OAC?
2. Substrate modification in catheter-based management of AF—particularly for persistent AF: What is the proper lesion set required beyond pulmonary vein isolation? Do lines and complex fractionated atrial electrogram (CFAE) have any remaining role? Are these approaches ill-advised or simply discouraged?

Table 6
Types of ambulatory cardiac monitoring devices

Type of recorder	Typical monitoring duration	Continuous recording	Event recording	Auto trigger	Unique features
Holter monitor	24–48 hours, approximately 7–30 days	Yes	Yes	N/A	Short term, provides quantitative data on arrhythmia burden
Patch monitor	1–3 weeks	Yes	Yes	N/A	Intermediate term, can provide continuous data for up to several weeks; improved patient compliance without lead wires
External loop recorder	1 month	Yes	Yes	Variable	Good correlation between symptoms and even brief arrhythmias
External nonloop recorder	Months	No	Yes	No	May be used long term and intermittently; will not capture very brief episodes
Smartphone monitor	Indefinite	No	Yes	No	Provides inexpensive long-term intermittent monitoring; dependent on patient compliance; requires a smartphone
Mobile cardiac telemetry	30 days	Yes	Yes	Yes	Real time central monitoring and alarms; relatively expensive
Implantable loop recorder	Up to 3 years	Yes	Yes	Yes	Improved patient compliance for long-term use; not able to detect 30-second episodes of AF due to detection algorithm; presence of AF needs to be confirmed by EGM review because specificity of detection algorithm is imperfect; expensive
Pacemakers or ICDs with atrial leads	Indefinite	Yes	Yes	Yes	Excellent AF documentation of burden and trends; presence of AF needs to be confirmed by electrogram tracing review because specificity of detection algorithms is imperfect; expensive
Wearable multisensor ECG monitors	Indefinite	Yes	Yes	Yes	ECG 3 leads, temp, heart rate, HRV, activity tracking, respiratory rate, galvanic skin response

AF = atrial fibrillation; ICD = implantable cardioverter defibrillator; ECG = electrocardiogram; HRV = heart rate variability.

Table 7
Selected clinical trials of catheter ablation of atrial fibrillation and/or for FDA approval

Trial	Year	Type	N	AF type	Ablation strategy	Initial time frame	Effectiveness endpoint	Ablation success	Drug/Control success	P value for success	Ablation complications	Drug/Control complications	Comments
Clinical Trials Performed for FDA Approval													
JAMA 2010; 303: 333–340 (ThermoCoolAF) ¹⁴	2010	Randomized to RF ablation or AAD, multicenter	167	Paroxysmal	PVI, optional CFAEs and lines	12 months	Freedom from symptomatic paroxysmal atrial fibrillation, acute procedural failure, or changes in specified drug regimen	66%	16%	< 0.001	4.5%	8.8%	FDA approval received
JACC 2013; 61: 1713–1723 (STOP AF) ⁹	2013	Randomized to cryo-balloon ablation or AAD, multicenter	245	Paroxysmal	PVI	12 months	Freedom from any detectable AF, use of nonstudy AAD, or nonprotocol intervention for AF	70%	7%	< 0.001	3.1%	NA	FDA approval received
Heart Rhythm 2014; 11: 202–209 (TTOP) ¹²	2014	Randomized to phased RF ablation or AAD/ cardioversion, multicenter	210	Persistent	PVI + CFAEs	6 months	Acute procedural success, ≥ 90% reduction in AF burden, off AAD	56%	26%	< 0.001	12.3%	NA	Not FDA approved
JACC 2014; 64: 647–656 (SMART-AF) ¹³	2014	Nonrandomized multicenter study of	172	Paroxysmal	PVI, optional	12 months	Freedom from symptomatic AF	72.5%	N/A	< 0.0001	7.5%	NA	

Study	Year	Design	Sample Size	Intervention	Follow-up	Primary Endpoint	Success Rate	Secondary Endpoints	Significance	Adverse Events	FDA Approval								
First-Line Therapy Trials	2015	Randomized to contact force-sensing RF catheter, comparing to performance goals	300	Paroxysmal PVI, optional CFAEs and lines in both arms	12 months	Flutter, tachycardia, acute procedural failure, or changes in AAD	67.8%	69.4%	0.0073 for noninferiority	7.2%	9.1%	FDA approval received							
													Randomized to contact force sensing RF catheter or approved RF catheter, multicenter	61.1%	61.7%	0.003 for noninferiority	5.3%	6.4%	FDA approval received
													Randomized to laser-balloon or approved RF catheter, multicenter	84%	37%	< 0.01	9%	11%	
First-Line Therapy Trials	2012	Randomized to drug, multicenter	294	Paroxysmal AF PVI, roof line, optional mitral and tricuspid line	24 months	Cumulative AF burden	13% AF burden	19% AF burden	NS	17%	15%								
													Randomized to drug, multicenter	45%	28%	0.02	9%	4.9%	
													Randomized to drug, multicenter	86%	22%	< 0.001	1%	23%	
Other Paroxysmal AF Ablation Trials	2016	Randomized to drug, multicenter	762	Paroxysmal AF PVI	12 months	Freedom from detectable AF, flutter, tachycardia	64.1% (RF)	65.4% (Cryo)	NS	12.8%	10.2%								
													Randomized to drug, multicenter	59%	5%	< 0.001	10.4%	4.7%	
													Randomized to drug, multicenter	74%	58%	0.05	1.3%	1.4%	
Other Persistent AF Ablation Trials	2014	Randomized to drug, multicenter	146	Persistent PVI, roof, mitral line	12 months	Freedom from AF/flutter lasting > 24h	70%	44%	0.002	6.1%	4.20%								
													Randomized to drug, multicenter	59% (PVI alone)	49% & 46%	NS	6%	4.3% & 7.6%	
													Randomized to drug, multicenter	74%	58%	0.05	1.3%	1.4%	

Table 7 (continued)

Trial	Year	Type	N	AF type	Ablation strategy	Initial time frame	Effectiveness endpoint	Ablation success	Drug/Control success	P value for success	Ablation complications	Drug/Control complications	Comments
Other Mixed Paroxysmal and Persistent AF Ablation Trials													
J Med Assoc Thai 2003; 86 (Suppl 1): S8–S16 ²⁴	2003	Randomized to RF ablation or amiodarone	30	Paroxysmal (70%), Persistent (30%)	PVI, mitral line, CTI, SVC to IVC	12 months	Freedom from AF	79%	40%	0.018	6.70%	47%	
EHI 2006; 27: 216–221 ¹⁷	2006	Randomized to RF ablation or drug, multicenter	137	Paroxysmal (67%), Persistent (33%)	PVI, mitral line, CTI	12 months	Freedom from AF, flutter, tachycardia	66%	9%	<0.001	4.40%	2.90%	
JCVEP 2009; 20: 22–28 ¹⁶	2009	Randomized to RF ablation or drug, multicenter	70	Paroxysmal (41%), Persistent (59%) & Type 2 DM	PVI, CTI, optional mitral line and roof line	12 months	Freedom from AF and atypical atrial flutter	80%	43%	0.001	2.90%	17%	
Randomized Trials of AF Ablation in Patients with Heart Failure													
NEJM 2008; 359: 1778–1785 (PABAF) ³⁶	2008	Randomized to RF ablation of AVJ and BV pacing	81	Persistent (50%), Paroxysmal (50%), EF 27% abl, 29% AVJ	PVI, optional line, ear abl and CFAEs	6 months	Composite EF, 6 min walk, MLWHF score; freedom from AF (secondary, mult proc, +/- AA drugs) with abl	88% AF free, EF 35% abl, 28% AVJ [P < .001], > QOL and 6 min walk increase		<0.001	14.60%	17.50%	
Heart 2011; 97: 740–747 ²⁰	2011	Randomized to RF ablation or pharmacological rate control	41	Persistent, EF 20% abl, 16% rate control	PVI, roof line, CFAEs	6 months	Change in LVEF, sinus rhythm at 6 months (secondary)	50% in NSR, LVEF increase 4.5%	0% in NSR, LVEF increase 2.8%	0.6 (for EF increase)	15%	Not reported	Not reported
JACC 2013; 61: 1894–1903 ⁴⁶	2013	Randomized to RF ablation or pharmacological rate control	52	Persistent AF (100%), EF 22% abl, 25% rate control	PVI, optional line, ear abl and CFAEs	12 months	Change in peak O ₂ consumption (also reported single procedure off drug ablation success)	Peak O ₂ consumption increase greater with abl, 72% abl success		0.018	15%	Not reported	
Circ A and E 2014; 7:31–38 ³⁰	2014	Randomized to RF ablation or pharmacological rate control	50	Persistent AF (100%), EF 32% abl, 34% rate control	PVI, optional line, ear abl and CFAEs	6 months	Change in LVEF at 6 months, multiple procedure freedom from AF also reported	LVEF 40% with abl, 31% rate control, 81% AF free with abl		0.015	7.70%		

AF = atrial fibrillation; RF = radiofrequency; AVJ = atrioventricular junction; abl = ablation; BV = biventricular; EF = ejection fraction; PVI = pulmonary vein isolation; CFAEs = complex fractionated atrial electrograms; MLWHF = Minnesota Living with Heart Failure; LVEF = left ventricular ejection fraction; QOL = quality of life; NSR = normal sinus rhythm.

Table 8
Definitions of complications associated with AF ablation

Asymptomatic cerebral embolism	Asymptomatic 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.
Atrioesophageal fistula	An atrioesophageal 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 is the most common method of documentation of an atrioesophageal 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 hematocrit.
Bleeding following cardiac surgery	Excessive bleeding following a surgical AF ablation procedure is defined as bleeding requiring reoperation or ≥ 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 observed during surgery; (3) one of the following conditions: chest pain, sternal instability, or fever ($> 38^{\circ}\text{C}$), 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.
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.
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 observed during surgery; (3) one of the following conditions: chest pain, sternal instability, or fever ($> 38^{\circ}\text{C}$), in combination with either purulent discharge from the mediastinum or an organism isolated from blood culture or culture of mediastinal drainage.
Myocardial infarction in the context of AF ablation	The universal definition of myocardial infarction ³⁹⁵ 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 that occurs following catheter ablation. We therefore propose that a myocardial infarction, 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 wave changes or new LBBB) that persist for more than 1 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.
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.
Stiff left atrial syndrome	Stiff left atrial syndrome is a clinical syndrome defined by the presence of signs of right heart failure in the presence of preserved LV function, pulmonary hypertension (mean PA pressure > 25 mm Hg or during exercise > 30 mm Hg), and large V waves ≥ 10 mm Hg or higher) on PCWP or left atrial pressure tracings in the absence of significant mitral valve disease or PV stenosis.
Stroke or TIA postablation	Stroke diagnostic criteria <ul style="list-style-type: none"> • 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 ≥ 24 hours; OR < 24 hours if therapeutic intervention (s) were performed (e.g., 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 (e.g., brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences).*

Table 8 (continued)

	<ul style="list-style-type: none"> • Confirmation of the diagnosis by at least one of the following: neurology or neurosurgical specialist; neuroimaging procedure (MRI or CT scan or cerebral angiography); lumbar puncture (i.e., spinal fluid analysis diagnostic of intracranial hemorrhage)
	Stroke definitions
	<ul style="list-style-type: none"> • 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 ≥ 2 at 30 and 90 days
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. 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.

AF = atrial fibrillation; CT = computed tomography; MRI = magnetic resonance imaging; PRBC = packed red blood cell; AFL = atrial flutter; AT = atrial tachycardia; CPK = creatine phosphokinase; ECG = electrocardiogram; LBBB = left bundle branch block.

* Patients with nonfocal global encephalopathy will not be reported as a stroke without unequivocal evidence based on 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.

What is the role of targeting localized rotational activations? How do we ablate a localized rotational activation? How can scar be characterized and targeted for ablation? Do we need to replicate the MAZE procedure? Does the right atrium need to be targeted as well as the left atrium?

3. Autonomic influence in AF: Is clinical AF really an autonomic mediated arrhythmia? Is elimination of ganglionated plexi required? Is there a role for autonomic modulation, for example, spinal cord or vagal stimulation?
4. Contribution and modulation of risk factors on outcomes of AF ablation: Obesity reduction has been shown to reduce AF burden and recurrence in patients undergoing ablation. What is the role of bariatric surgery? Does the modulation of other risk factors influence outcome such as hypertension, sleep apnea, and diabetes?
5. Outcomes in ablation of high-risk populations: Do high-risk populations benefit from AF ablation? Congestive heart failure has been assessed in smaller trials, but larger trials are required. Outcome data are needed in patients with very enlarged LAs, hypertrophic cardiomyopathy, patients with renal failure on dialysis, and the very elderly.
6. Surgical vs catheter-based vs hybrid ablation: There should be more comparative work between percutaneous and minimally invasive surgical approaches. Both report similar outcomes, but there is a dearth of comparative data. Is there any patient benefit to hybrid procedures?
7. How do we characterize patients who are optimal candidates for ablation? Preablation late gadolinium-enhanced (LGE)-

magnetic resonance imaging (MRI) might identify patients with heavy burdens of scar who are unlikely to respond to ablation. These techniques must become reproducible and reliable and must be assessed in multicenter trials. Other markers need to be investigated, including genetic markers, biochemical markers, and clinical markers based on aggregated risk scores.

8. The incremental role of new technologies: As newer and often more expensive technologies are produced for AF ablation, their definitive incremental value must be determined in order to justify change in practice or case cost. These technologies include global (basket) mapping techniques, newer ablation indices for assessing lesion durability, advanced imaging for viewing lesions in the myocardium, etc. New energy sources, including laser, low-intensity ultrasound, photonic particle therapy, external beam ablation, and MRI-guided ablation, must be assessed in comparative fashion.
9. Outcomes of AF ablation: We need to better understand the clinical relevance of ablation outcomes. What is the significance of time to recurrence of 30 seconds of arrhythmia? How do we best quantify AF burden? How do these outcomes relate to quality of life and stroke risk?
10. What is the role of surgical LA reduction? Does left atrial appendage (LAA) occlusion or obliteration improve outcome of persistent AF ablation with an accompanying reduction in stroke? Does ablation work through atrial size reduction? What is the incidence of "stiff atrial" syndrome and does this mitigate the clinical impact of ablation?

Table 9
Incidence, prevention, diagnosis, and treatment of selected complications of AF ablation

Complication	Incidence	Selected prevention techniques	Diagnostic testing	Selected treatment options	References
Air embolism	< 1%	Sheath management	Nothing or cardiac catheterization	Supportive care with fluid, oxygen, head down tilt, hyperbaric oxygen	398,399–401
Asymptomatic cerebral emboli (ACE)	2% to 15%	Anticoagulation, catheter and sheath management, TEE	Brain MRI	None	402–419
Atrial esophageal fistula	0.02% to 0.11%	Reduce power, force, and RF time on posterior wall, monitor esophageal temp, use proton pump inhibitors; avoid energy delivery over esophagus	CT scan of chest, MRI; avoid endoscopy with air insufflation	Surgical repair	337–365,420–456
Cardiac tamponade	0.2% to 5%	Catheter manipulation, transseptal technique, reduce power, force, and RF time	Echocardiography	Pericardiocentesis or surgical drainage	338,343,347,458,467
Coronary artery stenosis/occlusion	< 0.1%	Avoid high-power energy delivery near coronary arteries	Cardiac catheterization	PTCA	468–476
Death	< 0.1% to 0.4%	Meticulous performance of procedure, attentive post-procedure care	NA	NA	338,343,347,458,477
Gastric hypomotility	0% to 17%	Reduce power, force, and RF time on posterior wall	Endoscopy, barium swallow, gastric emptying study	Metoclopramide, possibly intravenous erythromycin	478–486
Mitral valve entrapment	< 0.1%	Avoid circular catheter placement near or across mitral valve; clockwise torque on catheter	Echocardiography	Gentle catheter manipulation, surgical extraction	489–498
Pericarditis	0% to 50%	None proven	Clinical history, ECG, sedimentation rate, echocardiogram	NSAID, colchicine, steroids	499–508
Permanent phrenic nerve paralysis	0% to 0.4%	Monitor diaphragm during phrenic pacing, CMAP monitoring, phrenic pacing to identify location and adjust lesion location	CXR, sniff test	Supportive care	9,11,156,347,387,486,487,478,479,487–490,507–528
Pulmonary vein stenosis	< 1%	Avoid energy delivery within PV	CT or MRI, V/Q wave scan	Angioplasty, stent, surgery	9,11,713,316–335,457,529–531
Radiation injury	< 0.1%	Minimize fluoroscopy exposure, especially in obese and repeat ablation patients, X-ray equipment	None	Supportive care, rarely skin graft	513,532–550
Stiff left atrial syndrome	< 1.5%	Limit extent of left atrial ablation	Echocardiography, cardiac catheterization	Diuretics	551–558
Stroke and TIA	0% to 2%	Pre-, post-, and intraprocedure anticoagulation, catheter and sheath management, TEE	Head CT or MRI, cerebral angiography	Thrombolytic therapy, angioplasty	10–12,336,347,367,458,550–565
Vascular complications	0.2% to 1.5%	Vascular access techniques, ultrasound-guided access, anticoagulation management	Vascular ultrasound, CT scan	Conservative treatment, surgical repair, transfusion	338,347,371,373,374,380,458,511,566–575

AF = atrial fibrillation; CT = computed tomography; MRI = magnetic resonance imaging; TEE = transesophageal electrocardiogram; RF = radiofrequency; PTCA = percutaneous transluminal coronary angioplasty; NA = not applicable; ECC = electrocardiogram; NSAID = nonsteroidal anti-inflammatory drug; CMAP = compound motor action potentials; CXR = chest X-ray; TIA = transient ischemic attack.

Table 10
Definitions for use when reporting outcomes of AF ablation and in designing clinical trials of catheter or surgical ablation of AF

Acute procedural success (pulmonary vein isolation)	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 PVI, including exit block and/or the use of provocative agents such as adenosine or isoproterenol, they should be prespecified. 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.
Acute procedural success (not related by pulmonary vein isolation)	Typically, this would apply to substrate ablation performed in addition to PVI for persistent AF. Although some have proposed AF termination as a surrogate for acute procedural success, its relationship to long-term success is controversial. Complete elimination of the additional substrate (localized rotational activation, scar region, non-PV trigger, or other target) and/or demonstration of bidirectional conduction block across a linear ablation lesion would typically be considered the appropriate endpoint.
One-year success*	One-year success is defined as freedom from AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure. Because cavotricuspid isthmus-dependent atrial flutter is easily treated with cavotricuspid isthmus ablation and is not an iatrogenic arrhythmia following a left atrial ablation procedure for AF, it is reasonable for clinical trials to choose to prespecify that occurrence of isthmus-dependent atrial flutter, if confirmed by entrainment maneuvers during electrophysiology testing, should not be considered an ablation failure or primary effectiveness endpoint.
Alternative one-year success	Although the one-year success definition provided above remains the recommended end point that should be reported in all AF ablation trials, and the endpoint for which the objective performance criteria listed below were developed, the Task Force recognizes that alternative definitions for success can be used if the main goal of therapy in the study is to relieve AF-related symptoms and to improve patient QOL. In particular, it is appropriate for clinical trials to define success as freedom from only symptomatic AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure if the main goal of therapy in the study is to relieve AF-related symptoms and to improve patient QOL. However, because symptoms of AF can resolve over time, and because studies have shown that asymptomatic AF represents a greater proportion of all AF postablation than prior to ablation, clinical trials need to continue to report freedom from both symptomatic and asymptomatic AF even if this alternative one year success definition is used as the primary trial endpoint.
Clinical/partial success*	It is reasonable for clinical trials to define and incorporate one or more secondary definitions of success that can be referred to as "clinical success" or "partial success." If these alternative definitions of success are included, they should be defined prospectively. In prior Consensus Documents the Task Force has proposed that clinical/partial success be 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." Because there is no firm scientific basis for selecting the cutoff of 75% rather than a different cutoff, this prior recommendation is provided only as an example of what future clinical trials may choose to use as a definition of clinical/partial success.
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-month follow-up from the date of the ablation procedure in the absence of Class I and III antiarrhythmic drug therapy.
Recurrent AF/AFL/AT	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 postablation blanking period is not considered a failure of AF ablation.
Early recurrence of AF/AFL/AT	Early recurrence of AF/AFL/AT 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." These are not counted toward the success rate if a blanking period is specified.
Recurrence of AF/AFL/AT	Recurrence of AF/AFL/AT postablation 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/AFL/AT	Late recurrence of AF/AFL/AT 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 chosen, it should be prespecified and included in the Methods section.
Stroke screening	A risk-based approach to determine the level of postablation stroke screening in clinical trials is recommended by the Task Force. For ablation devices with a lower risk of stroke and for which a stroke signal has not been reported, a minimum standardized neurological assessment of stroke should be conducted by a physician at baseline and at hospital discharge or 24 hours after the procedure, whichever is later. If this neurological assessment demonstrates new abnormal findings, the patient should have a formal neurological consult and examination with appropriate imaging (i.e., DW-MRI), used to confirm any suspected diagnosis of stroke. For devices in which a higher risk of stroke is suspected or revealed in prior trials, a formal neurological examination by a neurologist at discharge or 24 hours after the procedure, whichever is later, is recommended. Appropriate imaging should be obtained if this evaluation reveals a new neurological finding. In some studies in which delayed stroke is a concern, repeat neurological screening at 30 days postablation might be appropriate.
Detectable AF/AFL/AT	Detectable AF is defined as AF/AFL/AT 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 prespecified 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.

Table 10 (continued)

AF/AFL/AT burden	It is reasonable for clinical trials to incorporate AF/AFL/AT burden as a secondary endpoint in a clinical trial of AF ablation. In stating this it is recognized that there are no conclusive data that have validated a rate of AF burden reduction as a predictor of patient benefit (i.e. reduction in mortality and major morbidities such as stroke, CHF, QOL, or hospitalization). If AF burden is included, it is important to predefine and standardize the monitoring technique that will be used to measure AF burden. Available monitoring techniques have been discussed in this document. Should AF burden be selected as an endpoint in a clinical trial, the chosen monitoring technique should be employed at least a month prior to ablation to establish a baseline burden of AF.
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 can also be assessed using detailed point-by-point mapping of the PV antrum guided by an electroanatomical 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. It is recommended that reassessment of entrance block be performed a minimum of 20 minutes after initial establishment of PV isolation.
Procedural endpoints for AF ablation strategies not targeting the PVs	Procedural endpoints for AF ablation strategies not targeting the PVs vary depending on the specific ablation strategy and tool. It is important that they be prespecified in all clinical trials. For example, if a linear ablation strategy is used, documentation of bidirectional block across the ablation line must be shown. For ablation of CFAEs, rotational activity, or non-PV triggers, the acute endpoint should at a minimum be elimination of CFAEs, rotational activity, or non-PV triggers. Demonstration of AF slowing or termination is an appropriate procedural endpoint, but it is not required as a procedural endpoint for AF ablation strategies not targeting the PVs.
Esophageal temperature monitoring	Esophageal temperature monitoring should be performed in all clinical trials of AF ablation. At a minimum, a single thermocouple should be used. The location of the probe should be adjusted during the procedure to reflect the location of energy delivery. Although this document does not provide formal recommendations regarding the specific temperature or temperature change at which energy delivery should be terminated, the Task Force does recommend that all trials prespecify temperature guidelines for termination of energy delivery.
Enrolled subject	An enrolled subject is defined as a subject who has signed written informed consent to participate in the trial in question.
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.
Nonablative strategies	The optimal nonablative therapy for patients with persistent and long-standing persistent AF who are randomized to the control arm of an AF ablation trial is a trial of a new Class I or III antiarrhythmic agent or a higher dose of a previously failed antiarrhythmic agent. For patients with persistent or long-standing persistent AF, performance of a direct-current cardioversion while taking the new or dose adjusted antiarrhythmic agent should be performed, if restoration of sinus rhythm is not achieved following initiation and/or dose adjustment of antiarrhythmic drug therapy. Failure of pharmacological cardioversion alone is not adequate to declare this pharmacological strategy unsuccessful.
Noninducibility of atrial fibrillation	Noninducibility of atrial fibrillation is defined as the inability to induce atrial fibrillation with a standardized prespecified pharmacological or electrical stimulation protocol. The stimulation protocol should be prespecified in the specific clinical trial. Common stimulation approaches include a high-dose isoproterenol infusion protocol or repeated atrial burst pacing at progressively more rapid rates. It is considered optimal for clinical trials to enroll patients with only one type of AF: paroxysmal, persistent, or long-standing 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 that in those with long-standing persistent AF.
Patient populations for inclusion in clinical trials	Following a 3-month blanking period, it is reasonable for clinical trials to incorporate an additional 1- to 3-month therapy consolidation period. During this time, adjustment of antiarrhythmic medications and/or cardioversion can be performed. Should a consolidation period be incorporated into a clinical trial design, the minimum follow-up duration should be 9 months following the therapy consolidation period. Performance of a repeat ablation procedure during the blanking or therapy consolidation period would "reset" the endpoint of the study and trigger a new 3-month blanking period. Incorporation of a therapy consolidation period can be especially appropriate for clinical trials evaluating the efficacy of AF ablation for persistent or long-standing persistent AF. The challenge of this approach is that it prolongs the overall study duration. Because of this concern regarding overall study duration, we suggest that the therapy consolidation period be no more than 3 months in duration following the 3-month blanking period.
Therapy consolidation period	It is recommended that all clinical trials report the single procedure efficacy of catheter ablation. Success is defined as freedom from symptomatic or asymptomatic AF/AFL/AT of 30 seconds or longer at 12 months postablation. Recurrences of AF/AFL/AT during the first 3-month blanking period post- AF ablation are not considered a failure. Performance of a repeat ablation procedure at any point after the initial ablation procedure should be considered a failure of a single procedure strategy. It is acceptable for a clinical trial to choose to prespecify and use a multiprocedure success rate as the primary endpoint of a clinical trial. When a multiprocedure success is selected as the primary endpoint, efficacy should be defined as freedom from AF/flutter or tachycardia at 12 months after the final ablation procedure. In the case of multiple procedures, repeat ablation procedures can be performed at any time following the initial ablation procedure. All ablation procedures are subject to a 3-month post blanking window, and all ablation trials should report efficacy at 12 months after the final ablation procedure.
Recommendations regarding repeat ablation procedures	
Cardioversion definitions	
Failed electrical cardioversion	

Table 10 (continued)

Successful 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 is defined as the ability to restore sinus rhythm for at least 30 seconds following cardioversion.
Immediate AF recurrence postcardioversion	Immediate AF recurrence postcardioversion 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 postcardioversion.
Early AF recurrence postcardioversion	Early AF recurrence postcardioversion is defined as a recurrence of AF within 30 days of a successful cardioversion.
Late AF recurrence postcardioversion	Late AF recurrence postcardioversion is defined as recurrence of AF more than 30 days following a successful cardioversion.
Surgical ablation definitions	
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 preplanned separate ablation procedures separated by no more than 6 months.
Surgical Maze ablation procedure	Surgical Maze ablation procedure is defined as a surgical ablation procedure for AF that 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 left atrium; (5) line from MV to the PVs; (6) management of the LA appendage.
Stand-alone surgical AF ablation	A surgical AF ablation procedure during which other cardiac surgical procedures are not performed such as CABG, valve replacement, or valve repair.
Nomenclature for types of surgical AF ablation procedures	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 biatrial Cox-Maze procedure; (2) PVI alone; and (3) PVI combined with left atrial lesion sets.
Hybrid epicardial and endocardial AF ablation	This term refers to a combined AF ablation procedure involving an off-pump minimally invasive surgical AF ablation as well as a catheter-based AF ablation procedure designed to complement the surgical lesion set. Hybrid ablation procedures may be performed in a single-procedure setting in a hybrid operating room or a cardiac catheterization laboratory environment, or it can be staged. When staged, it is most typical to have the patient undergo the minimally invasive surgical ablation procedure first followed by a catheter ablation procedure 1 to 3 months later. This latter approach is referred to as a "staged Hybrid AF ablation procedure."
Minimum AF documentation, endpoints, TEE performance, 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 episode within 6 months prior to the ablation procedure.
Minimum documentation for persistent AF	The minimum AF documentation requirement for persistent AF is (1) physician's note indicating continuous AF > 7 days but no more than 1 year and (2) a 24-hour Holter within 90 days of the ablation procedure showing continuous AF.
Minimum documentation for early persistent AF	The minimum AF documentation requirement for persistent AF is (1) physician's note indicating continuous AF > 7 days but no more than 3 months and (2) a 24-hour Holter showing continuous AF within 90 days of the ablation procedure.
Minimum documentation for long-standing persistent AF	The minimum AF documentation requirement for long-standing persistent AF is as follows: 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 long-standing persistent.
Symptomatic AF/AFL/AT	AF/AFL/AT that results in symptoms that are experienced by the patient. These symptoms can include but are not limited to palpitations, presyncope, syncope, fatigue, and shortness of breath. For patients in continuous AF, reassessment of symptoms after restoration of sinus rhythm is recommended to establish the relationship between symptoms and AF.
Documentation of AF-related symptoms	Documentation by a physician evaluating the patient that the patient experiences symptoms that could be attributable to AF. This does not require a time-stamped ECG, Holter, or event monitor at the precise time of symptoms. For patients with persistent AF who initially report no symptoms, it is reasonable to reassess symptom status after restoration of sinus rhythm with cardioversion.
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, free from antiarrhythmic drug therapy, and 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: long-standing 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 long-standing 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 (e.g., 12 months); and (3) event recording with an event monitor regularly and when symptoms occur from the end of the 3-month blanking period to the end of follow-up (e.g., 12 months).
Minimum follow-up screening for persistent or long-standing AF recurrence	For persistent and long-standing 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.
Requirements for transesophageal echocardiogram	It is recommended that the minimum requirement for performance of a TEE in a clinical trial should be those requirements set forth in ACC/AHA/HRS 2014 Guidelines for AF Management pertaining to anticoagulation at the time of cardioversion. Prior to undergoing an AF ablation procedure a TEE

Table 10 (continued)

	should be performed in all patients with AF of > 48 hours' duration or of unknown duration if adequate systemic anticoagulation has not been maintained for at least 3 weeks prior to AF ablation. If a TEE is performed for this indication, it should be performed within 24 hours of the ablation procedure.
--	---

AF = atrial fibrillation; DW-MRI = diffusion-weighted magnetic resonance imaging; CHF = congestive heart failure; QOL = quality of life; ECG = electrocardiogram; CABG = coronary artery bypass grafting; PV = pulmonary vein; SVC = superior vena cava; IVC = inferior vena cava; CFAE = complex fractionated atrial electrogram; PVI = pulmonary vein isolation; AFL = atrial flutter; AT = atrial tachycardia; ACC = American College of Cardiology; AHA = American Heart Association; HRS = Heart Rhythm Society.

* 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.

Table 11
Quality-of-life scales, definitions, and strengths

Scale	Definition/Details	Strengths/Weaknesses
Short Form (36) Health Survey (SF36)38 (General)	Consists of 8 equally weighted, scaled scores in the following sections: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health. Each section receives a scale score from 0 to 100. Physical component summary (PCS) and mental component summary (MCS) is an average of all the physically and mentally relevant questions, respectively. The Short Form (12) Health Survey (SF12) is a shorter version of the SF-36, which uses just 12 questions and still provides scores that can be compared with SF-36 norms, especially for summary physical and mental functioning. Gives more precision in measuring QOL than EQ-5D but can be harder to transform into cost utility analysis.	Advantages: extensively validated in a number of disease and health states. Might have more resolution than EQ-50 for AF QOL. Disadvantages: not specific for AF, so might not have resolution to detect AF-specific changes in QOL.
EuroQoL Five Dimensions Questionnaire (EQ-5D)39 (General)	Two components: Health state description is measured in five dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Answers may be provided on a three-level (3L) or five-level (5L) scale. In the Evaluation section, respondents evaluate their overall health status using a visual analogue scale (EQ-VAS). Results can easily be converted to quality-adjusted life years for cost utility analysis.	Advantages: extensively validated in a number of disease and health states. Can easily be converted into quality-adjusted life years for cost-effectiveness analysis. Disadvantages: might not be specific enough to detect AF-specific changes in QOL. Might be less specific than SF-36.
AF effect on Quality of Life Survey (AFEQT) 40 (AF specific)	20 questions: 4 targeting AF-related symptoms, 8 evaluating daily function, and 6 assessing AF treatment concerns. Each item scored on a 7-point Likert scale.	Advantages: brief, simple, very responsive to AF interventions. Good internal validity and well validated against a number of other global and AF-specific QOL scales. Used in CABANA. Disadvantages: validation in only two published studies (approximately 219 patients).
Quality of Life Questionnaire for Patients with AF (AF-QoL)41 (AF specific)	18-item self-administered questionnaire with three domains: psychological, physical, and sexual activity. Each item scores on a 5-point Likert scale.	Advantages: brief, simple, responsive to AF interventions; good internal validity; used in SARA trial. Disadvantages: external validity compared only to SF-36; formal validation in 1 study (approximately 400 patients).
Arrhythmia-Related Symptom Checklist (SCL)42 (AF specific)	16 items covering AF symptom frequency and symptom severity.	Advantages: most extensively validated in a number of arrhythmia cohorts and clinical trials. Disadvantages: time-consuming and uncertain generalizability.
Mayo AF Specific Symptom Inventory (MAFSI)43 (AF specific)	10 items covering AF symptom frequency and severity. Combination of 5- point and 3-point Likert scale responses. Used in CABANA trial.	Advantages: validated in an AF ablation population and responsive to ablation outcome; used in CABANA trial. Disadvantages: external validity compared only to SF-36; 1 validation study (approximately 300 patients).
University of Toronto Atrial Fibrillation Severity Scale (AFSS) (AF specific)44	10 items covering frequency, duration, and severity. 7-point Likert scale responses.	Advantages: validated and reproducible; used in CTAFA trial. Disadvantages: time-consuming and uncertain generalizability.
Arrhythmia Specific Questionnaire in Tachycardia and Arrhythmia (ASTA)45 (AF specific)	Records number of AF episodes and average episode duration during last 3 months. 8 symptoms and 2 disabling symptoms are recorded with scores from 1–4 for each.	Advantages: validated in various arrhythmia groups; external validity compared with SCL, EQ5D, and SF-36; used in MANTRA-PAF; brief, simple. Disadvantages: one validation study (approximately 300 patients).
European Heart Rhythm Association (EHRA)46 (AF specific)	Like NYHA scale. I = no symptoms, II = mild symptoms not affecting daily activity, III = severe symptoms affecting daily activity, and IV = disabling symptoms terminating daily activities.	Advantage: very simple, like NYHA. Disadvantages: not used in studies and not well validated; not very specific; unknown generalizability.
Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale (CCS-SAF)47 (AF specific)	Like NYHA scale. 0 = asymptomatic, I = AF symptoms have minimal effect on patient's QOL, II = AF symptoms have minor effect on patient QOL, III = symptoms have moderate effect on patient QOL, IV = AF symptoms have severe effect on patient QOL.	Advantages: very simple, like NYHA; validated against SF-36 and University of Toronto AFSS. Disadvantages: poor correlation with subjective AF burden; not very specific.

AF = atrial fibrillation; QOL = quality of life; CABANA = Catheter Ablation vs Anti-arrhythmic Drug Therapy for Atrial Fibrillation; SARA = Study of Ablation Versus antiArrhythmic Drugs in Persistent Atrial Fibrillation; CTAFA = Canadian Trial of Atrial Fibrillation; MANTRA-PAF = Medical ANTIarrhythmic Treatment or Radiofrequency Ablation in Paroxysmal Atrial Fibrillation; NYHA = New York Heart Association; AFSS = atrial fibrillation severity scale.

Table 12
Non-AF recurrence-related endpoints for reporting in AF ablation trials

Stroke and bleeding endpoints	Definitions/Details
Stroke (2014 ACC/AHA Key Data Elements)	An acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction. Symptoms or signs must persist ≥ 24 hours, or if documented by CT, MRI or autopsy, the duration of symptoms/signs may be less than 24 hours. Stroke may be classified as ischemic (including hemorrhagic transformation of ischemic stroke), hemorrhagic, or undetermined. Stroke disability measurement is typically performed using the modified Rankin Scale (mRS).
Transient ischemic attack (2014 ACC/AHA Key Data Elements)	Transient episode of focal neurological dysfunction caused by brain, spinal cord, or retinal ischemia without acute infarction and with signs and symptoms lasting less than 24 hours.
Major bleeding (ISTH definition)	Fatal bleeding AND/OR symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome AND/OR bleeding causing a fall in hemoglobin level of 2 g/dL (1.24 mmol/L) or more, or leading to transfusion of two or more units of blood.
Clinically relevant nonmajor bleed (ISTH definition)	An acute or subacute clinically overt bleed that does not meet the criteria for a major bleed but prompts a clinical response such that it leads to one of the following: hospital admission for bleeding; physician-guided medical or surgical treatment for bleeding; change in antithrombotic therapy (including interruption or discontinuation).
Minor bleeding (ISTH definition)	All nonmajor bleeds. Minor bleeds are further divided into clinically relevant and not.
Incidence and discontinuation of oral anticoagulation	The number of patients receiving oral anticoagulation and the type of oral anticoagulation should be documented at the end of follow-up. If patients have their oral anticoagulation discontinued, the number of patients discontinuing, the timing of discontinuation, and the reasons for discontinuation of oral anticoagulation, as well as the clinical characteristics and stroke risk profile of the patients should be reported.

AF = atrial fibrillation; CT = computed tomography; MRI = magnetic resonance imaging.

Table 13
Advantages and disadvantages of AF-related endpoints in AF ablation trials

Endpoint	Advantages	Disadvantages	Relevance and Comments
Freedom from AF/AFL/AT recurrence "gold standard" is 30 seconds	<ul style="list-style-type: none"> - Has been in use for many years - Can be used to compare results of new trials with historical trials - Sets a high bar for AF elimination 	<ul style="list-style-type: none"> - Can systematically underestimate the efficacy of AF ablation, particularly for persistent AF, if 30-second cutoff is used 	<ul style="list-style-type: none"> - Particularly well suited for paroxysmal AF outcomes - Reporting of cutoffs other than 30 seconds encouraged as secondary endpoints to better contextualize results - May be reported as proportion of patients free from arrhythmia or time to recurrence
Freedom from stroke-relevant AF/AFL/AT-duration cutoff of 1 hour	<ul style="list-style-type: none"> - Useful for trials in which interest is more for prognostic change conferred by ablation rather than elimination of all arrhythmias 	<ul style="list-style-type: none"> - No consistent definition of what a stroke-relevant duration of AF is: ranges from 6 minutes to 24 hours in literature 	<ul style="list-style-type: none"> - More than 1 hour could be a useful cutoff based on results of 505 trial - May be reported as proportion of patients free from arrhythmia or time to recurrence
Freedom from AF/AFL/AT requiring intervention (emergency visits, cardioversion, urgent care visit, reablation, etc.)	<ul style="list-style-type: none"> - Can provide an endpoint more relevant to systemic costs of AF recurrence - Clinically relevant 	<ul style="list-style-type: none"> - Will overestimate efficacy of ablation by ignoring shorter episodes not requiring intervention that still might be important to quality of life or stroke 	<ul style="list-style-type: none"> - Determination of what is an "intervention" must be prespecified in protocol and biases mitigated to avoid over- or under-intervention in the trial
Freedom from persistent AF/AFL/AT-duration cutoff of 7 days	<ul style="list-style-type: none"> - Useful for trials assessing additional substrate modification in persistent AF 	<ul style="list-style-type: none"> - Can systematically overestimate the efficacy of AF ablation, particularly for persistent AF 	<ul style="list-style-type: none"> - Can require continuous monitoring to definitively assess if episode is > 7 days
Freedom from AF/AFL/AT on previously ineffective antiarrhythmic therapy	<ul style="list-style-type: none"> - If patient maintains sinus rhythm on previously ineffective drug therapy, this may be considered a clinically relevant, successful outcome 	<ul style="list-style-type: none"> - Will increase the success rate compared with off-drug success - May not be relevant to patients hoping to discontinue drug therapy 	<ul style="list-style-type: none"> - Postablation drug and dosage of drug should be identical to preablation drug and dosage
Significant reduction in AF burden: > 75% reduction from pre- to postablation and/or total postablation burden < 12%.	<ul style="list-style-type: none"> - Can be useful in persistent AF studies, but might not be suited for early, paroxysmal AF studies 	<ul style="list-style-type: none"> - Ideally requires continuous monitoring using an implantable device - No scientific basis exists showing that a 75% reduction in AF burden impacts hard endpoints, including heart failure, stroke, and mortality 	<ul style="list-style-type: none"> - AF burden can be estimated by intermittent monitoring and reporting of patient symptoms and recurrences like a "time in therapeutic range" report for oral anticoagulation; see text - Could also see 75% reduction in number and duration of AF episodes - Because there is no firm scientific basis for selecting the cutoff of 75%, this prior recommendation is provided only as an example of what future clinical trials may choose to use as a definition of clinical/partial success
Prevention in AF progression: time to first episode of persistent AF (> 7 days)	<ul style="list-style-type: none"> - Does not assume that total elimination of AF is required - Well suited for paroxysmal or "early" AF studies in which goal is to prevent progression to persistent AF 	<ul style="list-style-type: none"> - Prevention in progression might be irrelevant for stroke or thromboembolic outcomes - Long follow-up time might be required unless population is "enriched" - Can ideally require continuous implantable monitoring 	<ul style="list-style-type: none"> - Might be useful for specific populations such as heart failure or hypertrophic cardiomyopathy, in which progression to persistent AF can lead to increased hospitalization
Regression of AF: reduction in burden to a given threshold or conversion of persistent to paroxysmal AF	<ul style="list-style-type: none"> - Does not assume that total elimination of AF is required - Well suited for persistent "late" AF studies in which goal is to regress to 	<ul style="list-style-type: none"> - Regression endpoint will overestimate efficacy of AF ablation - Might ideally require continuous implantable monitoring 	<ul style="list-style-type: none"> - Could be particularly useful for long-standing persistent AF populations with structural heart disease, heart failure, etc.

Table 13 (continued)

Endpoint	Advantages	Disadvantages	Relevance and Comments
Acute AF termination during ablation procedure	<ul style="list-style-type: none"> paroxysmal AF, which might be easier to control with drug therapy - Could provide indication of successful modification of substrate responsible for maintaining AF, most relevant to persistent or long-standing persistent AF - Limited studies have linked acute AF termination to long-term success 	<ul style="list-style-type: none"> - Patients will require ongoing drug therapy - Relevance of acute AF termination has not consistently been shown to correlate to long-term success - Endpoint might not be relevant to paroxysmal AF patients in whom AF might terminate spontaneously - Some studies employ administration of intravenous or oral antiarrhythmics during ablation that could cause spontaneous termination - Studies consider termination as reversion to sinus rhythm, whereas others consider reversion to any regular tachycardia as termination 	<ul style="list-style-type: none"> - Intraprocedural administration of pre-procedural oral antiarrhythmics or intraprocedural intravenous antiarrhythmics are discouraged - If antiarrhythmics are used, their use and dosage before and during the ablation should be clearly documented - Termination to sinus rhythm and termination to another regular tachycardia (AT or AFL) should be separately reported

AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia.

11. Working in teams: What is the role of the entire heart team in AF ablation? Does a team approach achieve better outcomes than a "silo" approach?
12. Improving the safety of catheter ablation: As ablation extends to more operators and less experienced operators, the statistical occurrence of complications will increase. We need newer techniques to minimize complications and institute standards for operators to improve the reproducibility of ablation results and safety profiles at a variety of centers worldwide.
13. How does catheter ablation affect mortality, stroke, and hospitalization in broad and selected patient populations receiving catheter ablation for AF?
14. Management of patients who fail initial attempts at catheter ablation: Should there be specific criteria for repeat ablations (e.g., atrial size, body mass index)? Should patients be referred for surgery for repeat ablation?

In order to address these and other important questions in the field of catheter and surgical AF ablation, we urge investigators to create and participate in multisite collaborations and electrophysiology research networks with involvement of senior and junior investigators on the steering committees to push forward the next phase of AF research. We also urge funding bodies to support these important initiatives.

Section 14: Conclusion

Catheter ablation of AF is a very commonly performed procedure in hospitals 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. Also included within this document are recommendations concerning indications for AF ablation, technical performance of this procedure, and training. It is our hope to improve patient care by providing a foundation for those involved with care of patients with AF as well as those who perform AF ablation. 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 cardiologists, electrophysiologists, and surgeons to ensure appropriate indications, procedure selection, and follow-up.

Acknowledgments

The authors acknowledge the support of Jun Dong, MD, PhD; Kan Fang, MD; and Mark Fellman at the Division of Cardiovascular Devices, Center for Devices and Radiological Health, U.S. Food and Drug Administration (FDA) during the preparation of this document. This document does not necessarily represent the opinions, policies, or recommendations of the FDA.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.joa.2017.08.001>.

Table A1
Author disclosure table

Writing group member	Institution	Consultant/Advisory board/Honoraria	Speakers' bureau	Research grant	Fellowship support	Stock options/Partner	Board Mbs/Other
Hugh Calkins, MD (Chair)	Johns Hopkins Medical Institutions, Baltimore, MD	1: Abbott Laboratories, 1: Atrio-Cure, Inc., 1: Boston Scientific Corp., 1: Pfizer Inc., 1: St. Jude Medical, 1: Toray Industries Inc., 2: IRhythm, 3: Boehringer Ingelheim, 3: Medtronic, Inc.	None	2: Medtronic, Inc., 2: Boston Scientific Corp.	None	None	None
Gerhard Hindricks, MD (Vice-Chair)	Heart Center Leipzig, Leipzig, Germany	None	None	1: SIEMENS, 3: Biosense Webster, Inc., 3: Stereotaxis, Inc., 4: BIOTRONIK, 5: Boston Scientific Corp., 5: St. Jude Medical	None	None	None
Riccardo Cappato, MD (Vice-Chair)	Humanitas Research Hospital, Arrhythmias and Electrophysiology Research Center, Milan, Italy	None	None	None	None	None	None
Young-Hoon Kim, MD, PhD (Vice-Chair)	Korea University, Seoul, South Korea	None	1: St. Jude Medical	2: St. Jude Medical	None	None	None
Eduardo B. Saad, MD, PhD (Vice-Chair)	Hospital Pro-Cardiaco and Hospital Samaritano, Botafogo, Rio de Janeiro, Brazil	None	None	None	None	None	None
Luis Aguinaga, MD, PhD	Centro Privado de Cardiología, Tucuman, Argentina	None	None	None	None	None	None
Joseph G. Akar, MD, PhD	Yale University School of Medicine, New Haven, CT	1: Biosense Webster	None	None	None	None	None
Vinay Badhwar, MD	West Virginia University School of Medicine, Morgantown, WV	None	None	None	None	None	None
Josep Brugada, MD, PhD	Cardiovascular Institute, Hospital Clinic, University of Barcelona, Catalonia, Spain	None	None	None	None	None	None
John Camm, MD	St. George's University of London, London, United Kingdom	1: Acrelion Pharmaceuticals, 1: Daiichi-Sankyo, 1: Eli Lilly, 1: Gilead Sciences, Inc., 1: Heart Metabolites, 1: InCardia Therapeutics, 1: Infobionic, 1: Johnson and Johnson, 1: Medtronic, Inc., 1: Milestone, 1: Pfizer, Inc., 2: Boehringer Ingelheim, 2: Boston Scientific Corp., 2: Novartis 3: Bayer HealthCare, LLC	1: Daiichi-Sankyo, 1: Servier, 2: Bayer/Schering Pharma, 2: Boehringer Ingelheim	3: Boehringer Ingelheim, 3: Daiichi-Sankyo, 3: Pfizer, Inc.	None	None	0: European Heart Rhythm Association, 1: Oxford
Peng-Sheng Chen, MD	Indiana University School of Medicine, Indianapolis, IN	None	None	5: National Institutes of Health	None	5: Arrhythmotech	None
Shih-Ann Chen, MD	National Yang-Ming University, Taipei, Taiwan	1: Bayer/Schering Pharma, 1: Biosense Webster, 1: Boehringer Ingelheim, 1: Boston Scientific Corp., 1: Daiichi-Sankyo, 1: Medtronic Inc., 1: Pfizer Inc., 1: St. Jude Medical	1: St. Jude Medical	2: Biosense Webster, 2: St. Jude Medical	None	None	None
Mina K. Chung, MD	Cleveland Clinic, Cleveland, OH	0: Amarin, 0: BIOTRONIK, 0: Boston Scientific Corp., 0: Medtronic, Inc., 0: St. Jude Medical, 0: Zoll Medical Corporation	1: American College of Cardiology	None	None	None	1: Up to Date.
Jens Cosedis Nielsen, DMSc, PhD	Aarhus University Hospital, Skejby, Denmark	None	None	5. Novo Nordisk Foundation	None	None	None

Anne B. Curtis, MD	University at Buffalo, Buffalo, NY	1: Daiichi-Sankyo, 1: Medtronic, Inc., 1: Projects in Knowledge, 2: St. Jude Medical	None	None	None	None	None	None
D. Wyn Davies, MD	Imperial College Healthcare NHS Trust, London, United Kingdom	1: Boston Scientific Corp., 1: Janssen Pharmaceuticals, 1: Medtronic, Inc., 1: Rhythmia Medical	None	None	None	None	3: Rhythmia Medical	None
John D. Day, MD	Intermountain Medical Center Heart Institute, Salt Lake City, UT	1: Biotronik, 1: Boston Scientific Corp., 3: St. Jude Medical	None	None	None	None	None	None
André d'Avila, MD, PhD	Hospital SOS Cardio, Florianópolis, SC, Brazil	0: Biotronik, 0: St. Jude Medical	None	None	None	None	None	None
N.M.S. (Natasja) de Groot, MD, PhD	Erasmus Medical Center, Rotterdam, the Netherlands	None	None	None	None	None	None	None
Luigi Di Biase, MD, PhD	Albert Einstein College of Medicine, Montefiore-Einstein Center for Heart & Vascular Care, Bronx, NY	1: Atricure, 1: Biosense Webster, Inc., 1: Biotronik, 1: Boston Scientific Corp., 1: EpiEP, 1: Medtronic, Inc., 1: St. Jude Medical, 1: Stereotaxis, Inc.	None	None	None	None	None	None
Martias Duytschaever, MD, PhD	Universitair Ziekenhuis Gent (Ghent University Hospital), Ghent, Belgium	None	None	None	None	None	None	None
James R. Edgerton, MD	The Heart Hospital, Baylor Plano, Plano, TX	2: AtriCure, Inc.	1: AtriCure, Inc.	2: AtriCure, Inc.	None	None	None	None
Kenneth A. Ellenbogen, MD	Virginia Commonwealth University School of Medicine, Richmond, VA	1: American Heart Association, 1: Heart Rhythm Society, 2: Boston Scientific Corp.	1: AtriCure, Inc., 1: Biosense Webster, Inc., 2: Biotronik, 1: St. Jude Medical, 2: Boston Scientific Corp., 2: Medtronic, Inc.	2: Biosense Webster, Inc., 2: Daiichi-Sankyo, 2: National Institutes of Health, 4: Boston Scientific Corp., 4: Medtronic, Inc.	None	None	None	1: Elsevier, 1: Wiley-Blackwell
Patrick T. Ellinor, MD, PhD	Massachusetts General Hospital, Boston, MA	1: Bayer HealthCare, LLC, 1: Quest Diagnostics	None	1: Leducq Foundation, 3: American Heart Association, 3: National Institutes of Health, 5: Bayer HealthCare, LLC, 4: Spectrum Dynamics	None	None	None	None
Sabine Ernst, MD, PhD	Royal Brompton and Harefield NHS Foundation Trust, National Heart and Lung Institute, Imperial College London, London, United Kingdom	2: Biosense Webster, Inc.	None	None	None	None	None	None
Guilherme Fenealon, MD, PhD	Albert Einstein Jewish Hospital, Federal University of São Paulo, São Paulo, Brazil	1: Biosense Webster, Inc., 1: Biotronik, 1: St. Jude Medical	None	None	None	None	None	None
Edward P. Gerstenfeld, MS, MD	University of California, San Francisco, San Francisco, CA	1: Boehringer Ingelheim, 1: Boston Scientific Corp., 1: Medtronic, Inc., 1: St. Jude Medical	None	4: Biosense Webster, Inc., 4: St. Jude Medical	None	2: Biosense Webster, Inc., 2: Biotronik, 2: Boston Scientific Corp., 2: Medtronic, Inc.	1: Rhythm Diagnostic Systems Inc.	None
David E. Haines, MD	Beaumont Health System, Royal Oak, MI	1: Lake Region Medical, 1: Terumo Medical Corp	None	None	None	None	None	1: Biosense Webster, Inc., 1: Boston Scientific Corp., 1: Medtronic, Inc., 1: St. Jude Medical
Michel Haissaguerre, MD	Hôpital Cardiologique du Haut-Lévêque, Pessac, France	None	None	None	None	None	None	None
Robert H. Helm, MD	Boston University Medical Center, Boston, MA	None	None	None	None	None	None	1: Boston Scientific Corp.
Elaïne Hylek, MD, MPH	Boston University School of Medicine, Boston, MA	1: Bayer, 1: Boehringer Ingelheim, 1: Bristol-Myers Squibb, 1: Daiichi-Sankyo, 1: Medtronic, 1: Pfizer	None	2: Janssen Pharmaceuticals	None	None	None	None
Warren M. Jackman, MD	None	1: ACT, 1: Vytronis, Inc., 2: Biosense Webster, Inc., 2: Boston	1: Biotronik, 1: St. Jude Medical, 2:	None	None	None	None	None

Table A1 (continued)

Writing group member	Institution	Consultant/Advisory board/ Honorary	Speakers' bureau	Research grant	Fellowship support	Stock options/ Partner	Board Mbs/Other
Jose Jalife, MD	Heart Rhythm Institute, University of Oklahoma Health Sciences Center, Oklahoma City, OK	Scientific Corp., 2: Spectrum Dynamics	Biosense Webster, Inc., 2: Boston Scientific Corp.	1: Medtronic, Inc.	None	None	None
Jonathan M. Kalman, MBBS, PhD	University of Michigan, Ann Arbor, MI, the National Center for Cardiovascular Research Carlos III (CNIC) and CIBERCV, Madrid, Spain	None	1: Boston Scientific Corp., 1: Medtronic, Inc.	4: Medtronic, Inc.	3: St. Jude Medical, 4: Biosense Webster, Inc., 4: Medtronic, Inc.	None	2: Biosense Webster, Inc., 4: Boston Scientific Corp.
Josef Kautzner, MD, PhD	Royal Melbourne Hospital and University of Melbourne, Melbourne, Australia	1: Bayer/Schering Pharma, 1: Boehringer Ingelheim, 1: Boston Scientific Corp., 1: Daiichi-Sankyo, 1: Sorin Group, 1: St. Jude Medical, 1: Biosense Webster, Inc., 2: Medtronic, Inc.	1: BIOTRONIK	None	None	None	None
Hans Kottkamp, MD	Institute for Clinical and Experimental Medicine, Prague, Czech Republic	1: Biosense Webster, Inc., 1: Kardium	None	None	None	1: Kardium	None
Karl Heinz Kuck, MD, PhD	Hirslanden Hospital, Dept. of Electrophysiology, Zurich, Switzerland	1: Biosense Webster, Inc., 1: BIOTRONIK, 1: St. Jude Medical, 1: Stereotaxis, Inc.	None	1: Biosense Webster, Inc., 1: BIOTRONIK, 1: St. Jude Medical, 1: Stereotaxis, Inc.	None	1: Endosense	None
Koichiro Kumagai, MD, PhD	Asklepios Klinik St. Georg, Hamburg, Germany	None	None	None	None	None	None
Richard Lee, MD, MBA	Heart Rhythm Center, Fukuoka Sanno Hospital, Fukuoka, Japan	None	None	None	None	None	None
Thorsten Lewalter, MD, PhD	Saint Louis University Medical School, St. Louis, MO	None	None	None	None	None	None
Bruce D. Lindsay, MD	Dept. of Cardiology and Intensive Care, Hospital Munich-Thalkirchen, Munich, Germany	1: BIOTRONIK, 1: Medtronic, Inc., 1: St. Jude Medical	1: Abbott Vascular, 1: BIOTRONIK, 1: Medtronic, Inc., 1: St. Jude Medical	None	None	None	None
Laurent Macle, MD	Cleveland Clinic, Cleveland, OH	0: Medtronic, Inc., 1: Abbott Vascular, 1: Biosense Webster, Inc.	None	None	3: Boston Scientific Corp., 3: Medtronic, Inc., 3: St. Jude Medical	None	None
Moussa Mansour, MD	Montréal Heart Institute, Department of Medicine, Université de Montréal, Montréal, Canada	1: Bayer HealthCare, LLC, 1: Biosense Webster, Inc., 1: Boehringer Ingelheim, 1: Bristol-Myers Squibb, 1: Medtronic, Inc., 1: Pfizer, Inc., 1: Servier, 1: St. Jude Medical	None	4: Biosense Webster, Inc., 5: St. Jude Medical	None	None	None
Francis E. Marchlinski, MD	Massachusetts General Hospital, Boston, MA	1: Biosense Webster, Inc., 1: St. Jude Medical	None	None	None	4: NewPace Ltd.	None
Gregory F. Michaud, MD	Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine, Philadelphia, PA	1: Abbot Medical, 1: Biosense Webster, Inc., 2: BIOTRONIK, 1: Medtronic, Inc., 1: Boston Scientific Corp., 1: St. Jude Medical	None	1: Boehringer Ingelheim, 3: Medtronic, Inc., 4: Biosense Webster, Inc.	1: BIOTRONIK, 3: Boston Scientific Corp., 3: Medtronic, Inc., 4: Biosense Webster, Inc., 5: St. Jude Medical	None	None
	Brigham and Women's Hospital, Boston, MA	1: Biosense Webster, Inc., 1: Boston Scientific Corp., 1: Medtronic, Inc., 1: St. Jude Medical	None	4: Biosense Webster, Inc., 4: Boston Scientific Corp.	None	None	None

Table A1 (continued)

Writing group member	Institution	Consultant/Advisory board/Honoraria	Speakers' bureau	Research grant	Fellowship support	Stock options/Partner	Board Mbs/Other
David J. Wilber, MD	Southlake Regional Health Centre, University of Toronto, Toronto, Canada Loyola University of Chicago, Chicago, IL	1: Bayer HealthCare, LLC, 1: Boehringer Ingelheim 1: Biosense Webster, Inc., 1: Medtronic, Inc., 1: St. Jude Medical, 1: Janssen Pharmaceuticals, 1: Medtronic, Inc., 1: St. Jude Medical, 1: Thermedical 1: Bayer HealthCare, 1: Medtronic, 2: Abbott Japan, 2: Daiichi-Sankyo, 2: Boehringer Ingelheim, 2: Bristol-Myers Squibb	None	5: Bayer HealthCare, LLC, 5: Biosense Webster, Inc., 5: BIO-TRONIK, 5: Medtronic, Inc. 1: Abbott Vascular, 1: Medtronic, Inc., 1: St. Jude Medical, 1: Thermedical, 3: Biosense Webster, Inc. 1: Boehringer Ingelheim, 1: Bayer HealthCare	3: Biosense Webster, Inc., 3: Medtronic, Inc., 3: St. Jude Medical None	None	1: Elsevier, 1: Wiley-Blackwell, 4: American College of Cardiology Foundation None
Teitichi Yamane, MD, PhD	Jikei University School of Medicine, Tokyo, Japan		None				

Number Value: 0 = \$0; 1 = ≤ \$10,000; 2 = > \$10,000 to ≤ \$25,000; 3 = > \$25,000 to ≤ \$50,000; 4 = > \$50,000 to ≤ \$100,000; 5 = > \$100,000.

* Dr. Cappato is now with the Department of Biomedical Sciences, Humanitas University, Milan, Italy, and IRCCS, Humanitas Clinical and Research Center, Milan, Italy

Table B1
Reviewer disclosure table

Peer reviewer	Institution	Consultant/Advisory board/Honoraria	Speakers' bureau	Research grant	Fellowship support	Stock options/ Partner	Board Mbs/Other
Carina Blomström-Lundqvist, MD, PhD	Department of Cardiology and Medical Science, Uppsala University, Uppsala, Sweden	1: Bayer/Schering Pharma, 1: Boston Scientific Corp., 1: Medtronic, Inc., 1: Sanofi, 1: Pfizer, MSD, Bristol-Myers Squibb, Biosense Webster, Inc.	None	1: Cardione Pharma/Astellas, 1: Medtronic, Inc.	None	None	None
Angelo A.V. De Paola, MD, PhD	Hospital São Paulo – Federal University of São Paulo, São Paulo, Brazil	None	None	None	None	None	None
Peter M. Kistler, MBBS, PhD	The Alfred Hospital Heart Centre, Melbourne, Australia	None	1: St. Jude Medical	None	None	None	None
Gregory Y.H. Lip, MD	University of Birmingham, Birmingham, United Kingdom; Aalborg University, Aalborg, Denmark	1: Medtronic, 3: Bayer/Janssen, BMS/Pfizer, Boehringer Ingelheim, Daiichi-Sankyo	3: Bayer, BMS/Pfizer, Boehringer Ingelheim, Daiichi-Sankyo. No fees are received personally	None	None	None	None
Nicholas S. Peters, MD	St Mary's Hospital, Imperial College London, London, United Kingdom	1: Boston Scientific Corp., 1: Cardialogs, 1: Magnetics, 1: Medtronic, Inc., 1: St. Jude Medical	None	None	None	None	None
Cristiano F. Pisani, MD	InCor, Heart Institute, HCFMUSP, Arrhythmia Unit	None	None	None	None	None	None
Antonio Raviolo, MD	ALFA-Alliance to Fight Atrial Fibrillation, Rimini, Italy	None	None	None	None	None	None
Eduardo B. Saad, MD, PhD	Hospital Pro-Cardiaco and Hospital Samaritano, Botafogo, Rio de Janeiro, Brazil	None	None	None	None	None	None
Kazuhiro Satomi, MD, PhD	Tokyo Medical University, Tokyo, Japan	1: Bayer/Schering Pharma, 1: Boehringer Ingelheim, 1: Bristol-Myers Squibb, 1: Japan Lifeline, 1: Johnson and Johnson, 1: Medtronic, Inc., 1: Sankyo Pharmaceuticals, 1: St. Jude Medical	None	None	None	None	None
Martin K. Stiles, MB ChB, PhD	Waikato Hospital, Hamilton, New Zealand	1: Boston Scientific Corp., 1: Biosense Webster, Inc., 1: BIOTRONIK, 1: Medtronic, Inc.	None	None	1: Medtronic, Inc.	None	None
Stephan Willems, MD, PhD	University Medical Center Hamburg-Eppendorf, Hamburg, Germany	1: Bayer HealthCare, LLC, 1: Biosense Webster, Inc., 1: Boehringer Ingelheim, 1: Bristol-Myers Squibb, 1: Sanofi, 1: St. Jude Medical, 1: Medtronic	None	None	None	None	None

Number Value: 0 = \$0; 1 = ≤ \$10,000; 2 = > \$10,000 to ≤ \$25,000; 3 = > \$25,000 to ≤ \$50,000; 4 = > \$50,000 to ≤ \$100,000; 5 = > \$100,000.

References

- 1 Calkins H, et al. HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm* 2007;4(6):816–61.
- 2 Calkins H, et al. 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. *Heart Rhythm* 2012;9(4):632–696, e21.
- 3 Jacobs AK, Anderson JL, Halperin JL. The evolution and future of ACC/AHA clinical practice guidelines: a 30-year journey: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014;64(13):1373–84.
- 4 Anderson JL. Evolution of the ACC/AHA clinical practice guidelines in perspective: guiding the guidelines. *J Am Coll Cardiol* 2015;65(25):2735–8.
- 5 January CT, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol* 2014;64(21):e1–76.
- 6 Kirchhof P, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur J Cardiothorac Surg* 2016;50(5):e1–88.
- 7 Jais P, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. *Circulation* 2008;118(24):2498–505.
- 8 Calkins H, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. *Circ Arrhythm Electrophysiol* 2009;2(4):349–61.
- 9 Packer DL, et al. Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. *J Am Coll Cardiol* 2013;61(16):1713–23.
- 10 Kuck KH, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. *N Engl J Med* 2016;374(23):2235–45.
- 11 Dukkipati SR, et al. Pulmonary vein isolation using the visually guided laser balloon: a prospective, multicenter, and randomized comparison to standard radiofrequency ablation. *J Am Coll Cardiol* 2015;66(12):1350–60.
- 12 Reddy VY, et al. Randomized, controlled trial of the safety and effectiveness of a contact force-sensing irrigated catheter for ablation of paroxysmal atrial fibrillation: results of the TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) study. *Circulation* 2015;132(10):907–15.
- 13 Natale A, et al. Paroxysmal AF catheter ablation with a contact force sensing catheter: results of the prospective, multicenter SMART-AF trial. *J Am Coll Cardiol* 2014;64(7):647–56.
- 14 Wilber DJ, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. *JAMA* 2010;303(4):333–40.
- 15 Sahara H, et al. HotBalloon ablation of the pulmonary veins for paroxysmal AF: a multicenter randomized trial in Japan. *J Am Coll Cardiol* 2016;68(25):2747–57.
- 16 Pappone C, et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. *J Am Coll Cardiol* 2006;48(11):2340–7.
- 17 Stabile G, et al. Catheter ablation treatment in patients with drug-refractory atrial fibrillation: a prospective, multi-centre, randomized, controlled study (Catheter Ablation For The Cure Of Atrial Fibrillation Study). *Eur Heart J* 2006;27(2):216–21.
- 18 Forleo GB, et al. Catheter ablation of atrial fibrillation in patients with diabetes mellitus type 2: results from a randomized study comparing pulmonary vein isolation versus antiarrhythmic drug therapy. *J Cardiovasc Electrophysiol* 2009;20(1):22–8.
- 19 Verma A, et al. Approaches to catheter ablation for persistent atrial fibrillation. *N Engl J Med* 2015;372(19):1812–22.
- 20 Scherr D, et al. Five-year outcome of catheter ablation of persistent atrial fibrillation using termination of atrial fibrillation as a procedural endpoint. *Circ Arrhythm Electrophysiol* 2015;8(1):18–24.
- 21 Tamboreto D, et al. Left atrial posterior wall isolation does not improve the outcome of circumferential pulmonary vein ablation for atrial fibrillation: a prospective randomized study. *Circ Arrhythm Electrophysiol* 2009;2(1):35–40.
- 22 Hummel J, et al. Phased RF ablation in persistent atrial fibrillation. *Heart Rhythm* 2014;11(2):202–9.
- 23 Bassiouny M, et al. Randomized study of persistent atrial fibrillation ablation: ablate in sinus rhythm versus ablate complex-fractionated atrial electrograms in atrial fibrillation. *Circ Arrhythm Electrophysiol* 2016;9(2):e003596.
- 24 Krittayaphong R, et al. A randomized clinical trial of the efficacy of radiofrequency catheter ablation and amiodarone in the treatment of symptomatic atrial fibrillation. *J Med Assoc Thai* 2003;86(Suppl 1):S8–16.
- 25 Oral H, et al. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. *N Engl J Med* 2006;354(9):934–41.
- 26 Mont L, et al. Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicenter, randomized, controlled trial (SARA study). *Eur Heart J* 2014;35(8):501–7.
- 27 Calvo N, et al. Efficacy of circumferential pulmonary vein ablation of atrial fibrillation in endurance athletes. *Europace* 2010;12(1):30–6.
- 28 Furfanello F, et al. Radiofrequency catheter ablation of atrial fibrillation in athletes referred for disabling symptoms preventing usual training schedule and sport competition. *J Cardiovasc Electrophysiol* 2008;19(5):457–62.
- 29 Wazni OM, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA* 2005;293(21):2634–40.
- 30 Cosedis Nielsen J, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. *N Engl J Med* 2012;367(17):1587–95.
- 31 Morillo CA, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAF-2): a randomized trial. *JAMA* 2014;311(7):692–700.
- 32 Hakalahti A, et al. Radiofrequency ablation vs antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis. *Europace* 2015;17(3):370–8.
- 33 Hocini M, et al. Reverse remodeling of sinus node function after catheter ablation of atrial fibrillation in patients with prolonged sinus pauses. *Circulation* 2003;108(10):1172–5.
- 34 Chen YW, et al. Pacing or ablation: which is better for paroxysmal atrial fibrillation-related tachycardia-bradycardia syndrome? *Pacing Clin Electrophysiol* 2014;37(4):403–11.
- 35 Inada K, et al. The role of successful catheter ablation in patients with paroxysmal atrial fibrillation and prolonged sinus pauses: outcome during a 5-year follow-up. *Europace* 2014;16(2):208–13.
- 36 Chen MS, et al. Pulmonary vein isolation for the treatment of atrial fibrillation in patients with impaired systolic function. *J Am Coll Cardiol* 2004;43(6):1004–9.
- 37 Gentlesk PJ, et al. Reversal of left ventricular dysfunction following ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2007;18(1):9–14.
- 38 Khan MN, et al. Pulmonary-vein isolation for atrial fibrillation in patients with HF. *N Engl J Med* 2008;359(17):1778–85.
- 39 MacDonald MR, et al. Radiofrequency ablation for persistent atrial fibrillation in patients with advanced heart failure and severe left ventricular systolic dysfunction: a randomized controlled trial. *Heart* 2011;97(9):740–7.
- 40 Hunter RJ, et al. A randomized controlled trial of catheter ablation versus medical treatment of atrial fibrillation in heart failure (the CAMTAF trial). *Circ Arrhythm Electrophysiol* 2014;7(1):31–8.
- 41 Tondo C, et al. Pulmonary vein vestibule ablation for the control of atrial fibrillation in patients with impaired left ventricular function. *Pacing Clin Electrophysiol* 2006;29(9):962–70.
- 42 Lutomsly BA, et al. Catheter ablation of paroxysmal atrial fibrillation improves cardiac function: a prospective study on the impact of atrial fibrillation ablation on left ventricular function assessed by magnetic resonance imaging. *Europace* 2008;10(5):593–9.
- 43 Choi AD, et al. Ablation vs medical therapy in the setting of symptomatic atrial fibrillation and left ventricular dysfunction. *Congest Heart Fail* 2010;16(1):10–4.
- 44 De Potter T, et al. Left ventricular systolic dysfunction by itself does not influence outcome of atrial fibrillation ablation. *Europace* 2010;12(1):24–9.
- 45 Cha YM, et al. Success of ablation for atrial fibrillation in isolated left ventricular diastolic dysfunction: a comparison to systolic dysfunction and normal ventricular function. *Circ Arrhythm Electrophysiol* 2011;4(5):724–32.
- 46 Jones DC, et al. A randomized trial to assess catheter ablation versus rate control in the management of persistent atrial fibrillation in HF. *J Am Coll Cardiol* 2013;61(18):1894–903.
- 47 Machino-Ohtsuka T, et al. Efficacy, safety, and outcomes of catheter ablation of atrial fibrillation in patients with heart failure with preserved ejection fraction. *J Am Coll Cardiol* 2013;62(20):1857–65.
- 48 Al Halabi S, et al. Catheter ablation for atrial fibrillation in heart failure patients: a meta-analysis of randomized controlled trials. *JACC Clin Electrophysiol* 2015;1(3):200–9.
- 49 Bunch TJ, et al. Five-year outcomes of catheter ablation in patients with atrial fibrillation and left ventricular systolic dysfunction. *J Cardiovasc Electrophysiol* 2015;26(4):363–70.
- 50 Lobo TJ, et al. Atrial fibrillation ablation in systolic dysfunction: clinical and echocardiographic outcomes. *Arq Bras Cardiol* 2015;104(1):45–52.
- 51 Ling LH, et al. Sinus rhythm restores ventricular function in patients with cardiomyopathy and no late gadolinium enhancement on cardiac magnetic resonance imaging who undergo catheter ablation for atrial fibrillation. *Heart Rhythm* 2013;10(9):1334–9.
- 52 Hsu LF, et al. Catheter ablation for atrial fibrillation in congestive HF. *N Engl J Med* 2004;351(23):2373–83.
- 53 Spragg DD, et al. Complications of catheter ablation for atrial fibrillation: incidence and predictors. *J Cardiovasc Electrophysiol* 2008;19(6):627–31.
- 54 Kusumoto F, et al. Radiofrequency catheter ablation of atrial fibrillation in older patients: outcomes and complications. *J Interv Card Electrophysiol* 2009;25(1):31–5.
- 55 Bunch TJ, et al. Long-term clinical efficacy and risk of catheter ablation for atrial fibrillation in octogenarians. *Pacing Clin Electrophysiol* 2010;33(2):146–52.
- 56 Santangeli P, et al. Catheter ablation of atrial fibrillation in octogenarians: safety and outcomes. *J Cardiovasc Electrophysiol* 2012;23(7):687–93.
- 57 Nademanee K, et al. Benefits and risks of catheter ablation in elderly patients with atrial fibrillation. *Heart Rhythm* 2015;12(1):44–51.
- 58 Bunch TJ, et al. The impact of age on 5-year outcomes after atrial fibrillation catheter ablation. *J Cardiovasc Electrophysiol* 2016;27(2):141–6.

- 59 Metzner I, et al. Ablation of atrial fibrillation in patients ≥ 75 years: long-term clinical outcome and safety. *Europace* 2016;18(4):543–9.
- 60 Bunch TJ, et al. Substrate and procedural predictors of outcomes after catheter ablation for atrial fibrillation in patients with hypertrophic cardiomyopathy. *J Cardiovasc Electrophysiol* 2008;19(10):1009–14.
- 61 Olivetto I, et al. Impact of atrial fibrillation on the clinical course of hypertrophic cardiomyopathy. *Circulation* 2001;104(21):2517–24.
- 62 Providencia R, et al. Catheter ablation for atrial fibrillation in hypertrophic cardiomyopathy: a systematic review and meta-analysis. *Heart* 2016;102(19):1533–43.
- 63 Leong-Sit P, et al. Efficacy and risk of atrial fibrillation ablation before 45 years of age. *Circ Arrhythm Electrophysiol* 2010;3(5):452–7.
- 64 Chun KR, et al. Catheter ablation of atrial fibrillation in the young: insights from the German Ablation Registry. *Clin Res Cardiol* 2013;102(6):459–68.
- 65 Koopman P, et al. Efficacy of radiofrequency catheter ablation in athletes with atrial fibrillation. *Europace* 2011;13(10):1386–93.
- 66 Forleo GB, et al. Clinical impact of catheter ablation in patients with asymptomatic atrial fibrillation: the IRON-AF (Italian registry on NavX atrial fibrillation ablation procedures) study. *Int J Cardiol* 2013;168(4):3968–70.
- 67 Wu L, et al. Comparison of radiofrequency catheter ablation between asymptomatic and symptomatic persistent atrial fibrillation: a propensity score matched analysis. *J Cardiovasc Electrophysiol* 2016;27(5):531–5.
- 68 Mohanty S, et al. Catheter ablation of asymptomatic longstanding persistent atrial fibrillation: impact on quality of life, exercise performance, arrhythmia perception, and arrhythmia-free survival. *J Cardiovasc Electrophysiol* 2014;25(10):1057–64.
- 69 U.S. Food and Drug Administration. Summary of Safety and Effectiveness Data: AtriCure Synergy Ablation System, PMA P100046. 2011.
- 70 Badhwar V, et al. The Society of Thoracic Surgeons Mitral Repair/Replacement Composite Score: a report of the Society of Thoracic Surgeons Quality Measurement Task Force. *Ann Thorac Surg* 2016;101(6):2265–71.
- 71 Abreu Filho CA, et al. Effectiveness of the maze procedure using cooled-tip radiofrequency ablation in patients with permanent atrial fibrillation and rheumatic mitral valve disease. *Circulation* 2005;112(9 Suppl):320–5.
- 72 Doukas G, et al. Left atrial radiofrequency ablation during mitral valve surgery for continuous atrial fibrillation: a randomized controlled trial. *JAMA* 2005;294(18):2323–9.
- 73 Blomstrom-Lundqvist C, et al. A randomized double-blind study of epicardial left atrial cryoablation for permanent atrial fibrillation in patients undergoing mitral valve surgery: the SWEDISH Multicentre Atrial Fibrillation study (SWEDMAF). *Eur Heart J* 2007;28(23):2902–8.
- 74 Chevalier P, et al. Left atrial radiofrequency ablation during mitral valve surgery: a prospective randomized multicentre study (SAFIR). *Arch Cardiovasc Dis* 2009;102(11):769–75.
- 75 Cheng DC, et al. Surgical ablation for atrial fibrillation in cardiac surgery: a meta-analysis and systematic review. *Innovations (Phila)* 2010;5(2):84–96.
- 76 Budera P, et al. Comparison of cardiac surgery with left atrial surgical ablation vs. cardiac surgery without atrial ablation in patients with coronary and/or valvular heart disease plus atrial fibrillation: final results of the PRAGUE-12 randomized multicentre study. *Eur Heart J* 2012;33(21):2644–52.
- 77 Phan K, et al. Surgical ablation for treatment of atrial fibrillation in cardiac surgery: a cumulative meta-analysis of randomised controlled trials. *Heart* 2014;100(9):722–30.
- 78 Gillinov AM, et al. Surgical ablation of atrial fibrillation during mitral-valve surgery. *N Engl J Med* 2015;372(15):1399–409.
- 79 Rankin JS, et al. The Society of Thoracic Surgeons risk model for operative mortality after multiple valve surgery. *Ann Thorac Surg* 2013;95(4):1484–90.
- 80 Louagie Y, et al. Improved patient survival with concomitant Cox Maze III procedure compared with heart surgery alone. *Ann Thorac Surg* 2009;87(2):440–6.
- 81 Chiappini B, Di Bartolomeo R, Marinelli G. Radiofrequency ablation for atrial fibrillation: different approaches. *Asian Cardiovasc Thorac Ann* 2004;12(3):272–7.
- 82 Barnett SD, Ad N. Surgical ablation as treatment for the elimination of atrial fibrillation: a meta-analysis. *J Thorac Cardiovasc Surg* 2006;131(5):1029–35.
- 83 Edgerton JR, Jackman WM, Mack MJ. A new epicardial lesion set for minimal access left atrial maze: the Dallas lesion set. *Ann Thorac Surg* 2009;88(5):1655–7.
- 84 Edgerton JR, et al. Totally thorascopic surgical ablation of persistent AF and long-standing persistent atrial fibrillation using the “Dallas” lesion set. *Heart Rhythm* 2009;6(12 Suppl):S64–70.
- 85 Lockwood D, et al. Linear left atrial lesions in minimally invasive surgical ablation of persistent atrial fibrillation: techniques for assessing conduction block across surgical lesions. *Heart Rhythm* 2009;6(12 Suppl):S50–63.
- 86 Malaisrie SC, et al. Atrial fibrillation ablation in patients undergoing aortic valve replacement. *J Heart Valve Dis* 2012;21(3):350–7.
- 87 Cherniavsky A, et al. Assessment of results of surgical treatment for persistent atrial fibrillation during coronary artery bypass grafting using implantable loop recorders. *Interact Cardiovasc Thorac Surg* 2014;18(6):727–31.
- 88 Yoo JS, et al. Impact of concomitant surgical atrial fibrillation ablation in patients undergoing aortic valve replacement. *Circ J* 2014;78(6):1364–71.
- 89 Driessen AH, et al. Ganglion Plexus Ablation in Advanced Atrial Fibrillation: The AFACT Study. *J Am Coll Cardiol* 2016;68(11):1155–65.
- 90 Boersma LV, et al. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): a 2-center randomized clinical trial. *Circulation* 2012;125(1):23–30.
- 91 Henn MC, et al. Late outcomes after the Cox maze IV procedure for atrial fibrillation. *J Thorac Cardiovasc Surg* 2015;150(5):1168–76 e1–2.
- 92 Krul SP, et al. Navigating the mini-maze: systematic review of the first results and progress of minimally-invasive surgery in the treatment of atrial fibrillation. *Int J Cardiol* 2013;166(1):132–40.
- 93 Cox JL, et al. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure. *J Thorac Cardiovasc Surg* 1991;101(4):569–83.
- 94 Rodriguez E, et al. Minimally invasive bi-atrial CryoMaze operation for atrial fibrillation. *Oper Tech Thorac Cardiovasc Surg* 2009;14(3):208–23.
- 95 Wolf RK, et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;130(3):797–802.
- 96 Edgerton JR, et al. Minimally invasive pulmonary vein isolation and partial autonomic denervation for surgical treatment of atrial fibrillation. *Ann Thorac Surg* 2008;86(1):35–8 discussion 39.
- 97 Edgerton JR, et al. Minimally invasive surgical ablation of atrial fibrillation: six-month results. *J Thorac Cardiovasc Surg* 2009;138(1):109–13 discussion 114.
- 98 Beyer E, Lee R, Lam BK. Point: Minimally invasive bipolar radiofrequency ablation of lone atrial fibrillation: early multicenter results. *J Thorac Cardiovasc Surg* 2009;137(3):521–6.
- 99 Kearney K, et al. A systematic review of surgical ablation versus catheter ablation for atrial fibrillation. *Ann Cardiothorac Surg* 2014;3(1):15–29.
- 100 Ad N, et al. Surgical ablation of atrial fibrillation trends and outcomes in North America. *J Thorac Cardiovasc Surg* 2012;144(5):1051–60.
- 101 Driessen AH, et al. Electrophysiologically guided thoracoscopic surgery for advanced atrial fibrillation: 5-year follow-up. *J Am Coll Cardiol* 2017;69(13):1753–4.
- 102 Khargi K, et al. Surgical treatment of atrial fibrillation: a systematic review. *Eur J Cardiothorac Surg* 2005;27(2):258–65.
- 103 Wazni OM, et al. Atrial arrhythmias after surgical maze: findings during catheter ablation. *J Am Coll Cardiol* 2006;48(7):1405–9.
- 104 Magnano AR, et al. Mechanisms of atrial tachyarrhythmias following surgical atrial fibrillation ablation. *J Cardiovasc Electrophysiol* 2006;17(4):366–73.
- 105 McFildery HT, et al. Proarrhythmic aspects of atrial fibrillation surgery: mechanisms of postoperative macroreentrant tachycardias. *Circulation* 2008;117(2):155–62.
- 106 McCarthy PM, et al. Where does atrial fibrillation surgery fail? Implications for increasing effectiveness of ablation. *J Thorac Cardiovasc Surg* 2010;139(4):860–7.
- 107 Zeng Y, et al. Recurrent atrial arrhythmia after minimally invasive pulmonary vein isolation for atrial fibrillation. *Ann Thorac Surg* 2010;90(2):510–5.
- 108 Lee R, et al. Surgical treatment for isolated atrial fibrillation: minimally invasive vs. classic cut and sew maze. *Innovations (Phila)* 2011;6(6):373–7.
- 109 Kuck KH, et al. Impact of complete versus incomplete circumferential lines around the pulmonary veins during catheter ablation of paroxysmal atrial fibrillation: results from the Gap-Atrial Fibrillation-German Atrial Fibrillation Competence Network I Trial. *Circ Arrhythm Electrophysiol* 2016;9(1):e003337.
- 110 Verma A, et al. Response of atrial fibrillation to pulmonary vein antrum isolation is directly related to resumption and delay of pulmonary vein conduction. *Circulation* 2005;112(5):627–35.
- 111 Macle L, et al. Adenosine-guided pulmonary vein isolation for the treatment of paroxysmal atrial fibrillation: an international, multicentre, randomised superiority trial. *Lancet* 2015;386(9994):672–9.
- 112 Cheema A, et al. Incidence and time course of early recovery of pulmonary vein conduction after catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2007;18(4):387–91.
- 113 Rajappan K, et al. Acute and chronic pulmonary vein reconnection after atrial fibrillation ablation: a prospective characterization of anatomical sites. *Pacing Clin Electrophysiol* 2008;31(12):1598–605.
- 114 Bansch D, et al. Circumferential pulmonary vein isolation: wait or stop early after initial successful pulmonary vein isolation? *Europace* 2013;15(2):183–8.
- 115 Nakamura K, et al. Optimal observation time after completion of circumferential pulmonary vein isolation for atrial fibrillation to prevent chronic pulmonary vein reconnections. *Int J Cardiol* 2013;168(6):5300–10.
- 116 Wang XH, et al. Early identification and treatment of PV reconnections: role of observation time and impact on clinical results of atrial fibrillation ablation. *Europace* 2007;9(7):481–6.
- 117 Sauer WH, et al. Atrioventricular nodal reentrant tachycardia in patients referred for atrial fibrillation ablation: response to ablation that incorporates slow-pathway modification. *Circulation* 2006;114(3):191–5.
- 118 Ninomiya Y, et al. Usefulness of the adenosine triphosphate with a sufficient observation period for detecting reconnection after pulmonary vein isolation. *Pacing Clin Electrophysiol* 2009;32(10):1307–12.
- 119 Yamane T, et al. Repeated provocation of time- and ATP-induced early pulmonary vein reconnections after pulmonary vein isolation: eliminating paroxysmal atrial fibrillation in a single procedure. *Circ Arrhythm Electrophysiol* 2011;4(5):601–8.
- 120 Kobori A, et al. Adenosine triphosphate-guided pulmonary vein isolation for atrial fibrillation: the UNmasking Dormant Electrical Reconnection by Adenosine TriPhosphate (UNDER-ATP) trial. *Eur Heart J* 2015;36(46):3276–87.
- 121 Pratola C, et al. Radiofrequency ablation of atrial fibrillation: is the persistence of all intraprocedural targets necessary for long-term maintenance of sinus rhythm? *Circulation* 2008;117(2):136–43.

- 122 Jiang RH, et al. Incidence of pulmonary vein conduction recovery in patients without clinical recurrence after ablation of paroxysmal atrial fibrillation: mechanistic implications. *Heart Rhythm* 2014;11(6):969–76.
- 123 Arentz T, et al. "Dormant" pulmonary vein conduction revealed by adenosine after ostial radiofrequency catheter ablation. *J Cardiovasc Electrophysiol* 2004;15(9):1041–7.
- 124 Tritto M, et al. Adenosine restores atrio-venous conduction after apparently successful ostial isolation of the pulmonary veins. *Eur Heart J* 2004;25(23):2155–63.
- 125 Datino T, et al. Mechanisms by which adenosine restores conduction in dormant canine pulmonary veins. *Circulation* 2010;121(8):963–72.
- 126 Dallaglio PD, et al. The role of adenosine in pulmonary vein isolation: a critical review. *Cardiol Res Pract* 2016;2016:8632509.
- 127 Kapa S, et al. Dose-dependent pulmonary vein reconnection in response to adenosine: relevance of atrioventricular block during infusion. *J Interv Card Electrophysiol* 2016;47(1):117–23.
- 128 Andrade JG, et al. Pulmonary vein isolation using "contact force" ablation: the effect on dormant conduction and long-term freedom from recurrent atrial fibrillation—a prospective study. *Heart Rhythm* 2014;11(11):1919–24.
- 129 Eitel C, et al. Circumferential pulmonary vein isolation and linear left atrial ablation as a single-catheter technique to achieve bidirectional conduction block: the pace-and-ablate approach. *Heart Rhythm* 2010;7(2):157–64.
- 130 Steven D, et al. Loss of pace capture on the ablation line: a new marker for complete radiofrequency lesions to achieve pulmonary vein isolation. *Heart Rhythm* 2010;7(3):323–30.
- 131 Andrade JG, et al. Pulmonary vein isolation using a pace-capture-guided versus an adenosine-guided approach: effect on dormant conduction and long-term freedom from recurrent atrial fibrillation—a prospective study. *Circ Arrhythm Electrophysiol* 2013;6(6):1103–8.
- 132 Steven D, et al. Benefit of pulmonary vein isolation guided by loss of pace capture on the ablation line: results from a prospective 2-center randomized trial. *J Am Coll Cardiol* 2013;62(1):44–50.
- 133 Schaeffer B, et al. Loss of pace capture on the ablation line during pulmonary vein isolation versus "dormant conduction": is adenosine expendable? *J Cardiovasc Electrophysiol* 2015;26(10):1075–80.
- 134 Gerstenfeld EP, et al. Utility of exit block for identifying electrical isolation of the pulmonary veins. *J Cardiovasc Electrophysiol* 2002;13(10):971–9.
- 135 Vijayaraman P, et al. Assessment of exit block following pulmonary vein isolation: far-field capture masquerading as entrance without exit block. *Heart Rhythm* 2012;9(10):1653–9.
- 136 Ip JE, et al. Method for differentiating left superior pulmonary vein exit conduction from pseudo-exit conduction. *Pacing Clin Electrophysiol* 2013;36(3):299–308.
- 137 Spector P. Principles of cardiac electric propagation and their implications for re-entrant arrhythmias. *Circ Arrhythm Electrophysiol* 2013;6(3):655–61.
- 138 Chen S, et al. Blocking the pulmonary vein to left atrium conduction in addition to the entrance block enhances clinical efficacy in atrial fibrillation ablation. *Pacing Clin Electrophysiol* 2012;35(5):524–31.
- 139 Kim JY, et al. Achievement of successful pulmonary vein isolation: methods of adenosine testing and incremental benefit of exit block. *J Interv Card Electrophysiol* 2016;46(3):315–24.
- 140 Perez FJ, et al. Long-term outcomes after catheter ablation of cavo-tricuspid isthmus dependent atrial flutter: a meta-analysis. *Circ Arrhythm Electrophysiol* 2009;2(4):393–401.
- 141 Patef NJ, et al. Contemporary utilization and safety outcomes of catheter ablation of atrial flutter in the United States: Analysis of 89,638 procedures. *Heart Rhythm* 2016;13(6):1317–25.
- 142 Wazni O, et al. Randomized study comparing combined pulmonary vein-left atrial junction disconnection and cavotricuspid isthmus ablation versus pulmonary vein-left atrial junction disconnection alone in patients presenting with typical atrial flutter and atrial fibrillation. *Circulation* 2003;108(20):2479–83.
- 143 Natale A, et al. Prospective randomized comparison of antiarrhythmic therapy versus first-line radiofrequency ablation in patients with atrial flutter. *J Am Coll Cardiol* 2000;35(7):1898–904.
- 144 Pappone C, et al. Prevention of iatrogenic atrial tachycardia after ablation of atrial fibrillation: a prospective randomized study comparing circumferential pulmonary vein ablation with a modified approach. *Circulation* 2004;110(19):3036–42.
- 145 Sawhney N, et al. Circumferential pulmonary vein ablation with additional linear ablation results in an increased incidence of left atrial flutter compared with segmental pulmonary vein isolation as an initial approach to ablation of paroxysmal atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010;3(3):243–8.
- 146 Chae S, et al. Atrial tachycardia after circumferential pulmonary vein ablation of atrial fibrillation: mechanistic insights, results of catheter ablation, and risk factors for recurrence. *J Am Coll Cardiol* 2007;50(18):1781–7.
- 147 Ouyang F, et al. Characterization of reentrant circuits in left atrial macro-reentrant tachycardia: critical isthmus block can prevent atrial tachycardia recurrence. *Circulation* 2002;105(16):1934–42.
- 148 Matsuo S, et al. Peri-mitral atrial flutter in patients with atrial fibrillation ablation. *Heart Rhythm* 2010;7(1):2–8.
- 149 Tzeis S, et al. The modified anterior line: an alternative linear lesion in peri-mitral flutter. *J Cardiovasc Electrophysiol* 2010;21(6):665–70.
- 150 Chen SA, Tai CT. Catheter ablation of atrial fibrillation originating from the non-pulmonary vein foci. *J Cardiovasc Electrophysiol* 2005;16(2):229–32.
- 151 Haissaguerre M, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339(10):659–66.
- 152 Lee SH, et al. Predictors of non-pulmonary vein ectopic beats initiating paroxysmal atrial fibrillation: implication for catheter ablation. *J Am Coll Cardiol* 2005;46(6):1054–9.
- 153 Hsieh MH, et al. Alterations of heart rate variability after radiofrequency catheter ablation of focal atrial fibrillation originating from pulmonary veins. *Circulation* 1999;100(22):2237–43.
- 154 Shah D, et al. Nonpulmonary vein foci: do they exist? *Pacing Clin Electrophysiol* 2003;26(7 Pt 2):1631–5.
- 155 Lin D, et al. Provocability of atrial fibrillation triggers during pulmonary vein isolation in patients with infrequent AF [abstract]. *Heart Rhythm* 2004;1(Suppl):S231.
- 156 Di Biase L, et al. Left atrial appendage: an underrecognized trigger site of atrial fibrillation. *Circulation* 2010;122(2):109–18.
- 157 Santangeli P, et al. Prevalence and distribution of focal triggers in persistent and long-standing persistent atrial fibrillation. *Heart Rhythm* 2016;13(2):374–82.
- 158 Lin WS, et al. Catheter ablation of paroxysmal atrial fibrillation initiated by non-pulmonary vein ectopy. *Circulation* 2003;107(25):3176–83.
- 159 Lee R, et al. Percutaneous alternative to the Maze procedure for the treatment of persistent or long-standing persistent atrial fibrillation (aMAZE trial): Rationale and design. *Am Heart J* 2015;170(6):1184–94.
- 160 Zhao Y, et al. Importance of non-pulmonary vein triggers ablation to achieve long-term freedom from paroxysmal atrial fibrillation in patients with low ejection fraction. *Heart Rhythm* 2016;13(1):141–9.
- 161 Dixit S, et al. Randomized ablation strategies for the treatment of persistent atrial fibrillation: RASTA study. *Circ Arrhythm Electrophysiol* 2012;5(2):287–94.
- 162 Neuzil P, et al. Electrical reconnection after pulmonary vein isolation is contingent on contact force during initial treatment: results from the EFFICAS I study. *Circ Arrhythm Electrophysiol* 2013;6(2):327–33.
- 163 Yokoyama K, et al. Novel contact force sensor incorporated in irrigated radiofrequency ablation catheter predicts lesion size and incidence of steam pop and thrombus. *Circ Arrhythm Electrophysiol* 2008;1(5):354–62.
- 164 Ikeda A, et al. Relationship between catheter contact force and radiofrequency lesion size and incidence of steam pop in the beating canine heart: electrogram amplitude, impedance, and electrode temperature are poor predictors of electrode-tissue contact force and lesion size. *Circ Arrhythm Electrophysiol* 2014;7(6):1174–80.
- 165 Nakagawa H, et al. Locations of high contact force during left atrial mapping in atrial fibrillation patients: electrogram amplitude and impedance are poor predictors of electrode-tissue contact force for ablation of atrial fibrillation. *Circ Arrhythm Electrophysiol* 2013;6(4):746–53.
- 166 Nakagawa H, et al. Prospective study to test the ability to create RF lesions at predicted depth and diameter using a new formula incorporating contact force, radiofrequency power and application time (force-power-time index) in the beating heart [abstract]. *Heart Rhythm* 2014;11(Suppl):S548.
- 167 Kumar S, et al. Predictive value of impedance changes for real-time contact force measurements during catheter ablation of atrial arrhythmias in humans. *Heart Rhythm* 2013;10(7):962–9.
- 168 Kumar S, et al. Prospective characterization of catheter-tissue contact force at different anatomic sites during atrial pulmonary vein isolation. *Circ Arrhythm Electrophysiol* 2012;5(6):1124–9.
- 169 Reddy VY, et al. The relationship between contact force and clinical outcome during radiofrequency catheter ablation of atrial fibrillation in the TOCCATA study. *Heart Rhythm* 2012;9(11):1789–95.
- 170 Haidar S, et al. Contact force sensing technology identifies sites of inadequate contact and reduces acute pulmonary vein reconnection: a prospective case control study. *Int J Cardiol* 2013;168(2):1160–6.
- 171 Perna F, et al. Assessment of catheter tip contact force resulting in cardiac perforation in swine atria using force sensing technology. *Circ Arrhythm Electrophysiol* 2011;4(2):218–24.
- 172 Kimura M, et al. Comparison of lesion formation between contact force-guided and non-guided circumferential pulmonary vein isolation: a prospective, randomized study. *Heart Rhythm* 2014;11(6):984–91.
- 173 Sohns C, et al. Quantitative magnetic resonance imaging analysis of the relationship between contact force and left atrial scar formation after catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2014;25(2):138–45.
- 174 Martinek M, et al. Clinical impact of an open-irrigated radiofrequency catheter with direct force measurement on atrial fibrillation ablation. *Pacing Clin Electrophysiol* 2012;35(11):1312–8.
- 175 Marjion E, et al. Real-time contact force sensing for pulmonary vein isolation in the setting of paroxysmal atrial fibrillation: procedural and 1-year results. *J Cardiovasc Electrophysiol* 2014;25(2):130–7.
- 176 Sigmund E, et al. Optimizing radiofrequency ablation of paroxysmal and persistent atrial fibrillation by direct catheter force measurement—a case-matched comparison in 193 patients. *Pacing Clin Electrophysiol* 2015;38(2):201–8.
- 177 Ullah W, et al. Randomized trial comparing pulmonary vein isolation using the SmartTouch catheter with or without real-time contact force data. *Heart Rhythm* 2016;13(9):1761–7.
- 178 Wakili R, et al. Impact of real-time contact force and impedance measurement in pulmonary vein isolation procedures for treatment of atrial fibrillation. *Clin Res Cardiol* 2014;103(2):97–106.

- 179 Kumagai K, et al. A new approach for complete isolation of the posterior left atrium including pulmonary veins for atrial fibrillation. *J Cardiovasc Electrophysiol* 2007;18(10):1047–52.
- 180 Yamaguchi Y, et al. Long-term effects of box isolation on sympathovagal balance in atrial fibrillation. *Circ J* 2010;74(6):1096–103.
- 181 Kumagai K. Catheter ablation of atrial fibrillation. State of the Art. *Circ J* 2011;75(10):2305–11.
- 182 Kim JS, et al. Does isolation of the left atrial posterior wall improve clinical outcomes after radiofrequency catheter ablation for persistent atrial fibrillation? A prospective randomized clinical trial. *Int J Cardiol* 2015;181:277–83.
- 183 He X, et al. Left atrial posterior wall isolation reduces the recurrence of atrial fibrillation: a meta-analysis. *J Interv Card Electrophysiol* 2016;46(3):267–74.
- 184 Di Biase L, et al. Left atrial appendage isolation in patients with long-standing persistent AF undergoing catheter ablation: BELIEF trial. *J Am Coll Cardiol* 2016;68(18):1929–40.
- 185 Di Biase L, et al. Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial. *Circulation* 2016;133(17):1637–44.
- 186 Morillo CA, et al. Chronic rapid atrial pacing. Structural, functional, and electrophysiological characteristics of a new model of sustained atrial fibrillation. *Circulation* 1995;91(5):1588–95.
- 187 Harada A, et al. Atrial activation during chronic atrial fibrillation in patients with isolated mitral valve disease. *Ann Thorac Surg* 1996;61(1):104–11 discussion 111–112.
- 188 Gray RA, Pertsov AM, Jalife J. Spatial and temporal organization during cardiac fibrillation. *Nature* 1998;392(6671):75–8.
- 189 Berenfeld O, et al. Spatially distributed dominant excitation frequencies reveal hidden organization in atrial fibrillation in the Langendorff-perfused sheep heart. *J Cardiovasc Electrophysiol* 2000;11(8):869–79.
- 190 Mansour M, et al. Left-to-right gradient of atrial frequencies during acute atrial fibrillation in the isolated sheep heart. *Circulation* 2001;103(21):2631–6.
- 191 Lazar S, et al. Presence of left-to-right atrial frequency gradient in paroxysmal but not persistent atrial fibrillation in humans. *Circulation* 2004;110(20):3181–6.
- 192 Atenza F, et al. Real-time dominant frequency mapping and ablation of dominant frequency sites in atrial fibrillation with left-to-right frequency gradients predicts long-term maintenance of sinus rhythm. *Heart Rhythm* 2009;6(1):33–40.
- 193 Atenza F, et al. Comparison of radiofrequency catheter ablation of drivers and circumferential pulmonary vein isolation in atrial fibrillation: a noninferiority randomized multicenter RADAR-AF trial. *J Am Coll Cardiol* 2014;64(23):2455–67.
- 194 Vogler J, et al. Pulmonary vein isolation versus defragmentation: the CHASE-AF clinical trial. *J Am Coll Cardiol* 2015;66(24):2743–52.
- 195 Haissaguerre M, et al. Catheter ablation of long-lasting persistent atrial fibrillation: clinical outcome and mechanisms of subsequent arrhythmias. *J Cardiovasc Electrophysiol* 2005;16(11):1138–47.
- 196 Nademanee K, et al. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. *J Am Coll Cardiol* 2004;43(11):2044–53.
- 197 O'Neill MD, et al. Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint. *Eur Heart J* 2009;30(9):1105–12.
- 198 Lo LW, et al. Predicting factors for atrial fibrillation acute termination during catheter ablation procedures: implications for catheter ablation strategy and long-term outcome. *Heart Rhythm* 2009;6(3):311–8.
- 199 Zhang Z, et al. Linear ablation following pulmonary vein isolation in patients with atrial fibrillation: a meta-analysis. *Pacing Clin Electrophysiol* 2016;39(6):623–30.
- 200 Kim TH, et al. Linear ablation in addition to circumferential pulmonary vein isolation (Dallas lesion set) does not improve clinical outcome in patients with paroxysmal atrial fibrillation: a prospective randomized study. *Europace* 2015;17(3):388–95.
- 201 Wynn GJ, et al. Batrial linear ablation in sustained nonpermanent AF: results of the substrate modification with ablation and antiarrhythmic drugs in nonpermanent atrial fibrillation (SMAN-PAF) trial. *Heart Rhythm* 2016;13(2):399–406.
- 202 Kottkamp H, et al. Box Isolation of Fibrotic Areas (BIFA): a patient-tailored substrate modification approach for ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2016;27(1):22–30.
- 203 Kottkamp H, Bender R, Berg J. Catheter ablation of atrial fibrillation: how to modify the substrate? *J Am Coll Cardiol* 2015;65(2):196–206.
- 204 Rolf S, et al. Tailored atrial substrate modification based on low-voltage areas in catheter ablation of atrial fibrillation. *Circ Arrhythm Electrophysiol* 2014;7(5):825–33.
- 205 Bai R, et al. Proven isolation of the pulmonary vein antrum with or without left atrial posterior wall isolation in patients with persistent atrial fibrillation. *Heart Rhythm* 2016;13(1):132–40.
- 206 Cutler MJ, et al. Impact of voltage mapping to guide whether to perform ablation of the posterior wall in patients with persistent atrial fibrillation. *J Cardiovasc Electrophysiol* 2016;27(1):13–21.
- 207 Yang G, et al. Catheter ablation of nonparoxysmal atrial fibrillation using electrophysiologically guided substrate modification during sinus rhythm after pulmonary vein isolation. *Circ Arrhythm Electrophysiol* 2016;9(2):e003382.
- 208 Verma A, et al. Pre-existent left atrial scarring in patients undergoing pulmonary vein antrum isolation: an independent predictor of procedural failure. *J Am Coll Cardiol* 2005;45(2):285–92.
- 209 Kapa S, et al. Contact electroanatomic mapping derived voltage criteria for characterizing left atrial scar in patients undergoing ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2014;25(10):1044–52.
- 210 Oakes RS, et al. Detection and quantification of left atrial structural remodeling with delayed-enhancement magnetic resonance imaging in patients with atrial fibrillation. *Circulation* 2009;119(13):1758–67.
- 211 McGann C, et al. Atrial fibrillation ablation outcome is predicted by left atrial remodeling on MRI. *Circ Arrhythm Electrophysiol* 2014;7(1):23–30.
- 212 Dagues M, et al. Current ablation techniques for persistent atrial fibrillation: results of the European Heart Rhythm Association Survey. *Europace* 2015;17(10):1596–600.
- 213 Nademanee K, et al. Clinical outcomes of catheter substrate ablation for high-risk patients with atrial fibrillation. *J Am Coll Cardiol* 2008;51(8):843–9.
- 214 Haissaguerre M, et al. Localized sources maintaining atrial fibrillation organized by prior ablation. *Circulation* 2006;113(5):616–25.
- 215 Haissaguerre M, et al. Catheter ablation of long-lasting persistent atrial fibrillation: critical structures for termination. *J Cardiovasc Electrophysiol* 2005;16(11):1125–37.
- 216 Takahashi Y, et al. Characterization of electrograms associated with termination of chronic atrial fibrillation by catheter ablation. *J Am Coll Cardiol* 2008;51(10):1003–10.
- 217 Singh SM, et al. Intraprocedural use of ibutilide to organize and guide ablation of complex fractionated atrial electrograms: preliminary assessment of a modified step-wise approach to ablation of persistent atrial fibrillation. *J Cardiovasc Electrophysiol* 2010;21(6):608–16.
- 218 Narayan SM, et al. Classifying fractionated electrograms in human atrial fibrillation using monophasic action potentials and activation mapping: evidence for localized drivers, rate acceleration, and nonlocal signal etiologies. *Heart Rhythm* 2011;8(2):244–53.
- 219 Verma A, et al. Selective CFAE targeting for atrial fibrillation study (SELECT AF): clinical rationale, design, and implementation. *J Cardiovasc Electrophysiol* 2011;22(5):541–7.
- 220 Quintanilla JG, et al. Mechanistic approaches to detect, target, and ablate the drivers of atrial fibrillation. *Circ Arrhythm Electrophysiol* 2016;9(1):e002481.
- 221 Hansen BJ, et al. Atrial fibrillation driven by micro-anatomic intramural re-entry revealed by simultaneous sub-epicardial and sub-endocardial optical mapping in explanted human hearts. *Eur Heart J* 2015;36(35):2390–401.
- 222 Cuculich PS, et al. Noninvasive characterization of epicardial activation in humans with diverse atrial fibrillation patterns. *Circulation* 2010;122(5):1364–72.
- 223 Haissaguerre M, et al. Driver domains in persistent atrial fibrillation. *Circulation* 2014;130(7):530–8.
- 224 Narayan SM, et al. Ablation of rotor and focal sources reduces late recurrence of atrial fibrillation compared with trigger ablation alone: extended follow-up of the CONFIRM trial (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation). *J Am Coll Cardiol* 2014;63(17):1761–8.
- 225 Lin YJ, et al. Prevalence, characteristics, mapping, and catheter ablation of potential rotors in nonparoxysmal atrial fibrillation. *Circ Arrhythm Electrophysiol* 2013;6(5):851–8.
- 226 Lin YJ, et al. Benefits of atrial substrate modification guided by electrogram similarity and phase mapping techniques to eliminate rotors and focal sources versus conventional defragmentation in persistent atrial fibrillation. *JACC: Clinical Electrophysiology* 2016;2(6):667–78.
- 227 Miller JM, et al. Initial independent outcomes from focal impulse and rotor modulation ablation for atrial fibrillation: multicenter FIRM registry. *J Cardiovasc Electrophysiol* 2014;25(9):921–9.
- 228 Lin YJ, et al. Electrophysiological characteristics and catheter ablation in patients with paroxysmal right atrial fibrillation. *Circulation* 2005;112(12):1692–700.
- 229 Narayan SM, et al. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) trial. *J Am Coll Cardiol* 2012;60(7):628–36.
- 230 Rappel WJ, Narayan SM. Theoretical considerations for mapping activation in human cardiac fibrillation. *Chaos* 2013;23(2):023113.
- 231 Gianni C, et al. Acute and early outcomes of focal impulse and rotor modulation (FIRM)-guided rotors-only ablation in patients with nonparoxysmal atrial fibrillation. *Heart Rhythm* 2016;13(4):830–5.
- 232 Narayan SM, Zaman JA. Mechanistically based mapping of human cardiac fibrillation. *J Physiol* 2016;594(9):2399–415.
- 233 Sommer P, et al. Successful repeat catheter ablation of recurrent long-standing persistent atrial fibrillation with rotor elimination as the procedural endpoint: a case series. *J Cardiovasc Electrophysiol* 2016;27(3):274–80.
- 234 Buch E, et al. Long-term clinical outcomes of focal impulse and rotor modulation for treatment of atrial fibrillation: A multicenter experience. *Heart Rhythm* 2016;13(3):636–41.
- 235 Benharash P, et al. Quantitative analysis of localized sources identified by focal impulse and rotor modulation mapping in atrial fibrillation. *Circ Arrhythm Electrophysiol* 2015;8(3):554–61.
- 236 Ramanathan C, et al. Noninvasive electrocardiographic imaging for cardiac electrophysiology and arrhythmia. *Nat Med* 2004;10(4):422–8.

- 237 Lim HS, et al. Noninvasive mapping to guide atrial fibrillation ablation. *Card Electrophysiol Clin* 2015;7(1):89–98.
- 238 Yamashita S, et al. Body surface mapping to guide atrial fibrillation ablation. *Arrhythm Electrophysiol Rev* 2015;4(3):172–6.
- 239 Guillem MS, et al. Noninvasive mapping of human atrial fibrillation. *J Cardiovasc Electrophysiol* 2009;20(5):507–13.
- 240 Guillem MS, et al. Noninvasive localization of maximal frequency sites of atrial fibrillation by body surface potential mapping. *Circ Arrhythm Electrophysiol* 2013;6(2):294–301.
- 241 Rodrigo M, et al. Body surface localization of left and right atrial high-frequency rotors in atrial fibrillation patients: a clinical-computational study. *Heart Rhythm* 2014;11(9):1584–91.
- 242 Armour JA, et al. Gross and microscopic anatomy of the human intrinsic cardiac nervous system. *Anat Rec* 1997;247(2):289–98.
- 243 Po SS, Nakagawa H, Jackman WM. Localization of left atrial ganglionated plexi in patients with atrial fibrillation. *J Cardiovasc Electrophysiol* 2009;20(10):1186–9.
- 244 Patterson E, et al. Triggered firing in pulmonary veins initiated by in vitro autonomic nerve stimulation. *Heart Rhythm* 2005;2(6):624–31.
- 245 Choi EK, et al. Intrinsic cardiac nerve activity and paroxysmal atrial tachyarrhythmia in ambulatory dogs. *Circulation* 2010;121(24):2615–23.
- 246 Katriotis DG, et al. Autonomic denervation added to pulmonary vein isolation for paroxysmal atrial fibrillation: a randomized clinical trial. *J Am Coll Cardiol* 2013;62(24):2318–25.
- 247 Nakagawa H, et al. Pathophysiological basis of autonomic ganglionated plexus ablation in patients with atrial fibrillation. *Heart Rhythm* 2009;6(12 Suppl):S26–34.
- 248 Bettoni M, Zimmermann M. Autonomic tone variations before the onset of paroxysmal atrial fibrillation. *Circulation* 2002;105(23):2753–9.
- 249 Pauza DH, et al. Morphology, distribution, and variability of the epicardial neural ganglionated subplexuses in the human heart. *Anat Rec* 2000;259(4):353–82.
- 250 Scherlag BJ, et al. Electrical stimulation to identify neural elements on the heart: their role in atrial fibrillation. *J Interv Card Electrophysiol* 2005;13(Suppl 1):37–42.
- 251 Patterson E, et al. Sodium-calcium exchange initiated by the Ca²⁺ transient: an arrhythmia trigger within pulmonary veins. *J Am Coll Cardiol* 2006;47(6):1196–206.
- 252 Lemola K, et al. Pulmonary vein region ablation in experimental vagal atrial fibrillation: role of pulmonary veins versus autonomic ganglia. *Circulation* 2008;117(4):470–7.
- 253 Nishida K, et al. The role of pulmonary veins vs. autonomic ganglia in different experimental substrates of canine atrial fibrillation. *Cardiovasc Res* 2011;89(4):825–33.
- 254 Nishida K, et al. Atrial fibrillation ablation: translating basic mechanistic insights to the patient. *J Am Coll Cardiol* 2014;64:823–31.
- 255 Stavrakis S, et al. The role of the autonomic ganglia in atrial fibrillation. *JACC Clin Electrophysiol* 2015;1(1–2):1–13.
- 256 Pokushalov E, et al. Left atrial ablation at the anatomic areas of ganglionated plexi for paroxysmal atrial fibrillation. *Pacing Clin Electrophysiol* 2010;33(10):1231–8.
- 257 Pokushalov E, et al. Ganglionated plexi ablation for long-standing persistent atrial fibrillation. *Europace* 2010;12(3):342–6.
- 258 Pokushalov E, et al. Catheter versus surgical ablation of atrial fibrillation after a failed initial pulmonary vein isolation procedure: a randomized controlled trial. *J Cardiovasc Electrophysiol* 2013;24(12):1338–43.
- 259 Pokushalov E, et al. Ganglionated plexus ablation vs linear ablation in patients undergoing pulmonary vein isolation for persistent/long-standing persistent atrial fibrillation: a randomized comparison. *Heart Rhythm* 2013;10(9):1280–6.
- 260 Lloyd-Jones DM, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation* 2004;110(9):1042–6.
- 261 Mahajan R, et al. Electrophysiological, electroanatomical, and structural remodeling of the atria as consequences of sustained obesity. *J Am Coll Cardiol* 2015;66(1):1–11.
- 262 Wokhlu A, et al. Long-term outcome of atrial fibrillation ablation: impact and predictors of very late recurrence. *J Cardiovasc Electrophysiol* 2010;21(10):1071–8.
- 263 Dublin S, et al. Risk of new-onset atrial fibrillation in relation to body mass index. *Arch Intern Med* 2006;166(21):2322–8.
- 264 Gami AS, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. *J Am Coll Cardiol* 2007;49(5):565–71.
- 265 Tedrow UB, et al. The long- and short-term impact of elevated body mass index on the risk of new atrial fibrillation the WHS (Women's Health Study). *J Am Coll Cardiol* 2010;55(21):2319–27.
- 266 Huxley RR, et al. Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: the Atherosclerosis Risk in Communities (ARIC) study. *Circulation* 2011;123(14):1501–8.
- 267 Munger TM, et al. Electrophysiological and hemodynamic characteristics associated with obesity in patients with atrial fibrillation. *J Am Coll Cardiol* 2012;60(9):851–60.
- 268 Abed HS, et al. Obesity results in progressive atrial structural and electrical remodeling: implications for atrial fibrillation. *Heart Rhythm* 2013;10(1):90–100.
- 269 Richter B, et al. Is inducibility of atrial fibrillation after radio frequency ablation really a relevant prognostic factor? *Eur Heart J* 2006;27(21):2553–9.
- 270 Jongnarangsin K, et al. Body mass index, obstructive sleep apnea, and outcomes of catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2008;19(7):668–72.
- 271 Shah AN, et al. Long-term outcome following successful pulmonary vein isolation: pattern and prediction of very late recurrence. *J Cardiovasc Electrophysiol* 2008;19(7):661–7.
- 272 Chang SL, et al. Comparison of outcome in catheter ablation of atrial fibrillation in patients with versus without the metabolic syndrome. *Am J Cardiol* 2009;103(1):67–72.
- 273 Letsas KP, et al. Pre-ablative predictors of atrial fibrillation recurrence following pulmonary vein isolation: the potential role of inflammation. *Europace* 2009;11(2):158–63.
- 274 Tang RB, et al. Metabolic syndrome and risk of recurrence of atrial fibrillation after catheter ablation. *Circ J* 2009;73(3):438–43.
- 275 Jin Hwang H, et al. Atrial electroanatomical remodeling as a determinant of different outcomes between two current ablation strategies: circumferential pulmonary vein isolation vs pulmonary vein isolation. *Clin Cardiol* 2010;33(3):E69–74.
- 276 Patel D, et al. Outcomes and complications of catheter ablation for atrial fibrillation in females. *Heart Rhythm* 2010;7(2):167–72.
- 277 Patel D, et al. Safety and efficacy of pulmonary vein antral isolation in patients with obstructive sleep apnea: the impact of continuous positive airway pressure. *Circ Arrhythm Electrophysiol* 2010;3(5):445–51.
- 278 Patel D, et al. The impact of statins and rexin-angiotensin-aldosterone system blockers on pulmonary vein antrum isolation outcomes in post-menopausal females. *Europace* 2010;12(3):322–30.
- 279 Chao TF, et al. Associations between renal function, atrial substrate properties and outcome of catheter ablation in patients with paroxysmal atrial fibrillation. *Circ J* 2011;75(10):2326–32.
- 280 Winkle RA, et al. Relation of early termination of persistent atrial fibrillation by cardioversion or drugs to ablation outcomes. *Am J Cardiol* 2011;108(3):374–9.
- 281 Wong CX, et al. Pericardial fat is associated with atrial fibrillation severity and ablation outcome. *J Am Coll Cardiol* 2011;57(17):1745–51.
- 282 Kang JH, et al. Prediction of long-term outcomes of catheter ablation of persistent atrial fibrillation by parameters of preablation DC cardioversion. *J Cardiovasc Electrophysiol* 2012;23(11):1165–70.
- 283 Mohanty S, et al. Impact of metabolic syndrome on procedural outcomes in patients with atrial fibrillation undergoing catheter ablation. *J Am Coll Cardiol* 2012;59(14):1295–301.
- 284 Ejima K, et al. Impact of diastolic dysfunction on the outcome of catheter ablation in patients with atrial fibrillation. *Int J Cardiol* 2013;164(1):88–93.
- 285 Letsas KP, et al. The impact of body mass index on the efficacy and safety of catheter ablation of atrial fibrillation. *Int J Cardiol* 2013;164(1):94–8.
- 286 Wong CX, et al. Obesity and the risk of incident, post-operative, and post-ablation atrial fibrillation: a meta-analysis of 626,603 individuals in 51 studies. *JACC: Clinical Electrophysiology* 2015;1(3):139–52.
- 287 Alonso A, et al. Effect of an intensive lifestyle intervention on atrial fibrillation risk in individuals with type 2 diabetes: the Look AHEAD randomized trial. *Am Heart J* 2015;170(4):770–77.e5.
- 288 Pathak RK, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. *J Am Coll Cardiol* 2014;64(21):2222–31.
- 289 Bitter T, et al. Sleep-disordered breathing and cardiac arrhythmias. *Can J Cardiol* 2015;31(7):928–34.
- 290 Fletcher EC. Effect of episodic hypoxia on sympathetic activity and blood pressure. *Respir Physiol* 2000;119(2–3):189–97.
- 291 Kraicz H, et al. Increased vasoconstrictor sensitivity in obstructive sleep apnea. *J Appl Physiol* 1985;89(2):493–8.
- 292 Ghias M, et al. The role of ganglionated plexi in apnea-related atrial fibrillation. *J Am Coll Cardiol* 2009;54(22):2075–83.
- 293 Linz D, et al. Negative tracheal pressure during obstructive respiratory events promotes atrial fibrillation by vagal activation. *Heart Rhythm* 2011;8(9):1436–43.
- 294 Linz D, et al. Renal sympathetic denervation suppresses postapneic blood pressure rises and atrial fibrillation in a model for sleep apnea. *Hypertension* 2012;60(1):172–8.
- 295 Linz D, et al. Effect of renal denervation on neurohumoral activation triggering atrial fibrillation in obstructive sleep apnea. *Hypertension* 2013;62(4):767–74.
- 296 Iwasaki YK, et al. Determinants of atrial fibrillation in an animal model of obesity and acute obstructive sleep apnea. *Heart Rhythm* 2012;9(9):1409–416.e1.
- 297 Iwasaki YK, et al. Atrial fibrillation promotion with long-term repetitive obstructive sleep apnea in a rat model. *J Am Coll Cardiol* 2014;64(19):2013–23.
- 298 Dimitri H, et al. Atrial remodeling in obstructive sleep apnea: implications for atrial fibrillation. *Heart Rhythm* 2012;9(3):321–7.
- 299 Stevenson IH, et al. Atrial electrophysiology is altered by acute hypercapnia but not hypoxemia: implications for promotion of atrial fibrillation in pulmonary disease and sleep apnea. *Heart Rhythm* 2010;7(9):1263–70.
- 300 Holmqvist F, et al. Impact of obstructive sleep apnea and continuous positive airway pressure therapy on outcomes in patients with atrial fibrillation—Results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *Am Heart J* 2015;169(5):647–654.e2.
- 301 Kwon Y, et al. Association of sleep characteristics with atrial fibrillation: the Multi-Ethnic Study of Atherosclerosis. *Thorax* 2015;70(9):873–9.

- 302 Kanagala R, et al. Obstructive sleep apnea and the recurrence of atrial fibrillation. *Circulation* 2003;107(20):2589–94.
- 303 Fein AS, et al. Treatment of obstructive sleep apnea reduces the risk of atrial fibrillation recurrence after catheter ablation. *J Am Coll Cardiol* 2013;62(4):300–5.
- 304 Matiello M, et al. Low efficacy of atrial fibrillation ablation in severe obstructive sleep apnoea patients. *Europace* 2010;12(8):1084–9.
- 305 Naruse Y, et al. Concomitant obstructive sleep apnea increases the recurrence of atrial fibrillation following radiofrequency catheter ablation of atrial fibrillation: clinical impact of continuous positive airway pressure therapy. *Heart Rhythm* 2013;10(3):331–7.
- 306 Neilan TG, et al. Effect of sleep apnea and continuous positive airway pressure on cardiac structure and recurrence of atrial fibrillation. *J Am Heart Assoc* 2013;2(6):e000421.
- 307 Li L, et al. Efficacy of catheter ablation of atrial fibrillation in patients with obstructive sleep apnoea with and without continuous positive airway pressure treatment: a meta-analysis of observational studies. *Europace* 2014;16(9):1309–14.
- 308 Raitt MH, et al. Reversal of electrical remodeling after cardioversion of persistent atrial fibrillation. *J Cardiovasc Electrophysiol* 2004;15(5):507–12.
- 309 Chalfoun N, et al. Reverse electrical remodeling of the atria post cardioversion in patients who remain in sinus rhythm assessed by signal averaging of the P-wave. *Pacing Clin Electrophysiol* 2007;30(4):502–9.
- 310 Igarashi M, et al. Effect of restoration of sinus rhythm by extensive antiarrhythmic drugs in predicting results of catheter ablation of persistent atrial fibrillation. *Am J Cardiol* 2010;106(1):62–8.
- 311 Rivard L, et al. Improved outcome following restoration of sinus rhythm prior to catheter ablation of persistent atrial fibrillation: a comparative multicenter study. *Heart Rhythm* 2012;9(7):1025–30.
- 312 Mohanty S, et al. Effect of periprocedural amiodarone on procedure outcome in patients with long-standing persistent atrial fibrillation undergoing extended pulmonary vein antrum isolation: results from a randomized study (SPECULATE). *Heart Rhythm* 2015;12(3):477–83.
- 313 Robbins JM, et al. Pulmonary vein stenosis after catheter ablation of atrial fibrillation. *Circulation* 1998;98(17):1769–75.
- 314 Ernst S, et al. Total pulmonary vein occlusion as a consequence of catheter ablation for atrial fibrillation mimicking primary lung disease. *J Cardiovasc Electrophysiol* 2003;14(4):366–70.
- 315 Mansour M, et al. Assessment of pulmonary vein anatomic variability by magnetic resonance imaging: implications for catheter ablation techniques for atrial fibrillation. *J Cardiovasc Electrophysiol* 2004;15(4):387–93.
- 316 Holmes Jr DR, Monahan KH, Packer D. Pulmonary vein stenosis complicating ablation for atrial fibrillation: clinical spectrum and interventional considerations. *JACC Cardiovasc Interv* 2009;2(4):267–76.
- 317 Fender EA, Packer DL, Holmes Jr DR. Pulmonary vein stenosis after atrial fibrillation ablation. *EuroIntervention* 2016;12(Suppl X):X31–4.
- 318 Di Biase L, et al. Pulmonary vein total occlusion following catheter ablation for atrial fibrillation: clinical implications after long-term follow-up. *J Am Coll Cardiol* 2006;48(12):2493–9.
- 319 Prieto LR, et al. Comparison of stent versus balloon angioplasty for pulmonary vein stenosis complicating pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2008;19(7):673–8.
- 320 Packer DL, et al. Clinical presentation, investigation, and management of pulmonary vein stenosis complicating ablation for atrial fibrillation. *Circulation* 2005;111(5):546–54.
- 321 Taylor GW, et al. Pathological effects of extensive radiofrequency energy applications in the pulmonary veins in dogs. *Circulation* 2000;101(14):1736–42.
- 322 Arentz T, et al. Incidence of pulmonary vein stenosis 2 years after radiofrequency catheter ablation of refractory atrial fibrillation. *Eur Heart J* 2003;24(10):963–9.
- 323 Tse HF, et al. Pulmonary vein isolation using transvenous catheter cryoablation for treatment of atrial fibrillation without risk of pulmonary vein stenosis. *J Am Coll Cardiol* 2003;42(4):752–8.
- 324 Kasper L, et al. Hemoptysis and lung disease as a manifestation of pulmonary vein stenosis after cryoballoon catheter ablation for atrial fibrillation. *Pol Arch Med Wewn* 2016;126(1–2):94–6.
- 325 Dong J, et al. Incidence and predictors of pulmonary vein stenosis following catheter ablation of atrial fibrillation using the anatomic pulmonary vein ablation approach: results from paired magnetic resonance imaging. *J Cardiovasc Electrophysiol* 2005;16(8):845–52.
- 326 Hoyt RH, et al. Transvenous catheter cryoablation for treatment of atrial fibrillation: results of a feasibility study. *Pacing Clin Electrophysiol* 2005;28(Suppl 1):S78–82.
- 327 Saad EB, et al. Pulmonary vein stenosis after catheter ablation of atrial fibrillation: emergence of a new clinical syndrome. *Ann Intern Med* 2003;138(8):634–8.
- 328 Hilbert S, et al. Pulmonary vein collateral formation as a long-term result of post-interventional pulmonary vein stenosis. *Eur Heart J* 2016;37(31):2474.
- 329 Hilbert S, Sommer P, Bollmann A. Pulmonary vein dilatation in a case of total pulmonary vein occlusion: contemporary approach using a combination of 3D-mapping system and image integration. *Catheter Cardiovasc Interv* 2016;88(7):E227–32.
- 330 Fender EA, et al. Severe pulmonary vein stenosis resulting from ablation for atrial fibrillation: presentation, management, and clinical outcomes. *Circulation* 2016;134(23):1812–21.
- 331 De Potter TJ, et al. Drug-eluting stents for the treatment of pulmonary vein stenosis after atrial fibrillation ablation. *Europace* 2011;13(1):57–61.
- 332 Kanter KR, Kirshbom PM, Kogon BE. Surgical repair of pulmonary venous stenosis: a word of caution. *Ann Thorac Surg* 2014;98(5):1687–91 discussion 1691–1692.
- 333 Patel NS, et al. Successful surgical repair of iatrogenic pulmonary vein stenosis. *J Cardiovasc Electrophysiol* 2012;23(6):656–8.
- 334 Bharat A, et al. Lung transplant is a viable treatment option for patients with congenital and acquired pulmonary vein stenosis. *J Heart Lung Transplant* 2013;32(6):621–5.
- 335 Ponomaghi SP, et al. Catheter-based intervention for pulmonary vein stenosis due to fibrosing mediastinitis: the Mayo Clinic experience. *Int J Cardiol Heart Vasc* 2015;8:103–7.
- 336 Mohanty S, et al. Impact of alcohol intake on thromboembolic events following catheter ablation for atrial fibrillation. *J Am Coll Cardiol* 2014;63(12_5).
- 337 Di Biase L, et al. Esophageal capsule endoscopy after radiofrequency catheter ablation for atrial fibrillation: documented higher risk of luminal esophageal damage with general anesthesia as compared with conscious sedation. *Circ Arrhythm Electrophysiol* 2009;2(2):108–12.
- 338 Cappato R, et al. Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation* 2005;111(9):1100–5.
- 339 Pappone C, et al. Atrio-esophageal fistula as a complication of percutaneous transcatheter ablation of atrial fibrillation. *Circulation* 2004;109(22):2724–6.
- 340 Martinek M, et al. Identification of a high-risk population for esophageal injury during radiofrequency catheter ablation of atrial fibrillation: procedural and anatomical considerations. *Heart Rhythm* 2010;7(9):1224–30.
- 341 Singh SM, et al. Clinical outcomes after repair of left atrial esophageal fistulas occurring after atrial fibrillation ablation procedures. *Heart Rhythm* 2013;10(11):1591–7.
- 342 Bunch TJ, et al. Temporary esophageal stenting allows healing of esophageal perforations following atrial fibrillation ablation procedures. *J Cardiovasc Electrophysiol* 2006;17(4):435–9.
- 343 Cappato R, et al. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. *J Am Coll Cardiol* 2009;53(19):1798–803.
- 344 Tan C, Coffey A. Atrioesophageal fistula after surgical unipolar radiofrequency atrial ablation for atrial fibrillation. *Ann Thorac Surg* 2013;95(3):e61–2.
- 345 Mohanty S. Outcomes of atrio-esophageal fistula following catheter ablation of atrial fibrillation treated with surgical repair versus esophageal stenting. *J Cardiovasc Electrophysiol* 2014;25(9):E6.
- 346 Mohanty S, et al. Outcomes of atrioesophageal fistula following catheter ablation of atrial fibrillation treated with surgical repair versus esophageal stenting. *J Cardiovasc Electrophysiol* 2014;25(6):579–84.
- 347 Cappato R, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010;3(1):32–8.
- 348 Gillinov AM, Pettersson C, Rice TW. Esophageal injury during radiofrequency ablation for atrial fibrillation. *J Thorac Cardiovasc Surg* 2001;122(6):1239–40.
- 349 Mohr FW, et al. Curative treatment of atrial fibrillation with intraoperative radiofrequency ablation: short-term and midterm results. *J Thorac Cardiovasc Surg* 2002;123(5):919–27.
- 350 Doll N, et al. Esophageal perforation during left atrial radiofrequency ablation: is the risk too high? *J Thorac Cardiovasc Surg* 2003;125(4):836–42.
- 351 Sonmez B, et al. A fatal complication due to radiofrequency ablation for atrial fibrillation: atrio-esophageal fistula. *Ann Thorac Surg* 2003;76(1):281–3.
- 352 Scanavacca ML, et al. Left atrial-esophageal fistula following radiofrequency catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2004;15(8):960–2.
- 353 Borchert B, et al. Lethal atrioesophageal fistula after pulmonary vein isolation using high-intensity focused ultrasound (HIFU). *Heart Rhythm* 2008;5(1):145–8.
- 354 Chia KK, et al. A nationwide survey on the prevalence of atrioesophageal fistula after left atrial radiofrequency catheter ablation. *J Interv Card Electrophysiol* 2009;24(1):33–6.
- 355 Gilcrease GW, Stein JB. A delayed case of fatal atrioesophageal fistula following radiofrequency ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2010;21(6):708–11.
- 356 Stockigt F, et al. Atrioesophageal fistula after cryoballoon pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2012;23(11):1254–7.
- 357 Yousuf O, Calkins H. Sounding the warning on the potential for oesophageal injury resulting from use of the nMARQ for ablation of atrial fibrillation. *Europace* 2015;17(3):343–4.
- 358 Jackson PG, et al. The vagus plays a role in the anti-reflux barrier by controlling both the lower esophageal sphincter pressure and crural diaphragm activity. *J Am Coll Surg* 2005;201(3 Suppl):S11.
- 359 Nolkner G, et al. Esophageal acid levels after pulmonary vein isolation for atrial fibrillation. *Pacing Clin Electrophysiol* 2009;32(Suppl 1):S228–30.
- 360 Medeiros De Vasconcelos JT, et al. Atrial-oesophageal fistula following percutaneous radiofrequency catheter ablation of atrial fibrillation: the risk still persists. *Europace* 2017;19(2):250–8.
- 361 Rillig A, et al. Modified energy settings are mandatory to minimize oesophageal injury using the novel multipolar irrigated radiofrequency ablation catheter for pulmonary vein isolation. *Europace* 2015;17(3):396–402.
- 362 Chavez P, et al. Atrioesophageal fistula following ablation procedures for atrial fibrillation: systematic review of case reports. *Open Heart* 2015;2(1):e000257.

- 363 Mateos JC, et al. Simplified method for esophagus protection during radiofrequency catheter ablation of atrial fibrillation—prospective study of 704 cases. *Rev Bras Cir Cardiovasc* 2015;30(2):139–47.
- 364 Shim HB, et al. Successful management of atrio-esophageal fistula after cardiac radiofrequency catheter ablation. *Korean J Thorac Cardiovasc Surg* 2013;46(2):142–5.
- 365 Black-Maier E, et al. Risk of atrioesophageal fistula formation with contact-force sensing catheters. *Heart Rhythm* 2017 S1547–5271(17) 30452–30456.
- 366 Santangeli P, et al. Ablation of atrial fibrillation under therapeutic warfarin reduces periprocedural complications: evidence from a meta-analysis. *Circ Arrhythm Electrophysiol* 2012;5(2):302–11.
- 367 Di Biase L, et al. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. *Circulation* 2010;121(23):2550–6.
- 368 Wazni OM, et al. Atrial fibrillation ablation in patients with therapeutic international normalized ratio: comparison of strategies of anticoagulation management in the periprocedural period. *Circulation* 2007;116(22):2531–4.
- 369 Schmidt M, et al. Atrial fibrillation ablation in patients with therapeutic international normalized ratios. *Pacing Clin Electrophysiol* 2009;32(8):995–9.
- 370 Hakalahti A, et al. Catheter ablation of atrial fibrillation in patients with therapeutic oral anticoagulation treatment. *Europace* 2011;13(5):640–5.
- 371 Di Biase L, et al. Periprocedural stroke and bleeding complications in patients undergoing catheter ablation of atrial fibrillation with different anticoagulation management: results from the Role of Coumadin in Preventing Thromboembolism in Atrial Fibrillation (AF) Patients Undergoing Catheter Ablation (COMPARE) randomized trial. *Circulation* 2014;129(25):2638–44.
- 372 Hohnloser SH, Camm AJ. Safety and efficacy of dabigatran etexilate during catheter ablation of atrial fibrillation: a meta-analysis of the literature. *Europace* 2013;15(10):1407–11.
- 373 Calkins H, et al. RE-CIRCUIT study—randomized evaluation of Dabigatran etexilate compared to warfarin in pulmonary vein ablation: assessment of an uninterrupted periprocedural anticoagulation strategy. *Am J Cardiol* 2015;115(1):154–5.
- 374 Cappato R, et al. Uninterrupted rivaroxaban vs. uninterrupted vitamin K antagonists for catheter ablation in non-valvular atrial fibrillation. *Eur Heart J* 2015;36(28):1805–11.
- 375 Di Biase L, et al. Feasibility and safety of uninterrupted periprocedural apixaban administration in patients undergoing radiofrequency catheter ablation for atrial fibrillation: results from a multicenter study. *Heart Rhythm* 2015;12(6):1162–8.
- 376 Bassiouny M, et al. Use of dabigatran for periprocedural anticoagulation in patients undergoing catheter ablation for atrial fibrillation. *Circ Arrhythm Electrophysiol* 2013;6(3):460–6.
- 377 Bin Abdulhak AA, et al. Safety and efficacy of interrupted dabigatran for periprocedural anticoagulation in catheter ablation of atrial fibrillation: a systematic review and meta-analysis. *Europace* 2013;15(10):1412–20.
- 378 Providencia R, et al. Rivaroxaban and dabigatran in patients undergoing catheter ablation of atrial fibrillation. *Europace* 2014;16(8):1137–44.
- 379 Winkle RA, et al. Peri-procedural interrupted oral anticoagulation for atrial fibrillation ablation: comparison of aspirin, warfarin, dabigatran, and rivaroxaban. *Europace* 2014;16(10):1443–9.
- 380 Armbruster HL, et al. Safety of novel oral anticoagulants compared with uninterrupted warfarin for catheter ablation of atrial fibrillation. *Ann Pharmacother* 2015;49(3):278–84.
- 381 Ren JF, Marchlinski FE, Callans DJ. Left atrial thrombus associated with ablation for atrial fibrillation: identification with intracardiac echocardiography. *J Am Coll Cardiol* 2004;43(10):1861–7.
- 382 Saksena S, et al. A prospective comparison of cardiac imaging using intracardiac echocardiography with transesophageal echocardiography in patients with atrial fibrillation: the intracardiac echocardiography guided cardioversion helps interventional procedures study. *Circ Arrhythm Electrophysiol* 2010;3(6):571–7.
- 383 Baran J, et al. Intracardiac echocardiography for detection of thrombus in the left atrial appendage: comparison with transesophageal echocardiography in patients undergoing ablation for atrial fibrillation: the Action-Ice I Study. *Circ Arrhythm Electrophysiol* 2013;6(6):1074–81.
- 384 Ren JF, et al. Intracardiac echocardiographic diagnosis of thrombus formation in the left atrial appendage: a complementary role to transesophageal echocardiography. *Echocardiography* 2013;30(1):72–80.
- 385 Anter E, et al. Comparison of intracardiac echocardiography and transesophageal echocardiography for imaging of the right and left atrial appendages. *Heart Rhythm* 2014;11(11):1890–7.
- 386 Sriram CS, et al. Detection of left atrial thrombus by intracardiac echocardiography in patients undergoing ablation of atrial fibrillation. *J Interv Card Electrophysiol* 2015;43(3):227–36.
- 387 Maleki K, et al. Intracardiac ultrasound detection of thrombus on transseptal sheath: incidence, treatment, and prevention. *J Cardiovasc Electrophysiol* 2005;16(6):561–5.
- 388 Wazni OM, et al. Embolic events and char formation during pulmonary vein isolation in patients with atrial fibrillation: impact of different anticoagulation regimens and importance of intracardiac echo imaging. *J Cardiovasc Electrophysiol* 2005;16(6):576–81.
- 389 Shah D. Filamentous thrombi during left-sided sheath-assisted catheter ablations. *Europace* 2010;12(12):1657–8.
- 390 Ren JF, et al. Increased intensity of anticoagulation may reduce risk of thrombus during atrial fibrillation ablation procedures in patients with spontaneous echo contrast. *J Cardiovasc Electrophysiol* 2005;16(5):474–7.
- 391 Bruce CJ, et al. Early heparinization decreases the incidence of left atrial thrombi detected by intracardiac echocardiography during radiofrequency ablation for atrial fibrillation. *J Interv Card Electrophysiol* 2008;22(3):211–9.
- 392 Asbach S, et al. Early heparin administration reduces risk for left atrial thrombus formation during atrial fibrillation ablation procedures. *Cardiol Res Pract* 2011;2011:615087.
- 393 Briceno DF, et al. Clinical impact of heparin kinetics during catheter ablation of atrial fibrillation: meta-analysis and meta-regression. *J Cardiovasc Electrophysiol* 2016;27(6):683–93.
- 394 Chilukuri K, et al. Incidence and outcomes of protamine reactions in patients undergoing catheter ablation of atrial fibrillation. *J Interv Card Electrophysiol* 2009;25(3):175–81.
- 395 Thygesen K, et al. Universal definition of myocardial infarction. *J Am Coll Cardiol* 2007;50(22):2173–95.
- 396 Helps SC, et al. The effect of gas emboli on rabbit cerebral blood flow. *Stroke* 1990;21(1):94–9.
- 397 Krivonyak GS, Warren SG. Cerebral arterial air embolism treated by a vertical head-down maneuver. *Catheter Cardiovasc Interv* 2000;49(2):185–7.
- 398 Cauchemez B, et al. High-flow perfusion of sheaths for prevention of thromboembolic complications during complex catheter ablation in the LA. *J Cardiovasc Electrophysiol* 2004;15(3):276–83.
- 399 Kuwahara T, et al. Clinical characteristics of massive air embolism complicating left atrial ablation of atrial fibrillation: lessons from five cases. *Europace* 2012;14(2):204–8.
- 400 Franzen OW, et al. Mechanisms underlying air aspiration in patients undergoing left atrial catheterization. *Catheter Cardiovasc Interv* 2008;71(4):553–8.
- 401 Ryu KH, et al. Heparin reduces neurological impairment after cerebral arterial air embolism in the rabbit. *Stroke* 1996;27(2):303–9 discussion 310.
- 402 Gaita F, et al. Incidence of silent cerebral thromboembolic lesions after atrial fibrillation ablation may change according to technology used: comparison of irrigated radiofrequency, multipolar nonirrigated catheter and cryoballoon. *J Cardiovasc Electrophysiol* 2011;22(9):961–8.
- 403 Herrera Siklody C, et al. Incidence of asymptomatic intracranial embolic events after pulmonary vein isolation: comparison of different atrial fibrillation ablation technologies in a multicenter study. *J Am Coll Cardiol* 2011;58(7):681–8.
- 404 Verma A, et al. Evaluation and reduction of asymptomatic cerebral embolism in ablation of atrial fibrillation, but high prevalence of chronic silent infarction: results of the evaluation of reduction of asymptomatic cerebral embolism trial. *Circ Arrhythm Electrophysiol* 2013;6(5):835–42.
- 405 De Greef Y, et al. Low rate of asymptomatic cerebral embolism and improved procedural efficacy with the novel pulmonary vein ablation catheter GOLD: results of the PRECISION GOLD trial. *Europace* 2016;18(5):687–95.
- 406 Deneke T, et al. Silent cerebral events/lesions related to atrial fibrillation ablation: a clinical review. *J Cardiovasc Electrophysiol* 2015;26(4):455–63.
- 407 Merchant FM, Delurgio DB. Catheter ablation of atrial fibrillation and risk of asymptomatic cerebral embolism. *Pacing Clin Electrophysiol* 2014;37(3):389–97.
- 408 Lickfett L, et al. Cerebral diffusion-weighted magnetic resonance imaging: a tool to monitor the thrombogenicity of left atrial catheter ablation. *J Cardiovasc Electrophysiol* 2006;17(1):1–7.
- 409 Gaita F, et al. Radiofrequency catheter ablation of atrial fibrillation: a cause of silent thromboembolism? Magnetic resonance imaging assessment of cerebral thromboembolism in patients undergoing ablation of atrial fibrillation. *Circulation* 2010;122(17):1667–73.
- 410 Schrickel JW, et al. Incidence and predictors of silent cerebral embolism during pulmonary vein catheter ablation for atrial fibrillation. *Europace* 2010;12(1):52–7.
- 411 Deneke T, et al. Postablation asymptomatic cerebral lesions: long-term follow-up using magnetic resonance imaging. *Heart Rhythm* 2011;8(11):1705–11.
- 412 Sauren LD, et al. Transcranial measurement of cerebral microembolic signals during endocardial pulmonary vein isolation: comparison of three different ablation techniques. *J Cardiovasc Electrophysiol* 2009;20(10):1102–7.
- 413 Wleczorek M, et al. Investigation into causes of abnormal cerebral MRI findings following PVAC duty-cycled, phased RF ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2013;24(2):121–8.
- 414 Bendszus M, Stoll G. Silent cerebral ischaemia: hidden fingerprints of invasive medical procedures. *Lancet Neurol* 2006;5(4):364–72.
- 415 Kruis RW, Vlasveld PA, Van Dijk D. The (un)importance of cerebral microemboli. *Semin Cardiothorac Vasc Anesth* 2010;14(2):111–8.
- 416 Medi C, et al. Subtle post-procedural cognitive dysfunction after atrial fibrillation ablation. *J Am Coll Cardiol* 2013;62(6):531–9.
- 417 Ichiki H, et al. The incidence of asymptomatic cerebral microthromboembolism after atrial fibrillation ablation: comparison of warfarin and dabigatran. *Pacing Clin Electrophysiol* 2013;36(11):1328–35.
- 418 Nagy-Balo E, et al. Transcranial measurement of cerebral microembolic signals during pulmonary vein isolation: a comparison of two ablation techniques. *Circ Arrhythm Electrophysiol* 2013;6(3):473–80.
- 419 Vermeer SE, et al. Silent brain infarcts and the risk of dementia and cognitive decline. *N Engl J Med* 2003;348(13):1215–22.
- 420 Neven K, et al. Fatal end of a safety algorithm for pulmonary vein isolation with use of high-intensity focused ultrasound. *Circ Arrhythm Electrophysiol* 2010;3(3):260–5.

- 421 Ripley KL, et al. Time course of esophageal lesions after catheter ablation with cryothermal and radiofrequency ablation: implication for atrio-esophageal fistula formation after catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2007;18(6):642–6.
- 422 Ahmed H, et al. The esophageal effects of cryoenergy during cryoablation for atrial fibrillation. *Heart Rhythm* 2009;6(7):962–9.
- 423 Kawasaki R, et al. Atrioesophageal fistula complicating cryoballoon pulmonary vein isolation for paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 2014;25(7):787–92.
- 424 Lim HW, et al. Atrioesophageal fistula during cryoballoon ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2014;25(2):208–13.
- 425 Yokoyama K, et al. Canine model of esophageal injury and atrial-esophageal fistula after applications of forward-firing high-intensity focused ultrasound and side-firing unfocused ultrasound in the left atrium and inside the pulmonary vein. *Circ Arrhythm Electrophysiol* 2009;2(1):41–9.
- 426 Singh SM, et al. Esophageal injury and temperature monitoring during atrial fibrillation ablation. *Circ Arrhythm Electrophysiol* 2008;1(3):162–8.
- 427 Kuwahara T, et al. Safe and effective ablation of atrial fibrillation: importance of esophageal temperature monitoring to avoid periesophageal nerve injury as a complication of pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2009;20(1):1–6.
- 428 Contreras-Valdes FM, et al. Severity of esophageal injury predicts time to healing after radiofrequency catheter ablation for atrial fibrillation. *Heart Rhythm* 2011;8(12):1862–8.
- 429 Leite LR, et al. Luminal esophageal temperature monitoring with a deflectable esophageal temperature probe and intracardiac echocardiography may reduce esophageal injury during atrial fibrillation ablation procedures: results of a pilot study. *Circ Arrhythm Electrophysiol* 2011;4(2):149–56.
- 430 Tschabrunn CM, et al. Comparison between single- and multi-sensor esophageal temperature probes during atrial fibrillation ablation: thermodynamic characteristics. *Europace* 2015;17(6):891–7.
- 431 Deneke T, et al. Utility of esophageal temperature monitoring during pulmonary vein isolation for atrial fibrillation using duty-cycled phased radiofrequency ablation. *J Cardiovasc Electrophysiol* 2011;22(3):255–61.
- 432 Carroll BJ, et al. Multi-sensor esophageal temperature probe used during radiofrequency ablation for atrial fibrillation is associated with increased intraluminal temperature detection and increased risk of esophageal injury compared to single-sensor probe. *J Cardiovasc Electrophysiol* 2013;24(9):958–64.
- 433 Muller P, et al. Higher incidence of esophageal lesions after ablation of atrial fibrillation related to the use of esophageal temperature probes. *Heart Rhythm* 2015;12(7):1464–9.
- 434 Tsuchiya T, et al. Atrial fibrillation ablation with esophageal cooling with a cooled water-irrigated intraesophageal balloon: a pilot study. *J Cardiovasc Electrophysiol* 2007;18(2):145–50.
- 435 Arruda MS, et al. Feasibility and safety of using an esophageal protective system to eliminate esophageal thermal injury: implications on atrio-esophageal fistula following AF ablation. *J Cardiovasc Electrophysiol* 2009;20(11):1272–8.
- 436 Kuwahara T, et al. Esophageal cooling with ice water does not reduce the incidence of esophageal lesions complicating catheter ablation of atrial fibrillation: randomized controlled study. *Europace* 2014;16(6):834–9.
- 437 Kuwahara T, et al. Incidences of esophageal injury during esophageal temperature monitoring: a comparative study of a multi-thermocouple temperature probe and a deflectable temperature probe in atrial fibrillation ablation. *J Interv Card Electrophysiol* 2014;39(3):251–7.
- 438 Chugh A, et al. Mechanical displacement of the esophagus in patients undergoing left atrial ablation of atrial fibrillation. *Heart Rhythm* 2009;6(3):319–22.
- 439 Koruth JS, et al. Mechanical esophageal displacement during catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2012;23(2):147–54.
- 440 Zellerhoff S, Lenze F, Eckardt L. Prophylactic proton pump inhibition after atrial fibrillation ablation: is there any evidence? *Europace* 2011;13(9):1219–21.
- 441 Zellerhoff S, et al. Fatal course of esophageal stenting of an atrioesophageal fistula after atrial fibrillation ablation. *Heart Rhythm* 2011;8(4):624–6.
- 442 Khan M, et al. Medical treatments in the short term management of reflux oesophagitis. *Cochrane Database Syst Rev* 2007(2):CD003244.
- 443 Kabrilas PJ. Clinical practice. Gastroesophageal reflux disease. *N Engl J Med* 2008;359(16):1700–7.
- 444 Shaheen NJ, et al. Pantoprazole reduces the size of postbanding ulcers after variceal band ligation: a randomized, controlled trial. *Hepatology* 2005;41(3):588–94.
- 445 Halm U, et al. Thermal esophageal lesions after radiofrequency catheter ablation of left atrial arrhythmias. *Am J Gastroenterol* 2010;105(3):551–6.
- 446 Knopp H, et al. Incidental and ablation-induced findings during upper gastrointestinal endoscopy in patients after ablation of atrial fibrillation: a retrospective study of 425 patients. *Heart Rhythm* 2014;11(4):574–8.
- 447 Dagres N, et al. Rapid detection and successful treatment of esophageal perforation after radiofrequency ablation of atrial fibrillation: lessons from five cases. *J Cardiovasc Electrophysiol* 2006;17(11):1213–5.
- 448 Eitel C, et al. Successful nonsurgical treatment of esophagopericardial fistulas after atrial fibrillation catheter ablation: a case series. *Circ Arrhythm Electrophysiol* 2013;6(4):675–81.
- 449 Hazell W, et al. Atrio-oesophageal fistula: an emergent complication of radiofrequency ablation. *Emerg Med Australas* 2009;21(4):329–32.
- 450 Cazaver A, et al. Successful surgery for atrioesophageal fistula caused by transcatheter ablation of atrial fibrillation. *J Thorac Cardiovasc Surg* 2010;140(3):e43–5.
- 451 Podgaetz E, Deschamps C. Esophageal complications of catheter ablation for atrial fibrillation: a case report. *J Thorac Cardiovasc Surg* 2013;145(1):e9–13.
- 452 Queneherve L, et al. Endoscopic management of an esophagopericardial fistula after radiofrequency ablation for atrial fibrillation. *World J Gastroenterol* 2013;19(21):3352–3.
- 453 Gunes MF, et al. Ablating the posterior heart: cardioesophageal fistula complicating radiofrequency ablation in the coronary sinus. *J Cardiovasc Electrophysiol* 2015;26(12):1376–8.
- 454 Qadeer MA, et al. Endoscopic clips for closing esophageal perforations: case report and pooled analysis. *Gastrointest Endosc* 2007;66(3):605–11.
- 455 Ellis CR, et al. Successful treatment of esophageal perforation following atrial fibrillation ablation with a fully covered esophageal stent: prevention of atrio-esophageal fistula. *J Innov Cardiac Rhythm Management* 2012;3:874–8.
- 456 Markar SR, et al. Novel multimodality endoscopic closure of postoperative esophageal fistula. *Int J Surg Case Rep* 2012;3(11):577–9.
- 457 Andrade JG, et al. Efficacy and safety of cryoballoon ablation for atrial fibrillation: a systematic review of published studies. *Heart Rhythm* 2011;8(9):1444–51.
- 458 Deshmukh A, et al. In-hospital complications associated with catheter ablation of atrial fibrillation in the United States between 2000 and 2010: analysis of 93 801 procedures. *Circulation* 2013;128(19):2104–12.
- 459 Cappato R, et al. Delayed cardiac tamponade after radiofrequency catheter ablation of atrial fibrillation: a worldwide report. *J Am Coll Cardiol* 2011;58(25):2696–7.
- 460 Eick OJ, Gerritje B, Schumacher B. Popping phenomena in temperature-controlled radiofrequency ablation: when and why do they occur? *Pacing Clin Electrophysiol* 2000;23(2):253–8.
- 461 Fisher JD, et al. Internal transcatheter pericardiocentesis for acute tamponade. *Am J Cardiol* 2000;86(12):1388–9 A6.
- 462 Hsu LF, et al. Transcatheter pericardiocentesis: an emergency life-saving technique for cardiac tamponade. *J Cardiovasc Electrophysiol* 2003;14(9):1001–3.
- 463 Bunch TJ, et al. Outcomes after cardiac perforation during radiofrequency ablation of the atrium. *J Cardiovasc Electrophysiol* 2005;16(11):1172–9.
- 464 Hsu LF, et al. Incidence and prevention of cardiac tamponade complicating ablation for atrial fibrillation. *Pacing Clin Electrophysiol* 2005;28(Suppl 1):S106–9.
- 465 Michowitz Y, et al. Effects of sex on the incidence of cardiac tamponade after catheter ablation of atrial fibrillation: results from a worldwide survey in 34 943 atrial fibrillation ablation procedures. *Circ Arrhythm Electrophysiol* 2014;7(2):274–80.
- 466 Tsang TS, et al. Consecutive 1127 therapeutic echocardiographically guided pericardiocenteses: clinical profile, practice patterns, and outcomes spanning 21 years. *Mayo Clin Proc* 2002;77(5):429–36.
- 467 O'Neill MD, et al. Two techniques to avoid surgery for cardiac tamponade occurring during catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2008;19(3):323–5.
- 468 Takahashi Y, et al. Acute occlusion of the left circumflex coronary artery during mitral isthmus linear ablation. *J Cardiovasc Electrophysiol* 2005;16(10):1104–7.
- 469 Chugh A, et al. Manifestations of coronary arterial injury during catheter ablation of atrial fibrillation and related arrhythmias. *Heart Rhythm* 2013;10(11):1638–45.
- 470 Makhinoto H, et al. Aborted sudden cardiac death due to radiofrequency ablation within the coronary sinus and subsequent total occlusion of the circumflex artery. *J Cardiovasc Electrophysiol* 2013;24(8):929–32.
- 471 Kitamura T, et al. Transient sinus node dysfunction following sinus node artery occlusion due to radiofrequency catheter ablation of the septal superior vena cava-right atrium junction. *J Electrocardiol* 2016;49(1):18–22.
- 472 Ouali S, et al. Acute coronary occlusion during radiofrequency catheter ablation of typical atrial flutter. *J Cardiovasc Electrophysiol* 2002;13(10):1047–9.
- 473 Vlyktyse A, et al. Right coronary artery occlusion during RF ablation of typical atrial flutter. *J Cardiovasc Electrophysiol* 2010;21(7):818–21.
- 474 Sticherling C, Pfister O, Osswald S. Thrombo-embolic occlusion of the left anterior descending coronary artery complicating left atrial radiofrequency ablation. *Europace* 2009;11(1):117–8.
- 475 Wong KC, et al. High incidence of acute sub-clinical circumflex artery 'injury' following mitral isthmus ablation. *Eur Heart J* 2011;32(15):1881–90.
- 476 Fayad G, et al. Circumflex artery stenosis induced by intraoperative radiofrequency ablation. *Ann Thorac Surg* 2003;76(4):1291–3.
- 477 Piccini JP, et al. Outcomes of Medicare beneficiaries undergoing catheter ablation for atrial fibrillation. *Circulation* 2012;126(18):2200–7.
- 478 Lakireddy D, et al. Effect of atrial fibrillation ablation on gastric motility: the atrial fibrillation gut study. *Circ Arrhythm Electrophysiol* 2015;8(3):531–6.
- 479 Dumonceau JM, et al. Acute delayed gastric emptying after ablation of atrial fibrillation: treatment with botulinum toxin injection. *Endoscopy* 2006;38(5):543.
- 480 Bunch TJ, et al. Vagus nerve injury after posterior atrial radiofrequency ablation. *Heart Rhythm* 2008;5(9):1327–30.
- 481 Kuwahara T, et al. Clinical characteristics and management of periesophageal vagal nerve injury complicating left atrial ablation of atrial fibrillation: lessons from eleven cases. *J Cardiovasc Electrophysiol* 2013;24(8):847–51.

- 482 Miyazaki S, et al. Factors associated with periesophageal vagal nerve injury after pulmonary vein antrum isolation. *J Am Heart Assoc* 2014;3(5):e001209.
- 483 Chopra N, Shadchehr A. Achalasia cardia as a unique complication of pulmonary vein isolation. *Heart Rhythm* 2014;11(12):2297–9.
- 484 Schwartz TW, et al. Pancreatic-polypeptide response to food in duodenal-ulcer patients before and after vagotomy. *Lancet* 1976;1(7969):1102–5.
- 485 Ajaj W, et al. Real time high resolution magnetic resonance imaging for the assessment of gastric motility disorders. *Gut* 2004;53(9):1256–61.
- 486 Pisani CF, et al. Gastric hypomotility following epicardial vagal denervation ablation to treat atrial fibrillation. *J Cardiovasc Electrophysiol* 2008;19(2):211–3.
- 487 Kanaeda T, et al. Evaluation of periesophageal nerve injury after pulmonary vein isolation using the (13)C-acetate breath test. *J Arrhythm* 2015;31(6):364–70.
- 488 Lo LW, et al. A novel finding—impairment of gastric myoelectricity after catheter ablation of atrial fibrillation. *Circ J* 2013;77(8):2014–23.
- 489 Janssens J, et al. Improvement of gastric emptying in diabetic gastroparesis by erythromycin. Preliminary studies. *N Engl J Med* 1990;322(15):1028–31.
- 490 Jones MP, Maganti K. A systematic review of surgical therapy for gastroparesis. *Am J Gastroenterol* 2003;98(10):2122–9.
- 491 Tavernier R, Duytschaever M, Taeymans Y. Fracture of a circular mapping catheter after entrapment in the mitral valve apparatus during segmental pulmonary vein isolation. *Pacing Clin Electrophysiol* 2003;26(8):1774–5.
- 492 Grove R, et al. Demand for open heart surgery due to entrapment of a circular mapping catheter in the mitral valve in a patient undergoing atrial fibrillation ablation. *Clin Res Cardiol* 2008;9(7):528–9.
- 493 Lakireddy D, et al. Radiofrequency ablation of atrial fibrillation in patients with mitral or aortic mechanical prosthetic valves: a feasibility, safety, and efficacy study. *Heart Rhythm* 2011;8(7):975–80.
- 494 Zeljko HM, et al. Entrapment of the circular mapping catheter in the mitral valve in two patients undergoing atrial fibrillation ablation. *Europace* 2011;13(1):132–3.
- 495 Desimone CV, et al. Catheter ablation related mitral valve injury: the importance of early recognition and rescue mitral valve repair. *J Cardiovasc Electrophysiol* 2014;25(9):971–5.
- 496 Gurbuz O, et al. Case report: paravalvular leak as a complication of percutaneous catheter ablation for atrial fibrillation. *J Cardiothorac Surg* 2014;9:187.
- 497 Mansour M, et al. Successful release of entrapped circumferential mapping catheters in patients undergoing pulmonary vein isolation for atrial fibrillation. *Heart Rhythm* 2004;1(5):558–61.
- 498 Wu RC, et al. Circular mapping catheter entrapment in the mitral valve apparatus: a previously unrecognized complication of focal atrial fibrillation ablation. *J Cardiovasc Electrophysiol* 2002;13(8):819–21.
- 499 Deftereos S, et al. Colchicine for prevention of early atrial fibrillation recurrence after pulmonary vein isolation: a randomized controlled study. *J Am Coll Cardiol* 2012;60(18):1790–6.
- 500 Deftereos S, et al. Colchicine for prevention of atrial fibrillation recurrence after pulmonary vein isolation: mid-term efficacy and effect on quality of life. *Heart Rhythm* 2014;11(4):620–8.
- 501 Stabile G, et al. Low incidence of permanent complications during catheter ablation for atrial fibrillation using open-irrigated catheters: a multicentre registry. *Europace* 2014;16(8):1154–9.
- 502 Luckie M, et al. Dressler's syndrome following pulmonary vein isolation for atrial fibrillation. *Acute Card Care* 2008;10(4):234–5.
- 503 Lambert T, et al. Cardiac tamponade following pericarditis 18 days after catheter ablation of atrial fibrillation. *Clin Res Cardiol* 2010;99(9):595–7.
- 504 Torihashi S, et al. Two cases of delayed cardiac tamponade due to pericarditis after pulmonary vein (PV) isolation for atrial fibrillation. *Intern Med* 2015;54(7):791–6.
- 505 Kim DR, et al. Comparison of two different doses of single bolus steroid injection to prevent atrial fibrillation recurrence after radiofrequency catheter ablation. *Yonsei Med J* 2015;56(2):324–31.
- 506 Kesk M, et al. Entrapment of circular mapping catheter in the mitral valve. *Heart Rhythm* 2007;4(1):17–9.
- 507 Kuck KH, et al. Cryoballoon or radiofrequency ablation for symptomatic paroxysmal atrial fibrillation: reintervention, rehospitalization, and quality-of-life outcomes in the FIRE AND ICE trial. *Eur Heart J* 2016;37(38):2858–65.
- 508 Sahara H, et al. Feasibility of the radiofrequency hot balloon catheter for isolation of the posterior left atrium and pulmonary veins for the treatment of atrial fibrillation. *Circ Arrhythm Electrophysiol* 2009;2(3):225–32.
- 509 Evonich RF, Nori DM, Haines DE. Efficacy of pulmonary vein isolation with a novel hot balloon ablation catheter. *J Interv Card Electrophysiol* 2012;34(1):29–36.
- 510 Chun RR, et al. The 'single big cryoballoon' technique for acute pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a prospective observational single centre study. *Eur Heart J* 2009;30(6):699–709.
- 511 Hoyt H, et al. Complications arising from catheter ablation of atrial fibrillation: temporal trends and predictors. *Heart Rhythm* 2011;8(12):1869–74.
- 512 Gühl EN, et al. Efficacy of cryoballoon pulmonary vein isolation in patients with persistent atrial fibrillation. *J Cardiovasc Electrophysiol* 2016;27(4):423–7.
- 513 Earley MJ, et al. Radiofrequency ablation of arrhythmias guided by non-fluoroscopic catheter location: a prospective randomized trial. *Eur Heart J* 2006;27(10):1223–9.
- 514 Sarabanda AV, et al. Efficacy and safety of circumferential pulmonary vein isolation using a novel cryothermal balloon ablation system. *J Am Coll Cardiol* 2005;46(10):1902–12.
- 515 Guiot A, et al. Collateral nervous damages after cryoballoon pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2012;23(4):346–51.
- 516 Metzner A, et al. The incidence of phrenic nerve injury during pulmonary vein isolation using the second-generation 28 mm cryoballoon. *J Cardiovasc Electrophysiol* 2014;25(5):466–70.
- 517 Okumura Y, et al. Distortion of right superior pulmonary vein anatomy by balloon catheters as a contributor to phrenic nerve injury. *J Cardiovasc Electrophysiol* 2009;20(10):1151–7.
- 518 Arruda M, et al. Electrical isolation of the superior vena cava: an adjunctive strategy to pulmonary vein antrum isolation improving the outcome of AF ablation. *J Cardiovasc Electrophysiol* 2007;18(12):1261–6.
- 519 Miyazaki S, et al. Prevalence and clinical outcome of phrenic nerve injury during superior vena cava isolation and circumferential pulmonary vein antrum isolation using radiofrequency energy. *Am Heart J* 2014;168(6):846–53.
- 520 Wissner E, et al. Catheter ablation of atrial fibrillation in patients with persistent left superior vena cava is associated with major intraprocedural complications. *Heart Rhythm* 2010;7(12):1755–60.
- 521 Elayi CS, et al. Left superior vena cava isolation in patients undergoing pulmonary vein antrum isolation: impact on atrial fibrillation recurrence. *Heart Rhythm* 2006;3(9):1019–23.
- 522 Liu H, et al. Electrogram-guided isolation of the left superior vena cava for treatment of atrial fibrillation. *Europace* 2007;9(9):775–80.
- 523 Yong Ji S, et al. Phrenic nerve injury: an underrecognized and potentially preventable complication of pulmonary vein isolation using a wide-area circumferential ablation approach. *J Cardiovasc Electrophysiol* 2013;24(10):1086–91.
- 524 Franceschi F, et al. Phrenic nerve monitoring with diaphragmatic electromyography during cryoballoon ablation for atrial fibrillation: the first human application. *Heart Rhythm* 2011;8(7):1068–71.
- 525 Miyazaki S, et al. Prospective evaluation of bilateral diaphragmatic electromyograms during cryoballoon ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2015;26(6):622–8.
- 526 Mondesert B, et al. Clinical experience with a novel electromyographic approach to preventing phrenic nerve injury during cryoballoon ablation in atrial fibrillation. *Circ Arrhythm Electrophysiol* 2014;7(4):605–11.
- 527 Sacher F, et al. Phrenic nerve injury after atrial fibrillation catheter ablation: characterization and outcome in a multicenter study. *J Am Coll Cardiol* 2006;47(12):2498–503.
- 528 Andrade JG, et al. Histopathology of cryoballoon ablation-induced phrenic nerve injury. *J Cardiovasc Electrophysiol* 2014;25(2):187–94.
- 529 Pappone C, et al. Circumferential radiofrequency ablation of pulmonary vein ostia: a new anatomic approach for curing atrial fibrillation. *Circulation* 2000;102(21):2619–28.
- 530 Dulkipati SR, et al. Pulmonary vein isolation using a visually guided laser balloon catheter: the first 200-patient multicenter clinical experience. *Circ Arrhythm Electrophysiol* 2013;6(3):467–72.
- 531 Katz BS, et al. Surgical left atrial appendage ligation is frequently incomplete: a transesophageal echocardiographic study. *J Am Coll Cardiol* 2000;36(2):468–71.
- 532 Caponi D, et al. Ablation of atrial fibrillation: does the addition of three-dimensional magnetic resonance imaging of the left atrium to electroanatomic mapping improve the clinical outcome? A randomized comparison of Carto-Merge vs. Carto-XP three-dimensional mapping ablation in patients with paroxysmal and persistent atrial fibrillation. *Europace* 2010;12(8):1098–104.
- 533 Proietti R, et al. Remote magnetic with open-irrigated catheter vs. manual navigation for ablation of atrial fibrillation: a systematic review and meta-analysis. *Europace* 2013;15(9):1241–8.
- 534 Ferguson JD, et al. Catheter ablation of atrial fibrillation without fluoroscopy using intracardiac echocardiography and electroanatomic mapping. *Circ Arrhythm Electrophysiol* 2009;2(6):611–9.
- 535 Calkins H, et al. Radiation exposure during radiofrequency catheter ablation of accessory atrioventricular connections. *Circulation* 1991;84(6):2376–82.
- 536 Lindsay BD, et al. Radiation exposure to patients and medical personnel during radiofrequency catheter ablation for supraventricular tachycardia. *Am J Cardiol* 1992;70(2):218–23.
- 537 Kovoor P, et al. Risk to patients from radiation associated with radiofrequency ablation for supraventricular tachycardia. *Circulation* 1998;98(15):1534–40.
- 538 Macle L, et al. Radiation exposure during radiofrequency catheter ablation for atrial fibrillation. *Pacing Clin Electrophysiol* 2003;26(1 Pt 2):288–91.
- 539 Lickfett L, et al. Radiation exposure during catheter ablation of atrial fibrillation. *Circulation* 2004;110(19):3003–10.
- 540 Ector J, et al. Obesity is a major determinant of radiation dose in patients undergoing pulmonary vein isolation for atrial fibrillation. *J Am Coll Cardiol* 2007;50(3):234–42.
- 541 Chen J, et al. Cumulative exposure to ionizing radiation from diagnostic and therapeutic cardiac imaging procedures: a population-based analysis. *J Am Coll Cardiol* 2010;56(9):702–11.
- 542 Khaykin Y, et al. CARTO-guided vs. NavX-guided pulmonary vein antrum isolation and pulmonary vein antrum isolation performed without 3-D mapping: effect of the 3-D mapping system on procedure duration and fluoroscopy time. *J Interv Card Electrophysiol* 2011;30(3):233–40.

- 543 Stabile G, et al. Reduced fluoroscopy exposure during ablation of atrial fibrillation using a novel electroanatomical navigation system: a multicentre experience. *Europace* 2012;14(1):60–5.
- 544 De Ponti R, et al. Simulator training reduces radiation exposure and improves trainees' performance in placing electrophysiologic catheters during patient-based procedures. *Heart Rhythm* 2012;9(8):1280–5.
- 545 Kleemann T, et al. Development of radiation exposure in patients undergoing pulmonary vein isolation in Germany between 2007 and 2014: great potential to minimize radiation dosage. *Clin Res Cardiol* 2016;105(10):858–64.
- 546 Steven D, et al. Reduced fluoroscopy during atrial fibrillation ablation: benefits of robotic guided navigation. *J Cardiovasc Electrophysiol* 2010;21(1):6–12.
- 547 Weiss JP, et al. A comparison of remote magnetic irrigated tip ablation versus manual catheter irrigated tip catheter ablation with and without force sensing feedback. *J Cardiovasc Electrophysiol* 2016;27(Suppl 1):S5–10.
- 548 Dragusin O, et al. Evaluation of a radiation protection cabin for invasive electrophysiological procedures. *Eur Heart J* 2007;28(2):183–9.
- 549 Reddy VY, et al. Catheter ablation of atrial fibrillation without the use of fluoroscopy. *Heart Rhythm* 2010;7(11):1644–53.
- 550 Bulava A, Hanis J, Eisenberger M. Catheter ablation of atrial fibrillation using zero-fluoroscopy technique: a randomized trial. *Pacing Clin Electrophysiol* 2015;38(7):797–806.
- 551 Cochet H, et al. Atrial structure and function 5 years after successful ablation for persistent atrial fibrillation: an MRI study. *J Cardiovasc Electrophysiol* 2014;25(7):671–9.
- 552 Gibson DN, et al. Stiff left atrial syndrome after catheter ablation for atrial fibrillation: clinical characterization, prevalence, and predictors. *Heart Rhythm* 2011;8(9):1364–71.
- 553 Shoemaker MB, et al. Left atrial hypertension after repeated catheter ablations for atrial fibrillation. *J Am Coll Cardiol* 2011;57(19):1918–9.
- 554 Weich TD, et al. Symptomatic pulmonary hypertension with giant left atrial v waves after surgical maze procedures: evaluation by comprehensive hemodynamic catheterization. *Heart Rhythm* 2013;10(12):1839–42.
- 555 Witt C, et al. Recurrent dyspnea following multiple ablations for atrial fibrillation explained by the "stiff left atrial syndrome". *Catheter Cardiovasc Interv* 2013;82(5):E747–9.
- 556 Pilote L, et al. Stiff left atrial syndrome. *Can J Cardiol* 1988;4(6):255–7.
- 557 Khurram IM, et al. Association between left atrial stiffness index and atrial fibrillation recurrence in patients undergoing left atrial ablation. *Circ Arrhythm Electrophysiol* 2016;9(3).
- 558 Kosiuk J, et al. Prevalence and predictors of worsened left ventricular diastolic dysfunction after catheter ablation of atrial fibrillation. *Int J Cardiol* 2013;168(4):3613–5.
- 559 Ghanbari H, et al. Mortality and cerebrovascular events after radiofrequency catheter ablation of atrial fibrillation. *Heart Rhythm* 2014;11(9):1503–11.
- 560 Scherr D, et al. Incidence and predictors of left atrial thrombus prior to catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2009;20(4):379–84.
- 561 Liu Y, et al. Incidence and outcomes of cerebrovascular events complicating catheter ablation for atrial fibrillation. *Europace* 2016;18(9):1357–65.
- 562 Noseworthy PA, et al. Risk of stroke after catheter ablation versus cardioversion for atrial fibrillation: a propensity-matched study of 24,244 patients. *Heart Rhythm* 2015;12(6):1154–61.
- 563 Patel D, et al. Long-term functional and neurocognitive recovery in patients who had an acute cerebrovascular event secondary to catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2010;21(4):412–7.
- 564 Kochhauser S, et al. Comparison of outcomes after cardioversion or atrial fibrillation ablation in patients with differing periprocedural anticoagulation regimens. *Can J Cardiol* 2014;30(12):1541–6.
- 565 Kosiuk J, et al. Early cerebral thromboembolic complications after radiofrequency catheter ablation of atrial fibrillation: incidence, characteristics, and risk factors. *Heart Rhythm* 2014;11(11):1934–40.
- 566 Abhishek F, et al. Effectiveness of a strategy to reduce major vascular complications from catheter ablation of atrial fibrillation. *J Interv Card Electrophysiol* 2011;30(3):211–5.
- 567 Aldhoun B, et al. Complications of catheter ablation for atrial fibrillation in a high-volume centre with the use of intracardiac echocardiography. *Europace* 2013;15(1):24–32.
- 568 Mugnai G, et al. Complications in the setting of percutaneous atrial fibrillation ablation using radiofrequency and cryoballoon techniques: a single-center study in a large cohort of patients. *Int J Cardiol* 2015;196:42–9.
- 569 Murakawa Y, et al. Nationwide survey of catheter ablation for atrial fibrillation: the Japanese catheter ablation registry of atrial fibrillation (J-CARAF)-A report on periprocedural oral anticoagulants. *J Arrhythm* 2015;31(1):29–32.
- 570 Palaniswamy C, et al. Catheter ablation of postinfarction ventricular tachycardia: ten-year trends in utilization, in-hospital complications, and in-hospital mortality in the United States. *Heart Rhythm* 2014;11(1):2056–63.
- 571 Peichi P, et al. Complications of catheter ablation of ventricular tachycardia: a single-center experience. *Circ Arrhythm Electrophysiol* 2014;7(4):684–90.
- 572 Waigand J, et al. Percutaneous treatment of pseudoaneurysms and arteriovenous fistulas after invasive vascular procedures. *Catheter Cardiovasc Interv* 1999;47(2):157–64.
- 573 Lakireddy D, et al. Feasibility and safety of uninterrupted rivaroxaban for periprocedural anticoagulation in patients undergoing radiofrequency ablation for atrial fibrillation: results from a multicenter prospective registry. *J Am Coll Cardiol* 2014;63(10):982–8.
- 574 Tanaka-Esposito CC, et al. Real-time ultrasound guidance reduces total and major vascular complications in patients undergoing pulmonary vein antral isolation on therapeutic warfarin. *J Interv Card Electrophysiol* 2013;37(2):163–8.
- 575 Errahmouni A, et al. Ultrasound-guided venous puncture in electrophysiological procedures: a safe method, rapidly learned. *Pacing Clin Electrophysiol* 2014;37(8):1023–8.