

## 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary

### A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

*Developed in Collaboration With the Society of Thoracic Surgeons*

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### Preamble

The medical profession should play a central role in evaluating the evidence related to drugs, devices, and procedures for the detection, management, and prevention of disease. When properly applied, expert analysis of available data on the benefits and risks of these therapies and procedures can improve the quality of care, optimize patient outcomes, and favorably

affect costs by focusing resources on the most effective strategies. An organized and directed approach to a thorough review of evidence has resulted in the production of clinical practice guidelines that assist clinicians in selecting the best management strategy for an individual patient. Moreover, clinical practice guidelines can provide a foundation for other applications, such as performance measures, appropriate use criteria, and both quality improvement and clinical decision support tools.

The American College of Cardiology (ACC) and the American Heart Association (AHA) have jointly engaged in the production of guidelines in the area of cardiovascular disease since 1980. The ACC/AHA Task Force on Practice Guidelines (Task Force), whose charge is to develop, update, or revise practice guidelines for cardiovascular diseases and procedures, directs this effort. Writing committees are charged with the task of performing an assessment of the evidence and acting as an independent group of authors to develop, update, or revise written recommendations for clinical practice.

Experts in the subject under consideration are selected from both organizations to examine subject-specific data and write guidelines. Writing committees are specifically charged to perform a literature review; weigh the strength of evidence for or against particular tests, treatments, or procedures; and include estimates of expected health outcomes where such data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that may influence the choice of tests or therapies are considered, as well as frequency of follow-up and cost-effectiveness. When available, information from studies on cost is considered; however, review of data on efficacy and outcomes constitutes the primary basis for preparing recommendations in this guideline.

In analyzing the data, and developing recommendations and supporting text, the writing committee uses evidence-based methodologies developed by the Task Force.<sup>1</sup> The Classification of Recommendation (COR) is an estimate of the size of the treatment effect, with consideration given to risks versus benefits, as well as evidence and/or agreement that a given treatment or procedure is or is not useful/effective or in some situations may cause harm; this is defined in Table 1. The Level of Evidence (LOE) is an estimate of the certainty or precision of the treatment effect. The writing committee reviews and ranks evidence supporting each recommendation, with the weight of evidence ranked as LOE A, B, or C, according to specific definitions that are included in Table 1. Studies are identified as observational, retrospective, prospective, or randomized, as appropriate. For certain conditions for which inadequate data are available, recommendations are based on expert consensus and clinical experience and are ranked as LOE C. When recommendations at LOE C are supported by historical clinical data, appropriate references (including clinical reviews) are cited if available.

For issues with sparse available data, a survey of current practice among the clinician members of the writing committee is the basis for LOE C recommendations and no references are cited.

The schema for COR and LOE is summarized in Table 1, which also provides suggested phrases for writing recommendations within each COR.

Table 1. Applying Classification of Recommendations and Level of Evidence

|   |  | SIZE OF TREATMENT EFFECT   |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
|---|--|--|---|--|--|---------------------|----------------|--------------------|---------------------|------------------|-------------------|--|--|------------------------------------|--|
|   |  | CLASS I<br><i>Benefit &gt;&gt;&gt; Risk</i><br>Procedure/Treatment <b>SHOULD</b> be performed/administered   | CLASS IIa<br><i>Benefit &gt;&gt; Risk</i><br><i>Additional studies with focused objectives needed</i><br><b>IT IS REASONABLE</b> to perform procedure/administer treatment  | CLASS IIb<br><i>Benefit ≥ Risk</i><br><i>Additional studies with broad objectives needed; additional registry data would be helpful</i><br>Procedure/Treatment <b>MAY BE CONSIDERED</b>                  | CLASS III <i>No Benefit</i> or CLASS III <i>Harm</i>   |                     |                |                    |                     |                  |                   |  |  |                                    |  |
|   |  |  |   |  | <table border="1"> <thead> <tr> <th></th> <th>Procedure/Test</th> <th>Treatment</th> </tr> </thead> <tbody> <tr> <td>COR III: No benefit</td> <td>Not Helpful</td> <td>No Proven Benefit</td> </tr> <tr> <td>COR III: Harm</td> <td>Excess Cost w/o Benefit or Harmful</td> <td>Harmful to Patients</td> </tr> </tbody> </table>   |                     | Procedure/Test | Treatment          | COR III: No benefit | Not Helpful      | No Proven Benefit | COR III: Harm                              | Excess Cost w/o Benefit or Harmful         | Harmful to Patients                |  |
|   | Procedure/Test   | Treatment  |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| COR III: No benefit                                   | Not Helpful  | No Proven Benefit  |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| COR III: Harm   | Excess Cost w/o Benefit or Harmful   | Harmful to Patients  |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT | LEVEL A<br>Multiple populations evaluated*<br>Data derived from multiple randomized clinical trials or meta-analyses   | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul> | <ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>      | <ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Greater conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>      | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
|   | LEVEL B<br>Limited populations evaluated*<br>Data derived from a single randomized trial or nonrandomized studies      | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Evidence from single randomized trial or nonrandomized studies</li> </ul>       | <ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Some conflicting evidence from single randomized trial or nonrandomized studies</li> </ul> | <ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Greater conflicting evidence from single randomized trial or nonrandomized studies</li> </ul> | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Evidence from single randomized trial or nonrandomized studies</li> </ul>  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
|   | LEVEL C<br>Very limited populations evaluated*<br>Only consensus opinion of experts, case studies, or standard of care | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Only expert opinion, case studies, or standard of care</li> </ul>               | <ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Only diverging expert opinion, case studies, or standard of care</li> </ul>                | <ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Only diverging expert opinion, case studies, or standard of care</li> </ul>                   | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Only expert opinion, case studies, or standard of care</li> </ul>  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| Suggested phrases for writing recommendations         |  | should<br>is recommended<br>is indicated<br>is useful/effective/beneficial   | is reasonable<br>can be useful/effective/beneficial<br>is probably recommended<br>or indicated  | may/might be considered<br>may/might be reasonable<br>usefulness/effectiveness is unknown/unclear/uncertain or not well established  | <table border="1"> <thead> <tr> <th>COR III: No Benefit</th> <th>COR III: Harm</th> </tr> </thead> <tbody> <tr> <td>is not recommended</td> <td>potentially harmful</td> </tr> <tr> <td>is not indicated</td> <td>causes harm</td> </tr> <tr> <td>should not be performed/administered/other</td> <td>associated with excess morbidity/mortality</td> </tr> <tr> <td>is not useful/beneficial/effective</td> <td>should not be performed/administered/other</td> </tr> </tbody> </table> | COR III: No Benefit | COR III: Harm  | is not recommended | potentially harmful | is not indicated | causes harm       | should not be performed/administered/other | associated with excess morbidity/mortality | is not useful/beneficial/effective | should not be performed/administered/other |
| COR III: No Benefit                                   | COR III: Harm  |  |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| is not recommended                                    | potentially harmful  |  |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| is not indicated                                      | causes harm  |  |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| should not be performed/administered/other            | associated with excess morbidity/mortality   |  |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| is not useful/beneficial/effective                    | should not be performed/administered/other   |  |   |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |
| Comparative effectiveness phrases†                    |  | treatment/strategy A is recommended/indicated in preference to treatment B<br>treatment A should be chosen over treatment B  | treatment/strategy A is probably recommended/indicated in preference to treatment B<br>it is reasonable to choose treatment A over treatment B  |  |  |                     |                |                    |                     |                  |                   |  |  |                                    |  |

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

\*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes mellitus, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative-effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

A new addition to this methodology is the separation of the Class III recommendations to delineate whether the recommendation is determined to be of “no benefit” or is associated with “harm” to the patient. In addition, in view of the increasing number of comparative effectiveness studies, comparator verbs and suggested phrases for writing recommendations for the comparative effectiveness of one treatment or strategy versus another are included for COR I and IIa, LOE A or B only.

In view of the advances in medical therapy across the spectrum of cardiovascular diseases, the Task Force has designated the term *guideline-directed medical therapy* to represent optimal medical therapy as defined by ACC/AHA guideline (primarily Class I)–recommended therapies. This

new term, *guideline-directed medical therapy*, is used herein and throughout subsequent guidelines.

Therapies not available in the United States are discussed in the text without a specific COR. For studies performed in large numbers of subjects outside North America, each writing committee reviews the potential impact of different practice patterns and patient populations on the treatment effect and relevance to the ACC/AHA target population to determine whether the findings should inform a specific recommendation.

The ACC/AHA practice guidelines are intended to assist clinicians in clinical decision making by describing a range of generally acceptable approaches to the diagnosis, management, and prevention of specific diseases or conditions. The guidelines attempt to define practices that meet the needs of most patients in



most circumstances. The ultimate judgment about care of a particular patient must be made by the clinician and patient in light of all the circumstances presented by that patient. As a result, situations may arise in which deviations from these guidelines may be appropriate. Clinical decision making should involve consideration of the quality and availability of expertise in the area where care is provided. When these guidelines are used as the basis for regulatory or payer decisions, the goal should be improvement in quality of care. The Task Force recognizes that situations arise in which additional data are needed to inform patient care more effectively; these areas are identified within each respective guideline when appropriate.

Prescribed courses of treatment in accordance with these recommendations are effective only if followed. Because lack of patient understanding and adherence may adversely affect outcomes, clinicians should make every effort to engage the patient's active participation in prescribed medical regimens and lifestyles. In addition, patients should be informed of the risks, benefits, and alternatives to a particular treatment and should be involved in shared decision making whenever feasible, particularly for COR IIa and IIb, for which the benefit-to-risk ratio may be lower.

The Task Force makes every effort to avoid actual, potential, or perceived conflicts of interest that may arise as a result of relationships with industry and other entities (RWI) among the members of the writing committee. All writing committee members and peer reviewers of the guideline are required to disclose all current healthcare-related relationships, including those existing 12 months before initiation of the writing effort.

In December 2009, the ACC and AHA implemented a new RWI policy that requires the writing committee chair plus a minimum of 50% of the writing committee to have no relevant RWI (Appendix 1 includes the ACC/AHA definition of *relevance*). The Task Force and all writing committee members review their respective RWI disclosures during each conference call and/or meeting of the writing committee, and members provide updates to their RWI as changes occur. All guideline recommendations require a confidential vote by the writing committee and require approval by a consensus of the voting members. Members may not draft or vote on any recommendations pertaining to their RWI. Members who recused themselves from voting are indicated in the list of writing committee members, and specific section recusals are noted in Appendix 1. Authors' and peer reviewers' RWI pertinent to this guideline are disclosed in Appendixes 1 and 2. In addition, to ensure complete transparency, writing committee members' comprehensive disclosure information—including RWI not pertinent to this document—is available as an [online supplement](#). Comprehensive disclosure information for the Task Force is also available online at <http://www.cardiosource.org/en/ACC/About-ACC/Who-We-Are/Leadership/Guidelines-and-Documents-Task-Forces.aspx>. The ACC and AHA exclusively sponsor the work of the writing committee, without commercial support. Writing committee members volunteered their time for this activity. Guidelines are official policy of both the ACC and AHA.

In an effort to maintain relevance at the point of care for clinicians, the Task Force continues to oversee an ongoing process improvement initiative. As a result, in response to pilot

projects, several changes to this guideline will be apparent, including limited narrative text, a focus on summary and evidence tables (with references linked to abstracts in PubMed), and more liberal use of summary recommendation tables (with references that support the LOE) to serve as a quick reference.

In April 2011, the Institute of Medicine released 2 reports: *Finding What Works in Health Care: Standards for Systematic Reviews* and *Clinical Practice Guidelines We Can Trust*.<sup>2,3</sup> It is noteworthy that the Institute of Medicine cited ACC/AHA practice guidelines as being compliant with many of the proposed standards. A thorough review of these reports and of our current methodology is under way, with further enhancements anticipated.

The recommendations in this guideline are considered current until they are superseded by a focused update, the full-text guideline is revised, or until a published addendum declares it out of date and no longer official ACC/AHA policy. The reader is encouraged to consult the full-text guideline<sup>4</sup> for additional guidance and details about atrial fibrillation (AF), because the executive summary contains mainly the recommendations.

Jeffrey L. Anderson, MD, FACC, FAHA  
Chair, ACC/AHA Task Force on Practice Guidelines

## 1. Introduction

### 1.1. Methodology and Evidence Review

The recommendations listed in this document are, whenever possible, evidence based. An extensive evidence review was conducted, focusing on 2006 through October 2012 and selected other references through March 2014. The relevant data are included in evidence tables in the [Online Data Supplement](#). Searches were extended to studies, reviews, and other evidence conducted in human subjects, published in English, and accessible through PubMed, EMBASE, Cochrane, Agency for Healthcare Research and Quality Reports, and other selected databases relevant to this guideline. Key search words included but were not limited to the following: *age, antiarrhythmic, atrial fibrillation, atrial remodeling, atrioventricular conduction, atrioventricular node, cardioversion, classification, clinical trial, complications, concealed conduction, cost-effectiveness, defibrillator, demographics, epidemiology, experimental, heart failure, hemodynamics, human, hyperthyroidism, hypothyroidism, meta-analysis, myocardial infarction, pharmacology, postoperative, pregnancy, pulmonary disease, quality of life, rate control, rhythm control, risks, sinus rhythm, symptoms, and tachycardia-mediated cardiomyopathy*. Additionally, the writing committee reviewed documents related to AF previously published by the ACC and AHA. References selected and published in this document are representative and not all-inclusive.

### 1.2. Organization of the Writing Committee

The 2014 AF writing committee was composed of clinicians with broad expertise related to AF and its treatment, including adult cardiology, electrophysiology, cardiothoracic surgery, and heart failure (HF). The writing committee was assisted by staff from the ACC and AHA. Under the guidance of the Task Force, the Heart Rhythm Society was invited to be a partner organization and provided representation. The writing

committee also included a representative from the Society of Thoracic Surgeons. The rigorous methodological policies and procedures noted in the Preamble differentiate ACC/AHA guidelines from other published guidelines and statements.

**1.3. Document Review and Approval**

This document was reviewed by 2 official reviewers each nominated by the ACC, AHA, and Heart Rhythm Society, as well as 1 reviewer from the Society of Thoracic Surgeons and 43 individual content reviewers (from the ACC Electrophysiology Section Leadership Council, ACC Adult Congenital and Pediatric Cardiology Section Leadership Council, ACC Association of International Governors, ACC Heart Failure and Transplant Section Leadership Council, ACC Imaging

Section Leadership Council, ACC Interventional Section Leadership Council, ACC Surgeons' Council, and the Heart Rhythm Society Scientific Documents Committee). All information on reviewers' RWI was distributed to the writing committee and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACC, AHA, and Heart Rhythm Society and endorsed by the Society of Thoracic Surgeons.

**1.4. Scope of the Guideline**

The task of the 2014 writing committee was to establish revised guidelines for optimum management of AF. The new guideline incorporates new and existing knowledge derived from published clinical trials, basic science, and comprehensive

**Table 2. Associated Guidelines and Statements**

| Title  | Organization                   | Publication Year/Reference |
|--|--------------------------------|----------------------------|
| <b>Guidelines</b>  |                                |                            |
| Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)  | NHLBI                          | 2003 <sup>9</sup>          |
| Assessment of Cardiovascular Risk in Asymptomatic Adults   | ACC/AHA                        | 2010 <sup>10</sup>         |
| Coronary Artery Bypass Graft Surgery   | ACC/AHA                        | 2011 <sup>11</sup>         |
| Hypertrophic Cardiomyopathy  | ACC/AHA                        | 2011 <sup>12</sup>         |
| Percutaneous Coronary Intervention   | ACC/AHA/SCAI                   | 2011 <sup>13</sup>         |
| Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease  | AHA/ACC                        | 2011 <sup>14</sup>         |
| Atrial Fibrillation*   | CCS                            | 2012 <sup>15</sup>         |
| Atrial Fibrillation  | ESC                            | 2012 <sup>16</sup>         |
| Stable Ischemic Heart Disease  | ACC/AHA/ACP/AATS/PCNA/SCAI/STS | 2012 <sup>17</sup>         |
| Antithrombotic Therapy   | ACCP                           | 2012 <sup>18</sup>         |
| Device-Based Therapy   | ACC/AHA/HRS                    | 2012 <sup>19</sup>         |
| Heart Failure  | ACC/AHA                        | 2013 <sup>20</sup>         |
| ST-Elevation Myocardial Infarction   | ACC/AHA                        | 2013 <sup>21</sup>         |
| Unstable Angina/Non-ST-Elevation Myocardial Infarction   | ACC/AHA                        | 2014 <sup>22</sup>         |
| Valvular Heart Disease   | AHA/ACC                        | 2014 <sup>23</sup>         |
| Assessment of Cardiovascular Risk  | ACC/AHA                        | 2013 <sup>24</sup>         |
| Lifestyle Management to Reduce Cardiovascular Risk   | AHA/ACC                        | 2013 <sup>25</sup>         |
| Management of Overweight and Obesity in Adults   | AHA/ACC/TOS                    | 2013 <sup>26</sup>         |
| Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults   | ACC/AHA                        | 2013 <sup>27</sup>         |
| <b>Statements</b>  |                                |                            |
| Treatment of Atrial Fibrillation   | AHRQ                           | 2013 <sup>8a,8b</sup>      |
| Oral Antithrombotic Agents for the Prevention of Stroke in Nonvalvular Atrial Fibrillation: A Science Advisory for Healthcare Professionals  | AHA/ASA                        | 2012 <sup>28</sup>         |
| 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 | HRS/EHRA/ECAS                  | 2012 <sup>29</sup>         |

\*Includes the following sections: Catheter Ablation for AF/Atrial Flutter; Prevention and Treatment of AF Following Cardiac Surgery; Rate and Rhythm Management; Prevention of Stroke and Systemic Thromboembolism in AF and Flutter; Management of Recent-Onset AF and Flutter in the Emergency Department; Surgical Therapy; The Use of Antiplatelet Therapy in the Outpatient Setting; and Focused 2012 Update of the CCS AF Guidelines: Recommendations for Stroke Prevention and Rate/Rhythm Control.

AATS indicates American Association for Thoracic Surgery; ACC, American College of Cardiology; ACCP, American College of Chest Physicians; ACP, American College of Physicians; AF, atrial fibrillation; AHA, American Heart Association; AHRQ, Agency for Healthcare Research and Quality; ASA, American Stroke Association; CCS, Canadian Cardiology Society; ECAS, European Cardiac Arrhythmia Society; EHRA, European Heart Rhythm Association; ESC, European Society of Cardiology; HRS, Heart Rhythm Society; JNC, Joint National Committee; NHLBI, National Heart, Lung, and Blood Institute; PCNA, Preventive Cardiovascular Nurses Association; SCAI, Society for Cardiovascular Angiography and Interventions; STS, Society of Thoracic Surgeons; and TOS, The Obesity Society.

**Table 3. Definitions of AF: A Simplified Scheme**

| Term                        | Definition   |
|-----------------------------|--|
| Paroxysmal AF               | <ul style="list-style-type: none"> <li>AF that terminates spontaneously or with intervention within 7 d of onset.</li> <li>Episodes may recur with variable frequency.</li> </ul>  |
| Persistent AF               | <ul style="list-style-type: none"> <li>Continuous AF that is sustained &gt;7 d.</li> </ul>   |
| Long-standing persistent AF | <ul style="list-style-type: none"> <li>Continuous AF &gt;12 mo in duration.</li> </ul>   |
| Permanent AF                | <ul style="list-style-type: none"> <li>The term “permanent AF” is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm.</li> <li>Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of AF.</li> <li>Acceptance of AF may change as symptoms, efficacy of therapeutic interventions, and patient and clinician preferences evolve.</li> </ul> |
| Nonvalvular AF              | <ul style="list-style-type: none"> <li>AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.</li> </ul>   |

AF indicates atrial fibrillation.

review articles, along with evolving treatment strategies and new drugs. This guideline supersedes the “ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation”<sup>5</sup> and the 2 subsequent focused updates from 2011.<sup>6,7</sup> In addition, the ACC, AHA, American College of Physicians, and American Academy of Family Physicians submitted a proposal to the Agency for Healthcare Research and Quality to perform a systematic review on specific questions related to the treatment of AF. The data from that report

were reviewed by the writing committee and incorporated where appropriate.<sup>8a,8b</sup>

The 2014 AF guideline is organized thematically, with recommendations, where appropriate, provided with each section. Some recommendations from earlier guidelines have been eliminated or updated as warranted by new evidence or a better understanding of earlier evidence. In developing the 2014 AF guideline, the writing committee reviewed prior published guidelines and related statements. Table 2 lists these publications and statements deemed pertinent to this effort and is intended for use as a resource.

## 2. Clinical Characteristics and Evaluation of AF

### 2.1. AF Classification

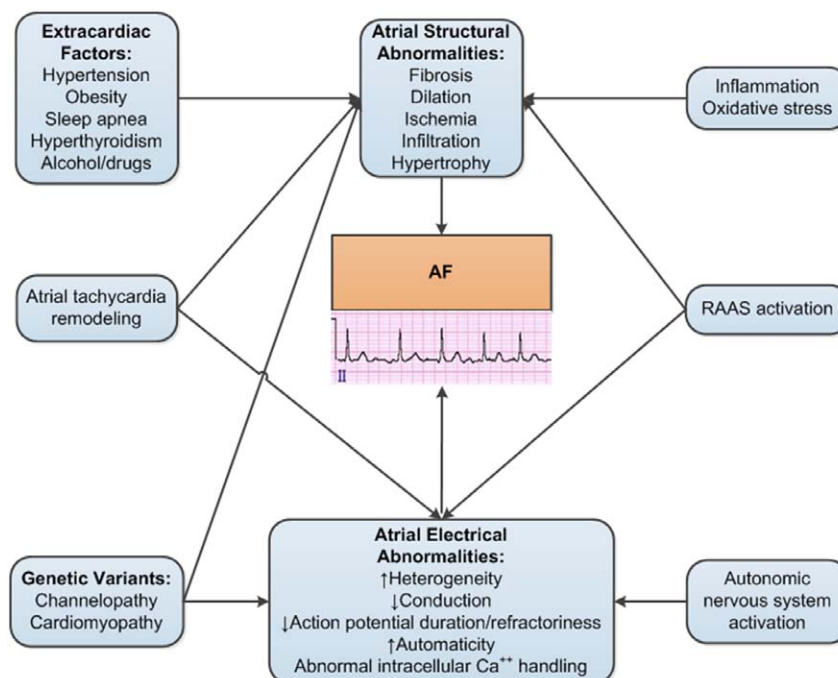
AF may be described in terms of the duration of episodes using a simplified scheme shown in Table 3.<sup>5,29,30</sup> Implanted loop recorders, pacemakers, and defibrillators offer the possibility of reporting frequency, rate, and duration of abnormal atrial rhythms, including AF.<sup>31,32</sup> Episodes often increase in frequency and duration over time.

### 2.2. Mechanisms of AF and Pathophysiology

AF occurs when structural and/or electrophysiological abnormalities alter atrial tissue to promote abnormal impulse formation and/or propagation (Figure 1). These abnormalities are caused by diverse pathophysiological mechanisms,<sup>29,33,34</sup> such that AF represents a final common phenotype for multiple disease pathways and mechanisms that are incompletely understood.

### 2.3. Risk Factors and Associated Heart Disease

Multiple clinical risk factors, electrocardiographic and echocardiographic features, and biochemical markers are associated with an increased risk of AF (Table 4).



**Figure 1.** Mechanisms of AF. AF indicates atrial fibrillation; Ca<sup>++</sup> ionized calcium; and RAAS, renin-angiotensin-aldosterone system.

**Table 4. Selected Risk Factors and Biomarkers for AF**

| Clinical Risk Factors              | References |
|------------------------------------|------------|
| Increasing age                     | 35         |
| Hypertension                       | 35         |
| Diabetes mellitus                  | 35         |
| MI                                 | 35         |
| VHD                                | 35         |
| HF                                 | 35,36      |
| Obesity                            | 37–39      |
| Obstructive sleep apnea            | 39         |
| Cardiothoracic surgery             | 40         |
| Smoking                            | 41         |
| Exercise                           | 42–44      |
| Alcohol use                        | 45–47      |
| Hyperthyroidism                    | 48–50      |
| Increased pulse pressure           | 51         |
| European ancestry                  | 52         |
| Family history                     | 53         |
| Genetic variants                   | 54–57      |
| ECG                                |            |
| LVH                                | 58         |
| Echocardiographic                  |            |
| LA enlargement                     | 58,59      |
| Decreased LV fractional shortening | 58         |
| Increased LV wall thickness        | 58         |
| Biomarkers                         |            |
| Increased CRP                      | 60,61      |
| Increased BNP                      | 62,63      |

AF indicates atrial fibrillation; BNP, B-type natriuretic peptide; CRP, C-reactive protein; ECG, electrocardiographic; HF, heart failure; LA, left atrial; LV, left ventricular; LVH, left ventricular hypertrophy; MI, myocardial infarction; and VHD, valvular heart disease.

**2.4. Clinical Evaluation: Recommendation**

See Appendix 3 for information on initial clinical evaluation in patients with AF.

**Class I**

- 1. Electrocardiographic documentation is recommended to establish the diagnosis of AF. (Level of Evidence: C)

**3. Thromboembolic Risk and Treatment**

**3.1. Risk-Based Antithrombotic Therapy: Recommendations**

See Table 5 for a summary of recommendations from this section.

**Class I**

- 1. In patients with AF, antithrombotic therapy should be individualized based on shared decision making after discussion of the absolute and relative risks

- of stroke and bleeding and the patient’s values and preferences. (Level of Evidence: C)
- 2. Selection of antithrombotic therapy should be based on the risk of thromboembolism irrespective of whether the AF pattern is paroxysmal, persistent, or permanent.<sup>64–67</sup> (Level of Evidence: B)
- 3. In patients with nonvalvular AF, the CHA<sub>2</sub>DS<sub>2</sub>-VASc\* score is recommended for assessment of stroke risk.<sup>68–70</sup> (Level of Evidence: B)
- 4. For patients with AF who have mechanical heart valves, warfarin is recommended, and the target international normalized ratio (INR) intensity (2.0 to 3.0 or 2.5 to 3.5) should be based on the type and location of the prosthesis.<sup>71–73</sup> (Level of Evidence: B)
- 5. For patients with nonvalvular AF with prior stroke, transient ischemic attack (TIA), or a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 or greater, oral anticoagulants are recommended. Options include warfarin (INR 2.0 to 3.0)<sup>68–70</sup> (Level of Evidence: A), dabigatran<sup>74</sup> (Level of Evidence: B), rivaroxaban<sup>75</sup> (Level of Evidence: B), or apixaban.<sup>76</sup> (Level of Evidence: B)
- 6. Among patients treated with warfarin, the INR should be determined at least weekly during initiation of antithrombotic therapy and at least monthly when anticoagulation (INR in range) is stable.<sup>77–79</sup> (Level of Evidence: A)
- 7. For patients with nonvalvular AF unable to maintain a therapeutic INR level with warfarin, use of a direct thrombin or factor Xa inhibitor (dabigatran, rivaroxaban, or apixaban) is recommended. (Level of Evidence: C)
- 8. Reevaluation of the need for and choice of antithrombotic therapy at periodic intervals is recommended to reassess stroke and bleeding risks. (Level of Evidence: C)
- 9. Bridging therapy with unfractionated heparin or low-molecular-weight heparin (LMWH) is recommended for patients with AF and a mechanical heart valve undergoing procedures that require interruption of warfarin. Decisions on bridging therapy should balance the risks of stroke and bleeding. (Level of Evidence: C)
- 10. For patients with AF without mechanical heart valves who require interruption of warfarin or new anticoagulants for procedures, decisions about bridging therapy (LMWH or unfractionated heparin) should balance the risks of stroke and bleeding and the duration of time a patient will not be anticoagulated. (Level of Evidence: C)
- 11. Renal function should be evaluated before initiation of direct thrombin or factor Xa inhibitors and should be reevaluated when clinically indicated and at least annually.<sup>80–82</sup> (Level of Evidence: B)
- 12. For patients with atrial flutter, antithrombotic therapy is recommended according to the same risk profile used for AF. (Level of Evidence: C)

\*CHA<sub>2</sub>DS<sub>2</sub>-VASc indicates Congestive heart failure, Hypertension, Age ≥75 years (doubled), Diabetes mellitus, prior Stroke or TIA or thromboembolism (doubled), Vascular disease, Age 65 to 74 years, Sex category.



**Table 5. Summary of Recommendations for Risk-Based Antithrombotic Therapy**

| Recommendations  | COR             | LOE | References   |
|--|-----------------|-----|--------------|
| Antithrombotic therapy based on shared decision making, discussion of risks of stroke and bleeding, and patient's preferences  | I               | C   | N/A          |
| Selection of antithrombotic therapy based on risk of thromboembolism   | I               | B   | 64–67        |
| CHA <sub>2</sub> DS <sub>2</sub> -VASc score recommended to assess stroke risk   | I               | B   | 68–70        |
| Warfarin recommended for mechanical heart valves and target INR intensity based on type and location of prosthesis   | I               | B   | 71–73        |
| With prior stroke, TIA, or CHA <sub>2</sub> DS <sub>2</sub> -VASc score ≥2, oral anticoagulants recommended. Options include:  |                 |     |              |
| Warfarin   | I               | A   | 68–70        |
| Dabigatran, rivaroxaban, or apixaban   | I               | B   | 74–76        |
| With warfarin, determine INR at least weekly during initiation of therapy and monthly when stable  | I               | A   | 77–79        |
| Direct thrombin or factor Xa inhibitor recommended if unable to maintain therapeutic INR   | I               | C   | N/A          |
| Reevaluate the need for anticoagulation at periodic intervals  | I               | C   | N/A          |
| Bridging therapy with UFH or LMWH recommended with a mechanical heart valve if warfarin is interrupted. Bridging therapy should balance risks of stroke and bleeding   | I               | C   | N/A          |
| For patients without mechanical heart valves, bridging therapy decisions should balance stroke and bleeding risks against duration of time patient will not be anticoagulated  | I               | C   | N/A          |
| Evaluate renal function before initiation of direct thrombin or factor Xa inhibitors, and reevaluate when clinically indicated and at least annually   | I               | B   | 80–82        |
| For atrial flutter, antithrombotic therapy is recommended as for AF  | I               | C   | N/A          |
| With nonvalvular AF and CHA <sub>2</sub> DS <sub>2</sub> -VASc score of 0, it is reasonable to omit antithrombotic therapy   | IIa             | B   | 80,81        |
| With CHA <sub>2</sub> DS <sub>2</sub> -VASc score ≥2 and end-stage CKD (CrCl <15 mL/min) or on hemodialysis, it is reasonable to prescribe warfarin for oral anticoagulation   | IIa             | B   | 82           |
| With nonvalvular AF and a CHA <sub>2</sub> DS <sub>2</sub> -VASc score of 1, no antithrombotic therapy or treatment with oral anticoagulant or aspirin may be considered   | IIb             | C   | N/A          |
| With moderate-to-severe CKD and CHA <sub>2</sub> DS <sub>2</sub> -VASc scores ≥2, reduced doses of direct thrombin or factor Xa inhibitors may be considered   | IIb             | C   | N/A          |
| For PCI,* BMS may be considered to minimize duration of DAPT   | IIb             | C   | N/A          |
| After coronary revascularization in patients with CHA <sub>2</sub> DS <sub>2</sub> -VASc score ≥2, it may be reasonable to use clopidogrel concurrently with oral anticoagulants but without aspirin                                   | IIb             | B   | 83           |
| Direct thrombin dabigatran and factor Xa inhibitor rivaroxaban are not recommended in patients with AF and end-stage CKD or on dialysis because of a lack of evidence from clinical trials regarding the balance of risks and benefits | III: No Benefit | C   | 74–76, 84–86 |
| Direct thrombin inhibitor dabigatran should not be used with a mechanical heart valve  | III: Harm       | B   | 87           |

\*See the 2011 PCI guideline for type of stent and duration of DAPT recommendations.<sup>13</sup>

AF indicates atrial fibrillation; BMS, bare-metal stent; CHA<sub>2</sub>DS<sub>2</sub>-VASc, Congestive heart failure, Hypertension, Age ≥75 years (doubled), Diabetes mellitus, Prior Stroke or TIA or thromboembolism (doubled), Vascular disease, Age 65 to 74 years, Sex category; CKD, chronic kidney disease; COR, Class of Recommendation; CrCl, creatinine clearance; DAPT, dual antiplatelet therapy; INR, international normalized ratio; LMWH, low-molecular-weight heparin; LOE, Level of Evidence; N/A, not applicable; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; and UFH, unfractionated heparin.

## Class IIa

1. For patients with nonvalvular AF and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 0, it is reasonable to omit antithrombotic therapy.<sup>80,81</sup> (*Level of Evidence: B*)
2. For patients with nonvalvular AF with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 or greater and who have end-stage chronic kidney disease (CKD) (creatinine clearance <15 mL/min) or are on hemodialysis, it is reasonable to prescribe warfarin (INR 2.0 to 3.0) for oral anticoagulation.<sup>82</sup> (*Level of Evidence: B*)

## Class IIb

1. For patients with nonvalvular AF and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 1, no antithrombotic therapy or treatment with

an oral anticoagulant or aspirin may be considered. (*Level of Evidence: C*)

2. For patients with nonvalvular AF and moderate-to-severe CKD with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 2 or greater, treatment with reduced doses of direct thrombin or factor Xa inhibitors may be considered (eg, dabigatran, rivaroxaban, or apixaban), but safety and efficacy have not been established. (*Level of Evidence: C*)
3. In patients with AF undergoing percutaneous coronary intervention,† bare-metal stents may be considered to minimize the required duration of dual antiplatelet therapy. Anticoagulation may be interrupted at the time of the procedure to reduce the risk of bleeding at the site of peripheral arterial puncture. (*Level of Evidence: C*)

†See the 2011 percutaneous coronary intervention guideline for type of stent and duration of dual antiplatelet therapy recommendations.<sup>13</sup>



4. Following coronary revascularization (percutaneous or surgical) in patients with AF and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 or greater, it may be reasonable to use clopidogrel (75 mg once daily) concurrently with oral anticoagulants but without aspirin.<sup>83</sup> (Level of Evidence: B)

**Class III: No Benefit**

1. The direct thrombin inhibitor dabigatran and the factor Xa inhibitor rivaroxaban are not recommended in patients with AF and end-stage CKD or on dialysis because of the lack of evidence from clinical trials regarding the balance of risks and benefits.<sup>74-76,84-86</sup> (Level of Evidence: C)

**Class III: Harm**

1. The direct thrombin inhibitor dabigatran should not be used in patients with AF and a mechanical heart valve.<sup>87</sup> (Level of Evidence: B)

**3.2. Risk Stratification Schemes (CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc)**

One meta-analysis has stratified ischemic stroke risk among patients with nonvalvular AF using the following scoring systems: AF Investigators,<sup>88</sup> CHADS<sub>2</sub> (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Prior Stroke or TIA or Thromboembolism [doubled]),<sup>89</sup> or CHA<sub>2</sub>DS<sub>2</sub>-VASc (Congestive heart failure, Hypertension, Age ≥75 years [doubled], Diabetes mellitus, Prior Stroke or TIA or thromboembolism [doubled], Vascular disease, Age 65 to 74 years, Sex category) (Table 6).

**3.3. Considerations in Selecting Anticoagulants**

For patients with CKD, dose modifications of the new agents are available (Table 7); however, for those with severe or end-stage CKD, warfarin remains the anticoagulant of choice, as there are no or very limited data for these patients. Among patients on hemodialysis, warfarin has been used with acceptable risks of hemorrhage.<sup>82</sup>

**3.4. Cardiac Surgery—Left Atrial Appendage Occlusion/Excision: Recommendation**

**Class IIb**

1. Surgical excision of the left atrial appendage may be considered in patients undergoing cardiac surgery. (Level of Evidence: C)

**4. Rate Control: Recommendations**

See Table 8 for a summary of recommendations for this section and Table 9 for common medication dosages for rate control of AF.

**Class I**

1. Control of the ventricular rate using a beta blocker or nondihydropyridine calcium channel antagonist is

**Table 6. Comparison of the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc Risk Stratification Scores for Subjects With Nonvalvular AF**

| Definition and Scores for CHADS <sub>2</sub> and CHA <sub>2</sub> DS <sub>2</sub> -VASc | Stroke Risk Stratification With the CHADS <sub>2</sub> and CHA <sub>2</sub> DS <sub>2</sub> -VASc Scores |  |                                |
|---|--|--|--------------------------------|
|   | Score  |  | Adjusted Stroke Rate (% per y) |
| <b>CHADS<sub>2</sub></b>  |  | <b>CHADS<sub>2</sub>*</b>                  |                                |
| Congestive HF   | 1  | 0  | 1.9                            |
| Hypertension  | 1  | 1  | 2.8                            |
| Age ≥75 y   | 1  | 2  | 4.0                            |
| Diabetes mellitus   | 1  | 3  | 5.9                            |
| Stroke/TIA/TE   | 2  | 4  | 8.5                            |
| Maximum score   | 6  | 5  | 12.5                           |
|   |  | 6  | 18.2                           |
| <b>CHA<sub>2</sub>DS<sub>2</sub>-VASc</b>   |  | <b>CHA<sub>2</sub>DS<sub>2</sub>-VASc†</b> |                                |
| Congestive HF   | 1  | 0  | 0                              |
| Hypertension  | 1  | 1  | 1.3                            |
| Age ≥75 y   | 2  | 2  | 2.2                            |
| Diabetes mellitus   | 1  | 3  | 3.2                            |
| Stroke/TIA/TE   | 2  | 4  | 4.0                            |
| Vascular disease (prior MI, PAD, or aortic plaque)                                      | 1  | 5  | 6.7                            |
| Age 65–74 y   | 1  | 6  | 9.8                            |
| Sex category (ie, female sex)   | 1  | 7  | 9.6                            |
| Maximum score   | 9  | 8  | 6.7                            |
|   |  | 9  | 15.20                          |

\*These adjusted stroke rates are based on data for hospitalized patients with AF and were published in 2001.<sup>89</sup> Because stroke rates are decreasing, actual stroke rates in contemporary nonhospitalized cohorts might vary from these estimates.

†Adjusted stroke rate scores are based on data from Lip and colleagues.<sup>16,30,68,90,91</sup> Actual rates of stroke in contemporary cohorts might vary from these estimates.

AF indicates atrial fibrillation; CHADS<sub>2</sub>, Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Prior Stroke or TIA or Thromboembolism (doubled); CHA<sub>2</sub>DS<sub>2</sub>-VASc, Congestive heart failure, Hypertension, Age ≥75 years (doubled), Diabetes mellitus, Prior Stroke or TIA or thromboembolism (doubled), Vascular disease, Age 65–74 years, Sex category; HF, heart failure; MI, myocardial infarction; PAD, peripheral artery disease; TE, thromboembolism; and TIA, transient ischemic attack.<sup>90,91</sup>

- recommended for patients with paroxysmal, persistent, or permanent AF.<sup>93-95</sup> (Level of Evidence: B)
2. Intravenous administration of a beta blocker or nondihydropyridine calcium channel blocker is recommended to slow the ventricular heart rate in the acute setting in patients without pre-excitation. In hemodynamically unstable patients, electrical cardioversion is indicated.<sup>96-99</sup> (Level of Evidence: B)
3. In patients who experience AF-related symptoms during activity, the adequacy of heart rate control should be assessed during exertion, adjusting pharmacological treatment as necessary to keep the ventricular rate within the physiological range. (Level of Evidence: C)

**Table 7. Dose Selection of Oral Anticoagulant Options for Patients With Nonvalvular AF and CKD (Based on Prescribing Information for the United States)\***

| Renal Function                | Warfarin <sup>92</sup>         | Dabigatran <sup>†74</sup>          | Rivaroxaban <sup>†75</sup>                         | Apixaban <sup>†76</sup>   |
|-------------------------------|--------------------------------|------------------------------------|--|---|
| Normal/mild impairment        | Dose adjusted for INR 2.0–3.0  | 150 mg BID (CrCl >30 mL/min)       | 20 mg QD with the evening meal (CrCl >50 mL/min)   | 5.0 or 2.5 mg BID‡  |
| Moderate impairment           | Dose adjusted for INR 2.0–3.0  | 150 mg BID (CrCl >30 mL/min)       | 15 mg QD with the evening meal (CrCl 30–50 mL/min) | 5.0 or 2.5 mg BID‡  |
| Severe impairment             | Dose adjusted for INR 2.0–3.0§ | 75 mg BID¶ (CrCl 15–30 mL/min)     | 15 mg QD with the evening meal (CrCl 15–30 mL/min) | No recommendation. See Section 4.2.2.2 in the full-text guideline¶  |
| End-stage CKD not on dialysis | Dose adjusted for INR 2.0–3.0§ | Not recommended¶ (CrCl <15 mL/min) | Not recommended¶ (CrCl <15 mL/min)                 | No recommendation. See Section 4.2.2.2 in the full-text guideline¶  |
| End-stage CKD on dialysis     | Dose adjusted for INR 2.0–3.0§ | Not recommended¶ (CrCl <15 mL/min) | Not recommended¶ (CrCl <15 mL/min)                 | No recommendation. See Section 4.2.2.2 in the full-text guideline¶# |

\*Renal function should be evaluated before initiation of direct thrombin or factor Xa inhibitors and should be reevaluated when clinically indicated and at least annually. CrCl should be measured using the Cockcroft-Gault method.

†The concomitant use of P-glycoprotein inducers or inhibitors with dabigatran or the concomitant use of dual P-glycoprotein and strong CYP3A4 inducers or inhibitors with either rivaroxaban or apixaban, particularly in the setting of CKD, may require dosing adjustment or avoidance of concomitant drug use (see the FDA drug label at [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/202155s002lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/202155s002lbl.pdf), Section 8.6 in the full-text guideline).

‡Use apixaban 2.5 mg BID if any 2 patient characteristics are present: Cr ≥1.5 mg/dL, ≥80 y of age, body weight ≤60 kg.<sup>76</sup> Apixaban is not recommended in patients with severe hepatic impairment.

§Dose-adjusted warfarin has been used, but observational data on safety and efficacy are conflicting.

¶Modeling studies suggest that dabigatran 75 mg BID might be safe for patients with CrCl 15–30 mL/min, but this has not been validated in a prospective cohort. Some countries outside the United States use 110 mg BID.<sup>74</sup>

¶¶No published studies support a dose for this level of renal function.

#In patients with end-stage CKD on stable hemodialysis, prescribing information indicates the use of apixaban 5 mg BID with dose reduction to 2.5 mg BID if the patient is ≥80 y of age or body weight is ≤60 kg.

AF indicates atrial fibrillation; BID, twice daily; CKD, chronic kidney disease; Cr, creatinine; CrCl, creatinine clearance; FDA, Food and Drug Administration; INR, international normalized ratio; and QD, once daily.

## Class IIa

1. A heart rate control (resting heart rate <80 beats per minute [bpm]) strategy is reasonable for symptomatic management of AF.<sup>95,100</sup> (Level of Evidence: B)
2. Intravenous amiodarone can be useful for rate control in critically ill patients without pre-excitation.<sup>101–103</sup> (Level of Evidence: B)
3. Atrioventricular (AV) nodal ablation with permanent ventricular pacing is reasonable to control heart rate when pharmacological therapy is inadequate and rhythm control is not achievable.<sup>104–106</sup> (Level of Evidence: B)

## Class IIb

1. A lenient rate-control strategy (resting heart rate <110 bpm) may be reasonable as long as patients remain asymptomatic and left ventricular systolic function is preserved.<sup>100</sup> (Level of Evidence: B)
2. Oral amiodarone may be useful for ventricular rate control when other measures are unsuccessful or contraindicated. (Level of Evidence: C)

## Class III: Harm

1. AV nodal ablation with permanent ventricular pacing should not be performed to improve rate control without prior attempts to achieve rate control with medications. (Level of Evidence: C)
2. Nondihydropyridine calcium channel antagonists should not be used in patients with decompensated

HF as these may lead to further hemodynamic compromise. (Level of Evidence: C)

3. In patients with pre-excitation and AF, digoxin, nondihydropyridine calcium channel antagonists, or intravenous amiodarone should not be administered as they may increase the ventricular response and may result in ventricular fibrillation.<sup>107</sup> (Level of Evidence: B)
4. Dronedarone should not be used to control the ventricular rate in patients with permanent AF as it increases the risk of the combined endpoint of stroke, myocardial infarction, systemic embolism, or cardiovascular death.<sup>108,109</sup> (Level of Evidence: B)

## 5. Rhythm Control: Recommendations

See Table 10 for a summary of recommendations for rhythm control.

### 5.1. Prevention of Thromboembolism

#### Class I

1. For patients with AF or atrial flutter of 48 hours' duration or longer, or when the duration of AF is unknown, anticoagulation with warfarin (INR 2.0 to 3.0) is recommended for at least 3 weeks before and 4 weeks after cardioversion, regardless of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score and the method (electrical or pharmacological) used to restore sinus rhythm.<sup>110–113</sup> (Level of Evidence: B)
2. For patients with AF or atrial flutter of more than 48 hours' duration or unknown duration that requires immediate cardioversion for hemodynamic instability,

**Table 8. Summary of Recommendations for Rate Control**

| Recommendations  | COR       | LOE | References |
|--|-----------|-----|------------|
| Control ventricular rate using a beta blocker or nondihydropyridine calcium channel antagonist for paroxysmal, persistent, or permanent AF   | I         | B   | 93–95      |
| IV beta blocker or nondihydropyridine calcium channel blocker is recommended to slow ventricular heart rate in the acute setting in patients without pre-excitation. In hemodynamically unstable patients, electrical cardioversion is indicated | I         | B   | 96–99      |
| For AF, assess heart rate control during exertion, adjusting pharmacological treatment as necessary  | I         | C   | N/A        |
| A heart rate control (resting heart rate <80 bpm) strategy is reasonable for symptomatic management of AF  | IIa       | B   | 95,100     |
| IV amiodarone can be useful for rate control in critically ill patients without pre-excitation   | IIa       | B   | 101–103    |
| AV nodal ablation with permanent ventricular pacing is reasonable when pharmacological therapy is inadequate and rhythm control is not achievable  | IIa       | B   | 104–106    |
| A lenient rate-control strategy (resting heart rate <110 bpm) may be reasonable when patients remain asymptomatic and LV systolic function is preserved  | IIb       | B   | 100        |
| Oral amiodarone may be useful for ventricular rate control when other measures are unsuccessful or contraindicated   | IIb       | C   | N/A        |
| AV nodal ablation should not be performed without prior attempts to achieve rate control with medications  | III: Harm | C   | N/A        |
| Nondihydropyridine calcium channel antagonists should not be used in decompensated HF  | III: Harm | C   | N/A        |
| With pre-excitation and AF, digoxin, nondihydropyridine calcium channel antagonists, or amiodarone should not be administered  | III: Harm | B   | 107        |
| Dronedarone should not be used to control ventricular rate with permanent AF   | III: Harm | B   | 108,109    |

AF indicates atrial fibrillation; AV, atrioventricular; bpm, beats per minute; COR, Class of Recommendation; HF, heart failure; IV, intravenous; LOE, Level of Evidence; LV, left ventricular; and N/A, not applicable.

anticoagulation should be initiated as soon as possible and continued for at least 4 weeks after cardioversion unless contraindicated. (*Level of Evidence: C*)

- For patients with AF or atrial flutter of less than 48 hours' duration and with high risk of stroke, intravenous heparin or LMWH, or administration of a factor Xa or direct thrombin inhibitor, is recommended as soon as possible before or immediately after cardioversion, followed by long-term anticoagulation therapy. (*Level of Evidence: C*)
- Following cardioversion for AF of any duration, the decision about long-term anticoagulation therapy should be based on the thromboembolic risk profile (Section 3). (*Level of Evidence: C*)

### Class IIa

- For patients with AF or atrial flutter of 48 hours' duration or longer or of unknown duration who have not been anticoagulated for the preceding 3 weeks, it is reasonable to perform transesophageal echocardiography before cardioversion and proceed with cardioversion if no left atrial thrombus is identified, including in the left atrial appendage, provided that anticoagulation is achieved before transesophageal echocardiography and maintained after cardioversion for at least 4 weeks.<sup>114</sup> (*Level of Evidence: B*)
- For patients with AF or atrial flutter of 48 hours' duration or longer or when duration of AF is unknown, anticoagulation with dabigatran, rivaroxaban, or apixaban is reasonable for at least 3 weeks before and 4 weeks after cardioversion.<sup>115–117</sup> (*Level of Evidence: C*)

### Class IIb

- For patients with AF or atrial flutter of less than 48 hours' duration who are at low thromboembolic risk, anticoagulation (intravenous heparin, LMWH, or a new oral anticoagulant) or no antithrombotic therapy may be considered for cardioversion, without the need for postcardioversion oral anticoagulation.<sup>118</sup> (*Level of Evidence: C*)

## 5.2. Direct-Current Cardioversion

### Class I

- In pursuing a rhythm-control strategy, cardioversion is recommended for patients with AF or atrial flutter as a method to restore sinus rhythm. If cardioversion is unsuccessful, repeated attempts at direct-current cardioversion may be made after adjusting the location of the electrodes, applying pressure over the electrodes or following administration of an antiarrhythmic medication.<sup>119</sup> (*Level of Evidence: B*)
- Cardioversion is recommended when a rapid ventricular response to AF or atrial flutter does not respond promptly to pharmacological therapies and contributes to ongoing myocardial ischemia, hypotension, or HF. (*Level of Evidence: C*)
- Cardioversion is recommended for patients with AF or atrial flutter and pre-excitation when tachycardia is associated with hemodynamic instability. (*Level of Evidence: C*)

**Table 9. Common Medication Dosage for Rate Control of AF**

|   | Intravenous Administration  | Usual Oral Maintenance Dose |
|---|---|-----------------------------|
| <b>Beta blockers</b>                                  |   |                             |
| Metoprolol tartrate                                   | 2.5–5.0 mg IV bolus over 2 min; up to 3 doses   | 25–100 mg BID               |
| Metoprolol XL (succinate)                             | N/A   | 50–400 mg QD                |
| Atenolol  | N/A   | 25–100 mg QD                |
| Esmolol   | 500 mcg/kg IV bolus over 1 min, then 50–300 mcg/kg/min IV   | N/A                         |
| Propranolol   | 1 mg IV over 1 min, up to 3 doses at 2-min intervals  | 10–40 mg TID or QID         |
| Nadolol   | N/A   | 10–240 mg QD                |
| Carvedilol  | N/A   | 3.125–25 mg BID             |
| Bisoprolol  | N/A   | 2.5–10 mg QD                |
| <b>Nondihydropyridine calcium channel antagonists</b> |   |                             |
| Verapamil   | 0.075–0.15 mg/kg IV bolus over 2 min; may give an additional 10.0 mg after 30 min if no response, then 0.005 mg/kg/min infusion | 180–480 mg QD (ER)          |
| Diltiazem   | 0.25 mg/kg IV bolus over 2 min, then 5–15 mg/h  | 120–360 mg QD (ER)          |
| <b>Digitalis glycosides</b>                           |   |                             |
| Digoxin   | 0.25 mg IV with repeat dosing to a maximum of 1.5 mg over 24 h  | 0.125–0.25 mg QD            |
| <b>Others</b>   |   |                             |
| Amiodarone*   | 300 mg IV over 1 h, then 10–50 mg/h over 24 h   | 100–200 mg QD               |

\*Multiple dosing schemes exist for the use of amiodarone.

AF indicates atrial fibrillation; BID, twice daily; ER, extended release; IV, intravenous; N/A, not applicable; QD, once daily; QID, 4 times a day; and TID, 3 times a day.

### Class IIa

1. It is reasonable to perform repeated cardioversions in patients with persistent AF, provided that sinus rhythm can be maintained for a clinically meaningful period between cardioversion procedures. Severity of AF symptoms and patient preference should be considered when embarking on a strategy requiring serial cardioversion procedures. (*Level of Evidence: C*)

### 5.3. Pharmacological Cardioversion

#### Class I

1. Flecainide, dofetilide, propafenone, and intravenous ibutilide are useful for pharmacological cardioversion of AF or atrial flutter, provided contraindications to the selected drug are absent.<sup>120–125</sup> (*Level of Evidence: A*)

#### Class IIa

1. Administration of oral amiodarone is a reasonable option for pharmacological cardioversion of AF.<sup>126,127</sup> (*Level of Evidence: A*)
2. Propafenone or flecainide (“pill-in-the-pocket”) in addition to a beta blocker or nondihydropyridine calcium channel antagonist is reasonable to terminate AF outside the hospital once this treatment has been observed to be safe in a monitored setting for selected patients.<sup>120</sup> (*Level of Evidence: B*)

#### Class III: Harm

1. Dofetilide therapy should not be initiated out of hospital because of the risk of excessive QT prolongation that can cause torsades de pointes.<sup>124,128</sup> (*Level of Evidence: B*)

### 5.4. Antiarrhythmic Drugs to Maintain Sinus Rhythm

Table 11 summarizes the range of antiarrhythmic drugs useful in the maintenance of sinus rhythm along with toxicity profiles.

#### Class I

1. Before initiating antiarrhythmic drug therapy, treatment of precipitating or reversible causes of AF is recommended. (*Level of Evidence: C*)
2. The following antiarrhythmic drugs are recommended in patients with AF to maintain sinus rhythm, depending on underlying heart disease and comorbidities (*Level of Evidence: A*):
  - a. Amiodarone<sup>129–132</sup>
  - b. Dofetilide<sup>124,128</sup>
  - c. Dronedarone<sup>133–135</sup>
  - d. Flecainide<sup>130,136</sup>
  - e. Propafenone<sup>130,137–140</sup>
  - f. Sotalol<sup>130,138,141</sup>
3. The risks of the antiarrhythmic drug, including proarrhythmia, should be considered before initiating therapy with each drug. (*Level of Evidence: C*)
4. Because of its potential toxicities, amiodarone should only be used after consideration of risks and when other agents have failed or are contraindicated.<sup>129,137,142–145</sup> (*Level of Evidence: C*)

#### Class IIa

1. A rhythm-control strategy with pharmacological therapy can be useful in patients with AF for the treatment of tachycardia-induced cardiomyopathy. (*Level of Evidence: C*)



**Table 10. Summary of Recommendations for Electrical and Pharmacological Cardioversion of AF and Atrial Flutter**

| Recommendations   | COR       | LOE | References |
|---|-----------|-----|------------|
| <b>Prevention of thromboembolism</b>  |           |     |            |
| With AF or atrial flutter for $\geq 48$ h, or unknown duration, anticoagulate with warfarin for at least 3 wk before and 4 wk after cardioversion   | I         | B   | 110–113    |
| With AF or atrial flutter for $> 48$ h or unknown duration, requiring immediate cardioversion, anticoagulate as soon as possible and continue for at least 4 wk   | I         | C   | N/A        |
| With AF or atrial flutter $< 48$ h and high stroke risk, IV heparin or LMWH, or factor Xa or direct thrombin inhibitor, is recommended before or immediately after cardioversion, followed by long-term anticoagulation   | I         | C   | N/A        |
| Following cardioversion of AF, long-term anticoagulation should be based on thromboembolic risk   | I         | C   | N/A        |
| With AF or atrial flutter for $\geq 48$ h or unknown duration and no anticoagulation for preceding 3 wk, it is reasonable to perform TEE before cardioversion and then cardiovert if no LA thrombus is identified, provided anticoagulation is achieved before TEE and maintained after cardioversion for at least 4 wk | IIa       | B   | 114        |
| With AF or atrial flutter $\geq 48$ h or unknown duration, anticoagulation with dabigatran, rivaroxaban, or apixaban is reasonable for $\geq 3$ wk before and 4 wk after cardioversion  | IIa       | C   | 115–117    |
| With AF or atrial flutter $< 48$ h and low thromboembolic risk, IV heparin, LMWH, a new oral anticoagulant, or no antithrombotic may be considered for cardioversion  | IIb       | C   | 118        |
| <b>Direct-current cardioversion</b>   |           |     |            |
| Cardioversion is recommended for AF or atrial flutter to restore sinus rhythm. If unsuccessful, cardioversion attempts may be repeated.   | I         | B   | 119        |
| Cardioversion is recommended for AF or atrial flutter with RVR, that does not respond to pharmacological therapies  | I         | C   | N/A        |
| Cardioversion is recommended for AF or atrial flutter and pre-excitation with hemodynamic instability   | I         | C   | N/A        |
| It is reasonable to repeat cardioversion in persistent AF when sinus rhythm can be maintained for a clinically meaningful time period between procedures  | IIa       | C   | N/A        |
| <b>Pharmacological cardioversion</b>  |           |     |            |
| Flecainide, dofetilide, propafenone, and IV ibutilide are useful for cardioversion of AF or atrial flutter, provided contraindications to the selected drug are absent  | I         | A   | 120–125    |
| Amiodarone is reasonable for pharmacological cardioversion of AF  | IIa       | A   | 126,127    |
| Propafenone or flecainide (“pill-in-the-pocket”) to terminate AF out of hospital is reasonable once observed to be safe in a monitored setting  | IIa       | B   | 120        |
| Dofetilide should not be initiated out of hospital  | III: Harm | B   | 124,128    |

AF indicates atrial fibrillation; COR, Class of Recommendation; IV, intravenous; LA, left atrial; LMWH, low-molecular-weight heparin; LOE, Level of Evidence; N/A, not applicable; RVR, rapid ventricular response; and TEE, transesophageal echocardiography.

### Class IIb

1. It may be reasonable to continue current antiarrhythmic drug therapy in the setting of infrequent, well-tolerated recurrences of AF when the drug has reduced the frequency or symptoms of AF. (Level of Evidence: C)

### Class III: Harm

1. Antiarrhythmic drugs for rhythm control should not be continued when AF becomes permanent (Level of Evidence: C), including dronedarone.<sup>108</sup> (Level of Evidence: B)
2. Dronedarone should not be used for treatment of AF in patients with New York Heart Association class III and IV HF or patients who have had an episode of decompensated HF in the past 4 weeks.<sup>109</sup> (Level of Evidence: B)

## 5.5. Upstream Therapy

### Class IIa

1. An angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker (ARB) is reasonable

for primary prevention of new-onset AF in patients with HF with reduced left ventricular ejection fraction.<sup>147–149</sup> (Level of Evidence: B)

### Class IIb

1. Therapy with an ACE inhibitor or ARB may be considered for primary prevention of new-onset AF in the setting of hypertension.<sup>150</sup> (Level of Evidence: B)
2. Statin therapy may be reasonable for primary prevention of new-onset AF after coronary artery surgery.<sup>151,152</sup> (Level of Evidence: A)

### Class III: No Benefit

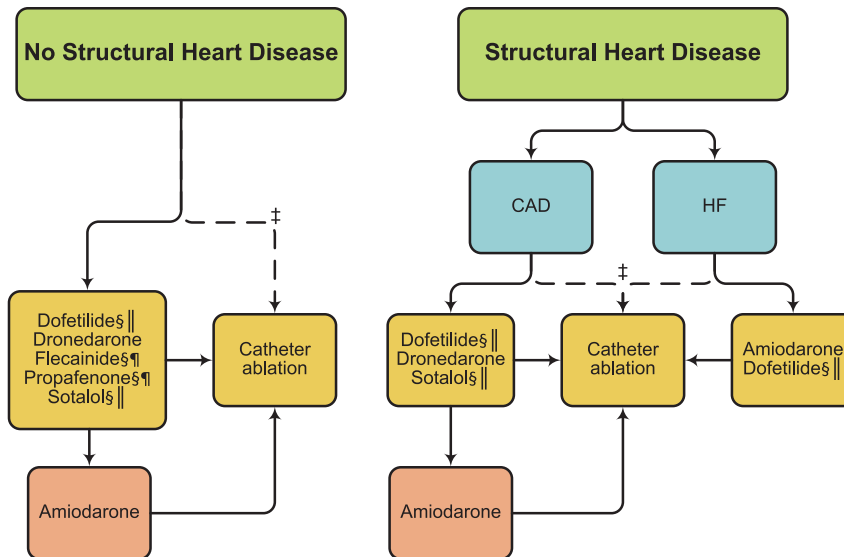
1. Therapy with an ACE inhibitor, ARB, or statin is not beneficial for primary prevention of AF in patients without cardiovascular disease.<sup>153</sup> (Level of Evidence: B)

**Table 11. Dosage and Safety Considerations for Maintenance of Sinus Rhythm in AF**

| Drug                       | Usual Doses  | Exclude/Use With Caution   | Major Pharmacokinetic Drug Interactions  |
|----------------------------|--|--|--|
| Vaughan Williams class IA  |  |  |  |
| Disopyramide               | <ul style="list-style-type: none"> <li>• Immediate release: 100–200 mg once every 6 h</li> <li>• Extended release: 200–400 mg once every 12 h</li> </ul>   | <ul style="list-style-type: none"> <li>• HF</li> <li>• Prolonged QT interval</li> <li>• Prostatism, glaucoma</li> <li>• Avoid other QT interval–prolonging drugs</li> </ul>  | <ul style="list-style-type: none"> <li>• Metabolized by CYP3A4: caution with inhibitors (eg, verapamil, diltiazem, ketoconazole, macrolide antibiotics, protease inhibitors, grapefruit juice) and inducers (eg, rifampin, phenobarbital, phenytoin)</li> </ul>  |
| Quinidine                  | <ul style="list-style-type: none"> <li>• 324–648 mg every 8 h</li> </ul>   | <ul style="list-style-type: none"> <li>• Prolonged QT interval</li> <li>• Diarrhea</li> </ul>  | <ul style="list-style-type: none"> <li>• Inhibits CYP2D6: ↑concentrations of tricyclic antidepressants, metoprolol, antipsychotics; ↓efficacy of codeine</li> <li>• Inhibits P-glycoprotein: ↑digoxin concentration</li> </ul>   |
| Vaughan Williams class IC  |  |  |  |
| Flecainide                 | <ul style="list-style-type: none"> <li>• 50–200 mg once every 12 h</li> </ul>  | <ul style="list-style-type: none"> <li>• Sinus or AV node dysfunction</li> <li>• HF</li> <li>• CAD</li> <li>• Atrial flutter</li> <li>• Infranodal conduction disease</li> <li>• Brugada syndrome</li> <li>• Renal or liver disease</li> </ul>   | <ul style="list-style-type: none"> <li>• Metabolized by CYP2D6 (inhibitors include quinidine, fluoxetine, tricyclics; also genetically absent in 7%–10% of population) and renal excretion (dual impairment can ↑↑plasma concentration)</li> </ul>   |
| Propafenone                | <ul style="list-style-type: none"> <li>• Immediate release: 150–300 mg once every 8 h</li> <li>• Extended release: 225–425 mg once every 12 h</li> </ul>   | <ul style="list-style-type: none"> <li>• Sinus or AV node dysfunction</li> <li>• HF</li> <li>• CAD</li> <li>• Atrial flutter</li> <li>• Infranodal conduction disease</li> <li>• Brugada syndrome</li> <li>• Liver disease</li> <li>• Asthma</li> </ul>  | <ul style="list-style-type: none"> <li>• Metabolized by CYP2D6 (inhibitors include quinidine, fluoxetine, tricyclics; also genetically absent in 7%–10% of population)—poor metabolizers have ↑beta blockade</li> <li>• Inhibits P-glycoprotein: ↑digoxin concentration</li> <li>• Inhibits CYP2C9: ↑warfarin concentration (↑INR 25%)</li> </ul>  |
| Vaughan Williams class III |  |  |  |
| Amiodarone                 | <ul style="list-style-type: none"> <li>• Oral: 400–600 mg daily in divided doses for 2–4 wk; maintenance typically 100–200 mg QD</li> <li>• IV: 150 mg over 10 min; then 1 mg/min for 6 h; then 0.5 mg/min for 18 h or change to oral dosing; after 24 h, consider decreasing dose to 0.25 mg/min</li> </ul> | <ul style="list-style-type: none"> <li>• Sinus or AV node dysfunction</li> <li>• Infranodal conduction disease</li> <li>• Lung disease</li> <li>• Prolonged QT interval</li> </ul>   | <ul style="list-style-type: none"> <li>• Inhibits most CYPs to cause drug interaction: ↑concentrations of warfarin (↑INR 0%–200%), statins, many other drugs</li> <li>• Inhibits P-glycoprotein: ↑digoxin concentration</li> </ul>   |
| Dofetilide                 | <ul style="list-style-type: none"> <li>• 125–500 mcg once every 12 h</li> </ul>  | <ul style="list-style-type: none"> <li>• Prolonged QT interval</li> <li>• Renal disease</li> <li>• Hypokalemia</li> <li>• Hypomagnesemia</li> <li>• Diuretic therapy</li> <li>• Avoid other QT interval–prolonging drugs</li> </ul>  | <ul style="list-style-type: none"> <li>• Primary renal elimination involving glomerular filtration and active tubular secretion: verapamil, HCTZ, cimetidine, ketoconazole, trimethoprim, prochlorperazine, and megestrol are contraindicated; discontinue amiodarone at least 3 mo before initiation</li> </ul>   |
| Dronedarone                | <ul style="list-style-type: none"> <li>• 400 mg once every 12 h</li> </ul>   | <ul style="list-style-type: none"> <li>• Bradycardia</li> <li>• HF</li> <li>• Long-standing persistent AF/flutter</li> <li>• Liver disease</li> <li>• Prolonged QT interval</li> </ul>   | <ul style="list-style-type: none"> <li>• Metabolized by CYP3A: caution with inhibitors (eg, verapamil, diltiazem, ketoconazole, macrolide antibiotics, protease inhibitors, grapefruit juice) and inducers (eg, rifampin, phenobarbital, phenytoin)</li> <li>• Inhibits CYP3A, CYP2D6, P-glycoprotein: ↑concentrations of some statins, sirolimus, tacrolimus, beta blockers, digoxin</li> </ul> |
| Sotalol                    | <ul style="list-style-type: none"> <li>• 40–160 mg once every 12 h</li> </ul>  | <ul style="list-style-type: none"> <li>• Prolonged QT interval</li> <li>• Renal disease</li> <li>• Hypokalemia</li> <li>• Hypomagnesemia</li> <li>• Diuretic therapy</li> <li>• Avoid other QT interval–prolonging drugs</li> <li>• Sinus or AV nodal dysfunction</li> <li>• HF</li> <li>• Asthma</li> </ul> | <ul style="list-style-type: none"> <li>• None (renal excretion)</li> </ul>   |

AF indicates atrial fibrillation; AV, atrioventricular; CAD, coronary artery disease; HCTZ, hydrochlorothiazide; HF, heart failure; INR, international normalized ratio; IV, intravenous; and QD, once daily.

Adapted with permission from Roden et al.<sup>146</sup>



**Figure 2.** Strategies for rhythm control in patients with paroxysmal\* and persistent AF. †Catheter ablation is only recommended as first-line therapy for patients with paroxysmal AF (Class IIa recommendation). †Drugs are listed alphabetically. ‡Depending on patient preference when performed in experienced centers. §Not recommended with severe LVH (wall thickness >1.5 cm). ¶Should be used with caution in patients at risk for torsades de pointes ventricular tachycardia. ¶Should be combined with AV nodal blocking agents. AF indicates atrial fibrillation; AV, atrioventricular; CAD, coronary artery disease; HF, heart failure; and LVH, left ventricular hypertrophy.

## 5.6. AF Catheter Ablation to Maintain Sinus Rhythm

Figure 2 shows an approach to the integration of antiarrhythmic drugs and catheter ablation of AF in patients without and with structural heart disease.

### Class I

1. AF catheter ablation is useful for symptomatic paroxysmal AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm-control strategy is desired.<sup>154–160</sup> (Level of Evidence: A)
2. Before consideration of AF catheter ablation, assessment of the procedural risks and outcomes relevant to the individual patient is recommended. (Level of Evidence: C)

### Class IIa

1. AF catheter ablation is reasonable for some patients with symptomatic persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication.<sup>157,161–163</sup> (Level of Evidence: A)
2. In patients with recurrent symptomatic paroxysmal AF, catheter ablation is a reasonable initial rhythm-control strategy before therapeutic trials of antiarrhythmic drug therapy, after weighing the risks and outcomes of drug and ablation therapy.<sup>164–166</sup> (Level of Evidence: B)

### Class IIb

1. AF catheter ablation may be considered for symptomatic long-standing (>12 months) persistent AF

refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm-control strategy is desired.<sup>154,167</sup> (Level of Evidence: B)

2. AF catheter ablation may be considered before initiation of antiarrhythmic drug therapy with a class I or III antiarrhythmic medication for symptomatic persistent AF when a rhythm-control strategy is desired. (Level of Evidence: C)

### Class III: Harm

1. AF catheter ablation should not be performed in patients who cannot be treated with anticoagulant therapy during and after the procedure. (Level of Evidence: C)
2. AF catheter ablation to restore sinus rhythm should not be performed with the sole intent of obviating the need for anticoagulation. (Level of Evidence: C)

## 5.7. Surgical Maze Procedures

### Class IIa

1. An AF surgical ablation procedure is reasonable for selected patients with AF undergoing cardiac surgery for other indications. (Level of Evidence: C)

### Class IIb

1. A stand-alone AF surgical ablation procedure may be reasonable for selected patients with highly symptomatic AF not well managed with other approaches.<sup>168</sup> (Level of Evidence: B)

## 6. Specific Patient Groups and AF: Recommendations

See Table 12 for a summary of recommendations for this section.

### 6.1. Hypertrophic Cardiomyopathy

#### Class I

1. Anticoagulation is indicated in patients with hypertrophic cardiomyopathy (HCM) with AF independent of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score.<sup>169,170</sup> (*Level of Evidence: B*)

#### Class IIa

1. Antiarrhythmic medications can be useful to prevent recurrent AF in patients with HCM. Amiodarone or disopyramide combined with a beta blocker or nondihydropyridine calcium channel antagonists are reasonable for therapy. (*Level of Evidence: C*)
2. AF catheter ablation can be beneficial in patients with HCM in whom a rhythm-control strategy is desired when antiarrhythmic drugs fail or are not tolerated.<sup>171-174</sup> (*Level of Evidence: B*)

#### Class IIb

1. Sotalol, dofetilide, and dronedarone may be considered for a rhythm-control strategy in patients with HCM.<sup>12</sup> (*Level of Evidence: C*)

### 6.2. AF Complicating Acute Coronary Syndromes

#### Class I

1. Urgent direct-current cardioversion of new-onset AF in the setting of acute coronary syndromes (ACS) is recommended for patients with hemodynamic compromise, ongoing ischemia, or inadequate rate control. (*Level of Evidence: C*)
2. Intravenous beta blockers are recommended to slow a rapid ventricular response to AF in patients with ACS who do not display HF, hemodynamic instability, or bronchospasm. (*Level of Evidence: C*)
3. For patients with ACS and AF with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 or greater, anticoagulation with warfarin is recommended unless contraindicated. (*Level of Evidence: C*)

#### Class IIb

1. Administration of amiodarone or digoxin may be considered to slow a rapid ventricular response in patients with ACS and AF associated with severe left ventricular dysfunction and HF or hemodynamic instability. (*Level of Evidence: C*)

2. Administration of nondihydropyridine calcium antagonists might be considered to slow a rapid ventricular response in patients with ACS and AF only in the absence of significant HF or hemodynamic instability. (*Level of Evidence: C*)

### 6.3. Hyperthyroidism

#### Class I

1. Beta blockers are recommended to control ventricular rate in patients with AF complicating thyrotoxicosis unless contraindicated. (*Level of Evidence: C*)
2. In circumstances in which a beta blocker cannot be used, a nondihydropyridine calcium channel antagonist is recommended to control the ventricular rate. (*Level of Evidence: C*)

### 6.4. Pulmonary Disease

#### Class I

1. A nondihydropyridine calcium channel antagonist is recommended to control the ventricular rate in patients with AF and chronic obstructive pulmonary disease. (*Level of Evidence: C*)
2. Direct-current cardioversion should be attempted in patients with pulmonary disease who become hemodynamically unstable as a consequence of new-onset AF. (*Level of Evidence: C*)

### 6.5. Wolff-Parkinson-White and Pre-Excitation Syndromes

#### Class I

1. Prompt direct-current cardioversion is recommended for patients with AF, Wolff-Parkinson-White syndrome, and rapid ventricular response who are hemodynamically compromised.<sup>175</sup> (*Level of Evidence: C*)
2. Intravenous procainamide or ibutilide to restore sinus rhythm or slow the ventricular rate is recommended for patients with pre-excited AF and rapid ventricular response who are not hemodynamically compromised.<sup>175</sup> (*Level of Evidence: C*)
3. Catheter ablation of the accessory pathway is recommended in symptomatic patients with pre-excited AF, especially if the accessory pathway has a short refractory period that allows rapid antegrade conduction.<sup>175</sup> (*Level of Evidence: C*)

#### Class III: Harm

1. Administration of intravenous amiodarone, adenosine, digoxin (oral or intravenous), or nondihydropyridine calcium channel antagonists (oral or intravenous) in patients with Wolff-Parkinson-White syndrome who have pre-excited AF is potentially harmful because these drugs accelerate the ventricular rate.<sup>176-178</sup> (*Level of Evidence: B*)



**Table 12. Summary of Recommendations for Specific Patient Groups and AF**

| Recommendations   | COR       | LOE | References      |
|---|-----------|-----|-----------------|
| <b>Hypertrophic cardiomyopathy</b>  |           |     |                 |
| Anticoagulation is indicated in HCM with AF independent of the CHA <sub>2</sub> DS <sub>2</sub> -VASc score   | I         | B   | 169,170         |
| Antiarrhythmic drugs can be useful to prevent recurrent AF in HCM. Amiodarone or disopyramide combined with a beta blocker or nondihydropyridine calcium channel antagonist are reasonable  | IIa       | C   | N/A             |
| AF catheter ablation can be beneficial for HCM to facilitate a rhythm-control strategy when antiarrhythmics fail or are not tolerated   | IIa       | B   | 171–174         |
| Sotalolol, dofetilide, and dronedarone may be considered for a rhythm-control strategy in HCM   | IIb       | C   | 12              |
| <b>AF complicating ACS</b>  |           |     |                 |
| Urgent cardioversion of new-onset AF in the setting of ACS is recommended for patients with hemodynamic compromise, ongoing ischemia, or inadequate rate control  | I         | C   | N/A             |
| IV beta blockers are recommended to slow RVR with ACS and no HF, hemodynamic instability, or bronchospasm   | I         | C   | N/A             |
| With ACS and AF with CHA <sub>2</sub> DS <sub>2</sub> -VASc score ≥2, anticoagulation with warfarin is recommended unless contraindicated   | I         | C   | N/A             |
| Amiodarone or digoxin may be considered to slow RVR with ACS and AF and severe LV dysfunction and HF or hemodynamic instability   | IIb       | C   | N/A             |
| Nondihydropyridine calcium antagonists might be considered to slow RVR with ACS and AF only in the absence of significant HF or hemodynamic instability   | IIb       | C   | N/A             |
| <b>Hyperthyroidism</b>  |           |     |                 |
| Beta blockers are recommended to control ventricular rate with AF complicating thyrotoxicosis unless contraindicated  | I         | C   | N/A             |
| When beta blockers cannot be used, a nondihydropyridine calcium channel antagonist is recommended to control ventricular rate   | I         | C   | N/A             |
| <b>Pulmonary diseases</b>   |           |     |                 |
| A nondihydropyridine calcium channel antagonist is recommended to control ventricular rate with AF and COPD   | I         | C   | N/A             |
| Cardioversion should be attempted for patients with pulmonary disease who become hemodynamically unstable with new-onset AF   | I         | C   | N/A             |
| <b>WPW and pre-excitation syndromes</b>   |           |     |                 |
| Cardioversion is recommended for patients with AF, WPW syndrome, and RVR who are hemodynamically compromised  | I         | C   | 175             |
| IV procainamide or ibutilide to restore sinus rhythm or slow ventricular rate is recommended for patients with pre-excited AF and RVR who are not hemodynamically compromised   | I         | C   | 175             |
| Catheter ablation of the accessory pathway is recommended in symptomatic patients with pre-excited AF, especially if the accessory pathway has a short refractory period  | I         | C   | 175             |
| IV amiodarone, adenosine, digoxin, or nondihydropyridine calcium channel antagonists in patients with WPW syndrome who have pre-excited AF is potentially harmful   | III: Harm | B   | 176–178         |
| <b>Heart failure</b>  |           |     |                 |
| A beta blocker or nondihydropyridine calcium channel antagonist is recommended for persistent or permanent AF in patients with HFpEF  | I         | B   | 95              |
| In the absence of preexcitation, an IV beta blocker (or a nondihydropyridine calcium channel antagonist with HFpEF) is recommended to slow ventricular response to AF in the acute setting, with caution in patients with overt congestion, hypotension, or HF/EF | I         | B   | 179–182         |
| In the absence of pre-excitation, IV digoxin or amiodarone is recommended to control heart rate acutely   | I         | B   | 103,180,183,184 |
| Assess heart rate during exercise and adjust pharmacological treatment in symptomatic patients during activity  | I         | C   | N/A             |
| Digoxin is effective to control resting heart rate with HF/EF   | I         | C   | N/A             |
| A combination of digoxin and beta blocker (or a nondihydropyridine calcium channel antagonist with HFpEF) is reasonable to control resting and exercise heart rate with AF  | IIa       | B   | 93,180          |
| It is reasonable to perform AV node ablation with ventricular pacing to control heart rate when pharmacological therapy is insufficient or not tolerated  | IIa       | B   | 95,185,186      |
| IV amiodarone can be useful to control heart rate with AF when other measures are unsuccessful or contraindicated   | IIa       | C   | N/A             |

(Continued)

Table 12. Continued

| Recommendations  | COR       | LOE | References |
|--|-----------|-----|------------|
| With AF and RVR causing or suspected of causing tachycardia-induced cardiomyopathy, it is reasonable to achieve rate control by AV nodal blockade or a rhythm-control strategy                                 | IIa       | B   | 187–189    |
| In patients with chronic HF who remain symptomatic from AF despite a rate-control strategy, it is reasonable to use a rhythm-control strategy  | IIa       | C   | N/A        |
| Amiodarone may be considered when resting and exercise heart rate cannot be controlled with a beta blocker (or a nondihydropyridine calcium channel antagonist with HFpEF) or digoxin, alone or in combination | IIb       | C   | N/A        |
| AV node ablation may be considered when rate cannot be controlled and tachycardia-mediated cardiomyopathy is suspected   | IIb       | C   | N/A        |
| AV node ablation should not be performed without a pharmacological trial to control ventricular rate   | III: Harm | C   | N/A        |
| For rate control, IV nondihydropyridine calcium channel antagonists, IV beta blockers, and dronedarone should not be given with decompensated HF   | III: Harm | C   | N/A        |
| Familial (genetic) AF  |           |     |            |
| For patients with AF and multigenerational family members with AF, referral to a tertiary care center for genetic counseling and testing may be considered   | IIb       | C   | N/A        |
| Postoperative cardiac and thoracic surgery   |           |     |            |
| A beta blocker is recommended to treat postoperative AF unless contraindicated   | I         | A   | 190–193    |
| A nondihydropyridine calcium channel blocker is recommended when a beta blocker is inadequate to achieve rate control with postoperative AF  | I         | B   | 194        |
| Preoperative amiodarone reduces AF with cardiac surgery and is reasonable as prophylactic therapy for patients at high risk of postoperative AF  | IIa       | A   | 195–197    |
| It is reasonable to restore sinus rhythm pharmacologically with ibutilide or direct-current cardioversion with postoperative AF  | IIa       | B   | 198        |
| It is reasonable to administer antiarrhythmic medications to maintain sinus rhythm with recurrent or refractory postoperative AF   | IIa       | B   | 194        |
| It is reasonable to administer antithrombotic medications for postoperative AF   | IIa       | B   | 199        |
| It is reasonable to manage new-onset postoperative AF with rate control and anticoagulation with cardioversion if AF does not revert spontaneously to sinus rhythm during follow-up                            | IIa       | C   | N/A        |
| Prophylactic sotalol may be considered for patients with AF risk after cardiac surgery   | IIb       | B   | 193,200    |
| Colchicine may be considered postoperatively to reduce AF after cardiac surgery  | IIb       | B   | 201        |

ACS indicates acute coronary syndromes; AF, atrial fibrillation; AV, atrioventricular; CHA<sub>2</sub>DS<sub>2</sub>-VASc, Congestive heart failure, Hypertension, Age  $\geq$ 75 years (doubled), Diabetes mellitus, Prior Stroke or TIA or thromboembolism (doubled), Vascular disease, Age 65 to 74 years, Sex category; COPD, chronic obstructive pulmonary disease; COR, Class of Recommendation; HCM, hypertrophic cardiomyopathy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HF/rEF, heart failure with reduced ejection fraction; IV, intravenous; LOE, Level of Evidence; LV, left ventricular; N/A, not applicable; RVR, rapid ventricular response; and WPW, Wolff-Parkinson-White.

## 6.6. Heart Failure

### Class I

1. Control of resting heart rate using either a beta blocker or nondihydropyridine calcium channel antagonist is recommended for patients with persistent or permanent AF and compensated HF with preserved ejection fraction (HFpEF).<sup>95</sup> (Level of Evidence: B)
2. In the absence of pre-excitation, intravenous beta-blocker administration (or a nondihydropyridine calcium channel antagonist in patients with HFpEF) is recommended to slow the ventricular response to AF in the acute setting, with caution needed in patients with overt congestion, hypotension, or HF with reduced left ventricular ejection fraction.<sup>179–182</sup> (Level of Evidence: B)
3. In the absence of pre-excitation, intravenous digoxin or amiodarone is recommended to control heart rate acutely in patients with HF.<sup>103,180,183,184</sup> (Level of Evidence: B)
4. Assessment of heart rate control during exercise and adjustment of pharmacological treatment to keep the

rate in the physiological range is useful in symptomatic patients during activity. (Level of Evidence: C)

5. Digoxin is effective to control resting heart rate in patients with HF with reduced ejection fraction. (Level of Evidence: C)

### Class IIa

1. A combination of digoxin and a beta blocker (or a nondihydropyridine calcium channel antagonist for patients with HFpEF) is reasonable to control resting and exercise heart rate in patients with AF.<sup>93,180</sup> (Level of Evidence: B)
2. It is reasonable to perform AV node ablation with ventricular pacing to control heart rate when pharmacological therapy is insufficient or not tolerated.<sup>95,185,186</sup> (Level of Evidence: B)
3. Intravenous amiodarone can be useful to control heart rate in patients with AF when other measures are unsuccessful or contraindicated. (Level of Evidence: C)

4. For patients with AF and rapid ventricular response causing or suspected of causing tachycardia-induced cardiomyopathy, it is reasonable to achieve rate control by either AV nodal blockade or a rhythm-control strategy.<sup>187–189</sup> (*Level of Evidence: B*)
5. For patients with chronic HF who remain symptomatic from AF despite a rate-control strategy, it is reasonable to use a rhythm-control strategy. (*Level of Evidence: C*)

#### Class IIb

1. Oral amiodarone may be considered when resting and exercise heart rate cannot be adequately controlled using a beta blocker (or a nondihydropyridine calcium channel antagonist in patients with HFpEF) or digoxin, alone or in combination. (*Level of Evidence: C*)
2. AV node ablation may be considered when the rate cannot be controlled and tachycardia-mediated cardiomyopathy is suspected. (*Level of Evidence: C*)

#### Class III: Harm

1. AV node ablation should not be performed without a pharmacological trial to achieve ventricular rate control. (*Level of Evidence: C*)
2. For rate control, intravenous nondihydropyridine calcium channel antagonists, intravenous beta blockers, and dronedarone should not be administered to patients with decompensated HF. (*Level of Evidence: C*)

#### 6.7. Familial (Genetic) AF

##### Class IIb

1. For patients with AF and multigenerational family members with AF, referral to a tertiary care center for genetic counseling and testing may be considered. (*Level of Evidence: C*)

#### 6.8. Postoperative Cardiac and Thoracic Surgery

##### Class I

1. Treating patients who develop AF after cardiac surgery with a beta blocker is recommended unless contraindicated.<sup>190–193</sup> (*Level of Evidence: A*)
2. A nondihydropyridine calcium channel blocker is recommended when a beta blocker is inadequate to achieve rate control in patients with postoperative AF.<sup>194</sup> (*Level of Evidence: B*)

##### Class IIa

1. Preoperative administration of amiodarone reduces the incidence of AF in patients undergoing cardiac surgery and is reasonable as prophylactic therapy for patients at high risk for postoperative AF.<sup>195–197</sup> (*Level of Evidence: A*)

2. It is reasonable to restore sinus rhythm pharmacologically with ibutilide or direct-current cardioversion in patients who develop postoperative AF, as advised for nonsurgical patients.<sup>198</sup> (*Level of Evidence: B*)
3. It is reasonable to administer antiarrhythmic medications in an attempt to maintain sinus rhythm in patients with recurrent or refractory postoperative AF, as advised for other patients who develop AF.<sup>194</sup> (*Level of Evidence: B*)
4. It is reasonable to administer antithrombotic medication in patients who develop postoperative AF, as advised for nonsurgical patients.<sup>199</sup> (*Level of Evidence: B*)
5. It is reasonable to manage well-tolerated, new-onset postoperative AF with rate control and anticoagulation with cardioversion if AF does not revert spontaneously to sinus rhythm during follow-up. (*Level of Evidence: C*)

#### Class IIb

1. Prophylactic administration of sotalol may be considered for patients at risk of developing AF after cardiac surgery.<sup>193,200</sup> (*Level of Evidence: B*)
2. Administration of colchicine may be considered for patients postoperatively to reduce AF after cardiac surgery.<sup>201</sup> (*Level of Evidence: B*)

### 7. Evidence Gaps and Future Research Directions

The past decade has seen substantial progress in the understanding of mechanisms of AF, clinical implementation of ablation for maintaining sinus rhythm, and new drugs for stroke prevention. Further studies are needed to better inform clinicians about the risks and benefits of therapeutic options for an individual patient. Continued research is needed into the mechanisms that initiate and sustain AF. It is hoped that better understanding of these tissue and cellular mechanisms will lead to more defined approaches to treating and abolishing AF. This includes new methodological approaches for AF ablation that would favorably impact survival, thromboembolism, and quality of life across different patient profiles. New pharmacological therapies are needed, including antiarrhythmic drugs that have atrial selectivity and drugs that target fibrosis, which will hopefully reach clinical evaluation. The successful introduction of new anticoagulants is encouraging, and further investigations will better inform clinical practices for optimizing beneficial applications and minimizing the risks of these agents, particularly in the elderly, in the presence of comorbidities and in the periprocedural period. Further investigations must be performed to better understand the links between the presence of AF, AF burden, and stroke risk, and to better define the relationship between AF and dementia. The roles of emerging surgical and procedural therapies to reduce stroke will be defined. Great promise lies in prevention. Future strategies for reversing the growing epidemic of AF will come from basic science and genetic, epidemiological, and clinical studies.

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KEY WORDS: AHA Scientific Statements ■ atrial fibrillation ■ cardio-renal physiology/pathophysiology ■ cardiovascular surgery: transplantation, ventricular assistance, cardiomyopathy ■ epidemiology ■ full revision ■ health policy and outcome research ■ other atrial fibrillation.



**Appendix 1. Author Relationships With Industry and Other Entities (Relevant)—2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation**

| Committee Member            | Employment   | Consultant  | Speaker's Bureau | Ownership/ Partnership/ Principal | Personal Research  | Institutional, Organizational, or Other Financial Benefit   | Expert Witness | Voting Recusals by Section*      |
|-----------------------------|--|---|------------------|-----------------------------------|--|---|----------------|----------------------------------|
| Craig T. January (Chair)    | University of Wisconsin-Madison—Professor of Medicine, Cardiovascular Medicine Division              | None  | None             | None                              | None   | None  | None           | None                             |
| L. Samuel Wann (Vice Chair) | Columbia St. Mary's Cardiovascular Physicians—Clinical Cardiologist                                  | <ul style="list-style-type: none"> <li>• United Healthcare</li> </ul>   | None             | None                              | None   | None  | None           | 4.1<br>5.0<br>6.3<br>7.3<br>7.10 |
| Joseph S. Alpert            | University of Arizona Health Sciences Center—Professor of Medicine                                   | <ul style="list-style-type: none"> <li>• Bayer Pharmaceuticals (DSMB)†</li> <li>• Boehringer Ingelheim</li> <li>• Daiichi-Sankyo</li> <li>• Johnson &amp; Johnson</li> <li>• Roche Diagnostics</li> <li>• Sanofi-aventis</li> <li>• Servier Pharmaceuticals</li> </ul>  | None             | None                              | None   | None  | None           | 4.1<br>5.0                       |
| Hugh Calkins                | Johns Hopkins Hospital—Professor of Medicine, Director of Electrophysiology                          | <ul style="list-style-type: none"> <li>• AtriCure</li> <li>• Biosense Webster</li> <li>• CareCore</li> <li>• iRhythm</li> <li>• Medtronic‡</li> <li>• Sanofi-aventis</li> </ul>   | None             | None                              | None   | None  | None           | 5.0<br>6.3<br>7.8                |
| Joaquin E. Cigarroa         | Oregon Health and Science University—Clinical Professor; Clinical Chief of Cardiology                | None  | None             | None                              | None   | None  | None           | None                             |
| Joseph C. Cleveland, Jr     | University of Colorado—Professor of Surgery; Denver Veterans Affairs Hospital—Chief, Cardiac Surgery | None  | None             | None                              | None   | None  | None           | None                             |
| Jamie B. Conti              | University of Florida—Professor of Medicine; Division of Cardiovascular Medicine—Chief               | None  | None             | None                              | <ul style="list-style-type: none"> <li>• Boston Scientific‡</li> <li>• Medtronic‡</li> <li>• St. Jude Medical‡</li> </ul>                              | <ul style="list-style-type: none"> <li>• Boston Scientific‡</li> <li>• Medtronic‡</li> <li>• St. Jude Medical‡</li> </ul> | None           | 5.0<br>6.3<br>7.8                |
| Patrick T. Ellinor          | Massachusetts General Hospital Heart Center, Cardiac Arrhythmia Service—Director                     | None  | None             | None                              | None   | None  | None           | None                             |
| Michael D. Ezekowitz        | Jefferson Medical College—Professor  | <ul style="list-style-type: none"> <li>• ARYx Therapeutics‡</li> <li>• AstraZeneca</li> <li>• Boehringer Ingelheim‡</li> <li>• Bristol-Myers Squibb‡</li> <li>• Daiichi-Sankyo‡</li> <li>• Eisai</li> <li>• Johnson &amp; Johnson‡</li> <li>• Medtronic‡</li> <li>• Pfizer‡</li> <li>• Portola‡</li> <li>• Sanofi-aventis‡</li> </ul> | None             | None                              | <ul style="list-style-type: none"> <li>• ARYx Therapeutics‡</li> <li>• Boehringer Ingelheim‡</li> <li>• Daiichi-Sankyo‡</li> <li>• Portola‡</li> </ul> | None  | None           | 4.1<br>5.0<br>6.3<br>7.8         |

(Continued)

Appendix 1. Continued

| Committee Member     | Employment  | Consultant               | Speaker's Bureau | Ownership/ Partnership/ Principal          | Personal Research   | Institutional, Organizational, or Other Financial Benefit | Expert Witness | Voting Recusals by Section* |
|----------------------|---|--------------------------|------------------|--|---------------------|---|----------------|-----------------------------|
| Michael E. Field     | University of Wisconsin School of Medicine and Public Health—Assistant Professor of Medicine, Director of Cardiac Arrhythmia Service            | None                     | None             | None                                       | None                | None  | None           | None                        |
| Katherine T. Murray  | Vanderbilt University School of Medicine, Divisions of Clinical Pharmacology and Cardiology—Professor of Medicine                               | None                     | None             | None                                       | • GlaxoSmithKline†  | None  | None           | None                        |
| Ralph L. Sacco       | University of Miami, Miller School of Medicine, Department of Neurology—Chairman  | • Boehringer Ingelheim†§ | None             | None                                       | None                | None  | None           | None                        |
| William G. Stevenson | Brigham and Women's Hospital, Cardiac Arrhythmia Program—Director; Harvard Medical School—Professor of Medicine                                 | None                     | None             | • Biosense Webster—Needle Ablation Patent† | • Biosense Webster‡ | None  | None           | 5.0<br>6.3<br>7.8           |
| Patrick J. Tchou     | Cleveland Clinic Foundation—Section of Cardiac Electrophysiology and Pacing, Department of Cardiovascular Medicine Heart and Vascular Institute | None                     | None             | None                                       | None                | None  | None           | None                        |
| Cynthia M. Tracy     | George Washington University Medical Center—Associate Director and Professor of Medicine  | None                     | None             | None                                       | None                | None  | None           | None                        |
| Clyde W. Yancy       | Northwestern University, Feinberg School of Medicine—Magerstadt Professor of Medicine; Division of Cardiology—Chief                             | None                     | None             | None                                       | None                | None  | None           | None                        |

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥\$10 000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

According to the ACC/AHA, a person has a *relevant* relationship IF: a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) the *person, or a member of the person's household*, has a reasonable potential for financial, professional, or other personal gain or loss as a result of the issues/content addressed in the *document*.

\*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply. Section numbers pertain to those in the full-text guideline.

†No financial benefit.

‡Indicates significant relationship.

§Dr. Sacco's relationship with Boehringer Ingelheim was added just after final balloting of the recommendations and before organizational review, so it was not relevant during the writing or voting stages of the guideline's development.

ACC indicates American College of Cardiology; AHA, American Heart Association; DSMB, data safety monitoring board; and HRS, Heart Rhythm Society.

**Appendix 2. Reviewer Relationships With Industry and Other Entities (Relevant)—2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation**

| Reviewer             | Representation  | Employment  | Consultant  | Speaker's Bureau   | Ownership/ Partnership/ Principal | Personal Research   | Institutional, Organizational, or Other Financial Benefit   | Expert Witness |
|----------------------|---|---|---|--|-----------------------------------|---|---|----------------|
| A. John Camm         | Official Reviewer—HRS                                       | St. George's, University of London—Professor of Clinical Cardiology     | <ul style="list-style-type: none"> <li>• Bayer</li> <li>• Biotronik</li> <li>• Boehringer Ingelheim</li> <li>• Boston Scientific</li> <li>• Bristol-Myers Squibb</li> <li>• ChanRx</li> <li>• Daiichi-Sankyo</li> <li>• Forest Laboratories</li> <li>• Johnson &amp; Johnson</li> <li>• Medtronic</li> <li>• Novartis*</li> <li>• Sanofi-aventis</li> <li>• Servier</li> <li>• St. Jude Medical</li> <li>• Takeda</li> <li>• Xention</li> </ul> | <ul style="list-style-type: none"> <li>• Pfizer</li> </ul> | None                              | <ul style="list-style-type: none"> <li>• Biotronik†</li> <li>• Servier (DSMB)</li> <li>• St. Jude Medical (DSMB)</li> </ul> | None  | None           |
| John Fisher          | Official Reviewer—AHA                                       | Albert Einstein College of Medicine—Professor of Medicine               | <ul style="list-style-type: none"> <li>• Medtronic*</li> </ul>  | None   | None                              | None  | <ul style="list-style-type: none"> <li>• Biotronik*</li> <li>• Boston Scientific*</li> <li>• Medtronic*</li> <li>• St. Jude Medical*</li> </ul> | None           |
| Jonathan L. Halperin | Official Reviewer—ACC/AHA Task Force on Practice Guidelines | Mt. Sinai Medical Center—Professor of Medicine                          | <ul style="list-style-type: none"> <li>• AstraZeneca</li> <li>• Bayer</li> <li>• Biotronik*</li> <li>• Boehringer Ingelheim*</li> <li>• Boston Scientific</li> <li>• Bristol-Myers Squibb</li> <li>• Daiichi-Sankyo</li> <li>• Janssen Pharmaceuticals</li> <li>• Johnson &amp; Johnson</li> <li>• Medtronic</li> <li>• Pfizer</li> <li>• Sanofi-aventis</li> </ul>   | None   | None                              | None  | None  | None           |
| Jose Joglar          | Official Reviewer—AHA                                       | UT Southwestern Medical Center—Associate Professor of Internal Medicine | None  | None   | None                              | None  | <ul style="list-style-type: none"> <li>• Medtronic*</li> <li>• St. Jude Medical*</li> </ul>   | None           |

(Continued)

Appendix 2. Continued

| Reviewer            | Representation   | Employment  | Consultant   | Speaker's Bureau   | Ownership/ Partnership/ Principal                              | Personal Research   | Institutional, Organizational, or Other Financial Benefit  | Expert Witness   |
|---------------------|--|---|--|--|--|---|--|--|
| Peter Kowey         | Official Reviewer—HRS  | Lankenau Medical Office Building—Chief of Cardiology  | <ul style="list-style-type: none"> <li>• Astellas†</li> <li>• AstraZeneca*</li> <li>• Boehringer Ingelheim*</li> <li>• Bristol-Myers Squibb</li> <li>• Daiichi-Sankyo*</li> <li>• Forest Laboratories</li> <li>• GlaxoSmithKline*</li> <li>• Johnson &amp; Johnson*</li> <li>• Medtronic</li> <li>• Merck*</li> <li>• Pfizer*</li> <li>• Portola</li> <li>• Sanofi-aventis*</li> </ul> | None   | <ul style="list-style-type: none"> <li>• CardioNet*</li> </ul> | None  | None   | None   |
| John Strobel        | Official Reviewer—ACC Board of Governors                       | Premier Healthcare, LLC—Clinical Cardiac EP; Indiana University—Assistant Clinical Professor of Medicine            | None   | <ul style="list-style-type: none"> <li>• Boehringer Ingelheim</li> <li>• Bristol-Myers Squibb</li> <li>• Pfizer</li> <li>• Sanofi-aventis</li> </ul> | None   | None  | None   | <ul style="list-style-type: none"> <li>• Plaintiff, ICD, 2012</li> </ul> |
| Stuart Winston      | Official Reviewer—ACC Board of Trustees                        | Michigan Heart, P. C. Michigan Heart and Vascular Institute—Cardiologist  | None   | None   | None   | None  | <ul style="list-style-type: none"> <li>• Biotronik†</li> <li>• Medtronic†</li> </ul>   | None   |
| James R. Edgerton   | Organizational Reviewer—STS                                    | The Heart Hospital Baylor Plano—Cardiologist; University of Texas at Arlington—Adjunct Assistant Clinical Professor | None   | <ul style="list-style-type: none"> <li>• AtriCure*</li> </ul>  | None   | None  | None   | None   |
| Jeffrey L. Anderson | Content Reviewer—ACC/AHA Task Force on Practice Guidelines     | Intermountain Medical Center—Associate Chief of Cardiology  | <ul style="list-style-type: none"> <li>• The Medicines Company</li> <li>• Sanofi-aventis</li> </ul>  | None   | None   | None  | None   | None   |
| Nancy Berg          | Content Reviewer—ACC EP Section Leadership Council             | Park Nicollet Health Services—Registered Nurse  | <ul style="list-style-type: none"> <li>• Medtronic</li> </ul>  | None   | None   | <ul style="list-style-type: none"> <li>• Mayo Clinic</li> </ul> | <ul style="list-style-type: none"> <li>• Medtronic†</li> </ul>   | None   |
| Emmanouil Brilakis  | Content Reviewer—ACC Interventional Section Leadership Council | UT Southwestern Medical School—Director, Cardiac Catheterization Laboratory, VA North Texas Healthcare System       | <ul style="list-style-type: none"> <li>• Boston Scientific*</li> <li>• Bridgepoint Medical*</li> <li>• Janssen Pharmaceuticals</li> <li>• Sanofi-aventis</li> <li>• St. Jude Medical</li> </ul>  | None   | None   | None  | <ul style="list-style-type: none"> <li>• Abbott Vascular†</li> <li>• AstraZeneca†</li> <li>• Cordis*</li> <li>• Daiichi-Sankyo*</li> <li>• Medtronic*</li> <li>• The Medicines Company*</li> </ul> | None   |

(Continued)



## Appendix 2. Continued

| Reviewer            | Representation   | Employment   | Consultant  | Speaker's Bureau | Ownership/ Partnership/ Principal | Personal Research  | Institutional, Organizational, or Other Financial Benefit  | Expert Witness  |
|---------------------|--|--|---|------------------|-----------------------------------|--|--|---|
| Yong-Mei Cha        | Content Reviewer—AHA                                       | Mayo Clinic, Division of Cardiovascular Diseases—Professor of Medicine   | None  | None             | None                              | None   | None   | None  |
| Jafna Cox           | Content Reviewer—ACC Board of Governors                    | Queen Elizabeth II Health Sciences Center—Professor, Departments of Medicine, Community Health, and Epidemiology | <ul style="list-style-type: none"> <li>• AstraZeneca</li> <li>• Bayer</li> <li>• Boehringer Ingelheim</li> </ul>  | None             | None                              | <ul style="list-style-type: none"> <li>• Bayer*</li> <li>• Pfizer*</li> </ul>  | None   | None  |
| Anne Curtis         | Content Reviewer   | University of Buffalo—Charles and Mary Bauer Professor of Medicine   | <ul style="list-style-type: none"> <li>• Biosense Webster</li> <li>• Bristol-Myers Squibb</li> <li>• Medtronic*</li> <li>• Pfizer</li> <li>• Sanofi-aventis</li> <li>• St. Jude Medical</li> </ul>  | None             | None                              | None   | None   | None  |
| Lesley H. Curtis    | Content Reviewer—ACC/AHA Task Force on Practice Guidelines | Duke University School of Medicine—Associate Professor of Medicine   | None  | None             | None                              | None   | <ul style="list-style-type: none"> <li>• Medtronic*</li> <li>• GE Healthcare*</li> <li>• GlaxoSmithKline*</li> <li>• Johnson &amp; Johnson*</li> </ul>   | None  |
| Kenneth Ellenbogen  | Content Reviewer   | VCU Medical Center—Director, Clinical EP Laboratory  | <ul style="list-style-type: none"> <li>• Biosense Webster</li> <li>• Biotronik*</li> <li>• Boston Scientific*</li> <li>• Cameron Health</li> <li>• Janssen Pharmaceuticals</li> <li>• Medtronic*</li> <li>• Sanofi-aventis</li> <li>• St. Jude Medical</li> </ul> | None             | None                              | <ul style="list-style-type: none"> <li>• Biosense Webster*</li> <li>• Boston Scientific*</li> <li>• Medtronic*</li> <li>• Sanofi-aventis*</li> </ul> | <ul style="list-style-type: none"> <li>• Biosense Webster*</li> <li>• Boston Scientific*</li> <li>• CardioNet</li> <li>• Medtronic*</li> <li>• Sanofi-aventis*</li> <li>• St. Jude Medical*</li> </ul> | <ul style="list-style-type: none"> <li>• Represented hospital, ICD, 2012</li> </ul> |
| N.A. Mark Estes III | Content Reviewer   | Tufts University School of Medicine—Professor of Medicine  | <ul style="list-style-type: none"> <li>• Boston Scientific*</li> <li>• Medtronic</li> </ul>   | None             | None                              | <ul style="list-style-type: none"> <li>• Boston Scientific</li> </ul>  | <ul style="list-style-type: none"> <li>• Boston Scientific*</li> <li>• Medtronic*</li> <li>• St. Jude Medical*</li> </ul>  | None  |
| Gregg Fonarow       | Content Reviewer   | Ahmanson—UCLA Cardiomyopathy Center, Division of Cardiology  | <ul style="list-style-type: none"> <li>• Boston Scientific</li> <li>• Johnson &amp; Johnson</li> <li>• The Medicines Company</li> <li>• Medtronic</li> </ul>  | None             | None                              | <ul style="list-style-type: none"> <li>• Novartis*</li> </ul>  | <ul style="list-style-type: none"> <li>• Medtronic†</li> </ul>   | None  |

(Continued)

Appendix 2. Continued

| Reviewer          | Representation   | Employment   | Consultant   | Speaker's Bureau  | Ownership/ Partnership/ Principal                                     | Personal Research  | Institutional, Organizational, or Other Financial Benefit                                   | Expert Witness   |
|-------------------|--|--|--|---|---|--|---|--|
| Valentin Fuster   | Content Reviewer   | Mount Sinai School of Medicine—<br>Director, Zena and Michael A. Wiener Cardiovascular Institute   | None   | None  | None  | None   | None  | None   |
| Richard Goodman   | Content Reviewer—<br>HHS                                       | HHS Office of the Assistant Secretary for Health and National Center for Chronic Disease Prevention and Health Promotion Centers for Disease Control and Prevention—<br>Senior Medical Advisor | None   | None  | None  | None   | None  | None   |
| Judith S. Hochman | Content Reviewer—<br>ACC/AHA Task Force on Practice Guidelines | New York University School of Medicine—<br>Clinical Chief of Cardiology  | <ul style="list-style-type: none"> <li>• GlaxoSmithKline</li> <li>• Janssen Pharmaceuticals</li> </ul>           | None  | None  | None   | None  | None   |
| Warren Jackman    | Content Reviewer   | University of Oklahoma Health Sciences Center for Cardiac Arrhythmia Research Institute—<br>Professor of Medicine  | <ul style="list-style-type: none"> <li>• Biosense Webster*</li> <li>• Endosense*</li> <li>• VytronUS*</li> </ul> | <ul style="list-style-type: none"> <li>• Biotronik*</li> <li>• Boston Scientific*</li> </ul>  | <ul style="list-style-type: none"> <li>• Rhythmia Medical*</li> </ul> | <ul style="list-style-type: none"> <li>• Boston Scientific*</li> <li>• Rhythmia Medical*</li> </ul>      | None  | None   |
| Samuel Jones      | Content Reviewer—<br>ACC Board of Governors                    | USUHS—<br>Associate Professor of Medicine  | None   | None  | None  | None   | <ul style="list-style-type: none"> <li>• Medtronic†</li> <li>• St. Jude Medical†</li> </ul> | None   |
| Paulus Kirchhof   | Content Reviewer—<br>HRS                                       | University of Birmingham, School of Clinical and Experimental Medicine—<br>Chair in Cardiovascular Medicine  | None   | None  | None  | <ul style="list-style-type: none"> <li>• Sanofi-aventis (DSMB)</li> </ul>                                | None  | None   |
| Bradley Knight    | Content Reviewer   | Northwestern Medical Center Division of Cardiology—<br>Director of Clinical Cardiac EP   | <ul style="list-style-type: none"> <li>• Boston Scientific</li> <li>• Cameron Health†</li> </ul>                 | <ul style="list-style-type: none"> <li>• Biosense Webster</li> <li>• Biotronik</li> <li>• Boston Scientific</li> <li>• Medtronic</li> </ul> | None  | <ul style="list-style-type: none"> <li>• Catheter Robotics</li> </ul>                                    | None  | <ul style="list-style-type: none"> <li>• Plaintiff, pacemaker surgery, 2012</li> </ul> |
| Austin Kutscher   | Content Reviewer   | Hunterdon Cardiovascular Associates—<br>Cardiologist   | <ul style="list-style-type: none"> <li>• Pfizer</li> </ul>   | <ul style="list-style-type: none"> <li>• Bristol-Myers Squibb</li> <li>• Forest Laboratories</li> </ul>                                     | None  | <ul style="list-style-type: none"> <li>• Boehringer Ingelheim</li> <li>• Bristol-Myers Squibb</li> </ul> | None  | None   |

(Continued)

Appendix 2. Continued

| Reviewer              | Representation                                     | Employment   | Consultant   | Speaker's Bureau   | Ownership/ Partnership/ Principal | Personal Research  | Institutional, Organizational, or Other Financial Benefit | Expert Witness |
|-----------------------|--|--|--|--|-----------------------------------|--|---|----------------|
| Gregory Michaud       | Content Reviewer                                   | Harvard Medical School, Brigham and Women's Hospital—Assistant Professor   | <ul style="list-style-type: none"> <li>• Boston Scientific</li> <li>• Medtronic</li> </ul>   | None   | None                              | <ul style="list-style-type: none"> <li>• Boston Scientific*</li> <li>• St. Jude Medical*</li> </ul>  | None  | None           |
| William Miles         | Content Reviewer                                   | University of Florida, Department of Medicine—Cardiologist                 | None   | None   | None                              | <ul style="list-style-type: none"> <li>• Medtronic—STOP-AF (PI)</li> <li>• Zoll Medical</li> </ul>   | None  | None           |
| Simone Musco          | Content Reviewer—ACC Board of Governors            | Saint Patrick Hospital—Cardiologist  | None   | <ul style="list-style-type: none"> <li>• Bristol-Myers Squibb</li> <li>• Sanofi-aventis</li> </ul> | None                              | None   | None  | None           |
| Brian Olshansky       | Content Reviewer—ACC EP Section Leadership Council | University of Iowa Hospital—Professor of Medicine                          | <ul style="list-style-type: none"> <li>• Boehringer Ingelheim</li> <li>• Boston Scientific</li> <li>• Guidant</li> <li>• Medtronic*</li> <li>• Sanofi-aventis</li> </ul>   | None   | None                              | <ul style="list-style-type: none"> <li>• Boston Scientific (DSMB)</li> <li>• Sanofi-aventis (DSMB)</li> </ul>  | None  | None           |
| Huseyin Murat Ozdemir | Content Reviewer—AIG                               | Gazi University School of Medicine—Professor of Cardiology                 | <ul style="list-style-type: none"> <li>• Bayer</li> <li>• Boehringer Ingelheim</li> <li>• Bristol-Myers Squibb</li> <li>• Novartis</li> <li>• Pfizer</li> <li>• Servier</li> </ul>   | None   | None                              | None   | None  | None           |
| Douglas Packer        | Content Reviewer                                   | Mayo Foundation St. Mary's Hospital Complex—Professor of Medicine          | <ul style="list-style-type: none"> <li>• Abiomed†</li> <li>• Biosense Webster†</li> <li>• Boston Scientific†</li> <li>• InfoBionic†</li> <li>• Johnson &amp; Johnson†</li> <li>• Medtronic†</li> <li>• Janssen Pharmaceuticals†</li> <li>• Sanofi-aventis†</li> <li>• Siemens†</li> <li>• St. Jude Medical†</li> </ul> | None   | None                              | <ul style="list-style-type: none"> <li>• Biosense Webster*</li> <li>• Boston Scientific*</li> <li>• CardioFocus</li> <li>• Endosense*</li> <li>• Hansen Medical</li> <li>• Medtronic*</li> <li>• Siemens</li> <li>• St. Jude Medical*</li> <li>• Thermedical*</li> </ul> | • St. Jude Medical*                                       | None           |
| Richard Page          | Content Reviewer                                   | University of Wisconsin Hospital and Clinics—Chair, Department of Medicine | None   | None   | None                              | None   | None  | None           |
| Robert Page           | Content Reviewer—AHA PharmD                        | University of Colorado School of Pharmacy—Associate Professor              | None   | None   | None                              | None   | None  | None           |

(Continued)

## Appendix 2. Continued

| Reviewer            | Representation  | Employment  | Consultant  | Speaker's Bureau | Ownership/ Partnership/ Principal   | Personal Research  | Institutional, Organizational, or Other Financial Benefit                              | Expert Witness |
|---------------------|---|---|---|------------------|---|--|--|----------------|
| Gurusher Panjrath   | Content Reviewer—ACC HF and Transplant Section Leadership Council                         | George Washington University—Assistant Professor of Medicine                                    | None  | None             | None  | None   | None   | None           |
| Eric Prystowsky     | Content Reviewer—HRS  | St. Vincent Hospital and Health Center—Director, Clinical EP Laboratory                         | <ul style="list-style-type: none"> <li>• Bard*</li> <li>• Medtronic*</li> </ul> | None             | <ul style="list-style-type: none"> <li>• CardioNet*</li> <li>• Topera*</li> <li>• Stereotaxis*</li> </ul> | None   | <ul style="list-style-type: none"> <li>• CardioNet*</li> <li>• Stereotaxis*</li> </ul> | None           |
| Pasala Ravichandran | Content Reviewer—ACC Surgeons' Council  | Oregon Health and Science University—Associate Professor  | None  | None             | None  | None   | None   | None           |
| Anitra Romfh        | Content Reviewer—ACC Adult Congenital and Pediatric Cardiology Section Leadership Council | Children's Hospital Boston—Cardiologist   | None  | None             | None  | None   | None   | None           |
| Elizabeth Saarel    | Content Reviewer—ACC Adult Congenital and Pediatric Cardiology Section Leadership Council | University of Utah School of Medicine and Primary Children's Medical Center—Associate Professor | None  | None             | None  | None   | None   | None           |
| Marcel Salive       | Content Reviewer—HHS  | National Institute on Aging, Division of Geriatrics and Clinical Gerontology                    | None  | None             | <ul style="list-style-type: none"> <li>• Express Scripts*</li> </ul>                                      | None   | None   | None           |
| John Sapp           | Content Reviewer—HRS  | Dalhousie University—Director of EP   | <ul style="list-style-type: none"> <li>• Biosense Webster</li> </ul>            | None             | None  | <ul style="list-style-type: none"> <li>• Biosense Webster*</li> <li>• St. Jude Medical*</li> </ul> | None   | None           |
| Frank W. Sellke     | Content Reviewer—ACC/AHA Task Force on Practice Guidelines                                | Cardiovascular Institute, Rhode Island Hospital and Lifespan—Chief of Cardiothoracic Surgery    | None  | None             | None  | None   | <ul style="list-style-type: none"> <li>• The Medicines Company</li> </ul>              | None           |
| Win-Kuang Shen      | Content Reviewer—ACC/AHA Task Force on Practice Guidelines                                | Mayo Clinic Arizona—Professor of Medicine, Consultant   | None  | None             | None  | None   | None   | None           |

(Continued)



## Appendix 2. Continued

| Reviewer            | Representation                          | Employment   | Consultant  | Speaker's Bureau  | Ownership/ Partnership/ Principal   | Personal Research   | Institutional, Organizational, or Other Financial Benefit   | Expert Witness |
|---------------------|---|--|---|---|---|---|---|----------------|
| David J. Slotwiner  | Content Reviewer                        | Long Island Jewish Medical Center—Associate Director, EP Laboratory  | None  | None  | None  | None  | • Boston Scientific   | None           |
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| Albert Waldo        | Content Reviewer— HRS                   | Case Western Reserve University— The Walter H. Pritchard Professor of Cardiology, Professor of Medicine, and Professor of Biomedical Engineering | <ul style="list-style-type: none"> <li>• Abbott Vascular</li> <li>• AtriCure</li> <li>• Biosense Webster</li> <li>• Biotronik</li> <li>• Daiichi-Sankyo</li> <li>• Gilead</li> <li>• Janssen Pharmaceuticals*</li> <li>• Merck</li> <li>• Pfizer</li> <li>• Sanofi-aventis</li> </ul> | <ul style="list-style-type: none"> <li>• Janssen Pharmaceuticals*</li> <li>• Sanofi-aventis*</li> </ul> | None  | <ul style="list-style-type: none"> <li>• Biotronik</li> <li>• Daiichi-Sankyo</li> <li>• Gilead*</li> <li>• St. Jude Medical*</li> </ul> | None  | None           |

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\*Significant relationship.

†No financial benefit.

ACC indicates American College of Cardiology; AHA, American Heart Association; AIG, Association of International Governors; DSMB, data safety monitoring board; EP, electrophysiology; HF, heart failure; HHS, Health and Human Services; HRS, Heart Rhythm Society; ICD, implantable cardioverter-defibrillator; PI, principal investigator; STOP-AF, Sustained Treatment Of Paroxysmal Atrial Fibrillation; STS, Society of Thoracic Surgeons; UCLA, University of California, Los Angeles; USUHS, Uniformed Services University of the Health Sciences; UT, University of Texas; VA, Veterans Affairs; and VCU, Virginia Commonwealth University.

**Appendix 3. Initial Clinical Evaluation in Patients With AF**

## Minimum Evaluation

- |  |  |
|--|--|
| 1. History and physical examination, to define         | <ul style="list-style-type: none"> <li>• Presence and nature of symptoms associated with AF</li> <li>• Clinical type of AF (paroxysmal, persistent, or permanent)</li> <li>• Onset of first symptomatic attack or date of discovery of AF</li> <li>• Frequency, duration, precipitating factors, and modes of initiation or termination of AF</li> <li>• Response to any pharmacological agents that have been administered</li> <li>• Presence of any underlying heart disease or reversible conditions (eg, hyperthyroidism or alcohol consumption)</li> </ul> |
| 2. ECG, to identify                                    | <ul style="list-style-type: none"> <li>• Rhythm (verify AF)</li> <li>• LVH</li> <li>• P-wave duration and morphology or fibrillatory waves</li> <li>• Pre-excitation</li> <li>• Bundle-branch block</li> <li>• Prior MI</li> <li>• Other atrial arrhythmias</li> <li>• To measure and follow R-R, QRS, and QT intervals in conjunction with antiarrhythmic drug therapy</li> </ul>   |
| 3. TTE, to identify                                    | <ul style="list-style-type: none"> <li>• VHD</li> <li>• LA and RA size</li> <li>• LV and RV size and function</li> <li>• Peak RV pressure (pulmonary hypertension)</li> <li>• LV hypertrophy</li> <li>• LA thrombus (low sensitivity)</li> <li>• Pericardial disease</li> </ul>  |
| 4. Blood tests of thyroid, renal, and hepatic function | <ul style="list-style-type: none"> <li>• For a first episode of AF</li> <li>• When ventricular rate is difficult to control</li> </ul>   |

## Additional Testing (1 or several tests may be necessary)

- |                                  |   |
|----------------------------------|---|
| 1. 6-min walk test               | <ul style="list-style-type: none"> <li>• If adequacy of rate control is in question</li> <li>• If adequacy of rate control is in question</li> <li>• To reproduce exercise-induced AF</li> <li>• To exclude ischemia before treatment of selected patients with a type IC* antiarrhythmic drug</li> </ul>             |
| 2. Exercise testing              |   |
| 3. Holter or event monitoring    | <ul style="list-style-type: none"> <li>• If diagnosis of type of arrhythmia is in question</li> <li>• As a means of evaluating rate control</li> </ul>  |
| 4. TEE                           | <ul style="list-style-type: none"> <li>• To identify LA thrombus (in LAA)</li> <li>• To guide cardioversion</li> </ul>  |
| 5. Electrophysiological study    | <ul style="list-style-type: none"> <li>• To clarify the mechanism of wide-QRS-complex tachycardia</li> <li>• To identify a predisposing arrhythmia such as atrial flutter or paroxysmal supraventricular tachycardia</li> <li>• To seek sites for curative AF ablation or AV conduction block/modification</li> </ul> |
| 6. Chest radiograph, to evaluate | <ul style="list-style-type: none"> <li>• Lung parenchyma, when clinical findings suggest an abnormality</li> <li>• Pulmonary vasculature, when clinical findings suggest an abnormality</li> </ul>  |

\*Type IC refers to the Vaughan Williams classification of antiarrhythmic drugs.

AF indicates atrial fibrillation; AV, atrioventricular; ECG, electrocardiogram; LA, left atrial; LAA, left atrial appendage; LV, left ventricular; LVH, left ventricular hypertrophy; MI, myocardial infarction; RA, right atrial; RV, right ventricular; TEE, transesophageal echocardiography; TTE, transthoracic echocardiogram; and VHD, valvular heart disease.

Adapted with permission from Fuster et al.<sup>5</sup>