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

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PII: S0735-1097(14)01739-2

DOI: 10.1016/j.jacc.2014.03.021

Reference: JAC 20030

To appear in: *Journal of the American College of Cardiology*

Please cite this article as: January CT, Wann LS, Alpert JS, Field ME, Calkins H, Murray KT, Cleveland Jr JC, Sacco RL, Cigarroa JE, Stevenson WG, Conti JB, Tchou PJ, Ellinor PT, Tracy CM, Ezekowitz MD, Yancy CW, 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary, *Journal of the American College of Cardiology* (2014), doi: 10.1016/j.jacc.2014.03.021.

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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This document was approved by the American College of Cardiology Board of Trustees, the American Heart Association Science Advisory and Coordinating Committee, and the Heart Rhythm Society Board of Trustees in March 2014.

The American College of Cardiology requests that this document be cited as follows: January CT, Wann LS, Alpert JS, Calkins H, Cleveland JC, Cigarroa JE, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014; ●●:●●●●–●●●●.

This article is copublished in *Circulation.*

Copies: This document is available on the World Wide Web sites of the American College of Cardiology (www.cardiosource.org), the American Heart Association (my.americanheart.org), and the Heart Rhythm Society (www.hrsonline.org). A copy of the document is available at http://my.americanheart.org/statements by selecting either the “By Topic” link or the “By Publication Date” link. For copies of this document, please contact the Elsevier Inc. Reprint Department, fax (212) 633-3820, e-mail reprints@elsevier.com.

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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 procedure, 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 (1). 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 for which sparse data are available, 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.

A new addition to this methodology is 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* (GDMT) to represent optimal medical therapy as defined by ACC/AHA guideline (primarily Class I)-recommended therapies. This new term, GDMT, is used herein and throughout subsequent guidelines.

Because the ACC/AHA practice guidelines address patient populations (and clinicians) residing in North America, drugs that are not currently available in North America 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 (http://jaccjacc.cardiosource.com/DataSupp/2014_AF_GL_RWI_Table_Comprehensive_Only_0319.pdf). 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 these guidelines 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 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* (2, 3). 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 (4) for additional guidance and details about atrial fibrillation (AF), since the Executive Summary contains only the recommendations.

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

Table 1. Applying Classification of Recommendations and Level of Evidence

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* 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
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; should not be performed/ administered/ other; is not useful/ beneficial/ effective COR III: Harm: potentially harmful; causes harm; associated with excess morbidity/mortality; should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B 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.

1. Introduction

1.1. Methodology and Evidence Review

The recommendations listed in this document are, whenever possible, evidence based. An extensive evidence review, focusing on 2006 to the present, was conducted through October 2012, and selected other references through February 2014. The relevant data are included in evidence tables in the Data Supplement available online at (http://jaccjacc.cardiosource.com/DataSupp/MASTER_2014_AF_Evidence_Table_Supplement_03182014.pdf). Searches were extended to studies, reviews, and other evidence conducted in human subjects and that were published in English from 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 committee reviewed documents related to the subject matter 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); and 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 has provided representation. The writing committee also included a representative from the Society of Thoracic Surgery. The rigorous methodological policies and procedures noted in the Preamble act to 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, the AHA, and the Heart Rhythm Society, as well as 1 reviewer from the Society of Thoracic Surgeons, and 43 individual content reviewers (from the ACC Electrophysiology Committee, Adult Congenital and Pediatric Cardiology Council, Association of International Governors, Heart Failure and Transplant Council, Imaging Council, Interventional Council, Surgeons Council, and the HRS 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 Surgery.

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 review articles, along with evolving treatment strategies and new drugs. This guideline supersedes the "2006 ACC/AHA/ESC Guideline for the Management of Patients With Atrial Fibrillation" and the 2 subsequent focused updates from 2011 (5-8). 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 was reviewed by the writing committee and incorporated where appropriate (9).

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 is a list of these publications and statements deemed pertinent to this effort and is intended for use as a resource.

Table 2. Associated Guidelines and Statements

Title	Organization	Publication Year/ Reference
Guidelines		
Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII)	NHLBI	2003 (10)
Assessment of Cardiovascular Risk in Asymptomatic Adults	ACCF/AHA	2010 (11)
Coronary Artery Bypass Graft Surgery	ACCF/AHA	2011 (12)
Hypertrophic Cardiomyopathy	ACCF/AHA	2011 (13)
Percutaneous Coronary Intervention	ACCF/AHA/SCAI	2011 (14)
Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease	AHA/ACCF	2011 (15)
Atrial Fibrillation*	CCS	2011 (16)
Atrial Fibrillation	ESC	2012 (17)
Device-Based Therapy	ACCF/AHA/HRS	2012 (18)
Stable Ischemic Heart Disease	ACCF/AHA/ACP/ AATS/PCNA/SCAI/STS	2012 (19)
Antithrombotic Therapy	ACCP	2012 (20)
Heart Failure	ACCF/AHA	2013 (21)
ST-Elevation Myocardial Infarction	ACCF/AHA	2013 (22)
Non–ST-Elevation Acute Coronary Syndromes	ACC/AHA	2014 In Press (23)
Valvular Heart Disease	AHA/ACC	2014 (24)
Assessment of Cardiovascular Risk	ACC/AHA	2013 (25)
Lifestyle Management to Reduce Cardiovascular Risk	AHA/ACC	2013 (26)
Management of Overweight and Obesity in Adults	AHA/ACC/TOS	2013 (27)
Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults	ACC/AHA	2013 (28)

Statements		
Treatment of Atrial Fibrillation	AHRQ	2012 (9)
Oral Antithrombotic Agents for the Prevention of Stroke in Nonvalvular Atrial Fibrillation: a Science Advisory for Healthcare Professionals	AHA/ASA	2012 (29)
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 (30)

*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; ACCF, American College of Cardiology Foundation; ACP, American College of Physicians; ACCP, American College of Chest Physicians; AHA, American Heart Association; AHRQ, Agency for Healthcare Research and Quality; ASA, American Stroke Association; AF, atrial fibrillation; 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 Cardiac Angiography and Interventions; STS, Society of Thoracic Surgeons, and TOS, The Obesity Society.

2. Clinical Characteristics and Evaluation of AF

2.1. AF—Classification

AF may be described by the duration of episodes and a simplified scheme revised from the 2006 AF full-text guideline is given in Table 3 (30, 31). Implanted loop recorders, pacemakers, and defibrillators offer the possibility to report frequency, rate, and duration of abnormal atrial rhythms including AF (32, 33). Episodes often increase in frequency and duration over time.

Table 3. AF Definitions: A Simplified Scheme

Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 d of onset. • Episodes may recur with variable frequency.
Persistent AF	• Continuous AF that is sustained >7 d.
Longstanding persistent AF	• Continuous AF of >12 mo duration.
Permanent AF	• Permanent AF is used when there has been a joint decision by the patient and clinician to cease further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of the AF. • Acceptance of AF may change as symptoms, the efficacy of therapeutic interventions, and patient and clinician preferences evolve.

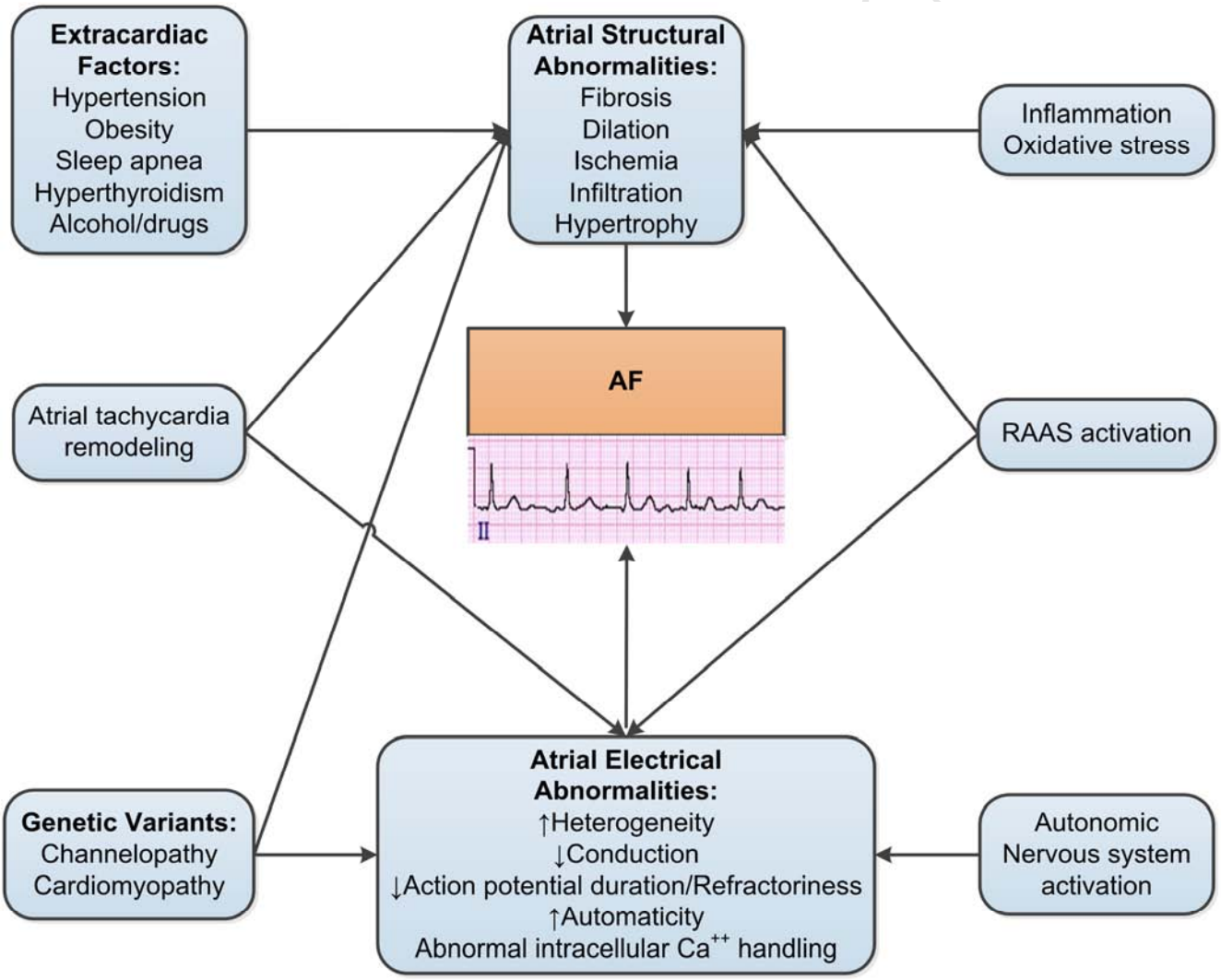
Nonvalvular AF	• AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

AF indicates atrial fibrillation.

2.2. Mechanisms of AF and Pathophysiology

AF occurs when structural and/or electrophysiologic abnormalities alter atrial tissue to promote abnormal impulse formation and/or propagation (Figure 1). These abnormalities are caused by diverse pathophysiologic mechanisms (5-8, 30, 34, 35), such that AF represents a final common phenotype for multiple disease pathways and mechanisms that are incompletely understood.

Figure 1. Mechanisms of AF



AF indicates atrial fibrillation; Ca^{++} ionized calcium; and RAAS, renin-angiotensin-aldosterone system.

2.3. Risk Factors and Associated Heart Disease

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

Table 4. Selected Risk Factors and Biomarkers for AF

Clinical Risk Factors	References
Increasing age	(36)
Hypertension	(36)
Diabetes mellitus	(36)
MI	(36)
VHD	(36)
HF	(36, 37)
Obesity	(38-40)
Obstructive sleep apnea	(40)
Cardiothoracic surgery	(41)
Smoking	(42)
Exercise	(43-45)
Alcohol use	(46-48)
Hyperthyroidism	(49-51)
Increased pulse pressure	(52)
European ancestry	(53)
Family history	(54)
Genetic variants	(55-58)
Electrocardiographic	
LVH	(59)
Echocardiographic	
LA enlargement	(59, 60)
Decreased LV fractional shortening	(59)
Increased LV wall thickness	(59)
Biomarkers	
Increased CRP	(61, 62)
Increased BNP	(63, 64)

AF indicates atrial fibrillation; BNP , B-type natriuretic peptide; CRP, C-reactive protein; 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 RRs 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 (65-68).** ***(Level of Evidence: B)***
3. **In patients with nonvalvular AF, the CHA_2DS_2-VASc score is recommended for assessment of stroke risk (69-71).** ***(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 (72-74).** ***(Level of Evidence: B)***
5. **For patients with nonvalvular AF with prior stroke, transient ischemic attack (TIA), or a CHA_2DS_2-VASc score of 2 or greater, oral anticoagulants are recommended. Options include: warfarin (INR 2.0 to 3.0) (69-71)** ***(Level of Evidence: A)*****, dabigatran (75)** ***(Level of Evidence: B)*****, rivaroxaban (76)** ***(Level of Evidence: B)*****, or apixaban (77).** ***(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 (78-80).** ***(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. **Re-evaluation 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 (UFH) 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 regarding 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 newer anticoagulants for procedures, decisions about bridging therapy (LMWH or UFH) 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 prior to initiation of direct thrombin or factor Xa inhibitors and should be re-evaluated when clinically indicated and at least annually (81-83).** ***(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)***

Class IIa

1. **For patients with nonvalvular AF and a CHA_2DS_2-VASc score of 0, it is reasonable to omit antithrombotic therapy (81, 82).** ***(Level of Evidence: B)***
2. **For patients with nonvalvular AF with a CHA_2DS_2-VASc score of 2 or greater and who have end-stage CKD (creatinine clearance [CrCl] <15 mL/min) or are on hemodialysis, it is reasonable to prescribe warfarin (INR 2.0 to 3.0) for oral anticoagulation (83).** ***(Level of Evidence: B)***

Class IIb

1. **For patients with nonvalvular AF and a CHA_2DS_2-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_2DS_2-VASc scores of 2 or greater, treatment with reduced doses of direct thrombin or factor Xa inhibitors may be considered (e.g., 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)***

4. **Following coronary revascularization (percutaneous or surgical) in patients with AF and a CHA_2DS_2-VASc score of 2 or greater, it may be reasonable to use clopidogrel (75 mg once daily) concurrently with oral anticoagulants but without aspirin (84).** ***(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 hemodialysis because of the lack of evidence from clinical trials regarding the balance of risks and benefits (75-77, 85-87).** ***(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 (88).** ***(Level of Evidence: B)***

*See the 2011 percutaneous coronary intervention guideline for type of stent and duration of dual antiplatelet therapy recommendations (14).

Table 5. Summary of Recommendations for Prevention of Thromboembolism in Patients With AF

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
Antithrombotic therapy selection based on risk of thromboembolism	I	B	(65-68)
CHA_2DS_2-VASc score recommended to assess stroke risk	I	B	(69-71)
Warfarin recommended with mechanical heart valves**.** Target INR intensity should be based on the type and location of prosthesis	I	B	(72-74)
With prior stroke, TIA, or CHA_2DS_2-VASc score ≥2, oral anticoagulants recommended. Options include:			
• Warfarin	I	A	(69-71)
• Dabigatran, rivaroxaban, or apixaban	I	B	(75-77)
With warfarin, determine INR at least weekly during initiation and monthly when stable	I	A	(78-80)
Direct thrombin or factor Xa inhibitor recommended, if unable to maintain therapeutic INR	I	C	N/A
Re-evaluate the need for anticoagulation at periodic intervals	I	C	N/A
Bridging therapy with LMWH or UFH recommended with a mechanical heart valve if warfarin is interrupted. Bridging therapy should balance risks of stroke and bleeding	I	C	N/A
Without a mechanical heart valve, bridging therapy decisions should balance stroke and bleeding risks against the duration of time patient will not be anticoagulated	I	C	N/A
Evaluate renal function prior to initiation of direct thrombin or factor Xa inhibitors, and re-evaluate when clinically indicated and at least annually	I	B	(81-83)
For atrial flutter, antithrombotic therapy is recommended as for AF	I	C	N/A
With nonvalvular AF and CHA_2DS_2-VASc score of 0, it is reasonable to omit antithrombotic therapy	IIa	B	(81, 82)
With CHA_2DS_2-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	(83)

With nonvalvular AF and a CHA_2DS_2-VASc score of 1, no antithrombotic therapy or treatment with an oral anticoagulant or aspirin may be considered	IIb	C	N/A
With moderate-to-severe CKD and CHA_2DS_2-VASc scores of ≥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
Following coronary revascularization in patients with CHA_2DS_2-VASc score of ≥2, it may be reasonable to use clopidogrel concurrently with oral anticoagulants, but without aspirin	IIb	B	(84)
Direct thrombin, dabigatran, and factor Xa inhibitor, rivaroxaban, are not recommended with AF and end-stage CKD or on hemodialysis because of the lack of evidence from clinical trials regarding the balance of risks and benefits	III: No Benefit	C	(75-77, 85-87)
Direct thrombin inhibitor, dabigatran, should not be used with a mechanical heart valve	III: Harm	B	(88)

*See the 2011 percutaneous coronary intervention guideline for type of stent and duration of dual antiplatelet therapy recommendations (14).
AF indicates atrial fibrillation; BMS, bare-metal stent; CKD, chronic kidney disease; COR, Class of Recommendation; CrCl, creatinine clearance; DAPT, dual antiplatelet therapy; INR, international normalized ratio; LOE, Level of Evidence; LMWH, low-molecular-weight heparin; N/A, not applicable; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; and UFH, unfractionated heparin.

3.2. Risk Stratification Schemes ($CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED)

One meta-analysis has stratified ischemic stroke risk among patients with nonvalvular AF using either the AF Investigators (89), the Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Prior Stroke or TIA or Thromboembolism (doubled) ($CHADS_2$) (90), or the Congestive heart failure, Hypertension, Age ≥75 years (doubled), Diabetes mellitus, Prior Stroke or TIA or thromboembolism (doubled), Vascular disease, Age 65 to74 years, Sex category (CHA_2DS_2-VASc) point score systems (Table 6) (17).

Table 6. Comparison of the $CHADS_2$ and CHA_2DS_2-VASc Risk Stratification Scores for Subjects With Nonvalvular AF

Definition and Scores for $CHADS_2$ and CHA_2DS_2-VASc	
	Score
$CHADS_2$ acronym	
Congestive HF	1
Hypertension	1
Age ≥75 y	1
Diabetes mellitus	1
Stroke/TIA/TE	2
Maximum Score	6
CHA_2DS_2-VASc acronym	
Congestive HF	1
Hypertension	1
Age ≥75 y	2

Stroke Risk Stratification With the $CHADS_2$ and CHA_2DS_2-VASc scores	
	Adjusted stroke rate (% per y)
$CHADS_2$ acronym*	
0	1.9%
1	2.8%
2	4.0%
3	5.9%
4	8.5%
5	12.5%
6	18.2%
CHA_2DS_2-VASc acronym†	
0	0%
1	1.3%

Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Age 65–74 y	1
Sex category (i.e., female sex)	1
Maximum Score	9

2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
7	9.6%
8	6.7%
9	15.20%

* These adjusted-stroke rates are based on data for hospitalized patients with AF and were published in 2001 (90). 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 (91). Actual rates of stroke in contemporary cohorts might vary from these estimates.

AF indicates atrial fibrillation; $CHADS_2$, Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Prior Stroke or TIA or Thromboembolism (doubled); CHA_2DS_2-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; LV, left ventricular; MI, myocardial infarction; PAD, peripheral artery disease; TE, thromboembolic; and TIA, transient ischemic attack (91, 92).

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 (83).

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** (93)	**Dabigatran**† (75)	**Rivaroxaban**† (76)	**Apixaban**† (77)
Normal/Mild Impairment	Dose adjusted for INR 2.0–3.0	150 mg BID (CrCl >30 mL/min)	20 mg HS (CrCl >50 mL/min)	5.0 or 2.5 mg BID‡
Moderate Impairment	Dose adjusted for INR 2.0–3.0	150 mg BID or 75 mg BID§ (CrCl >30 mL/min)	15 mg HS (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 HS (CrCl 15–30 mL/min)	No recommendation, See section 4.2.2.2.¶
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.¶
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.¶#

*Renal function should be evaluated prior to initiation of direct thrombin or factor Xa inhibitors and should be re-evaluated when clinically indicated and at least annually. CrCl should be measured using the Crockoft-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; Section 8.6).

‡Use apixaban 2.5 mg BID if any 2 patient characteristics present: Cr ≥1.5 mg/dL, ≥80 years of age, body weight ≤60 kg (77). Apixaban is not recommended in patients with severe hepatic impairment.
§Modeling studies suggest that dabigatran 75 mg BID might be safe for patients with CrCl 15–30mL/min, but this has not been validated in a prospective cohort. Some countries outside the United States use 110 mg BID (75).
‖Dose-adjusted warfarin has been used, but observational data regarding safety and efficacy are conflicting.
¶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 either ≥80 years of age or body weight ≤60 kg.

AF indicates atrial fibrillation; BID, twice daily; CKD, chronic kidney disease; Cr, creatinine; CrCl, creatinine clearance; HS, once daily in evening with food; and INR, international normalized ratio.

3.4. Cardiac Surgery—LAA Occlusion/Excision: Recommendation

Class IIb

1. **Surgical excision of the LAA 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 AF rate control common medication dosages.

Class I

1. **Control of the ventricular rate using a beta blocker or nondihydropyridine calcium channel antagonist is recommended for patients with paroxysmal, persistent, or permanent AF (94-96). *(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 (97-100). *(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)***

Class IIa

1. **A heart rate control (resting heart rate <80 bpm) strategy is reasonable for symptomatic management of AF (96, 101). *(Level of Evidence: B)***
2. **Intravenous amiodarone can be useful for rate control in critically ill patients without pre-excitation (102-104). *(Level of Evidence: B)***
3. **AV nodal ablation with permanent ventricular pacing is reasonable to control the heart rate when pharmacological therapy is inadequate and rhythm control is not achievable (105-107). *(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 LV systolic function is preserved (101). *(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 (108).** ***(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, MI, systemic embolism, or cardiovascular death (109, 110).** ***(Level of Evidence: B)***

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	(94-96)
IV beta blockers or nondihydropyridine calcium channel blocker 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	(97-100)
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	(96, 101)
IV amiodarone can be useful for rate control in critically ill patients without pre-excitation	IIa	B	(102-104)
AV nodal ablation with permanent ventricular pacing is reasonable when pharmacological management is inadequate and rhythm control is not achievable	IIa	B	(105-107)
Lenient rate control strategy (resting heart rate <110 bpm) may be reasonable with asymptomatic patients and LV systolic function is preserved	IIb	B	(101)
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	(108)
Dronedarone should not be used to control ventricular rate with permanent AF	III: Harm	B	(109, 110)

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

Table 9. AF Rate Control Common Medication Dosage

	Intravenous Administration	Usual Oral Maintenance Dose
Beta blockers		
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
Nondihydropyridine calcium channel antagonists		
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)
Digitalis glycosides		
Digoxin	0.25 mg IV with repeat dosing to a maximum of 1.5 mg over 24 h	0.125–0.25 mg QD
Others		
Amiodarone	300 mg IV over 1 h, then 10–50 mg/h over 24 h	100–200 mg QD

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

5. Rhythm Control

See Table 10 for a summary of recommendations from this section.

5.1. Thromboembolism Prevention: Recommendations

Class I

1. **For patients with AF or atrial flutter of 48-hour 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 prior to and 4 weeks after cardioversion, regardless of the CHA_2DS_2-VASc score and the method (electrical or pharmacological) used to restore sinus rhythm (111-114).** ***(Level of Evidence: B)***
2. **For patients with AF or atrial flutter of more than 48 hours or unknown duration that requires immediate cardioversion for hemodynamic instability, anticoagulation should be initiated as soon as possible and continued for at least 4 weeks after cardioversion unless contraindicated.** ***(Level of Evidence: C)***
3. **For patients with AF or atrial flutter of less than 48-hour 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)***
4. **Following cardioversion for AF of any duration, the decision regarding long-term anticoagulation therapy should be based on the thromboembolic risk profile (Section 4).** ***(Level of Evidence: C)***

Class IIa

1. **For patients with AF or atrial flutter of 48-hour duration or longer or of unknown duration who have not been anticoagulated for the preceding 3 weeks, it is reasonable to perform a TEE prior to cardioversion and proceed with cardioversion if no LA thrombus is identified, including in the LAA, provided that anticoagulation is achieved before TEE and maintained after cardioversion for at least 4 weeks (115).** ***(Level of Evidence: B)***

2. **For patients with AF or atrial flutter of 48-hour duration or longer, or when the duration of AF is unknown, anticoagulation with dabigatran, rivaroxaban, or apixaban is reasonable for at least 3 weeks prior to and 4 weeks after cardioversion (116-118).** ***(Level of Evidence: C)***

Class IIb

1. **For patients with AF or atrial flutter of less than 48-hour 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 (119).** ***(Level of Evidence: C)***

5.2. Direct-Current Cardioversion: Recommendations

Class I

1. **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 direct-current cardioversion attempts may be made after adjusting the location of the electrodes or applying pressure over the electrodes, or following administration of an antiarrhythmic medication (120).** ***(Level of Evidence: B)***
2. **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)***
3. **Cardioversion is recommended for patients with AF or atrial flutter and pre-excitation when tachycardia is associated with hemodynamic instability.** ***(Level of Evidence: C)***

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: Recommendations

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 (121-126).** ***(Level of Evidence: A)***

Class IIa

1. **Administration of oral amiodarone is a reasonable option for pharmacological cardioversion of AF (127, 128).** ***(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 (121).** ***(Level of Evidence: B)***

Class III: Harm

1. **Dofetilide therapy should not be initiated out of hospital owing to the risk of excessive QT prolongation that can cause torsades de pointes (125, 129).** ***(Level of Evidence: B)***

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

Recommendations	COR	LOE	References
Thromboembolism prevention			
With AF or atrial flutter for ≥48 h, or unknown duration, anticoagulate with warfarin for at least 3 wk prior to and 4 wk after cardioversion	I	B	(111-114)
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 ≥48 h or unknown duration and no anticoagulation for preceding 3 wk, it is reasonable to perform a TEE prior to 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	(115)
With AF or atrial flutter ≥48 h, or unknown duration, anticoagulation with dabigatran, rivaroxaban, or apixaban is reasonable for ≥3 wk prior to and 4 wk after cardioversion	IIa	C	(116-118)
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	(119)
Direct-current cardioversion			
Cardioversion is recommended for AF or atrial flutter to restore sinus rhythm. If unsuccessful, repeat cardioversion attempts may be made	I	B	(120)
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 cardioversions in persistent AF when sinus rhythm is maintained for a clinically meaningful time period between procedures	IIa	C	N/A
Pharmacological cardioversion			
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	(121-126)
Amiodarone is reasonable for pharmacological cardioversion of AF	IIa	A	(127, 128)
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	(121)
Dofetilide should not be initiated out of hospital	III: Harm	B	(125, 129)

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

5.4. Antiarrhythmic Drugs to Maintain Sinus Rhythm: Recommendations

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 (130-133)**
    b. **Dofetilide (125, 129)**
    c. **Dronedarone (134-136)**

   d. **Flecainide (131, 137)**
   e. **Propafenone (131, 138-141)**
   f. **Sotalol (131, 139, 142)**
3. **The risks of the antiarrhythmic drug, including proarrhythmia, should be considered before initiating therapy with each drug.** ***(Level of Evidence: C)***
4. **Owing to its potential toxicities, amiodarone should only be used after consideration of risks and when other agents have failed or are contraindicated. (130, 138, 143-146).** ***(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)***

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 (109).** ***(Level of Evidence: B)***
2. **Dronedarone should not be used for treatment of AF in patients with New York Heart Association (NYHA) class III and IV HF or patients who have had an episode of decompensated HF in the past 4 weeks (110).** ***(Level of Evidence: B)***

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

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	• Immediate release: 100–200 mg once every 6 h • Extended release: 200–400 mg once every 12 h	• HF • Prolonged QT interval • Prostatism, glaucoma • Avoid other QT interval-prolonging drugs	• Metabolized by *CYP3A4*: caution with inhibitors (e.g., verapamil, diltiazem, ketoconazole, macrolide antibiotics, protease inhibitors, grapefruit juice) and inducers (e.g., rifampin, phenobarbital, phenytoin)
Quinidine	• 324–648 mg every 8 h	• Prolonged QT interval • Diarrhea	• Inhibits *CYP2D6*: ↑concentrations of tricyclic antidepressants, metoprolol, antipsychotics; ↓efficacy of codeine • Inhibits P-glycoprotein: ↑digoxin concentration
Vaughan Williams Class IC			
Flecainide	• 50–200 mg once every 12 h	• Sinus or AV node dysfunction • HF • CAD • Atrial flutter • Infranodal conduction	• Metabolized by *CYP2D6* (inhibitors include quinidine, fluoxetine, tricyclics; also genetically absent in 7%–10% of population) and renal excretion (dual impairment can ↑↑plasma

		• disease • Brugada syndrome • Renal or liver disease	concentration)
Propafenone	• Immediate release: 150–300 mg once every 8 h • Extended release: 225–425 mg once every 12 h	• Sinus or AV node dysfunction • HF • CAD • Atrial flutter • Infranodal conduction disease • Brugada syndrome • Liver disease • Asthma	• Metabolized by *CYP2D6* (inhibitors include quinidine, fluoxetine, tricyclics; also genetically absent in 7%–10% of population)—poor metabolizers have ↑beta blockade • Inhibits P-glycoprotein: ↑digoxin concentration • Inhibits *CYP2C9*: ↑warfarin concentration (↑INR 25%)
Vaughan Williams Class III			
Amiodarone	• Oral: 400–600 mg daily in divided doses for 2-4 wk; maintenance typically 100-200 mg QD • 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	• Sinus or AV node dysfunction • Infranodal conduction disease • Lung disease • Prolonged QT interval	• Inhibits most CYPs to cause drug interaction:↑concentrations of warfarin (↑INR 0%–200%), statins, many other drugs • Inhibits P-glycoprotein: ↑digoxin concentration
Dofetilide	• 125–500 mcg once every 12 h	• Prolonged QT interval • Renal disease • Hypokalemia • Diuretic therapy • Avoid other QT interval prolonging drugs	• Metabolized by *CYP3A*: verapamil, HCTZ, cimetidine, ketoconazole, trimethoprim, prochlorperazine, and megestrol are contraindicated; discontinue amiodarone at least 3 mo before initiation
Dronedarone	• 400 mg once every 12 h	• Bradycardia • HF • Long-standing persistent AF/flutter • Liver disease • Prolonged QT interval	• Metabolized by *CYP3A*: caution with inhibitors (e.g., verapamil, diltiazem, ketoconazole, macrolide antibiotics, protease inhibitors, grapefruit juice) and inducers (e.g., rifampin, phenobarbital, phenytoin) • Inhibits *CYP3A*, *CYP2D6*, P-glycoprotein: ↑concentrations of some statins, sirolimus, tacrolimus, beta blockers, digoxin
Sotalol	• 40–160 mg once every 12 h	• Prolonged QT interval • Renal disease • Hypokalemia • Diuretic therapy • Avoid other QT interval prolonging drugs • Sinus or AV nodal dysfunction • HF • Asthma	• None (renal excretion)

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 from Brunton et al. (147).

5.5. Upstream Therapy: Recommendations

Class IIa

1. **An ACE inhibitor or angiotensin-receptor blocker (ARB) is reasonable for primary prevention of new-onset AF in patients with HF with reduced LVEF (148-150).** ***(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 (34, 151).** ***(Level of Evidence: B)***
2. **Statin therapy may be reasonable for primary prevention of new-onset AF after coronary artery surgery (152, 153).** ***(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 (34, 154).** ***(Level of Evidence: B)***

5.6. AF Catheter Ablation to Maintain Sinus Rhythm: Recommendations

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 (155-161).** ***(Level of Evidence: A)***
2. **Prior to 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 selected patients with symptomatic persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication (158, 162-164).** ***(Level of Evidence: A)***
2. **In patients with recurrent symptomatic paroxysmal AF, catheter ablation is a reasonable initial rhythm control strategy prior to therapeutic trials of antiarrhythmic drug therapy, after weighing risks and outcomes of drug and ablation therapy (165-167).** ***(Level of Evidence: B)***

Class IIb

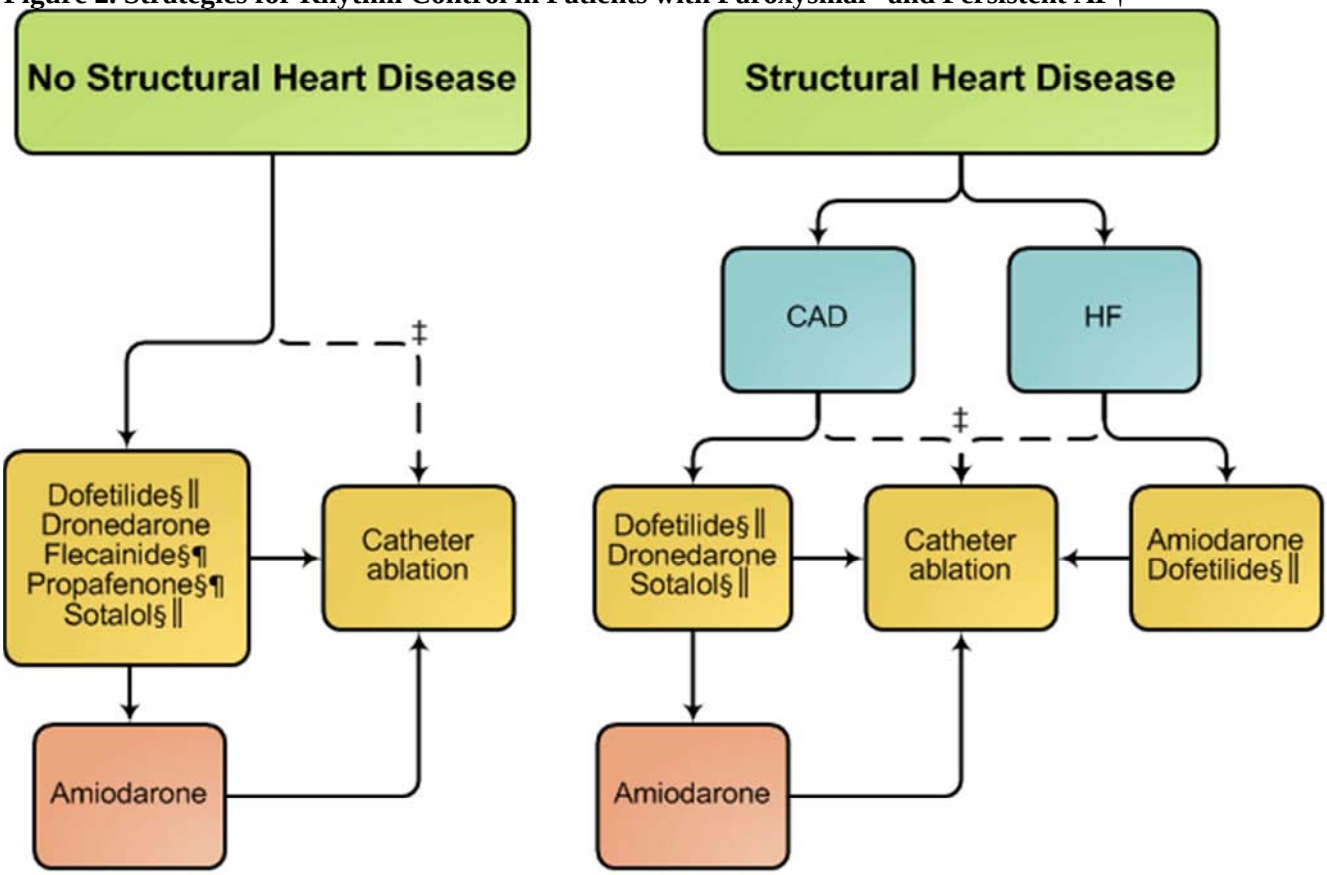
1. **AF catheter ablation may be considered for symptomatic long-standing (>12 months) persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication, when a rhythm control strategy is desired (155, 168).** ***(Level of Evidence: B)***
2. **AF catheter ablation may be considered prior to 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 following 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)***

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

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; CAD, coronary artery disease; HF, heart failure; and LVH, left ventricular hypertrophy.

5.7. Surgery Maze Procedures: Recommendations

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 (169). *(Level of Evidence: B)***

6. Specific Patient Groups and AF

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

6.1. Hypertrophic Cardiomyopathy: Recommendations

Class I

1. **Anticoagulation is indicated in patients with HCM with AF independent of the CHA_2DS_2-VASc score (170, 171).** ***(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 therapies.** ***(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 (172-175).** ***(Level of Evidence: B)***

Class IIb

1. **Sotalol, dofetilide, and dronedarone may be considered for a rhythm-control strategy in patients with HCM (13).** ***(Level of Evidence: C)***

6.2. AF Complicating Acute Coronary Syndrome: Recommendations

Class I

1. **Urgent direct-current cardioversion of new-onset AF in the setting of 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 CHA_2DS_2-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 LV 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: Recommendations

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: Recommendations

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: Recommendations

Class I

1. **Prompt direct-current cardioversion is recommended for patients with AF, WPW, and rapid ventricular response who are hemodynamically compromised (176). *(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 (176). *(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 (176). *(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 WPW syndrome who have pre-excited AF is potentially harmful as these treatments accelerate the ventricular rate (177-179). *(Level of Evidence: B)***

6.6. Heart Failure: Recommendations

Class I

1. **Control of resting heart rate using either a beta blocker or a nondihydropyridine calcium channel antagonist is recommended for patients with persistent or permanent AF and compensated HF with preserved EF (HF*p*EF) (96). *(Level of Evidence: B)***
2. **In the absence of pre-excitation, intravenous beta blocker administration (or a nondihydropyridine calcium channel antagonist in patients with HF*p*EF) 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 LVEF (180-183). *(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 (104, 181, 184, 185). *(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 EF. *(Level of Evidence: C)***

Class IIa

1. **A combination of digoxin and a beta blocker (or a nondihydropyridine calcium channel antagonist for patients with HF*p*EF), is reasonable to control resting and exercise heart rate in patients with AF (94, 181). *(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 (96, 186, 187). *(Level of Evidence: B)***
3. **Intravenous amiodarone can be useful to control the 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 (188-190). (*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 HF*p*EF) 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: Recommendation

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: Recommendations

Class I

1. **Treating patients who develop AF after cardiac surgery with a beta blocker is recommended unless contraindicated (191-194). *(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 (195). *(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 (196-198). *(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 (199). *(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 (195). *(Level of Evidence: B)***
4. **It is reasonable to administer antithrombotic medication in patients who develop postoperative AF, as advised for nonsurgical patients (200). *(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 following cardiac surgery (194, 201). *(Level of Evidence: B)***
2. **Administration of colchicine may be considered for patients postoperatively to reduce AF following cardiac surgery (202). *(Level of Evidence: B)***

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

Recommendations	COR	LOE	References
Hypertrophic cardiomyopathy			
Anticoagulation indicated in HCM with AF independent of the CHA_2DS_2-VASc score	I	B	(170, 171)
Antiarrhythmic drugs can be useful to prevent recurrent AF in HCM. Amiodarone, or disopyramide combined with beta blockers 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	(172-175)
Sotalol, dofetilide, and dronedarone may be considered for a rhythm-control strategy in HCM	IIb	C	(13)
AF complicating ACS			
Urgent cardioversion of new onset AF in 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_2DS_2-VASc (score $\geq$2), anticoagulation with warfarin is recommended unless contraindicated	I	C	N/A
Amiodarone or digoxin may be considered to slow a 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 a RVR with ACS and AF only in the absence of significant HF or hemodynamic instability	IIb	C	N/A
Hyperthyroidism			
Beta blockers are recommended to control ventricular rate with AF complicating thyrotoxicosis, unless contraindicated	I	C	N/A
Nondihydropyridine calcium channel antagonist is recommended to control the ventricular rate with AF and thyrotoxicosis when beta blocker cannot be used	I	C	N/A
Pulmonary diseases			
Nondihydropyridine calcium channel antagonist is recommended to control the ventricular rate with COPD and AF	I	C	N/A
Cardioversion should be attempted with pulmonary disease patients who become hemodynamically unstable with new onset AF	I	C	N/A
WPW and pre-excitation syndromes			
Cardioversion recommended with AF, WPW, and RVR who are hemodynamically compromised	I	C	(176)
IV procainamide or ibutilide to restore sinus rhythm or slow ventricular rate recommended with pre-excited AF and RVR who are not hemodynamically compromised	I	C	(176)
Catheter ablation of accessory pathway is recommended in symptomatic patients with pre-excited AF, especially if the accessory pathway has a short refractory period	I	C	(176)
IV amiodarone, adenosine, digoxin, or nondihydropyridine calcium channel antagonists with WPW who have pre-excited AF is potentially harmful	III: Harm	B	(177-179)
Heart failure			
Beta blocker or nondihydropyridine calcium channel antagonist is recommended for persistent or permanent AF in patients with HF*p*EF	I	B	(96)
In the absence of pre-excitation, IV beta blocker (or a nondihydropyridine calcium channel antagonist with HF*p*EF) is recommended to slow ventricular response to AF in the acute setting, exercising caution in patients with overt congestion, hypotension or	I	B	(180-183)

HF*r*EF			
In the absence of pre-excitation, IV digoxin or amiodarone is recommended to acutely control heart rate	I	B	(104, 181, 184, 185)
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*r*EF	I	C	N/A
Combination digoxin and beta blocker (or a nondihydropyridine calcium channel antagonist with HF*p*EF), is reasonable to control rest and exercise heart rate with AF	IIa	B	(94, 181)
Reasonable to perform AV node ablation with ventricular pacing to control heart rate when pharmacological therapy insufficient or not tolerated	IIa	B	(96, 186, 187)
IV amiodarone can be useful to control the heart rate with AF when other measures are unsuccessful or contraindicated	IIa	C	N/A
With AF and RVR, causing or suspected of causing tachycardia-induced cardiomyopathy, it is reasonable to achieve rate control by AV nodal blockade or rhythm control strategy	IIa	B	(188-190)
In chronic HF patients 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 HF*p*EF) 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 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			
With AF and multigenerational AF family members, referral to a tertiary care center for genetic counseling and testing may be considered	IIb	C	N/A
Postoperative cardiac and thoracic surgery			
Beta blocker is recommended to treat postoperative AF unless contraindicated	I	A	(191-194)
A nondihydropyridine calcium channel blocker is recommended when a beta blocker is inadequate to achieve rate control with postoperative AF	I	B	(195)
Preoperative amiodarone reduces AF with cardiac surgery and is reasonable as prophylactic therapy for high risk of postoperative AF	IIa	A	(196-198)
It is reasonable to restore sinus rhythm pharmacologically with ibutilide or direct-current cardioversion with postoperative AF	IIa	B	(199)
It is reasonable to administer antiarrhythmic medications to maintain sinus rhythm with recurrent or refractory postoperative AF	IIa	B	(195)
It is reasonable to administer antithrombotic medications for postoperative AF	IIa	B	(200)
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 following cardiac surgery	IIb	B	(194, 201)
Colchicine may be considered postoperatively to reduce AF following cardiac surgery	IIb	B	(202)

AF indicates atrial fibrillation; AV, atrioventricular; COPD, chronic obstructive pulmonary disease; COR, Class of Recommendation; HCM, hypertrophic cardiomyopathy; HF, heart failure; HF*p*EF, heart failure with preserved ejection fraction; HF*r*EF, 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.

7. Evidence Gaps and Future Research Directions

The past decade has seen substantial progress in the understanding of AF mechanisms, clinical implementation of ablation for maintaining sinus rhythm, and new drugs for stroke prevention. Further studies are needed to better inform clinicians as to the risks and benefits of therapeutic options for an individual patient. Continued research is needed into the mechanisms that initiate and sustain AF. Better understanding of these tissue and cellular mechanisms will, hopefully, lead to more defined approaches to treat and abolish AF. This includes new methodological approaches for AF ablation that would favorably impact survival, thromboembolism, and quality of life across different patient profiles. New pharmacologic 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 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 link between the presence of AF, AF burden, and stroke risk, and also 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, epidemiologic, and clinical studies.

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Key Words: ACC/AHA Practice Guidelines ■ 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	• United Healthcare	None	None	None	None	None	4.1 5.0 6.3 7.3 7.10
Joseph S. Alpert	University of Arizona Health Sciences Center—Professor of Medicine	• Bayer Pharmaceuticals (DSMB)‡ • Boehringer Ingelheim • Daiichi-Sankyo • Johnson & Johnson • Roche Diagnostics • Sanofi-aventis • Servier Pharmaceuticals	None	None	None	None	None	4.1 5.0
Hugh Calkins	Johns Hopkins Hospital—Professor of Medicine, Director of Electrophysiology	• Atricure • Biosense Webster • Carecore • iRhythm • Medtronic† • Sanofi-aventis	None	None	None	None	None	5.0 6.3 7.8
Joaquin E. Cigarroa	Oregon Health & Science University—Clinical	None	None	None	None	None	None	None

	Professor; Clinical Chief of Cardiology							
Joseph C. Cleveland, Jr	University of Colorado—Professor of Surgery; Denver Veteran's Administration 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	• Boston Scientific† • Medtronic† • St. Jude Medical†	• Boston Scientific† • Medtronic† • St. Jude Medical†	None	5.0 6.3 7.8
Patrick T. Ellinor	Massachusetts General Hospital Heart Center, Cardiac Arrhythmia Service—Director	None	None	None	None	None	None	None
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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	None	None	None	• GlaxoSmith Kline‡	None	None	None

	Pharmacology and Cardiology—Professor of Medicine							
Ralph L. Sacco	University of Miami, Miller School of Medicine, Department of Neurology—Chairman	• Boehringer Ingelheim‡§	None	None	None	None	None	None
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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.

†Indicates significant relationship.
‡No financial benefit.
§Dr. Sacco's relationship with Boehringer Ingelheim was added just after final balloting of the recommendations and prior to 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	• Bayer • Biotronik • Boehringer Ingelheim • Boston Scientific • Bristol-Myers Squibb • ChanRx • Daiichi-Sankyo • Forest Laboratories • Johnson & Johnson • Medtronic • Novartis* • Sanofi-aventis • Servier • St. Jude Medical • Takeda • Xention	• Pfizer	None	• Biotronik† • Servier (DSMB) • St. Jude Medical (DSMB)	None	None
John Fisher	Official Reviewer—AHA	Albert Einstein College of Medicine—Professor of Medicine	• Medtronic*	None	None	None	• Biotronik* • Boston Scientific* • Medtronic* • St. Jude Medical*	None
Jonathan Halperin	Official Reviewer—ACC/AHA Task Force on Practice Guidelines	Mt. Sinai Medical Center—Professor of Medicine	• AstraZeneca • Bayer • Biotronik* • Boehringer Ingelheim* • Boston Scientific • Bristol-Myers Squibb • Daiichi-Sankyo	None	None	None	None	None

			• Janssen Pharmaceuticals • Johnson & Johnson • Medtronic • Pfizer • Sanofi-aventis					
Jose Joglar	Official Reviewer—AHA	UT Southwestern Medical Center—Associate Professor of Internal Medicine	None	None	None	None	• Medtronic* • St. Jude Medical*	None
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Appendix 3. Initial Clinical Evaluation in Patients With AF

Minimum Evaluation	
1. History and physical examination, to define	• Presence and nature of symptoms associated with AF
	• Clinical type of AF (paroxysmal, persistent, or permanent)
	• Onset of the first symptomatic attack or date of discovery of AF
	• Frequency, duration, precipitating factors, and modes of initiation or termination of AF
	• Response to any pharmacological agents that have been administered
	• Presence of any underlying heart disease or reversible conditions (e.g., hyperthyroidism or alcohol consumption)
2. ECG, to identify	• Rhythm (verify AF)
	• LVH
	• P-wave duration and morphology or fibrillatory waves
	• Pre-excitation
	• Bundle-branch block
	• Prior MI
	• Other atrial arrhythmias
	• To measure and follow the R-R, QRS, and QT intervals in conjunction with antiarrhythmic drug therapy
3. TTE, to identify	• VHD
	• LA and RA size
	• LV and RV size and function
	• Peak RV pressure (pulmonary hypertension)
	• LV hypertrophy
	• LA thrombus (low sensitivity)
	• Pericardial disease
4. Blood tests of thyroid, renal, and hepatic function	• For a first episode of AF
	• When the ventricular rate is difficult to control
Additional Testing (1 or several tests may be necessary)	
1. 6-min walk test	• If the adequacy of rate control is in question
2. Exercise testing	• If the adequacy of rate control is in question
	• To reproduce exercise-induced AF
	• To exclude ischemia before treatment of selected patients with a type IC* antiarrhythmic drug
3. Holter or event monitoring	• If diagnosis of the type of arrhythmia is in question
	• As a means of evaluating rate control
4. TEE	• To identify LA thrombus (in the LAA)
	• To guide cardioversion
5. Electrophysiological study	• To clarify the mechanism of wide-QRS-complex tachycardia
	• To identify a predisposing arrhythmia such as atrial flutter or paroxysmal supraventricular tachycardia

	• To seek sites for curative AF ablation or AV conduction block/modification
6. Chest radiograph, to evaluate	• Lung parenchyma, when clinical findings suggest an abnormality
	• Pulmonary vasculature, when clinical findings suggest an abnormality

*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. Modified from Fuster, et al. (5-8).

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