Atrial fibrillation clinical practice guidelines(2019)

Notes on NICE Guidance CG180 **Atrial Fibrillation [AF] : management**

Key points:	Why the is important for for patients:	Implementation tips:

• New evidence related to stroke prevention led to NICE Guidance (2014 + updates) key points:
  • Assess, & where indicated offer anticoagulation
  • Patient choice paramount
  • Personalised packages of care
  • Use of Risk Scoring
  • CHA2DS2 – VASC stroke risk
  • HASBLED – risk of bleeding especially:
  • If uncontrolled B/P
  • Poor INR control
  • Use of NSAIDS
  • Harmful alcohol consumption
	• ***Risk of stroke if Atrial Fibrillation [AF] is left untreated***
	• ***Latest evidence shows aspirin not to be effective***
	• ***There were a large number of people with AF who have not had the condition reviewed (click for best practice examples)***
	• ***Introduces a Patient Decision Aid [PDA] (click for link, go to last page to see how it's scored)***
	• ***Patient choice, and assessment of other illnesses (co-morbidity) are key to the new guidelines***
		• Assess the needs of your local community
		• Identify those most at risk & review
		• Implement simple changes e.g. Pulse checking for over 65s
		• Develop an inter-disciplinary pathway
		• Consider new models of working
		  • Self-monitoring
		  • 'One stop shops'
		  • Pharmacy monitoring
		  • Adherence support from Pharmacists / specialist Nurses etc.

#MedLearn

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Steve & Associates develop & deliver Patient Led Clinical Education services.
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Notes from Steve Turner @MedicineGovUK to subscribe to my email updates on medicines & prescribing send details to info@carerightnow.co.uk (#GDPR compliant)
Link to Guidance: https://www.nice.org.uk/guidance/cg180 (accessed 11/1/2018)

Table 13 Drugs for rate control in AF[a] (2)

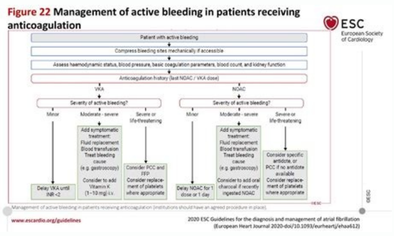
	Intravenous administration	Usual oral maintenance dose	Contraindicated
Non-dihydropyridine calcium channel antagonists			
Verapamil	2.5–10 mg i.v. bolus over 5 min	40 mg b.i.d. to 480 mg (extended release) o.d.	Contraindicated in HFrEF Adapt doses in hepatic and renal impairment
Diltiazem	0.25 mg/kg i.v. bolus over 5 min, then 5–15 mg/h	60 mg t.i.d. to 360 mg (extended release) o.d.	
Digitalis glycosides			
Digoxin	0.5 mg i.v. bolus (0.75–1.5 mg over 24 hours in divided doses)	0.0625–0.25 mg o.d.	High plasma levels associated with increased mortality Check renal function before starting and adapt dose in CKD patients
Digitoxin	0.4–0.6 mg	0.05–0.1 mg o.d.	High plasma levels associated with increased mortality

[a]All rate control drugs are contraindicated in Wolff-Parkinson-White syndrome, also i.v. amiodarone.

www.escardio.org/guidelines

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation (European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

Figure 22 Management of active bleeding in patients receiving anticoagulation



Management of active bleeding in patients receiving anticoagulation (institutions should have an agreed procedure in place).

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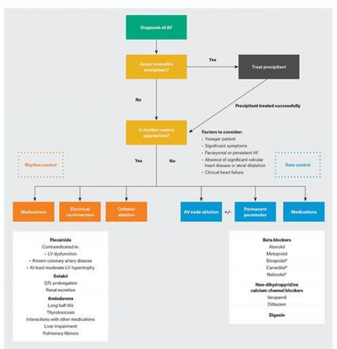
2020 ESC Guidelines for the diagnosis and management of atrial fibrillation (European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

IIb	B-R	**14. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and moderate-to-severe CKD (serum creatinine ≥1.5 mg/dL [apixaban], CrCl 15 to 30 mL/min [dabigatran], CrCl ≤50 mL/min [rivaroxaban], or CrCl 15 to 50 mL/min [edoxaban]) with an elevated CHA_2DS_2-VASc score, treatment with reduced doses of direct thrombin or factor Xa inhibitors may be considered (e.g., dabigatran, rivaroxaban, apixaban, or edoxaban) (S4.1.1-11).** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and this recommendation has been changed in response to the approval of edoxaban. LOE was updated from C to B-R. (Section 4.1. in the 2014 AF Guideline)
IIb	C- LD	**15. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and a CHA_2DS_2-VASc score of 1 in men and 2 in women, prescribing an oral anticoagulant to reduce thromboembolic stroke risk may be considered (S4.1.1-31–S4.1.1-35).** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and evidence was added to support separate risk scores by sex. LOE was updated from C to C-LD. (Section 4.1. in the 2014 AF Guideline)
III: No Benefit	C-EO	**16. In patients with AF and end-stage CKD or on dialysis, the direct thrombin inhibitor dabigatran or the factor Xa inhibitors rivaroxaban or edoxaban are not recommended because of the lack of evidence from clinical trials that benefit exceeds risk (S4.1.1-8–S4.1.1-11, S4.1.1-36–S4.1.1-38).** **MODIFIED**: New data have been included. Edoxaban received FDA approval and has been added to the recommendation. LOE was updated from C to C-EO. (Section 4.1. in the 2014 AF Guideline)
III: Harm	B-R	**17. The direct thrombin inhibitor dabigatran should not be used in patients with AF and a mechanical heart valve (S4.1.1-39).** **MODIFIED**: Evidence was added. LOE was updated from B to B-R. Other NOACs are addressed in the supportive text. (Section 4.1. in the 2014 AF Guideline)



Atrial fibrillation guidelines 2019. Clinical practice guideline for atrial fibrillation.

ACC/AHA/ESC 2006 Guidelines 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 European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzey JY, Kay GN, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann S, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Halperin JL, Hunt SA, Nishimura R, Ornato JP, Page RL, Riegel B, Priori SG, Blanc JJ, Budaj A, Camm AJ, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Tamargo JL, Zamorano JL; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; European Society of Cardiology Committee for Practice Guidelines; European Heart Rhythm Association; Heart Rhythm Society. Fuster V, et al. Circulation. 2006 Aug 15;114(7):e257-354. doi: 10.1161/CIRCULATIONAHA.106.177292. Circulation. 2006. PMID: 16908781 No abstract available. Atrial fibrillation, often called AFib or AF, is the most common type of treated heart arrhythmia. An arrhythmia is when the heart beats too slowly, too fast, or in an irregular way. When a person has AFib, the normal beating in the upper chambers of the heart (the two atria) is irregular, and blood doesn't flow as well as it should from the atria to the lower chambers of the heart (the two ventricles). AFib may happen in brief episodes, or it may be a permanent condition. Facts About AFib It is estimated that 12.1 million people in the United States will have AFib in 2030.1,2 In 2019, AFib was mentioned on 183,321 death certificates and was the underlying cause of death in 26,535 of those deaths.3 People of European descent are more likely to have AFib than African Americans. Because the number of AFib cases increases with age and women generally live longer than men, more women than men experience AFib. What are the symptoms of AFib? Some people who have AFib don't know they have it and don't have any symptoms. Others may experience one or more of the following symptoms: Irregular heartbeat Heart palpitations (rapid, fluttering, or pounding) Lightheadedness Extreme fatigue Shortness of breath Chest pain What are the risk factors for AFib? The risk for AFib increases with age. High blood pressure, the risk for which also increases with advancing age, accounts for about 1 in 5 cases of AFib.4 Risk factors for AFib include4,5 Advancing age High blood pressure Obesity European ancestry Diabetes Heart failure Ischemic heart disease Hyperthyroidism Chronic kidney disease Moderate to heavy alcohol use Smoking Enlargement of the chambers on the left side of the heart How is AFib related to stroke? AFib increases a person's risk for stroke. When standard stroke risk factors were accounted for, AFib was associated with an approximately fivefold increased risk of ischemic stroke.6 AFib causes about 1 in 7 strokes.7 Strokes caused by complications from AFib tend to be more severe than strokes with other underlying causes. Strokes happen when blood flow to the brain is blocked by a blood clot or by fatty deposits called plaque in the blood vessel lining. How is AFib treated? Treatment for AFib can include Medicines to control the heart's rhythm and rate Blood-thinning medicine to prevent blood clots from forming and reduce stroke risk Surgery Medicine and healthy lifestyle changes to manage AFib risk factors What are the consequences of AFib? More than 454,000 hospitalizations with AFib as the primary diagnosis happen each year in the United States.4 The condition contributes to about 158,000 deaths each year.3 The death rate from AFib as the primary or a contributing cause of death has been rising for more than two decades.7 More Information Miyasaka Y, Barnes ME, Gersh BJ, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation. 2006;114:199–225. Colilla S, Crow A, Petkun W, Singer DE, Simon T, Liu X. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. Am J Cardiol. 2013;112:1142–1147. doi: 10.1016/j.amjcard.2013.05.063. Centers for Disease Control and Prevention, National Center for Health Statistics. About Multiple Cause of Death, 1999–2019. CDC WONDER Online Database website. Atlanta, GA: Centers for Disease Control and Prevention; 2019. Accessed February 1, 2021. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. Circulation. 2019;139(10):e56–528. Benjamin E, Levy D, Vaziri SM. Independent risk facors for atrial fibrillation in a population based cohort. JAMA. 1994;271(11):840-844. Tsao CW, Aday AW, Almarzooq ZI, Beaton AZ, Bittencourt MS, Boehme AK, et al. Heart Disease and Stroke Statistics—2022 Update: A Report From the American Heart Association. Circulation. 2022;145(8):e153–e639. Heart Rhythm Society. (2019). Complications from Atrial Fibrillation. Accessed May 9, 2019. Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December 2018. Data are from the Multiple Cause of Death Files, 1999-2017, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at October 4, 2019 Preamble (Full Version) e1261. Introduction e1281.1. Methodology and Evidence Review e1291.2. Organization of the Writing Group e1291.3. Document Review and Approval e1291.4. Abbreviations e1294. Prevention of Thromboembolism e1304.1. Risk-Based Anticoagulant Therapy (Modified From Section 4.1., "Risk-Based Antithrombotic Therapy," in the 2014 AF Guideline) e1304.1.1. Selecting an Anticoagulant Regimen—Balancing Risks and Benefits (Modified From Section 4.1.1., "Selecting an Antithrombotic Regimen—Balancing Risks and Benefits," in the 2014 AF Guideline) e1304.2. Anticoagulant Options (Modified From Section 4.2., "Antithrombotic Options," in the 2014 AF Guideline) e1344.3. Interruption and Bridging Anticoagulation e1344.4. Nonpharmacological Stroke Prevention e1354.4.1. Percutaneous Approaches to Occlude the LAA e1354.4.2. Cardiac Surgery—LAA Occlusion/Excision e1366. Rhythm Control e1366.1. Electrical and Pharmacological Cardioversion of AF and Atrial Flutter e1366.1.1. Prevention of Thromboembolism e1366.3. AF Catheter Ablation to Maintain Sinus Rhythm e1386.3.4. Catheter Ablation in HF e1387. Specific Patient Groups and AF e1387.4. AF Complicating ACS e1387.12. Device Detection of AF and Atrial Flutter (New) e1417.13. Weight Loss (New) e142References e143Appendix 1: Author Relationships With Industry and Other Entities (Relevant) e148Appendix 2: Abbreviated Reviewer Relationships With Industry and Other Entities e150Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines with recommendations to improve cardiovascular health. These guidelines, which are based on systematic methods to evaluate and classify evidence, provide a foundation for the delivery of quality cardiovascular care. The ACC and AHA sponsor the development and publication of clinical practice guidelines without commercial support, and members volunteer their time to the writing and review efforts. Guidelines are official policy of the ACC and AHA. For some guidelines, the ACC and AHA partner with other organizations. This guideline is a collaboration of the ACC and AHA with the Heart Rhythm Society (HRS) as a partner and the Society of Thoracic Surgeons as a collaborator.Intended UseClinical practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease. The focus is on medical practice in the United States, but these guidelines are relevant to patients throughout the world. Although guidelines may be used to inform regulatory or payer decisions, the intent is to improve quality of care and align with patients' interests. Guidelines are intended to define practices meeting the needs of patients in most, but not all, circumstances, and should not replace clinical judgment.Clinical ImplementationManagement, in accordance with guideline recommendations, is effective only when followed by both practitioners and patients. Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions on the basis of individual values, preferences, and associated conditions and comorbidities.Methodology and ModernizationThe ACC/AHA Task Force on Clinical Practice Guidelines (Task Force) continuously reviews, updates, and modifies guideline methodology on the basis of published standards from organizations, including the Institute of Medicine,P-1,P-2 and on the basis of internal reevaluation. Similarly, presentation and delivery of guidelines are reevaluated and modified in response to evolving technologies and other factors to optimally facilitate dissemination of information to healthcare professionals at the point of care.Beginning in 2017, numerous modifications to the guidelines have been and continue to be implemented to make guidelines shorter and enhance "user friendliness." Guidelines are written and presented in a modular knowledge chunk format, in which each chunk includes a table of recommendations, a brief synopsis, recommendation-specific supportive text and, when appropriate, flow diagrams or additional tables. Hyperlinked references are provided for each modular knowledge chunk to facilitate quick access and review. More structured guidelines—including word limits ("targets") and a web guideline supplement for useful but noncritical tables and figures—are 2 such changes. Also, to promote conciseness, the Preamble is presented in abbreviated form in the executive summary and full-text guideline documents.In recognition of the importance of cost–value considerations in certain guidelines, when appropriate and feasible, an analysis of value for a drug, device, or intervention may be performed in accordance with the ACC/AHA methodology.P-3To ensure that guideline recommendations remain current, new data are reviewed on an ongoing basis, with full guideline revisions commissioned ideally in approximate 6-year cycles. Publication of potentially practice-changing new study results relevant to an existing or new drug, device, or management strategy prompts evaluation by the Task Force, in consultation with the relevant guideline writing committee, to determine whether a focused update should be commissioned. For additional information and policies on guideline development, we encourage readers to consult the ACC/AHA guideline methodology manualP-4 and other methodology articles.P-5–P-8Selection of Writing Committee MembersThe Task Force strives to ensure that the guideline writing committee both contains requisite expertise and is representative of the broader medical community by selecting experts from a broad array of backgrounds, representing different geographic regions, sexes, races, ethnicities, intellectual perspectives/biases, and scopes of clinical practice, and by inviting organizations and professional societies with related interests and expertise to participate as partners or collaborators.Relationships With Industry and Other EntitiesThe ACC and AHA have rigorous policies and methods to ensure that documents are developed without bias or improper influence. The complete policy on relationships with industry and other entities (RWI) can be found online. Appendix 1 of the guideline lists writing committee members' relevant RWI; for the purposes of full transparency, their comprehensive disclosure information is available online. Comprehensive disclosure information for the Task Force is also available online.Evidence Review and Evidence Review CommitteesIn developing recommendations, the writing committee uses evidence-based methodologies that are based on all available data.P-4–P-6 Literature searches focus on randomized controlled trials (RCTs) but also include registries, nonrandomized comparative and descriptive studies, case series, cohort studies, systematic reviews, and expert opinion. Only key references are cited.An independent evidence review committee is commissioned when there are one or more questions deemed of utmost clinical importance that merit formal systematic review to determine which patients are most likely to benefit from a drug, device, or treatment strategy, and to what degree. Criteria for commissioning an evidence review committee and formal systematic review include absence of a current authoritative systematic review, feasibility of defining the benefit and risk in a timeframe consistent with the writing of a guideline, relevance to a substantial number of patients, and likelihood that the findings can be translated into actionable recommendations. Evidence review committee members may include methodologists, epidemiologists, clinicians, and biostatisticians. Recommendations developed by the writing committee on the basis of the systematic review are marked "SR."Guideline-Directed Management and TherapyThe term guideline-directed management and therapy encompasses clinical evaluation, diagnostic testing, and both pharmacological and procedural treatments. For these and all recommended drug treatment regimens, the reader should confirm dosage with product insert material and evaluate for contraindications and interactions. Recommendations are limited to drugs, devices, and treatments approved for clinical use in the United States.Class of Recommendation and Level of EvidenceThe Class of Recommendation (COR) indicates the strength of recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. The Level of Evidence (LOE) rates the quality of scientific evidence supporting the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources (Table 1).P-5Glenn N. Levine, MD, FACC, FAHAChair, ACC/AHA Task Force on Clinical Practice GuidelinesTable 1. Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated August 2015)1. IntroductionThe purpose of this document is to update the "2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation"S1.3-1 (2014 AF Guideline) in areas for which new evidence has emerged since its publication. The scope of this focused update of the 2014 AF Guideline includes revisions to the section on anticoagulation (because of the approval of new medications and thromboembolism protection devices), revisions to the section on catheter ablation of atrial fibrillation (AF), revisions to the section on the management of AF complicating acute coronary syndrome (ACS), and new sections on device detection of AF and weight loss. The areas of the 2014 AF Guideline that were updated were limited to those for which important new data from clinical trials had emerged and/or new US Food and Drug Administration (FDA) indications for thromboembolism protection devices have appeared in the data available to the writing group up to August 2018.All recommendations (new, modified, and unchanged) for each updated clinical section are included to provide a comprehensive assessment. The text explains new and modified recommendations, whereas recommendations from the previous guideline that have been deleted or superseded no longer appear. Please consult the full-text version of the 2014 AF GuidelineS1.3-1 for text and evidence tables supporting the unchanged recommendations and for clinical areas not addressed in this focused update. Individual recommendations in this focused update will be incorporated into the full-text guideline in the future. Recommendations from

the prior guideline that remain current have been included for completeness, but the LOE reflects the COR/LOE system used when initially developed. New and modified recommendations in this focused update reflect the latest COR/LOE system, in which LOE B and C are subcategorized for greater specificity.S1.3-2–S1.3-4 The section numbers correspond to the full-text guideline sections.1.1. Methodology and Evidence ReviewClinical trials presented at the annual scientific meetings of the ACC, AHA, Heart Rhythm Society (HRS), and European Society of Cardiology, as well as other selected data published in a peer-reviewed format through August 2018, were reviewed by the Task Force and members of the 2014 AF Guideline writing group to identify trials and other key data that might affect guideline recommendations. The information considered important enough to prompt updated recommendations is included in evidence tables in the Online Data Supplement. The complete section of recommendations (new, modified, and unchanged) for each clinical section is included to provide a comprehensive overview for the reader. Recommendations that have been deleted or superseded are not incorporated. The text supporting the new and modified recommendations is provided.After the preliminary recommendation and text were drafted for percutaneous approaches to occlusion of the left atrial appendage (LAA), it was appreciated that the primary author of the section had, by strict criteria, an RWI relevant to the section. Task Force and organizational leadership directed that both the recommendation and text be discarded and the section be constructed de novo by both a new primary author and new primary reviewer, both without RWI. This new section was thoroughly reviewed by the entire writing group, and the de novo formulated recommendation, as with all recommendations in the focused update, was formally voted on by the writing group.1.2. Organization of the Writing GroupFor this focused update, representative members of the 2014 AF writing committee were invited to participate, and they were joined by additional invited members to form a new writing group, referred to as the 2018 AF Guideline Focused Update Writing Group. Members were required to disclose all RWI relevant to the data under consideration. The group was composed of clinicians with broad expertise related to AF and its treatment, including the areas of adult cardiology, electrophysiology, cardiothoracic surgery, and heart failure (HF). The writing group included representatives from the ACC, AHA, HRS, and the Society of Thoracic Surgeons.1.3. Document Review and ApprovalThe focused update was reviewed by 2 official reviewers each nominated by the ACC, AHA, and HRS; 1 AHA/ACC lay reviewer; 1 organizational reviewer from the Society of Thoracic Surgeons; and 29 individual content reviewers. Reviewers' abbreviated RWI information is published in this document (Appendix 2), and their detailed disclosures are available online.This document was approved for publication by the governing bodies of the ACC, AHA, and HRS and was endorsed by the Society of Thoracic Surgeons.1.4. AbbreviationsAbbreviationMeaning/PhraseACSacute coronary syndromeAFatrial fibrillationAHREatrial high-rate episodesCHADS2congestive heart failure, hypertension, age >75 years, diabetes mellitus, stroke/transient ischemia attack/ thromboembolismCHA2DS2-VAScongestive heart failure, hypertension, age ≥75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism (doubled), vascular disease, age 65 to 74 years, sex categoryCIconfidence intervalCKDchronic kidney diseaseCMSUS Centers for Medicare & Medicaid ServicesCrClcreatinine clearanceDAPTdual-antiplatelet therapyFDAUS Food and Drug AdministrationHFheart failureHFrEFheart failure with reduced left ventricular ejection fractionHRhazard ratioINRinternational normalized ratioLAAleft atrial appendageLVleft ventricularMImyocardial infarctionNOACnon–vitamin K oral anticoagulantPCIpercutaneous coronary interventionRCTrandomized controlled trialTIMIThrombolysis in Myocardial Infarction4. Prevention of Thromboembolism4.1. Risk-Based Anticoagulant Therapy (Modified From Section 4.1., "Risk-Based Antithrombotic Therapy," in the 2014 AF Guideline)4.1.1. Selecting an Anticoagulant Regimen—Balancing Risks and Benefits (Modified From Section 4.1.1., "Selecting an Antithrombotic Regimen—Balancing Risks and Benefits," in the 2014 AF Guideline)Introductory TextThe distinction between nonvalvular and valvular AF has confused clinicians, varying among AF clinical trials of non–vitamin K oral anticoagulants (NOACs) (ie, dabigatran [a direct thrombin inhibitor] and rivaroxaban, apixaban, and edoxaban [factor Xa inhibitors]; also referred to as direct-acting oral anticoagulants [DOACs]) and between North American and European AF guidelines. Valvular AF generally refers to AF in the setting of moderate-to-severe mitral stenosis (potentially requiring surgical intervention) or in the presence of an artificial (mechanical) heart valve. Valvular AF is considered an indication for long-term anticoagulation with warfarin. In contrast, nonvalvular AF does not imply the absence of valvular heart disease. Instead, as used in the present focused update, nonvalvular AF is AF in the absence of moderate-to-severe mitral stenosis or a mechanical heart valve. This is because in most AF NOAC clinical trials, up to approximately 20% of patients were enrolled with various valvular defects, including mild mitral stenosis, mitral regurgitation, aortic stenosis, aortic regurgitation, and tricuspid regurgitation;S4.1.1-1,S4.1.1-2 some trials enrolled small numbers of patients with valve repair, valvuloplasty, and bioprosthetic valves. Furthermore, meta-analysis–derived data from the original clinical trials suggest that, among patients with AF and these valvular lesions and operations, NOACs reduce stroke and systemic embolism compared with warfarin, but with differences in bleeding risk.S4.1.1-3 For recommendations from the 2014 AF guideline that were modified only to define the exclusion criteria for valvular AF or to change "antithrombotic" to "anticoagulant," LOE and supportive text have not been updated. A fifth NOAC, betrixaban, has not been approved by the FDA for use in patients with AF. Antithrombotic (anticoagulant combined with antiplatelet) therapy is discussed in Sections 4.4.1. and 7.4.S4.1.1-4Recommendation-Specific Supportive Text (New or Modified)1. New data are available for edoxaban. Edoxaban (30 or 60 mg once daily) was studied in a large randomized prospective AF trial; it was found to be noninferior to warfarin with regard to the prevention of stroke or systemic embolization and was associated with significantly lower rates of bleeding and death from cardiovascular causes.S4.1.1-11 Treatment of patients with AF with edoxaban, either 30 mg or 60 mg, should be based on assessment of the risks of stroke and bleeding. In ENGAGE-TIMI 48 (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation—Thrombolysis in Myocardial Infarction 48), the rate of systemic embolism and stroke was 1.5% with warfarin, compared with 1.2% with 60 mg of edoxaban (hazard ratio [HR]: 0.79; 97.5% CI: 0.63–0.99; p120 kg)Assessment of patient adherence.4.3. Interruption and Bridging AnticoagulationRecommendation-Specific Supportive Text (New or Modified)2. The BRIDGE (Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for an Elective Invasive Procedure or Surgery) study was a randomized, double-blind, placebo-controlled trial of bridging versus no bridging in 1 884 patients with AF (except with moderate to severe mitral stenosis or a mechanical heart valve) requiring periprocedural interruption of warfarin therapy.S4.3-1 Absence of bridging was found to be noninferior to bridging with low-molecular-weight heparin for prevention of arterial thromboembolism and was found to decrease the risk of bleeding. Bridging anticoagulation may be appropriate only in patients (on warfarin) with a very high thromboembolic risk.3. The analysis of 503 patients from the RE-VERSE AD (Reversal Effects of Idarucizumab on Active Dabigatran) trial found that idarucizumab, a monoclonal antibody fragment that binds dabigatran, rapidly normalized hemostasis and reduced levels of circulating dabigatran in subjects on dabigatran who had serious bleeding or required an urgent procedure.S4.3-2 Idarucizumab has received full FDA approval.4. Andexanet alfa (coagulation factor Xa [recombinant], inactivated-zhzo) is a bioengineered, recombinant modified protein designed to serve as an antidote against direct factor Xa inhibitors. It was reported to reverse the effects of rivaroxaban and apixabanS4.3-3,S4.3-4 and was approved under the FDA's accelerated-approval pathway on the basis of effects in healthy volunteers. Continued approval may be contingent on postmarketing studies to demonstrate an improvement in hemostasis in patients.4.4. Nonpharmacological Stroke Prevention4.4.1. Percutaneous Approaches to Occlude the LAARecommendation-Specific Supportive Text (New)1. Percutaneous LAA occlusion with the Watchman device has been compared with warfarin in patients with AF (in the absence of moderate to severe mitral stenosis or a mechanical heart valve) at increased risk of stroke in 2 RCTs: the PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation)S4.4.1-1 and the PREVAIL (Evaluation of the WATCHMAN LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy)S4.4.1-2 trials. A meta-analysis combining data from these 2 trials and their registries demonstrated that patients receiving the device had significantly fewer hemorrhagic strokes than did those receiving warfarin, but there was an increase in ischemic strokes in the device group.S4.4.1-3 However, when periprocedural events were excluded, the difference in ischemic strokes was not significant.Oral anticoagulation remains the preferred therapy for stroke prevention for most patients with AF and elevated stroke risk. However, for patients who are poor candidates for long-term oral anticoagulation (because of the propensity for bleeding or poor drug tolerance or adherence), the Watchman device provides an alternative. There are important differences in wording between the FDA approval and the Centers for Medicare & Medicaid Services (CMS) approval. In the FDA approval, the device was restricted to patients who were deemed suitable for long-term warfarin (mirroring the inclusion criteria for enrollment in the clinical trials) but had an appropriate rationale to seek a nonpharmacological alternative to warfarin. Conversely, CMS states that the device is an option for patients who are suitable for short-term warfarin but deemed unable to take long-term oral anticoagulation. CMS has specified that patients should have a CHADS2 score ≥2 or a CHA2DS2-VASc score ≥3 to be considered for the device. A number of unresolved issues remain, including the optimal patient selection and periprocedural antithrombotic regimen. The current FDA labeling specifies that patients should be deemed suitable for anticoagulation and, in particular, a period of periprocedural anticoagulation. Patients unable to take oral anticoagulation were excluded from the Watchman RCTs. However, there is increasing experience outside the United States with LAA closure in oral anticoagulation–ineligible patients using an antiplatelet regimen only,S4.4.1-6,S4.4.1-7 and this is the focus of an ongoing RCT.S4.4.1-84.4.2. Cardiac Surgery—LAA Occlusion/ExcisionRecommendation-Specific Supportive Text (Modified)1. New evidence exists supporting surgical LAA occlusion in patients with a history of AF. An observational study evaluated the association between surgical LAA occlusion (usually with surgical atrial ablation) performed concurrently with cardiac operations in older patients with a history of AF and the risk of postoperative thromboembolic complications.S4.4.2-1 The authors used patient information from the Society of Thoracic Surgeons Adult Cardiac Surgery Database registry, which contains perioperative information with short-term (mainly 30-day) outcomes. The study linked the Society of Thoracic Surgeons Adult Cardiac Surgery Database patient information to Medicare claims data (age ≥65 years), with the primary outcome of readmission within 3 years of operation for thromboembolism (stroke, transient ischemic attack, or systemic embolism). The study identified 10 524 patients who underwent cardiac surgical procedures, including 3 892 patients (37%) with surgical LAA occlusion. At a mean follow-up of 2.6 years, surgical LAA occlusion, compared with no LAA occlusion, was associated with lower unadjusted rates of readmission for thromboembolism (4.2% versus 6.2%), all-cause mortality (17.3% versus 23.9%), and the composite endpoint (20.5% versus 28.7%) but no significant difference in rates of hemorrhagic stroke (0.9% each). These findings suggest that surgical LAA occlusion may be associated with reduced postoperative thromboembolic events in older patients with a history of AF.In subgroup analyses stratified by anticoagulation status at hospital discharge, patients with a history of AF who received LAA occlusion without postoperative anticoagulation had a significantly lower thromboembolism rate than those who received neither LAA occlusion nor anticoagulation. There also was no significant difference in the risk of thromboembolism among patients with a history of AF discharged with anticoagulation therapy, whether they received surgical LAA occlusion or not. These data support a role for anticoagulation in patients with a history of AF, particularly in patients not receiving LAA occlusion.A propensity-matched analysis of prophylactic surgical LAA occlusion in patients undergoing cardiac surgery did not demonstrate an association between LAA occlusion and long-term thromboembolic events.S4.4.2-2 The propensity-matched LAA occlusion and non–LAA occlusion groups were relatively small (461 patients per group), and fewer than half the patients in each group had a history of AF. The study did show that surgical LAA occlusion, which often was incomplete, was associated with increased risk of early postoperative AF, but it did not influence the risk of stroke or death.There are several important limitations to these studies, and future RCTs may be valuable.6. Rhythm Control6.1. Electrical and Pharmacological Cardioversion of AF and Atrial Flutter6.1.1. Prevention of ThromboembolismRecommendation-Specific Supportive Text (New or Modified)1. Three prospective RCTs have evaluated the safety and efficacy of newly initiated factor Xa inhibitors (rivaroxaban and apixaban) for cardioversion as an alternative to warfarin.S6.1.1-7,S6.1.1-8,S6.1.1-17 In addition, retrospective analyses have been performed on the subset of patients undergoing cardioversion within the context of the larger randomized trials that compared each of the FDA-approved NOACs with warfarin for thromboembolism prevention with AF. The results were consistent and support the assertion that NOACs are an effective and safe alternative to warfarin for patients undergoing cardioversion. An alternative to waiting 3 weeks before cardioversion is to perform transesophageal echocardiography to exclude thrombus (see separate recommendation in this section). The decision about long-term anticoagulant therapy (beyond 4 weeks) is based on the thromboembolic risk profile (Section 4) and bleeding risk profile. The "48-hour rule" has also been questioned, because delay to cardioversion of 12 hours or longer from symptom onset was associated with a greater risk of thromboembolic complications compared to cardioversion of less than 12 hours (1.1% versus 0.3%)S6.1.1-18 and the risk of thromboembolic complications with cardioversion of 12 hour or longer increases substantially in patients >75 years of age and in women.S6.1.1-19"4. The data supporting the safety of current practices of cardioversion of AF without oral anticoagulation in patients with AF duration

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