2018 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay

Web Supplement

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Preamble (full version)

Since 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).

Intended Use

Clinical 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 Implementation

Management, 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 Modernization

The 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 (1, 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 (3).

To 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 manual (4) and other methodology articles (5-8).

Selection of Writing Committee Members

The 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 Entities

The 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 at http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy. Appendix 1 of the guideline lists writing committee members' relevant RWI; for the purposes of full transparency, their comprehensive disclosure information is available online http://jaccjacc.acc.org/Clinical_Document/Bradycardia_GL_Comprehensive_Author_RWI.pdf. Comprehensive disclosure information for the Task Force is also available at http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/guidelines-and-documents-task-forces.

Evidence Review and Evidence Review Committees

In developing recommendations, the writing committee uses evidence-based methodologies that are based on all available data (4–6). 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 Therapy

The 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 Evidence

The 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 (see Table 2 in the guideline) (5).

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Table S1. Nutraceuticals and Herbs That May Be Associated With Bradycardia and Possible Active Ingredient or Mechanism (Section 4.1. in the guideline)*

Possible Active Ingredient or Mechanism	Nutraceutical or Herb
Aconitine	• Monkshood • Wolfsbane
Ajmaline	• Indian Snakeroot
Amiodarone	• Khella seed
Beta blocker	• Kudzu root • Lobelia
Calcium channel blocker	• Ginseng • Hawthorne
Glycoside containing	• Foxglove • Lily of the Valley • Oleander • Squill • Stropanthus
Hypokalemia	• Licorice root
Unknown/poorly defined	• Motherwort • Queen of the Night • Skullcap • Valerian

*Incomplete list.

Table S2. Additional Testing for Patients With Evidence of Atrioventricular Block (Section 6.4.3. in the guideline)

Electrocardiographic monitoring • **Holter monitor:** Typically continuous recording 24-48 h duration; useful when symptoms occur daily. Longer monitoring 7-14 d with monitor patches. Patient returns the monitor or patch and the data are accessed and information is sent to the caregiver. • **Event monitor:** Continuous recording with patient activation for symptoms or detection of abnormally fast or slow heart rates. Monitor sends the data to another device (often at 24-h intervals), which then transmits the electrocardiographic data to a central station and then information is sent to the caregiver. • **Mobile cardiac outpatient telemetry:** Continuous recording and real-time monitoring of the heart rhythm. • **Implantable cardiac monitor:** Often will automatically trigger for bradycardic (and tachycardic) events and also allow patient activated episodes.
Exercise treadmill testing: Useful when assessing exertional symptoms or determining whether atrioventricular block is vagally mediated.
Electrophysiology study: Useful to determine if AV block is infranodal.
Endomyocardial biopsy: Useful to determine specific causes for AV block (e.g. sarcoidosis).
Cardiac imaging: Echocardiography (transthoracic or transesophageal), computed tomography, magnetic resonance imaging can provide information on specific causes for AV block.
Pharmacologic testing • **Atropine:** Can paradoxically worsen AV block if underlying infranodal disease is present. • **Procainamide:** Can increase HV interval if underlying infranodal disease is present. • **Isoproterenol:** Can paradoxically worsen AV block if underlying infranodal disease is present.

AV indicates atrioventricular; and HV, His-ventricular.

Table S3. Possible Etiologies for Conduction Disorders With 1:1 Atrioventricular Conduction (Section 7.2. in the guideline)

Etiology	Comments
Physiologic	• First-degree AV block may occur in the absence of organic heart disease caused by increased vagal tone and may be present in athletes or during sleep. • First-degree AV block with moderate PR prolongation is generally a benign condition. • Functional fascicular or bundle branch block may occur in the setting of large beat-to-beat heart rate variations.
Developmental	• Spontaneous AV block occurs at a rate of 2% per year in patients with ccTGA, including well into adulthood (9, 10). • AV septal defects in the setting of left atrial isomerism are other lesions where the AV conduction tissue may be congenitally displaced and at risk, and AV block is a risk factor for mortality in this setting (11).
Hereditary/genetic	• Conduction defects are among the major features of several neuromuscular disorders including myotonic dystrophy and Emery-Dreifuss muscular dystrophy. • Within families with suspected Brugada syndrome, first-degree AV block is more prevalent among carriers of SCN5A mutations and may help further refine risk stratification in selected cases (12). • Conduction delay in arrhythmogenic right ventricular cardiomyopathy may present as QRS fragmentation, bundle branch block, or QRS prolongation on standard or signal-averaged ECG. These parameters have been associated with an increased risk of ventricular arrhythmias and/or sudden death. • Mitochondrial genetic disorders, such as Kearns-Sayre syndrome, may manifest cardiac conduction defects.
Metabolic	• Anderson-Fabry disease, an X-linked lysosomal storage disorder, can mimic hypertrophic cardiomyopathy in adults and present with conduction abnormalities (13-15).
Inflammatory, immune, or infiltrative	• Sarcoidosis, scleroderma, amyloidosis, and hemochromatosis are systemic infiltrative disorders that commonly affect the heart and can be associated with conduction abnormalities that are associated with sudden cardiac death (16).
Infectious	• Endocarditis • Chagas disease • Lyme carditis • Toxoplasmosis
Iatrogenic	• Catheter or wire insertion into the right or left ventricle may “bump” a bundle branch, producing temporary bundle branch block. In the presence of preexisting contralateral bundle branch block transient complete AV block may ensue and require temporary pacing support. • Alcohol septal ablation, a treatment for left ventricular outflow tract obstruction in hypertrophic cardiomyopathy, results in RBBB in about 50% of cases. • Surgical myectomy • Valve surgery: Particularly transcatheter aortic valve replacement
Ischemic	• Intraventricular conduction disturbances may develop in the setting of myocardial infarction as a result of specific blood supply conditions (17, 18).
Degenerative	• The prevalence of RBBB increases with age, such that those >80 years of age have more than a 10% likelihood of having acquired this abnormality (19). • LBBB prevalence also increases with age, although it is about half that of RBBB.

	• Lev's and Lenegre's disease generally refers to fibrosis of the left side of the cardiac skeleton, resulting in fascicular, bundle branch, or complete AV block, as well as calcification of the aortic and mitral rings. Lenegre described fibrosis and progressive degenerative disease in younger patients while Lev described a similar process in older patients that was associated with calcification.

AV indicates atrioventricular; ECG, electrocardiogram; LBBB, left bundle branch block; and RBBB, right bundle branch block.

Table S4. Summary of Neuromuscular Disorders and Disease-Specific Recommendations for Permanent Pacemaker Implantation for the Treatment of Bradycardia (Section 8.4. in the guideline)

Disease	Summary	Disease-Specific Bradycardia Considerations
Dystrophinopathies (Duchenne, Becker)	• Most common form of neuromuscular disorder (80%) (20, 21) • Intraventricular conduction abnormalities (50% RBBB) (20, 21) • Rare infranodal block (20, 21)	• None
Myotonic dystrophy • Type 1	• Most common neuromuscular disorder in adults (20, 22, 23) • AV conduction abnormalities including His Purkinje disease (first-degree AV block: 33%; LBBB: 10%; RBBB: 9%) (20, 22, 23) • Electrocardiographic abnormalities associated with risk of sudden death (20, 22, 23)	• Section 6.4.4., Recommendation 2 in the full-text guideline • Section 6.4.4., Recommendation 8 in the full-text guideline
• Type 2	• Conduction abnormalities and His Purkinje disease less frequently observed than Type 1 (PR >0.2 s; DM2: 10% vs. DM1 31%) (20, 24)	• Similar to myotonic dystrophy type 1 if same conduction abnormalities are present
Emery Dreifuss	• Early onset of AV conduction abnormalities (20) • Progressive His Purkinje disease (20)	• Section 6.4.4., Recommendation 6 in the full-text guideline • Similar to myotonic dystrophy type 1 if same conduction abnormalities are present
Limb Girdle	• Diverse group of multiple diseases (20) • Progressive conduction disease in patients with laminopathies (also referred to as type 1B) (20)	• Section 6.4.4., Recommendation 6 in the full-text guideline • Similar to myotonic dystrophy type 1 if same conduction abnormalities are present
Facioscapulohumeral	• Rare cardiac involvement (20)	• None

AV indicates atrioventricular; DM1, type 1 diabetes mellitus; DM2, type 2 diabetes mellitus; LBBB, left bundle branch block; and RBBB, right bundle branch block.

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