

Table 1. Vascular supply of the conduction system.

Sinus Node: RCA (60%) or Cx (40%)

AV node: RA (90%) or Cx (10%)

His bundle: AV nodal branch of RCA, and septal perforators of the LAD

RBB: septal perforators of the LAD

LBB: septal perforators of the LAD, and AV nodal branch of RCA

Katrtsis DG, Morady F. Clinical Cardiac Electrophysiology. Elsevier 2013.

Table 2. ACC/AHA/HRS 2018 GL on bradycardia. Medications That Can Induce/Exacerbate Bradycardia or Conduction Disorders*

Antihypertensive	Antiarrhythmic	Psychoactive	Other
• Beta-adrenergic receptor blockers (including beta-adrenergic blocking eye drops used for glaucoma) • Clonidine • Methyldopa • Non-dihydropyridine calcium channel blockers • Reserpine	• Adenosine • Amiodarone • Dronedarone • Flecainide • Procainamide • Propafenone • Quinidine • Sotalol	• Donepezil • Lithium • Opioid analgesics • Phenothiazine antiemetics and antipsychotics • Phenytoin • Selective serotonin reuptake inhibitors • Tricyclic antidepressants	• Anesthetic drugs (propofol) • Cannabis • Digoxin • Ivabradine • Muscle relaxants (e.g., succinylcholine)

***: Cytotoxic chemotherapy** agents in different classes have been associated with benign sinus bradycardia, and, rarely, symptomatic bradycardia and advanced atrioventricular block.

Table 3. ACC/AHA/HRS 2018 GL on bradycardia. Conditions associated with Bradycardia or Conduction Disorders

Intrinsic	
Cardiomyopathy (ischemic or nonischemic)	
Congenital heart disease	
Degenerative fibrosis	
Infection/inflammation	
• Chagas disease • Diphtheria • Infectious endocarditis • Lyme disease • Myocarditis • Sarcoidosis • Toxoplasmosis	
Infiltrative disorders	
• Amyloidosis • Hemochromatosis • Lymphoma	
Ischemia/infarction	
Rheumatological conditions	
• Rheumatoid arthritis • Scleroderma • Systemic lupus erythematosus	
Surgical or procedural trauma	
• Cardiac procedures such as ablation or cardiac catheterization • Congenital heart disease surgery • Septal myomectomy for hypertrophic obstructive cardiomyopathy • Valve surgery (including percutaneous valve replacement)	
Extrinsic	
Autonomic perturbation	
• Carotid sinus hypersensitivity • Neurally-mediated syncope/presyncope • Physical conditioning • Situational syncope ○ Cough ○ Defecation ○ Glottic stimulation ○ Medical procedures ○ Micturition ○ Vomiting • Sleep (with or without sleep apnea)	
Metabolic	
• Acidosis • Hyperkalemia • Hypokalemia • Hypothermia • Hypothyroidism • Hypoxia	

Table 4. ESC 2021 GL on pacing and CRT. Intrinsic and extrinsic causes of bradycardia

	Sinus bradycardia or SND	AVJ disturbances
Intrinsic		
Idiopathic (ageing, degenerative)	+	+
Infarction/ischaemia	+	+
Cardiomyopathies	+	+
Genetic disorders	+	+
Infiltrative diseases		
Sarcoidosis	+	+
Amyloidosis	+	+
Haemochromatosis	+	+
Collagen vascular diseases		
Rheumatoid arthritis	+	+
Scleroderma	+	+
Systemic lupus erythematosus	+	+
Storage diseases	+	+
Neuromuscular diseases	+	+
Infectious diseases		
Endocarditis (perivalvular abscess)	–	+
Chagas disease	+	+
Myocarditis	–	+
Lyme disease	–	+
Diphtheria	–	+
Toxoplasmosis	–	+
Congenital heart diseases	+	+
Cardiac surgery		
Coronary artery bypass grafting	+	+
Valve surgery (including transcatheter aortic valve replacement)	+	+
Maze operation	+	–
Heart transplant	+	+
Radiation therapy	+	+
Intended or iatrogenic AVB	–	+
Sinus tachycardia ablation	+	–
Extrinsic		
Physical training (sports)	+	+
Vagal reflex	+	+
Drug effects	+	+
Idiopathic paroxysmal AVB	–	+
Electrolyte imbalance		
Hypokalaemia	+	+
Hyperkalaemia	+	+
Hypercalcaemia	+	+
Hypermagnesaemia	+	+
Metabolic disorders		
Hypothyroidism	+	+
Anorexia	+	+
Hypoxia	+	+
Acidosis	+	+
	Sinus bradycardia or SND	AVJ disturbances
Hypothermia	+	+
Neurological disorders		
Increased intracranial pressure	+	+
Central nervous system tumours	+	+
Temporal epilepsy	+	+
Obstructive sleep apnoea	+	+

AV = atrioventricular; AVB = atrioventricular block; AVJ = atrioventricular junction; SND = sinus node dysfunction

Table 5. ESC 2021 GL on pacing and CRT. Drugs that may cause bradycardia conduction disorders

	Sinus node bradycardia	AVB
Beta-blockers	+	+
Antihypertensives		
Non-dihydropyridine calcium channel blockers	+	+
Methyldopa	+	-
Clonidine	+	-
Antiarrhythmics		
Amiodarone	+	+
Dronedarone	+	+
Sotalol	+	+
Flecainide	+	+
Propafenone	+	+
Procainamide	-	+
Disopyramide	+	+
Adenosine	+	+
Digoxin	+	+
Ivabradine	+	-
Psychoactive and neuroactive drugs		
Donepezil	+	+
Lithium	+	+
Opioid analgesics	+	-
Phenothiazine	+	+
Phenytoin	+	+
Selective serotonin reuptake inhibitors	-	+
Tricyclic antidepressants	-	+
Carbamazepine	+	+
	Sinus node bradycardia	AVB
Others		
Muscle relaxants	+	-
Cannabis	+	-
Propofol	+	-
Ticagrelor	+	+
High-dose corticosteroids	+	-
Chloroquine	-	+
H ₂ antagonists	+	+
Proton pump inhibitors	+	-
Chemotherapy		
Arsenic trioxide	+	+
Bortezomib	+	+
Capecitabine	+	-
Cisplatin	+	-
Cyclophosphamide	+	+
Doxorubicin	+	-
Epirubicin	+	-
5-fluorouracil	+	+
Ifosfamide	+	-
Interleukin-2	+	-
Methotrexate	+	-
Mitoxantrone	+	+
Paclitaxel	+	-
Rituximab	+	+
Thalidomide	+	+
Anthracycline	-	+
Taxane	-	+

AVB = atrioventricular block.

Table 6. ACC/AHA/HRS 2018 GL on bradycardia. Evaluation of patients with documented or suspected Bradycardia or Conduction Disorders

History and physical examination

Comprehensive history and physical examination I-C-EO

Resting ECG

A 12-lead ECG to document rhythm, rate, and conduction, and to screen for structural heart disease or systemic illness I-B-NR

Exercise testing

In suspected chronotropic incompetence, to ascertain the diagnosis and provide information on prognosis IIa-B-NR

In patients with exercise-related symptoms suspicious for bradycardia or conduction disorders, or 2:1 atrioventricular block of unknown level IIa-C-LD

Ambulatory electrocardiography

In the evaluation of patients with documented or suspected bradycardia or conduction disorders, to establish correlation between heart rate or conduction abnormalities with symptoms, with the specific type of cardiac monitor chosen based on the frequency and nature of symptoms, as well as patient preferences I-B-NR

Imaging

Transthoracic echocardiography in newly identified LBBB, second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, or third-degree atrioventricular block with or without apparent structural heart disease or coronary artery disease. I-B-NR

Transthoracic echocardiography in bradycardia or conduction disorders other than LBBB, second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, or third-degree atrioventricular block if structural heart disease is suspected IIa-B-NR

In bradycardia or bundle branch block, disease-specific advanced imaging (e.g., transesophageal echocardiography, computed tomography, cardiac magnetic resonance imaging, or nuclear imaging) if structural heart disease is suspected yet not confirmed by other diagnostic modalities. IIa-C-LD

In asymptomatic sinus bradycardia or first degree AV block and no clinical evidence of structural heart disease, routine cardiac imaging is not indicated III-B-NR (no benefit)

Laboratory testing

In bradycardia, laboratory tests (e.g., thyroid function tests, Lyme titer, potassium, pH) based on clinical suspicion for a potential underlying cause IIa-C-LD

Genetic testing

In patients in whom a conduction disorder-causative mutation has been identified, genetic counseling and mutation-specific genetic testing of first degree relatives to identify similarly affected individuals. I-C-EO

In patients with inherited conduction disease, genetic counseling and targeted testing to facilitate cascade screening of relatives as part of the diagnostic evaluation. IIb-C-EO

Sleep apnoea

In documented or suspected bradycardia or conduction disorder during sleep, screening for symptoms of sleep apnea syndrome with subsequent confirmatory testing directed by clinical suspicion I-B-NR

Treatment directed specifically at the sleep apnea (e.g., continuous positive airway pressure and weight loss) in sleep-related bradycardia or conduction disorder and documented obstructive sleep apnea. I-B-NR

Screening for sleep apnea syndrome in patients who have previously received or are being considered for a PPM for bradycardia or conduction disorder. IIa-B-NR

Invasive testing***Implantable cardiac monitor***

In patients with infrequent symptoms (>30 days between symptoms) suspected to be caused by bradycardia, long-term ambulatory monitoring with an implantable cardiac monitor if initial noninvasive evaluation is nondiagnostic IIa-C-LD

Electrophysiology study

In symptoms suspected to be attributable to bradycardia, an electrophysiology study for diagnosis of, and elucidation of bradycardia mechanism, if initial noninvasive evaluation is nondiagnostic IIa-C-LD

Table 7. ESC 2021 GL on pacing and CRT. Evaluation of the patient with bradycardia**Non-invasive evaluation**

Once carotid stenosis is ruled out,^a carotid sinus massage in patients with syncope of unknown origin compatible with a reflex mechanism or with symptoms related to pressure/manipulation of the carotid sinus area. I B

^a Carotid sinus massage (CSM) should not be undertaken in patients with previous transient ischaemic attack, stroke, or known carotid stenosis. Carotid auscultation should be performed before CSM. If a carotid bruit is present, carotid ultrasound should be performed to exclude the presence of carotid disease.

Ambulatory electrocardiographic monitoring

Ambulatory ECG monitoring for the evaluation of patients with suspected bradycardia to correlate rhythm disturbances with symptoms. I C

Choice of ambulatory electrocardiographic monitoring depending on symptom frequency

Frequency of symptom	
Daily	24-h Holter ECG or in-hospital telemetric monitoring
Every 48–72 h	24–48–72 h Holter ECG
Every week	7-day Holter ECG/external loop recorder/external patch recorder
Every month	External loop recorder/external patch recorder/handheld ECG recorder
<1 per month	ILR

ECG = electrocardiogram; ILR = implantable loop recorder.

Exercise testing

Exercise testing for patients who experience symptoms suspicious of bradycardia during or immediately after exertion. I C

In patients with suspected chronotropic incompetence, exercise testing to confirm the diagnosis. IIa B

In patients with intraventricular conduction disease or AVB of unknown level, exercise testing to expose infranodal block. IIb C

Imaging before implantation

Cardiac imaging in patients with suspected or documented symptomatic bradycardia to evaluate the presence of structural heart disease, to determine LV systolic function, and to diagnose potential causes of conduction disturbances. I C

Multimodality imaging (CMR, CT, or PET) for myocardial tissue characterization in the diagnosis of specific pathologies associated with conduction abnormalities needing pacemaker implantation, particularly in patients younger than 60 years.. IIa C

CMR = cardiovascular magnetic resonance; CT = computed tomography; LV = left ventricular; PET = positron emission tomography.

Laboratory tests

In addition to pre-implantation laboratory tests,^a specific laboratory tests in patients with clinical suspicion for potential underlying causes of reversible bradycardia (e.g. thyroid function tests, Lyme titre, digitalis level, potassium, calcium, and pH) to diagnose and treat these conditions. I C

a Complete blood counts, prothrombin time, partial thromboplastin time, serum creatinine, and electrolytes.

Genetic testing

In patients with early onset (age <50 years) of progressive cardiac conduction disease.^a IIa C

In family members following the identification of a pathogenic genetic variant that explains the clinical phenotype of cardiac conduction disease in an index case IIa C

a Progressive cardiac conduction disease: prolonged P wave duration, PR interval, and QRS widening with axis deviation.

Sleep evaluation

Screening for sleep apnoea syndrome in patients with symptoms of S sleep apnoea syndrome and in the presence of severe bradycardia or advanced AV block during sleep. I C

Tilt testing

Tilt testing in patients with suspected recurrent reflex syncope. IIa B

Implantable loop recorders

Long-term ambulatory monitoring with an ILR in patients with infrequent (less than once a month) unexplained syncope or other symptoms suspected to be caused by bradycardia, in whom a comprehensive evaluation did not demonstrate a cause,. I A

ILR = implantable loop recorder.

Electrophysiology study

EPS in patients with syncope and bifascicular block, when syncope remains unexplained after non-invasive evaluation or when an immediate decision about pacing is needed due to severity, unless empirical pacemaker implantation is preferred (especially in elderly and frail patients). IIa B

EPS in patients with syncope and sinus bradycardia, when non-invasive tests have failed to show a correlation between syncope and bradycardia. IIb B

EPS = electrophysiology study.

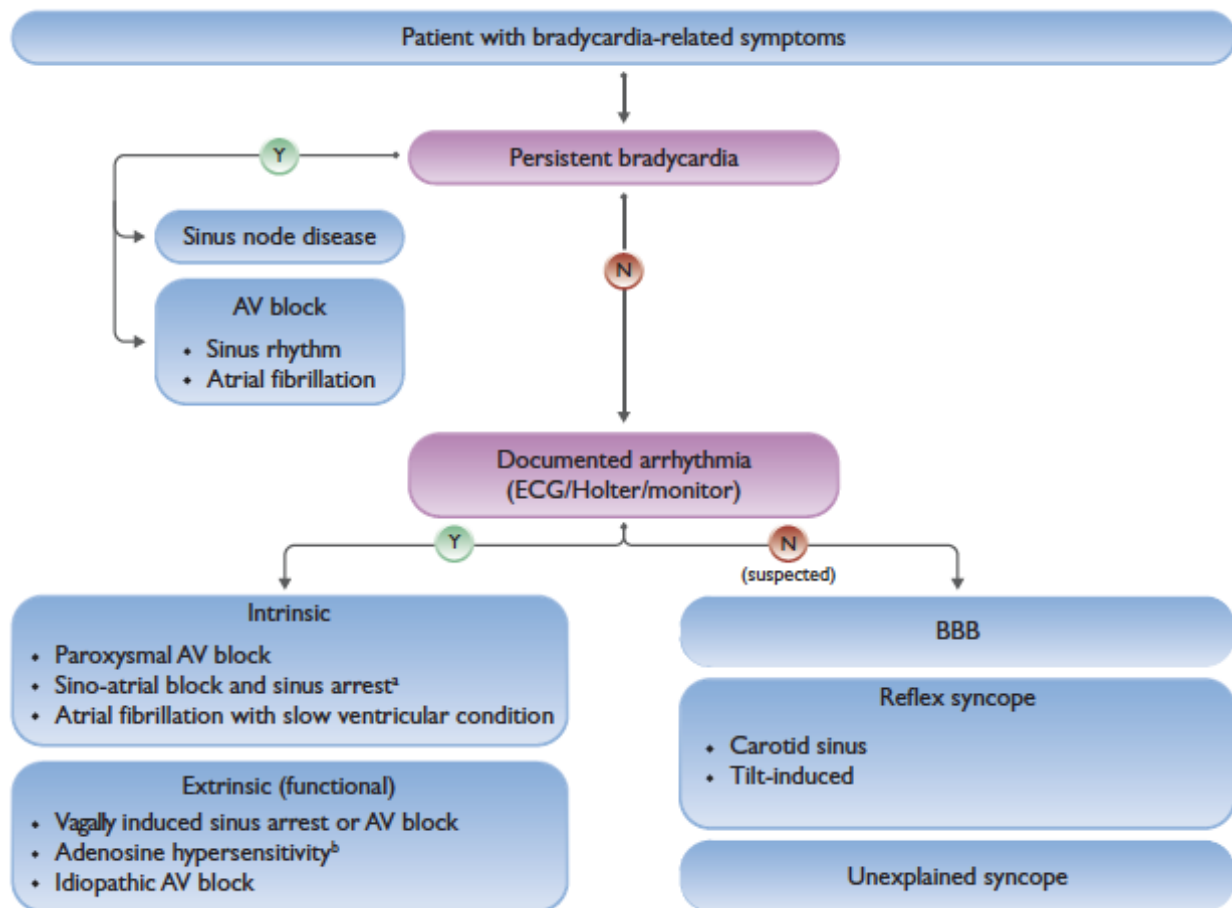


Figure 1. ESC 2021 GL on pacing and CRT. Classification of documented and suspected bradyarrhythmias.

AV = atrioventricular; BBB = bundle branch block; ECG = electrocardiogram.

A Including the bradycardia_tachycardia form of sick sinus syndrome.

B Deharo et al. Adenosine hypersensitivity and atrioventricular block. *Herzschrittmacherther Elektrophysiol* 2018;29:166-170.

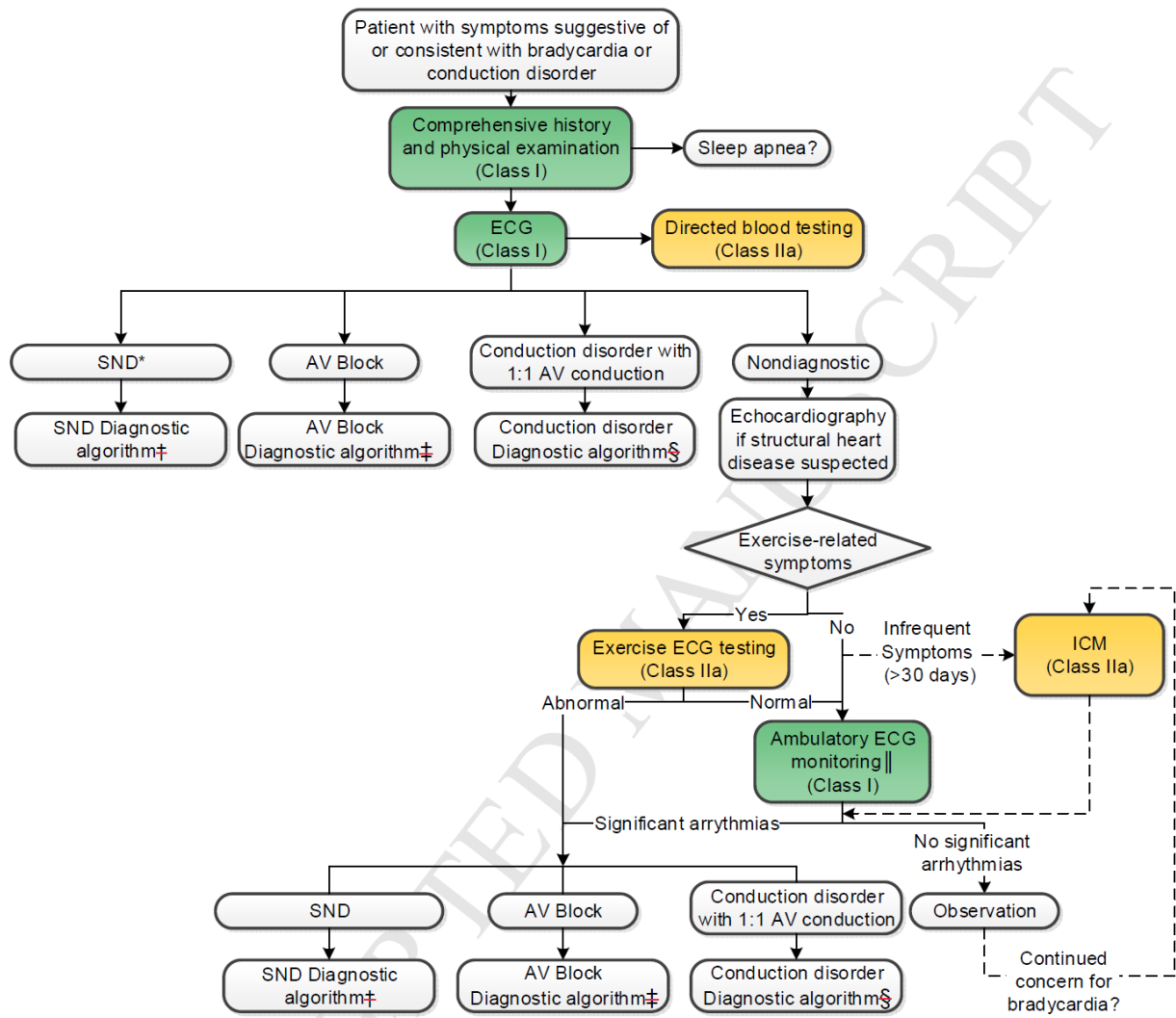


Figure 2. ACC/AHA/HRS 2018 GL on bradycardia. Evaluation of Bradycardia and Conduction Disease Algorithm.

Dashed lines indicate possible optional strategies based on the specific clinical situation.

*Sinus bradycardia, ectopic atrial rhythm, junctional rhythm, sinus pause.

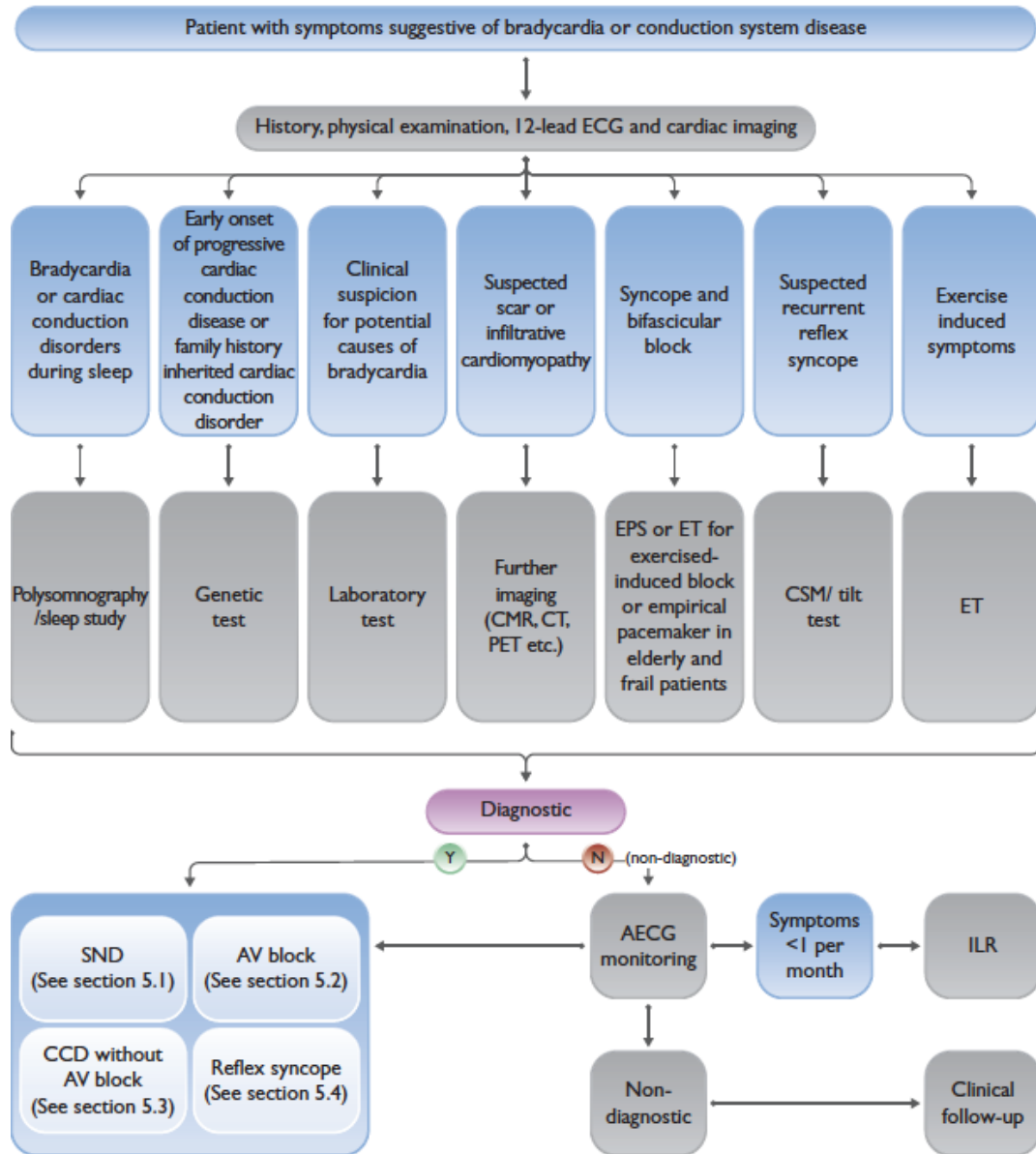


Figure 3. ESC 2021 GL on pacing and CRT. Evaluation of bradycardia and conduction disease algorithm.

AECG = ambulatory electrocardiographic monitoring; AV = atrioventricular; CCD = cardiac conduction disease (or disorder); CMR = cardiovascular magnetic resonance; CSM = carotid sinus massage; CT = computed tomography; ECG = electrocardiogram; EPS = electrophysiology study; ET = exercise test; ILR = implantable loop recorder; PET = positron emission tomography; SND = sinus node dysfunction.

Table 8. ACC/AHA/HRS 2018 GL on bradycardia. Acute Medical Management of Bradycardia Attributable to SND or Atrioventricular Block.

Medication	Dosage	Comments
Symptomatic sinus bradycardia or atrioventricular block		
Atropine	0.5-1 mg IV (may be repeated every 3-5 min to a maximum dose of 3 mg) (S5.3.2.4-20-S5.3.2.4-24)	
Dopamine	5 to 20 mcg/kg/min IV, starting at 5 mcg/kg/min and increasing by 5 mcg/kg/min every 2 min (S5.3.2.4-25)	Dosages of >20 mcg/kg/min may result in vasoconstriction or arrhythmias
Isoproterenol	20-60 mcg IV bolus followed doses of 10-20 mcg, or infusion of 1-20 mcg/min based on heart rate response (S5.3.2.4-26-S5.3.2.4-32)	Monitor for potential development of ischemic chest pain
Epinephrine	2-10 mcg/min IV or 0.1-0.5 mcg/kg/min IV titrated to desired effect (S5.3.2.4-17, S5.3.2.4-31, S5.3.2.4-33)	
Second- or third-degree atrioventricular block associated with acute inferior MI		
Aminophylline	250-mg IV bolus	
Calcium channel blocker overdose		
10% calcium chloride	1-2 g IV every 10-20 min or an infusion of 0.2-0.4 mL/kg/h (S5.3.2.4-34-S5.3.2.4-36)	
10% calcium gluconate	3-6 g IV every 10-20 min or an infusion at 0.6-1.2 mL/kg/h (S5.3.2.4-34-S5.3.2.4-36)	
Beta-blocker or calcium channel blocker overdose		
Glucagon	3-10 mg IV with infusion of 3-5 mg/h (S5.3.2.4-37, S5.3.2.4-38)	
High dose insulin therapy	IV bolus of 1 unit/kg followed by an infusion of 0.5 units/kg/h (S5.3.2.4-36, S5.3.2.4-39, S5.3.2.4-40).	Follow glucose and potassium levels
Digoxin overdose		
Digoxin antibody fragment	Dosage is dependent on amount ingested or known digoxin concentration (S5.3.2.4-41-S5.3.2.4-48)	• One vial binds approximately 0.5 mg of digoxin • Administer over at least 30 min • May be repeated
Post-heart transplant		
Aminophylline	6 mg/kg in 100-200 mL of IV fluid over 20-30 min	
Theophylline	300 mg IV, followed by oral dose of 5-10 mg/kg/d titrated to effect	• Therapeutic serum levels range from 10-20 mcg/mL • Usual posttransplant dosages average 450 mg±100 mg/d
Spinal cord injury		
Aminophylline	6 mg/kg in 100-200 mL of IV fluid over 20-30 min (S5.3.2.4-7)	
Theophylline	Oral dose of 5-10 mg/kg/d titrated to effect (S5.3.2.4-6)	Effective dosages often result in serum levels below the usual effective range of 10-20 mcg/mL

IV indicates intravenous; and MI, myocardial infarction.

Table 9. ACC/AHA/HRS 2018 GL on bradycardia. Therapy of Beta Blocker and Calcium Channel Blocker Mediated Bradycardia Attributable to SND or Atrioventricular Block

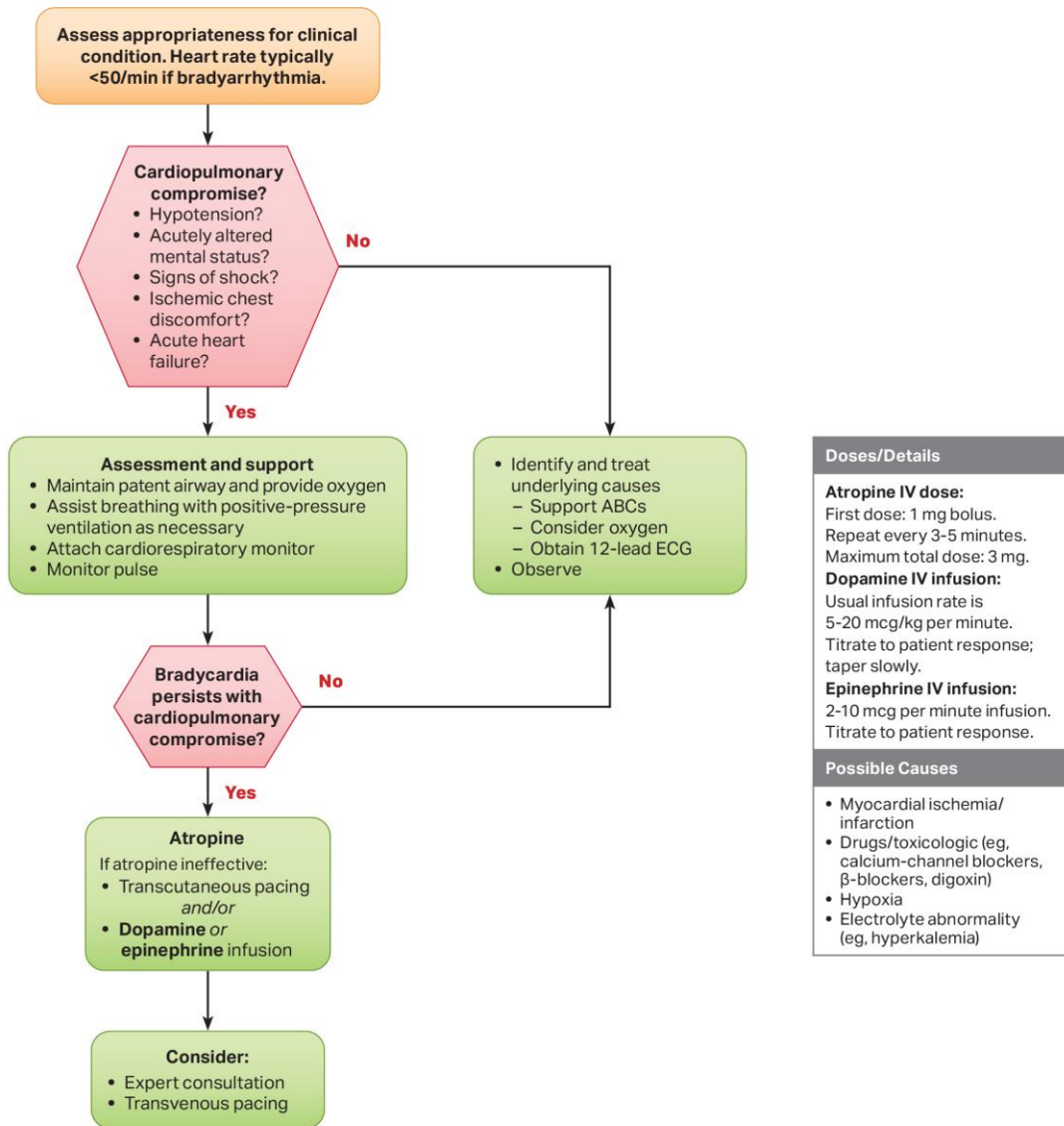
Intravenous calcium in bradycardia associated with symptoms or hemodynamic compromise because of beta-blocker or calcium channel blocker overdose.	IIa-C-LD
Glucagon in bradycardia associated with symptoms or hemodynamic compromise because of calcium channel blocker overdose.	IIa-C-LD
High-dose insulin in bradycardia associated with symptoms or hemodynamic compromise because of calcium channel blocker overdose.	IIa-C-LD

Table 10. ACC/AHA/HRS 2018 GL on bradycardia. Therapy of Digoxin Mediated Bradycardia Attributable to SND or Atrioventricular Block

Digoxin Fab antibody fragment in bradycardia associated with symptoms or hemodynamic compromise	IIa-C-LD
Dialysis is not recommended for removal of digoxin	III-C-LD (No benefit)

Table 11. AHA 2025 GL on CPR. Adult Advanced Life Support Initial Management of Bradycardia

1	C-EO	1. In adult patients presenting with acute symptomatic bradycardia, evaluation and treatment of reversible causes are recommended.
2a	B-NR	2. In adult patients with acute bradycardia associated with hemodynamic compromise, administration of atropine is reasonable to increase heart rate.
2a	C-LD	3. In adult patients with persistent hemodynamically unstable bradycardia refractory to medical therapy, temporary transvenous pacing is reasonable to increase heart rate and improve symptoms.
2b	C-LD	4. If bradycardia is unresponsive to atropine, IV adrenergic agonists with rate-accelerating effects (eg, epinephrine, dopamine) or transcutaneous pacing may be effective while the adult patient is prepared for emergent transvenous temporary pacing if required.
2b	C-EO	5. Immediate pacing might be considered in unstable adult patients with high-degree AV block when IV/IO access is not available.



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Figure 4. AHA 2025 GL on CPR. Adult Bradycardia With a Pulse Algorithm.

Table 12. ESC 2021 GL on pacing and CRT. Recommendations regarding temporary cardiac pacing

Temporary transvenous pacing in cases of haemodynamic-compromising bradyarrhythmia refractory to intravenous chronotropic drugs.	I C
Transcutaneous pacing in cases of haemodynamic-compromising bradyarrhythmia when temporary transvenous pacing is not possible or available.	IIa C
Temporary transvenous pacing when immediate pacing is indicated and pacing indications are expected to be reversible, such as in the context of myocardial ischaemia, myocarditis, electrolyte disturbances, toxic exposure, or after cardiac surgery.	IIa C
Temporary transvenous pacing as a bridge to permanent pacemaker implantation when this procedure is not immediately available or possible due to concomitant infection.	IIa C
For long-term temporary transvenous pacing, an active fixation lead inserted through the skin and connected to an external pacemaker.	IIa C