

Indications for permanent cardiac pacing

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Key points

- Permanent cardiac pacing is indicated for treatment of nonreversible symptomatic bradycardia or atrioventricular (AV) block with high-risk features for progression to third-degree AV block.
- Pacemaker is rarely indicated as a primary strategy in reflex bradycardia or asymptomatic nighttime bradycardia.
- Primary indication for pacing to treat tachyarrhythmias is limited and generally not recommended except in patients with nonreversible bradycardia-dependent torsades de pointes ventricular tachycardia.
- Pacemaker algorithms should be used to minimize right ventricular pacing if intact AV conduction is present to minimize pacing-induced cardiomyopathy.
- If >40% ventricular pacing is expected, conduction system lead or biventricular lead should be considered, especially for patients with ejection fraction (EF) 36–50%.
- If pacemaker is indicated for bradycardia with $EF \leq 35\%$, implantable cardioverter–defibrillator (ICD) with or without resynchronization therapy should be considered.
- Benefit of cardiac resynchronization therapy (CRT) is strongest in patients with NYHA class II–IV symptoms, sinus rhythm, and left bundle branch block.
- Conduction system pacing may be considered in patients with unsuccessful left ventricular (LV) lead implant or suboptimal results following biventricular pacing.
- In children with congenital heart disease, pacemaker is indicated for symptomatic bradycardia with special attention to the choice of the lead and device, based on age and congenital abnormality present.

Introduction

Disorders of cardiac impulse formation and propagation may occur at any level of the specialized conduction system, extending from the sinus node through the AV node, His–Purkinje system, and

intramyocardial Purkinje network. Intrinsic conduction system pathology is frequently multifocal and progressive; thus, an apparently isolated abnormality at one level rarely excludes concomitant or future dysfunction elsewhere. For example, normal AV conduction neither can be presumed in

a patient undergoing pacemaker implantation for sinus node dysfunction (SND) nor can intact sinus node function be assumed in an individual paced for AV block.

Clinically important bradyarrhythmias and pauses may result from transient, potentially reversible conditions, such as drug toxicity, metabolic or electrolyte derangements, acute ischemia, and inflammatory processes, or may reflect fixed, degenerative conduction disease. Distinguishing reversible from irreversible etiologies is fundamental, as correction of reversible factors may eliminate the need for permanent pacing. Contemporary indications for permanent pacemaker implantation (PPI), therefore, incorporate not only the anatomic level of conduction disturbance but also symptom burden, the hemodynamic significance of the bradyarrhythmia, the probability of reversibility, and the broader clinical context. This chapter reviews the major conduction system disorders that lead to cardiac pacing and summarizes current guideline-based recommendations for device therapy, including the evolving role of conduction system pacing (CSP).

Anatomy and physiology of the conduction system

The current understanding of the anatomy and physiology of the cardiac conduction system is continually evolving and has been substantially informed by both research and clinical practice of CSP. A thorough appreciation of rhythm generation and intracardiac conduction, as well as their pathological manifestations, requires a focused review of the anatomy and physiology of the specialized conduction system.

Sinus node

The sinoatrial (SA) node is a crescent-shaped, predominantly subepicardial structure located at the junction of the superior vena cava (SVC) and right atrium along the long axis of the terminal crest. Contemporary high-resolution anatomic and structural mapping studies confirm that the node typically measures 10–25 mm in length, with some extensions projecting superiorly toward the SVC or inferiorly along the crista terminalis. The node possesses rich autonomic innervation and a robust

arterial supply with multiple arterial branches or dual supply patterns [1]. The SA node's location adjacent to the sinus nodal artery facilitates exceptionally rapid modulation of firing rate in response to fluctuations in autonomic tone and metabolic demand.

The crista terminalis is an endocardial structure that overlies the majority of nodal tissue, but newer imaging demonstrates that the inferior and lateral extensions may course more deeply in a subendocardial plane. Histologically, the node contains specialized pacemaker and transitional cell types embedded within a dense collagenous matrix. The boundaries of the SA node are indistinct, with nodal extensions and “fingers” interdigitating with adjacent atrial myocardium, particularly toward the intercaval region and SVC. This anatomic heterogeneity and distal fragmentation explain the multiple potential exit sites and the absence of a single, discrete breakthrough point of atrial activation.

Despite the presence of distinct pacemaker and transitional cell phenotypes, no sharply demarcated SA junction exists, because radiating fibers are not electrically insulated from the surrounding atrial myocardium. Instead, a gradient of intercellular coupling and ion-channel expression, from loosely coupled, low-conductance central pacemaker cells to more tightly coupled peripheral cells, helps preserve the node's ability to maintain automaticity in the face of electrotonic loading from the surrounding atria. The periphery exhibits higher expression of HCN4-mediated I_f (funny current, a mixed sodium and potassium current carried by the HCN channels), as well as increased I_{Na} availability relative to the center, supporting successful propagation of impulses into atrial tissue [2].

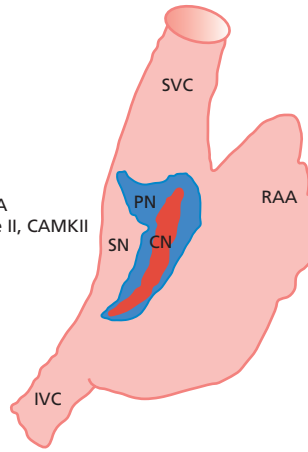
Recent mechanistic studies emphasize that impulse initiation is governed by an interplay between the voltage clock (HCN-dependent I_P , I_{CaL} , and I_{CaT}) and the calcium clock. Central nodal cells exhibit low maximum diastolic potentials (approximately -50 to -60 mV) and slow, I_{CaL} -dependent action potentials, while peripheral nodal and paranodal regions rely more heavily on I_{Na} to overcome the electrical load of the adjacent atrial myocardium. Disruption of either the voltage- or calcium-clock components due to genetic channelopathies,

Molecular and Biophysical Defects

Ion Channels
Fast sodium current
L-Type calcium current
 I_f current
Repolarizing K^+ current

Connexins
Intracellular calcium cycling
Sarcoendoplasmic reticulum ATPase, SERCA
 Ca^{2+} calmodulin-dependent protein kinase II, CAMKII
Calsequestrin II, CASQ2
Ryanodine receptors, RyR

Popeye proteins
Ankyrin B
Alpha myosin heavy chain
Micro RNA (Pitx 2)
Angiotensin II
Adenosine



Other Intrinsic and Extrinsic Factors

Fibrosis
Infiltration
Amyloid
Malignancy
Sarcoid
Scleroderma
Hemochromatosis

Inflammation
Rheumatic fever
Diphtheria
Chagas disease
Lyme disease

Atherosclerosis
Ischemia
Pericardial disease

Drugs
Sympatholytics
Parasympathomimetics
Antiarrhythmics
Cimetidine
Lithium

Toxins
Trauma
Endocrine
Hypothyroidism
Thermoregulatory
Hypothermia
Metabolic
Hypoxia

Figure 1.1 Summary of factors contributing to sinus node (SN) dysfunction. The central node (CN) shown in red is surrounded by the peripheral nodal (PN) structure in blue. RAA, right atrial appendage; SVC, superior vena cava; IVC, inferior

vena cava. Source: Modified from Monfredi O, Boyett MR. Sinus sinus syndrome and atrial fibrillation in older persons: a view from the sinoatrial nodal myocyte. *J Mol Cell Cardiol* 2015;83:88–100. Reproduced with permission of Elsevier.

fibrosis, aging-related remodeling, or metabolic dysregulation contribute to sinus node dysfunction (SND) [3] (Figure 1.1).

Functionally, the SA node remains the dominant pacemaker of the heart due to its intrinsic highest rate of spontaneous diastolic (phase 4) depolarization. Electrophysiological mapping demonstrates that functionally active pacemaker tissue can be distributed across a broad, elongated region of the intercaval atrium. Thus, the SA node exhibits longitudinal pacemaker shift, with superior pacemaker sites preferentially recruited during adrenergic stimulation and inferior regions activated during increased vagal tone. These dynamic shifts underscore the multicentric potential of pacemaker activity. Premature atrial stimulation, autonomic perturbations, and certain medications can further modulate pacemaker location and exit pathways, producing variable atrial activation patterns. This accounts for the variability of the sinus P-wave morphology and axis between patients and within individual patients.

Atrioventricular node

The compact AV node is a subendocardial structure located at the apex of the triangle of Koch, with substantial interindividual variability in its exact position and morphology. Rather than the older estimates of 2–5 mm, the compact node more consistently measures approximately 5–7 mm in length and 1–1.5 mm in width, reflecting its tightly packed cellular architecture. The node is contiguous with atrial myocardium on its proximal (atrial) side, whereas distally it becomes progressively insulated by the central fibrous body, marking the transition to the His bundle. The atrionodal (AN) and nodal-His (NH) transitional zones remain functionally important bridges, with gradual shifts in cell size, connexin expression, and ion-channel profiles that generate the unique conduction properties of the AV junction.

Histologically, the compact node (N-region) is composed of small, irregularly oriented cells with low connexin-43 expression and a predominance of L-type Ca^{2+} -dependent depolarization, producing

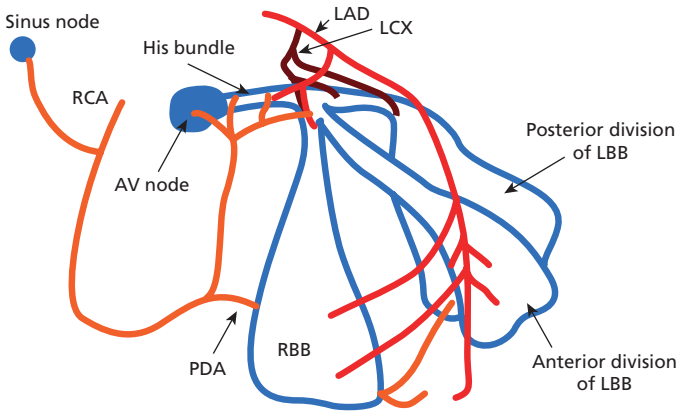


Figure 1.2 Schematic of the conduction system with arterial supply shown. LAD, left anterior descending coronary artery; LBB, left bundle branch; LCX, left circumflex coronary artery; RBB, right bundle branch; RCA, right coronary artery.

slow upstroke velocity and decremental conduction. Modern molecular profiling confirms that action potential characteristics evolve gradually across the AN $\rightarrow$ N $\rightarrow$ NH continuum, rather than existing as sharply demarcated cell types. Posterior nodal extensions, now more commonly termed inferior nodal extensions (INEs), extend rightward and leftward and form the principal anatomic substrate for “slow-pathway” conduction in AV nodal reentrant tachycardia.

The AV node receives dense autonomic innervation, with both sympathetic and parasympathetic fibers exerting strong modulation of conduction velocity and refractoriness. Its blood supply is provided by the AV nodal artery, arising from the right coronary artery in roughly 80–90% of individuals and from the left circumflex in the remainder, with occasional dual or variant supply patterns. Distal nodal and proximal His tissues can generate junctional escape rhythms, and adrenergic stimulation (e.g. isoproterenol) can accelerate junctional rate while shifting the dominant pacemaker site proximally into AN transitional cells or inferior extensions. The AV node is a dynamically coupled micro-network, whose architecture optimizes reliability, protects against atrial tachyarrhythmias, and provides flexible modulation of AV conduction [4].

His–Purkinje system

Specialized conduction fibers (Purkinje fibers) emerging from the distal AV node converge to form the Bundle of His. The His bundle traverses the fibrous (membranous) septum and courses toward the crest of the muscular interventricular

septum, where it bifurcates into the right and left bundle branches (RBB and LBB) (Figure 1.2). In most human hearts, the LBB contains the greater share of specialized conduction tissue, whereas the RBB is often a narrower, more cord-like structure. Histologically, the His–Purkinje axis is composed of longitudinal strands of Purkinje-type cells (and transitional cells), ensheathed by a dense collagenous matrix; this structural compartmentalization supports high longitudinal conduction velocities while minimizing lateral electrotonic spread to adjoining myocardium.

The distal architecture of the conduction system is markedly variable among individuals. In many hearts, the LBB fans out rapidly into the anterior and posterior (or septal) fascicle but may also branch into a tri- or multifascicular pattern. In other hearts, a highly interwoven Purkinje network may predominate. This has important implications for CSP. It is this arborization that may contribute the overall successful outcomes of CSP with LBB area pacing relative to the His bundle pacing (HBP). The RBB is generally more consistent in its course: it travels subendocardially along the right aspect of the septum, typically giving off multiple arborizing branches distally that conduct to the right ventricular (RV) free wall and papillary muscle insertions.

Historically, the His–Purkinje system was thought to have minimal autonomic innervation; however, recent studies challenge this assumption by showing regionally variable sympathetic and parasympathetic fibers, suggesting possible modulation of conduction under physiological and pathophysiological conditions [5].

Vascular supply to the His bundle and bundle branches is typically robust and often dual: the proximal His and penetrating portion are most often supplied by branches of the AV-nodal artery (when present) and by septal perforators derived from the left anterior descending coronary artery (LAD). The exact pattern depends on coronary dominance and individual septal perforator anatomy, explaining the variety of conduction disturbances seen in ischemic disease (Figure 1.2).

Functionally, the rapid conduction through the insulated His–Purkinje network enables near-simultaneous activation of the right and left ventricles, ensuring coordinated systolic contraction. The combination of specialized cell types (Purkinje-type and transitional cells), abundant gap junctions, and longitudinal fiber alignment underlies the high conduction velocities.

From a clinical and translational perspective, the recognition of considerable interindividual anatomic variability, combined with the insulated, rapidly conducting microarchitecture of the His–Purkinje system, has underpinned the expansion of CSP, including both HBP and left bundle branch area pacing (LBBAP). Targeting distal sites in the LBB region may accommodate anatomic variation while preserving physiological ventricular activation, improving outcomes compared with conventional ventricular pacing [6].

CSP has provided several important insights into the functional anatomy, physiology, and pathophysiology of the native cardiac conduction system that were not fully appreciated from anatomic studies or surface electrocardiography alone. These insights have reshaped contemporary understanding of intraventricular activation and have direct implications for pacing strategies.

1 Functional anatomy of the His–Purkinje system is more extensive and heterogeneous than previously recognized

CSP has demonstrated that the His bundle and bundle branches form a broad, arborizing network rather than a narrow, cable-like structure. HBP frequently captures adjacent septal myocardium or distal conduction fibers, revealing longitudinal dissociation within the His bundle and variable spatial separation of fibers destined for the RBB and LBB. Left bundle branch pacing (LBBP) has further highlighted the extensive subendocardial and

intraseptal course of the left bundle and its fascicles, with capture possible at multiple septal depths and longitudinal levels.

2 Longitudinal dissociation and selective recruitment within the His bundle are clinically relevant

Selective and nonselective His bundle capture has shown that discrete fiber populations within the His bundle can be differentially recruited. This has provided functional confirmation of longitudinal dissociation, explaining phenomena such as rate-dependent bundle branch block, intermittent AV block, and the ability of His pacing to normalize bundle branch block by capturing fibers distal to a site of functional or proximal block.

3 Bundle branch blocks are often functional or proximal rather than distal

CSP has shown that a substantial proportion of left bundle branch block (LBBB), particularly in nonischemic cardiomyopathy, can be corrected by HBP or proximal LBB capture. This implies that conduction delay often resides in the proximal His–Purkinje system rather than in diffuse distal Purkinje or myocardial disease, challenging the assumption that most LBBB reflects irreversible distal conduction system damage.

4 The left bundle branch is accessible and capturable deep within the interventricular septum

LBBP has provided direct evidence that the LBB and its fascicles can be consistently captured from the RV septal approach. Electrophysiologic markers, such as left bundle potentials, short and constant LV activation times, and selective capture, have clarified the spatial relationship between septal myocardium and the conduction system and confirmed the feasibility of engaging the left-sided Purkinje network without left-sided vascular access.

5 Physiologic ventricular activation depends more on conduction system recruitment than AV or VV timing alone

CSP has underscored that restoration of rapid, synchronous ventricular activation requires engagement of the His–Purkinje system itself, not merely optimization of AV or interventricular timing. This insight explains why biventricular pacing may fail in some patients despite optimal programming and why CSP can produce narrower QRS complexes and more physiologic activation patterns.

6 Septal myocardial pacing is not equivalent to conduction system capture

Experience with CSP has clarified that pacing from the septum, even when producing a relatively narrow QRS, does not replicate true Purkinje-mediated activation unless the conduction system is directly captured. This distinction has refined interpretations of paced QRS morphology and emphasized the importance of electrogram criteria and activation timing rather than surface ECG appearance alone.

7 AV conduction disease is often dynamic and modifiable

HBP has demonstrated that infra-Hisian block may be intermittent or functional, with conduction restored at higher pacing outputs or different pacing sites. This has provided mechanistic insight into paroxysmal AV block, phase-dependent block, and the influence of autonomic tone and membrane potential on conduction system excitability.

8 The conduction system has a limited safety margin for injury but significant capacity for functional recruitment

CSP implant experience has revealed both the vulnerability of the His–Purkinje system to trauma, ischemia, or fibrosis and its ability to support normal activation when appropriately recruited. This duality has refined understanding of pacing thresholds, lead positioning, and long-term performance of conduction system leads.

9 Ventricular dyssynchrony is fundamentally an electrical disease of the conduction system

CSP has reinforced the concept that electrical dyssynchrony primarily reflects disordered His–Purkinje activation rather than myocardial conduction delay per se. Correction of dyssynchrony by CSP, even without multisite pacing, has provided strong physiologic evidence supporting this paradigm.

10 Clinical pacing strategies can now be guided by conduction system physiology rather than anatomic surrogates

CSP has shifted pacing from an anatomic approach (RV apex or coronary sinus branches) toward a physiology-driven strategy focused on preserving or restoring native conduction. This represents a conceptual advance in how the conduction system is understood and therapeutically engaged.

Permanent cardiac pacing—Indications and guideline considerations

Permanent cardiac pacing is a cornerstone therapy for patients with clinically significant bradyarrhythmias. The decision to implant a pacemaker can be nuanced, requiring careful assessment of symptoms, conduction-system pathology, and the likelihood of progression or reversibility of conduction disease. Current guidelines from the American College of Cardiology (ACC), American Heart Association (AHA), Heart Rhythm Society (HRS), and the European Society of Cardiology (ESC) provide a structured framework for evaluating the need for pacing while emphasizing individualized patient assessment and shared decision-making.

Determinants of pacing requirement

Several key factors determine the indication for permanent pacing.

1 Symptoms related to bradyarrhythmia:

Syncope, presyncope, exercise intolerance, or heart failure symptoms attributable to slow heart rates remain primary triggers for pacing evaluation. Objective documentation of bradycardia or conduction pauses (via electrocardiography, Holter, or implantable monitors) is essential to establish a causal relationship.

2 Site and severity of conduction abnormality:

The location of conduction delay within the cardiac conduction system significantly influences pacing strategy. High-grade atrioventricular (AV) block (second-degree type 2 or third-degree), infranodal block, or symptomatic SND generally warrant permanent pacing, irrespective of transient or intermittent manifestations. The decision may be guided by extended electrocardiographic monitoring, electrophysiologic study, or advanced imaging when required.

3 Progressive or genetic conduction disorders:

Conditions associated with progressive conduction system disease, including hereditary cardiomyopathies or inherited conduction disorders, may justify earlier implantation, even in minimally symptomatic patients. Early intervention can prevent symptomatic deterioration and mitigate the risk of sudden cardiac events.

4 Potential for reversibility: Bradyarrhythmias caused by reversible factors, including drug toxicity, electrolyte imbalance, acute ischemia, or inflammatory myocarditis, typically do not necessitate permanent pacing unless the conduction defect persists after correction of the underlying cause. Accurate differentiation between transient and permanent disease is critical

All guideline recommendations are subdivided into three classes to reflect the magnitude of treatment effect (Table 1.1). A class I indication pertains to a condition in which the procedure or intervention confers definite benefits. A class III indication is one in which the intervention is not helpful and potentially harmful and hence not recommended.

Additionally, the evidence supporting recommendations is ranked by the following criteria for level of evidence.

- **Level A:** Data derived from multiple randomized controlled trials (RCTs) involving a large number of patients; meta-analysis of high-quality RCTs; one or more RCTs corroborated by high-quality registry studies.
- **Level B-R (randomized):** Moderate-quality evidence from one or more RCTs or from meta-analyses of moderate-quality RCTs.

- **Level B-NR (non-randomized):** Moderate-quality evidence from one or more non-randomized studies, observational studies, or registry studies; meta-analyses of such studies.
- **Level C-LD (limited data):** Randomized or non-randomized observational or registry studies with limitations of design or execution; meta-analyses of such studies; physiological or mechanistic studies in human subjects.
- **Level C-EO (expert opinion):** Consensus based on clinical experience.

Some class I indications will necessarily lack support from level A evidence due to early non-randomized studies documenting clear benefits such that randomized trials become unethical. The key current guidelines, their scope, and relevance as referenced throughout this chapter are summarized in Table 1.2. Important concepts and elements are highlighted where appropriate.

Sinus node dysfunction

Definition and classification of sinus node dysfunction

Disorders of the sinus node can be broadly categorized as follows:

- **Intrinsic SND:** due to primary pathology of the sinus node or adjacent atrial tissue (e.g. fibrosis, atrial myopathy, and structural remodeling).
- **Extrinsic SND:** due to external influences such as autonomic imbalance or the effects of medications.

The terms *sinus node dysfunction (SND)*, *sick sinus syndrome*, and *SA-node disease* are used interchangeably. They encompass a wide range of abnormalities in sinus node impulse generation and atrial conduction. Typical manifestations include persistent sinus bradycardia, chronotropic incompetence, intermittent or persistent sinus arrest, and SA exit block. In many cases, atrial tachyarrhythmias coexist with SND, resulting in symptomatic pauses (e.g. at termination of an atrial arrhythmia), commonly referred to as “tachycardia/bradycardia syndrome” (Figure 1.3).

Table 1.1 Classes of guideline recommendations

<i>Class I</i>	Conditions for which there is evidence and/or general agreement that a pacemaker implantation is beneficial, useful, and effective
<i>Class II</i>	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of pacemaker implantation
<i>Class IIa</i>	Weight of evidence/opinion in favor of efficacy
<i>Class IIb</i>	Usefulness/efficacy less well established by evidence/opinion
<i>Class III</i>	Conditions for which there is evidence and/or general agreement that a pacemaker is not useful/effective and in some cases may be harmful

Table 1.2 Summary of key current guidelines referenced throughout this chapter

2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay [7]	Foundational guideline for permanent pacing decisions (symptomatic bradycardia, AV block, sinus node dysfunction, conduction abnormalities), device-based therapy, and general evaluation of conduction disease/bradycardia in adults.
2021 ESC Guidelines on Cardiac Pacing and Cardiac Resynchronization Therapy [8]	European guideline for pacing/CRT: complements ACC/AHA guidance, offers recommendations on evaluation of bradyarrhythmia, conduction disease, and includes updated considerations (e.g. reflex syncope evaluation, non-invasive assessment, and genetic testing in younger patients).
2023 HRS/APHRS/LAHRS Guideline on Cardiac Physiologic Pacing for the Avoidance and Mitigation of Heart Failure [9]	Recent guideline focusing on physiologic pacing strategies (conduction-system pacing, CRT) particularly for patients at risk of or with heart failure—includes patient selection, pre-implant assessment, procedural guidance, follow-up, and optimization.
2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy [10]	Device/ICD selection and pacing-related therapy when indicated. The guideline emphasizes shared decision-making concerning the choice between single-chamber, dual-chamber, or subcutaneous ICDs—in part based on the potential need for pacing (e.g. for bradycardia or atrioventricular conduction disease).
ACC/AHA/ASE/HFSA/HRS/SCAI/SCCT/SCMR 2025 Appropriate Use Criteria for Implantable [11]	Updated comprehensive “Appropriate Use Criteria (AUC)” covering 335 clinical scenarios for ICDs, CRT, leadless pacing, conduction-system pacing, and traditional pacing—helps clinicians judge whether device implantation is “Appropriate,” “May Be Appropriate,” or “Rarely Appropriate,” complementing formal guideline recommendations.

Pathophysiology of intrinsic SND

Intrinsic SND is common and its prevalence increases with age. Several underlying pathologic patterns have been described.

1 Atrial myopathy/atriopathy: Structural remodeling of the atrium, often affecting the region near the sinus node and along the crista terminalis. This remodeling may lead to a more caudal (lower) shift of the dominant pacemaker site over time. Atriopathy is also associated with atrial arrhythmias, particularly atrial fibrillation that develops in 50% of patients with SND

2 Cellular changes: For example, downregulation of L-type calcium channels ($I_{Ca,L}$) and reduced expression of gap-junction proteins (e.g. connexin-43) have been demonstrated in animal models. Although direct evidence in humans is more limited, such remodeling likely contributes to impaired impulse generation and conduction

3 Anatomic abnormalities: Including hypoplasia or atrophy of the sinus node (rare) or congenital anomalies

4 Channelopathies: Mutations involving HNC4 (LV noncompaction syndrome), SCN5A (Brugada

syndrome), and GNB2 (familial sick sinus syndrome and Sturge–Weber syndrome) have all been linked to sinus node dysfunction

5 MYH6 mutation: A structural gene for myosin; variations can affect cardiac muscle contraction, increasing SND risk

6 “Idiopathic” SND: In some patients, no structural or histologic abnormality can be identified; dysfunction may in part result from abnormalities in neural (autonomic) innervation of the sinus node

SND frequently coexists with atrial arrhythmias [notably atrial fibrillation (AF)]. In such cases, the arrhythmia itself may worsen SND, and conversely, SND may predispose to arrhythmia. Prior observational data suggested that restoring sinus rhythm (e.g. via ablation of AF or flutter) can reverse some adverse electrical remodeling of the sinus node. More recent data question whether minimizing atrial pacing truly prevents recurrent AF (see below).

Clinical presentation and diagnostic considerations

Symptoms in SND may be quite variable. When symptomatic, patients may present with syncope,

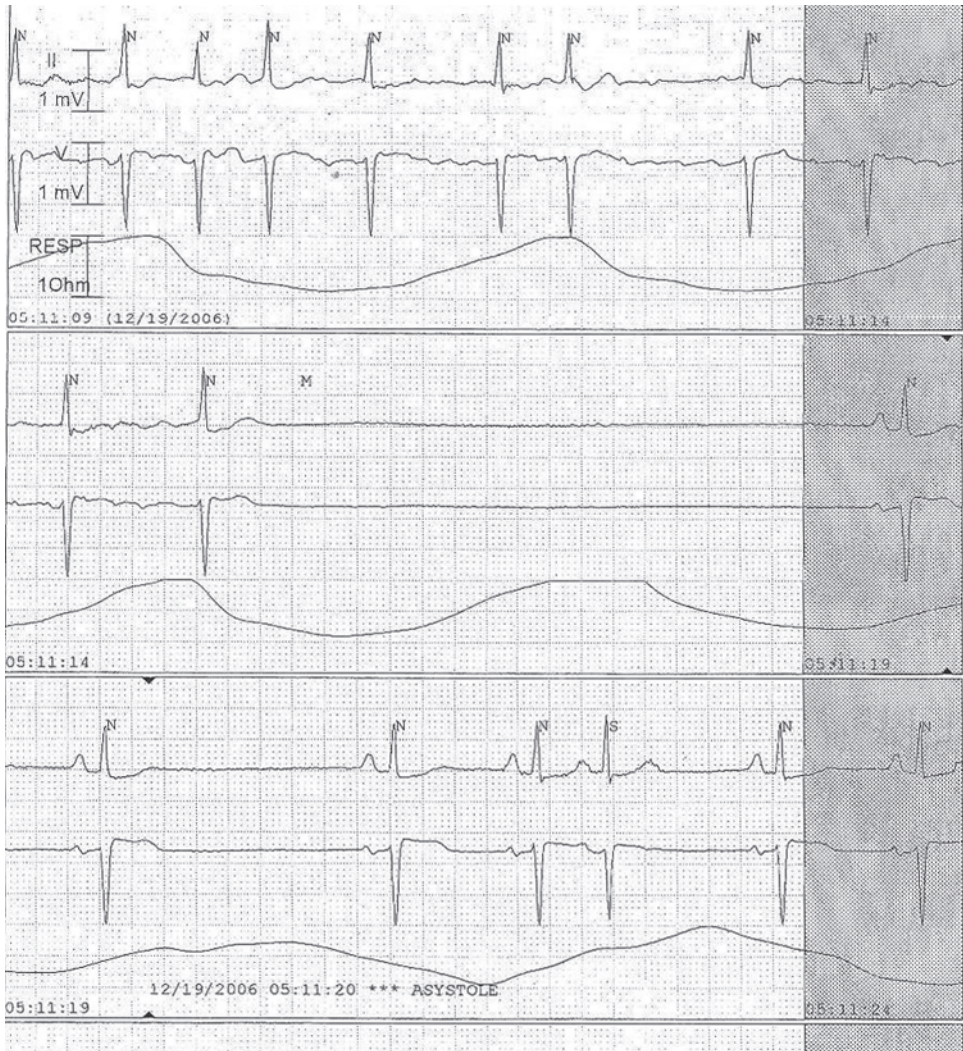


Figure 1.3 This figure shows a telemetry recording the termination of atrial fibrillation with a prolonged pause of nearly 5s before sinus node function returns and nearly 10s for total sinus node recovery, typical of tachycardia-bradycardia syndrome.

presyncope, dizziness, lightheadedness, exercise intolerance, fatigue, or less specific complaints (e.g. lethargy and cognitive slowing). In older individuals, nonspecific symptoms, such as reduced exercise tolerance, fatigue, or subtle cognitive decline, are often misattributed to aging or other comorbidities.

Diagnosis requires demonstration of a *causal relationship* between bradyarrhythmia and symptoms. This is often difficult, particularly when symptoms are mild or intermittent. Key diagnostic

tools include prolonged ambulatory ECG monitoring, event recorders (patient-triggered or auto-triggered), and exercise testing (to assess chronotropic competence). Electrophysiological study (EPS) performed specifically for the diagnosis of SND is rarely indicated. Non-invasive monitoring with symptom correlation remains the diagnostic method with the highest yield. Manifestations of SND are summarized in Table 1.3

The overarching goal in SND management is to relieve symptoms (e.g. syncope, presyncope, dizziness,

Table 1.3 Manifestations of sinus node dysfunction

<i>Sinus bradycardia</i>	Sinus rates persistently <50 bpm and associated with symptoms. Prolonged sinus node recovery time (following atrial pacing) is helpful in diagnosing sinus node disease but has low sensitivity.
<i>Chronotropic incompetence</i>	Inadequate sinus rate response to exercise, defined as failure to achieve 80% of expected heart rate during exercise. Diagnosis made with exercise test or ambulatory ECG monitoring.
<i>Sinoatrial (SA) block</i>	Sinus beats are “dropped” in a regular pattern (e.g. 2: 1 SA block and 3: 2 SA Wenckebach) due to blocking of impulses in the perinodal area between the sinus node and atrial muscle (by disease, medications, etc.). Diagnosis is by ECG or ambulatory monitoring.
<i>Sinus pause >3.0s</i>	Failure of impulse formation in the sinus node due to pathology, medications, etc. The diagnosis is made electrocardiographically by an absence of sinus P waves that occurs without any discernible pattern.
<i>Tachy-brady syndrome</i>	The diagnosis is made electrocardiographically by alternating periods of bradycardia and tachycardia. It may be due to (i) overdrive suppression of sinus node by atrial fibrillation, flutter, or tachycardia with sinus pauses that occur at the termination of tachycardia; (ii) periods of paroxysmal atrial arrhythmia with rapid rates superimposed on underlying sinus bradycardia; or (iii) persistent atrial fibrillation with periods of fast and slow AV conduction. Note that the tachy-brady syndrome associated with persistent atrial fibrillation is related to disease in the AV node and not sinus node

and fatigue) that are attributable to inadequate heart rate or pauses. Since SND is rarely associated with increased mortality, the decision to institute permanent pacing is driven primarily by symptom burden and quality-of-life considerations, rather than prognostic benefit.

Current guideline-based recommendations (e.g. ESC and ACC/AHA/HRS) emphasize the importance of a clear causal relationship between bradycardia (or chronotropic failure) and symptoms before recommending permanent pacing.

Key indications for permanent pacing in sinus node dysfunction

Class I indications (pacing is recommended/clear benefit)

- 1 Symptomatic SND:** Includes symptomatic sinus bradycardia, sinus arrest, SA block, and symptomatic chronotropic incompetence when *clearly causing symptoms* (syncope, presyncope, dizziness, and exercise intolerance).
- 2 Tachycardia-bradycardia syndrome with symptomatic bradycardia or symptomatic pauses:** Especially pauses occurring at termination of atrial tachyarrhythmias.
- 3 Symptomatic bradycardia due to essential drug therapy:** When the drug is required for treatment and no acceptable alternative exists.

Class IIa indications (reasonable/benefit likely exceeds risk)

- 1 Symptomatic chronotropic incompetence** requiring rate-responsive pacing: When symptoms occur because the heart cannot appropriately increase its rate with exertion

Class III (not indicated/potential harm)

- 1 Asymptomatic SND.**
- 2 Symptoms not correlated with bradycardia.**
- 3 Sleep-related sinus bradycardia or nocturnal pauses alone,** unless another class I or IIa indication is also present.

Contemporary data, evolving insights and recommendations for clinical practice

The recent randomized trial DANPACE II [12] evaluated whether minimizing atrial pacing in patients with SND reduces incidence of AF. Patients receiving dual-chamber pacemakers were randomized to a higher base rate with rate-adaptive pacing (DDDR-60) versus a lower base rate without rate adaptation (DDD-40). After 2 years, the incidence of AF was similar in both groups ($\approx 46\%$). However, syncope or presyncope occurred significantly more often in the DDD-40 (low-rate) group. This suggests that minimizing atrial pacing does *not* reliably prevent AF in SND and may increase risk of symptomatic

bradycardia or pauses. Thus, pacing decisions should prioritize symptom relief rather than attempting to minimize atrial pacing solely to delay or prevent AF. In patients with intact AV conduction, atrial (or dual-chamber) pacing is preferred to preserve AV synchrony and physiologic activation and minimize ventricular pacing burden.

Essential drugs used for coexisting conditions can accentuate SND. If cessation of a drug is anticipated to cause deterioration of the primary condition, permanent pacing may be needed to allow continuation of medical therapy in some patients. Chronotropic incompetence is an underdiagnosed condition in which patients fail to augment their heart rate with exercise, with marked exercise intolerance in some patients. Although no specific parameter has been established as a diagnostic standard, the most commonly used definition for chronotropic incompetence is the inability to achieve 80% of expected heart rate reserve for age; expected heart rate reserve is defined as the difference between the age-predicted maximal heart rate ($220 - \text{age}$) and the resting heart rate.

Patients with SND may have associated disease in the AV node and His–Purkinje conduction system. However, the rate of lone SND progressing to AV block is low. The mean annual incidence of complete AV block developing in patients implanted with AAI pacemakers for SND is 0.4–1.7% and as high as 3–4% in patients with a prolonged PR interval or preexisting bundle branch block. The natural history of untreated SND is highly variable. Syncope resulting from sinus arrest tends to be recurrent and may result in falls and significant orthopedic injuries, especially in the elderly. The incidence of sudden death is low, and SND very rarely affects survival regardless of whether or not it is treated with a pacemaker.

Conduction system disease: Pathophysiology, classification, and clinical implications for acquired atrioventricular block

While age-related degenerative (sclerodegenerative) changes remain a dominant cause of progressive conduction system disease in older individuals, a substantial subset of younger or middle-aged patients presenting with advanced AV block harbors underlying structural or inflammatory cardiomyopathy rather than purely degenerative disease. In a recent

cohort of 119 patients (mean age 49 ± 15 years) undergoing cardiovascular magnetic resonance (CMR) for advanced conduction system disease (complete heart block, Mobitz II, or bifascicular block), late gadolinium enhancement (LGE) was present in ~27% [13]. Most common among these non-degenerative causes is cardiac sarcoidosis (CS), but other inflammatory disorders (e.g. giant cell myocarditis/GCM) or infiltrative/storage diseases may also underlie conduction disease. This has major therapeutic implications: conduction system disease may not simply be “benign AV block” requiring pacing, but a harbinger of progressive cardiomyopathy, risk of ventricular arrhythmias (VA), sudden cardiac death (SCD), or heart failure, prompting consideration of an ICD in addition to pacing therapy.

AV block is classified on the basis of ECG, but anatomical site (supra-His, intra-His, and infra-His) governs the reliability of escape rhythms and long-term behavior.

- **First-degree AV block:** PR interval >200 ms, commonly due to AV nodal delay, independent of QRS width.
- **Second-degree AV block**
 - **Type I (Wenckebach):** Progressive PR prolongation culminating in a non-conducted P wave, then shorter PR after the block. Block occurs at the level of the AV node and is usually, but not necessarily, associated with a narrow QRS (Figure 1.4).
 - **Type II:** Fixed PR intervals before and after blocked beats. It is often associated with a wide QRS, implying a distal (His–Purkinje or infra-His) location of block (Figure 1.5). It carries a higher risk of progression to more advanced forms of block.
 - **2 : 1 AV block:** Could be nodal, intranodal (Figure 1.6), or infranodal. The QRS duration and PR interval can help identify the most likely level of block.
 - **“High-grade/advanced” second-degree AV block:** Two or more non-conducted sinus P waves with intermittent resumed conduction (Figure 1.7). In AF/flutter, prolonged pauses (>5 seconds) may reflect high-grade AV block.
- **Third-degree AV block (complete AV block):** Absence of any AV conduction. In the case of AF, complete AV block often manifests as a regularized slow ventricular rate (Figure 1.8).

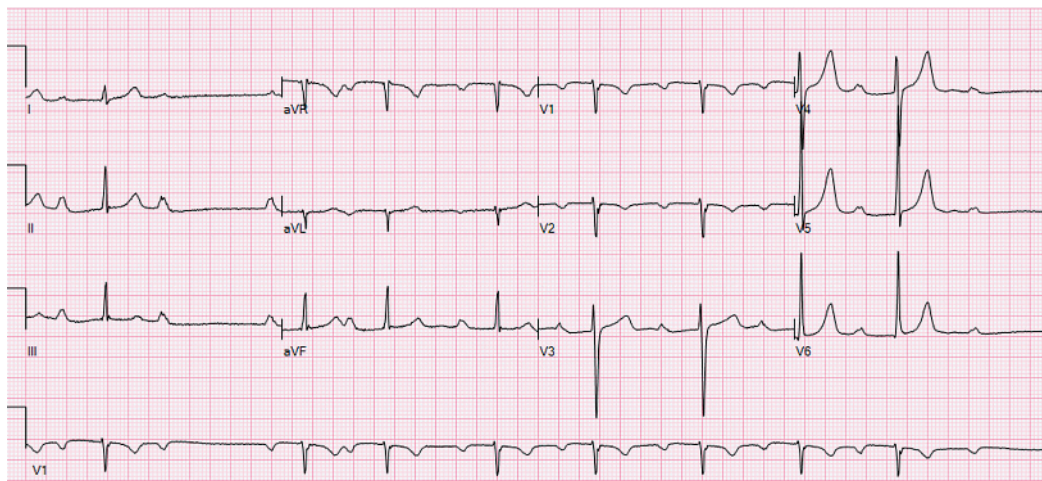


Figure 1.4 This is an example of second-degree Mobitz Type I AV block (Wenckebach).

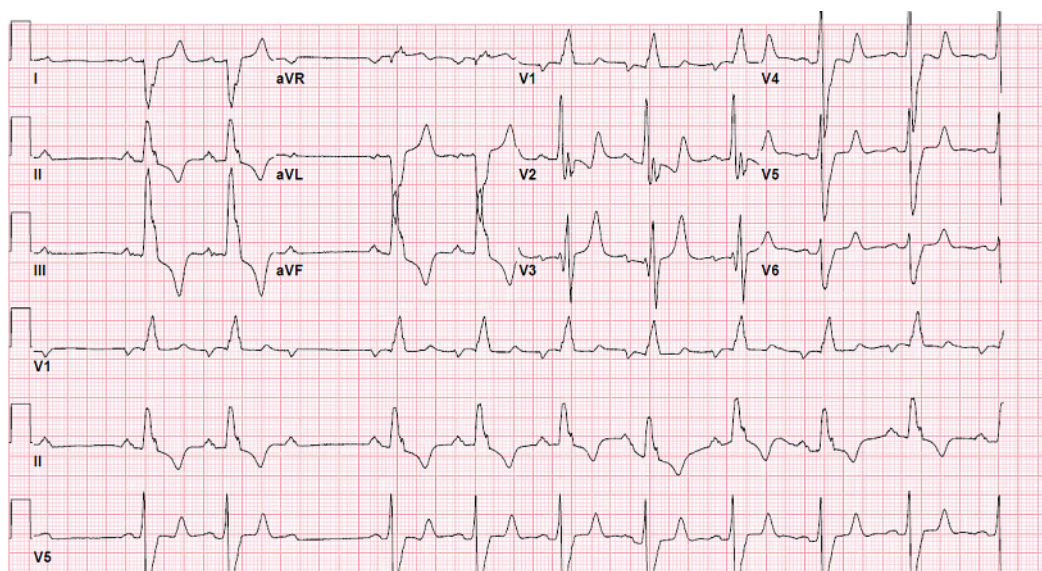


Figure 1.5 This is an example of Mobitz Type II AV block. Note the fixed PR interval throughout and the presence of right bundle branch block and left posterior fascicular block.

The site of AV block will to a great extent determine the adequacy and reliability of the underlying escape rhythm. Although ECG features provide important clues to the likely anatomical level of block, they are not always reliable. An electrophysiology study (EPS) may be required in ambiguous cases (e.g. narrow QRS but suspected infranodal block). Type I second-degree block, for example, can occasionally be infranodal, even with a narrow QRS, and may warrant the consideration of pacing

clinical maneuvers (exercise, atropine, carotid massage, and vagal maneuvers) may help: improved conduction with exercise/atropine suggests a nodal block; slowing atrial rate (e.g. carotid massage) may unmask infra-His recovery (Table 1.4).

The clinical manifestations of AV block span from entirely asymptomatic, through fatigue, exertional intolerance, syncope, to SCD. Historically, first-degree AV block and asymptomatic type I second-degree (Wenckebach) have been considered

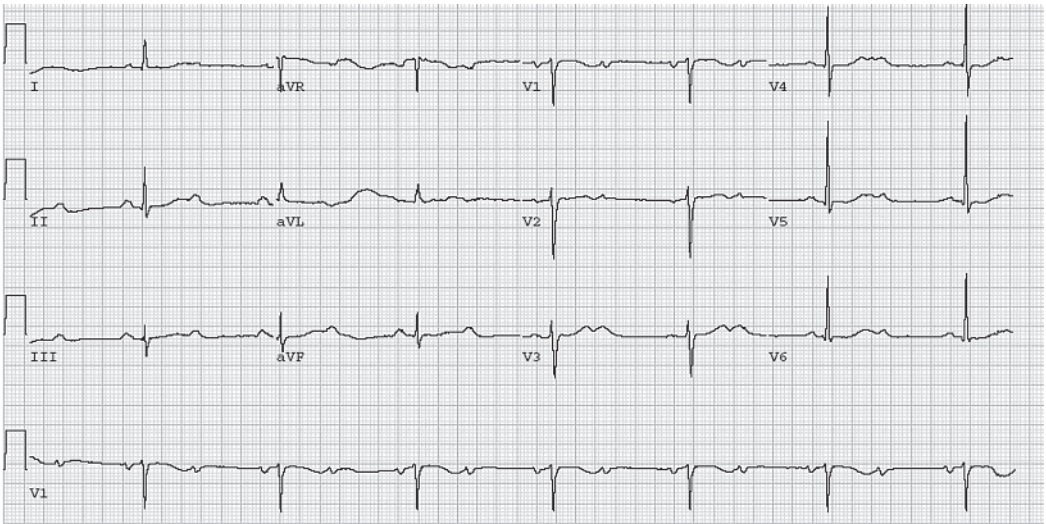


Figure 1.6 This is an example of fixed ratio 2 : 1 AV block. Note the narrow QRS and PR interval of 170ms with the conducted beats. The site of block is likely to be intra-His.

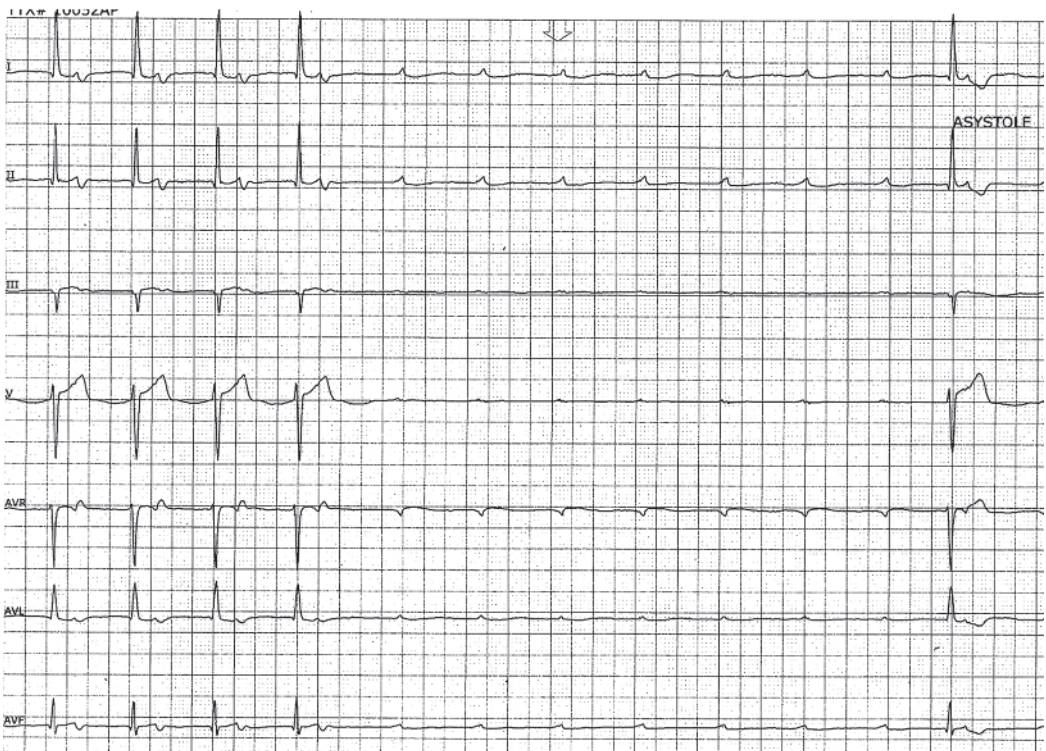


Figure 1.7 High-grade AV block. This 60-year-old female with hypertension and coronary artery disease presented with syncope. Baseline ECG showed marked first-degree AV block and voltage changes of left ventricular hypertrophy. Telemetry recorded abrupt interruption of

AV conduction with multiple non-conducted P waves with spontaneous recovery. Her β -adrenergic blockers were continued as essential treatment for coronary artery disease and a permanent pacemaker was implanted.

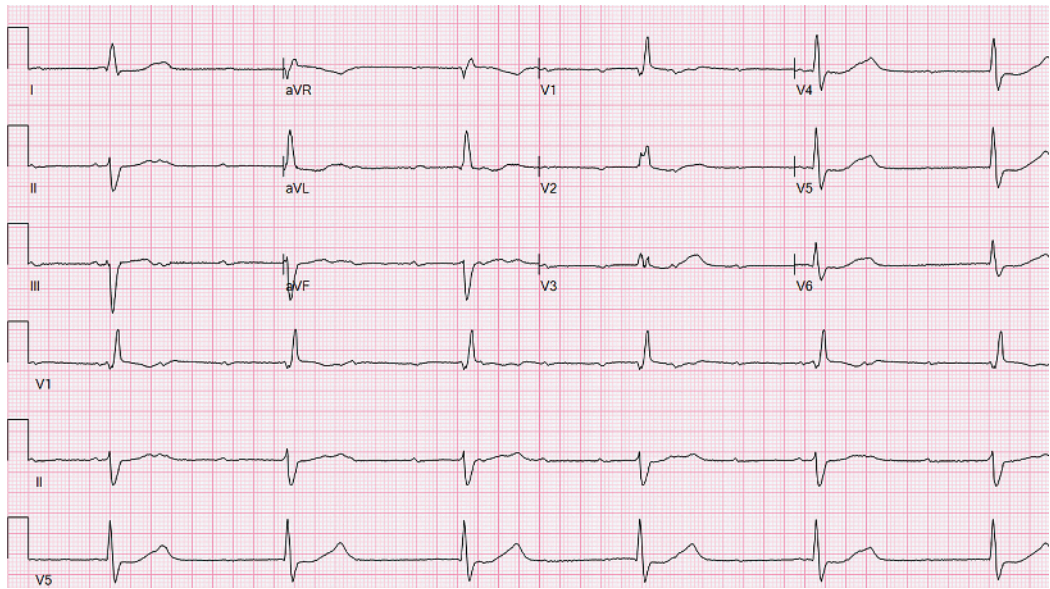


Figure 1.8 Example of complete heart block with a ventricular escape rate of 35bpm. Note the QRS morphology is right bundle branch block and left anterior fascicular block (left anterior fascicular block is diagnosed

by left-axis deviation, qR in aVL, R peak time in aVL >45ms, and rS pattern in leads II, III, and aVF). The escape rhythm may originate from the posterior fascicle.

Table 1.4 Responses to maneuvers to identify level of block in patients with 2 : 1 atrioventricular (AV) block

	<i>Block above AV node</i>	<i>Block below AV node</i>
Exercise	+	± or –
Atropine	+	± or –
Carotid sinus massage	–	+ or ±
Isoproterenol	+	– or ±

+, improved AV conduction; –, worsened AV conduction.

benign, with pacing rarely indicated. However, marked PR prolongation (e.g. PR > 250–300 ms), particularly in patients with LV dysfunction, may impair LV filling, increase pulmonary capillary wedge pressure, reduce cardiac output, and manifest with symptoms of “pacemaker syndrome.” Similarly, even type I second-degree block (despite narrow QRS and presumed nodal block) may lead to significant symptoms or hemodynamic compromise. The atrial rate at which the AV block occurs

may also be a factor in determining the indication for pacing. Mobitz I AV block occurring at an atrial rate of <60bpm in an awake patient is usually pathologic and likely requires pacing. Importantly, when conduction disease reflects underlying inflammatory/infiltrative cardiomyopathy (e.g. CS and GCM), the risk extends beyond bradycardia: such patients are at elevated risk for sustained VA [ventricular tachycardia (VT)/ventricular fibrillation (VF)], heart failure, and SCD independent of LV function.

Type II second-degree AV block is important as it has a high rate of progression to third-degree AV block. It usually reflects diffuse conduction system disease and often warrants permanent pacing even in the absence of symptoms. Third-degree AV block with a wide QRS escape rhythm often presents with fatigue, dyspnea, presyncope, or frank unheralded syncope. Rarely, VF and torsades de pointes VT can result from marked bradycardia and prolonged pauses. Permanent cardiac pacing should be strongly considered even if the escape rate is greater than 40bpm because it is not necessarily the escape rate that determines a safe and

reliable heart rhythm but the site of origin of the escape rhythm. Infra-His escape rhythms are more likely associated with prolonged asystole, syncope, and death.

AV block, usually with 2 : 1 AV conduction, can be provoked by exercise. Patients typically complain of exertional dyspnea and dizziness. The abnormality is often reproducible by exercise testing. Once ischemia is excluded as a cause, permanent pacing is remarkably effective for symptom relief. Without pacing, these patients have a poor prognosis because the site of conduction block is below the AV nodal level.

In general, the presence of symptoms documented to be due to AV block is an indication for permanent pacing regardless of the site of the block (e.g. above as well as below the His bundle). However, it is important to recognize potentially reversible causes of AV block despite their presentation with symptoms. Important examples include acute myocarditis (particularly that associated with Lyme carditis), AV block related to drug toxicity, transient vagotonia, and hypoxic events. Many of these conditions tend to resolve with disease-specific treatment and although temporary pacing may be required, permanent pacing is seldom necessary.

Key indications for permanent pacing in acquired AV block

Class I indications

- 1 Acquired second-degree Mobitz type II AV block, high-grade (advanced) AV block, or third-degree (complete) AV block not due to reversible/physiologic causes.
- 2 Permanent (or paroxysmal) atrial arrhythmia (e.g. AF) with permanent or paroxysmal high-degree AV block—pacing indicated irrespective of symptoms.
- 3 Permanent AF with symptomatic bradycardia.
- 4 Symptomatic AV block occurring during necessary guideline-directed medical therapy (GDMT) (for which there is no reasonable alternative).

Class IIa (reasonable/should be considered)

- 1 Second-degree type I (Mobitz I/Wenckebach) AV block causing symptoms, especially when EPS demonstrates intra- or infra-His conduction delay.

- 2 Marked first-degree AV block (e.g. prolonged PR) with persistent symptoms clearly attributable to AV conduction delay (e.g. pacemaker syndrome-type symptoms).

- 3 Patients with infiltrative or inflammatory cardiomyopathies (e.g. sarcoidosis and amyloidosis) who manifest Mobitz II, high-grade or third-degree AV block—pacing (with or without defibrillator) may be reasonable if prognosis >1 year.

- 4 Patients with genetic/neuromuscular conduction disease (e.g. lamin A/C mutations and muscular dystrophies) with significant conduction delay [e.g. PR prolongation (>240 ms) and bundle branch block]—pacing (possibly with defibrillator) may be reasonable.

Contemporary data, evolving insights and recommendations for clinical practice

Given the growing recognition of non-degenerative causes of AV block, cardiovascular magnetic resonance imaging (CMR) is strongly recommended for patients with unexplained AV block, even when conventional echocardiography shows normal LV function. Recent ESC guidelines (2025) designate this as a class I, Level B indication in suspected cardiac inflammatory disease (e.g. CS) [14]. 18F-FDG positron emission tomography (PET) is also recommended (class I, level B) in diagnostic work-up of suspected CS, to detect active inflammation and guide therapy/follow-up. These approaches increasingly unmask subclinical or isolated cardiac inflammatory disease in patients whose only presentation may be arrhythmia or conduction block. As such, the idea that AV block simply requires a pacemaker is outdated. In the context of inflammatory or infiltrative disease (e.g. CS and GCM), an ICD with pacing capability should be considered (class IIa or IIb) in patients with persistent high-degree AV block requiring permanent pacing, particularly when left ventricular ejection fraction (LVEF) > 35%, but there is significant LGE, syncope, inducible VA on EPS, or documented arrhythmias. A recent prospective study of 112 patients with CS presenting with AV block found that 50% of those experienced sustained VA during follow-up [15]. Use physiologic ventricular activation (HBP, CSP, or CRT when indicated) preferentially over conventional RV

apical pacing, especially in patients expected to require frequent ventricular pacing, to reduce risk of pacing-induced cardiomyopathy.

Conduction system disease in the setting of 1 : 1 AV conduction

Conduction disease of the distal conduction system most commonly affects the bundle branches and the individual fascicles of the LBB. Bifascicular block is defined by block in two of the three major fascicular pathways, most commonly complete right bundle branch block (RBBB) with either left anterior fascicular block (LAFB) or left posterior fascicular block (LPFB), or complete LBBB alone. Alternating (or bilateral) bundle branch block occurs when there are RBBB and LBBB morphologies in the same patient on separate ECGs or even beat-to-beat; this behavior implies highly unstable and advanced conduction disease. Trifascicular block is best defined as disease in all three fascicles (RBBB + alternating block of the left-sided fascicles) or the combination of bifascicular block with intermittent third-degree AV block. Historically, the term has also been used more loosely to describe bifascicular block plus first-degree AV block, but this latter pattern may reflect a mix of AV nodal and infra-His disease and therefore should be described precisely (e.g. “bifascicular block with PR prolongation”) rather than automatically labeled trifascicular. The prevalence of bundle branch block rises markedly with age and with the presence of structural heart disease. Population studies demonstrate that the cumulative prevalence of any complete bundle branch block increases from ~1% at age ~50 years to ~17% by age 80 in long-term cohort data. LBBB is less common than RBBB but is more frequently associated with underlying structural heart disease (hypertensive heart disease, coronary disease, and cardiomyopathy) [16]. New-onset LBBB often signals coexistent cardiac pathology and is associated with adverse cardiovascular outcomes. The absolute annual incidence of progression from asymptomatic bifascicular block to advanced AV block in unselected cohorts is low (typically ~0.5–1% per year), but the presence of syncope or presyncope markedly increases the risk. Multiple observational series and guideline reviews report substantially higher annual progression/major event rates in

symptomatic patients (estimates vary by study), and syncope is the single most consistent clinical predictor of progression to high-grade AV block. Because high-grade AV block may be transient, intermittent, and difficult to capture, evaluation strategies should be directed at documenting the rhythm during symptoms.

Invasive EPS can identify infranodal conduction disease that is not apparent on surface ECG. A prolonged baseline His-ventricular (HV) interval and demonstration of intra- or infra-His block during pacing or pharmacologic challenge predict a higher likelihood of progression to high-grade AV block. Contemporary guideline documents (ACC/AHA/HRS, ESC) and consensus statements use an HV interval threshold of ≥ 70 ms as an actionable cut-off: an HV ≥ 70 ms in patients with bifascicular block and/or unexplained syncope supports permanent pacing if reversible causes have been excluded. Some EP studies and meta-analyses have considered lower thresholds (55–60 ms) in specific contexts (and clinical judgment may justify individualized consideration for HV 55–70 ms), but guideline recommendations retain HV ≥ 70 ms as the threshold for a pacing recommendation. Demonstration of second- or third-degree intra- or infra-His block during incremental atrial pacing (or an abnormal pharmacologic response) is likewise considered an indication to pace (Figure 1.9).

Because high-grade AV block is often paroxysmal and may not be captured during a short hospitalization or by surface monitoring, ILRs have an established role in the evaluation of unexplained syncope in patients with bundle branch block and nondiagnostic EPS. Prospective series and registry data show that ILRs frequently capture bradyarrhythmic causes of syncope (including sudden-onset paroxysmal AV block) that were not identified by ambulatory ECG or EPS; observations from this body of work inform a strategy of targeted ILR use when the diagnosis is uncertain rather than immediate empiric permanent pacing in all patients. Nevertheless, several randomized and observational studies have debated whether empirical pacemaker implantation is preferable to an EPS/ILR-guided strategy in selected patients with bundle branch block and syncope; the choice should therefore be individualized, weighing patient age, comorbidity, syncope severity, local EP resources, and patient preference [17].

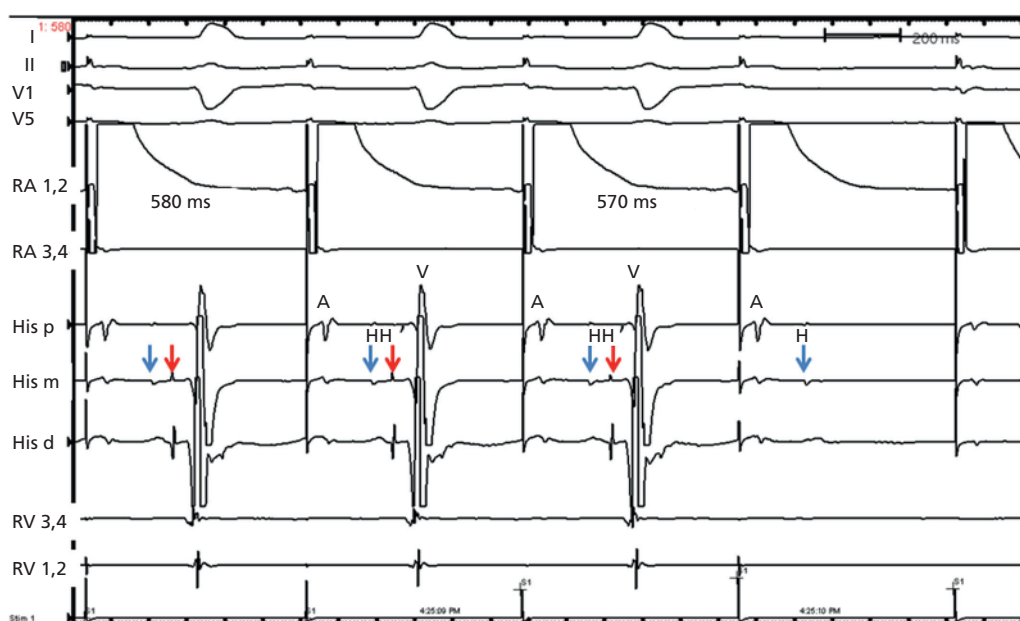


Figure 1.9 Intra- and infra-His AV block induced with atrial pacing. A 68-year-old male was admitted complaining of recurrent dizziness and syncope. His baseline 12-lead ECG showed a PR interval of 0.25 s and a left bundle branch block QRS morphology. The His bundle is split and denoted by H and H' (blue and red arrows). With decremental atrial pacing, intra-His block (blue arrow) is demonstrated at a cycle length of 570 ms (105 bpm). These findings are indicative of severe diffuse conduction system

disease. A permanent dual-chamber pacemaker was implanted, and the patient's symptoms resolved. From top to bottom: I, II, V1, and V5 are standard ECG leads; intracardiac recording from the right atrial appendage (RA 1, 2 and RA 3, 4); and His bundle (His-p, His-m, and His-d are proximal, mid, and distal His recordings, respectively). A, atrial depolarization; H, proximal His bundle depolarization; H', distal His bundle depolarization; V, ventricular depolarization.

Key indications for permanent pacing in conduction system disease in the setting of 1 : 1 conduction

Class I indications

- 1 Bifascicular block and explained syncope.
- 2 Alternating bundle branch block.
- 3 EPS demonstrates a baseline HV interval ≥ 70 ms with syncope, second- or third-degree intra- or infra-His block during atrial pacing (at rates <150 bpm).

Reflex syncope

Reflex (neurally mediated) syncope comprises a spectrum of conditions in which an abnormal autonomic reflex produces a characteristic cardiovascular response of vasodilation and/or increased parasympathetic outflow with bradycardia, leading to transient cerebral hypoperfusion and loss of

consciousness. Any episode may be dominated by the cardioinhibitory or the vasodepressor component; the cardioinhibitory phenotype is typified by sinus slowing, sinus arrest (Figure 1.10), PR-interval prolongation, and, less commonly, AV block, whereas the vasodepressor phenotype reflects a fall in sympathetic vascular tone with marked hypotension that can occur independent of heart rate changes. These core pathophysiologic concepts and the contemporary diagnostic framework are consistent with current U.S. and European guideline statements [18].

The most commonly encountered forms of reflex syncope are vasovagal (neurocardiogenic) syncope and carotid sinus hypersensitivity; other variants are typically categorized as situational syncope (for example, cough, micturition, defecation, and swallowing, postexercise or postprandial) or less common atypical subtypes (adenosine-sensitive syncope or forms without a clear precipitant)

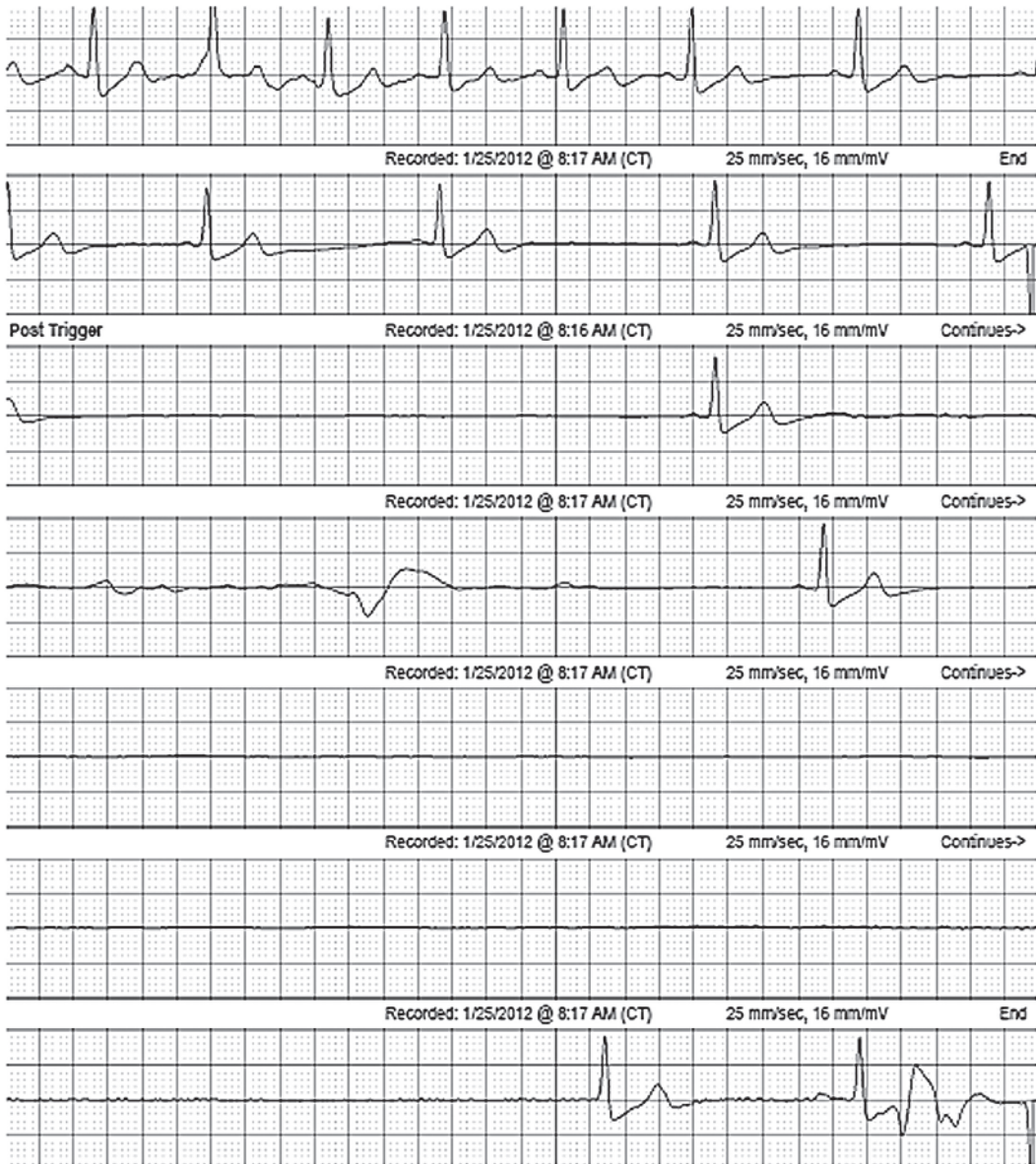


Figure 1.10 Marked cardioinhibitory response to neurally mediated syncope. This 45-year-old female presented with syncope preceded by nausea while wearing an event monitor. There was gradual sinus slowing with prolonged sinus arrest resulting in syncope. Intense vagal stimulation can suppress junctional escape rhythms.

(Table 1.5). Triggers may vary between and within patients, and a careful history that documents provoking factors, prodromal symptoms (nausea, diaphoresis, lightheadedness, and visual changes), and temporal relation to posture or specific activities remains the single most informative diagnostic element.

Clinical presentation is age dependent: classic vasovagal syncope with prolonged prodrome and isolated episodes is more typical in younger patients, whereas older adults more often have attenuated or absent prodrome and are therefore at higher risk for sudden falls and injury. When vasovagal-type episodes begin at an older age or are

Table 1.5 Types of neurally mediated syncope

<i>Vasovagal</i>	Mediated by emotional stress, such as fear, pain, sight of blood, and instrumentation Mediated by orthostatic stress
<i>Carotid sinus syncope</i>	Mediated by pressure to the carotid sinus area, e.g. shaving, turning of the head, and tight neck collar
<i>Situational</i>	Cough and sneeze Gastrointestinal stimulation: swallow, defecation, and visceral pain Micturition syncope Postexercise Postprandial
<i>Other</i>	Triggered by increased intrathoracic pressure, e.g. laughing, playing brass instruments, and weightlifting
<i>Atypical forms</i>	No identified precipitant Adenosine-sensitive syncope

associated with progressive autonomic failure, secondary causes should be sought, and neurologic or systemic disorders should be considered. The 2017 ACC/AHA/HRS guideline emphasizes tailored evaluation driven by history, physical examination, and targeted testing (orthostatic vitals, ECG, ambulatory monitoring, and tilt-table testing when appropriate) to establish the mechanism and to exclude cardiac causes of syncope. While tilt-table testing may be helpful when the diagnosis is unclear after initial evaluation, it is not recommended in the 2018 ESC guidelines to predict a response to medical therapy [19].

Management begins with education and structured, non-pharmacologic measures. Avoidance of identifiable triggers, liberalization of dietary salt and fluids when appropriate, physical counter-pressure maneuvers, and supervised tilt-training are first-line strategies and can meaningfully reduce recurrence and symptoms in many patients; these interventions are recommended before committing to long-term drug therapy or device implantation for most patients. For situational forms, trigger avoidance and specific counseling are usually sufficient.

Pharmacologic therapy is reserved for patients with frequent, disabling recurrences despite

conservative measures. Current randomized and observational data provide at best modest and inconsistent benefit for agents, such as fludrocortisone and the α -agonist midodrine, which principally target the vasodepressor component; high-quality trial data are limited, and guideline panels conclude evidence is inconclusive for routine use in all patients. Beta-blockers have not shown consistent benefit in randomized trials and may be unhelpful or harmful in some patients (for example, in carotid sinus syncope); ongoing trials (for example, trials comparing midodrine versus fludrocortisone) seek to clarify comparative effectiveness. Clinicians should individualize drug choices to the dominant pathophysiology, comorbidities, and tolerability.

One variant of neurally mediated syncope is the hypersensitive carotid sinus syndrome. A mildly abnormal response to vigorous carotid sinus massage may occur in up to 25% of patients, especially if coexisting vascular disease is present. Some patients with an abnormal response to carotid sinus massage may have no symptoms suggestive of carotid sinus syncope. On the other hand, the typical history of syncope, such as blurred vision, lightheadedness, or confusion in the standing or sitting position, especially during movement of the head or neck, should suggest the diagnosis. Classical triggers of carotid sinus syncope are head turning, tight neckwear, shaving, and neck hyperextension. Syncopal episodes are generally reproducible in a given patient. Because of the predominantly bradycardic (cardioinhibitory) response to carotid hypersensitivity, permanent pacing has a significant role for alleviating symptoms (Figure 1.11).

Permanent cardiac pacing has a role in carefully selected patients with recurrent, severe neurally mediated syncope when an objectively documented, predominantly cardioinhibitory mechanism (for example, prolonged asystole captured on implantable loop recorder or during monitored syncope) correlates with symptoms. Randomized trials and meta-analyses have produced variable results, but trials that used implantable loop recorders to confirm clinically relevant asystole (for example, ISSUE-3) [20] and those that used dual-chamber closed-loop stimulation (CLS) technology (for example, the SPAIN CLS trial) have demonstrated meaningful reductions in recurrence

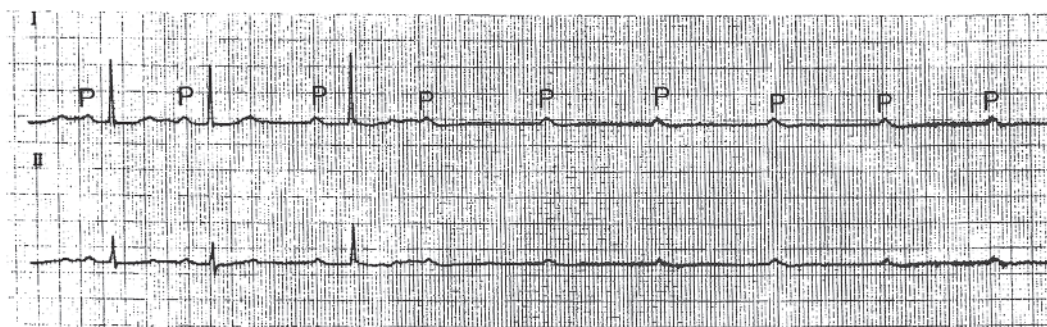


Figure 1.11 Response to gentle carotid massage in carotid hypersensitivity syndrome. A 69-year-old male complained of near-syncope, which typically occurred while shaving or turning his neck. Carotid sinus massage was performed

shortly before the second QRS complex. Note that the sinus rate slows prior to the third QRS complex, followed by complete heart block with ventricular asystole.

in appropriately selected older patients (generally ≥ 40 years) with recurrent, refractory syncope and proven asystolic events [21]. Dual-chamber pacing is generally preferred over single-chamber ventricular pacing because the latter can worsen symptoms in some patients; CLS pacing has shown benefit in head-to-head randomized studies in carefully selected populations. Patients should be counseled that a vasodepressor component may persist despite pacing and that device implantation carries procedure-related and long-term lead/generator risks that are particularly important for younger patients.

Paroxysmal AV block

Paroxysmal AV block is increasingly recognized as a heterogeneous clinical and electrophysiological syndrome encompassing several distinct mechanisms rather than a single disease entity. Among these, an idiopathic or “extrinsic” adenosine-mediated form has been well described in otherwise structurally normal hearts. Patients typically present with abrupt, unpredictable syncope, often without prodromal symptoms, associated with the sudden onset of advanced or complete AV block, frequently accompanied by prolonged ventricular asystole, followed by spontaneous and complete restoration of normal AV conduction. The episodic nature and dramatic presentation distinguish this entity from more common forms of functional or degenerative AV block.

Baseline electrocardiography and invasive electrophysiologic assessment are characteristically normal in the adenosine-mediated form, with preserved PR intervals and normal AH and HV conduction times during sinus rhythm. Autonomic

testing, including tilt-table evaluation, is usually unrevealing. Importantly, in contrast to vagally mediated (reflex) AV block, there is typically no antecedent sinus slowing, PR prolongation, or other progressive markers of heightened parasympathetic tone immediately preceding the block. The absence of these vagal signatures, coupled with abrupt AV conduction failure, should prompt consideration of an adenosine-sensitive mechanism.

Mechanistic and translational studies support a primary role for adenosinergic signaling in this phenotype. Affected individuals have been shown to exhibit relatively low baseline plasma adenosine concentrations and altered expression or sensitivity of adenosine receptors within the AV node, particularly involving A1 and A2A receptor pathways. This receptor milieu may predispose to an exaggerated AV nodal response to transient adenosine surges, resulting in sudden conduction block. Consistent with this hypothesis, exogenous adenosine administration frequently induces transient high-grade AV block in these patients (adenosine challenge), a finding that is uncommon in patients with typical vasovagal syncope, who generally demonstrate higher baseline adenosine levels and a different autonomic-humoral profile (Figure 1.12).

In addition to adenosine-mediated mechanisms, paroxysmal AV block may arise from intrinsic conduction system properties, most notably phase 4 block and concealed conduction. Phase 4 block reflects abnormal diastolic depolarization within diseased His–Purkinje tissue, whereby spontaneous membrane potential drift during pauses or slowing of the preceding cycle renders the tissue inexcitable to subsequent impulses. This mechanism is

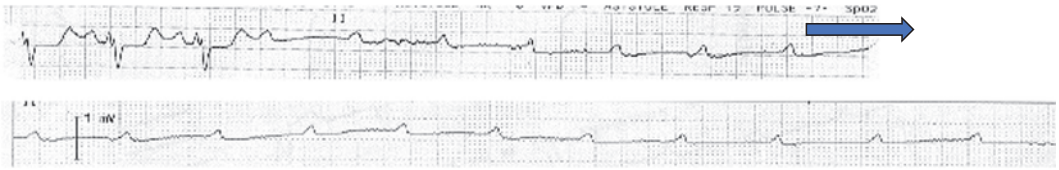


Figure 1.12 Example of paroxysmal AV block with no preceding deceleration of the atrial rate suggesting the mechanism for the transient block was not vagally

mediated. There is no premature atrial contraction or premature ventricular contraction triggering the heart block.

classically pause-dependent and may be precipitated by sinus slowing or post-extrasystolic pauses. Concealed conduction further modulates this process: premature atrial or ventricular extrasystoles that fail to propagate to the ventricles may nonetheless penetrate the AV node or His–Purkinje system, partially depolarizing the tissue and prolonging refractoriness without producing a surface ECG manifestation. The combination of concealed penetration and subsequent phase 4 depolarization can abruptly render the conduction system refractory to the next sinus impulse, resulting in sudden high-grade or complete AV block (Figure 1.13). These mechanisms are particularly relevant in patients with subtle or early His–Purkinje disease, even when baseline conduction intervals are normal.

From a therapeutic standpoint, available long-term observational data and case series support two pragmatic management strategies. Permanent cardiac pacing is highly effective in preventing recurrent syncope in patients with documented paroxysmal AV block associated with prolonged asystole and remains the cornerstone of therapy when episodes are recurrent, unpredictable, or associated with injury. Alternatively, because adenosine signaling plays a central role in a subset of patients, pharmacologic antagonism with oral theophylline, a nonselective adenosine receptor antagonist, has been reported to reduce or suppress episodes in selected cases. However, the evidence base for theophylline is limited to small series and anecdotal reports, and it should be regarded as an adjunctive or temporizing strategy rather than a substitute for definitive pacing in patients with recurrent or life-threatening pauses. Emerging interventional approaches, including cardioneuroablation, have shown promise in highly selected patients with functional or adenosine-sensitive AV block, but these techniques remain investigational and require rigorous prospective evaluation before widespread adoption.

Because paroxysmal AV block is episodic and frequently absent on routine electrocardiography, prolonged rhythm surveillance is often essential to establish the diagnosis. Extended ambulatory monitoring, and in many cases implantable loop recorders, play a critical role in documenting transient high-grade AV block and confirming a temporal correlation between symptoms and bradyarrhythmia prior to committing to long-term therapy.

Key indications for permanent pacing in conduction system disease in neurally mediated syncope and hypersensitive carotid sinus syndrome (2018 European Society of Cardiology guidelines)

Class I indication

1 Syncope due to paroxysmal AV block with electrocardiographic correlation.

Class IIa indications

- 1 In patients aged ≥ 40 years, permanent pacing should be considered to reduce syncopal recurrence when there is documented symptomatic asystolic pause ≥ 3.0 seconds or asymptomatic pause ≥ 6 seconds due to sinus arrest, AV block, or a combination of both.
- 2 In patients with cardioinhibitory carotid sinus syndrome (CSS), permanent pacing should be considered when syncope is recurrent, frequent, unpredictable, and likely due to the reflex.

Class IIb indications

- 1 Cardiac pacing may be considered in patients aged ≥ 40 years with recurrent, frequent, unpredictable syncope and a tilt-induced asystolic (cardioinhibitory) response on tilt-table testing.
- 2 Cardiac pacing may be considered in patients with clinical features consistent with an “adenosine-sensitive syncope” (also termed “idiopathic paroxysmal AV block” or “low-adenosine syncope”), i.e. unexplained syncope, normal heart and conduction system, negative tilt test, and evidence (clinical/biological) of adenosine mediation.

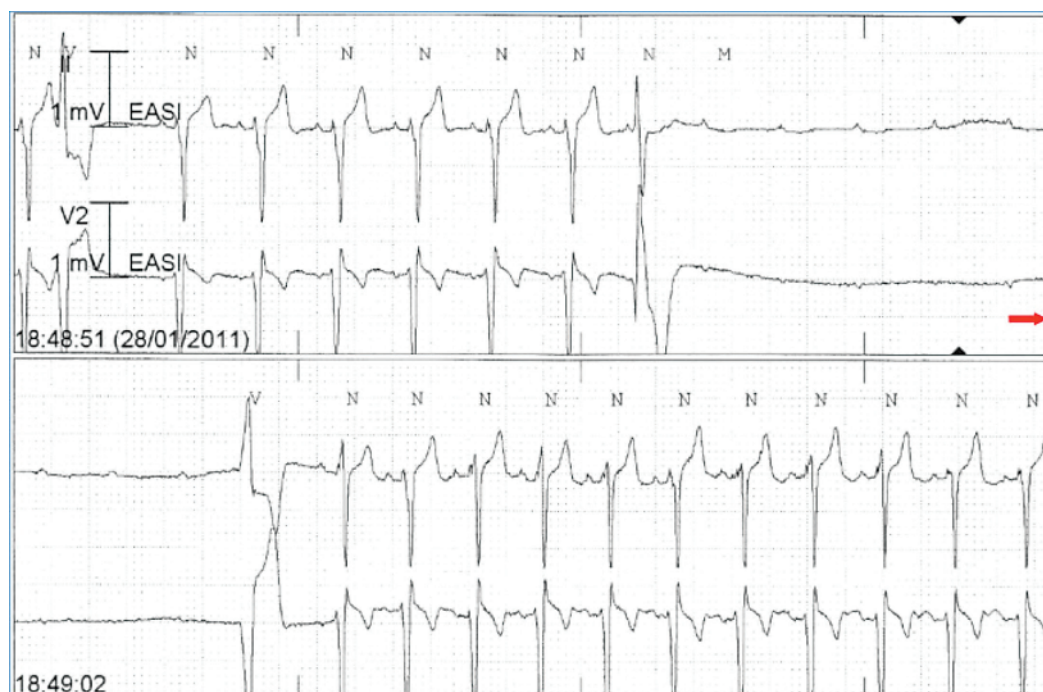


Figure 1.13 This is an example of paroxysmal AV block triggered by a combination of a PVC causing concealed conduction and subsequent phase 4 block. Note, the another PVC terminates the block by concealed conduc-

tion into the distal His-Purkinje system (retrograde penetration), allowing these cells to repolarize to a more negative maximum diastolic potential and restoring sodium-channel availability.

Class III (not indicated)

1 Pacing is not indicated in patients with reflex syncope in the absence of a documented cardioinhibitory response (i.e. no asystole or AV block documented)

Contemporary data, evolving insights and recommendations for clinical practice

Permanent cardiac pacing has a role in carefully selected patients with recurrent, severe neurally mediated syncope when an objectively documented, predominantly cardioinhibitory mechanism (for example, prolonged asystole captured on implantable loop recorder or during monitored syncope) correlates with symptoms. A more recent randomized trial showed that in patients ≥ 40 years with severe recurrent reflex syncope and tilt-induced asystole, a dual-chamber pacemaker with CLS significantly reduced syncope recurrences

compared to no pacing (1-year recurrence 19% versus 53%; 2-year 22% versus 68%) [20]. Dual-chamber pacing is generally preferred over single-chamber ventricular pacing because the latter can worsen symptoms in some patients; CLS pacing has shown benefit in head-to-head randomized studies in carefully selected populations. Leadless pacemakers may also have a promising role in the management of these patients [22]. Patients should be counseled that a vasodepressor component may persist despite pacing and that device implantation carries procedure-related and long-term lead/generator risks that are particularly important for younger patients.

Spinal cord injury

Bradycardia remains a frequent and important complication after acute spinal cord injury (SCI), reflecting loss of sympathetic outflow with relative parasympathetic predominance; this is most pronounced with high cervical injuries and is typically

greatest in the acute/subacute phase (most commonly within the first days to 2–4 weeks after injury). Patients with high cervical SCI are at risk for severe sinus bradycardia, sinus arrest and prolonged pauses/asystole that may be life-threatening.

Initial management follows standard ACLS/critical care algorithms: atropine is first-line for symptomatic bradycardia, with escalation to intravenous sympathomimetics (e.g. dopamine, epinephrine) when required. When pharmacologic measures fail or when there is recurrent, prolonged asystole, temporary transvenous pacing (or external pacing in the very short term) is indicated and is effective for immediate stabilization.

Methylxanthines (aminophylline/theophylline) remain the most studied non-device pharmacologic option for atropine-refractory bradycardia in SCI. Recent case series and small observational reports support use of aminophylline/theophylline as an adjunct to raise heart rate and reduce pauses in selected patients, and they may permit avoidance of temporary or permanent pacing in some cases. Evidence, however, is limited to small, nonrandomized series; there are no contemporary randomized trials to define optimal dosing, duration, or long-term outcomes, and drug levels/side effects (arrhythmia, CNS stimulation, and interactions) require careful monitoring. Thus, methylxanthines are a reasonable second-line or bridging therapy in selected patients but are not a proven substitute for pacing when pauses are recurrent or life-threatening.

PPI is reserved for patients with intractable, recurrent, or persistent bradyarrhythmia/asystole that does not resolve as autonomic function recovers or when prolonged dependence on pacing is clearly documented. The decision to implant should weigh the benefits against increased long-term risks in this population (recurrent device infection, bacteremia and lead-related endocarditis are greater concerns in medically complex, frequently catheterized patients), and device timing/strategy should involve an infection-prevention plan.

Ictal bradycardia

Rarely (<0.5%), profound bradycardia due to sinus arrest or AV block at the nodal level can complicate seizures, mostly temporal lobe epilepsy. Prolonged ictal asystole (>6.0 s) is more common with left

temporal lobe epilepsy than right and can worsen and extend the duration of syncope associated with such seizures. Pacing has been shown to reduce syncopal events and is a consideration if antiepileptic measures such as drugs and surgery fail to control epilepsy. In the 2018 guidelines for bradycardia, permanent pacing is considered a class IIa indication based on limited data

Specific conditions associated with cardiac conduction disease

Chronic neuromuscular disorders

A number of neuromuscular disorders are associated with progressive cardiomyopathy and an increased incidence of conduction system disease, bradyarrhythmias, and SCD. Although respiratory failure remains a major determinant of overall survival in many of these conditions, cardiac involvement, particularly disease of the His–Purkinje system, can be a dominant contributor to morbidity and mortality. Conduction disease is often unpredictable, may progress rapidly, and can be asymptomatic until the onset of high-grade AV block or ventricular arrhythmia (VA).

Both the 2021 ESC Pacing Guidelines and the ACC/AHA/HRS 2018 Bradycardia Guidelines identify several neuromuscular disorders in which conduction disease is a recognized and potentially malignant manifestation. Because SCD may be the first presentation, pacing recommendations are deliberately conservative.

High-grade AV block (Mobitz II, high-grade, or complete AV block) is a Class I indication for permanent pacing, even when asymptomatic, in patients with neuromuscular diseases known to involve the cardiac conduction system. The rationale is the high likelihood of disease progression, unpredictable timing, and risk of sudden death from asystole.

Suggestive symptoms, such as syncope or presyncope, warrant urgent evaluation with ECG, ambulatory monitoring, and often EP-guided risk assessment. Annual ECG and periodic 24-hour or longer ambulatory monitoring to detect evolving conduction abnormalities before symptoms develop is appropriate. Pacemaker therapy reduces the risk of bradyarrhythmic death, but does not prevent SCD

related to ventricular tachyarrhythmias (VTAs), which may occur in settings of LV dysfunction or coexisting cardiomyopathy; an ICD may be preferred when ventricular arrhythmia risk is significant.

Neuromuscular disorders most frequently associated with clinically important conduction disease

Myotonic dystrophy type 1 (DM1, Steinert disease)

DM1 is the most common adult muscular dystrophy and frequently involves the cardiac conduction system. Conduction abnormalities (PR prolongation, fascicular block, and bundle branch block) are common and may progress abruptly. Approximately one-third of deaths are sudden, attributed to complete heart block or malignant VA.

Permanent pacing is indicated for second- or third-degree AV block regardless of symptoms. Contemporary observational data continue to support an invasive EP-guided strategy in patients with PR > 200 ms and/or QRS > 100 ms, where an HV interval > 70 ms predicts imminent progression to complete AV block. Patients receiving prophylactic pacemakers based on abnormal HV intervals demonstrate a lower rate of sudden death compared with non-invasively managed cohorts [23]. Recent studies also emphasize the need to stratify for VA, with ICD therapy considered when there is LV dysfunction or documented VT.

Duchenne muscular dystrophy (DMD)

Duchenne muscular dystrophy (DMD) is an X-linked dystrophinopathy with near-universal cardiac involvement. Conduction disturbances may occur, though progressive dilated cardiomyopathy (DCM) is often the dominant cause of mortality. Because high-grade AV block can develop and may be unpredictable, it is reasonable to implant a permanent pacemaker when second-degree or higher AV block occurs, particularly when associated with a wide QRS or evidence of His–Purkinje disease. In the presence of LV dysfunction, risk of malignant VA should prompt ICD consideration rather than pacing alone.

Becker muscular dystrophy (BMD)

Becker muscular dystrophy (BMD) is an allelic, milder dystrophinopathy with similar but slower cardiac involvement. Conduction disease and VA

occur but typically later than in DMD. Although data are more limited, pacing indications mirror those in DMD: second- or third-degree AV block warrants permanent pacing, and ICD therapy should be considered when LV dysfunction or VT risk is present.

Emery–Dreifuss muscular dystrophy (EDMD)

Emery–Dreifuss muscular dystrophy (EDMD) (X-linked or autosomal dominant) features early and prominent cardiac conduction system disease. SNS, AV block, atrial standstill, and sudden death due to bradyarrhythmias are well documented. Most recent guidelines continue to state that permanent pacing is frequently required, and prophylactic consideration is appropriate when progressive PR prolongation or conduction delay develops. Because atrial paralysis and VA also occur, device selection (pacemaker versus ICD) should be individualized.

Limb-girdle muscular dystrophies (LGMD)

This is a genetically diverse group with variable cardiac involvement. Several subtypes [e.g. lamin A/C gene (LMNA)-related dystrophy] have a high incidence of conduction disease, VA, and sudden death. In LMNA-related disease in particular, early conduction disease often predicts malignant VA; thus ICD rather than pacemaker may be indicated when LV dysfunction, non-sustained VT, or significant conduction disease is present. Permanent pacing is indicated when second- or third-degree AV block develops, even in the absence of symptoms, and early device implantation may be considered in families with a history of sudden death.

Kearns–Sayre syndrome (KSS)

Kearns–Sayre syndrome (KSS) is a mitochondrial DNA deletion syndrome with a high prevalence of progressive conduction system disease. Distal His–Purkinje involvement is expected, and complete AV block is common. Because progression can be rapid and unpredictable, contemporary recommendations favor prophylactic PPI when marked first-degree AV block (PR prolongation) or fascicular/bundle branch block appears, even before high-grade AV block develops. ICD therapy may be considered when VA or LV dysfunction coexist.

Key indications for permanent pacing in conduction system disease chronic neuromuscular disorders

Class I indications

- 1 Any Mobitz II, high-grade, or complete AV block, even if asymptomatic.
- 2 Any syncope attributable to conduction disease.

Class IIa/IIb indications

- 1 Prophylactic pacing may be considered in disorders with *high risk of sudden progression* [DM1, EDMD, LMNA-related limb-girdle muscular dystrophies (LGMD), KSS] even before high-grade block appears.
- 2 **ICD consideration:** When ventricular arrhythmia risk or LV dysfunction is present (common in DMD, BMD, LMNA-LGMD, and DM1).

Infiltrative and inflammatory disorders

Infiltrative cardiomyopathies are characterized by the deposition or accumulation of abnormal substances within the myocardium, leading to ventricular stiffening, restrictive filling, and progressive diastolic dysfunction. Many of these disorders produce increased myocardial wall thickness that can mimic hypertrophic cardiomyopathy (HCM), and several may present with small ventricular cavity size or dynamic LV outflow tract obstruction. Importantly, some infiltrative or inflammatory processes produce only subtle structural changes on transthoracic echocardiography but affect the specialized conduction system early, such that initial presentation may involve bradyarrhythmias, advanced AV block, or VA. Disorders particularly associated with conduction disease include CS, giant cell myocarditis, amyloidosis, hemochromatosis, Fabry disease, Danon disease, certain glycogen-storage cardiomyopathies, primary oxalosis, and infiltration from hematologic malignancies or cardiac tumors. AV block remains well recognized across these conditions, although its prevalence varies by disease mechanism and stage. In endemic areas of South America, Chagas disease persists as a major cause of severe conduction disease and is a leading indication for pacing.

Prognosis across infiltrative and inflammatory cardiomyopathies depends primarily on the underlying systemic disorder, yet cardiac complications,

including high-grade conduction block, malignant VA, heart failure, and sudden death, contribute to morbidity and mortality. Solid tumors infiltrating the myocardium typically portend a poor overall prognosis. When infiltration or inflammation directly disrupts the conduction system, permanent pacemakers or ICDs are indicated.

Sarcoidosis

CS remains a relatively common granulomatous inflammatory disorder of unknown etiology. It is characterized by non-caseating granulomas that may regress, remain stable, or progress to scarring and remodeling. Autopsy studies suggest far greater cardiac involvement than is clinically recognized, and isolated CS accounts for approximately 5% of cases. Granulomas most often involve the basal interventricular septum and inferoposterior LV myocardium, explaining the high prevalence of conduction system disease, chronotropic incompetence, VA, and regional aneurysm formation.

Endomyocardial biopsy has limited sensitivity ($\approx 25\text{--}30\%$) due to the patchy nature of involvement. Cardiac MRI with LGE and fluorodeoxyglucose positron emission tomography (FDG-PET) are essential for diagnosis. CMR is particularly useful for identifying scar, while FDG-PET identifies active inflammation and guides immunosuppressive therapy decisions.

High-grade AV block is one of the most common clinical presentations, but the risk of SCD from VA is substantial even when conduction disease is the dominant finding. Current consensus statements (ACC/AHA/HRS 2023–2024) emphasize a low threshold for ICD implantation in confirmed CS when there is high-grade AV block, significant LGE or PET-active disease, or VA. Corticosteroids and additional immunosuppressants may stabilize or improve LV function but have inconsistent effects on conduction disease progression or arrhythmia burden.

Amyloidosis

Cardiac amyloidosis is caused by extracellular deposition of misfolded precursor proteins, most commonly immunoglobulin light chains (AL amyloid) or transthyretin (TTR). Transthyretin amyloidosis (ATTR) includes both hereditary variants (caused by TTR gene mutations) and wild-type ATTR

(formerly “senile” amyloidosis), which predominantly affects older men and is increasingly recognized through improved diagnostic pathways.

Amyloid infiltration produces concentric wall thickening, biatrial enlargement, and a restrictive filling pattern, while ECG voltages remain disproportionately low relative to the degree of hypertrophy. Conduction system involvement is common across all subtypes, manifesting as SND, bundle branch block, intraventricular delay, or progressive AV block. Patients with wild-type ATTR are particularly prone to developing high-grade conduction disease requiring pacing.

Although permanent pacing alleviates symptoms attributable to bradyarrhythmia, there is no evidence of a survival benefit. Disease-modifying therapies, including TTR stabilizers, TTR silencers (e.g. RNA-based therapies), and plasma-cell-directed AL amyloidosis treatment have reshaped prognosis, but conduction disease often progresses despite systemic improvement.

Collagen vascular and systemic inflammatory diseases

A variety of systemic autoimmune disorders, including systemic lupus erythematosus, systemic sclerosis, polymyositis/dermatomyositis, and antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides may involve the myocardium, pericardium, and coronary vasculature. Myocarditis or vasculitis may lead to arrhythmias, although sustained arrhythmias remain relatively uncommon. Conduction system fibrosis is most frequently reported in granulomatosis with polyangiitis (formerly Wegener granulomatosis) and inflammatory myopathies. AV block from active inflammation may occasionally reverse with immunosuppressive therapy.

Congenital complete heart block resulting from transplacental passage of maternal anti-SSA/Ro antibodies remains an important cause of permanent AV block in neonates of mothers with systemic lupus erythematosus or primary Sjögren syndrome. Contemporary guidelines emphasize careful fetal surveillance and early recognition of high-risk maternal antibody profiles.

Chagas disease

Chagas disease, caused by *Trypanosoma cruzi*, remains one of the most important infectious

causes of bradyarrhythmias worldwide. While acute infection is often mild or unrecognized, approximately 20–30% of infected individuals progress to chronic Chagas cardiomyopathy over decades. Conduction abnormalities, including SND, RBBB, LAFB, and progressive AV block, typically precede the development of ventricular aneurysms, cardioembolic complications, and DCM with severe LV dysfunction.

Even early conduction abnormalities (e.g. isolated RBBB with fascicular block) confer increased risk of malignant arrhythmias and SCD. VA are common, often scar-related, and may require ICD therapy. In endemic regions, Chagas disease continues to be one of the leading indications for permanent pacing.

Dilated cardiomyopathy: genetic forms associated with conduction system disease and arrhythmia

Mutations in the LMNA and in SCN5A (encoding the cardiac sodium channel Nav1.5) define genetic forms of DCM in which conduction-system disease and malignant VA are prominent and may precede systolic dysfunction. Both LMNA-related cardiomyopathy and SCN5A-related disease show a predilection for early AV conduction disturbance, atrial arrhythmias, and a high burden of VTAs compared with many other non-ischemic DCM genotypes. The phenotype spectrum in SCN5A variants is broad (overlap with Brugada syndrome, sick sinus syndrome, and isolated conduction disease), but when associated with DCM, it is highly arrhythmogenic.

LMNA pathogenic variants are highly penetrant: most genotype-positive carriers will demonstrate some form of cardiac involvement by mid-to-late adult life, and AV conduction abnormalities (ranging from first-degree AV block to high-grade AV block) commonly represent an initial manifestation several years before the development of overt LV systolic dysfunction. A multivariate risk model for life-threatening VTA in laminopathies (the Wahbi LMNA-VTA score) incorporates sex, type of LMNA variant (missense versus non-missense), presence and degree of AV block, history of non-sustained VT, and LVEF to estimate 5-year arrhythmic risk and guide consideration of primary-prevention ICD therapy [24].

In a young patient presenting with unexplained high-grade AV block or early conduction disease,

or in any patient with DCM plus conduction delay, a genetic etiology should be suspected and genetic testing considered (especially when there is a family history of DCM or premature SCD). Cardiomyopathy guidelines discussed in subsequent chapters recommend targeted genetic evaluation in these scenarios because identification of a pathogenic variant alters downstream arrhythmic risk assessment, genetic testing of relatives, and device strategy.

All patients with genetically mediated conduction disease who receive pacing require periodic surveillance of LV function because (i) cardiomyopathy may evolve after the onset of conduction disease and (ii) chronic RV pacing can contribute to pacing-induced LV dysfunction. When pacing burden is expected to be high, or when LV systolic function is reduced or declines after pacing, cardiac resynchronization therapy (CRT) or CSP strategies should be considered to reduce the risk of heart-failure progression.

Hypertrophic cardiomyopathy

HCM is a common genetic myocardial disease most frequently caused by autosomal-dominant pathogenic variants in genes encoding sarcomere proteins and associated myofilament elements. The clinical phenotype is heterogeneous, ranging from isolated, asymmetric LV hypertrophy with preserved systolic function to diffuse hypertrophy with heart-failure symptoms, and may include dynamic left ventricular outflow tract (LVOT) obstruction, diastolic dysfunction, mitral regurgitation, myocardial ischemia, AF, and an increased risk of VTA and SCD. Contemporary guidelines emphasize that genotype and phenotype both inform risk stratification, family cascade (targeted genetic) testing, and longitudinal management [10].

LVOT obstruction remains recognized as a dynamic phenomenon in which systolic anterior motion (SAM) of the mitral valve and septal morphology interact to create a variable pressure gradient. Imaging and fluid-dynamic analyses stress the importance of altered mitral-valve geometry and systolic drag forces on an abnormally positioned mitral apparatus that displaces leaflets into the outflow tract during systole, in addition to septal hypertrophy and contractile encroachment. This mechanistic understanding underpins current

interventional strategies that target either the septum [surgical myectomy or alcohol septal ablation (ASA)] or mitral apparatus (surgical or transcatheter mitral interventions).

Early uncontrolled series suggested that AV-synchronized RV apical pacing could reduce LVOT gradients and improve symptoms in some patients, and mechanistic hypotheses included alteration of septal contraction and induced paradoxical septal motion. However, randomized, double-blind, and crossover trials (including M-PATHY and smaller double-blind crossover studies) [25] demonstrated only modest mean reductions in gradient and symptomatic benefit that were frequently indistinguishable from a placebo effect; benefit was highly variable among individuals and hard to predict from baseline hemodynamics or morphology. As a result, contemporary guideline documents (ESC and AHA/ACC) no longer endorse dual-chamber pacing as a primary therapy for obstructive HCM and reserve it for highly selected circumstances. Pacing may be considered as an alternative only when: (i) patients are poor candidates for septal reduction (surgical myectomy or ASA) or refuse those procedures; (ii) symptoms are refractory to maximally tolerated medical therapy; and (iii) realistic expectations have been established about the variable benefit. Older age (commonly >65 years) has been reported as a subgroup more likely to experience symptomatic improvement with AV-sequential pacing in some trials, but this remains a pragmatic rather than definitive selection criterion. When pacing is undertaken with the aim of reducing LVOT obstruction, careful AV-delay optimization (to produce ventricular pre-excitation without compromising diastolic filling), attention to rate-adaptive AV timing for exercise, and choice of ventricular lead site to achieve the desired activation pattern are recommended.

Surgical septal myectomy and ASA remain the guideline-recommended septal reduction therapies for medically refractory, symptomatic obstructive HCM; these procedures generally provide more consistent and durable gradient reduction and symptomatic improvement than pacing. ASA carries a nontrivial risk of conduction disturbance: the incidence of new complete heart block requiring permanent pacing in 6–11% of patients. The exact rate depends on procedural technique, target

septal branch anatomy, and operator experience. The literature on post-ASA ventricular arrhythmia risk is mixed: some meta-analyses and registries report comparable or modestly increased rates of VA compared with myectomy, but interpretation is confounded by patient selection, follow-up intensity, and use of implantable monitoring. Decisions about device implantation after septal reduction should therefore be individualized and guided by contemporary arrhythmic-risk assessment.

Choice between pacemaker and ICD is driven by separate indications: pacing is indicated for conventional bradyarrhythmia indications (SND, high-grade AV block) per standard device guidelines, whereas ICD therapy is indicated for prevention of SCD based on established HCM risk markers (personal history of cardiac arrest or sustained VT, NSVT, high scar burden on MRI, family history of SCD due to HCM, certain combinations of risk factors, unexplained syncope, extensive LV hypertrophy, LV systolic dysfunction, apical aneurysm, or otherwise high estimated 5-year SCD risk). Current HCM guidance (AHA/ACC and ESC updates) stresses that device decisions for primary prevention of SCD in HCM should use validated risk models where available, incorporate phenotype and family history, and be individualized rather than governed by LVOT status or septal reduction history alone. In patients undergoing device implantation for bradyarrhythmia who also meet criteria for primary-prevention ICD because of arrhythmic risk, implantation of an ICD (or an ICD-capable cardiac-resynchronization device, when indicated) at the index procedure is reasonable to avoid early re-intervention. Pacing therapy alone may be considered in the management of HCM patients with AF with rapid ventricular response with planned AV node ablation and who are not indicated for ICD implantation based on established guidelines (Table 1.6).

Pacing for systolic heart failure and conduction system pacing

Early observations suggested that dual-chamber pacing (with standard endocardial pacing) with short AV delay could improve hemodynamics by enhancing diastolic filling and reducing functional mitral regurgitation. However, subsequent randomized trials consistently failed to demonstrate

meaningful clinical benefit from isolated right-sided dual-chamber pacing in systolic heart failure. In contrast, the development of biventricular pacing for CRT fundamentally changed management of patients with electrical and mechanical dyssynchrony. Large randomized CRT trials, representing over 7,000 patients across multiple landmark studies have demonstrated substantial reductions in heart failure hospitalization and mortality, reverse LV remodeling, improved functional class, and reduction in secondary mitral regurgitation in appropriately selected patients. Approximately 65–75% of patients (“CRT responders”) experience measurable improvement in symptoms and ventricular function.

More recent experience in less symptomatic populations, including patients with NYHA class I–II heart failure, shows that CRT can reduce the composite of heart failure hospitalization and death, with mortality benefit most clearly demonstrated in class II patients with LBBB and wide QRS duration. Conversely, narrow-QRS populations do not benefit from CRT; the ECHO-CRT trial demonstrated increased cardiovascular mortality with CRT in patients with QRS <130 ms, firmly establishing the current QRS threshold for therapy. These data underpin the contemporary requirement that candidates for CRT must have QRS $\geq$ 130 ms, with the strongest benefit seen in LBBB morphology and QRS $\geq$ 150 ms.

Although most pivotal CRT trials implanted CRT-D devices, current guidelines emphasize selecting between CRT-P and CRT-D based on individual patient characteristics, comorbidity burden, competing mortality risks, and shared decision-making. CRT-P alone provides substantial improvement in quality of life and functional capacity and is often preferred in older patients or those with limited life expectancy in whom defibrillator therapy is unlikely to provide meaningful survival advantage. In patients with pacing-induced cardiomyopathy or high right-ventricular pacing burden leading to LV dysfunction, upgrade to CRT (with addition of an LV lead) can reverse LV remodeling and obviate the need for an ICD in individuals without independent arrhythmic risk.

CRT implantation remains more technically demanding than conventional pacemaker or ICD implantation because of the need for coronary

Table 1.6 Summary of pacing considerations versus ICD considerations in patients with hypertrophic cardiomyopathy

<i>Clinical scenario</i>	<i>Recommended device (class/LOE)</i>	<i>Practical notes/caveats</i>
Symptomatic sinus node dysfunction (SND) (any patient, incl HCM)	Pacemaker (dual- or single-chamber as appropriate) Class I/LOE C	Standard bradycardia indication; choose device type based on rhythm (sinus versus AF) and need for AV synchrony.
High-grade/advanced AV block (any patient, incl HCM)	Pacemaker Class I/LOE C	If coexisting high SCD risk → favor ICD rather than pacemaker (see below).
HCM with refractory symptoms, not candidate for septal reduction → consider AV-sequential pacing	AV-sequential RV pacing trial (select patients) Class IIb (selected older patients); LOE C–B (limited RCT data)	Pacing is not first-line for LVOT obstruction. Randomized trials show modest, variable benefit with substantial placebo effect; consider only after shared decision-making (older patients may benefit more). Optimize AV delay and rate-adaptive timing.
New persistent complete heart block after ASA/myectomy	Permanent pacemaker Class I (for persistent AV block)	If patient also meets primary-prevention ICD criteria, implant an ICD (or ICD-capable CRT) at index procedure to avoid early upgrade.
HCM patient with conventional bradycardia indication AND independent high SCD risk (meets ICD criteria)	ICD (rather than pacemaker) Class I when ICD indications met	Use guideline HCM SCD risk tools (AHA/ACC, ESC) and phenotype (massive LVH, apical aneurysm, prior VT/CA, extensive LGE, family history) to guide ICD decision. If pacing indicated, implant ICD at index procedure.
HFrEF, LVEF ≤35%, sinus rhythm, LBBB, QRS ≥ 150 ms, NYHA II–IV on GDMT	CRT-D or CRT-P (CRT indicated) Class I/LOE A (for NYHA III/IV); Class I (or IIa) varies with NYHA II across guidelines	Strongest evidence for LBBB ≥150 ms. Consider ICD-capable CRT (CRT-D) if patient has significant SCD risk and reasonable life expectancy.
HFrEF, LVEF ≤35%, sinus rhythm, LBBB, QRS 130–149 ms, NYHA II	CRT considered Class IIa/LOE B	Contemporary guidance supports CRT in this subgroup (benefit attenuated compared to ≥150 ms)
HFrEF, LVEF ≤35%, non-LBBB, QRS ≥150 ms	CRT may be considered Class IIa/IIb (guideline-dependent), LOE B	Benefit less consistent than LBBB; decision individualized.
QRS <130 ms (without need for ventricular pacing)	CRT not recommended Class III/LOE A	Echo-CRT showed harm in narrow QRS mechanical dyssynchrony populations; CRT generally contraindicated if QRS <130 ms unless RV pacing necessity.
Patients with high anticipated RV-pacing burden and LVEF ≤35% (or existing LV dysfunction)	Prefer CRT over RV pacing, CSP can be considered as alternative Class I (to avoid pacing-induced cardiomyopathy)	When permanent ventricular pacing is indicated and LVEF is reduced, use CRT to prevent further dyssynchrony and remodeling.
Atrial fibrillation with LVEF ≤35% and indications for CRT	CRT can be useful Class IIa if near-100% biventricular capture can be achieved (often requires AVJ ablation)	Ensure effective biventricular pacing (consider AV-node ablation when rate control inadequate).
When coronary-sinus LV lead placement fails or suboptimal	Consider conduction-system pacing (His bundle or LBB-area pacing) as alternative to BiV-CRT Class IIa (emerging evidence)	CSP (HBP or LBBAP) is recognized in guidelines as a reasonable alternative in select cases; randomized long-term outcomes still maturing.

sinus lead placement, which carries higher risks of acute and subacute complications, including lead dislodgement, phrenic nerve stimulation, venous occlusion, and procedural failure. Optimal patient selection is therefore essential, and multiple post hoc analyses have identified phenotypes most likely to benefit; non-ischemic cardiomyopathy, typical LBBB morphology, and QRS duration ≥ 150 ms are the strongest positive predictors of response. Non-LBBB morphologies have a more modest response profile, although patients with QRS ≥ 150 ms may still benefit.

The role of biventricular pacing in AF is well defined in current practice: CRT is effective when near-100% biventricular capture can be ensured. Because rapid or irregular ventricular response interferes with resynchronization, many AF patients require AV nodal ablation to achieve effective CRT delivery. Evidence shows that when consistent biventricular pacing is achieved, outcomes in AF patients are comparable to those in sinus rhythm.

An important development is the emergence of CSP, including HBP and LBBAP, which can provide physiologic ventricular activation. Current guidelines recognize CSP as a reasonable alternative when conventional CRT cannot be delivered (e.g. failed coronary sinus lead) and as a strategy for patients requiring substantial ventricular pacing who are at risk of pacing-induced cardiomyopathy. Although long-term randomized outcome trials are ongoing, early data show promising results and CSP is expected to assume a larger role in future guidelines.

Key indications for pacing and CRT in heart failure with reduced ejection fraction

Class I indications

1 Standard bradycardia indications: Permanent pacing for symptomatic SND or advanced AV block (per general pacing guidelines). Consider CSP.

2 CRT in HFrEF with LBBB and wide QRS: CRT is indicated for patients with LVEF $\leq 35\%$, sinus rhythm, typical LBBB morphology, QRS ≥ 150 ms, and NYHA class II–IV symptoms despite GDMT. Evidence level remains strongest for NYHA III–IV (LOE A), with NYHA II supported by high-quality data (LOE B).

3 CRT when ventricular pacing is required in HFrEF: For patients with LVEF $\leq 35\%$ who require frequent ventricular pacing, regardless of NYHA

class, CRT is recommended over RV pacing to prevent pacing-induced dyssynchrony and reduce morbidity.

Class IIa indications

1 LBBB with QRS 130–149 ms: CRT is reasonable for patients with LVEF $\leq 35\%$, sinus rhythm, LBBB morphology with QRS 130–149 ms, and NYHA II–ambulatory IV symptoms on GDMT. (ESC guidelines categorize these as Class I indications.)

2 Non-LBBB with QRS ≥ 150 ms: CRT can be useful in patients with LVEF $\leq 35\%$ and non-LBBB morphology when QRS ≥ 150 ms. Benefit is less robust than in LBBB but clinically meaningful in selected patients.

3 AF with requirement for near-100% biventricular pacing: CRT is reasonable in AF patients with LVEF $\leq 35\%$ when:

- a) they meet standard CRT criteria or require ventricular pacing; and
- b) rate control or AV nodal ablation can achieve near-complete biventricular capture.

4 Patients needing new or replacement devices with high expected RV pacing burden: CRT is reasonable for patients with LVEF $\leq 35\%$ on GDMT who are expected to require $>40\%$ ventricular pacing at initial implant or generator replacement.

Class IIb Indications

1 Non-LBBB QRS 130–149 ms: CRT may be considered in patients with LVEF $\leq 35\%$, sinus rhythm, non-LBBB morphology, QRS 130–149 ms, and NYHA III–ambulatory IV symptoms, acknowledging reduced likelihood of response

Class III (not recommended)

1 CRT for QRS < 130 ms: CRT is not indicated when QRS duration is < 130 ms in the absence of a need for ventricular pacing, due to lack of benefit and potential harm

Contemporary data, evolving insights and recommendations for clinical practice

CSP represents a major evolution in physiologic cardiac pacing and is already reshaping device therapy for bradycardia and heart failure. By directly engaging the His–Purkinje network through HPB or LBB area pacing, CSP preserves or

restores the native sequence of ventricular activation, thereby minimizing electrical dyssynchrony and reducing the risk of pacing-induced cardiomyopathy. Early and mid-term clinical data demonstrate that CSP can provide resynchronization comparable to and in selected patients superior to traditional biventricular CRT, particularly when coronary sinus lead placement is difficult or when CRT response is suboptimal. This approach has also expanded therapeutic options for patients who require a high burden of ventricular pacing, those with atypical conduction patterns, and individuals with failed or non-responsive CRT systems. As implantation techniques and device algorithms continue to improve, CSP may offer more consistent ventricular synchrony, greater procedural flexibility, and potentially broader applicability than conventional CRT. Its integration into clinical practice has the potential to reduce heart-failure progression, improve functional status, and simplify complex device therapy. Table 1.7 outlines clinical scenarios in which CSP should be considered. In individual patients, both CRT and CSP need to be considered if the initial approach does not yield satisfactory acute results. Figure 1.14 compares the QRS complexes using different pacing strategies.

Pacing to prevent or terminate tachycardias

Pacing techniques can terminate tachyarrhythmias that depend on a reentrant mechanism by delivering premature or overdrive stimuli that interrupt the circuit. In contemporary practice, the role of permanent pacing for treatment or prophylaxis of supraventricular tachycardias (SVTs) is highly selective because catheter ablation offers high efficacy and safety across most forms of AV nodal and accessory pathway-dependent tachycardias, as well as typical atrial flutter and many atrial tachycardias. Antiarrhythmic drug therapy remains an alternative in patients not suited for ablation. Consequently, pacing for termination of atrial tachyarrhythmias is now largely confined to patients with coexisting bradyarrhythmias in whom a pacemaker is already indicated. In rare circumstances, patients with symptomatic, recurrent, and drug- or ablation-refractory focal atrial tachycardia may benefit from antitachycardia pacing (ATP) when reproducible

and safe termination has been demonstrated without provoking more rapid atrial arrhythmias. Atrial ATP remains available only in atrial or dual-chamber pacemakers, as devices without defibrillation capability do not provide ventricular ATP. Ventricular ATP is delivered exclusively by ICDs, which offer both antitachycardia and shock therapy and remain the standard for VTAs (Figure 1.15).

VA may be precipitated by pauses, and pacing can prevent pause-dependent torsades de pointes in long-QT states. In congenital long-QT syndrome (LQTS), the onset of torsades de pointes is frequently preceded by long-short RR sequences, and pacing to prevent bradycardia or pauses can reduce arrhythmic risk (Figure 1.16). Pacing combined with β -blocker therapy has been shown to lower the incidence of syncope and malignant arrhythmias in selected genotypes, although high-risk patients, particularly those with prior cardiac arrest, recurrent syncope on optimal β -blockade, or high-risk genotypes (e.g. LQT2 and LQT3), are typically treated with an ICD capable of both pacing and defibrillation. In acquired LQTS, pacing is used only acutely or when QT prolongation cannot be mitigated by eliminating reversible causes.

Multiple pacing strategies have been evaluated for prevention of AF, including biatrial pacing, Bachmann bundle-region pacing, low interatrial septal pacing, and atrial overdrive algorithms. Despite initial promise, controlled trials have not demonstrated consistent or clinically meaningful benefit for AF prevention beyond standard atrial-based pacing. However, in SND, atrial pacing may reduce AF burden, stroke risk, and progression to persistent AF compared with ventricular-only pacing. Algorithms that reduce unnecessary ventricular pacing remain central strategy for AF prevention in patients with SND and dual-chamber pacemakers.

Key indications for pacing to prevent or terminate tachycardias

Class I indications

1 Permanent pacing is indicated for sustained pause-dependent VT, with or without QT prolongation. (Level of evidence: C)

Class IIa indications

1 Permanent pacing is reasonable in high-risk patients with congenital LQTS who have recurrent

Table 1.7 This table summarizes some potential clinical scenarios in which conduction system pacing (CSP) may be considered as an alternative to standard cardiac resynchronization therapy (CRT)

<i>Clinical scenario</i>	<i>CSP as alternative to CRT</i>	<i>Rationale/practical considerations</i>	<i>Guideline/evidence</i>
Primary CRT candidates with failed or unfeasible coronary-sinus (CS) LV lead (CS anatomy unsuitable, phrenic stimulation, high lead thresholds, CS lead failure)	Prefer CSP (HBP or LBBAP)	CSP can achieve physiologic activation and resynchronization when CS lead cannot be placed or provides inadequate capture; LBBAP often easier to implant and provides stable thresholds. Use operator expertise and intra-procedural electrophysiologic criteria to confirm correction of conduction delay.	Supported by ESC/HRS/EHRA consensus and multiple contemporary reviews. Consider CSP as first alternative after failed CS lead.
Patients with typical LBBB, LVEF $\leq 35\%$, and need for CRT	CRT remains accepted standard. CSP reasonable (especially LBBAP)	Randomized clinical trials in progress. Observational and physiologic studies show comparable electrical resynchronization and clinical outcomes for LBBAP versus BIV-CRT in many patients with LBBB. Choice may depend on local CSP experience and anatomic suitability.	Recognized in 2021–2024 consensus statements as an acceptable alternative in selected centers; randomized trial data still emerging.
Patients with non-LBBB conduction patterns or intraventricular conduction delay (unlikely to respond to BIV-CRT)	CSP can be considered	BIV-CRT response is variable in non-LBBB patterns; CSP may directly correct native conduction delay and restore more physiological activation, potentially improving response in non-LBBB patients. Individualize decision and confirm electrical resynchronization during implant.	Growing evidence and consensus suggest CSP may be advantageous for non-LBBB; still class IIb/IIa level in many guidelines pending RCTs [26].
Patients who require high % ventricular pacing (e.g. AV block) with LVEF mildly-moderately reduced (to avoid pacing-induced cardiomyopathy)	Prefer CSP over RV pacing; CSP vs CRT depends on LVEF & QRS	CSP preserves physiologic activation and reduces risk of pacing-induced dyssynchrony; for patients with reduced LVEF who need permanent pacing, CSP (or CRT) is preferable to RV apical pacing. CSP can be considered for EF > 35% with LBBB or non-LBBB wide QRS. CSP may be preferred for EF > 35% with narrow QRS.	Recommended by HRS/APHS/LA/HRS consensus and ESC documents as reasonable approach to mitigate pacing-induced cardiomyopathy. [26]
Atrial fibrillation requiring AVJ ablation with CRT indication and reduced EF.	CSP is an option, but ensure reliable capture; CRT via Biv often preferred if achievable	After AVJ ablation, consistent capture is essential; CSP can provide physiologic activation but may be vulnerable to threshold changes, LBBAP may be preferred over His Bundle Pacing. If CS lead provides stable Biv pacing, CRT remains standard; CSP is appropriate if CS lead fails.	Consensus statements recommend CSP as alternative in selected patients; individualize by capture reliability. [26]
Elderly, frail patients where procedural complexity/patient risk is limiting.	CSP may be preferred when shorter procedures and less hardware are advantageous, but depends on operator skill	LBBAP can be quicker in experienced hands and avoids complex CS maneuvers; however, CSP still requires specialized skill and may not uniformly shorten procedures.	Consider operator experience and patient risk/benefit; no universal recommendation. [27]
Patients with prior BIV-CRT non-responders	Consider CSP in selected nonresponders	CSP may correct residual electrical dyssynchrony or overcome suboptimal LV lead position; observational studies report symptomatic and echo improvement in some CRT nonresponders after CSP upgrade.	Supportive observational evidence; remain selective and evaluate for alternative causes of nonresponse. [26]

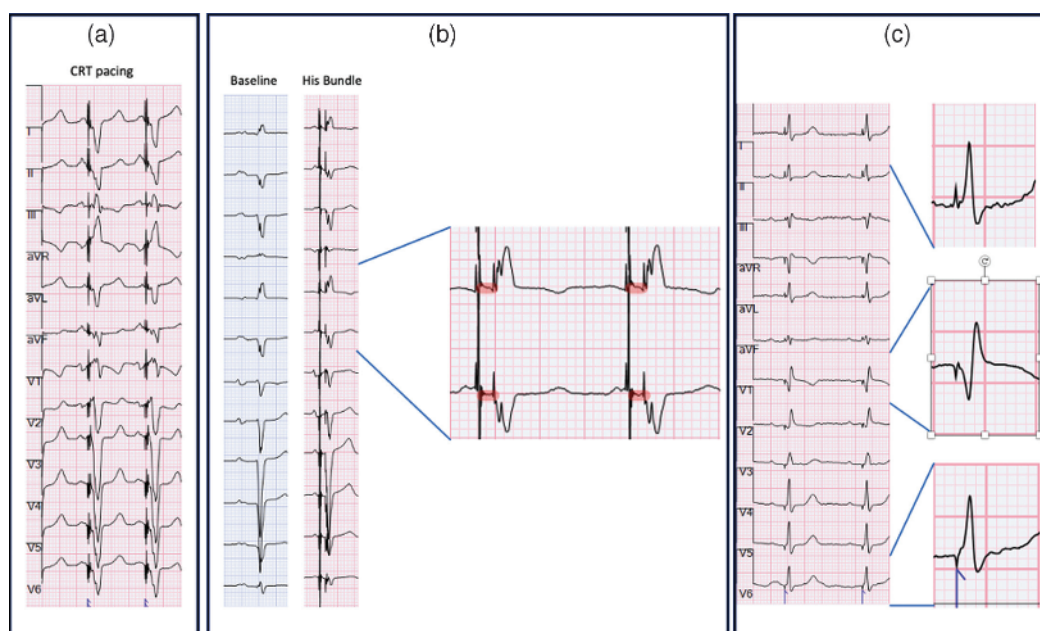


Figure 1.14 Panel A: Paced QRS complex measuring 128 ms from a CRT device. Panel B: Selective His bundle pacing can be identified on a surface ECG by an isoelectric line following the pacing spike (highlighted red line). The duration of the isoelectric line approximates the normal HV interval (35–55 ms). The QRS duration is 85 ms. The first

(large amplitude) spike is due to unipolar pacing from the His bundle lead. In this example, there is also a defibrillation lead in the RV, with back up RV pacing (second, low amplitude spike) and pseudofusion with the QRS. Panel C: Left bundle branch areas pacing with selective left bundle capture and a QRS duration of 110 ms.

arrhythmic events despite optimal β -blockade or in whom pause-dependent initiation of torsades de pointes is clearly documented. (Level of evidence: C). *Most such patients meet criteria for ICD therapy.*

2 Permanent pacing is reasonable for symptomatic, recurrent SVT that is reproducibly terminated by pacing when catheter ablation and antiarrhythmic drug therapy are either ineffective, contraindicated, or not tolerated. (Level of evidence: C)

Class IIb indications

1 Permanent pacing may be considered for prevention of symptomatic, drug-refractory recurrent AF in patients with coexisting SND, particularly when atrial pacing is expected to reduce AF triggers and ventricular pacing can be minimized. (Level of evidence: B)

Class III (not indicated or recommended)

1 Presence of accessory pathways with rapid anterograde conduction, irrespective of their role in tachycardia mechanism; pacing does not prevent nor terminate preexcited AF and may be harmful.

2 Frequent or complex ventricular ectopy without sustained VT in the absence of congenital LQTS.

3 Torsades de pointes due to reversible causes (e.g. drug exposure and electrolyte abnormalities), where pacing is not indicated once the cause is corrected.

Pacing for children and adolescents (including all patients with congenital heart block)

There remain no RCTs that specifically define pacing strategies for pediatric patients or for the full spectrum of congenital heart disease (CHD). The level of evidence for most recommendations remains consensus-based, informed by observational series, registry data, and expert consensus statements. Contemporary practice aligns with adult principles but requires multiple pediatric-specific considerations. The diagnosis of clinically important bradycardia in children is age dependent: heart rate thresholds that are physiologic for older children and adults may represent profound

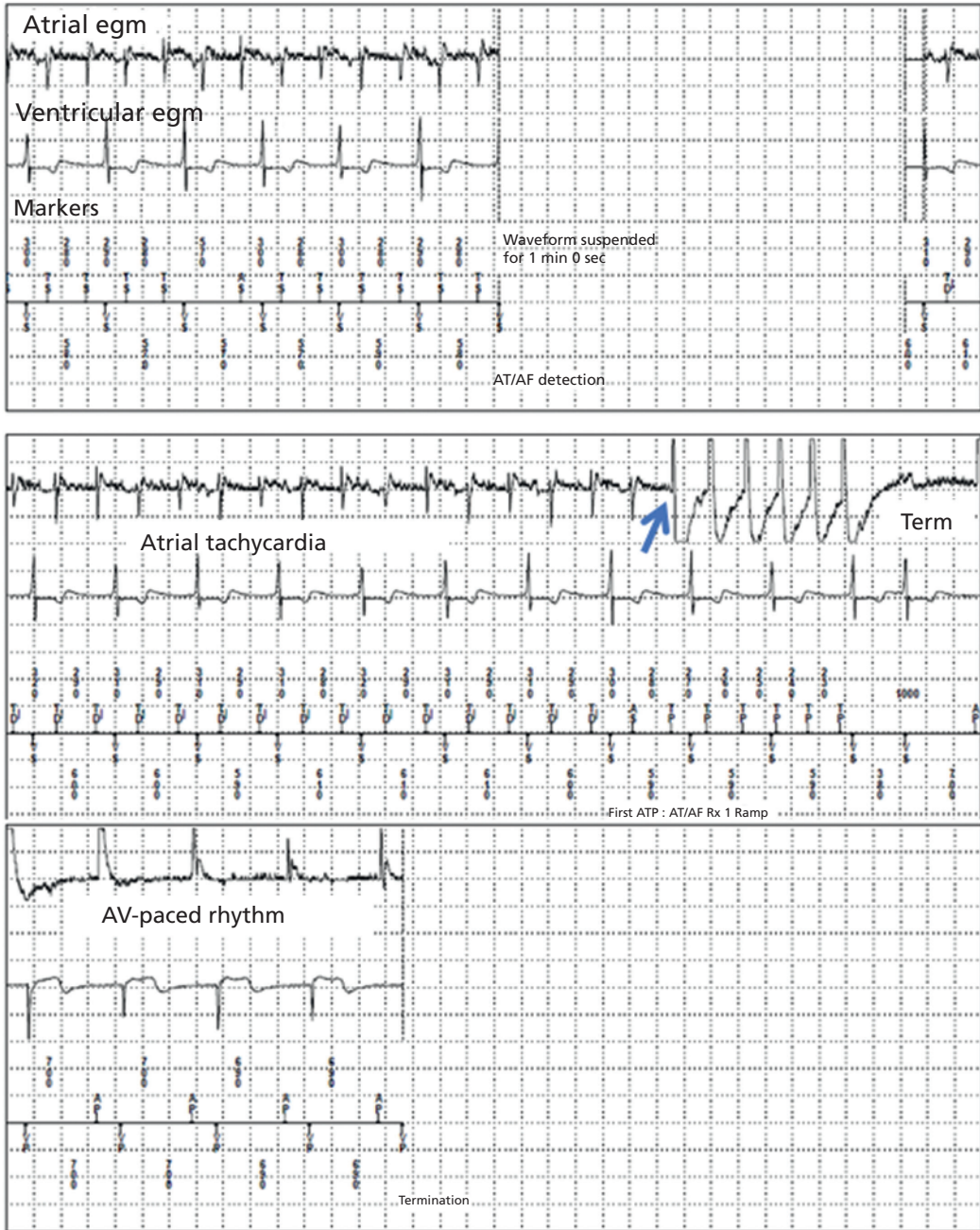


Figure 1.15 Atrial overdrive pacing to terminate atrial tachycardia. This 75-year-old woman with pulmonary hypertension and recurrent atrial tachycardia had a dual-chamber pacemaker implanted for tachy-brady syndrome. Her atrial arrhythmia was reproducibly terminated with atrial overdrive pacing. (Top to bottom)

Atrial bipolar electrograms, ventricular electrograms, and marker channels. At baseline, an atrial tachycardia at a cycle length of 250 ms (240 bpm) was present. A burst of atrial overdrive pacing (blue arrow) resulted in termination of the tachycardia (term) and restoration of AV-synchronous pacing.

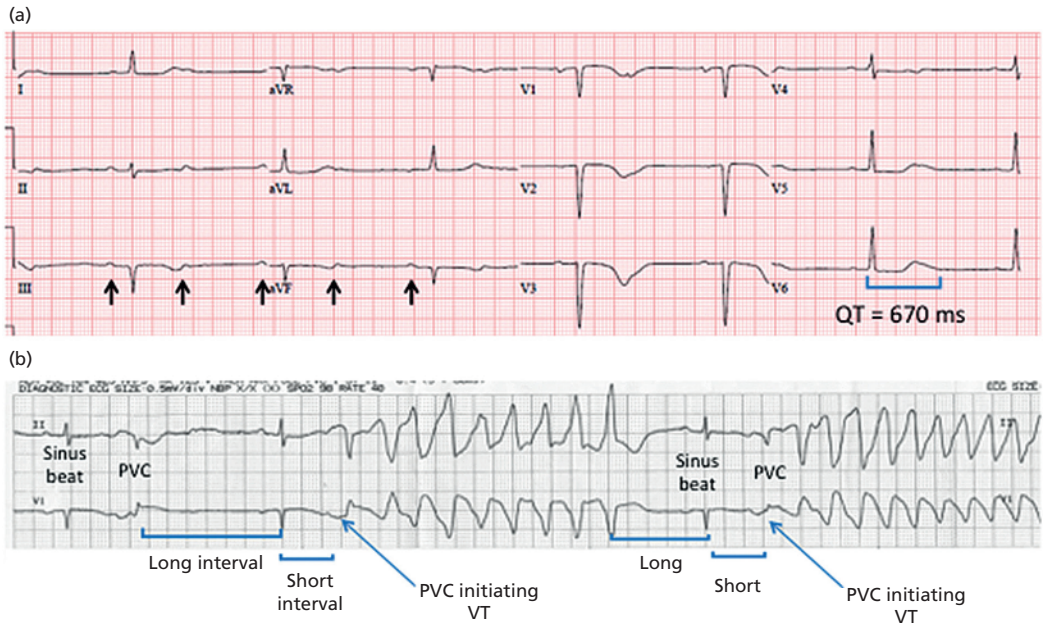


Figure 1.16 Bradycardia-related torsades de pointes ventricular tachycardia (VT). (a) Marked QT prolongation related to 2 : 1 AV block in an 80-year-old woman hospitalized with syncope and facial injuries. The black arrows denote P waves. (b) A premature ventricular

contraction (PVC) that arises on the T wave causes a post-PVC pause, further lengthening QT interval. Self-limiting torsades de pointes VT is initiated by a long-short RR interval and is repeated.

bradycardia in neonates and young infants and cause severe hemodynamic compromise. Likewise, the abnormal cardiovascular physiology that results from palliative or corrective surgery for CHD frequently renders postoperative patients more susceptible to decompensation from bradycardia or loss of AV synchrony than would be expected in structurally normal hearts. These anatomic and physiologic differences must inform both the indications and the timing of device therapy [28].

When intracardiac shunts or systemic venous–systemic arterial communications exist, the risk of paradoxical embolism from thrombus formation on endocardial leads becomes an important consideration and may favor epicardial systems or alternative strategies (including consideration of leadless systems where anatomically feasible). Vascular access challenges in neonates and small infants and the long-term sequelae of transvenous leads (venous stenosis/occlusion, lead fracture, and lead infection) frequently prompt early consideration of epicardial lead implantation. Epicardial

systems are commonly used in patients weighing less than ~10–15 kg or when venous anatomy or intracardiac shunts make transvenous access undesirable; however, epicardial leads carry higher procedural morbidity and a higher chronic lead-failure rate compared with modern transvenous leads, and these risks must be balanced against the longer-term risks of endovascular leads in growing children. Recent device innovations, including smaller generators, subcutaneous and leadless pacing technologies, and hybrid epicardial–endocardial strategies, have expanded options but require individualized patient selection and long-term planning for lead management and generator changes.

Chronic RV apical pacing in children can produce pacing-induced ventricular dyssynchrony and progressive ventricular dysfunction over years, particularly in patients with coexistent ventricular myocardial disease or genetic cardiomyopathies. Periodic surveillance by echocardiography (and where appropriate, cardiac MRI) is recommended to detect early LV systolic dysfunction. When

pacing-related ventricular dysfunction is suspected, strategies to minimize deleterious RV pacing and to provide physiologic ventricular activation (biventricular pacing/CRT or CSP where feasible) should be considered.

The common clinical indications for permanent pacing in children, adolescents, and patients with CHD remain broadly grouped as (i) sinus bradycardia (including symptomatic SND), (ii) tachy-brady syndrome (frequently postoperative intra-atrial reentrant tachycardia with impaired sinus-node recovery), and (iii) congenital or postoperative advanced second- or third-degree AV block. SND is uncommon in pediatric populations but, when present, may be associated with channelopathy or genetic variants (including SCN5A and other genes); pacing is typically reserved for correlation of symptoms (syncope, presyncope, and exercise intolerance) with documented bradyarrhythmia—commonly accepted triggers are mean awake rates that are pathologically low for age, or prolonged pauses (>3 s), although clinical context is paramount because apnea, seizure disorders, or neurocardiogenic mechanisms may produce transient bradycardia and are better treated by correcting the underlying disorder than by permanent pacing [28].

Tachy-brady syndrome in postoperative CHD patients commonly reflects intra-atrial reentrant tachycardia with associated SND and may present with hemodynamic compromise and prolonged post-tachycardia pauses. While permanent atrial-based pacing with atrial ATP algorithms can terminate some macro-reentrant atrial tachycardias and is a potential option in patients who already require pacing, catheter ablation remains the preferred therapy when anatomically feasible and efficacious.

Congenital complete AV block (CCHB) is an uncommon disorder that may arise from immune-mediated injury (transplacental maternal anti-SSA/Ro and/or anti-SSB/La antibodies) or from nonimmune developmental abnormalities of the conduction system. Immune-mediated block typically develops in utero or in the early neonatal period; late postnatal development has been described. The antibody-negative group often presents later in childhood and may demonstrate progressive AV conduction disease. The approximate incidence of antibody-associated CCHB among anti-SSA/Ro

positive pregnancies is low (reported live-birth incidence on the order of 1–2%), but the risk to an individual pregnancy depends on maternal autoimmune status and prior affected offspring.

Most children with isolated congenital complete AV block have a stable escape rhythm that is narrow complex. Current guidance and practice has moved toward slightly lower heart rate thresholds for immediate implantation in neonates to avoid premature device implantation in infants with stable hemodynamics; many centers now use a resting ventricular rate threshold of ≈ 50 bpm (instead of the historical 55 bpm) in structurally normal hearts as part of the overall decision algorithm, while higher ventricular rate thresholds (commonly <60 – 70 bpm) are often applied when significant structural or functional heart disease coexists. Regardless of numeric cutoffs, pacing is indicated for symptomatic bradycardia, ventricular dysfunction, complex ventricular ectopy, wide QRS escape rhythms, or significant pauses. In the asymptomatic child with congenital complete AV block, decisions consider average heart rate, frequency, and duration of pauses, presence of ventricular ectopy, LV function, exercise tolerance, and the QT interval [28].

Postoperative high-grade AV block (Mobitz II, advanced second-degree, or complete heart block) that does not show evidence of recovery within the expected postoperative window remains an indication for permanent pacing. Permanent pacing in patients with persistent advanced AV block that is not expected to resolve beyond 7–10 days after cardiac surgery, with earlier implantation considered when prolonged dependency on temporary pacing is anticipated or when there is hemodynamic instability.

Key indications for permanent pacing in children and adolescents

Class I indications

- 1 In patients with congenital complete third-degree AV block who are symptomatic because of bradycardia. (Level of evidence: C/Consensus)
- 2 In neonates/infants with congenital third-degree AV block and ventricular rate <50 bpm in a structurally normal heart, or ventricular rate <60 – 70 bpm when associated with structural heart disease, or in the presence of signs of poor perfusion, ventricular dysfunction, complex ventricular

ectopy, or wide-complex escape rhythm. (Level of evidence: C-EO/Expert Opinion)

3 Persistent postoperative high-grade AV block (Mobitz type II, advanced second-degree, or third-degree AV block) that is not expected to resolve. (Level of evidence: B-NR/consensus from surgical/EP practice)

4 Symptomatic SND (syncope, presyncope, and marked chronotropic incompetence) documented to be caused by bradyarrhythmia is an indication for atrial-based permanent pacing. (Level of evidence: B-NR)

Class IIa indications

1 In asymptomatic children or adolescents with congenital complete AV block who have concerning objective findings (e.g. mean daytime heart rate persistently low for age, significant pauses, complex ventricular ectopy, or impaired exercise tolerance), permanent pacing is reasonable. (Level of evidence: B-NR)

2 For children and adolescents with repaired CHD who require permanent pacing for bradycardia, a device that supports atrial antitachycardia pacing (if atrial tachyarrhythmia is a clinical problem) is reasonable when lead placement and anatomy permit. (Level of evidence: B-NR)

3 In children with preexisting sinus-node or AV conduction disease undergoing cardiac surgery, intraoperative placement of epicardial leads is reasonable when future transvenous access is likely to be problematic. (Level of evidence: C-EO)

Class IIb indications

1 Atrial-based permanent pacing for the sole purpose of preventing atrial arrhythmias may be considered in selected pediatric/ACHD patients with symptomatic tachy-brady syndrome or documented atrial tachyarrhythmias that are refractory to catheter therapy. (Level of evidence: B-NR)

Class III (not indicated or potentially harmful)

1 In patients with systemic venous-to-systemic arterial intracardiac shunts (right-to-left or bidirectional shunts), routine placement of transvenous endocardial leads is potentially harmful because of paradoxical embolism risk; alternative strategies (epicardial leads, surgical closure of the shunt where indicated, or individualized risk mitigation) are preferred. (Level of evidence: B-NR)

2 Permanent pacing is not indicated for transient, reversible causes of bradycardia (e.g. drug toxicity and reversible metabolic derangements) once the reversible cause has been corrected. (Level of evidence: C)

Permanent pacing after the acute phase of myocardial infarction

Bradyarrhythmias and conduction disturbances remain common in the setting of acute myocardial infarction (MI), although their incidence and prognostic implications have evolved with contemporary reperfusion strategies. Transient bradyarrhythmias frequently reflect enhanced vagal tone, ischemia of the sinus node or AV node, or reversible metabolic and autonomic disturbances. More persistent high-grade conduction disease generally reflects ischemic or necrotic injury to the His-Purkinje system and therefore carries a distinctly worse prognosis. With current primary PCI practices, the overall incidence of clinically meaningful AV block has declined substantially from historical thrombolytic-era rates. Inferior MI continues to account for the majority of transient, nodal-level AV block, whereas persistent, infranodal conduction disease remains most strongly associated with anterior MI.

The anatomic substrate of infarction determines the pattern of conduction disturbance. In inferior MI, AV block is typically supra-His or AV nodal, often accompanied by narrow-complex junctional escape rhythms and exaggerated vagal tone. These forms of AV block are usually transient, respond to reperfusion, and resolve within hours to a day, although persistent block may be present for several days. Permanent pacing is rarely required unless advanced block persists after recovery from the acute ischemic insult or is accompanied by features suggesting infranodal involvement (wide escape rhythm, alternating bundle branch block, or persistent high-grade block beyond the typical recovery window).

In anterior MI, conduction disturbances are usually infranodal, involving the His bundle or bundle branches as part of extensive antero-septal necrosis. These escape rhythms are typically wide-complex, unstable, and associated with a high in-hospital mortality. Even with early revascularization, persistent complete AV block after anterior MI strongly

Table 1.8 Pacing during acute inferior wall MI versus acute anterior wall MI

<i>Feature</i>	<i>Inferior MI</i>	<i>Anterior MI</i>
Primary blood supply to conduction system involved	AV node via RCA (or dominant LCx)	His–Purkinje system and proximal bundle branches via septal perforators of the LAD
Mechanism	Enhanced vagal tone and ischemia of the AV node; usually transient	Extensive septal necrosis involving the His bundle, bundle branches, and distal conduction system; generally irreversible
Typical AV block type	AV nodal block (Mobitz I or complete AV block with narrow QRS escape)	Infranodal block (Mobitz II or complete AV block with wide QRS escape)
Escape rhythm characteristics	Junctional, narrow QRS, stable	Ventricular or fascicular, wide QRS, often unstable and slow
Prognosis of AV block	Generally good; block usually resolves within 24–72 h	Poor prognosis; indicates large infarct size and high mortality
Need for temporary pacing	Sometimes required for bradycardia or hypotension, but less frequent	Often required due to unstable escape rhythms and hemodynamic compromise
Need for permanent pacing	Rare after resolution of ischemia	Common if block persists after recovery period due to structural conduction system destruction
Associated surface ECG findings	Prolonged PR interval, Wenckebach patterns, junctional escape beats	New RBBB, LBBB, bifascicular block, or alternating bundle branch block
Response to reperfusion	High likelihood of recovery with reperfusion or supportive therapy	Lower likelihood of recovery; persistent block reflects irreversible injury
Guideline approach	Observation is appropriate if block resolves and patient is asymptomatic	Persistent second-degree Mobitz II, high-grade block, or complete AV block → Class I indication for permanent pacing after waiting period

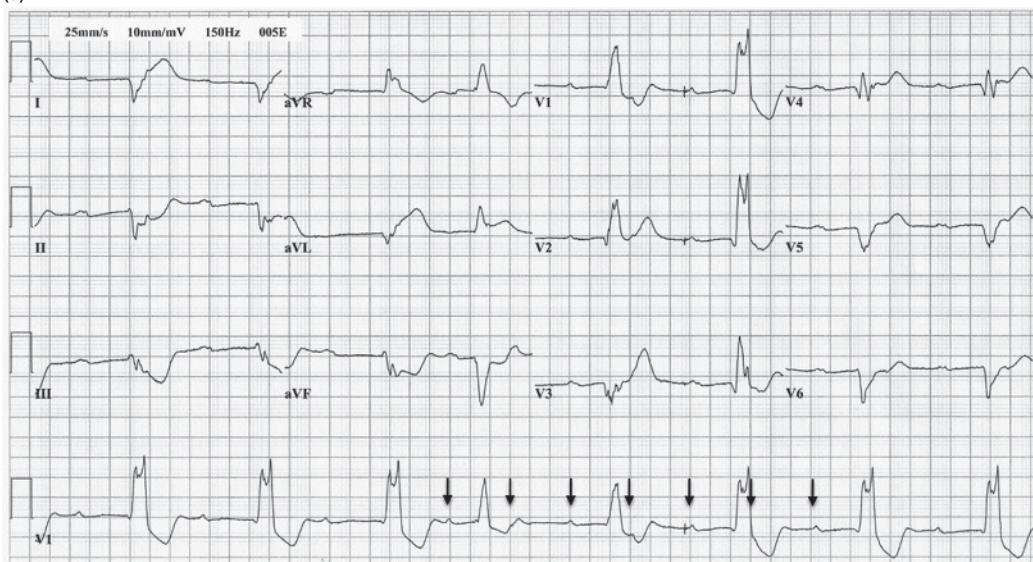
suggests irreversible injury to the conduction system. Thus, the requirement for permanent pacing is more frequent, and the prognosis is more strongly determined by the overall extent of myocardial damage and accompanying LV dysfunction. See Table 1.8 comparing conduction disturbances in anterior versus inferior wall MIs.

Intraventricular conduction disturbances (IVCDs), including new bundle branch block and bifascicular block, occur transiently in a significant proportion of patients during acute infarction and may persist in a minority. Persistent IVCDs, particularly bifascicular block or alternating bundle branch blocks, after MI are associated with an increased risk of progression to high-grade AV block, especially when preceded by transient AV block or when infarction involves the proximal septal conduction tissue. However, isolated LAFB

does not confer additional pacing risk in the post-MI setting.

Temporary pacing is often required in the acute phase of MI to stabilize hemodynamics or bridge patients until reperfusion reverses ischemia-related conduction block. However, the need for temporary pacing during the acute phase does not itself constitute an indication for permanent pacing. Decisions regarding permanent pacing should be based on the persistence and level of the conduction disturbance after the acute phase, site of block, and the patient’s recovery trajectory, rather than acute-phase instability (Figure 1.17–1.18). In patients with indications for permanent pacing after ST-elevation MI and persistent LV dysfunction, careful reassessment for primary-prevention ICD candidacy is essential once ventricular recovery has been fully evaluated.

(a)



(b)

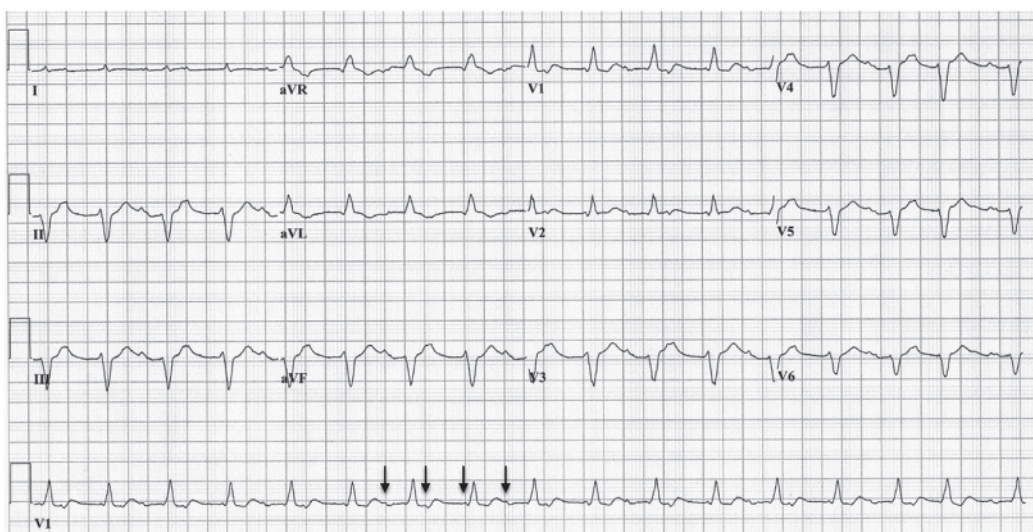


Figure 1.17 *Acute anterior myocardial infarction complicated by complete AV block.* This 82-year-old male presented with acute left main coronary occlusion and cardiogenic shock. (a) The initial ECG demonstrates complete AV block with a wide-complex escape rhythm and ST elevation. The fourth and likely the fifth QRS complexes are conducted beats. P waves are marked by arrows. He underwent temporary pacing, emergent revascularization, and hemodynamic support with a

percutaneous LV assist device. (b) The ECG the following day shows persistent complete AV block with an accelerated junctional rhythm and right bundle branch block with left anterior fascicular block, consistent with extensive conduction system injury. Although the conduction abnormalities meet criteria for permanent pacing, the prognosis was dominated by the severity of myocardial injury; the patient ultimately died from progressive multiorgan failure.

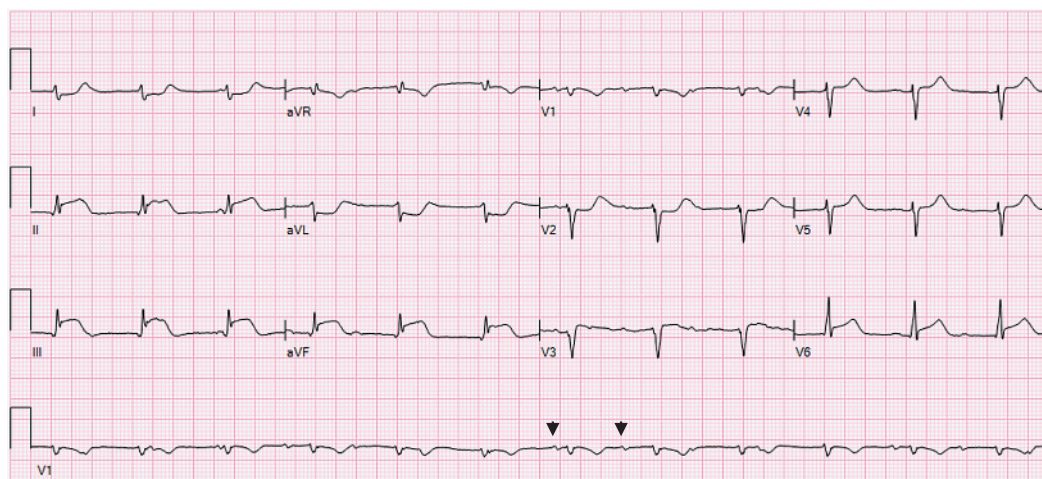


Figure 1.18 ECG showing complete heart block in the setting of the acute phase of an inferior wall myocardial infarction. The sinus rate is 90 bpm (black arrows) with

complete heart block and an accelerated junctional rhythm at 70 bpm.

Key indications for permanent pacing following acute myocardial infarction

Class I indications

1 A structured observation period is required before implanting a permanent pacemaker in patients who develop SND or AV block in the setting of acute MI, to allow determination of reversibility following reperfusion and stabilization. (Level of evidence: B-NR)

2 Permanent pacing is indicated in patients with acute MI who, after an appropriate waiting period, demonstrate:

- persistent Mobitz II second-degree AV block,
- persistent high-grade AV block,
- alternating bundle branch block, or
- persistent complete AV block, particularly when the block is infranodal or associated with unstable escape rhythms. (Level of evidence: B-NR)

Class III (not indicated or harm)

1 Permanent pacing should not be performed in patients with acute MI and transient AV block that fully resolves during the post-infarction recovery period. (Level of evidence: B-NR)

2 Permanent pacing is not indicated for patients with acute MI and isolated new bundle branch block or isolated fascicular block without associated second- or third-degree AV block. (Level of evidence: B-NR)

Pacing after cardiac surgery and transcatheter aortic valve implantation

Persistent bradyarrhythmias remain an important postoperative problem after cardiac surgery, although the epidemiology and management strategies have evolved with improvements in perioperative care and electrophysiology practice. The reported incidence of clinically important, persistent postoperative bradyarrhythmias requiring consideration of permanent pacing after open heart surgery ranges roughly from ~3–8% overall, with higher rates after multivalve procedures and repeat operations. SND after cardiopulmonary bypass often results from atrial cannulation, ischemia, or surgical trauma to the right atrium and is usually transient, with recovery occurring within days in the majority; however, SND that is prolonged, symptomatic, or limits rehabilitation or discharge may justify permanent pacing after an appropriate observation period. Perioperative atrial tachyarrhythmias frequently coexist and may complicate management; when sinus node function recovers, antiarrhythmic agents may be used more safely to suppress recurrent atrial arrhythmias.

Among postoperative conduction disturbances, persistent AV block is most commonly encountered after valvular surgery, particularly procedures involving the tricuspid or aortic valve or multivalve

operations: tricuspid valve replacement and complex multivalve surgery carry a higher incidence of persistent high-grade AV block (historical series report rates up to double-digit percentages in selected operations). Predictors of persistent postoperative AV block include preexisting RBBB, preoperative PR prolongation, advanced patient age, repeat sternotomy, and procedures involving the septal conduction tissue. Aortic valve interventions have particular proximity to the His bundle and proximal conduction system and therefore confer a higher risk for new AV conduction disturbances; mitral surgery may more often affect the AV nodal region through injury to the AV nodal artery and adjacent tissue. A 5–7-day observation period remains a practical strategy before committing to permanent device implantation when recovery is being observed and the patient is hemodynamically stable. If there is ongoing clinical evidence of improvement, extended observation is reasonable in select patients. An earlier implantation is appropriate when prolonged temporary pacing is required, recovery is unlikely, or persistent high-grade block produces hemodynamic compromise. Patients who ultimately undergo permanent pacing after surgery generally have favorable long-term outcomes, and many (up to 40%) are not permanently pacing-dependent upon long-term follow-up.

Procedures for septal reduction in obstructive HCM carry a recognized risk of AV conduction injury. Contemporary series report AV block requiring permanent pacing in ~10–15% after alcohol septal ablation and in a comparable or slightly lower proportion after surgical myectomy depending on operator experience and selection. The baseline annual risk of SCD after septal therapies is low and does not warrant routine ICD implantation. However, coexistence of other high-risk features for SCD (massive LV hypertrophy, family history of SCD, unexplained syncope, pathogenic sarcomere variants, or extensive LGE) necessitates individualized evaluation for ICD therapy rather than routine pacemaker alone. Current HCM and procedural guidance emphasize shared decision-making within dedicated HCM teams regarding septal reduction choice and the cardiac device strategy [29].

Transcatheter aortic valve replacement (TAVR) has introduced a distinct and common substrate for

new conduction disease. Unlike surgical aortic valve replacement, TAVR leaves the calcified native valve in place and applies inward radial force and potential trauma to the membranous septum and adjacent His–Purkinje tissue. Reported rates of new PPI after TAVR vary across valve type and generation, procedural technique, and patient selection. Pooled series and device-specific registries generally place the 30-day PPI rate in the range of ~5–15% for newer-generation devices, with higher rates historically for some self-expanding valves and lower rates for balloon-expandable valves and optimized implantation techniques. New LBBB occurs in a substantial minority of patients (historically 20–50%), and high-grade AV block evolves in ~5–15% acutely, though many conduction disturbances resolve before discharge. Important predictors of post-TAVR PPI include preexisting RBBB, greater implantation depth, shorter membranous septum, valve oversizing, and valve type/generation. The evolving literature shows reduced PPI rates with modern valve iterations and refined implantation strategies [29].

In patients with new LBBB after TAVR, EPS can risk-stratify for infra-His disease. Several observational studies have shown that an HV interval >65 ms (or identification of infra-His block) measured after TAVR is associated with a high likelihood of subsequent high-grade AV block and has been used to guide PPI decisions. Conversely, an HV ≤65 ms identifies a lower-risk group in whom conservative management with monitoring may be reasonable. While EPS is not mandated in all centers, it may be a valuable tool when new conduction abnormalities create equipoise about timing of PPI.

Patients discharged with new LBBB or intermittent conduction disturbances after TAVR remain at risk for late high-grade AV block. A structured outpatient monitoring (extended telemetry, event monitoring, or loop recorder) is recommended in patients managed conservatively after discharge. The timing of late events supports a strategy of vigilance in the first 30–90 days post-TAVR.

Where permanent pacing is indicated after cardiac surgery or TAVR, contemporary practice increasingly considers physiologic ventricular activation strategies when long-term ventricular pacing is anticipated. CSP (HBP or left-bundle branch area pacing) and cardiac resynchronization

approaches (when LV dysfunction coexists) are emerging options to reduce pacing-induced dys-synchrony; early series report feasibility and promising hemodynamic results after TAVR, but long-term comparative data in large cohorts of post-TAVR patients are still maturing. Leadless pacing may be attractive in select patients to avoid transvenous leads, especially when transvenous access is limited or infectious risk is high. Anatomical constraints and lack of AV synchronous solutions in some leadless systems limit universal applicability. Device choice should be individualized by the heart team, accounting for anticipated pacing burden, ventricular function, venous anatomy, and long-term lead management.

Drug-induced bradycardia

A broad range of cardiovascular and non-cardiovascular medications can precipitate clinically important bradyarrhythmias through effects on sinus node automaticity, AV nodal conduction, or the His–Purkinje system. These effects frequently occur in the setting of underlying conduction system vulnerability. Combinations of AV nodal-blocking agents substantially increase risk of bradarrhythmias. Agents most commonly implicated include beta-adrenergic blockers, nondihydropyridine calcium-channel blockers, digoxin, certain antiarrhythmic drugs (particularly class I and class III agents), and select psychotropic and neurologic medications with autonomic or sodium-channel blocking properties. Toxicity or supratherapeutic levels enhance these risks, but even therapeutic dosing can unmask previously silent disease.

Drug-induced bradycardia is typically transient, and cessation of the offending agent, supportive care, and sometimes, temporary pacing usually restore adequate conduction. However, accumulating evidence indicates that a meaningful subset of patients develops persistent or recurrent bradyarrhythmia after drug withdrawal. Recent observational studies continue to show that 40–60% of patients presenting with high-grade AV block while on AV nodal-blocking therapy ultimately require permanent pacing, reflecting intrinsic conduction system pathology rather than isolated pharmacologic suppression. Recovery of AV conduction is most reliably observed after

discontinuation of digoxin, whereas beta-blockers, nondihydropyridine calcium-channel blockers, and antiarrhythmic agents more commonly unmask irreversible conduction disease.

Decisions regarding permanent pacing should integrate the necessity of ongoing therapy with the implicated drug, the availability of therapeutic alternatives, the nature of the underlying conduction disorder, and the clinical consequences of bradyarrhythmia. When long-term continuation of essential AV nodal-blocking therapy is unavoidable or when conduction fails to recover after drug withdrawal and metabolic normalization, PPI is indicated.

Sleep-disordered breathing and bradycardia

Nocturnal bradyarrhythmias occur across a broad clinical spectrum and must be interpreted in relation to sleep physiology. In young, well-conditioned athletes and in healthy subjects during sleep, pronounced sinus bradycardia, brief sinus pauses, and transient, vagally mediated first-degree or Mobitz I AV block are common and sometimes transient complete heart block. These findings in asymptomatic individuals during sleep do not require intervention. The prevalence of physiologic nocturnal bradycardia declines with age, and the clinical significance of nocturnal pauses increases when they are prolonged, symptomatic, or occur outside sleep.

Obstructive sleep apnea (OSA) and other forms of sleep-disordered breathing substantially increase the frequency and severity of nocturnal bradyarrhythmias. Repetitive apneic events produce abrupt swings in blood gases, intrathoracic pressure, and autonomic tone that together provoke complex cardio-respiratory reflexes: hypoxemia and hypercapnia stimulate chemoreflexes and sympathetic surges, whereas arousal and the termination of apnea often invoke pronounced transient vagal activation. Large negative intrathoracic pressures during obstructed inspiration augment vagal afferent activity and can precipitate marked sinus slowing, sinus pauses, or high-grade AV block in susceptible patients. These pathophysiologic mechanisms are central to the arrhythmic manifestations of OSA.

Meta-analytic and observational data indicate that nocturnal bradycardia is common in patients

with OSA, with pooled estimates for nocturnal bradycardia often well above rates seen in unselected populations. Reported pooled prevalence of nocturnal bradyarrhythmia in OSA cohorts approaches 60–70% in some series, with sinus node abnormalities (sinus bradycardia and sinus arrest) as the most frequent findings and higher-grade AV block reported less commonly but not rarely. Prevalence correlates with OSA severity (apnea-hypopnea index) and with the degree of nocturnal hypoxemia. Importantly, many patients with OSA demonstrate normal rhythm during wakefulness, with the bradyarrhythmia confined to sleep [30].

Impact of OSA treatment on bradyarrhythmias. Effective treatment of OSA substantially reduces the frequency and magnitude of sleep-related bradyarrhythmias. Multiple observational studies and clinical series have demonstrated marked reductions in nocturnal sinus pauses and AV conduction disturbances after initiation of continuous positive airway pressure (CPAP), and in many cases, CPAP obviates the need for permanent pacing. Reductions in bradyarrhythmic episodes after adequate CPAP therapy are large (often cited as reductions of 60–80% in earlier series), and even complete resolution of previously observed high-grade block can be observed.

Nocturnal bradycardia or pauses are detected on monitoring or polysomnography; clinicians should actively evaluate for sleep-disordered breathing as a potentially reversible cause. History taking should target nocturnal symptoms (snoring, witnessed apneas, gasping, and daytime somnolence), and formal sleep testing (polysomnography or home sleep apnea testing, as appropriate) is indicated when suspicion is elevated. In the absence of daytime symptomatic bradycardia, immediate permanent pacing is generally deferred until reversible contributors, including OSA, drug effects, electrolyte abnormalities, and acute ischemia or inflammation, have been addressed. If moderate-to-severe OSA is confirmed, a trial of effective OSA therapy (with emphasis on CPAP adherence and objective improvement in nocturnal oxygenation and event indices) is the preferred initial strategy. Pacemaker implantation is reserved for patients with persistent, clinically consequential bradyarrhythmia despite optimal treatment of sleep apnea or for those who have daytime symptomatic bradycardia

or syncope attributable to pauses independent of sleep. Pacing guidelines and contemporary consensus statements therefore recommend screening for and treating OSA as part of the evaluation for nocturnal bradyarrhythmia [7].

Polysomnography remains the reference standard to characterize sleep-related arrhythmias and their temporal relation to respiratory events. When prolonged nocturnal pauses are identified, documentation of their sleep-state timing is essential (to distinguish physiologic sleep-related pauses from pathologic pauses occurring during wakefulness). Collaboration with sleep medicine improves diagnostic accuracy and treatment adherence. Where CPAP is poorly tolerated, alternative therapies for OSA (oral appliances, positional therapy, weight loss, upper airway surgery, or hypoglossal nerve stimulation in selected patients) should be considered and may also reduce arrhythmic burden. Finally, because the presence of concomitant structural heart disease or intrinsic conduction disease increases the likelihood that bradyarrhythmia will persist, individualized risk assessment and shared decision-making remain necessary when weighing pacemaker implantation after treatment of reversible causes

Summary

In patients with symptomatic and potentially life-threatening bradyarrhythmias, cardiac pacing is a cost-effective intervention to relieve symptoms and prevent death. However, the possible complications and the potentially complex longer-term management of permanent pacemaker systems require that careful consideration be given to the indications before implantation.

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