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REVIEW

Evaluation and management of bradycardia in neonates and children

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Abstract Heart rate is commonly used in pediatric early warning scores. Age-related changes in the anatomy and physiology of infants and children produce normal ranges for electrocardiogram features that differ from adults and vary with age. Bradycardia is defined as a heart rate below the lowest normal value for age. Pediatric bradycardia most commonly manifests as sinus bradycardia, junctional bradycardia, or atrioventricular block. As a result of several different etiologies, it may occur in an entirely structurally normal heart or in association with concomitant congenital heart disease. Genetic variants in multiple genes have been described to date in the pathogenesis of inherited sinus node dysfunction or progressive cardiac conduction disorders. Management and eventual prognosis of bradycardia in the young are entirely dependent upon the underlying cause. Reasons to intervene for bradycardia are the association of related symptoms and/or the downstream risk of heart failure or pause-dependent tachyarrhythmia. The simplest aspect of severe bradycardia management is reflected in the Pediatric and Advanced Life Support (PALS) guidelines.

Conclusion: Early diagnosis and appropriate management are critical in many cases in order to prevent sudden death, and

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this review critically assesses our current practice for evaluation and management of bradycardia in neonates and children.

What is Known:

- *Bradycardia is defined as a heart rate below the lowest normal value for age. Age related changes in the anatomy and physiology of infants and children produce normal ranges for electrocardiogram features that differ from adults and vary with age.*
- *Pediatric bradycardia most commonly manifests as sinus bradycardia, junctional bradycardia, or atrioventricular block.*

What is New:

- *Management and eventual prognosis of bradycardia in the young are entirely dependent upon the underlying cause. Bradycardia may occur in a structurally normal heart or in association with congenital heart disease. Genetic variants in multiple genes have been described.*
- *Reasons to intervene for bradycardia are the association of related symptoms and/or the downstream risk of heart failure or pause-dependent tachyarrhythmia. Early diagnosis and appropriate management are critical in order to prevent sudden death.*

Keywords Bradycardia · Atrioventricular block · Sinus node dysfunction · Sudden death · Pacemaker

Abbreviations

AV	atrioventricular
CHD	congenital heart disease
ECG	electrocardiogram
LQTS	long QT syndrome
PAC	premature atrial complex
PALS	Pediatric and Advanced Life Support
SACT	sinoatrial conduction time
SND	sinus node dysfunction
SNRT	sinus node recovery time

Introduction

Heart rate is an integral part of the clinical assessment of the child with acute illness and is commonly used in pediatric early warning scores [3, 22, 56, 61]. Age-related changes in the anatomy and physiology of infants and children produce normal ranges for electrocardiogram (ECG) features that differ from adults and vary with age [29]. Bradycardia is defined as a heart rate below the lowest normal value for age. But what is considered normal in a 15-year-old adolescent may be markedly abnormal in the neonate [25, 65]. Thus, it is critical when defining bradycardia in the pediatric population, to refer to normal values for age (Table 1). Bradycardia may be a sign of a healthy athletic heart and increased vagal tone, but can also be a sign of conductive tissue disease and lead to sudden death [53]. Thus both proper identification of rhythm and etiology and appropriate immediate therapeutic measures are necessary when assessing the child with a low heart rate. This review article aims to provide a comprehensive up-to-date approach for evaluation and management of bradycardia in neonates and children.

Table 1 Normal heart rate according to age

Age	Heart rate in beats per minute median (1–99th percentile)
Newborn (term)	127 (90–164)
0–3 months	143 (107–181)
3–6 months	140 (104–175)
6–9 months	134 (98–168)
9–12 months	128 (93–161)
12–18 months	123 (88–156)
18–24 months	116 (82–149)
2–3 years	110 (76–142)
3–4 years	104 (70–136)
4–6 years	98 (65–131)
6–8 years	91 (59–123)
8–12 years	84 (52–115)
12–15 years	78 (47–108)
15–18 years	73 (43–104)

Adapted from Fleming et al. [25]

Etiologies of pediatric bradycardia

Bradycardia most commonly manifests as sinus bradycardia, junctional bradycardia, or atrioventricular (AV) block in the pediatric population. These rhythms have several possible etiologies, which can be further divided into system-based groups (Table 2).

One of the main causes of bradycardia in the pediatric population is hypervagatonia, either secondary to athletic conditioning, or other factors including breath holding, increased intracranial pressure, or abdominal processes [2, 41, 72, 73]. Cardiac vagal hyperactivity significantly contributes to the sinus bradycardia observed in most malnourished adolescents with anorexia nervosa [20, 43] Electrolyte disturbances may also contribute to bradycardia in these patients, and heart rate is a predictor of spinal bone mineral density in adolescents hospitalized for anorexia nervosa [20]. Apnea and bradycardia of the premature newborn is another common cause of bradycardia in the infant [32, 51]. (Table 3)

Surgical procedures in patients with congenital heart disease can also result in sinus node dysfunction or AV block. Congenital heart surgery commonly associated with postoperative sinus node dysfunction is mainly represented by transposition of great arteries s/p atrial switch procedure [77, 83], whereas postoperative complete atrioventricular block is mainly associated with mitral valve repair/replacement, aortic

Table 2 Etiologies of Bradycardia

Type of bradycardia	Diagnosis setting	Causes
Sinus /junctional bradycardia	Respiratory	Hypoxia, apnea-bradycardia of prematurity
	Cardiac	Inherited sinus node dysfunction
		CHD, atrial septal defect
		Congenital heart surgery
	Neurocardiogenic	Increased vagal tone
		Bezold-Jarisch reflex
		Situational (eg. coughing, breath holding spells, sleep)
		Esophageal or nasopharyngeal stimulation
		Peritoneal and rectal stimulation
	Neurologic	Increased intracranial pressure
		Chiari malformation
	Psychiatric	Anorexia nervosa
	Endocrine	Hypothyroidism
	Toxicologic	Fentanyl, beta-blockers, alpha-2-agonists, phenylephrine, edophonium, physostigmine, neostigmine, methoxamine
	Miscellaneous	Hypothermia
		Electrolyte abnormalities
		hypo/hyper kalemia
		hypo/hyper calcemia
		hypomagnesemia
		hypoglycemia
Complete AV block	Cardiac	Inherited AV block
		Long QT syndrome
		CHD, L-transposition of great arteries
		Congenital heart surgery
		Coronary artery disease
	Immunologic	Maternal connective tissue disease
		Lupus erythematosus
		Sjögren syndrome
	Infectious	Acute or chronic infection
		Myocarditis
		Endocarditis
		Lyme disease, Chagas disease
		Diphtheria, rubella, mumps, trichinosis
		Rocky Mountain spotted fever
		Human immunodeficiency virus
		Acute rheumatic disease
	Metabolic	Kearns-Sayre syndrome
		Carnitine deficiency
		Glycogen storage disease
	Miscellaneous	Muscular dystrophy
		Eosinophilic cardiomyopathy
		Idiopathic

CHD congenital heart disease

valve repair/replacement, atrioventricular canal surgery, and ventricular septal defect surgery [47].

Congenital complete heart block, identified in utero or at birth in normal hearts, is found in 1 per 15,000 –20,000 live born infants [15, 53]. Maternal autoantibodies can be detected in over 95 % of fetuses or newborns presenting with atrioventricular block [18]. The pathophysiological process is believed to be due to immune-mediated injury of the developing conduction system, which occurs as a result of transplacental passage of maternal anti-SSA/Ro-SSB/La antibodies inducing a mechanistic sequence that inhibits or internalizes L-type calcium channels [5, 82]. Autoimmune congenital heart block is associated with an 8–16 % neonatal mortality rate and an approximately 10 % risk of dilated cardiomyopathy development in survivors [37, 55].

Non-immune heart block may be either inherited or acquired—due to acute or chronic infectious processes (Lyme disease, Chagas disease, infectious endocarditis), myocarditis, surgical- or catheterization-induced trauma, drug-induced, coronary artery disease, hypersensitivity cardiomyopathy, metabolic abnormalities, hypothyroidism, or infiltrative processes. The most common class of medications causing bradycardia are the beta-blockers [19, 50]. However, most antiarrhythmic medications can cause some sinus node slowing or, rarely, AV block [67]. Bradycardia is frequently observed after potentially cardiotoxic chemotherapeutic agents are administered [4].

Sinus node dysfunction or progressive cardiac conduction disease in structurally normal hearts may also be inherited, presenting as primary electrical diseases [8]. A recent rapid advance in molecular genetics enabled us to reveal a variety of genetic backgrounds underlying the pediatric bradycardia, especially of familial type, mainly using the candidate gene approach method.

The development of the conduction system is a complex process. Several transcription factors, including homeodomain proteins and T-box proteins, are essential for the morphogenesis of the cardiac conduction system and the activation or repression of key regulatory genes: *GATA4*, *NKX2-5*, *TBX3*, and *TBX5* [31, 33]. Mutations in the *TBX5* gene result in Holt-Oram syndrome [9, 35], consisting of upper limb abnormalities, atrial septal defect, or ventricular septal defect and first-degree heart block or sinus bradycardia [59].

Mutations in *SCN5A*, which encodes for the alpha subunit of the voltage-gated sodium channel have also been associated with multiple conduction abnormalities, including long QT syndrome (LQTS) type 3 and Brugada syndrome [63]. Patients with *SCN5A* mutations often display mixed arrhythmic phenotypes of cardiac sodium channelopathies (overlap syndrome) [49]. Interestingly, age appears to influence type of conduction abnormality seen; children with Brugada syndrome are more likely to present with bradycardia when compared to their adult counterparts [1]. LQTS type 3 infants with

Table 3 History of "red flags" requiring urgent referral to pediatric cardiology

History of "red flags"
History of heart murmur or congenital heart disease
Syncope, especially if unusual triggers such as loud noises, exercise, fright or extreme emotional stress
Other associated symptoms such as chest pain, palpitations, or dyspnea
Family history of sudden cardiac death, long QT syndrome, sensorineural hearing loss, familial heart disease, pacemaker implantation
Medications that can result in bradycardia
Absence of usual premonitory symptoms or precipitating factors associated with neutrally mediated lipothymia or syncope

gain-of-function type *SCN5A* mutations may display functional 2:1 AV block as a result of marked QT prolongation in addition to torsade de pointes form of ventricular arrhythmias [40]. Therefore, both *SCN5A* mutations with loss- and gain-of-function can lead to bradycardia in children. Several other ion-channel coding genes have been associated with bradycardia including the *TRPM4* gene, which results in familial AV block and right bundle branch block [44, 48, 70]. Genes associated with intracellular calcium handling such as the *RyR2* and *CASQ2*, while more commonly associated with catecholaminergic polymorphic ventricular tachycardia, have also been reported to produce sinus bradycardia [62], though it is unclear why this occurs.

Approach to the patient with suspected bradycardia

History The history in approaching a patient with bradycardia focuses on two primary goals: the first is to determine the presence of symptoms and establish symptom-rhythm correlation; the second is to identify an etiology for the bradycardia [50]. Bradycardia is most commonly an incidental finding in the presence of enhanced vagal tone [50, 54]. ECGs, Holter and bedside monitors, and telemetry frequently capture this normal and benign physiologic phenomenon [50]. The bradycardia in these instances is typically transient and due to sinus node slowing. Sometimes this is accompanied by concurrent slowing of AV nodal conduction [50]. A brief review of the clinical setting will quickly shed light on this common observation and, in such cases, no further evaluation or intervention is required.

Bradycardia can be accompanied by symptoms of feeding difficulties in the infant and exercise intolerance in older children. Syncope and presyncope are the most significant manifestations of bradycardia. The presence of symptoms attributable to bradycardia is an indication for intervention.

Most sinus bradycardia is secondary to a non-cardiac process, such as those causing increased vagal tone [54]. There are many pathologic conditions in which this occurs, notably with illness in the gastrointestinal system and also in the nervous system [19]. A very strong vagal stimulus, such as that seen during vomiting, can transiently depress the automaticity of the sinus node or block transmission across the atrioventricular node, even in healthy persons [50]. The history will elucidate the cause of nausea or enhanced vagal tone in most cases. An increasingly recognized group of patients are those preteen and teenagers presenting with a dysautonomia of adolescence [2, 13]. While these patients more commonly present with inappropriate sinus tachycardia, presyncope and syncope occur in the context of bradycardia [13, 52]. Vasovagal syncope is characterized by sympathoexcitation, followed by vagal overcoming via the Bezold-Jarisch reflex. This reflex is generated by the cerebral hypoperfusion due to vagal-activation-mediated sympathosuppression for the protection of myocardium. Several factors are known to exacerbate and accelerate the vasovagal syncope including (a) fatigue, dehydration, hypovolemia, and reduced venous return; (b) blood shift and pooling in the lower body; (c) hypersensitivity of the stretch receptors in the left ventricular wall; and (d) fear, emotional stress, and reaction to pain [36]. A detailed history excluding other causes is crucial and usually identifies the key elements of recent rapid growth, pervasive non-specific complaints of palpitations or dizziness, a decrease in exercise tolerance, and occasionally an inciting illness or injury (eg., concussion). A tilt table is not usually required, but can be helpful in reproducing elements of the symptom complex [2, 13, 52].

Medications are frequently the cause of bradycardia and have to be investigated.

Determining whether symptoms are secondary to bradycardia can be challenging. A chronically low heart rate should theoretically not contribute to a new onset of symptoms, but certainly during rapid growth phases, this appears to be the case. Additionally, meticulous documentation of the heart rate during symptoms should be attempted before committing the child to an intervention such as a pacemaker [50]. Smartphone technology can be helpful in this regard, with many children possessing this technology and a number of apps allowing recording and tracking of heart rates.

Family history A family history of individuals with early requirements for pacemaker insertion or septal defects may point to a familial inherited heart rhythm disorder. Several genes have been implicated in bradycardic rhythms [80]. A family history of sudden death in young, apparently healthy individuals may indicate LQTS [81]. In case of apparently idiopathic AV block, familial screening should be considered and may provide strong arguments for heritability [7]. Autoimmune disorders are often familial as well [68]. A history of maternal lupus or Sjogrens must be sought in any young individual presenting with complete AV block [54]. Trisomy 21 is associated with hypothyroidism [17].

Physical exam The physical exam does not usually contribute to determining the etiology of bradycardia. In the newborn with complete congenital AV block secondary to maternal antibodies, a neonatal lupus can exist, with a rash [14, 16, 54]. In the older patient, particularly young females, a low body mass index or significant weight loss in the absence of a physical cause, is consistent with an eating disorder. The gradual reduction in metabolic rate is accompanied by a lower body temperature and slow heart rate [20]. Physical manifestations of hypothyroidism include a goiter in long-standing cases. Thyroid receptor $\alpha 1$ activation is markedly reduced by thyroid hormone insufficiency, leading to a notable decline in expression of proteins such as enzymes that regulate Ca^{2+} uptake and other proteins involved in cardiac contractility. This impairment of myocardial contraction and relaxation leads to a reduction in heart rate [66, 74, 78].

Electrocardiogram and Holter The ECG is of paramount importance in documenting and understanding bradycardia. A slow sinus rate with a normal PR interval and QRS configuration indicates the sinus node as the cause, either as exit block or sinus node dysfunction [50, 54]. A gradually prolonging PR interval with non-conducted P waves is seen in Wenckebach AV block. Complete dissociation of the P waves from the QRS complexes is present in complete AV block. Care must be taken not to assume conduction is occurring if a P wave appears to precede the occasional QRS. A very regular ventricular rhythm not influenced by P waves is most consistent with absent AV conduction. Variability in the QRS rate suggests some degree of AV conduction [50, 54].

When cardiac repolarization is very long, the ensuing sinus beat may occur before the ventricle has repolarized. This occurs in LQTS with a markedly increased QT interval. This is usually a transient phenomenon in infants, but requires treatment directed at the underlying syndrome [11]. Another common cause of bradycardia presenting in fetal life, and often persisting in the first month of life, is atrial ectopy [6]. Non-conducted premature atrial complexes (PACs) occur during refractoriness of the conducting tissue and are not followed by a ventricular depolarization. PACs can also reset the sinus node, resulting in a pause in the atrium. In atrial bigeminy, one may observe a ventricular rate that is half the atrial rate. In the fetus, this may appear as a bradycardic rhythm, which is abruptly normalized by doubling as the atrial bigeminy ceases, or as the PACs are able to conduct [6].

An ambulatory ECG or Holter monitor is important in the work-up of bradycardia. Indications for pacemaker insertion in AV block are based on average heart rates, determined by a 24-h monitor. The Holter monitor also provides important information on the range of ventricular rates attained by the junctional escape rhythm in complete AV block [50]. The greater this range, the more favorable the prognosis in an early study in congenital complete AV block. The Holter is also useful in assessing chronotropic responses in children in whom a graded exercise test is not feasible, usually due to age or ability to perform a treadmill test [50]. The Holter monitor can be helpful in establishing rhythm-symptom correlation in patients with frequent complaints.

Echocardiography An echocardiogram is required to rule out complex forms of heart disease, which can be associated with bradycardia [54, 80]. While sinus bradycardia is a relatively common long-term complication of postoperative heart disease, particularly that involving the atria or systemic veins, these conditions will have been recognized and followed clinically [50]. Other conditions, which may have gone unrecognized, include atrial defects, isomerism, and AV-ventriculoatrial discordance [54, 80]. All of these conditions may exist without marked clinical findings and may present with bradycardia. In the current era of relatively widespread use of echocardiography, however, this is less common. The echocardiogram has an important role in documenting ventricular function and dimensions in the presence of known AV block. Ventricular dysfunction is an indication for intervention in the AV block.

Stress test A graded stress test can be performed using different methods. As alluded to above, a Holter monitor with a young patient given instructions to be very active and to annotate the activities well will give important information on the ability of the sinus and AV nodes to respond to enhanced adrenergic states. In older children, running on a treadmill is a preferred option to assessing the response to exercise. There are heart rate-determined definitions for chronotropic incompetence and the diagnosis depends on not attaining a linear heart rate increase, from baseline to peak heart rate, proportional to the maximal oxygen uptake ($V0_2$) [64]. This increase can be estimated using the age-predicted chronotropic index [64]. In the clinic or hospital setting, a patient being evaluated for bradycardia can be asked to perform a few simple calisthenics, such as jumping jacks or ascending stairs to crudely assess the heart rate response.

Invasive testing Sinus node dysfunction (SND) can be diagnosed both invasively and non-invasively [45]. As sporadic SND is more common than familial one, non-invasive pharmacological stimulation testing using atropine, isoproterenol, or adenosine infusion, can uncover the dysfunction [26, 60, 75]. Transesophageal electrophysiology studies also prove useful in SND diagnosis [34]. Intracardiac electrophysiology studies reveal the sinus node recovery time (SNRT) and sinoatrial conduction time (SACT), the gold standard for SND diagnosis [30, 39, 45, 58, 71]. The SNRT and SACT can be determined using atrial pacing and PAC. SNRT is a measurement of the time between the last PAB and first spontaneous sinus beat, and is corrected by subtracting the sinus cycle

length from the SNRT (cSNRT). A prolonged cSNRT is indicative of SND (>550 ms). SACT is a measure of the time required for a sinus impulse to activate the atrium. Increased SACT yields a SND diagnosis [30, 39, 45, 58, 71].

Management of bradycardia in neonates and children

Early management algorithms Management and eventual prognosis of bradycardia in the young are entirely dependent upon the underlying cause. The primary reasons to intervene for bradycardia, however defined, is the association of related symptoms. A secondary consideration is the downstream risk of heart failure or pause-dependent tachyarrhythmia. It must be said then that the simplest aspect of severe bradycardia management is reflected in the Pediatric and Advanced Life Support (PALS) guidelines (Fig. 1) [42]. Under this scenario, the bradycardia most frequently treated is sinus bradycardia, and is addressed by means of insuring adequate ventilation first, obtaining cardiac rhythm monitoring, intravenous access, and potentially utilizing exogenous catecholamine and/or atropine.

Outside of basic PALS guidelines, each discrete cause of bradycardia will have its own series of management options to consider. The majority of these causes tend to occur in the face of chronic conditions and require consideration of rarely acute and more often subacute interventions.

In addition to the PALS Guidelines, a schema can be utilized to help determine intervention for bradycardia that occurs with acute hemodynamic consequences and bradycardia that presents more potential long-term concerns (Fig. 2).

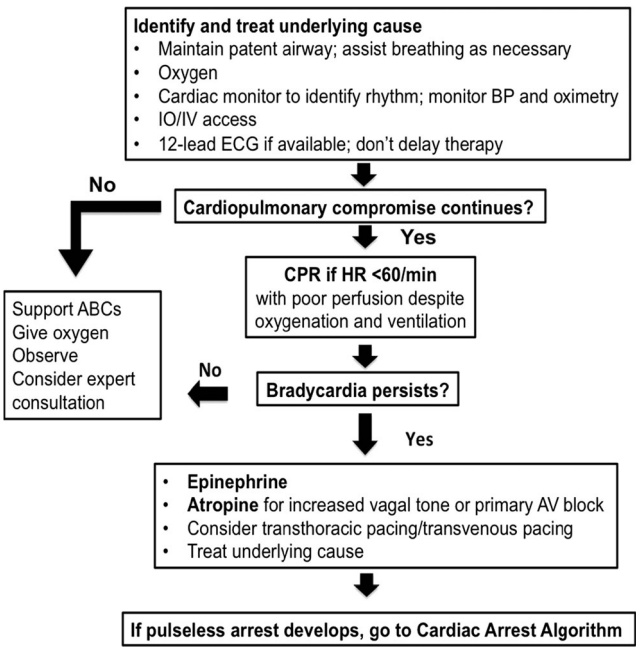

Fig. 1 Pediatric bradycardia with a pulse and poor perfusion algorithm (PALS). Cardiopulmonary compromise defined by hypotension and/or acutely altered mental status and/or signs of shock. *PALS* pediatric advanced life support. Adapted from Kleinman et al. Circulation 2010;122:S876-S908

Pacing guidelines The current AHA/HRS guidelines for pacing indications for children, adolescents, and patients with congenital heart disease (CHD) are shown and focus on patients with symptoms of slow rates, high-grade AV blocks, and slow rates for age or cardiac physiology [24]:

Class I

1. Permanent pacemaker implantation is indicated for advanced second- or third-degree AV block associated with symptomatic bradycardia, ventricular dysfunction, or low cardiac output. *(Level of Evidence: C)*
2. Permanent pacemaker implantation is indicated for SND with correlation of symptoms during age-inappropriate bradycardia. The definition of bradycardia varies with the patient's age and expected heart rate. *(Level of Evidence: B)*
3. Permanent pacemaker implantation is indicated for postoperative advanced second- or third-degree AV block that is not expected to resolve or that persists at least 7 days after cardiac surgery. *(Level of Evidence: B)*
4. Permanent pacemaker implantation is indicated for congenital third-degree AV block with a wide QRS escape rhythm, complex ventricular ectopy, or ventricular dysfunction. *(Level of Evidence: B)*
5. Permanent pacemaker implantation is indicated for congenital third-degree AV block in the infant with a ventricular rate less than 55 bpm or with congenital heart disease and a ventricular rate less than 70 bpm. *(Level of Evidence: C)*

Class IIa

1. Permanent pacemaker implantation is reasonable for patients with congenital heart disease and sinus bradycardia for the prevention of recurrent episodes of intra-atrial reentrant tachycardia; SND may be intrinsic or secondary to antiarrhythmic treatment. *(Level of Evidence: C)*
2. Permanent pacemaker implantation is reasonable for congenital third-degree AV block beyond the first year of life with an average heart rate less than 50 bpm, abrupt pauses in ventricular rate that are two or three times the basic cycle length, or associated with symptoms due to chronotropic incompetence. *(Level of Evidence: B)*

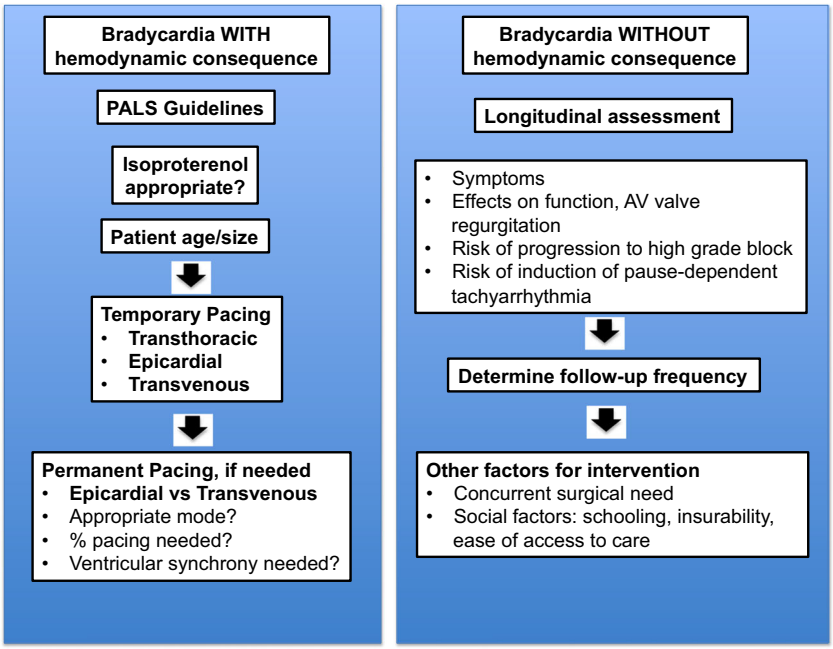

Fig. 2 Algorithm for management of bradycardia according to hemodynamic consequences

3. Permanent pacemaker implantation is reasonable for sinus bradycardia with complex congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 s. *(Level of Evidence: C)*
4. Permanent pacemaker implantation is reasonable for patients with congenital heart disease and impaired hemodynamics due to sinus bradycardia or loss of AV synchrony. *(Level of Evidence: C)*
5. Permanent pacemaker implantation is reasonable for unexplained syncope in the patient with prior congenital heart surgery complicated by transient complete heart block with residual fascicular block after a careful evaluation to exclude other causes of syncope. *(Level of Evidence: B)*

Class IIb

1. Permanent pacemaker implantation may be considered for transient postoperative third-degree AV block that reverts to sinus rhythm with residual bifascicular block. *(Level of Evidence: C)*
2. Permanent pacemaker implantation may be considered for congenital third-degree AV block in asymptomatic children or adolescents with an acceptable rate, a narrow QRS complex, and normal ventricular function. *(Level of Evidence: B)*
3. Permanent pacemaker implantation may be considered for asymptomatic sinus bradycardia after biventricular repair of congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 s. *(Level of Evidence: C)*

Class III

1. Permanent pacemaker implantation is not indicated for transient postoperative AV block with return of normal AV conduction in the otherwise asymptomatic patient. *(Level of Evidence: B)*
2. Permanent pacemaker implantation is not indicated for asymptomatic bifascicular block with or without first-degree AV block after surgery for congenital heart disease in the absence of prior transient complete AV block. *(Level of Evidence: C)*
3. Permanent pacemaker implantation is not indicated for asymptomatic type I second-degree AV block. *(Level of Evidence: C)*
4. Permanent pacemaker implantation is not indicated for asymptomatic sinus bradycardia with the longest relative risk interval less than 3 s and a minimum heart rate more than 40 bpm. *(Level of Evidence: C)*

Sinus bradycardia and/or sinus node dysfunction Sinus bradycardia and/or sinus node dysfunction occurs in a number of settings. Outside the spectrum of CHDs, sinus bradycardia is nearly always secondary to some other cause, such as increased intracranial pressure, seizures, certain drug overdoses, hypothyroidism, congenital central hypoventilation syndrome, athletic conditioning, LQTS, and eating disorders, which can manifest varying degrees of slow sinus rates. Managing the underlying cause is the primary approach. Temporary pacing is rarely needed, but when bradycardia is severe and treatment of the underlying cause not expected to resolve

it quickly enough, then a temporary transvenous pacing catheter can be placed, usually with balloon tipped or echo guidance, to the right ventricle. In very young infants, those with CHD, and those with myocarditis, a small surgical incision and epicardial temporary wire works quite well.

Sinus bradycardia in the newborn can be a sign of underlying LQTS and also be due to 2:1 conduction block due to very long QT intervals. Beta-blockade remains indicated for these patients and epicardial pacing, usually dual chamber, is needed long-term.

In congenital central hypoventilation syndrome (Ondine's curse), sinus arrest can be present and potentially contribute to morbidity and mortality. Epicardial VVI pacing systems are useful and, with bipolar leads, do not interfere with diaphragmatic pacemakers, if present.

High-grade AV block Perhaps the clearest indications for management of bradycardia are in the setting of high-grade atrioventricular blocks. Patients with congenital complete AV block who have rates that are too slow or manifest wide QRS escape rhythms require permanent pacing system implantation. In the newborn and very young patient, it is intuitively obvious that this requires an epicardial approach. There is remaining debate about the need for initial dual chamber over single chamber pacing for newborns, to optimize AV synchrony [28]. Those receiving single chamber (VVIR) devices are traditionally upgraded to dual chamber pacing when they are older/larger, often over ~40 kg. While transvenous pacing systems technically can be placed in younger, smaller children, the practice is fraught with consequences of repeated entry into those venous structures and risks of extraction of leads over many decades of life [79]. In recent years, it has been questioned whether all children with congenital complete AV block might undergo biventricular pacing implantation to avoid the risks of single site ventricular pacing on left ventricular function [31, 57]. Data exists, however, to support epicardial DDD systems with ventricular epicardial leads placed at the LV apex rather than the RV in most patients [38].

Myocarditis can include high grades of AV block and complete AV block requiring early pacing. As the disease is commonly encountered in younger patients, temporary epicardial pacing wires can bridge the gap to observe for recovery of conduction, by 1 week after presentation in 2/3, or until the patient is stable for a permanent pacing system, necessary in ~1/4 [10]. AV block may also be observed in Lyme carditis and Kawasaki disease. Management again depends on the patient's age and whether conduction returns, generally by 7–10 days, with a narrow QRS and return of ventricular function.

Management of progressive AV block in the patient with congenitally corrected transposition depends on the degree of block and patient age, as well as effect on underlying structural CHD. The patients warrant close ambulatory monitoring to assess for development of high grade AV block [69].

Two items likely to undergo scrutiny that remain widespread in the language of pediatric cardiology warrant comment regarding pacing guidelines: the "3-second rule" and the use of "critical" value lower heart rate cut-offs.

The first, the 3-second rule, was promulgated soon after the publication in 1982 [12] of a burst suppression pacing protocol performed in young patients with either surgical or congenital complete AV block in the early days following CHD operations, as a means to predict outcome and development of symptoms. Those with recovery times of 3.4 s or greater were more likely to be or to become symptomatic. This publication has served as the reference, perhaps erroneously, for pacing indications in children for many years, including patients without CHD and those well out of the early postoperative period. It has never been shown to be a risk factor for prolonged asystole or sudden cardiac death. Also often cited is a 1983 manuscript on ventricular pauses of 3 s or more [21]. This data refers to Holter findings in 53 individual adults over 19 years of age, 19 of whom had sinus arrest (none with normal heart), 29 with slow ventricular rates during atrial fibrillation and 5 with AV block. There are certainly no correlates from this report that should be drawn for young patients, with or without CHD.

The lower heart rate criteria advocated for pacing are also suspect. With the introduction of increasingly longer duration ambulatory cardiac rhythm monitoring systems, two weeks or more of heart rate data are now routinely obtainable. Therefore, the paradigms of what constitutes concerning or actionable bradycardia may be redefined in the coming years. It is unknown to what extent newly revealed frequencies of sinus pauses and slower heart rate averages and lowest rates may mean for management [27]. Important aspects concerning the long-term detrimental effects of bradycardia, larger stroke volumes and diastolic volumes, and their effect on developing heart failure over decades need to be investigated and open up new management schemes for therapy of bradycardia.

Prognosis

For much of the bradycardia population, prognosis is related to (a) cumulative risks of the need for pacing system revisions over many years, (b) physiologic effects of various pacing modes on cardiac size and function, (c) resolution of an underlying disease, such as myocarditis, and (d) status of CHD severity [23, 46, 76].

Pacemaker system complications, replacements, and revisions tend to be one to two time considerations in the average adult-age patient. Pediatric patients and those with CHD can look forward to multiple decades facing these issues. Risks of pacemaker implantation are relatively low, but accrue over

many years. There are few reports of short-term complications to be expected for pacemaker implantation in the young, but a surprising lack of long-term investigations.

Future efforts

It is clear that the guidelines for intervention for bradycardia are based on very loosely associated findings for most scenarios. There is a paucity of meaningful research to draw upon to understand the long-term effects of bradycardia on ventricular size and function that could alter our perception of proper timing and modes for pacing therapies. There are also vague notions of what constitute significant symptoms and what risk bradycardia bears for those symptoms and for increasing the likelihood of extrasystoles, which then serve as triggers for tachyarrhythmia.

Importantly, there have been very few efforts to assess actual reductions of symptoms and other risk prevention by pacemaker intervention in patients with sinus node dysfunction. Prior to the advent of catheter ablative therapies for tachyarrhythmias, there were insightful clinical and basic science investigations of tachyarrhythmia substrates and patient populations. The availability and sophistication of implantable cardiac rhythm management systems has run far ahead of what we understand of the bradyarrhythmia substrates and functional aspects of CHD care they are designed to address. Our field needs to play catch up.

Conclusion

Although rare, bradycardia is an important treatable cause of morbidity and mortality in neonates and children. Clinicians must be aware of various etiologies to look at, as well as immediate therapeutic measures to take for accurate evaluation and management of pediatric patients presenting with bradycardia. This review crystallizes these aspects, highlighting the ongoing investigation in all aspects of care related to this complex group of disorders. Future efforts are needed, especially regarding proper risk assesment and long-term outcomes of pediatric bradycardia. Several genes have been linked to inherited forms of sinus node dysfunction or cardiac conduction disorders, and it is evident that as new insights are gleaned, management strategies continue to evolve. Despite the many different etiologies, each with specific management and distinct outcomes, these patients can do well with a careful, considered approach to the diagnostic evaluation and management plan.

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Dr. Perry contributed to draft the paragraph on management of bradycardia in neonates and children. He approved the final manuscript as submitted.

Dr. Sanatani contributed to draft the paragraph on approach of the patient with suspected bradycardia.

Dr. Horie contributed to draft the paragraph on genetic basis of pediatric bradycardia.

Dr. Dubin critically reviewed the whole paper and approved the final manuscript as submitted.

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Compliance with ethical standards

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