A COMPARATIVE STUDY ON LONG TERM ELECTRICAL PERFORMANCE OF RIGHT VENTRICULAR OUTFLOW TRACT PACING VERSUS RIGHT VENTRICULAR APICAL PACING IN PATIENTS WITH PERMANENT PACEMAKERS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Dissertation Submitted In Partial Fulfillment of the Requirement for the

Degree of Masters of Medicine

(INTERNAL MEDICINE)

UNIVERSITI SAINS MALAYSIA

NOVEMBER 2010

ACKNOWLEDGEMENTS

Bismillahirrahmanirrahim

Praise to Allah s.w.t the most compassionate and most merciful, whose blessing have helped me through the entire completion of this dissertation.

I wish to express my great appreciation to my supervisor and lecturer, Associate Professor Dr Zurkurnai Yusof for his suggestion, interest, sharing the ideas and irreplaceable encouragement.

A special thanks to Head Department of Internal Medicine of School of Medical Sciences, USM, Associate Professor Dr Kamaliah Mohd Daud for her support.

My gratitude also goes to Dr Wan Mohd Zahiruddin and Dr Ng Seng Loong, my co-supervisors for their help and guidance throughout my work and study.

A special gratitude to my family especially to my beloved parents Mr Abdul Rahim bin Omar and Mrs Rahmah Abdul Rahman. Throughout my life, they have been and still ever ready to assist and support me in various endeavours for which I am truly greatful.

Special thanks to Dr Mohammad Najib Mat Pa for helping me in analyzing the data.

Lastly, but not least, many heartfelt thanks to all lecturers in the department of Internal Medicine, School of Medical Sciences, USM, all staffs of Invasive Cardiac Laboratory HUSM, friends and participants of this study of whom the list is endless for sharing their moments and knowledge with me.

Siti Mariam Ab.Rahim

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ABBREVIATIONS:

A	Atrium
ACC	American College of Cardiology
ACS	Acute Coronary Syndrome
AF	Atrial Fibrillation
AHA	American Heart Association
AV	Atrioventricular
CAD	Coronary Artery Disease
CHF	Congestive Heart Failure
CI	Confidence Interval
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
ECG	Electrocardiograph
ECHO	Echocardiogram
HUSM	Hospital Universiti Sains Malaysia
HV	His bundle-ventricular
LAD	Left Anterior Descending
LAO	Left Anterior Oblique
LBBB	Left Bundle Branch Block
LCx	Left Circumflex
LDL	Low Density Lipoprotein
LL	Left Lateral
LV	Left Ventricle
LVEF	Left Ventricular Ejection Fraction

MI	Myocardial Infarction
ms	milliseconds
mV	milivolt
NASPE	North American Society of Pacing and Electrophysiology
OR	Odd Ratio
PA	Postero-anterior
PCI	Primary Coronary Intervention
PPM	Permanent pacemaker
RAO	Right Anterior Oblique
RBBB	Right Bundle Branch Block
RCA	Right Coronary Artery
RV	Right Ventricle
RVA	Right Ventricular Apex
RVOT	Right Ventricular Outflow Tract
SSP	Selective Site Pacing
SSS	Sick Sinus Syndrome
V	Ventricle
VF	Ventricular Fibrillation
VT	Ventricular Tachycardia
≥	more or equal
≤	less or equal
±	plus-minus
Ω	ohm

ABSTRACT

ABSTRACT

Background: Since the introduction of the transvenous cardiac pacing almost five decades ago, the right ventricular apical (RVA) has been the preferred site for ventricular lead attachment. This is due to the ease of placement, stability and reliability. However, from experimental and clinical studies showed that prolonged pacing from the RVA has been shown to be associated with progressive left ventricular dysfunction as demonstrated by heart failure, atrial fibrillation and increased in morbidity and mortality. This led to an interest in alternative RV pacing sites particularly the right ventricular outflow tract (RVOT). It is theoretically associated with more physiological ventricular activation comparing with the conventional pacing site. However there is lack of data on procedural success and long term electrical performance that limits the adoption of RVOT septum pacing as an alternative site to RV apical pacing. The primary aim of the study is to investigate the long term safety of ventricular lead performance and changes in pacing parameters of RVOT pacing comparing with the conventional RVA pacing. From previous study, long term was referred to more than 6 months.

Methods: A total of 96 patients underwent permanent pacemaker implantation at Hospital Universiti Sains Malaysia from January 2002 until June 2008. Out of this number, only 66 patients had complete data. They were enrolled and collected data were analyzed retrospectively. The position of endocardial leads were confirmed by a retrospective analysis of the radiographic appearance. The patients were divided into two group based on the pacing site. One group of patients with RVA pacing and another group of patients with RVOT pacing. Data on stimulation threshold, R wave sensing and lead impedance at time of

pacemaker implantation and two years post implantation were collected and analyzed. Patients' demographic, symptoms at presentation and indications for pacing also been analyzed.

Results: Pacing thresholds, impedance values, and R wave amplitudes measured at implantation and 2 years post-implantation did not significantly differ between RVOT and RVA pacing except for the final lead impedance and threshold. The impedance of the RVOT lead was significantly higher than RVA site. The threshold of the RVOT lead was significantly better than RVA. However values for both parameters were within the accepted range. There was no lead dislodgement or any other procedural related complications during follow up.

Conclusion: The ventricular lead performance of right ventricular outflow tract pacing site is safe and better compared with the right ventricular group. The pacing parameters are comparable with conventional RVA pacing in the long term.

ABSTRAK (MELAYU)

Latarbelakang: Semenjak *pacemaker* diperkenalkan hampir lima dekad yang lalu, apeks ventrikel kanan (RVA) telah menjadi pilihan utama dalam pemasangan *pacemaker lead* dalam ventrikel. Ini adalah kerana cara pemasangan *lead* ventrikel pada RVA adalah mudah, kedudukannya yang stabil dan boleh dipercayai. Walau bagaimanapun, dari kajian experimental dan klinikal menunjukkan bahawa pemasangan *lead* ventrikel pada RVA untuk suatu jangka masa yang panjang akan menyebabkan fungsi ventrikel kiri terganggu. Kesan ini dapat dilihat sebagai kegagalan jantung, fibrillasi atrial dan berlaku peningkatan dalam morbiditi dan mortaliti pesakit. Keadaan ini mewujudkan minat pada para penyelidik untuk mencari tempat alternatif bagi pemasangan *lead* ventrikel terutamanya pada *right ventricle outflow tract* (RVOT). Ini adalah kerana secara teorinya, pemasangan *lead* ventrikel pada RVOT akan mengakibatkan aktivasi ventrikel secara lebih fisiologi. Walau bagaimanapun, kurang kajian berkenaan kejayaan proses pemasangan *lead* ventrikel pada RVOT dan prestasi elektrikal untuk suatu jangka masa panjang dijalankan. Ini telah menghadkan aplikasi RVOT sebagai tempat alternatif. Tujuan utama kajian ini dijalankan adalah untuk mengkaji keselamatan, prestasi *lead* ventrikel dan perubahan parameter-parameter *pacemaker* untuk jangka masa panjang. Kajian ini melibatkan perbandingan antara dua kumpulan iaitu RVA dan RVOT. Daripada kajian-kajian terdahulu, jangka masa panjang merujuk kepada lebih dari 6 bulan.

Kaedah kajian: Seramai 96 pesakit telah menjalani pemasangan *pacemaker* kekal di Universiti Sains Malaysia dari Januari 2002 sehingga Jun 2008. Hanya 66 pesakit

mempunyai rekod data berkaitan kajian ini yang lengkap. Kedudukan *lead* endokardial dipastikan melalui x-ray dada secara retrospektif. Pesakit-pesakit kemudiannya dibahagikan kepada dua kumpulan berdasarkan kedudukan *pacing lead* ventrikel. Satu kumpulan terdiri daripada pesakit-pesakit yang diimplan *pacemaker* pada RVA dan satu kumpulan lagi di RVOT. Data berkenaan bacaan stimulasi *threshold, R wave* dan *impedance* semasa proses pemasangan *pacemaker* kekal dan dua tahun selepas implantasi dikumpulkan dan dianalisa. Data-data pesakit-pesakit yang turut dianalisa dalam kajian ini termasuk sosio-demografik, penyakit lain yang dihidapi, gejala-gejala dan indikasi bagi pemasangan *pacemaker* kekal.

Keputusan: Kajian ini menunjukkan bahawa tiada perbezaan yang signifikan secara statistik bagi *pacing* parameter kecuali keputusan akhir *impedance* dan *threshold.* Nilai *impedance* bagi kumpulan RVOT selepas 2 tahun pemasangan *pacemaker* adalah lebih tinggi dibandingkan dengan kumpulan RVA. Nilai *threshold* bagi kumpulan RVOT lebih baik dibandingkan dengan kumpulan RVA. Walau bagaimanapun, semua keputusan adalah dalam dalam julat normal. Tiada insiden *lead dislodgement* berlaku.

Kesimpulan: Prestasi *lead* ventrikel yany dipasang pada RVOT adalah lebih baik dibandingkan dengan kumpulan RVA dan selamat digunakan sebagai tempat implantasi ventrikel alternatif dan parameter *pacing* adalah setanding dengan RVA untuk jangka masa panjang.

INTRODUCTION

1. INTRODUCTION

1.1 Overview

One of the main objectives of modern cardiac pacing is to optimize or at least to stabilize cardiac performance. It dependent on 3 main parameters which are chronotropic function, quality of AV synchrony and ventricular activation sequence in relation to site selected. The most common indications for permanent pacemaker implantation are heart block and sinus node dysfunction. Any condition that may cause alteration in heart structure or function may lead to the above condition.

Since the introduction of transvenous cardiac pacing almost 5 decades ago, the right ventricular (RV) apex has been preferred site for ventricular lead placement due to the ease of placement, stability and reliability. Unfortunately, pacing from this site produces left ventricular dyssynchrony as a result of an abnormal late activation of the lateral wall of the left ventricle. The ventricular remodelling resulting from neurohumoral and electrophysiological changes. The resultant changes in cardiac hemodynamics cause left ventricle cellular abnormalities, leads to left ventricular dysfunction. This led to an interest in alternative RV pacing sites particularly the RVOT which is associated with more physiological ventricular activation comparing with the conventional pacing site. However there is lack of data on procedural success and long term electrical performance that limiting the adoption of RVOT septum pacing as an alternative site to RV apical pacing.

1.2 Pathophysiology of normal heart conduction

In the normal heart, rhythmic sequence of cardiac contractions is coordinated by the sinoatrial (SA) and atrioventricular (AV) nodes. The SA node, often known as the cardiac pacemaker, is located in the upper wall of the right atrium. It is responsible for the wave of electrical stimulation that initiates atrial contraction by creating an action potential. The ECG recording shows P wave during this time. Once the wave reaches the AV node which is situated in the lower right atrium, it is delayed there before being conducted through the bundles of *His* and subsequently to the Purkinje fibres, leading to a contraction of the ventricles. During atrial, AV node and His-Purkinje conduction, the ECG recording shows PR segment. The delay at the AV node allows enough time for all of the blood in the atria to fill their respective ventricles. However, AV node can also act as a pacemaker in certain conditions. This is usually not the case because their rate of spontaneous firing is considerably lower than that of the pacemaker cells in the SA node and hence is overridden (Guyton and AC, 2006).

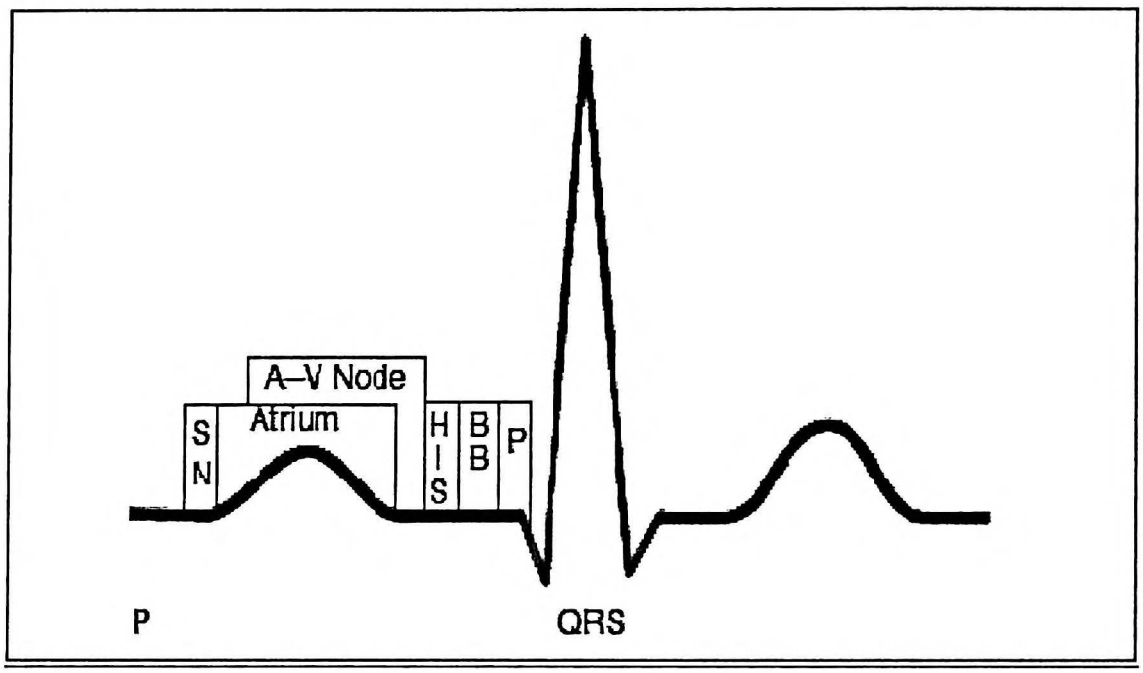

FIGURE 1.1: The conducting system is reflected in the normal QRS complex. SN = sinus node, His = His buddle, BB = bundle branches, P = Purkinje fibres

Adapted fromMalcolm Kirk. Basic principles of pacing. Chapter 1.2005;2.

1.3 ATRIOVENTRICULAR (AV) CONDUCTION DISTURBANCES

An atrioventricular (AV) block involves the impairment of conduction between the atria and ventricles of the heart. It occurs when the atrial depolarization fails to reach the ventricles or when atrial depolarization is conducted with a delay. Heart block results from various pathological conditions that causing infiltration, fibrosis, or loss of connection in portions of the normal conducting system.

Common causes of AV block are:

- Drugs: calcium channel blockers, beta blockers, quinidine, procainamide, lithium, digoxin, tricyclic antidepressant.
- Degenerative diseases: Lenegre disease (sclerodegenerative process involving only the conduction system.
- Infectious disease: Varicella zoster virus, valve ring abscess, rheumatic fever, myocarditis, Lyme borreliosis.
- Rheumatic disease: Ankylosing spondylitis, Reiter's syndrome, relapsing polychondritis, rheumatoid arthritis, scleroderma.
- Infiltrative processes: Amyloidosis, sarcoidosis, tumours, Hodgkin disease, multiple myeloma
- Neuromuscular disorder: Becker muscular dystrophy, myotonic muscular dystrophy
- Ischemic heart disease: Inferior wall myocardial infarction (AV nodal block), anterior wall myocardial infarction (His Purkinje block)
- Metabolic causes: Hypoxia, hyperkalemia, hypothyroidism
- Toxins

- Iatrogenic: Complicating aortic valve surgery, septal alcohol ablation, percutaneous coronary intervention to the left anterior descending artery or ablation of slow or fast pathway of the AV node.

The AV block can be divided into first, second and third degree AV block.

1.3.1. First degree AV block

First degree AV block consists of prolongation of the PR interval on the ECG (>0.20 seconds in adults and > 0.16 seconds in young children). The upper limit of the reference range for the PR interval is age-dependent in children. First-degree heart block is usually caused by a delay at the AV node level. All atrial impulses reach the ventricles in first-degree AV block, however, conduction is delayed within the AV node. First degree AV block may be associated with other conduction disturbances including bundle branch block and fascicular block (bifascicular or trifascicular block).

First-degree AV block can be found in healthy adults. Its incidence increases with age. The PR interval may exceed 0.20 s in 0.5-2% of healthy people at 20 years of age. At age 60 years, more than 5% of healthy individuals have PR intervals exceeding 0.20 seconds. First-degree AV block also may represent the first sign of a degenerative process of the AV conduction system. It is generally not indicated for permanent pacing. Indications for permanent pacemaker implantation including, if the patient develops symptoms attributable to the AV delay especially when the PR interval markedly prolonged (>0.30 s) and the patient has documented left ventricular systolic dysfunction and symptoms of heart failure (Epstein *et al.*, 2008).

Cheng et al found that first-degree AV block (i.e, PR interval >0.20 sec) is associated with an increased risk of atrial fibrillation, pacemaker implantation, and all-cause mortality. In a prospective, community-based cohort of 7,575 individuals from the Framingham Heart Study (mean age, 47 years old; 54% women) who underwent routine 12-lead electrocardiography in 1968-1974, 124 individuals had PR intervals >0.20 sec on the baseline examination. On follow-up of the cohort through 2007, individuals with first-degree AV block had a 2-fold adjusted risk of atrial fibrillation (hazard ratio [HR], 2.06; 95% CI, 1.36-3.12; P < .001), a 3-fold adjusted risk of pacemaker implantation (HR, 2.89; 95% CI, 1.83-4.57; P < .001), and a 1.4-fold adjusted risk of all-cause mortality (HR, 1.44; 95% CI, 1.09-1.91; P = .01). He found that each 20-msec increment in PR was associated with an increase in risk for all three outcomes (Cheng *et al.*, 2009).

1.3.2. Second degree AV block

Second-degree Mobitz I AV block are usually caused by a delay at the AV node level. Whereas second-degree Mobitz II AV block is generally caused by blockage in the His bundle or lower in the conduction system. Type I second-degree AV block (Wenckebach) is observed in 1-2% of healthy young people, especially during sleep. Type II second-degree AV block (Mobitz II) is rare in healthy individuals. Atrial impulses fail to conduct to the ventricles in one of the following 4 ways.

- Mobitz I second-degree AV block also known as Wenckebach block. It causes progressive prolongation of the PR interval with the subsequent occurrence of a single non conducted P wave that results in a pause. The pause is shorter than the sum of any 2 consecutive conducted beats (R-R interval). The block is generally in the AV node

but can occasionally occur in the His-Purkinje system and is termed infra-hisian Wenckebach.

- Mobitz II second-degree AV block is characterized by a constant PR interval followed by sudden failure of a P wave to be conducted to the ventricles, such that either an occasional dropped P wave or a regular conduction pattern of 2:1 (2 conducted and 1 blocked), 3:1 (3 conducted and 1 blocked), and so on is observed.
- High-grade AV block consists of multiple P waves in a row that should conduct, but do not. The conduction ratio can be 3:1 or more and the PR interval of conducted beats is constant. It is a distinct form of complete AV block in that the P waves that conduct to the QRS complexes occur at fixed intervals. For complete AV block, no relationship exists between the P waves and QRS complexes.
- 2:1 AV block could be Mobitz I or Mobitz II, but to distinguish one form from the other is nearly impossible.

1.3.3. Third degree AV block

Third degree AV block is also known as complete AV block. The prevalence is 0.04% internationally (Kojic *et al.*, 1999). It is often due to a lesion distal to the His bundle and associated with bilateral bundle branch block causing atrioventricular dissociation. The QRS complex is wide and the ventricular rate and thus the pulse is slower, usually less than 50 bpm. Transmission of atrial impulses through the AV node is completely blocked. Characteristically in this AV block, the atrial rate is rapid. Exercise does not increase the heart rate. Patients may be asymptomatic. They may experience of weakness, syncope or dyspnea if the rate is less than 35 bpm. Symptoms may occur at higher heart rate if the

patients have left ventricular dysfunction. In most cases of persistent complete heart block require permanent pacing.

1.3.4. Recommendation for permanent pacing in acquired AV block in adults. (ACC/AHA/HRS 2008 Guidelines).

CLASS I:

Permanent pacemaker implantation is indicated for:

- Third degree and advanced second degree atrioventricular (AV) block at any anatomic level associated with bradycardia with symptoms (including heart failure) or ventricular arrhythmias presumed to be due to AV block. *(LOE: C)*
- Third degree and advanced second degree AV block at any anatomic level associated with arrhythmias and other medical conditions that require drug therapy that results in symptomatic bradycardia. *(LOE: C)*
- Third degree and advanced second degree AV block at any anatomic level in awake, symptom free patients in sinus rhythm, with documented periods of asystole greater than or equal to 3.0 seconds or any escape rate less than 40 bpm, or with an escape rhythm that is below the AV node. *(LOE: C)*
- Third degree and advanced second degree AV block at any anatomic level in awake, symptoms free patients with atrial fibrillation and bradycardia with one or more pauses of at least 5 seconds or longer. *(LOE: C)*
- Third degree and advanced second degree AV block at any anatomic level after catheter ablation of the AV junction. *(LOE: C)*

- Third degree and advanced second degree AV block at any anatomic level associated with post-operative AV block that is not expected to resolve after cardiac surgery. *(LOE: C)*
- Third degree and advanced second degree AV block at any anatomic level associated with neuromuscular diseases with AV block, such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb dystrophy (limb girdle muscular dystrophy), and peroneal muscular atrophy, with or without symptoms. *(LOE: B)*
- Second degree AV block with associated symptomatic bradycardia regardless of type or site of block. *(LOE: B)*
- Asymptomatic persistent third degree AV block at any anatomic site with average awake ventricular rates of 40 bpm or faster if cardiomegaly or left ventricular (LV) dysfunction is present or if the site of block is below the AV node. *(LOE: B)*
- Second or third degree AV block during exercise in the absence of myocardial ischemia. *(LOE: C)*

CLASS IIa:

Permanent pacemaker implantation is reasonable for:

- Persistent third degree AV block with an escape rate greater than 40 bpm in asymptomatic adult patients without cardiomegaly. *(LOE: C)*
- Asymptomatic second degree AV block at intra or infra-His levels found at electrophysiological study. *(LOE: B)*
- First or second degree AV block with symptoms similar to those of pacemaker syndrome or hemodynamic compromise. *(LOE: B)*

- Asymptomatic type II second degree AV block with narrow QRS. When type II second degree AV block occurs with a wide QRS, including isolated right bundle branch block (RBBB), pacing becomes a Class I recommendation (see under "Chronic Bifascicular Block"). *(LOE: B)*

CLASS IIb:

Permanent pacemaker implantation may be considered for:

- Neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy (limb girdle muscular dystrophy), and peroneal muscular atrophy with any degree of AV block (including first degree AV block), with or without symptoms, because there may be unpredictable progression of AV conduction disease. *(LOE: B)*
- AV block in the setting of drug use and / or drug toxicity when the block is expected to recur even after the drug is withdrawn. *(LOE: B)*

CLASS III:

Permanent pacemaker implantation is not indicated for:

- Asymptomatic first degree AV block. *(LOE: B)*
- Asymptomatic type I second degree AV block at the supra-His (AV node) level or which is not known to be intra- or infra-Hisian. *(LOE: C)*
- AV block that is expected to resolve and is unlikely to recur (e.g., drug toxicity, Lyme disease or transient increases in vagal tone, or during hypoxia in sleep apnea syndrome in the absence of symptoms). *(LOE: B)*

1.3.5. Recommendation for permanent pacing in chronic bifascicular block (ACC/AHA/HRS 2008 Guidelines).

CLASS I:

Permanent pacemaker implantation is indicated for:

- Advanced second degree AV block or intermittent third degree AV block. *(LOE: B)*
- Type II second degree AV block. *(LOE: B)*
- Alternating bundle branch block. *(LOE: C)*

CLASS IIa:

Permanent pacemaker implantation is reasonable for:

- Syncope not demonstrated to be due to AV block when other likely causes have been excluded, especially ventricular tachycardia (VT). *(LOE: B)*
- Incidental finding at electrophysiological study of a markedly prolonged HV (His bundle-ventricular) interval (greater than or equal to 100 milliseconds) in asymptomatic patients. *(LOE: B)*
- Incidental finding at electrophysiological study of pacing induced infra-His block that is not physiological. *(LOE: B)*

CLASS IIb:

- Permanent pacemaker implantation may be considered in the setting of neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy (limb girdle muscular dystrophy), and peroneal muscular atrophy with bifascicular block or any fascicular block, with or without symptoms. *(LOE: C)*

CLASS III:

Permanent pacemaker implantation is not indicated for:

- Fascicular block without AV block or symptoms. *(LOE: B)*
- Fascicular block with first degree AV block without symptoms. *(LOE: B)*

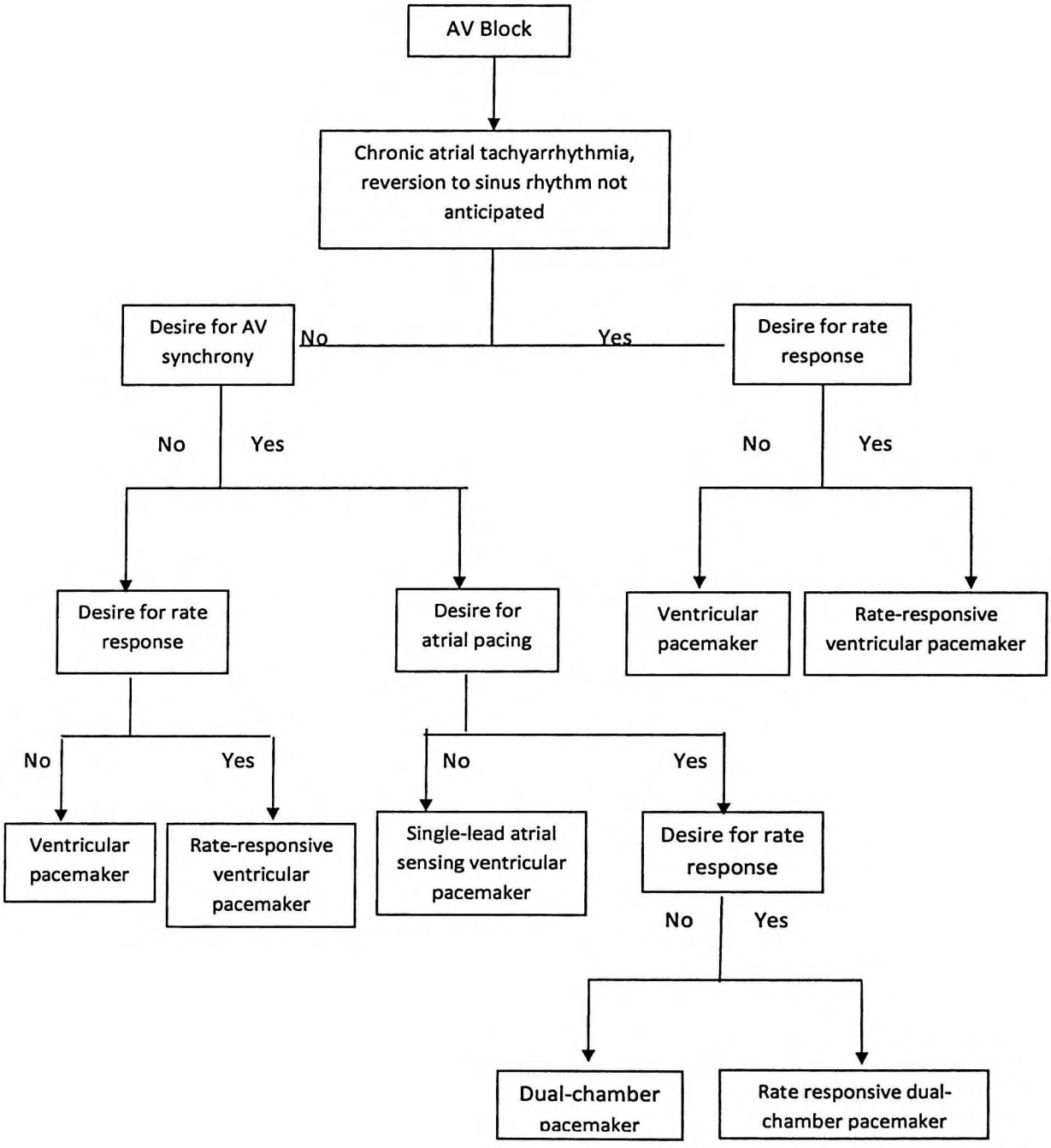

FIGURE 1.2: Selection of pacemaker system for patients with atrioventricular (AV) block.
Adapted from ACC/AHA/HRS 2008 Guidelines

1.4 SINUS NODE DYSFUNCTION

Sinus node dysfunction (SND) initially known as a clinical entity under the name of sick sinus syndrome (SSS) in 1968 (Ferrer, 1968). It is primarily a disease of the elderly. Sick sinus syndrome is a disorder characterized by a dysfunctional sinus node. It is often idiopathic and a result of degenerative fibrosis of nodal tissue and atrial muscle. The causes can be divided into intrinsic causes and extrinsic causes. Examples of intrinsic causes are such as amyloidosis, connective tissue disease, Chagas disease, and hemochromatosis (Table 1.1). Hypertensive heart disease and cardiomyopathies account for a smaller, but significant group that are also responsible for causing SSS. The extrinsic etiologies are pharmacological agents such as digitalis, calcium channel blockers, β-blockers, sympatholytic agents, and several antiarrhythmic drugs (Table 1.1) (Vlay, 2006).

Collected data from 28 different studies on atrial pacing for SND showed a median annual incidence of complete AV block of 0.6% (range 0% to 4.5%) and a total prevalence of 2.1% (range 0% to 11.9%) (Rosenqvist and Obel, 1989). This suggests that the degenerative process also affects the specialized conduction system, although the rate of progression is slow and does not dominate the clinical course of disease (Rosenqvist and Obel, 1989).

SND is typically diagnosed in the seventh and eighth decades of life. The mean age of patients with this condition is 68 years. Both sexes are affected equally. Similar clinical manifestations may occur at any age as a secondary phenomenon of any condition that results in destruction of sinus node cells, such as ischemia or infarction, infiltrative disease, collagen vascular disease, surgical trauma, endocrinologic abnormalities or autonomic insufficiency. The clinical manifestations of SND are broad, reflecting the range of typical sinoatrial rhythm

disturbances. The most dramatic presentation is syncope. The mechanism of syncope is a sudden pause in sinus impulse formation or sinus exit block, either spontaneously or after the termination of an atrial tachyarrhythmia, that causes cerebral hypoperfusion. The pause in sinus node activity is frequently accompanied by an inadequate, delayed, or absent response of subsidiary escape pacemakers in the AV junction or ventricular myocardium, which aggravates the hemodynamic consequences.

The natural history of untreated SND may be variable. The majority of patients who have experienced syncope because of a sinus pause or marked sinus bradycardia will have recurrent syncope (Menozzi *et al.*, 1998). The natural history of SND can be interrupted by medical therapies that aggravate the underlying tendency to bradycardia (Mangrum and DiMarco, 2000). About 50% of patients with SND develop tachy-brady syndrome over a lifetime. These patients have higher risk of stroke and death. The survival of patients with SND appears to depend primarily on the severity of underlying cardiac disease and is not significantly changed by pacemaker therapy (Simon and Janz, 1982; Alt *et al.*, 1985; Menozzi *et al.*, 1998). However, incidence of sudden death owing directly to SND is extremely low (Lamas *et al.*, 2002).

TABLE 1.1:
Causes of Sick Sinus Syndrome

Intrinsic Causes:

Amyloidosis
Arteritis
Cardiomyopathies
Cagas' disease
Collagen vascular disease
Diphteria
Familial sinoatrial node disorders
Fatty replacement
Friedreich's ataxia
Hemochromatosis
Idiopathic degeneration fibrotic infiltration*
Ischemia / Infarction
Leukemia
Metastatic disease
Muscular dystrophy
Myocarditis / percarditis
Rheumatic heart disease
Sarcoidosis
Surgical surgery

Extrinsic Causes:

Cholinesterase deficiency
Hyperkalemia
Hypoxia
Pharmacologic agents:
- Digitalis
- Calcium channel blocker
- Beta blocker
- Sympatholytic agents
- Antiarrhytmias

Toxins

Pediatric Causes:

Congenital abnormalities
Sinoatrial nodal artery deficiency

**Most common intrinsic cause*

Adapted from Wahls SA. Sick sinus syndrome. Am Fam Physician 1985;31:118

TABLE 1.2:
Symptoms of Sick Sinus Syndrome

Central nervous system	Cardiovascular System	Others
Dementia	Angina pectoris	Diggestive disturbances
Irritability	Arterial thromboemboli	Dizziness
Lethargy	Cerebrovascular accident	Errors in judgement
Lightheadedness	Congestive heart failure	Facial flushing
Memory loss	Palpitations	Fatigue
Nocturnal wakefulness		Oliguria
Syncope or presyncope		

Adapted from Wahls SA. Sick sinus syndrome. Am Fam Physician 1985;31:123

It is crucial to distinguish between physiological bradycardia due to autonomic conditions or training effects and inappropriate bradycardia that requires permanent cardiac pacing. For example, sinus bradycardia is accepted as a physiological finding that does not require cardiac pacing in trained athletes. They may have heart rates of 40 to 50 bpm while at rest and awake and may have a sleeping rate as slow as 30 bpm, with sinus pauses or progressive sinus slowing accompanied by AV conduction delay (PR prolongation), sometimes culminating in type I second-degree AV block (Meytes *et al.*, 1975; Talan *et al.*, 1982).

The physiological and pathological bradycardia may overlap in ECG presentation. Therefore it is pivots on correlation of episodic bradycardia with symptoms compatible with cerebral hypoperfusion. Intermittent ECG monitoring with Holter monitors and event recorders may be helpful (Zimetbaum and Josephson, 1999), although the duration of monitoring required to capture such evidence may be very long (Assar *et al.*, 2003). The use of insertable loop recorders offers the advantages of compliance and convenient during very long-term monitoring efforts (Krahn *et al.*, 2003). Normally, atropine significantly increases the SA rate and is used in the diagnosis of sinus node dysfunction. When atropine 1 mg intravenously fails to stimulate the sinus node and increase the heart rate over 90 bpm, it implies SA node dysfunction as SSS.

The optimal pacing system for prevention of symptomatic bradycardia in SND is unknown. Recent evidence suggests that ventricular desynchronization due to right ventricular apical (RVA) pacing may have adverse effects on left ventricular (LV) and left atrial structure and function (Prinzen *et al.*, 1990; Thambo *et al.*, 2004). These adverse effects likely explain the association of RVA pacing, independent of AV synchrony, with increased risks of atrial fibrillation (AF) and heart failure in randomized clinical trials of pacemaker therapy

(Sweeney and Hellkamp, 2006) and, additionally, ventricular arrhythmias and death during ICD therapy (Wilkoff *et al.*, 2002). Although simulation of the normal sinus node response to exercise in bradycardia patients with pacemaker sensors seems logical, a clinical benefit on a population scale has not been demonstrated in large randomized controlled trials of pacemaker therapy (Lamas *et al.*, 2007).

The ECG criteria for SND diagnosis including the following:

- Inappropriate sinus bradycardia:
    - The arbitrary cutoff for a low sinus rate at rest but awake is usually defined as <55-60 bpm. However, a study in healthy subjects suggests the low afternoon sinus rate should be around 46 bpm for men and 51 bpm for women. In the 2008 guidelines, pacemaker therapy is a class IIb indication for patients with minimal symptoms and who have a chronic heart rate of less than 40 bpm while awake.

- Sinus pause or arrest:
    - It is defined as absence of sinus P wave on the ECG for more than 2 seconds due to lack of sinus nodal pacemaker activity. The duration of the pauses should have no arithmetical relationship to the baseline sinus rate (i.e, the P-P interval should not be an interval of the pause), otherwise the diagnosis of sinoatrial exit block should be considered. Symptomatic long sinus pauses or arrests in patients with SND often occur after termination of atrial fibrillation or atrial flutter.

- A sinus pause of 2 seconds is not unusual in a healthy person. However, a sinus pause of more than 3 seconds is very uncommon except under certain conditions, such as sleep apnea, hypervagotonia state or seizure activity.

- Sinoatrial exit block (SA exit block):
  - First degree SA exit block reflects a conduction delay between the sinus node and atrium that cannot be recognized on regular ECG recordings.
  - Second degree SA exit block reflects intermittent conduction block between the sinus node and atrium. It has 2 classic types and likely some atypical types. Only the classic types can be recognized on regular ECG recordings
    - Type I (Wenckebach type) is manifested as group beating, which is progressive shortening of the P-P intervals, and then a pause that is less than twice the shortest P-P interval.
    - Type II is manifested as a pause that is a multiple of the baseline sinus P-P interval.
  - Third degree SA exit block reflects complete conduction block sinus node to atrium. It cannot be definitely distinguished from sinus arrest on regular ECG recordings.

- Chronotropic incompetence: Inadequate heart rate response to physical activity. It is defined as failure to achieve 70-80% of maximal predicted heart rate (maximal predicted heart rate = 220 minus age) at peak exercise. However, the clinical value of this definition has not been well validated. The peak exercise heart rate can be influenced by multiple factors.