CME

Ali A. Sovari, MD; Farhad Farokhi, DO, FACC; Abraham G. Kocheril, MD, FACC

The Physiology of Cardiac Pacing

Introduction

In a normal heart, the electrical impulse is generated in the sinus node (sinoatrial node), which is located near the junction of the superior vena cava and the right atrium. The specialized cells of the sinus node are capable of generating electrical impulses faster than other parts of the conduction system and with automaticity; therefore, they normally are the dominant natural pacemakers of the heart. The impulse is then conducted through the right and left atria and reaches the atrioventricular (AV) node. The AV junction, which is located at the base of the interatrial septum and extends into the interventricular septum, has two main parts: the AV node and the bundle of His in the upper and lower parts, respectively. In a normal heart, the AV node is the only electrical connection between the atria and the ventricles. With the delay in transmitting the impulse from the atria to the ventricles, the AV node provides the appropriate time in diastole for ventricular filling. The His bundle is divided into the left bundle branch and the right bundle branch and then into the Purkinje fibers that conduct the impulse rapidly through the ventricles, which results in rapid and simultaneous ventricular contraction.

Indications for Pacemaker Placement

In deciding whether pacemaker placement is clinically required, the single most important factor is the correlation of symptoms with the episodes of bradyarrhythmia. The most common symptoms include lightheadedness, dizziness, near syncope, syncope and fatigue. The other crucial factor is the type of conduction disorder. The most common reasons for pacemaker placement in the US are sinus node dysfunction and AV block.[1] Multifascicular block, hypersensitive carotid sinus syndrome and neurocardiogenic syncope, some forms of congenital heart disease (CHD), neuromuscular diseases, hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy are other less common indications for pacemaker implantation. There are four major conditions for which there is evidence and/or general agreement that permanent pacemaker implantation is required.[2] (Table 1) Pacemaker implantation requirement after acute myocardial infarction, in congenital heart diseases and in hypertrophic cardiomyopathy may need further evaluation by a cardiologist. There are other conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of pacemaker implantation.

Table 1. Conditions for which There Is Evidence and/or General Agreement That a Permanent Pacemaker Should Be Implanted.

1. Sinus node dysfunction with documented symptomatic bradycardia, including frequent sinus pauses that produce symptoms. In some patients, bradycardia is iatrogenic and will occur as a consequence of essential long-term drug therapy of a type and dose for which there are no acceptable alternatives.
2. Sinus node dysfunction with symptomatic chronotropic incompetence.
3. Third-degree and advanced second-degree AV block at any anatomic level, with some exceptions.
4. Multifascicular block with intermittent third-degree AV block or type II second-degree AV block or alternating bundle-branch block.

Parts of the Pacemaker System

A pacemaker has two main parts, the generator and the leads. The generator contains the circuits that deliver the pacing stimuli. The lead input and circuitry related to a specific chamber of the heart is called a channel (eg, the ventricular channel is the part of the generator that transmits the pulse to the ventricular lead). The generator also contains the battery. Pacemaker leads are wires that transfer the electrical impulses from the generator to the heart or vice versa. They are covered with insulation and are attached to the endocardium.

Pacing

Pacing is the process of delivering a small electrical current to the heart. The electrons leave the tip of the catheter (the negative pole) and go to a metal ring about 1 cm back from the tip (the positive pole). This system is called a bipolar system. In the unipolar system, which is older and now less common, the body of the pacemaker generator works as the positive pole. Since in unipolar pacing the electrical current passes through a large area of the heart to reach the positive pole, it creates a very large stimulus artifact on the surface ECG. With the bipolar system the stimulus artifact on the surface ECG can be very small and sometimes may be missed, which can lead to misinterpretation of the ECG as a wide-complex arrhythmia.

Although the Implantable Cardioverter Defibrillator (ICD) was originally designed to deliver a shock to terminate dangerous tachyarrhythmia, almost all of the new ICD devices also have a pacemaker function. Therefore, any patient who receives an ICD, depending on the patient's requirement, may have his/her heart paced by the ICD.

A pacemaker may have one, two, or three leads. A single-chamber pacemaker has one lead for pacing, which is placed either in the right ventricle or right atrium. A dual-chamber device has one lead in the right atrium and one lead in the right ventricle. A biventricular pacemaker is a device with an additional lead, which is placed within a branch of the coronary sinus to pace the posterolateral wall of the left ventricle nearly simultaneously with the right ventricle. This resynchronization strategy may improve heart function and the ejection fraction in certain patients with heart failure and conduction defects.[3-6]

Sensing

The intrinsic electrical activity in the heart appears as a P wave and QRS complex on the surface ECG for atrial and ventricular activity, respectively. This small electrical activity—in the range of a few millivolts—can be detected by the pacemaker lead. The unipolar pacing system senses any electrical activity between the lead and the metal body of the generator. Since this is a large area, there is always a chance that other electrical activity, such as diaphragm muscle activation, may be sensed by the lead, which will be interpreted by the pacemaker as the ventricular activity. With the bipolar system, this is less likely to happen because the electrical activity should be sensed between the two poles of the lead. The ventricular activity is usually sensed after the beginning of the QRS complex on the surface ECG because of the interval between the beginning of ventricular depolarization and the time that the pulse reaches the tip of the lead to be sensed.

Pacemaker Response to a Sensed Impulse (inhibition of output/triggered pacing)

A sensed intrinsic activity can inhibit the pacemaker output or can trigger the pacemaker to have an output. For example, in a patient with sinus bradycardia and third-degree AV block who has a dual-chamber pacemaker, the sensing of atrial activities with less than one second interval (heart rate >60 bpm) can be programmed to inhibit an output in the atrial lead and can trigger the output in the ventricular lead after a certain time (eg, after 250 msec, which is about the time needed for AV conduction). In this example, if the sinus rate is >60 bpm (atrial sensing of more than one second) the pacemaker will pace the atrium; however, with a normal rate of intrinsic atrial activity the pacemaker will not pace the atrium.

Pacing Modes

Once pacemaker placement is indicated, the next issue to address is the appropriate mode of pacing. The appropriate mode of pacing depends on the specific arrhythmia and the conduction disorder. There are standard codes that refer to the specific function of the pacemaker.

Nomenclature

Initially, in 1974, a three-digit code system was proposed by the American College of Cardiology/American Heart Association (ACC/AHA) for the basic functions of pacemakers. Then the North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and Electrophysiology Group (BPEG) continued to expand the codes. The system was last updated in 2002, and currently a code with five positions is used to describe the function of a pacemaker. The code is generic and is used for all brands.

Codes:

Position I: The first position indicates the chamber that is paced. A stands for atrium, V stands for ventricle and D stands for dual chamber, which means both the right atrium and right ventricle can be paced.

Position II: The same letters above refer to the chamber(s) that is sensed. Manufacturers may use the letter "S" to indicate that the pacemaker can pace only a single chamber. The letter "O" may be used to show that the pacemaker does not have the capability of sensing; these may be used in asynchronous pacing.

Position III: Indicates how the pacemaker responds to a sensed event. "I" means that the sensed event inhibits the pacemaker output, "T" means that the sensed event triggers the output and "D" means that both capabilities are available. It is important to know that a dual response is only possible in a dual chamber pacemaker. For example, a sensed event in the atrium can inhibit the output in the atrium and trigger the output in the ventricle. In this case, the output in the ventricle usually happens with a delay to mimic the normal PR interval, and it may be inhibited if the atrial pulse is conducted normally through the AV node.

Position IV: Indicates the rate modulation capability. The rate can be changed depending on whether the patient is active. "R" is the only mode available. "O," which may not be mentioned (ie, DDD is equal to DDDO), indicates that rate modulation is not available or is not used.

Position V: The fifth position of the code refers to multi-place pacing. "A" means that the pacemaker has the capability of pacing multiple places in one or both atria. "V" refers to the multi-place pacing ability in one or both ventricles. "D" means the multi-place pacing is done in both the atria and ventricles, and "O" means that the multi-place capability is not available or not used.

Pacing Modes:

VVI: Means the device paces the ventricle (the right ventricle) and also senses the ventricle, and a sensed event in the ventricle inhibits the pacemaker from pacing or having any output.

AAI: The pacemaker paces the atrium and senses the atrium, and sensing of an event (eg, sensing an atrial activity within one second) inhibits the pacemaker from pacing.

DDD: The pacemaker paces both the atrium and the ventricle. It can sense both of the chambers and the response can be both inhibitory and triggering.

DDDR: The pacemaker has the above-mentioned capabilities and rate modulation.

DDDRV: The device has the above capabilities and the capability of biventricular pacing.

Other features

AV delay

The AV delay is the time interval between an atrial sensed or atrial paced (sensed AV delay and paced AV delay, respectively) event and pacing of the ventricle by the pacemaker. It is analogous to the PR interval and allows for atrial contraction and ventricular filling to be completed. If a ventricular activity is sensed before this interval, then it inhibits the ventricular pacing.

Refractory period

In a normal conduction, the AV node will remain in a refractory period after conducting the electrical activity from the atria to the ventricles. However, with a pacemaker the AV node will not be in a refractory period when the ventricles are paced. Therefore, the ventricular electrical activity may be transmitted retrogradely to the atria and may activate the atria. This may result in pacemaker-mediated tachycardia (PMT). Setting a refractory period is essential and can prevent such events. The most important refractory period is the postventricular atrial refractory period (PVARP), and it is the period of time after a ventricular paced or sensed event that the atrial channel of the pacemaker does not respond to a sensed event in the atrium. Therefore, in this period a sensed atrial activity is not followed by a ventricular pacing event.

The lower rate limit

The lower rate limit is the programmed rate that the pacemaker will pace at unless a faster intrinsic activity is sensed. If the rate-modulating mode is available and used, then the actual lower rate may vary depending on the patient's activity. The *sleep function* is a feature of the pacemaker that allows a different lower rate limit (usually lower) during certain hours (usually during the night). Therefore, the patient will have a lower rate of pacing during the night when he/she is asleep and does not need a higher pacing rate.

The upper rate limit

The upper tracking rate limit is the maximum pacing rate in response to an intrinsic activity. For instance, if the upper sensor rate is 140 bpm, then the pacemaker will pace up to a maximum rate of 140 bpm when it is fully activated by the intrinsic activity. Therefore, if the intrinsic atrial activity in a patient with a pacemaker in DDD mode is 180 bpm, then the pacemaker may pace up to a 140 bpm and not faster. In this case the pacemaker will automatically increase the AV delay progressively until one P wave falls within the refractory period (ie, PVARP) and will not be conducted to the ventricles. This pacemaker behavior gives the appearance of Wenckebach on surface ECG and is called the *pacemaker-Wenckebach phenomenon*.

Mode switching

When the atrium is sensed (DDD/DDDR/VDD/VDDR) and the ventricle is paced following each atrial beat, up to a maximum rate, sensing of an atrial tachyarrhythmia, such as paroxysmal atrial tachycardia (PAT) results in a rapid ventricular rate during the atrial tachycardia episodes. The mode switching feature provides the option of switching to a VVI/VVIR mode when in the high tachycardic range (eg, 150 bpm) and then switching back to DDD/VDD mode when the atrial rate is below the set range.

Mode switching is used in paroxysmal atrial tachycardias (A Fib, A Flutter, PAT). It has been shown that not only did patients with atrial tachyarrhythmia prefer the mode switching (subjective benefit) but also their exercise capacity was improved in a randomized crossover study.[7] It has also been shown that the mode-switch algorithms for detection of atrial tachyarrhythmias are as accurate as Holter monitoring to detect the atrial tachyarrhythmia (98.1% and 100% sensitivity and specificity, respectively). Therefore, mode switching may serve as a valuable tool to detect atrial tachyarrhythmia episodes and help in clinical decision-making. [8]

Rate responsiveness or rate modulation (Position IV of the code)

A variety of sensors have been developed to detect vibration, oxygen saturation or minute ventilation as markers of the patient's activity. Then the range of heart rates, the pace of acceleration and deceleration, and the degree of activity required to initiate this response are programmed. This feature is different from the sleep function in which the minimum heart rate is programmed to be lower during the night hours.

Rate drop

Rate drop is a feature that gives the capability of pacing at an accelerated heart rate (eg, 100 bpm) for a short period of time (eg, three minutes) if the heart rate drops suddenly or if it drops below a certain rate. This feature is especially helpful in patients with neurocardiogenic syncope.

Managed ventricular pacing

Managed ventricular pacing is a very important feature, which actually is a kind of mode switching. In many patients who receive a pacemaker or ICD, native AV conduction is hemodynamically preferable to RV pacing. A dual-chamber device can be programmed to pace AAI (allowing native conduction), but if loss of AV conduction is sensed, the pacemaker will switch to DDD pacing for some period of time until the algorithm once again sees intrinsic AV conduction.[9-11] While in the DDD pacing mode the pacemaker is programmed to wait for a certain period of time (eg, 300 msec) after the atrial activity to sense the ventricular activity; in managed ventricular pacing the pacemaker allows an even longer AV conduction to stay in AAI mode and to avoid switching to ventricular pacing. In a patient with first-degree AV block, this appears on ECG as atrial pacing with a prolonged PR interval but no ventricular pacing as long as the P wave is conducted through the AV node.

Mortality Rate and Pacing Mode

In a landmark study evaluating the mortality rate in different pacing modes, the patients with sinus node dysfunction were randomized to two groups: one with AAI pacing and the other with VVI pacing. After five and a half years of follow-up, the patients who were paced with the AAI mode showed a lower mortality rate, a lower rate of atrial fibrillation and a lower rate of thromboembolism. Several other clinical trials, including the Pacemaker Selection in the Elderly (PASE) tria, the Mode Selection Trial (MOST), the United Kingdom Pacing and Cardiovascular Events (UKPACE) trial and the Canadian Trial of Physiologic Pacing (CTOPP), compared the survival in patients with VVI pacing versus patients with DDD or DDD/AAI pacing. Other than the Andersen study, the other studies could not show a significant survival benefit from DDD mode compared to VVI. Although there are several pacing modes available, the most commonly used modes are VVI, DDD and AAI.[12-16]

VVI mode

In VVI mode the right ventricle is paced and sensed, and the pacemaker is inhibited in response to a sensed beat. Advantages include requiring only one lead to be placed, and it gives protection against bradycardia with any etiology by pacing the ventricles. Disadvantages are the lack of AV synchrony, which results in pacemaker syndrome in the short-term and may induce heart failure in the long-term. However, it is the mode of choice for patients with chronic atrial fibrillation.

AAI mode

In AAI mode the atrium is paced and sensed, and the pacemaker is inhibited in response to sensed atrial beats. Advantages include requiring only a single lead to be placed, and it keeps the AV synchrony. Its disadvantage is a lack of protection against an AV conduction problem. It is appropriate for patients with sinus node dysfunction who have intact AV nodal function. If the patient with sinus node dysfunction is assessed carefully and does not have AV node disease at the time of pacemaker implantation, the occurrence of clinically significant AV nodal disease is low (less than 2% per year).[17] However, some clinicians prefer a dual chamber pacemaker for sinus node dysfunction even in the absence of an AV conduction problem.

DDD mode

In DDD mode it has sensing and pacing capabilities in both the atrium and the ventricle. The pacemaker will be totally inhibited in the presence of sinus rhythm with normal AV conduction if the sinus rate is faster than the programmed lower rate of the pacemaker and the intrinsic AV conduction is faster than the programmed AV interval; a normal sinus beat is seen on the surface 12-lead ECG. If there is sinus bradycardia but normal AV conduction with the intrinsic QRS occurring before the end of the programmed AV interval, there will be atrial pacing with a native QRS complex following each paced atrial beat. Both the atrium and ventricle will be paced if there is sinus bradycardia and delayed or absent AV conduction (ie, AV sequential pacing on ECG). The ventricle will be paced synchronously with the atrium if there is normal sinus rhythm with delayed or absent AV conduction (ie, atrial sensing and ventricular pacing on ECG).

The DDD pacing mode is appropriate for patients with AV block who have normal sinus node function. It is also indicated for patients who have combined sinus nodal and AV nodal dysfunction in whom DDDR pacing would restore rate responsiveness and AV synchrony. DDDR pacing is also appropriate for patients with sinus node dysfunction and normal AV conduction. Use of the DDDR pacing mode with an algorithm that will minimize ventricular pacing is often preferred. *A simplified general approach in the US would be choosing the DDDR mode for the majority of patients unless the patient has chronic atrial fibrillation, in which case the VVIR mode is the most appropriate.*

Pacemaker Syndrome

Pacemaker syndrome is defined as adverse hemodynamic effects of a VVI pacing mode while the pacemaker functions normally. Atrial contraction against a closed AV valve, which can happen in VVI mode with AV asynchrony, results in a cardiovascular impairment similar to that caused by a third-degree AV block. Symptoms include presyncope or syncope, fatigue, cough, dizziness, dyspnea, orthopnea, paroxysmal nocturnal dyspnea and a sensation of throat fullness. On physical examination, hypotension, increased jugular venous pressure with cannon A waves, peripheral edema, rales and murmurs of tricuspid and mitral regurgitation may be detected. The findings are nonspecific; therefore, presence of the above signs and symptoms in a patient who has a pacemaker with VVI mode may need further investigation and pacemaker interrogation.

Ali Sovari, MD recently completed his Internal Medicine residency at the University of Illinois College of Medicine at Urbana-Champaign, and is currently a cardiology research fellow at the UCLA and Olive View Center for the Health Sciences, Los Angeles, CA.

Farhad Farokhi, DO, FACC is a member of the cardiology department at Carle Clinic, Urbana, IL.

Abraham G. Kocheril, MD, FACC, FACP, is a Professor of Medicine and Director of Clinical Electrophysiology at the University of Illinois at Chicago, Chicago, IL.

References

1. Brinie D, Williams K, Guo A, Mielniczuk L, davis D, Lemery R, et al. Reasons for escalating pacemaker implants. Am J Cardiol 2006;98(1):93-97.

2. Gregoratos G, Abrams J, Epstein AE, Freedman RA, Hayes DL, Hlatka MA, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee to Update the 1998 Pacemaker Guidelines). J Cardiovasc Electrophysiol 2002;13(11):1183-1199

3. Leclercq C; Kass DA. Retiming the failing heart: principles and current clinical status of cardiac resynchronization. J Am Coll Cardiol 2002;39(2):194-201.

4. Leclercq C; Hare JM. Ventricular resynchronization: current state of the art. Circulation 2004;109(3):296-299.

5. Jarcho, JA. Resynchronizing ventricular contraction in heart failure. N Engl J Med 2005;352(15):1594-1597.

6. Lindenfeld J, Feldman AM, Saxon L,Boekme J, Carson P, Ghali JK, et al. Effects of cardiac resynchronization therapy with or without a defibrillator on survival and hospitalizations in patients with New York Heart Association Class IV Heart Failure. Circulation 2007;115(2):204-212.

7. Kamalvand K, Tan K, Kotsakis A, Bucknall C, Sulken N, et al. Is mode switching beneficial? A randomized study in patients with paroxysmal atrial tachyarrhythmias. J Am Coll Cardiol 1997;30(2):496-504.

8. Passman RS, Weinberg KM, Freher M, Denes P, Schaechter A, Goldberger JJ, et al. Accuracy of mode switch algorithms for detection of atrial tachyarrhythmias. J Cardiovasc Electrophysiol. 2004;15(7):773-777.

9. Sweeney MO, Shea JB, Fox V, Alden S, Nelson L, Mullen TJ, et al. Randomized pilot study of a new atrial-based minimal ventricular pacing mode in dual-chamber implantable cardioverter defibrillators. Heart Rhythm. 2004;1(2):160-167.

10. Sweeney MO, Ellenbogen KA, Casavant KJ, Betzold R, Sheldon T, Tang F, et al. Multicenter, prospective, randomized safety and efficacy study of a new atrial-based managed ventricular pacing mode (MVP) in dual chamber ICDs. J Cardiovasc Electrophysiol. 2005 Aug;16(8):811-817.

11. Gillis AM, Pürerfellner H, Israel CW, Santhorn H, Kacet S, Anelli-Prati M, et al. Reducing unnecessary right ventricular pacing with the managed ventricular pacing mode in patients with sinus node disease and AV block. Pacing Clin Electrophysiol 2006;29(7):697-705.

12. Andersen HR, Nielsen JC, Thomsen PE, Thuesen L, Mortensen PT, Vesterlundt T, et al: Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. Lancet1997;350(9086):1210-1216.

13. Lamas GA, Orav EJ, Stambler BS, Ellenbogen KA, Sgarbossa EB, Huang SK, et al. : Quality of life and clinical outcomes in elderly patients treated with ventricular pacing as compared with dual-chamber spacing. Pacemaker Selection in the Elderly Investigators. N Engl J Med 1998;338:1097-1104.

14. Lamas GA, Lee KL, Sweeney MO, Leon A, Ye R, Marinchak RA, et al. Ventricular pacing or dual-chamber pacing for sinus node dysfunction. N Engl J Med 2002; 346(24):1854-1862.

15. Toff WD, Skehan JD, De Bono DP, Camm RJ. The United Kingdom pacing and cardiovascular events (UKPACE) trial. United Kingdom Pacing and Cardiovascular Events. Heart 1997 78(3):221-223.

16. Connolly SJ, Kerr CR, Gent M, Roberts RS, Yusuf S, Gillis AM, et al: Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes Canadian Trial of Physiologic Pacing Investigators. N Engl J Med 2000;342(180):1385-1391.

17. Hayes DL; Furman S. Stability of AV conduction in sick sinus node syndrome patients with implanted atrial pacemakers. Am Heart J 1984;107(4):644-7.

CME Questions 4a-d

Please select the best answer for the following:

4a. Which one of the following patients least likely needs a permanent pacemaker implantation?

   a. A patient with third degree AV block
   b. A patient with symptomatic sinus node dysfunction and bradycardia due to a medication with no alternative available
   c. A patient with second-degree AV block Mobitz type 2
   d. A patient with sinus bradycardia following an inferior myocardial infarction

4b. In the nomenclature of pacing mode suggested by American Heart Association (AHA) and American College of Cardiology what do the first three letters stands for respectively?
   a. Pacing – Sensing – Response
   b. Sensing – Pacing – Response
   c. Pacing – Sensing – Rate modulation
   d. Sensing – Pacing – Rate modulation

4c. In general the DDDR pacing mode is chosen for the majority of patients unless the patient has chronic atrial fibrillation, in which case the VVIR mode is the most appropriate.
   a. True
   b. False

4d. A patient with paroxysmal atrial fibrillation and sinus node dysfunction who received a pacemaker with VVI pacing mode recently presented to you with complaint of dyspnea, dizziness, fatigue, near syncope, with elevated jugular venous pressure and cannon A waves in physical examination. Pacemaker syndrome should be considered as the cause of his/her signs and symptoms.
   a. True
   b. False