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Clinical Applications of Pacemakers in Patients with Bradycardia and Other Specific Conditions

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1. Introduction

This chapter explains the foundations for permanent pacing and proposes a rational and critical approach about the indications for stimulation which are supported by current scientific evidence. We also review stimulation mode selection in different clinical scenarios, technical aspects of implantation, and outline a follow-up program for patients who carry stimulation devices.

We consider convenient mentioning the initials used to designate the stimulation mode for pacemakers. The first letter refers to the paced chamber (could be 0=none, A=atrium, V=ventricle, D=dual), the second letter refers to the sensed chamber (could be 0=none, A=atrium, V=ventricle, D=dual), and the third letter to the type of response the pacemaker will have when detecting an intrinsic beat (could be 0=none, I=inhibitory, T=trigger, D=dual). There is a forth letter which confirms the presence of a sensor which modulates heart rate in to response physical activity (R=rate response). Thus, a VVI mode pacemaker paces and senses only the right ventricle, and it is inhibited if sensing an intrinsic beat. A DDD pacemaker paces and senses both chambers (right atrium and ventricle) and both leads can be inhibited by an intrinsic beat.

2. Main clinical indications for pacing

Cardiac stimulation through permanent pacing is a therapy that currently is clearly established for the treatment of patients with symptomatic bradycardia due to function alterations in the sinus and atrioventricular (AV) node. There are some indications in asymptomatic patients, which in general, are more controversial, with less scientific evidence in its favour.

2.1 Sinus node dysfunction (SND)
In 1923 Wenckebach described the electrocardiographic characteristics of SND, and in 1968 Ferrer published the manifestations considering it as a clinical entity.[1]

The node is formed, from a cytologic point of view, by P cells and transitional cells. P cells are responsible for the pacemaker function and present as groups of 3 or 4 cells. Transitional cells have two varieties: some connect P cells with the atria and the others form links

between the groups of P cells. Sinus node pacemaker activity is widely distributed and its automaticity is modulated by the autonomic function. Parasympathetic stimulation depresses automaticity and favors impulse propagation towards the lower part of the right atrium; on the contrary, sympathetic stimulation increases its automaticity and atrial activation starts in the upper part of the atrium.[2]

The sinus node has a central portion responsible for the origin of the stimulus, and another which is peripheral, in charge of the conduction towards the atria; the last one is separated from the atrial myocardium by a band of connective tissue. Aging is associated with structural changes in the sinus node: increase in the amount of collagen, decrease in connexin (Cx43) expression, and possibly decrease in I_{Na} flow in the node periphery (the center of the node does not express that flow). [3] These alterations, either in the formation and/or propagation of the atrial impulse, condition a broad variety of presentations such as:

- Persistent sinus bradycardia
- Chronotropic incompetence without identifiable causes
- Paroxysmal or persistent sinus arrest compensated by escape rhythms in the ventricular myocardium, in the AV junction and in some cases as paroxysmal or persistent atrial fibrillation (AF).

The bradycardia-tachycardia syndrome is the association between sinus bradycardia and/or sinus arrest and AF.[4] In this case tachycardia events depress node automatism by a suppression mechanism secondary to overstimulation. This way when tachycardia ceases abruptly, arrest or asystole supervene due to failure in the inferior pacemakers to rescue the heart rate. [5]

2.1.1 Epidemiology

SND presents in the elderly, usually between the sixth and seventh decades of life.[6,7] Although it can present at any age as a secondary phenomenon due to any alteration that implies sinus node cell destruction, such as heart surgery, inflammation or ischemia. It conditions an annual complete AV block incidence of 0.6%, with 2.1% prevalence. [7,8]

2.1.2 Clinical ma ions

Clinical manifestations are variable and can go from an asymptomatic stage, to subtle symptoms like dyspnea due to chronotropic incompetence (an inadequate response of heart rate to physical activity), to dizziness, to the most dramatic which is syncope. [9]

2.1.3 Diagnosis

The following are tests which can be helpful to diagnose SND:

- An electrocardiogram should be the initial test, although due to the briefness it may not completely correlate with the symptoms.
- A treadmill test is useful to evaluate chronotropic response, it should be considered positive when the patient cannot reach 70% of the expected heart rate according to the age. [10]
- 24-hour holter monitoring is recommended when symptoms are regular; when the symptoms are sporadic an implantable loop recorder is an excellent alternative. [11]

Electrophysiological studies evaluate sinus function through two methods: 1) sinus node recovery time, which analyzes node automaticity after a suppression period after

overstimulation; 2) sinoatrial conduction time, which analyzes the conduction time to the sinus node and from the sinus node to the atrium as a response to atrial extrastimuli. [12]

2.1.4 Treatment

For SND indications as for the rest of the chapter we refer to the classification of recommendations and level of evidence established by different cardiology societies. Currently the only effective method for the treatment of symptomatic SND is the implantation of a permanent pacemaker. See Table 1 for complete recommendations.

Class I
1.   Is indicated for SND with documented symptomatic bradycardia, including frequent sinus pauses that produce symptoms. (Level of Evidence: C)
2.   Is indicated for symptomatic chronotropic incompetence. (Level of Evidence: C)
3.   Is indicated for symptomatic sinus bradycardia that results from required drug therapy for medical conditions. (Level of Evidence: C)
Class IIa
1.   Is reasonable for SND with heart rate less than 40 bpm when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented. (Level of Evidence: C)
2.   Is reasonable for syncope of unexplained origin when clinically significant abnormalities of sinus node function are discovered or provoked in electrophysiological studies. (Level of Evidence: C)
Class IIb
1.   May be considered in minimally symptomatic patients with chronic heart rate less than 40 bpm while awake. (Level of Evidence: C)
Class III
1.   Is not indicated for SND in asymptomatic patients. (Level of Evidence: C)
2.   Is not indicated for SND in patients for whom the symptoms suggestive of bradycardia have been clearly documented to occur in the absence of bradycardia. (Level of Evidence: C)
3.   Is not indicated for SND with symptomatic bradycardia due to nonessential drug therapy. (Level of Evidence: C)

Table 1. Recommendations for permanent pacing in sinus node dysfunction[7]

2.2 Hypersensitive carotid sinus syndrome

It is defined as presyncope or syncope caused by an extreme reflex response to the stimulation of the carotid sinus. This hyperactive response is manifested as asystole equal or greater to 3 seconds, secondary to an AV block and an important decrease on systolic pressure. [13,14] It has two components:

3.   Cardioinhibitory: resulting from an increase in the parasympathetic tone and manifested by a decrease in the sinus rate or prolongation of the PR interval, an advanced AV block, alone or in combination.

4.   Vasopressor: conditioned by a reduction in the sympathetic activity, resulting in loss of vascular tone and hypotension. This effect is independent of the changes in the heart rate.

For the definite diagnosis it is important to rule out other potentially fatal causes such as ventricular tachycardia and/or ventricular fibrillation. Ultimately, the treatment for symptomatic patients is permanent pacing. See Table 2 for complete recommendations.

Class I
1.   Is indicated for recurrent syncope caused by spontaneously occurring carotid sinus stimulation and carotid sinus pressure that induces ventricular asystole of more than 3 seconds. (Level of Evidence: C)
Class IIa
1.   Is reasonable for syncope without clear, provocative events and with a hypersensitive cardioinhibitory response of 3 seconds or longer. (Level of Evidence: C)
Class IIb
1.   May be considered for significantly symptomatic neurocardiogenic syncope associated with bradycardia documented spontaneously or at the time of tilt-table testing. (Level of Evidence: B)
Class III
1.   Is not indicated for a hypersensitive cardioinhibitory response to carotid sinus stimulation without symptoms or with vague symptoms. (Level of Evidence: C)
2.   Is not indicated for situational vasovagal syncope in which avoidance behavior is effective and preferred. (Level of Evidence: C)

Table 2. Recommendations for permanent pacing in hypersensitive carotid sinus syndrome and neurocardiogenic syncope[7]

2.3 Acquired atrioventricular block

Patients with abnormalities in the AV conduction can vary from asymptomatic, to having episodes directly related to bradycardia, ventricular arrhythmias or both. It is vitally important to do an adequate clinical evaluation of symptomatic patients, and of the findings in the different diagnostic tests available. Identifying the different degrees of AV block is mandatory to make a satisfactory correlation and consequently an assertive therapeutic decision, which historically has been demonstrated to be a permanent pacemaker when there are symptoms conditioned by this alteration.[15-18] See Table 3 for complete recommendations.

The following is the classification of AV blocks:

4.   Anatomically, it is defined as supra-, intra-, or infra-His.

5.   AV block is classified as first-, second-, or third-degree (complete) block.

    a.   First-degree AV block is defined as abnormal prolongation of the PR interval (greater than 0.20 seconds).

    b.   Second-degree AV block is subclassified as type I and type II.

        i.   Type I second-degree AV block is characterized by progressive prolongation of the interval between the onset of atrial (P wave) and ventricular (R wave) conduction (PR) before a nonconducted beat and is usually seen in conjunction with QRS. Is characterized by progressive prolongation of the PR interval before a nonconducted beat and a shorter PR interval after the blocked beat.

        ii.   Type II second-degree AV block is characterized by fixed PR intervals before and after blocked beats and is usually associated with a wide QRS complex. When AV conduction occurs in a 2:1 pattern, block cannot be classified unequivocally as type I or type II, although the width of the QRS can be suggestive, as just described. Advanced second-degree AV block refers to the blocking of 2 or more consecutive P waves with some conducted beats, which indicates some preservation of AV conduction. In the setting of AF, a prolonged pause (e.g., greater than 5 seconds) should be considered to be due to advanced second-degree AV block.

    c.   Third-degree AV block (complete heart block) is defined as absence of AV conduction.

Class I
1. Is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with bradycardia with symptoms (including heart failure) or ventricular arrhythmias presumed to be due to AV block. (Level of Evidence: C)
2. Is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with arrhythmias and other medical conditions that require drug therapy that result in symptomatic bradycardia. (Level of Evidence: C)
3. Is indicated for 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 ≥3.0 seconds or any escape rate less than 40 bpm, or with an escape rhythm that is below the AV node. (Level of Evidence: C)
4. Is indicated for third-degree and advanced second-degree AV block at any anatomic level in awake, symptom-free patients with AF and bradycardia with 1 or more pauses of at least 5 seconds or longer. (Level of Evidence: C)
5. Is indicated for third-degree and advanced second-degree AV block at any anatomic level after catheter ablation of the AV junction. (Level of Evidence: C)
6. Is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with postoperative AV block that is not expected to resolve after cardiac surgery. (Level of Evidence: C)
7. Is indicated for 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. (Level of Evidence: B)
8. Is indicated for second-degree AV block with associated symptomatic bradycardia regardless of type or site of block. (Level of Evidence: B)
9. Is indicated for asymptomatic persistent third-degree AV block at any anatomic site with average awake ventricular rates of 40 bpm or faster if cardiomegaly or LV dysfunction is present or if the site of block is below the AV node. (Level of Evidence: B)
10. Is indicated for second- or third-degree AV block during exercise in the absence of myocardial ischemia. (Level of Evidence: C)

Class IIa
1. Is reasonable for persistent third-degree AV block with an escape rate greater than 40 bpm in asymptomatic adult patients without cardiomegaly. (Level of Evidence: C)
2. Is reasonable for first- or second-degree AV block with symptoms similar to those of pacemaker syndrome or hemodynamic compromise. (Level of Evidence: B)
3. Is reasonable for asymptomatic second-degree AV block at intra- or infra- His levels found at electrophysiological study. (Level of Evidence: B)
4. Is reasonable for asymptomatic type II second-degree AV block with a narrow QRS. When type II second-degree AV block occurs with a wide QRS, including isolated right bundle-branch block, pacing becomes a Class I recommendation. (Level of Evidence: B)

Class IIb
1. May be considered for neuromuscular diseases such as myotonic muscular dystrophy, Erb 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. (Level of Evidence: B)
2. May be considered for 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. (Level of Evidence: B)

Class III
1. Is not indicated for asymptomatic first-degree AV block. (Level of Evidence: B)
2. 2. Is not indicated for asymptomatic type I second-degree AV block at the supra-His (AV node) level or that which is not known to be intra- or infra-Hisian. (Level of Evidence: C)
3. Is not indicated for 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). (Level of Evidence: B)

Table 3. Recommendations for acquired atrioventricular block in adults[7]

2.4 Congenital atrioventricular block

Indications for permanent pacemaker implantation in patients under 18 year, are in general the same as for adults, there are only a few considerations. 1) There must be clinical correlation between the AV conduction alteration and the symptoms of the patient; 2) bradycardia

Class I
1.   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.   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.   Is indicated for post-operative 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.   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.   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.   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.   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 2 or 3 times the basic cycle length, or associated with symptoms due to chronotropic incompetence. (Level of Evidence: B)
3.   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 seconds. (Level of Evidence: C)
4.   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.   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.   May be considered for transient postoperative third-degree AV block that reverts to sinus rhythm with residual bifascicular block. (Level of Evidence: C)
2.   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.   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 seconds. (Level of Evidence: C)
Class III
1.   Is not indicated for transient postoperative AV block with return of normal AV conduction in the otherwise asymptomatic patient. (Level of Evidence: B)
2.   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.   Is not indicated for asymptomatic type I second-degree AV block. (Level of Evidence: C)
4.   Is not indicated for asymptomatic sinus bradycardia with the longest relative risk interval less than 3 seconds and a minimum heart rate more than 40 bpm. (Level of Evidence: C)

Table 4. Recommendations for permanent pacing in children, adolescents, and patients with congenital heart disease[7]

without associated symptoms is not a justification for permanent device implantation; 3) it is fundamental to consider the implantation site according to the size of the device and the height of the patient, keeping in mind alternatives such as the epicardic.

The most common indications for permanent pacing in this group of patients are:

a) advanced second-degree AV block; b) third-degree AV block; c) bradycardia-tachycardia syndromes, and d) symptomatic sinus bradycardia.[19,20] As always diagnosis should be done correlating clinical and tests findings. Exhaustive search of causes that could be triggering this disease should always be considered. See Table 4 for complete recommendations.

2.5 Chronic bifascicular block

Syncope is the most common manifestation in patients with bifascicular block, fortunately despite the recurrence, is not associated with increase on sudden death. [21,22] That cannot be stated for patients with third-degree AV block, in this case if they present syncope there is an increase in the incidence of sudden death.[23] It is important to consider an electrophysiological study to evaluate and treat ventricular arrhythmias.[24] Bifascicular block refers to ECG evidence of impaired conduction below the AV node in the right and left bundles. Alternating bundle-branch block (also known as bilateral bundle-branch block) refers to situations in which clear ECG evidence for block in all 3 fascicles is manifested on successive ECGs.

All of these considerations oblige us to make a certain diagnosis to give the optimal treatment to these patients. See Table 5 for complete recommendations.

Class I
1. Is indicated for advanced second-degree AV block or intermittent third- degree AV block. (Level of Evidence: B)
2. Is indicated for type II second-degree AV block. (Level of Evidence: B)
3. Is indicated for alternating bundle-branch block. (Level of Evidence: C)
Class IIa
1. Is reasonable for syncope not demonstrated to be due to AV block when other likely causes have been excluded specifically ventricular tachycardia. (Level of Evidence: B)
2. Is reasonable for an incidental finding at electrophysiological study of a markedly prolonged HV interval (greater than or equal to 100 milliseconds) in asymptomatic patients. (Level of Evidence: B)
3. Is reasonable for an incidental finding at electrophysiological study of pacing-induced infra-His block that is not physiological. (Level of Evidence: B)
Class IIb
1. May be considered in the setting of neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy, and peroneal muscular atrophy with bifascicular block or any fascicular block, with or without symptoms. (Level of Evidence: C)
Class III
1. Is not indicated for fascicular block without AV block or symptoms. (Level of Evidence: B)
2. Is not indicated for fascicular block with first-degree AV block without symptoms. (Level of Evidence: B)

Table 5. Recommendations for permanent pacing in chronic bifascicular block[7]

2.6 Pacing for atrioventricular block associated with Acute Myocardial Infarction

Pharmacological and mechanical reperfusion therapies have favored decrease in the incidence of AV block associated to acute myocardial infarction (AMI). [25] Indications for

permanent pacing in patients with AMI depend on the intraventricular conduction defect, which does not necessarily depends on the symptoms or on the fact that the patient required transitory pacing. When an AV block or an intraventricular conduction block appears after an AMI, the localization of the AMI and the type of conduction alteration should be considered for permanent pacing. [26, 27] See Table 6 for complete recommendations.

Class I
1.   Is indicated for persistent second-degree AV block in the His-Purkinje system with alternating bundle-branch block or third-degree AV block within or below the His-Purkinje system after ST-segment elevation MI. *(Level of Evidence: B)*
2.   Is indicated for transient advanced second-or third-degree infranodal AV block and associated bundle-branch block. If the site of block is uncertain, an electrophysiological study may be necessary. *(Level of Evidence: B)*
3.   Is indicated for persistent and symptomatic second- or third-degree AV block. *(Level of Evidence: C)*
Class IIb
1.   May be considered for persistent second- or third-degree AV block at the AV node level, even in the absence of symptoms. (Level of Evidence: B)
Class III
1.   Is not indicated for transient AV block in the absence of intraventricular conduction defects. *(Level of Evidence: B)*
2.   Is not indicated for transient AV block in the presence of isolated left anterior fascicular block. *(Level of Evidence: B)*
3.   Is not indicated for new bundle-branch block or fascicular block in the absence of AV block. *(Level of Evidence: B)*
4.   Is not indicated for persistent asymptomatic first-degree AV block in the presence of bundle-branch or fascicular block. *(Level of Evidence: B)*

Table 6. Recommendations for permanent pacing after the acute phase of myocardial infarction[7]

3. Indications for pacing in other specific conditions

There are other specific conditions in which stimulation through pacemakers can achieve beneficial clinical effects, with more or less scientific evidence in its favor.

3.1 Neurocardiogenic syncope

Syncope can be defined as a transitory loss of conscience related with the loss of posture (eventually falling to the floor). Frequently is referred as fainting, and can be the cause of hospitalization in 6% of patients admitted to a general hospital. Neurocardiogenic syncope is a frequent clinical entity in children and adults, generally associated to a benign prognosis. The concept known as neurally mediated syncopal syndrome can be represented by the hypersensitive carotid sinus syndrome, vasovagal syncope also known as neurocardiogenic syncope, and recently related with autonomic dysfunction and positional syncope. This is the origin in more than half of unexplained syncope at any age. Neurocardiogenic syncope has prevalence in general population of 22%[28] and it is conditioned by a triggering stimulus of a neural autonomic reflex, usually self-limited, which conditions arterial hypotension secondary to peripheral vasodilatation and/or important bradycardia or transitory asystole.

The majority of patients can be satisfactorily treated with drugs such as beta-blockers (atenolol), selective serotonin reuptake inhibitors (paroxetine), water retention drugs

(fludrocortisone) and some vasoconstrictors (midodrine) as well as dietary measures, such as high salt intake, exercise and lifestyle modifications. Nevertheless a small group of patients is affected by frequent fainting that can disturb daily living, and others can present episodes similar to sudden death which does not improve with the usual therapeutic measures. Some authors have called this type of manifestations as "malignant" neurocardiogenic syncope, because of recurrent falls and even physical trauma.[29] Some of these patients can have prolonged asystole or important bradycardia during the neurocardiogenic syncope, that is why the placement of a pacemaker has been proposed and could be justified, although this is highly controversial. Various randomized trials have shown important reduction in the number of syncopal events in selected patients, although in the first studies, the patients were assigned at random to receive or not cardiac stimulation and this could be related to a placebo effect.[30,31,32] Afterwards, in two trials the pacemaker was placed on all the patients and then randomized to have it "on" or "off" to avoid the placebo effect. Neither study demonstrated significant difference on a 6 month follow up. However one of the studies showed that the most benefited patients with this therapeutic where those with asystole, compared to those with marked bradycardia.[33,34,35] We must remember that up to 25% of patients with neurocardiogenic syncope have a dominant vasodepressor component without significant bradycardia, and most likely those patients have the least benefit with a pacemaker. It is estimated that approximately one third of the patients have bradycardia or asystole as cause of syncope in the tilt-table test or during the spontaneous syncopal episodes. The SYMPACE trial established that the recurrence of syncope was prolonged even more in the patients with asystole than the patients with bradycardia (91 days vs. 11 days).[35] Some studies demonstrated a beneficial effect on induced syncope during the tilt-table test.[36,37]

Seventy-seven patients included in 3 studies which had syncope during the tilt-table test, improved substantially after placement of a dual-chamber pacemaker.[38,39,40] However, other studies were not able to demonstrate the ability to avoid syncope, in some patients (82%) after placement of the pacemaker a tilt-table test was repeated and they only had presyncope. Thus it was possible to demonstrate that 80 to 90% of patients had marked symptomatic improvement reducing up to 90 to 95% the number of expected syncopal events.[13] Three randomized controlled studies commented nevertheless, that in selected patients it is possible to demonstrate benefits in most of them.[30,31,32] In the Second Vasovagal Pacemaker Study (VPS II), 100 patients were included and received a pacemaker. Then they were randomized to pacing with rate drop sensing, or sensing without pacing. The cumulative risk of syncope at 6 months was 40% for the control group and 31% for the actively paced group. The relative risk reduction in time to syncope with pacing was 30% (1 p = 0.14).[33] Nonetheless they concluded that pacemaker placement should not be used as a first line therapy in these patients.

Although since the 90s it has been accepted by the Therapeutic Guidelines of the Cardiac Stimulation British Group and the AHA/ACC, the use of pacemakers for the treatment of severe neurocardiogenic syncope, should not be considered as first line treatment. However it can be considered in those patients with recurrent syncope despite optimal medical treatment, mainly in patients without prodromal symptoms that allow them to have precautions at the beginning of the episode. Also, in those in which pacing can reduce the frequency of syncope and/or prolong the time since the beginning of symptoms to the loss of conscience episode, thus facilitating necessary measures to avoid falling, like sitting or lying down.

In the other hand we must have in mind that the symptoms in the patient with neurocardiogenic syncope are partially secondary to bradycardia, which can be prevented by pacing, but greatly peripheral vasodilatation is the producing mechanism. It is important to stress the fact that although prolonged asystole, provoked or spontaneous, can be worrying, usually the prognosis is benign in those patients even without pacemaker.41

In the patient with an intense cardioinhibitory response in the tilt-table test, placement of dual-chamber pacemaker can be an alternative to the medical therapy, especially in the highly symptomatic patient, and primarily when other therapeutic alternatives have failed.

Early detection of imminent neurocardiogenic syncope by the sensing system of the pacemaker is an important factor when defining the best strategy of stimulation, as it is the optimal method of stimulation. We must remember that the drop in the heart rate is usually insidious and not abrupt and it is usually accompanied by peripheral vasodilatation. Ammirati et al compared rate drop responsiveness and rate hysteresis. They demonstrated a benefit for those with rate drop responsiveness (0/12 fainted) compared with rate hysteresis (3/8 fainted).[42] Mc Leod et al compared three groups of symptomatic patients: 1) without pacemaker, 2) single-chamber pacemaker and, 3) dual-chamber pacemaker. They established that both pacing modes were equivalent, and more effective than no pacing, in preventing syncope. Dual-chamber pacing was superior to VVI pacing in preventing presyncope.[43] Some authors think that high stimulating frequency (120 beat per minute), can be superior to standard stimulating frequency (80 beats per minute) to improve symptoms and avoid syncopal episodes.[44]

Most of the patients with a pacemaker placed to correct the cardioinhibitory component of cardioneurogenic syncope, can also receive complementary medical therapy to inhibit the peripheral vasodilatation component. Patient-activated drug delivery systems using phenylephrine have been used to abort syncopal episodes with encouraging preliminary results.[45]

We can conclude that although pacing is not the first line therapy in patients with neurocardiogenic syncope, in some cases in which frequency and intensity of fainting deteriorates quality of life, and mainly in those in which the cardioinhibitory effect during the tilt-table test, could benefit with placement of dual-chamber pacemaker programmed with a drop response algorithm with high stimulating frequencies (120 beats per minute). For complete recommendations see Table 2.

3.2 Neuromuscular diseases

In some neuromuscular diseases such as myotonic dystrophy and Emery-Dreifuss muscular dystrophy, some patients can develop ventricular arrhythmias and atrioventricular disorders which can progress to complete AV block. In these patients permanent pacing will possibly be required.[47] Some authors have demonstrated disappearance of Stokes-Adams episodes through pacemaker implantation.[48] In these cases the recommendations will be those indicated for AV block.

3.3 Long-QT syndrome

In patients with congenital long-QT syndrome, therapy with ß-adrenergic blockers should be consider the first line of treatment, will be continued for life and should be supplemented with implantation of a permanent pacemaker only in cases where bradycardia or AV block is an important characteristic of the syndrome.[49] The use of oral ß-adrenergic blockers, is

considered the standard therapy and are usually successful in the long-term preventive treatment of important arrhythmias, however is has been demonstrated that in some patients a permanent pacing is fundamentally necessary, and even so the implantation of a cardioverter-defibrillator.

It is recommendable that besides the implantation of a pacemaker, ß-Adrenergic blocker therapy be continued.[50] Some consider that because of the availability of the cardioverter-defibrillator with dual-chamber pacing capabilities, and given the high risk in some patients it could be adequate to use it as first line therapy in symptomatic patients with high risk of sudden death. But since cardioverter-defibrillators do not prevent torsade de pointes, these patients should also continue with ß-adrenergic blockers.[51] See Table 7 for complete recommendations.

Class I
1.   Is indicated for sustained pause-dependent VT, with or without QT prolongation. (Level of Evidence: C)
Class IIa
1.   Is reasonable for high-risk patients with congenital long-QT syndrome. (Level of Evidence: C)
Class IIb
1.   May be considered for prevention of symptomatic, drug-refractory, recurrent AF in patients with coexisting SND. (Level of Evidence: B)
Class III
1.   Is not indicated for frequent or complex ventricular ectopic activity without sustained VT in the absence of the long-QT syndrome. (Level of Evidence: C)
2.   Is not indicated for torsade de pointes VT due to reversible causes. (Level of Evidence: A)

Table 7. Recommendations for pacing to prevent tachycardia[7]

3.4 Hypertrophic Obstructive Cardiomyopathy (HOCM)

HOCM is a primary myocardial disease, characterized by asymmetric hypertrophy of the interventricular basal septum, conditioning reduction between the posterior wall of the left ventricle (LV) and the septum, leading to abnormal systolic anterior motion of the anterior mitral leaflet, which generates dynamic obstruction of the LV outflow tract (LVOT). This obstruction causes significant gradient with important symptoms, predominantly during effort, such as dyspnea, angina, syncope, or even sudden death. Most of the patients with HOCM have normal or above normal systolic LV function. It is common to find stiffness of the LV due to hypertrophy, conditioning considerable diastolic dysfunction that generates a high LV end-diastolic pressure with reduced diastolic volumes, contributing to the symptoms (dyspnea). The clinical evolution is extremely variable, great proportions are asymptomatic, but 25% have important obstruction with abundant symptoms and bad prognosis. HOCM is considered the most frequent cause of effort-induced syncope or sudden death in people younger than 30 years.

Treatment has the primordial purpose of reducing LVOT gradient, facilitating systolic flow and improving diastolic filling, which also improves symptoms. The mayor conditioners of LVOT obstruction are systolic septal bulging, malposition of the anterior papillary muscle, drag forces, and hyperdynamic LV contraction conditioning the Venturi effect. Some investigators have demonstrated that afterload reduction with vasodilator agents, such as nitroglycerin, increases the gradient, as do positive inotropic drugs like digoxin, β-agonists, and exercise which also has positive inotropic effect.

The management of patients with HOCM comprises different areas: a) activity restriction to avoid volume depletion, b) improvement of symptoms and quality of life, c) improvement of survival rate and prevention of sudden death, d) to prevent and correct complications (syncope and arrhythmias), and finally e) screening of relatives.

Medical treatment has been used for chronic symptomatic HOCM patients, but in a small percentage (10%) of cases surgical options can be justified, if symptoms or an important LVOT gradient persist. Dual-chamber pacing (DDD) has been used in patients with HOCM without response to medical treatment.[52,53,54,55] In the early 90s permanent pacing was proposed not only as an alternative, but as a substitute of myectomy. The principle that explained the beneficial effect of DDD pacing was by achieving pre stimulation of the right ventricle apex, that way the LV empties before the basal portion contracts and conditions dynamic obstruction. It requires a precise adjustment on the ventricular stimulation (AV interval), that way at rest or exertion the pacemaker stimulates the apex and the distal septal region, without compromising ventricular filling or cardiac output. It improves the gradient and symptoms by 25%, although in most cases improvement has been measured based on the patient´s perception, which in most cases is only for short periods of time. Some think that pacing can condition deterioration of diastolic function[56], gradient decrease can be associated to important ventricular filling alterations and fall on the cardiac output, and LVOT gradient reduction can be quite modest and less than the one obtained by surgical myectomy.[53,54] Improvement on functional ability has not been demonstrated by pacing. Some authors even think that the perceived improvement after the pacemaker placement can be a placebo effect.[57,58,59,60,61]

Pacemakers have not demonstrated reduction in the risk of sudden death, nor conditions favourable LV remodelling. Some have suggested that DDD pacing can remodel and attenuate the hypertrophic septum as years goes by[54], but it has not been confirmed in prospective studies. There are three prospective randomized studies that analyzed the benefits of permanent pacing in the HOCM patient, without demonstrating the clinical or functional benefit. In fact, in one of the patients, after 9 months the LVOT gradient was similar to the one before surgery.[59,60]

The ACC/AHA guidelines for pacing consider it as class IIb in patients with symptomatic HOCM, and unresponsive to medical treatment, and class III in the patients that improve with β-blockers or calcium channel blockers. Even though the indications are clear, some studies in which the main objective is to define pacemaker utility, have included mildly symptomatic patients or even cases in which resting obstruction is not demonstrable, and only appears with provocation maneuvers[59] or even with dobutamine infusion.[62] Pacemaker implantation can be influenced by: a) implantation is simple and less invasive compared to myocardial ablation, b) common method, most cardiologists are familiarized with the technique, c) commonly used drugs are employed, without side effects like bradycardia, d) surgical myectomy or percutaneous transluminal septal myocardial ablation (PTSMA) can be done at a later time, e) it can be withdrawn or inactivated at any time. A useful strategy can be to place a temporary pacemaker and do hemodynamic measurements. If the gradient is not lowered, there will not be any benefit by placing a permanent pacemaker.[63,64,65] Some authors think that in patients over 65 years, pacing may condition clinical and hemodynamic improvement[60] and represents less risk than surgical myectomy and PTSMA. In patients with pacemakers we have the advantage of being able to increase β-blockers or verapamil doses, since they are protected from the deleterious effects like bradycardia. On the other hand, we can delay AV nodal conduction and facilitate synchronization and ventricular apex pre stimulation.

In 1995, a group of investigators placed a DDD pacemaker on a group of paediatric patients with non obstructive asymptomatic hypertrophic cardiomyopathy, in an attempt to interfere with genetic forces that later on, could develop LVOT obstruction. This was deeply criticized and nowadays is not considered as a therapeutic option in these patients.[66,67,68]

Maron et al demonstrated in a group of patients older than 65 years, objective improvement of symptoms after DDD pacing. Yufu et al analyzed results in one patient, after placement of one apical epicardial electrode on the LV, with apparent improvement. Komsuoglu et al reported the case of one patient with resting LVOT gradient of 130 mmHg, that reduced to 100 mmHg with DDD pacing with synchronized right auricular and ventricular stimulation, and reduced it to 20 mmHg after the placement of a biventricular pacemaker (atrial sensing and synchronous right and left ventricular pacing), placing percutaneously the LV electrode on the distal segment of the cardiac veins to have an early stimulation of the posterolateral LV wall. Unlike Yufu, they did not found improvement by stimulating only the LV.

In patients with high risk of severe ventricular arrhythmias or even on survivors of sudden death, the use of an implantable automatic defibrillator has been recommended. Results have been variable in these patients. In patients with ventricular tachycardia usefulness of an implantable defibrillator has been analyzed. In patients with high LVOT gradient in which an implantable cardioverter defibrillator (ICD) is indicated, we can obtain larger benefit if we use the DDD or biventricular component of the ICD.

4. Selecting the stimulation mode

The main issues to take into account in the decision-making process to determine the optimal pacing mode are: the diagnosis that is causing the permanent cardiac stimulation indication, the need to maintain AV synchrony and the presence of chronotropic incompetence that demands to implant a device with rate response sensor. Other special features can influence the pacemaker type and the stimulation mode selection, for example: devices with capability to deliver atrial therapies (AF prevention or antitachycardia stimulation), prolonged longevity battery, automatic capture verification, etc.

4.1 Sinus Node Dysfunction (SND)

The algorithm in Figure 1 synthesizes the critical path in pacing mode selection for SND.

Given the fact that in a patient with SND and normal AV conduction, the cardinal problem is sinus impulse generation, at least theoretically, ideal pacing mode is AAI. However, other methods have been studied, namely right ventricular pacing (VVI) and DDD. The current evidence that helps to guide the decision in this aspect is exposed in the next sections.

4.1.1 Risk of AV block development

An important matter is the concern about the risk of AV block in the following years after pacemaker implantation. In the Danish study directed by Nielsen et al, (atrial vs. dual-chamber pacing), the incidence of symptomatic AV block after a follow-up period of 2.9 years, was 1.9% per year.[69]

4.1.2 Atrial based versus ventricular pacing protocols

There is little information comparing atrial stimulation with other modalities. The only major randomized trial that included a true atrial pacing arm (AAI) compared with VVI was

the reported by Andersen and colleagues. They found a beneficial effect of atrial pacing sustained over time (8 years of follow-up), with improvement in survival, less atrial fibrillation, fewer thromboembolic complications, less heart failure, and a low-risk of atrioventricular block.[70,71]

In the Danish study, when atrial pacing was compared with dual-chamber stimulation, DDDR pacing caused increase in left atrium diameter and AF resulted significantly less common during AAIR pacing.[69]

Furthermore, there are few doubts about the obtained benefits by aiming to preserve the intrinsic ventricular activation. The MOST substudy linked the RV pacing rate with the risk of hospitalization due to heart failure and the probability to develop AF.[72] Moreover, in the DAVID study (patients with implantable defibrillator), primary outcome of death or heart failure (HF) hospitalization was less common (13.3 vs. 22.6%) in the group that maintained intrinsic ventricular rhythm in comparison with patients with predominant ventricular paced rhythm.[73]

A meta-analysis of the five main trials showed a significant reduction in the AF incidence and, possibly, ictus incidence, when selected pacing mode was an atrial based protocol (AAI/DDD) against ventricular single-chamber protocols.[74]

4.1.3 Algorithms to reduce ventricular stimulation in SND

Assuming the fact that ventricular stimulation has deleterious effects in cardiac function, stimulation protocols have been conceived attempting to reduce right ventricular pacing. Basically, there are two modalities: those who include AV interval (AVI) lengthening, and the minimal ventricular pacing (MVP) protocol. The first consist in programming a prolonged basal AV interval or an algorithm of AV hysteresis. AV hysteresis consists basically in a gradual lengthening of the programmed AV interval to determine if an intrinsic ventricular depolarization occurs within certain interval. In the MVP protocol, a DDDR stimulation mode changes to AAIR when spontaneous AV conduction is detected. When AV block occurs persistently, then AAIR mode turns into DDDR. This protocol has demonstrated to reduce ventricular stimulation rate in a larger proportion than other algorithms. In fact, the SAVEPACE trial, that included 1070 patients with dual chamber pacemaker, with and without MVP protocol, reported that patients without MVP showed 99.1% of ventricular pacing, while MVP patients had 9.1%. AF incidence was 7.9% in the MVP group and 12.7% in the other.[75]

4.1.4 Summary

In isolated SND, in absence of AV node conduction abnormalities, seems reasonable to choose an atrial based stimulation mode (AAI or DDD), while programming algorithms favoring intrinsic ventricular activation. This approach appears to be related with a reduction in the incidence of AF, HF related hospitalizations, and possibly, in the occurrence of stroke. Moreover, since AF is not infrequent in patients with SND, is essential to implant a pacemaker with automatic mode switching (AMS).[69-76]

4.2 Atrioventricular block

In most patients with AV block it is desirable to maintain AV synchrony, but mainly in those with LV dysfunction. As has been mentioned before, single-chamber RV stimulation eliminates cardiac activation synchrony, with negative effects in the risk of AF, LV failure,

and mitral regurgitation development.[69,70,71,75] That pathophysiological changes lead to negative clinical outcomes: increase in the incidence of death, HF hospitalizations and ictus.[72,73,74]

On the other hand, advanced age is sometimes advocated as a reason to prefer single-chamber stimulation. At this point, it is noteworthy to mention that almost every main trial was conducted in old people (the population at higher risk of conduction disturbances).[69-75]

When selecting the pacing mode in a patient with AV block, the first question to answer is if there is the desire to maintain the AV synchrony (if patient maintains sinus impulse generation and has no atrial arrhythmias precluding atrial sensing/pacing). The next aspect is to look for chronotropic incompetence, to evaluate the need of a rate response sensor. Then, one can ask if atrial stimulation is desired (for example to prevent AF or to treat supraventricular tachyarrhythmias).

The algorithm in Figure 2 shows a decision tree diagram to determine pacing mode for AV block.
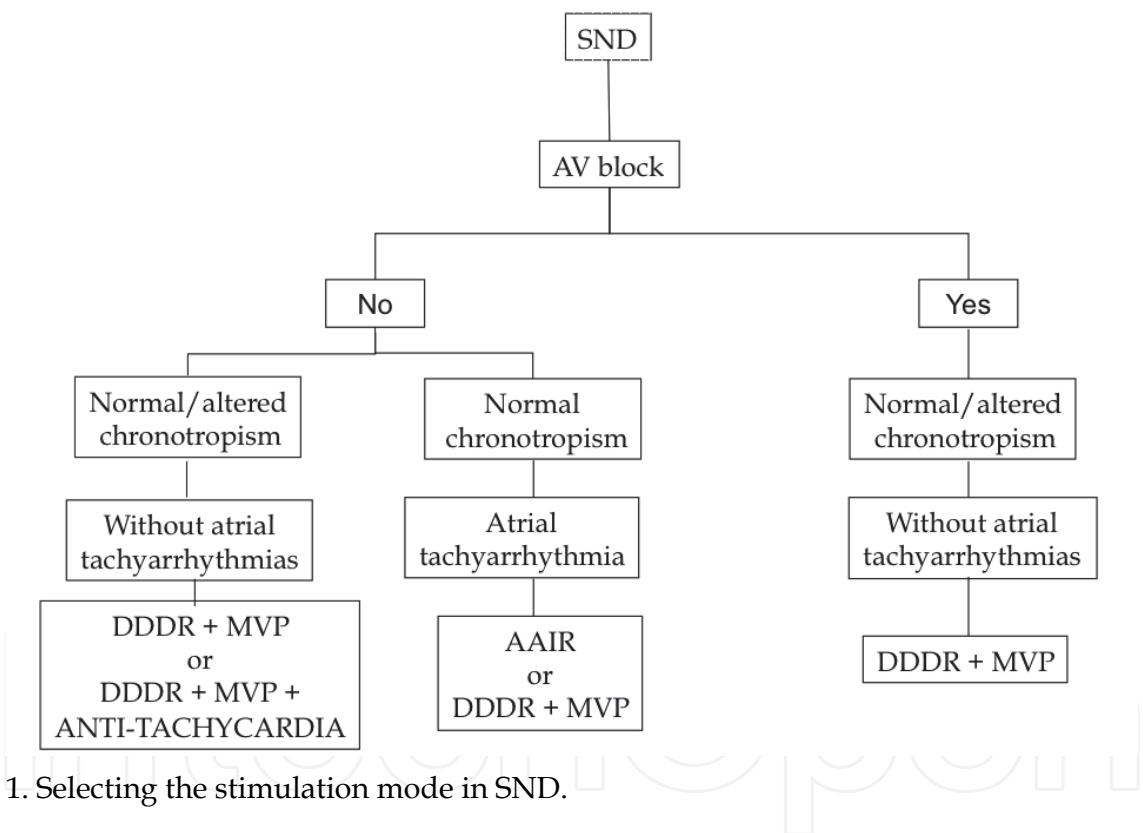
Fig. 1. Selecting the stimulation mode in SND.

4.3 Other indications

Apart from patients suffering from bradyarrhythmia (for example SND and AV block), other pacemaker indications deserve some specific comments about programming.

4.3.1 Neurocardiogenic syncope

Usually, patients do not have basal bradycardia and do not need permanent cardiac stimulation. Pacemaker only stimulates if patient develop bradycardia or asystole as part of a cardioinhibitory response. Moreover, some current devices contain programmable drop rate response algorithms, which activates if sudden bradycardia develops.

4.3.2 Heart failure

Cardiac resynchronization therapy optimal response depends on assuring a constant cardiac stimulation. For this reason, programming an appropriate AV delay and confirming ventricular pacing events (by reviewing counters and histograms) is essential.

4.3.3 Tachyarrhythmias

In the rare cases treated with a pacemaker, algorithms that automatically detects arrhythmia and applies antitachycardia pacing (ATP) exists. ATP needs to be individualized according to the arrhythmia rate and response to therapy.

4.3.4 Hypertrophic cardiomyopathy (HCM)

As in patients with heart failure, LV outflow tract gradient reduction in HCM depends on a constant ventricular stimulation. Attention needs to be paid in programming an appropriate AV delay and confirm ventricular pacing.
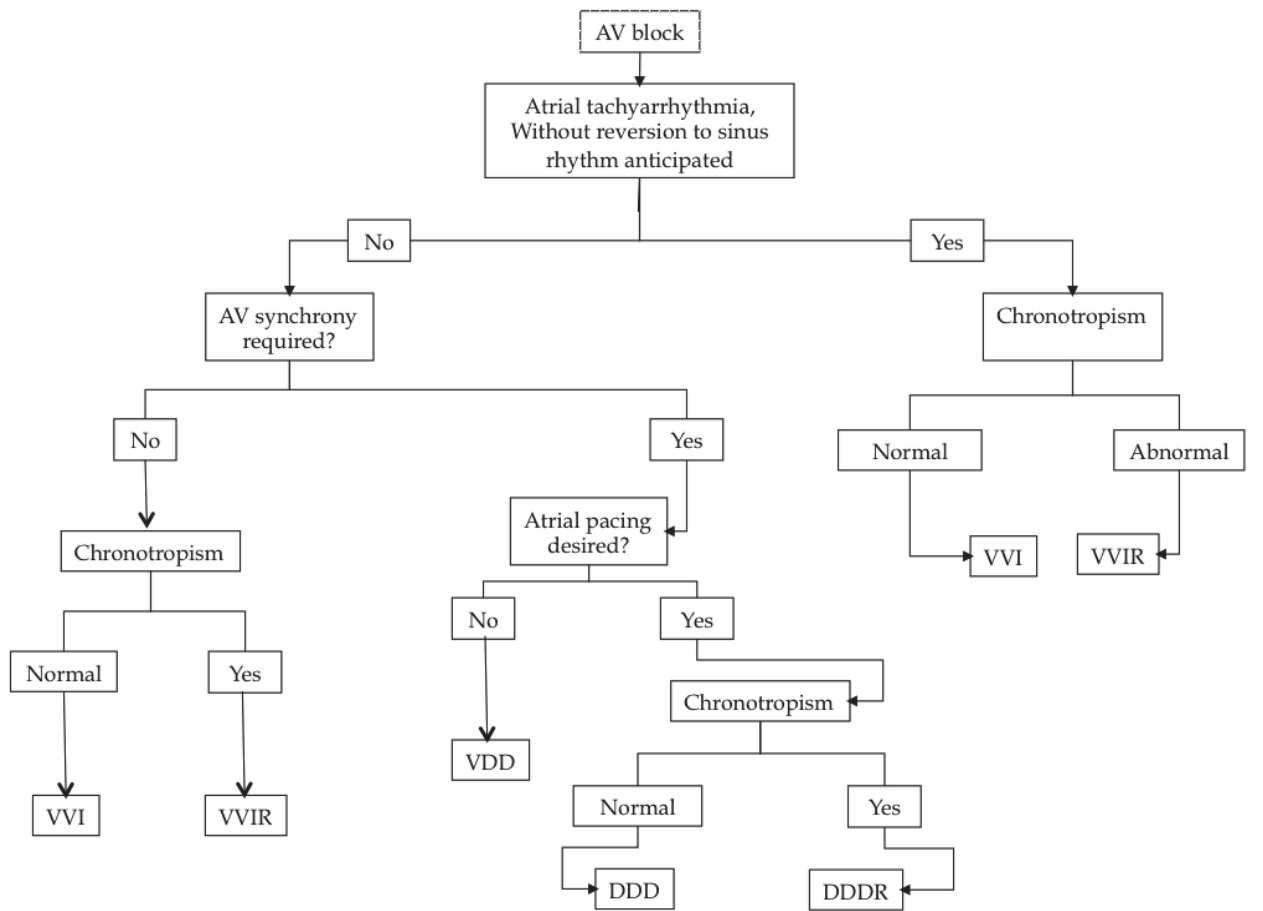
Fig. 2. Selecting the stimulation mode in AV block.

5. Device implantation techniques

A detailed description of the implantation techniques is beyond the scope of this chapter. We will approach some of the more important aspects to consider when a pacemaker is to be implanted.

5.1 Patient preparation

As in any invasive procedure, is mandatory to obtain written consent. A peripheral intravenous line must be placed, preferably in the arm of the planned implant side (of aid in case of requiring venography). Most of pacemaker implants are done in the left thoracic wall, mainly because of operator's choice and comfort. Conscious sedation is optional. Antibiotic prophylaxis is guaranteed and is determined by local antimicrobial guidelines, generally with coverage for G+ and staphylococcus. In the vast majority of cases, a single dose of a penicillin type antibiotic (for example a cephalosporin) can be used within 2 hours before operation. Antibiotics like vancomicyn and gentamicin are becoming more and more used, particularly in patients considered at high risk of infection.

Once in the operation room, implant area is prepared with antiseptic and delimited with sterile towels.[77,78]

5.2 Pocket formation

Three types of incisions are mostly used: deltopectoral, horizontal and oblique. By the time the incision site has been chosen, a local anesthetic is infiltrated at implantation area. In order to make the pacemaker pocket it should be decided if it will be subcutaneous or submuscular, depending on patient's characteristics (subcutaneous tissue thickness) and the pulse generator size. Subcutaneous pocket is easier to make and less painful, but it is imperative to reach the correct layer, the prepectoral fascia. The submuscular pocket requires a shallow incision in the pectoralis major, then blunt dissection up to pectoralis minor (intramuscular) or up to ribcage, beneath pectoralis minor (subpectoral). It is painful, but ordinarily can be performed under conscious sedation.

Pocket can be made before or after venous access, according to operator's preference.[77-79]

5.3 Venous access

Venous access is more frequently obtained by one of two techniques: dissection and vascular incision with direct vein visualization (commonly in the cephalic vein) and by venous puncture (usually directed to the subclavian vein). Cephalic vein dissection has lower pneumothorax and lead crush risk, however, more surgical skill is required and difficulties to introduce more than one lead can arise. Apart from the mentioned techniques, another venous access sites exists, for example, axillary, internal jugular or femoral veins. Nevertheless, although they can be used under certain circumstances, they are not of rutinary choice.[77-79]

5.4 Right ventricular lead placement

Lead placement is facilitated by positioning fluoroscopy in the right anterior oblique (RAO) projection, which helps to define the apex of the RV. The stylet is manually curved in a moderate angle (this action is learned with the experience). With the curved stylet in place, the lead is advanced across the tricuspid valve and then out to the pulmonary artery. Retracting the stylet 1-2 cm usually facilitates passage to the pulmonary artery. Once in the pulmonary artery, the stylet is advanced again to the lead tip. Now, the electrode body is gently retracted up to the midpoint of the interventricular septum. The stylet is retracted 1-2 cm and the floppy lead tip drops into the RV apex. Because the stylet is retracted, the lead tip is supple, precluding perforation of the RV. Adjustment of the tip position can be made by retracting and advancing the electrode, and, if necessary, by changing the curved one for

a straight stylet. Gently pulling the electrode is a reliable method to confirm that fixation of the lead has been achieved. This maneuver should not be performed in active fixation leads. Positioning an active fixation lead is similar, but once the lead tip is in the desired position, the helix fixation is released and the stylet removed. [77-79]

5.5 Atrial lead placement

Essentially, there are two techniques, depending on the type of lead selected. If a preformed, passive fixation mechanism, "J" curve lead is utilized, the straight stylet is used to straighten the preformed J. In this case, after the venous access, the lead is advanced to the mid right atrium, and then, the stylet is withdrawn several centimeters while the lead tip gains its J configuration. The lead body is then slowly advanced to push it into the right atrial appendage, which is confirmed by fluoroscopy (in the antero-posterior projection, the tip of the lead will move medial to lateral with each atrial contraction).

When a straight, active fixation lead is selected, then a preformed J stylet is used to take the lead tip to the desired position. Once in there, helix fixation is released and the J stylet removed. [77-79]

5.6 Measuring pacing and sensing thresholds

Every time each lead is positioned and suture-fixed, pacing and sensing thresholds are measured to determine its correct performance.

Table 8 summarizes the acceptable thresholds for the atrial, RV and coronary sinus (CS) leads. Once thresholds are measured, leads are screwed into pacemaker generator and pocket is sutured. [77-79]

	Atrial lead	RV lead	CS (LV) lead
Voltage threshold	<1.0 V (0.5 ms)	<1.0 V (0.5 ms)	<3.0 V (0.5 ms)
P/R amplitude	≥2.0 mV	≥4.0 mV	≥5.0 mV
Impedance	200-1000 ohm	200-1000 ohm	300-1000 ohm

Table 8. Acceptable pacing and sensing thresholds.

5.7 Procedure related complications

The more frequent procedure related complications are mentioned in Table 9.[80,81]

Eberhardt and colleagues reported the main factors related to procedural complications. They underwent a retrospective analysis of 1884 patients who received a pacemaker. The global complication rate was 4.5%. Complication occurrence was increased by age, reduced LV function, and RV dilatation. Dual-chamber system implantation led to a higher complication rate (6.3%) than implantation of single-chamber (2.6%) or VDD pacemakers (3.2%). These differences were encountered only among operators with a low or medium level of experience.[81]

Moreover, a recent study, with a very large cohort, reported that implant related infections are relatively rare (192 cases/236,888 pacemaker-years, which counts for an incidence rate of 4.82 cases/1000 pacemaker-years) after first implantation. Independent factors associated with an increased risk of infection were a greater number of surgical procedures (including

replacements), male sex, younger age, implantation during the earliest part of the study period, and absence of antibiotics.[82]

Pocket complications	Lead complications
Pocket hematoma Infection Erosion Migration of generator Twiddler´s syndrome Generator extrusion	Dislodgement Infection Vein thrombosis Air embolization Diaphragmatic stimulation CS dissection/perforation Myocardial perforation/tamponade

Table 9. Pacemaker implant complications

6. Clinical follow up for patients with pacemaker

Follow up office visits after a pacemaker implant, varies according to each center, but in general, may be performed twice in the first 6 months and then once every 6-12 months. More commonly, patients come to pacemaker checking several times during the first year, and then once or twice a year after that. As elective replacement is approaching, visits should be more frequent. The technician and/or nurse is a very valuable allied in this setting, because they carry out the majority of pacemaker checks at the outpatient consult.[83]

6.1 Main programming parameters

A normal follow-up visit to the outpatient pacemaker clinic may take a few minutes if patient is asymptomatic, there are no activated alarms and main parameters are normal. However, as technology advances, device complexity is arising and today we have multiple programmable parameters. The knowledge of theses parameters and its programmability enables the clinician in the follow-up problem solving process.[84,85]

Table 10 summarizes the main programming parameters and its possible applications.

7. Cost-benefit in pacemakers

Any measure oriented to optimize battery longevity will positively impact cost-efectiveness. Such measures may consist in improving pulse generator and leads technology or in optimizing pacemaker programming (above all, output voltage, pulse width and AV delay). In fact, reprogramming pulse generator may extend the estimated longevity by 4.25 years at a low cost, according to a report of Crossley et al.[86] It is expected that software algorithms, like automatic capture verification, help in increasing battery duration.

Obviously, dual-chamber systems are more expensive. However, considering aspects like quality of life is important in the evaluation of costs. Rinfret et al performed a cost-effectiveness analysis of pacemakers in SND and concluded that dual-chamber pacing increases quality-adjusted life expectancy at a cost that is generally considered acceptable.[87]

Parameter	Programmability	Application
Rate	Increase	Optimize cardiac output. After AV node RF ablation.
	Decrease	Minimize RV pacing. Adjust rate below angina threshold.
Voltage	Increase	Adapt to higher pacing threshold.
	Decrease	Enhance battery longevity. Reduce extracardiac stimulation (phrenic nerve, pectoral muscle).
Sensitivity	Increase	Correction of undersensing of P/R waves.
	Decrease	Correction of oversensing (T wave, myopotentials).
Refractory period	Increase	Atrial: minimize sensing of V far-field potentials. RV: minimize sensing of A far-field potentials (crosstalk).
	Decrease	Detection of early premature ventricular beats.
Hysteresis		Minimize RV pacing.
Detection/stimulation polarity	Conversion to unipolar mode	Optimize signal sensing. To obtain a more secure stimulation.
	Conversion to bipolar mode	Minimize electromagnetic or myopotential interference. Elimination of extracardiac anodal stimulation.
AV interval	Increase or decrease to optimize LV function	Increase: minimize RV pacing. Decrease: adaptative shortening according to heart rate (more physiologic). Optimize AV synchrony in HF.
PVARP	Increase	Prevent sensing of retrograde P waves, treatment of PMT.
PVARP extension after a PVC	On/off	Prevent sensing of retrograde P waves after a PVC
Post-atrial ventricular blanking period	Increase	Prevent crosstalk
Ventricular safety pacing	On/off	Assurance of ventricular stimulation in the presence of crosstalk

Abbreviations: AV= atrioventricular; RF= radiofrequency; RV= right ventricle; V= ventricular; LV= left ventricle; HF= heart failure; PVARP= post ventricular atrial refractory period; PMT= pacemaker mediated tachycardia; VPC= premature ventricular contraction.

Table 10. Main programming parameters and its applications.

8. Future perspectives on cardiac stimulation

There are many areas under investigation and others that need to be covered. The following is a selection of these areas.

Pacemakers availability. Above all in developing countries, further efforts needs to be done to extend pacemaker access to all eligible population.

Pacemakers technology. Improvements in hardware, software, battery and leads technology, will permit to obtain better clinical results as well as improved device performance and duration.

Pacemaker indications. Clinical applications of cardiac stimulation are under extensive research. Aspects like biventricular or LV pacing in patients with normal systolic function or in congenital heart disease needs to be determined.

Remote monitoring. This technology seems to represent a cost-effective tool to maintain an efficient and secure follow-up evaluation as a part of a well organized program. It is necessary to develop guidelines to norm its use.[7]

9. Conclusion

Permanent pacing is a therapy that can be lifesaving, established indications for main clinical syndromes and other specific conditions should be evaluated to offer the patient the best possible treatment. Once implanted determining the optimal stimulation mode is crucial, as it is to keep in mind all the possible complications inherent to the procedure. Clinical follow-up is as important as the implantation technique, to assure the patient the best quality of life possible.

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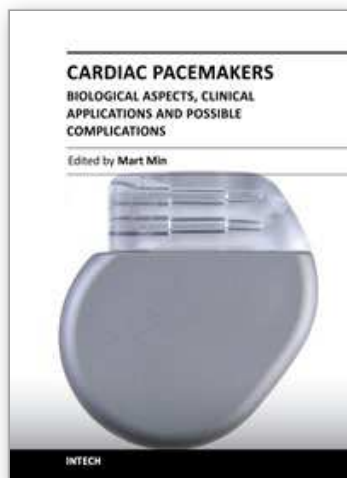
Cardiac Pacemakers - Biological Aspects, Clinical Applications and Possible Complications

Edited by Prof. Mart Min

Clinical usage of artificial pacing dates back to 1958, when the battery powered cardiac pacemakers became available. Modern implantable pacemakers are the complicated electronic devices operating 10 years continuously without battery exchange. Though the development of devices is not a primary topic of the book, certain efforts towards developing of biologic pacemakers through tissue engineering and studying of cell synchronization are discussed. The main attention is paid to implementations of pacemakers in different medical situations oriented towards widening the clinical indications for implanting the cardiac pacemakers. New methods and devices in cardiac resynchronization therapy (CRT) have received particular attention. Placing of pacing electrodes has been treated soundly. Furthermore, emerging of complexities and complications in new clinical situations and other safety problems have been discussed thoroughly. The authors have derived the used information from their own clinical practice and experiences of their medical colleagues. These and other pragmatic features can be acknowledged as the most valuable asset of the book.

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