

Evidence-based management of cardiac arrhythmias

(Ital Heart J 2004; 5 (Suppl 1): 1S-3S)

© 2004 CEPI Srl

PERMANENT CARDIAC PACING

Panos E. Vardas

Cardiology Department, Heraklion University Hospital, Heraklion, Crete, Greece

Cardiac pacing is an established treatment for the prevention of a systole, while recently it has been used as an adjunctive therapy in non-bradycardic diseases. For almost 45 years cardiac pacing has offered an improvement in quality of life and/or prolonged survival in patients with complete heart block and sick sinus syndrome. Additionally, during the last 10 years pacing has proved valuable in patients with congestive heart failure and ventricular conduction disturbances, improving quality of life and reducing morbidity and possibly mortality. Furthermore, the role of cardiac pacing has been evaluated in patients with hypertrophic cardiomyopathy and in those with atrial fibrillation (AF). Apart of indications for cardiac pacing, in recent years we have learned a great deal about the most appropriate mode of pacing for each disease and the proper patient follow-up.

It should be noted that our knowledge concerning various aspects of pacing comes either from large or small observational studies, or from better organized randomized studies.

The AHA, ACC and NASPE reviewed and ranked evidence supporting current recommendations, with the weight of evidence ranked as level A if the data were derived from multiple randomized clinical trials, as level B when the data were derived from a limited number of randomized trials or well organized observational studies, and as level C when the consensus of experts was the primary source of recommendation. In the text that follows we shall refer to the most basic classical indications for pacing, i.e. acquired atrioventricular (AV) block, sick sinus syndrome and neurocardiogenic syncope, as well as the latest indications relating to heart failure, hypertrophic cardiomyopathy and AF.

Conventional indications

Acquired atrioventricular block. AV block is classified as first, second, or third degree, as well as according to its location: supra-, intra-, or infra-His. Patients with AV conduction disturbances may be asymptomatic or may exhibit severe symptoms due to bradycardia, ventricular arrhythmias, or both. The decision to implant a permanent pacemaker is based mainly on the existence of symptoms that are directly related to bradycardia. The indications are based mainly on experience and to a lesser degree on randomized studies, since there are no accepted alternative treatments for most bradycardias. In the case of patients with third degree heart block, non-randomized studies have shown that pacing prolongs survival, especially in patients with syncope¹. In contrast, for patients with first degree heart block there is little evidence to suggest that cardiac pacing prolongs survival². However, it has been recognized that exaggerated first degree AV block (PR > 300 ms) can lead to symptoms that are due to the desynchronization of the atrial and ventricular systole³. In such cases, small, non-randomized studies have shown that cardiac pacing, by restoring the AV synchronization, improves patients' symptoms and functional capacity⁴.

For second degree type I heart block, which is usually due to delay within the AV node and rarely develops into higher degree block, cardiac pacing is not usually indicated, unless the patient is symptomatic or electrophysiological study shows the conduction disturbance to be infranodal³⁻⁴. However, this is still something of an open question⁵. In contrast, in second degree type II heart block the conduction disturbance is usually infranodal, especially when there is a wide QRS. In that case the patient is usually symptomatic, the prognosis is compromised and the appearance of third degree heart block is a frequent development^{3,6}. Thus, second degree, type II block with a wide QRS comprises an indication for permanent pacing even in asymptomatic patients.

In the case of third degree heart block cardiac pacing is absolutely indicated in symptomatic patients and also in asymptomatic patients, especially when the escape rhythm is low (< 40 b/min). Furthermore, heart block that appears on effort and is not due to myocardial ischemia indicates a disturbance of the His-Purkinje system and is associated with a bad prognosis. In this case, too, implantation of a permanent pacemaker is indicated⁷. In contrast, in patients with sleep apnea and high degree heart block without symptoms, the rhythm disturbances can usually be eliminated using nasal continuous positive airway pressure (nCPAP) treatment, so permanent pacing is not required⁸. Of course, if the patient is symptomatic pacemaker implantation is necessary. More generally, our decision should also take into account the existence of other treatable conditions, such as electrolyte disorders, hypothermia, hypervagotonia during surgery, and so on.

As regards the choice of pacing mode, if there is no permanent atrial arrhythmia then it is preferable to choose a mode that maintains the AV sequence. This may be achieved by implanting a DDD or a single-lead VDD system. Of course, if the atrial mechanical activation is permanently abolished then the most appropriate mode is VVIR.

Sinus node dysfunction. The term "sinus node dysfunction" is used to describe a wide range of arrhythmias, including sinus bradycardia, sinus pauses, brady-tachy syndrome and sick sinus syndrome. Permanent pacing has a role to play in those cases where the bradycardia causes symptoms, even though it is usually difficult to connect the symptoms with the bradycardia because of the sporadic nature of the episodes. The use of an implantable device for the long-term monitoring of cardiac rhythm can help in this connection. Indirect evidence that the patient's symptoms are due to sinus node dysfunction may be obtained from an electrophysiological study, i.e. a prolonged sinus node recovery time or sinoatrial conduction time. However, the sensitivity of the method is low. Pacing is indicated mainly for improvement of symptoms and not for prolongation of life⁹. There has been much discussion in recent years regarding the pacing mode that should be used in patients with sick sinus syndrome. Recent, well-organized studies have shown that the AAI(R) mode is the best, in that compared with VVI(R) and even DDD(R)¹⁰⁻¹² as it leads to better quality of life, better survival and a lower incidence of AF. Since, however, in a small percentage of patients the sinus node disorder may be followed by disturbances of AV conduction, a dual-chamber pacing device should be implanted and programmed so that the ventricle will not be paced unless such disturbances appear^{3,13}.

Neurocardiogenic syncope and hypersensitive carotid sinus syndrome. Neurocardiogenic syncope, in which triggering of a neural reflex results in arterial hypotension due to bradycardia and/or vasodilation, accounts for 10-40% of syncopal episodes. The role of cardiac pacing in neurocardiogenic syncope is controversial. Although three

randomized studies^{14,15} reported that pacemaker therapy reduces the risk of recurrent syncope in patients with vasovagal syncope, the results of the recently published VPS II study¹⁶ were different. This study, which was unique because of its double blind design, found that pacing produced no true benefit. We believe that there is more to learn about this syndrome and the role of cardiac pacing in its treatment. For the moment, cardiac pacing should be used only in highly symptomatic patients when all other kinds of therapy have failed.

Hypersensitive carotid sinus syndrome is a type of pathological response of the autonomic nervous system affecting the circulation and is classified as cardioinhibitory, vasodilatory or mixed. It is well known that some asymptomatic patients may exhibit a pathological response during carotid sinus massage. However, in certain patients with recurring episodes of syncope that occur during rotation or extension of the head or while wearing a tight tie, hypersensitive carotid sinus syndrome is very likely. In these patients carotid sinus massage usually reproduces the syncopal episode. Cardiac pacing is beneficial in the cardioinhibitory or mixed forms of the syndrome. Here, too, our knowledge comes from only a small number of studies^{17,18}.

Non-bradycardic pacing indications

During the last decade the role of cardiac pacing has been investigated as an adjunctive therapy in patients with hypertrophic cardiomyopathy or those with a hypertrophic left ventricle because of hypertension. In both cases we see an excessively strong systole, elevated end-diastolic pressures and reduced filling volumes, resulting in a lower cardiac reserve and symptoms such as fatigue and precordial discomfort, despite normal coronary arteries. Cardiac pacing with right apical preexcitation increases the end-systolic volume and reduces cavity obliteration, thus increasing systolic reserve¹⁹. Studies that have evaluated the clinical effect of permanent cardiac pacing have produced conflicting findings, and have shown that pacing benefits mainly elderly patients and those with severely reduced exercise tolerance²⁰.

More significant, perhaps, is the role of cardiac pacing in the treatment of patients with dilated cardiomyopathy and disturbances of intraventricular conduction. It has been shown that atrio-biventricular pacing in patients with an ejection fraction $< 35\%$, QRS > 120 or 130 ms, and in NYHA class III or IV leads to a direct improvement in the hemodynamic profile, while in the long term it reduces symptoms, improves quality of life and causes a reversal of remodeling. This means that it slows the progress of the disease, while in combination with an implantable cardioverter-defibrillator it can achieve a significant reduction in mortality. These observations have been confirmed by large, randomized, placebo-controlled studies²¹⁻²³.

AF is the most common chronic tachycardia. Therapeutic modalities to treat AF include antiarrhyth-

mic drugs, atrial pacing, ablation techniques, atrial defibrillators and combined (hybrid) therapies.

Atrial pacing could prevent the onset of AF through several mechanisms, such as the prevention of the relative bradycardia-induced dispersion of refractoriness, the suppression or reduction of atrial ectopic beats that initiate reentry or predispose to AF, the reduction of the interatrial conduction delay and dispersion of refractoriness and the preservation of AV and ventricular synchrony, which could prevent stretch-induced changes in atrial repolarization predisposing to AF.

Atrial pacing is beneficial in patients with conventional pacing indications. Preservation of the AV and, more importantly, the ventricular activation sequence is an important aspect of AF prevention^{10,11}. There is a strong association between the increased percentage of atria being paced and a decreased AF burden in patients with sick sinus syndrome. The utility of atrial pacing to prevent AF in patients with no conventional pacing indications has not been proven. Even though studies of specific preventive algorithms²⁴ and alternative²⁵ or dual pacing sites²⁶ have produced inconclusive results, these do seem to help in the prevention of atrial tachyarrhythmias in certain groups of patients. It seems likely that pacing combined with other therapeutic modalities (hybrid therapies) could be more effective.

References

- Edhag O, Swahn A. Prognosis of patients with complete heart block or arrhythmic syncope who were not treated with artificial pacemakers: a long-term follow-up study of 101 patients. *Acta Med Scand* 1976; 200: 457-63.
- Barold SS. Indications for permanent cardiac pacing in first degree AV block: class I, II, or III? *Pacing Clin Electrophysiol* 1996; 19: 747-51.
- Dhingra RC, Denes P, Wu D, Chuquimia R, Rosen KM. The significance of second degree atrioventricular block and bundle branch block: observations regarding site and type of block. *Circulation* 1974; 49: 638-46.
- Strasberg B, Amat-Y-Leon F, Dhingra RC, et al. Natural history of chronic second-degree atrioventricular nodal block. *Circulation* 1981; 63: 1043-9.
- Connelly DT, Steinhaus DM. Mobitz type I atrioventricular block: an indication for permanent pacing? *Pacing Clin Electrophysiol* 1996; 19: 261-4.
- Ranganathan N, Dhurandhar R, Phillips JH, Wigle ED. His Bundle electrogram in bundle-branch block. *Circulation* 1972; 45: 282-94.
- Barold SS, Falkoff MD, Ong LS, Vaughn MJ, Heinle RA. Atrioventricular block: new insights. In: Barold SS, Mugica J, eds. *New perspectives in cardiac pacing*. Mount Kisco, NY: Futura Publishing Company, 1991: 23-52.
- Grimm W, Koehler U, Fus E, et al. Outcome of patients with sleep apnea-associated severe bradyarrhythmias after continuous positive airway pressure therapy. *Am J Cardiol* 2000; 86: 688-92.
- Rasmussen K. Chronic sinus node disease: natural course and indications for pacing. *Eur Heart J* 1981; 2: 455-9.
- Andersen HR, Thuesen L, Bagger JP, Vesterlund T, Thomsen PE. Prospective randomised trial of atrial versus ventricular pacing in sick-sinus syndrome. *Lancet* 1994; 344: 1523-8.
- Andersen HR, Nielsen JC, Thomsen PE, et al. Long-term follow up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. *Lancet* 1997; 350: 1210-6.
- Nielsen JC, Kristensen L, Andersen HR, Mortensen PT, Pedersen OL, Pedersen AK. A randomized comparison of atrial and dual-chamber pacing in 177 consecutive patients with sick sinus syndrome: echocardiographic and clinical outcome. *J Am Coll Cardiol* 2003; 42: 614-23.
- Rosenqvist M, Obel IW. Atrial pacing and the risk for AV block: is there a time for change in attitude? *Pacing Clin Electrophysiol* 1989; 12: 97-101.
- Connolly SJ, Sheldon R, Roberts RS, Gent M. The North American Vasovagal Pacemaker Study (VPS): a randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. *J Am Coll Cardiol* 1999; 33: 16-20.
- Sutton R, Brignole M, Menozzi C, et al, for the Vasovagal Syncope International Study (VASIS) Investigators. Dual-chamber pacing in the treatment of neurally mediated tilt-positive cardioinhibitory syncope: pacemaker versus no therapy: a multicenter randomized study. *Circulation* 2000; 102: 294-9.
- Connolly SJ, Sheldon R, Thorpe KE, et al; VPS II Investigators. Pacemaker therapy for prevention of syncope in patients with recurrent severe vasovagal syncope: Second Vasovagal Pacemaker Study (VPS II): a randomized trial. *JAMA* 2003; 289: 2224-9.
- Brignole M, Menozzi C, Gianfranchi L, Oddone D, Lolli G, Bertulla A. Neurally mediated syncope detected by carotid sinus massage and head-up tilt test in sick sinus syndrome. *Am J Cardiol* 1991; 68: 1032-6.
- Kenny RA, Richardson DA, Steen N, Bexton RS, Shaw FE, Bond J. Carotid sinus syndrome: a modifiable risk factor for nonaccidental falls in older adults (SAFE PACE). *J Am Coll Cardiol* 2001; 38: 1491-6.
- Kappenberger L, Linde C, Daubert C, et al. Pacing in hypertrophic obstructive cardiomyopathy (PIC): a randomized crossover study. *Eur Heart J* 1997; 18: 1249-56.
- Maron BJ, Nishimura RA, McKenna WJ, Rakowski H, Josephson ME, Kieval RS. Assessment of permanent dual-chamber pacing as a treatment for drug-refractory symptomatic patients with obstructive hypertrophic cardiomyopathy: a randomized, double-blind, crossover study (M-PATHY). *Circulation* 1999; 99: 2927-33.
- Cazeau S, Leclercq C, Lavergne T, et al; Multisite Stimulation in Cardiomyopathies (MUSTIC) Study Investigators. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med* 2001; 344: 873-80.
- Abraham WT, Fisher WG, Smith AL, et al; MIRACLE Study Group. Multicenter InSync Randomized Clinical Evaluation. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002; 346: 1845-53.
- Young JB, Abraham WT, Smith AL, et al; Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) Trial Investigators. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. *JAMA* 2003; 289: 2685-94.
- Lee MA, Weachter R, Pollak S, et al; ATTEST Investigators. The effect of atrial pacing therapies on atrial tachyarrhythmia burden and frequency: results of a randomized trial in patients with bradycardia and atrial tachyarrhythmias. *J Am Coll Cardiol* 2003; 41: 1926-32.
- Padeletti L, Pieragnoli P, Ciapetti C, et al. Randomized crossover comparison of right atrial appendage pacing versus interatrial septum pacing for prevention of paroxysmal atrial fibrillation in patients with sinus bradycardia. *Am Heart J* 2001; 142: 1047-55.
- Delfaut P, Saksena S, Prakash A, Krol RB. Long-term outcome of patients with drug-refractory atrial flutter and fibrillation after single- and dual-site right atrial pacing for arrhythmia prevention. *J Am Coll Cardiol* 1998; 32: 1900-8.