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Pacing in older people

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Summary

The vast majority of cardiac pacemakers are implanted in older people. Pacing is a safe and effective treatment for patients with symptomatic bradyarrhythmias. This review provides a clinician's guide to the essential aspects of modern pacemaker therapy in older patients, including aetiology and epidemiology of bradycardia. We discuss some barriers to access to pacing. We review indications for pacemakers, and describe pacing system function, including the different types of pacemakers used. We also review clinical outcomes following pacing, follow-up requirements and problems encountered in clinical practice. Finally, we discuss ethical and end of life considerations with these devices.

Key words: cardiac pacemaker, bradycardia, conduction tissue disease, older people.

Introduction

Permanent cardiac pacing is a safe and effective treatment for patients with symptomatic bradyarrhythmias. The vast majority of pacemakers are implanted in older people; the mean age of patients receiving a first pacemaker is 75 years; over 85% of pacemakers are implanted in patients over 65 years old and approximately a third are implanted in patients aged over 80 years, a proportion that continues to increase as the population ages.[1] A knowledge of the evidence and issues related to pacing therapy in older patients is therefore important for physicians caring for older people. This review aims to provide a clinician's guide to the essential aspects of modern pacemaker therapy in older patients, including bradycardia aetiology, indications for pacemakers, and pacing system function. We will address the equity and under-provision of pacing therapy with particular reference to older patients. We also review clinical outcomes following pacing and ethical and end of life considerations with these devices. PubMed searches using the subject headings cardiac pacing and elderly were used in addition to detailed review of national and international guideline documents.

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Pathophysiology of bradyarrhythmias in older people

Diseases that disturb the cardiac conduction system at any point may lead to bradyarrhythmias, for which the only effective long-term treatment is cardiac pacing. The commonest indications for pacing are 'sinus node disease' (SND) and 'atrioventricular (AV) block', which together account for more than 97% of pacemaker implantations.[1] These clinical syndromes of heterogeneous aetiology occur with much higher frequency in elderly populations. It is not uncommon for SND and AV block to co-exist in older patients.

Atrioventricular block

AV block may be caused by disturbance of conduction at the level of the AV node, the bundle of His, or the bundle-branch Purkinje system. Acquired AV block in the older patient is characterized by increased collagen fibre deposition around the AV node and His-Purkinje system and abnormalities of apoptosis have been reported.[2] There are a number of secondary causes of AV block, which often occur more frequently in elderly populations, including coronary disease, annular calcification from valvular heart disease, particularly aortic stenosis, infiltrative cardiac disorders, inflammatory disorders, malignancy and trauma (particularly following cardiac valve replacement surgery). Sometimes AV block may be deliberately induced by catheter ablation to control the ventricular rate in refractory atrial tachyarrhythmias with a strategy of permanent pacing to maintain a stable heart rate.

AV block is classified according to the level and degree of the block.[3] First-degree AV block occurs when there is delay in conduction from the atria to the ventricles, and is manifest by prolongation of the PR interval on the surface ECG, with

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maintenance of a 1:1 relationship between the P waves and the QRS complexes. A relationship between P waves and QRS complexes is maintained in second-degree AV block, although it is no longer 1:1. Mobitz type I second-degree AV block describes intermittent failure of AV nodal conduction, with increasing prolongation of the PR interval, until a QRS complex is dropped. This often occurs at the level of the AV node and is also known as the Wenckebach phenomenon. In Mobitz type II block there are also dropped P waves, but the PR interval in conducted beats remains constant. The QRS complex is often wide, and the level of block is usually within the His-Purkinje system. When 2:1 or 3:1 block is observed, it is not usually possible to characterize it further; and it is sometimes called high grade AV block. Third-degree AV block occurs when there is complete dissociation between the P waves and the QRS complexes, and is also known as complete heart block.

Conduction system disease may be fixed, e.g. when there is chronic complete heart block, and it may then be associated with fatigue, exercise intolerance, heart failure, or other consequences of hypoperfusion. High grade and complete AV block may also be intermittent, and may then be associated with dizzy spells, falls, or syncope. Complete heart block may be intermittent in as many as two-thirds.[4,5] It may also be asymptomatic.

Escape rhythms originating from other parts of the conduction system usually occur in patients with complete AV block, the rate and QRS duration depending on the anatomical site of the escape rhythm. Rhythms arising proximally within the specialized conducting tissue tend to produce a narrow QRS complex typically at a rate of 45–60 per minute, while those arising more distally produce a wide QRS complex at a slower rate.

Sinus node disease

SND (or sick sinus syndrome) occurs when there is a problem with the generation of the action potential within the sinus node, producing a heart rate that is inappropriate for physiological requirements. This may result in resting bradycardia, inability to increase heart rate with exertion ('chronotropic incompetence'), or pauses due to sinus arrest or exit block. It may be associated with tachycardias, when it forms part of the tachy-brady syndrome.[6] Ageing is associated with a progressive loss of P cells, which are the main pacemaker cells of the sinus node,[7] and varying degrees of fibrosis and fat deposition within the node.[7,8] SND may also be secondary to other disease processes that are often more common in elderly people, including hypothyroidism, coronary disease, infiltrative cardiac disorders (haemochromatosis, amyloid), inflammatory disorders (pericarditis, myocarditis, connective tissue diseases), malignancy, and trauma. Older people are also at higher risk for the development of sinus node dysfunction due to extrinsic causes, in particular rate-limiting medications. Drugs such as beta-blockers, calcium channel blockers, and amiodarone are used more frequently in older people for co-morbidities such as hypertension, coronary disease and atrial fibrillation (AF), and older people tend to be more sensitive to the effects of such drugs.

Epidemiology of bradyarrhythmias

Epidemiological data on the incidence and prevalence of bradycardia, either symptomatic or not, are few. Much of the information available actually comes from series or registers of paced patients. Figure 1 shows the pacemaker implantation rate for each age decade in England and Wales. It is obvious that the need for pacing increases with age, and twice as many men receive pacemakers as do women. The need for pacing is therefore critically age and sex dependent.

Studies of older people describe the prevalence of first-degree AV block as 12–17%; second-degree AV block 1–2%, and complete heart block 1–2%.[9–11] In addition, 5% of the oldest old are already paced.[10] The incidence of left bundle branch block is 3.2/10,000/year in men;[4] of these, 2.3% will receive pacemakers during a 5–10 year follow-up period.[12] The prevalence of rhythms associated with sick sinus syndrome is 1–6%.

The only robust epidemiological data in the UK come from the Devon Heart Block and Bradycardia Survey, which was completed over 30 years ago.[5] The incidence of complete heart block was $97/10^6$ and of sick sinus syndrome $108/10^6$. The number identified potentially requiring pacing therapy was equivalent to $159–174/10^6$ (these figures are not age and sex adjusted). The prevalence of AV block in men aged over 80 years exceeded $5000/10^6$, and the prevalence of SND was twice as much as that of AV block, implying a total requirement for pacing

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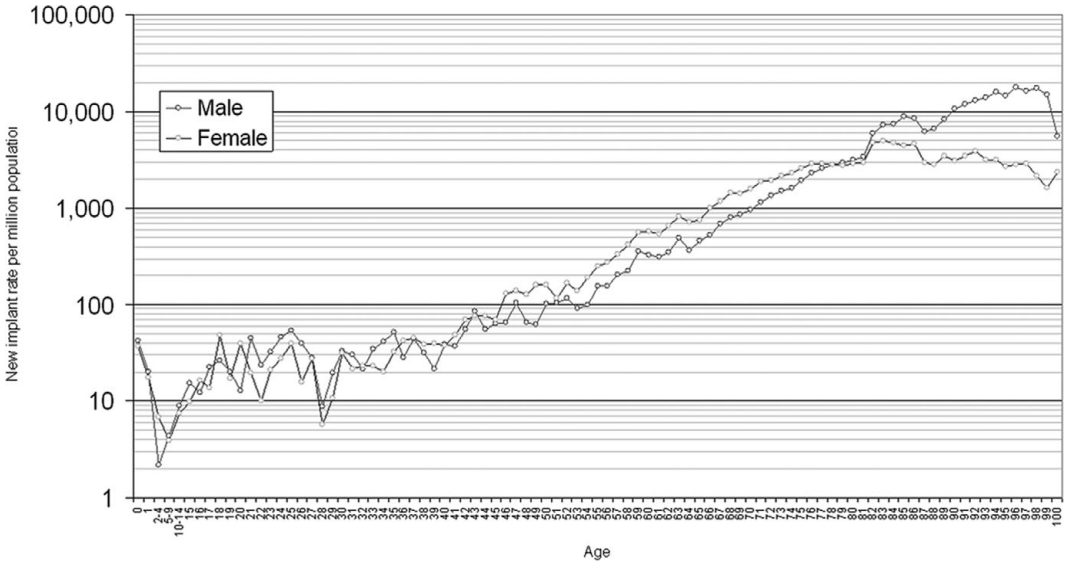


Figure 1. Graph illustrating new implant rates (per million population) of permanent pacemakers in the UK according to age and gender. Data are from 2006, courtesy of Dr David Cunningham, Central Cardiac Audit Database, NHS Information Centre.

in the over-80s of 15,000/10^6 (which is actually still more than the pacing rate in this age group now).

The prevalence of bundle branch block increases with age and is estimated at 1% of the population aged 35 and approximately 17% at age 80.[13] In patients without syncope, the rate of progression to high-degree AV block is low (0.6–0.8% per year)[14,15] and there is no non-invasive technique with a high predictive value.

Equity of provision of pacing

Pacing rates in western Europe, where the age structure of each country's population and economic factors are relatively similar, vary widely.[16] The reasons for this are not clear. Similar widespread variation is also seen within the United Kingdom, even after correction of implantation rates to take into account the age and sex structure of local populations.[16,17] So far there is no evidence that this is related to economic factors or local purchasing decisions.

Potential barriers to access to pacing

The only factors described which might influence pacing rates include concern about co-morbidities,[18] and lack of knowledge of pacing indications and difficulty with ECG interpretation in those to whom these patients present.[19,20]

Age

Figure 1 suggests that the pacing rate falls in the oldest old, implying that some of these patients are inappropriately not receiving pacemakers. It is not known whether this is due to failure of referral for pacing, or refusal of pacing. It is increasingly apparent that age itself should never be considered a barrier to pacing which improves quality of life.

Co-morbidity

Similarly, co-morbidities should not necessarily preclude pacing, particularly when not immediately life threatening. Thomas expressed surprise at the ease with which an elderly woman with a clear indication for pacing (complete heart block with symptoms) was accepted for pacing, because she had dementia.[18] Obviously such decisions need to be made on a case-by-case basis, but the default decision should probably be to pace, rather than not to, because of the improvement in quality of life offered by pacing.

Lack of knowledge

Recent work from the UK has suggested that failure to recognize pacing indications may contribute to

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Table 1. *A simplified summary of some of the common pacing indications*[13,22]

ECG finding	Clinical indication	Evidence class
Third-degree AV block/Mobitz II second-degree AV block	Symptomatic bradycardia*	I
	Asymptomatic with awake pauses >3 s or escape rate <40/min (in sinus rhythm); or pauses >5 s (in AF)	I
	Asymptomatic with cardiomegaly/LV dysfunction	I
	Asymptomatic Mobitz II with escape rate >40/min and broad QRS	IIa
	Asymptomatic with escape rate >40/min	
Mobitz I second-degree AV block (Wenckebach)	Symptomatic bradycardia	I
Bi- or trifascicular block	Alternating bundle branch block or intermittent high-degree AV block	I
	Syncope not demonstrated to be due to AV block when other likely causes have been excluded, specifically VT	IIa
Sinus node dysfunction	Documented symptomatic bradycardia*	I
	Symptomatic chronotropic incompetence	I
	Bradycardia <40/min when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented	IIa
	Unexplained syncope when clinically significant abnormalities of sinus node function are discovered	IIa
Hypersensitive carotid sinus syndrome	Recurrent syncope caused by spontaneously occurring carotid sinus stimulation and carotid sinus pressure that induces ventricular asystole >3 s	I
	Syncope without clear provocative events, with a hypersensitive cardioinhibitory response >3 s during CSM	IIa

*Bradycardia may be iatrogenic as a consequence of long term drug therapy. Class I: evidence and/or general agreement that pacing is beneficial, useful and effective and should be performed; class IIa: conflicting evidence and/or divergence of opinion about the usefulness of pacing, but weight of evidence/opinion is in favour of benefits outweighing risks and it is reasonable for pacing to be performed. AV block, atrioventricular block; LV, left ventricle; AF, atrial fibrillation; VT, ventricular tachycardia; CSM, carotid sinus massage.

relatively low pacing rates.[19,21] Roughly a third of patients who received pacemakers had a previous pacing indication which did not trigger a pacing referral, and by inference, not all patients who might benefit from pacing are referred for it. This resulted in significant delays to pacing, often with ongoing symptoms, additional hospitalizations, and unnecessary investigations.[19] A survey of the knowledge of pacing indications amongst those in hospital to whom potential pacemaker patients present suggested that physicians require further help in determining which patients should be referred for pacing.[21]

Indications for pacing

The European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) have published excellent detailed guidelines for cardiac device based therapy based on the available literature.[13 22] A simplified summary of some of the more common pacing indications is presented in Table 1. Essentially, pacing is indicated in all patients with symptomatic bradycardia. There are some conditions, such as advanced AV block, which carry a risk of progression and of life threatening bradyarrhythmias and pacing is indicated regardless of symptoms.

Atrioventricular block

Several studies have shown that permanent pacing improves survival in patients with acquired complete AV block. Siddons[23] showed that patients with complete AV block who received single

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chamber pacemakers had a survival curve not much different from that of the general population, matched for age and sex, while a similar group with complete AV block, who did not receive pacemakers, had a much higher mortality. Neither the presence of syncope, nor whether the AV block was established or intermittent, affected outcome.[24]

Mobitz type II second-degree AV block has a high incidence of progression to complete heart block (particularly if the QRS complexes are wide, as there is usually advanced disease within the His-Purkinje system, and any escape rhythm may be slow and unreliable) and of symptom development.[25,26] Pacing is therefore indicated for both complete AV block and Mobitz II AV block even in the absence of symptoms. Mobitz type I (Wenckebach) second-degree AV block has a lower rate of progression to advanced AV block and therefore clinical guidelines[13,22] suggest pacing is not routinely indicated (when the level of block has been shown to be above the His-Purkinje system) unless it is associated with symptoms. Wenkebach AV block has, however, been associated with increased mortality, especially in older patients, and benefit from pacing has been demonstrated.[26,27] Pacing should therefore be considered certainly when the patient has symptoms, and perhaps prophylactically in the older patient. Pacing is not generally considered for isolated first-degree AV block, although markedly prolonged PR intervals (>300 ms) sometimes lead to symptoms due to loss of AV synchrony (similar to pacemaker syndrome, where atrial contraction occurs when the AV valves are closed, resulting in cannon waves in the neck, and palpitation, fatigue and exercise intolerance) that may respond to pacing.[28] In AF, pauses of at least 5 s in awake, symptom-free patients indicate significant AV conduction defects and are a pacing indication. Shorter pauses in AF associated with symptoms are also a pacing indication.

Fascicular blocks

Bifascicular block refers to an electrocardiographic picture of right bundle branch block associated with block in the anterior or posterior fascicles of the left bundle (manifest as an axis deviation), or of left bundle branch block alone.[3,13] Trifascicular block is used to describe conduction disease in the right bundle and both fascicles of the left bundle. It may manifest as alternating bundle branch block, right bundle branch block with alternating right and left axis deviation, implying block in both fascicles of the left bundle, or bifasciclar block with first-degree AV block.[3] An example is shown in Figure 2. Asymptomatic bi- or trifascicular block is not considered an indication for pacing. However, once syncope has occurred, there is a high rate of progression to high grade AV block (19% per year),[29] particularly if the QRS is ≥120 ms at presentation (75% within 2 years).[30] Pacing is therefore indicated when other likely causes of syncope have been excluded. The other likely cardiac cause of syncope in this situation is ventricular tachycardia, and pragmatic use of echocardiography may be helpful; ventricular tachycardia is uncommon if ventricular function is normal or near normal, and bradycardia may be assumed, if syncope is thought to be cardiac. Studies of contemporary UK pacing suggest low awareness amongst physicians of this pacing indication and found evidence that pacing may be delayed unnecessarily in patients with syncope in the setting of bifascicular block, with consequent additional morbidity.[19,21,31]

Torsade de pointes

Torsade de pointes (twisting of the points) is an unusual form of polymorphic ventricular tachycardia associated with congenital or acquired lengthening of the QT interval.[32] It may be associated with bradycardia, in particular complete heart block.[33] It may be associated with hypokalaemia or hypocalcaemia, anti-arrhythmic drug therapy or with psychotropic drugs, and is commoner in older people, particularly women.[33] It is an indication for urgent pacing.

Sinus node disease

Symptomatic SND is an indication for pacing. Pacing in SND contributes more to relieving symptoms and reducing episodes of AF than to a definite reduction in mortality,[13,34] and hence sinus node dysfunction in the absence of symptoms attributable to bradycardia does not constitute a pacing indication. Symptom-rhythm correlation should be sought, with an ECG recorded during symptoms where possible. Even when a clear association between symptoms and bradycardia has not been documented, it is reasonable to consider pacing when there are other markers of SND, e.g. periods of junctional rhythm,

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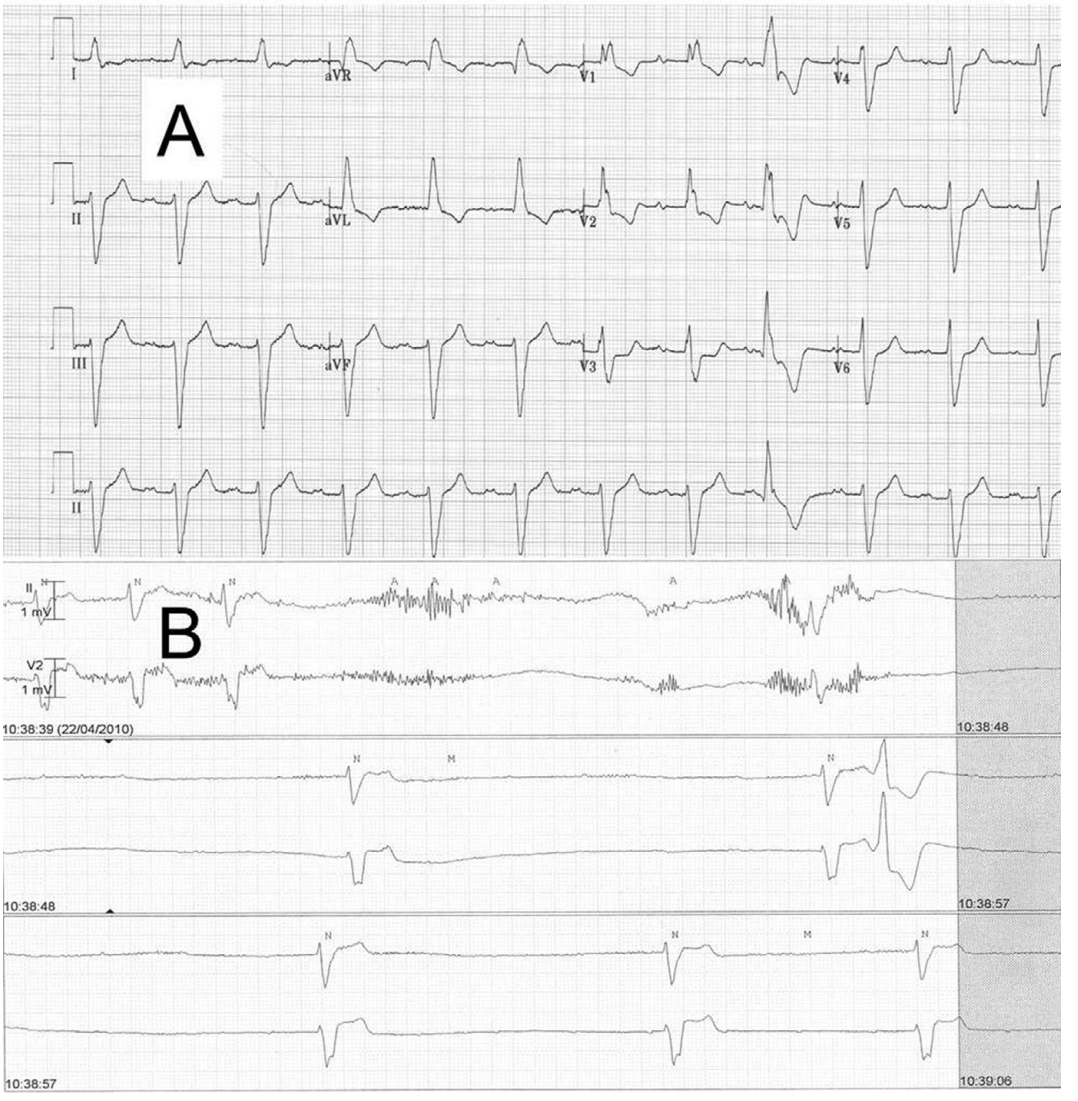


Figure 2. A, the 12-lead ECG of a 76-year-old patient who presented following an episode of syncope and shows RBBB, left axis and first-degree heart block (trifasicular block). B, the telemetry recording from an episode of dizziness whilst on the cardiology ward showing an episode of complete heart block with a slow broad complex ventricular escape rhythm at a rate less than 30 b.p.m. A dual chamber permanent pacemaker was inserted.

sinus bradycardia (≤40 b.p.m.) or chronotropic incompetence.[13,35] Exercise intolerance may be associated with chronotropic incompetence. This can be easily demonstrated by encouraging the patient to exercise during ambulatory monitoring (see Figure 3), or by formal exercise stress testing, when the heart rate will fail to rise above 100 b.p.m. during exercise.

Drug-associated bradycardia

It is important to note that both AV block and sinus bradycardia can occur in patients taking medications which may affect heart rate. In some instances the association is not causal, and pacing is therefore indicated. Patients who experience Mobitz II or complete heart block whilst taking beta-blockers or non-dihydropyridine calcium

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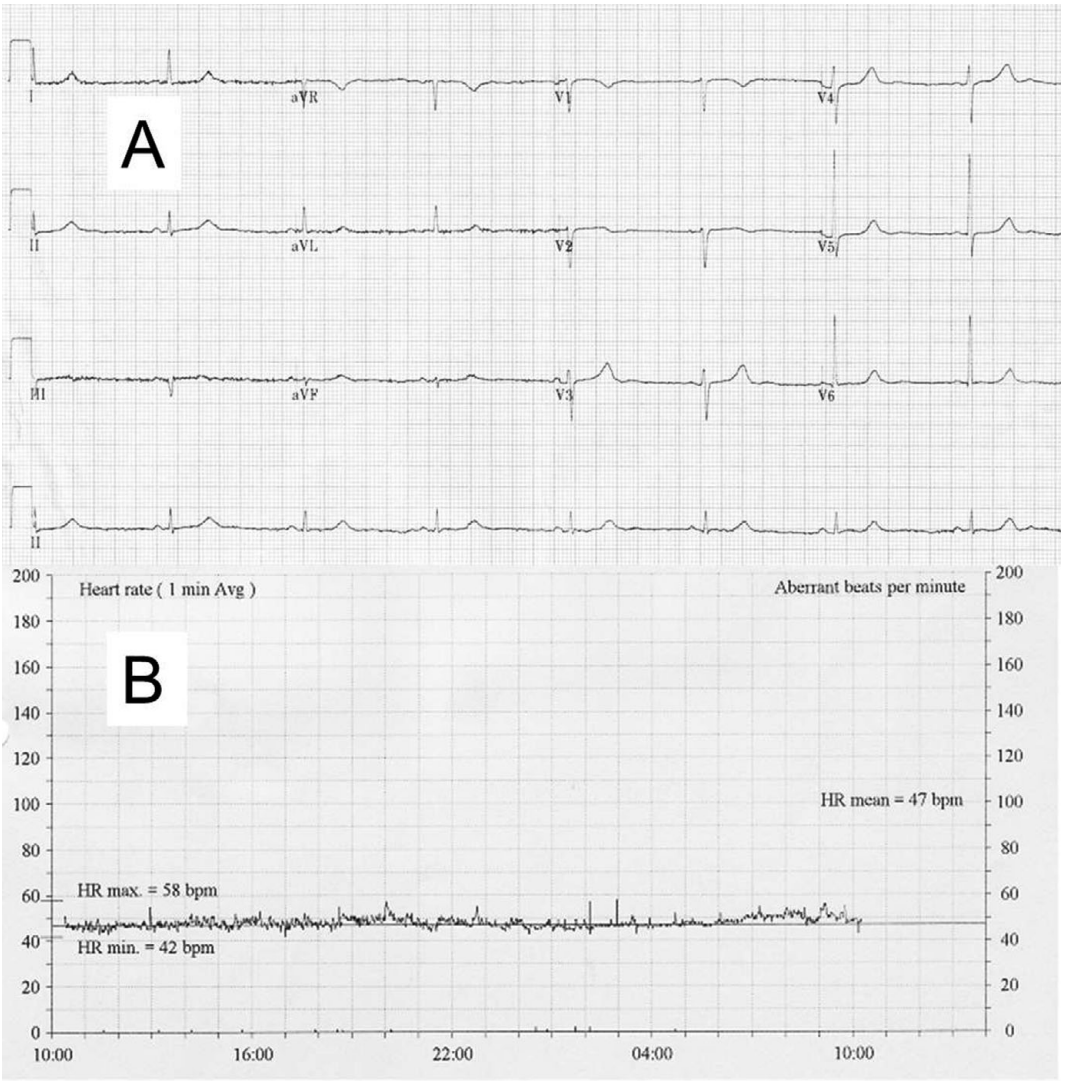


Figure 3. A, the 12-lead ECG of an 80-year-old patient presenting with dyspnoea and exercise intolerance. B, the heart rate trend over 24 hours during holter monitoring showing very poor heart rate variability with a maximum rate of 58 b.p.m. despite being active during this period. This is consistent with chronotropic incompetence secondary to sinus node disease and since the patient was not receiving any rate-limiting medications, a dual chamber permanent pacemaker was inserted.

channel blockers (verapamil and diltiazem) have a high chance of recurrence of AV block even with cessation of the 'culprit' medication.[30,36] This suggests that these medications unmask rather than cause AV block and pacing should be considered for high-degree AV block in this setting without a trial of stopping the medication.

When the relationship between drug and bradycardia is probably causal, pacing may be considered to allow continuation of a clinically useful drug. Bradycardias may occur as a consequence of long-term drug therapy required for another indication (such as control of tachyarrhythmias) which cannot easily be stopped. In particular, the use of amiodarone in AF is associated with an increased risk of pacemaker insertion, particularly in women, and when there is a previous history of SND.[37] The risk is dose

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related, and the need for pacing occurs relatively soon after initiation of therapy.[38] Digoxin is also associated with an increase in the need for pacing in these patients.[39] Newer drugs such as donezepil used to treat early Alzheimer's disease may be associated with a risk of sinus node and AV block and again, patients may be considered for pacing to allow continuation of a drug with clinical benefit.[40,41]

Neurocardiogenic syndromes

Neurocardiogenic syncope encompasses a spectrum of entities in which triggering of an autonomic neural reflex produces acute and inappropriate vasodilatation and/or bradycardia.[42,43] It includes vasovagal syncope, carotid sinus syndrome, and syncope related to cough, deglutition and micturition. Although neurocardiogenic syncope may be accompanied by bradycardia, there is frequently a substantial vasodepressor element which does not respond to pacing and there has been controversy over the benefit of pacemaker implantation for these conditions.

Vasovagal syncope

Vasovagal syncope is being recognized increasingly commonly in older people.[44] The typical vasovagal prodrome of nausea and diaphoresis is more likely to be absent in older patients.[44] It accounts for up to 50% of all admissions with syncope.[45–47] The role of pacing in vasovagal syndromes is not clear.[48] The early trials, randomizing patients who had vasovagal syncope with bradycardia to receive either pacemaker implantation or no pacemaker implantation, reported lower rates of syncope in the paced groups.[49,50] However, two subsequent double-blind trials in which all patients received a pacemaker which was randomly programmed to pacing on or off showed no reduction in syncope with pacing, suggesting that there is a significant and possibly useful placebo effect of pacemaker implantation.[51,52] It should be noted that, although older patients were not specifically excluded from these trials, the mean age of subjects recruited was 55 years,[48] much younger than the average paced patient. Pacing is therefore not indicated as first-line therapy for neurocardiogenic syncope but may be considered in some patients with refractory symptoms and a marked cardioinhibitory component.[13]

Carotid sinus hypersensitivity

Carotid sinus hypersensitivity (CSH) is characterized by a ventricular pause greater than 3 s and fall in systolic blood pressure of greater than 50 mmHg in response to carotid sinus massage (CSM). Between 25 and 40% of elderly patients with syncope or unexplained falls exhibit CSH,[53,54] but reproduction of syncope with these findings is required to define the carotid sinus syndrome. There is evidence to suggest that patients who have carotid sinus syndrome may have amnesia for loss of consciousness and will therefore present with falls rather than syncope.[55] Two trials have suggested a reduction in syncope following pacemaker implantation in patients with falls/syncope and an abnormal response to CSM.[56,57] However, both trials were unblinded (a pacemaker was implanted or not) and so did not include a placebo control. Guidelines, based on these data, suggest that permanent pacing is indicated in patients with recurrent syncope whose symptoms are reproduced by CSM associated with ventricular asystole of more than 3 s (during which the patient may be syncopal or pre-syncopal), particularly if usual symptoms appear to be precipitated by inadvertent carotid sinus pressure. However, the only blinded placebo-controlled trial, published recently, has not confirmed benefit from pacing. It included 25 subjects with unexplained falls and an abnormal response to CSM.[58] Patients all received pacemakers which were programmed randomly either to pace or not, with crossover to the other mode after 6 months. In this small study, the pacing intervention had no effect on the number of falls, raising the possibility that much of the positive effect of previous studies may have been placebo. The same group now suggest that CSH may be an age-related epiphenomenon, rather than a cause of syncope.[59] Further work in this controversial area will be of interest.

Cardiac resynchronization therapy

Cardiac resynchronization therapy (CRT) or biventricular pacing, with pacing leads positioned in the right atrium, right ventricle and left ventricle (usually via the coronary sinus, the branches of which run over the left ventricular epicardium) has also been shown to improve symptoms and survival in patients with advanced heart failure and cardiac dyssynchrony due to intraventricular

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conduction delay.[60] Modelling from trial data has shown that CRT is cost effective in all age groups, including those over 75.[61] Further discussion of the indications and benefits of CRT is beyond the scope of this review.

Outcome after pacing in older people

Mortality after pacing

Pacing reduces mortality in patients with AV block,[23,26,27] when compared with patients who did not receive pacemakers, but not in patients with SND.[5] However, despite this lack of reduction in mortality, older patients who receive pacemakers still have a life expectancy of some years. The proportion of older patients over 80 years of age who receive a pacemaker has increased in recent years from 18% in the 1970s, to 25% in the 1980s, to 32% in the 1990s.[62,63] Some are even implanted in centenarians.[17,62] The median survival in patients over the age of 80 who have received pacemakers in the last decade is 8 years,[62] and the annual mortality rate is about 7–15%.[64,65] Significant co-morbidities are associated, as might be expected, with reduced survival.[66] Pre-existing cardiac conditions, including coronary artery disease, heart failure and chronic AF, increase risk, as do diabetes, chronic kidney disease and chronic obstructive airways disease.[66] Despite this, about 50% of those with heart failure survive at least 4 years.[66,67]

Quality of life after pacing

Although it is very clear that quality of life improves after pacing,[68–70] it is less clear if dual chamber pacing leads to a greater improvement than single chamber ventricular pacing. This improvement in quality of life persists for at least 2–4 years after pacemaker implantation.[69,71] The improvement was significantly less in those over 75 years, but still greater than the decline expected with ageing.[71] Co-morbidities, particularly heart failure, may also affect quality of life in these patients. Pacing unfortunately does not prevent further decline in those with pre-existing cognitive impairment.[72]

Cost-effectiveness of pacing

There are no data on the cost-effectiveness of pacing for AV block and SND, as the practice was established long before randomized trials were required as evidence. More data are, however, available for the comparison of dual chamber pacing compared with single chamber ventricular pacing. As discussed above, dual chamber pacing is associated with benefits in morbidity and quality of life, particularly in patients with SND, although there is no clear effect on mortality. An economic evaluation[73] in 2005 estimated the cost of dual chamber pacing over 5 years as about £7400. The overall cost difference between single and dual chamber systems was not large – about £700. The cost-effectiveness of dual chamber compared with single chamber ventricular pacing was estimated to be about £8500 per quality adjusted life year (QALY) in AV block and £9500 in SND over 5 years, and about £5500 per QALY in both populations over 10 years. This is generally considered to be acceptable in health economics terms. Although this analysis was not carried out in an elderly population *per se*, the four large randomized trials which inform it include large numbers of older patients with an average age between 73 and 80 years.[73]

Pacemaker principles and nomenclature

Although the complexity and functionality of pacing systems is advancing rapidly, the fundamental concepts of a modern pacing system are simple. The pulse generator is a roughly circular unit comprising the battery and circuitry, which connects to one or more pacing leads. The leads are composed of electrode(s) positioned within a cardiac chamber and an insulated coiled wire attached to the pulse generator, which provides an electrical connection between the heart and the pulse generator. Electrical signals produced by intrinsic activity of the heart can be detected by the pulse generator (sensing) and electrical output to stimulate cardiac depolarization can be transmitted to the heart (pacing). Pacemakers are classified by a series of five letters (Table 2). The first letter indicates the chamber paced, either ventricle (V), atrium (A) or both (dual, D); the second letter indicates the chamber sensed, the third letter the response to a sensed beat, either inhibited (I), triggered (T) or both (dual, D); the fourth letter indicates the presence of a sensor which can give a rate adaptive response (increasing heart rate with exercise, R). The fifth letter is not widely used but indicates the presence of multisite pacing in one or

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Table 2. *The five letter classification scheme for cardiac pacemakers*

Chamber paced	Chamber sensed	Response to sensing	Presence of rate adaption	Presence of multisite pacing
A: atrium	O: no sensing	O: no sensing	O: no rate adaption	O: no multisite pacing
V: ventricle	A: atrium	I: inhibited	R: rate adaption	A: atrium
D: dual (ventricle and atrium)	V: ventricle	T: triggered		V: ventricle
	D: dual (ventricle and atrium)	D: dual response		D: dual (ventricle and atrium)

both chambers.[74] Multisite pacing in the ventricle is carried out during cardiac resynchronization therapy or biventricular pacing with pacing leads to pace the right atrium, right ventricle and left ventricle.

The commonest pacing modes encountered are VVIR and DDD±R. In VVIR pacing, there is a single lead in the right ventricle which senses the intrinsic depolarization and inhibits pacing. If no electrical activity is seen after a preset time, usually 1000 ms, a paced beat is initiated; the pacing rate is adapted according to level of physical activity using an activity sensor incorporated in the system. A DDD system is more complex and has leads in both atrium and ventricle. If an intrinsic beat is not sensed in the atrium, an atrial pacing stimulus will be initiated and given a chance to conduct through to the ventricles. If the ventricular lead does not sense an intrinsic ventricular depolarization in the appropriate time period, a ventricular pacing stimulus will be triggered. Thus an intrinsic stimulus in the atrium may lead to the inhibition of atrial pacing and the triggering of ventricular pacing (justifying the D-dual response in the third letter of the classification). Similarly, if the atrial rate is satisfactory and atrial pacing is inhibited but there is a lack of conduction to the ventricle, failure to sense an 'expected' ventricular intrinsic depolarization will also trigger a pacing stimulus. The minimum and maximum pacing rates may vary but often pacemakers are set to pace between 60 and 140 b.p.m. (with rate response, or tracking P waves). If the patient has an intrinsic heart rate greater than the minimum rate then no pacing will occur and no pacing spikes will be evident on the ECG. Various more complex algorithms exist which aim to improve symptoms and minimize inappropriate or unnecessary pacing, discussion of which is beyond the scope of this review.

Pacing modes: dual chamber *versus* single chamber pacing

The concept of dual chamber cardiac pacing in patients with sinus rhythm is appealing as it seems more physiological, and has the theoretical advantage of maintaining AV and subsequent mechanical synchrony. The potential disadvantages of a dual chamber system include increased implantation and follow-up costs, increased procedural complication rate and decreased battery longevity. Several large multicentre prospective randomized studies have evaluated pacing modes in patients with SND and AV block.[64,75–77] Two of these trials specifically excluded younger patients, recruiting only those over 65[75] or 70.[64] Although these trials fail to show any benefit in mortality between the two pacing modes, they do show a reduction in AF with dual chamber pacing, particularly in patients with SND,[77] which, perhaps surprisingly, does not translate into stroke reduction. Additionally, there is a reduction in heart failure symptoms and an increase in quality of life with dual chamber pacing compared with ventricular pacing in patients with SND.[77] It has been suggested that the apparent lack of benefit of dual chamber pacing may, in part, be related to the potentially deleterious effects of perhaps unnecessary right ventricular pacing in this group.[78] Pacing the right ventricular apex leads to abnormal left and right ventricular depolarization and dyssynchronous contraction.[78] Many patients, particularly with SND, have reliable AV conduction and so normal ventricular activation, and so do not need ventricular pacing. The dual chamber algorithms current at the time these trials were conducted will actually have promoted right ventricular pacing, with possible harm. New algorithms have been developed which promote intrinsic AV conduction and thus minimize pacing, where possible. Disappointingly, a recent randomized trial of one of these algorithms

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was not designed or powered to detect a change in mortality, although it did show that the incidence of AF was further reduced.[79] Despite this, dual chamber pacing has been shown to be a cost-effective measure to improve quality of life, and is recommended where possible.[80]

Pacemaker implantation: procedure and complications

Pacing may be either temporary, or permanent. Temporary pacing is appropriate if the condition causing symptomatic bradycardia is expected to resolve, or symptoms are so severe that pacing must be achieved as soon as possible. Otherwise, permanent pacing without prior temporary pacing is preferred.[81]

Temporary pacing

Temporary cardiac pacing can be achieved either by external pacing,[82,83] using large electrodes placed on the skin of the thorax, or by inserting a temporary electrode transvenously into the heart. External transcutaneous pacing is only suitable for emergency situations, such as cardiac arrest, as it is painful and not always well tolerated by the conscious patient.[83] It may not achieve pacing (in over a quarter),[83] and its effect may be difficult to assess, as movement and large stimulation artefacts recorded on the ECG may obscure the QRS complex. The equipment required should be available in ambulances, accident and emergency departments, and coronary care units. It cannot be used for prolonged periods, and ideally should be replaced by temporary transvenous or permanent pacing as soon as it can be arranged.

Temporary transvenous pacing is much better tolerated by the patient, but takes longer than transcutaneous pacing to achieve. One or more electrode catheters are inserted, through any large vein, and positioned under fluoroscopic guidance in usually the right ventricle (right atrial pacing may also be performed in the same way). The lead is secured to the skin with sutures, and the electrodes are attached to a temporary pacing box. Temporary transvenous pacing has a high complication rate (32%), particularly in inexperienced hands. Important complications include lead displacement, and infection, including septicaemia, leading to delays in permanent pacing in 23%,[84] and more than doubling the risk of infection of the subsequently implanted permanent pacing system.[85] The majority of patients who receive temporary pacing require permanent pacing (outside the context of acute myocardial infarction),[86] so if possible temporary pacing should be avoided, and a permanent system implanted as a first procedure.

Permanent pacing

Permanent pacemaker insertion is a surgical procedure carried out by cardiologists in most secondary and tertiary centres in the UK. It is usually performed under local anaesthetic and is well tolerated even in older patients with significant co-morbidities. The procedure may be performed electively, as a day case, even in the oldest old,[87] but commonly involves an overnight stay in hospital. A skin incision is made in the prepectoral area, usually on the left side, and a 'pocket' is created for the generator by blunt dissection in the plane immediately above the pectoral muscle. The leads are inserted into the central venous circulation and are positioned in the heart using X-ray fluoroscopic guidance. Lead fixation within the heart is either passive, where small tines at the end of the lead hold it in place within the cardiac trabeculations, or active, when a retractable screw mechanism is deployed, securing the lead to myocardium. The electrical parameters of the leads are measured, and when satisfactory, they are secured with sutures to the pectoral muscle and then inserted into the pacemaker pulse generator. The generator and any redundant lead loops are placed in the pocket and the wound is closed with sutures. The procedure typically takes less than an hour. The size of the generator can be a concern in thin patients where lack of overlying tissue increases the chance of subsequent erosion, but this can generally be overcome using a smaller device and/or implantation beneath the pectoral muscle.

Early procedural complications may occur but these are very seldom life-threatening. Lead displacement may occur at a rate of 0.7–2% for the ventricular lead and 0.5–4% for the atrial lead.[88] This usually requires an early repeat procedure to reposition the lead. When the subclavian approach for venous access is used, inadvertent pleural puncture may occur, leading to a pneumothorax in 0.7–2% of patients.[88] Although small asymptomatic pneumothoraces can usually be treated conservatively, insertion of a chest drain

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may be required. Cardiac perforation by the lead tip may occur at rates of 0.3–1% although this often does not cause any significant compromise.[88] Early infection rates of 0.2–1% have been reported and these usually respond to systemic antibiotics.[88] Rarely, a complete system extraction may be required. Given the natural history of indications for pacing, most of the patients in the large pacing trials informing these statistics are older. However, there are some data to evaluate the effect of age on complication rates. A recent study,[89] including >4800 patients, pooled data from three large pacing trials[64,76,90] and showed an increase in early pacemaker procedural complications from 3.4% in patients under 75 years to 5.1% in those over 75 years, particularly lead problems and pneumothorax. In contrast, late complications, such as lead fracture and need for generator replacement, were less likely among those over 75 years. In summary, the older old may have a slight increase in periprocedural complications, but these are generally not life threatening and are offset by a reduction in longer term complications, probably due to reduced life expectancy.

Pacemaker follow-up

Patients with cardiac pacemakers should remain under regular occasional follow-up to assess clinical status, optimize pacemaker function and assess battery status.[91] The frequency of device follow-up may be driven by clinical circumstances but typically patients are seen about 1 month after implantation to assess early complications such as lead displacement, and to optimize programming of the device. Subsequent follow-up is then at 6- or 12-monthly intervals, and allows evaluation of pacemaker function and identification of any problems with leads or the generator. Reprogramming of device parameters may be done in response to patient symptoms, or changes in status, but are often not required. Battery voltage is checked regularly, and this allows early identification of the need for generator replacement so that this can be planned ahead of the end of the battery life. Pacemaker generator replacement (for battery depletion) for certain pacing indications may be an essential life-sustaining treatment. Generator change should not, however, be undertaken without considering both the continued need for pacing and the patient's wishes. Some patients may not wish to undergo another procedure; however, even the extremely frail and oldest old should be offered generator change if they wish it and if the patient wishes to undergo the procedure, it should not be denied. Another interesting group are those patients with SND who develop permanent AF during follow-up. If AV node conduction is intact, these patients may no longer be at risk of bradycardia, and so may not need continued pacing. Over a third (38%) of patients paced for SND who subsequently developed permanent AF had a minimum intrinsic heart rate of over 60 b.p.m. and 18% had never used ventricular pacing during AF.[92] Although it is unlikely that a pacing system would ever be removed given the risks of lead extraction, a depleted battery may not be replaced in selected patients.

Recurrent syncope after pacing

Patients with pacemakers may experience syncope. This may occur in up to 13% of patients paced for SND over a period of 10 years.[93] It is commonly suspected that pacemaker malfunction is the cause, but in fact this is seldom the case.[93,94] A large series identified pacemaker malfunction as the cause of syncope in 6.5% of patients paced for SND with recurrent syncope. Other causes were vasovagal (18%), orthostatic hypotension (25.5%), rapid atrial tachyarrhythmias (11.5%), ventricular tachycardia (5%), acute myocardial ischaemia (2.5%) and in 29.5% of patients syncope remained unexplained. This reflects the multifactorial nature of syncope and the possible overlap between SND and neurocardiogenic syndromes (in up to 26%).[95] When syncope is attributable to the implanted device, it may occur as a result of lead failure or generator battery depletion or failure.

Atrial fibrillation

Another frequently encountered clinical problem identified at pacing follow-up is the development of AF. AF is common, particularly in older people. It occurs at a rate of about 3–4% per year in paced patients,[96,97] and occurs more commonly in the older old (≥74 years of age), those with a prior history of AF, those paced for SND, and in those who receive VVI (rather than DDD) pacemakers.[96]

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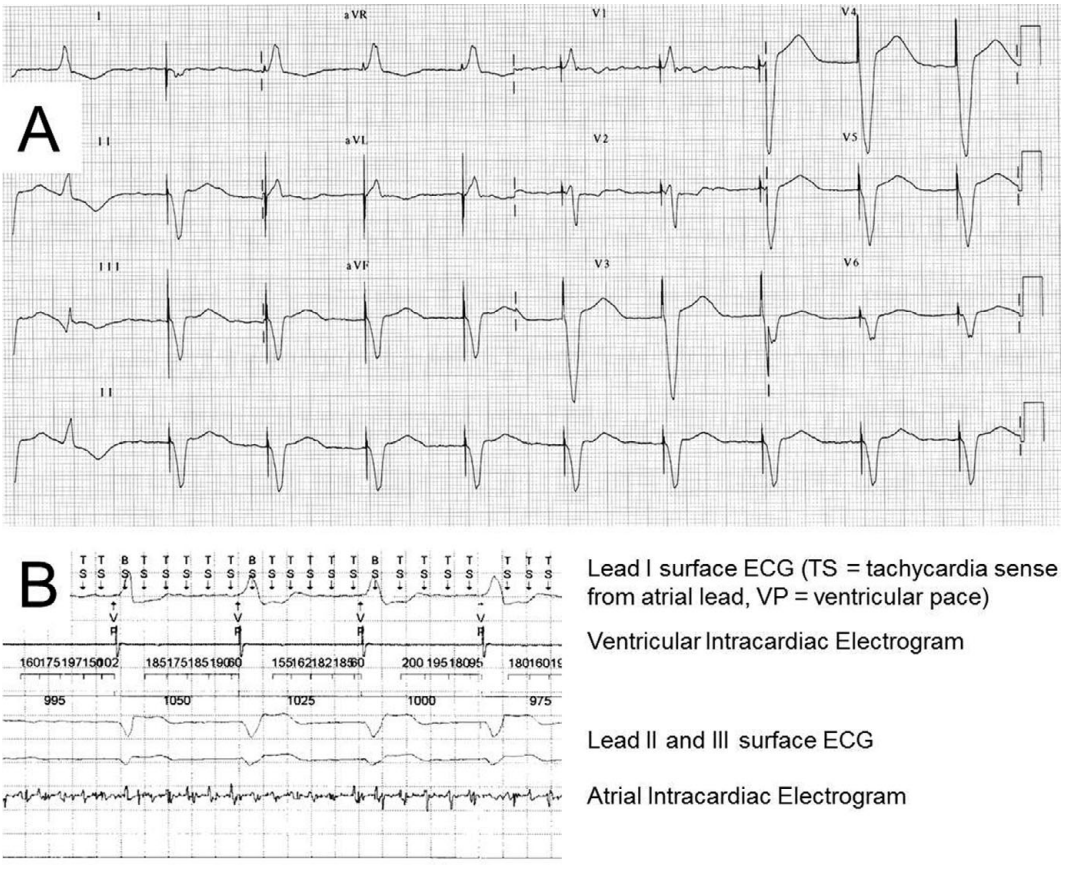


Figure 4. A, a 12-lead ECG from a patient with persistent atrial fibrillation and complete heart block with a dual chamber permanent pacemaker. The ventricular rhythm is paced and regular at the device base rate of 60 b.p.m. There are no visible P waves. B, the data from interrogation of the pacemaker. TS in the first column refers to pacemaker sensing of rapid atrial activity in AF, which is illustrated in the intracardiac recording from the tip of the atrial lead in the right atrium. The intracardiac recording from the tip of the ventricular lead shows the pacing spike and cardiac depolarization from the tip of the ventricular lead in the right ventricle. Leads II and III are also displayed in the figure and appear similar to the 12-lead ECG.

Identification of AF in paced patients at follow-up is important as patients are often asymptomatic, particularly if they have AV block, so that AF is not conducted rapidly to the ventricle. These patients may have a regular and normal (paced) heart rate at pulse check which will not raise suspicion of AF, but importantly will still have an increased risk of stroke associated with the arrhythmia,[98] which is particularly significant in elderly people. If AF is identified at follow-up, either by pacemaker recorded intracardiac electrograms, shown in Figure 3, or on the surface ECG, the responsible physician can assess stroke risk using a risk scoring system such as $CHADS_2$[99] or one of its refinements, CHA_2DS_2VASc[100] or HAS BLED[101] to guide decisions regarding anticoagulation.

Ethical and end of life decisions

Pacemaker implantation in older patients has increased rapidly in recent years and this means that the management of these devices in dying patients will be encountered increasingly in clinical practice. The withholding and withdrawal of life-sustaining treatments (e.g. cardiopulmonary resuscitation, mechanical ventilation, or haemodialysis) from terminally ill patients who do not want the treatments is ethical and legal.[102] There is no

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difference between a competent adult refusing implantation of a pacemaker and requesting its withdrawal.[103] Withdrawal of pacing can be done easily and non-invasively by programming; it rarely requires surgical removal of the device. If a pacemaker is programmed off in a pacemaker-dependent patient, death may be rapid, if there is no reliable escape rhythm. However, there may be a rhythm that sustains life for some time. As pacing is painless and the patient is rarely aware of it, it is uncommon to be asked to withdraw it. Equally, withdrawal of implantable cardioverter defibrillator (ICD) therapy may be done painlessly by programming, and bradycardia pacing support may be maintained despite disabling tachycardia therapy. Health professionals generally support withdrawal of ICD therapy for tachycardias in the terminally ill, particularly in those for whom a 'do not resuscitate' order has been agreed, as shocks delivered by the ICD are painful and unpleasant, and prevent sudden death.

These cases present a difficult dilemma, although with extensive counselling and a detailed informed consent may be considered an option on a case-by-case basis.[102] The key to managing these cases is early communication between the patient, their family and health professionals from both the cardiac team and any health professionals delivering care for a non-cardiac terminal illness. Advanced directives can provide useful guidance to medical teams when a patient's clinical condition deteriorates. Clinicians involved in device education do not commonly have discussions with patients about end of life issues and device deactivation[22] and it may be important to address these issues at the time of implantation.

Removal of devices after death

Pacemakers and ICDs should be removed after death if cremation of the body is to be undertaken, as the lithium iodide battery can explode, with possible damage.[104] Removal of pacemakers poses no electrical risk to the operator. In contrast, handling ICD generators or cutting the leads is an electrical hazard, and shocks can be delivered to the operator if shock therapy has not been disabled.[105]

Conclusions

Pacing is the only practical method of preventing bradycardia, and should be considered in all patients with symptoms probably related to bradycardia. Symptom rhythm correlation (ECG recording during symptoms) may be helpful, but is not always essential, as there may already be sufficient evidence to support a pacing indication. There is little to gain in stopping 'culprit' drugs such as beta-blockers or calcium antagonists, particularly in patients with AV block, as the block is likely to persist or recur. Most recipients of pacemakers are old, and some are among the oldest old. Despite this, pacing is associated with a significant improvement in quality of life, and in some patients increased longevity. The implantation procedure is straightforward, and well tolerated even in the oldest old, despite a small increase in the complication rate in this group. Routine pacemaker follow-up should not be onerous, but is important. Pacing therapy is seldom withdrawn, even at end of life, perhaps because it is painless. After death, the pacemaker generator should be removed prior to cremation.

Conflicts of interest

None of the authors had any conflicts of interest to declare.

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