EXPERT CONSENSUS DOCUMENT

HRS/ACCF Expert Consensus Statement on Pacemaker Device and Mode Selection

*Developed in partnership between the Heart Rhythm Society (HRS)
and the American College of Cardiology Foundation (ACCF)
and in collaboration with the Society of Thoracic Surgeons*

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Introduction

The most recent American College of Cardiology Foundation/American Heart Association/Heart Rhythm Society (ACCF/AHA/HRS) guidelines related to pacemaker implantation were published as part of a larger document related to device-based therapy (1). While this document provides some comments on pacemaker mode selection and algorithms to guide selection, it does not provide specific recommendations regarding choices for single- or dual-chamber devices. Over the past 15 years multiple randomized trials have compared a number of cardiovascular outcomes among patients randomized to atrial or dual-chamber pacing vs. those randomized to ventricular pacing. The purpose of this 2012 consensus statement is to provide a state-of-the-art review of the field and to report the recommendations of a consensus writing group, convened by HRS and ACCF, on pacemaker device and mode selection. This document focuses on pacemaker device and mode selection in the adult patient; therefore, many of the recommendations may not be applicable to unique situations encountered in the pediatric population. These recommendations summarize the opinion of the consensus writing group, based on an extensive literature review as well as their own experience.

This document should be used as a supplement to the published 2008 guidelines document, functioning as a guide to facilitate the selection of single- vs. dual-chamber devices for patients who already meet guidelines for pacemaker implantation (1). **It should be emphasized that recommendations for device selection in the current document apply to situations where the clinical decision for pacing has already been made.** In addition, specific recommendations for cardiac resynchronization therapy are not addressed in this document as the indications for cardiac resynchronization therapy have been published previously and guideline updates related to these indications are also in progress (2,3).

This document is directed to all health care professionals who are involved in the selection of devices and pacing mode as well as the subsequent management of patients with pacemakers.

All recommendations provided were agreed upon by at least 81% of the writing committee by anonymous vote. Writing group members were selected by HRS or ACCF based on their expertise in the field. The 11 participating cardiac electrophysiologists or surgeons include representatives from the United States, Canada, and Europe. The grading system for class of indication and level of evidence was adapted from that used by the ACCF and the AHA (4). However, it is important to state that this document is not a guideline. Nevertheless, we present recommendations with

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class and level of evidence designations to provide consistency with familiar guideline documents.

Classification of Recommendations

- Class I: Conditions for which there is evidence and/or general agreement that a given pacing mode is beneficial, useful and effective.
- Class II: Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a specific pacing mode.
  - Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
  - Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
- Class III: Conditions for which there is conflicting evidence and/or general agreement that a pacing mode is not useful/effective and in some cases may be harmful.

Level of Evidence

- Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
- Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.
- Level of Evidence C: Only consensus opinion of experts, case studies, or standard of care.

The writing group was divided into three subgroups to review aspects of pacing mode selection for patients with 1) sinus node dysfunction (SND), 2) atrioventricular (AV) conduction block, and 3) other less common indications for pacing. All members of the writing group, as well as peer reviewers of the document, provided disclosure statements for all relationships that might be perceived as real or potential conflicts of interest. These tables are shown at the end of this document.

1. Pacemaker Device and Mode Selection for SND

Expert Consensus Recommendations (see Table 1 for a summary of consensus recommendations)

CLASS I

1. **Dual-chamber pacing (DDD) or single-chamber atrial pacing (AAI) is recommended over single-chamber ventricular pacing (VVI) in patients with SND and intact AV conduction (Level of Evidence: A) (5–9).**
2. **Dual-chamber pacing is recommended over single-chamber atrial pacing in patients with SND (Level of Evidence: B) (10).**

CLASS IIa

1. **Rate adaptive pacing can be useful in patients with significant symptomatic chronotropic incompetence, and its need should be reevaluated during follow-up (Level of Evidence: C) (11,12).**
2. **In patients with SND and intact AV conduction, programming dual-chamber pacemakers to minimize ventricular pacing can**

be useful for prevention of atrial fibrillation (AF) (Level of Evidence: B) (13).

CLASS IIb

1. **AAI pacing may be considered in selected patients with normal AV and ventricular conduction (Level of Evidence: B) (14–16).**
2. **Single-chamber VVI pacing may be considered in instances where frequent pacing is not expected or the patient has significant comorbidities that are likely to influence survival and clinical outcomes (Level of Evidence: C) (5–8).**

CLASS III

1. **Dual-chamber pacing or single-chamber atrial pacing should not be used in patients in permanent or longstanding persistent AF where efforts to restore or maintain sinus rhythm are not planned (Level of Evidence: C) (1,5,10,17,18).**

SND is the most common cause of bradyarrhythmias requiring pacing therapy in North America and Western Europe. Arrhythmias associated with SND include sinus bradycardia, sinoatrial block, sinus arrest, chronotropic incompetence, and tachycardia–bradycardia syndrome characterized by paroxysms of supraventricular tachyarrhythmias (AF, atrial flutter, atrial tachycardia) alternating with bradycardia or asystole (17). Twenty percent of patients with SND will have some degree of AV block (8).

Two important developments in the natural history of SND should be emphasized: AV block and AF (17,19). The risk of developing AV block following pacemaker implantation within 5 years of follow-up is 3–35% (15,16,19,20). This risk varies with patient factors including age and comorbidities and likely increases further over time and with the addition of medications that have negative dromotropic effects. In patients with SND, the incidence of clinical AF at the time of initial diagnosis has been reported to range from approximately 40–70% (8,10,21). Among patients who do not have AF at initial diagnosis, the incidence of new AF in follow-up ranges from 3.9–22.3% (8,10,21). During long-term follow-up, 68% of patients receiving a dual pacemaker for SND have had AF documented by device diagnostics (21). The incidence of AF is significantly influenced by mode of pacing, percentage of ventricular pacing, and duration of follow-up (17,19,21).

In the absence of a reversible cause, the appropriate treatment for symptomatic SND is implantation of a permanent pacemaker. Available pacing modes include dual-chamber (DDD or DDI), ventricular single-chamber (VVI), and atrial single-chamber (AAI). Rate adaptive pacing may be programmed as required for symptomatic chronotropic incompetence. The optimal pacing mode for patients with SND has generated much debate until the completion and publication of several landmark clinical trials reporting the superiority of atrial or dual-chamber pacing over ventricular pacing with regard to their effect on some clinical outcomes.

Four major randomized clinical trials, specifically the Danish study, the Pacemaker Selection in the Elderly (PASE) study, the Canadian Trial of Physiologic Pacing (CTOPP), and the Mode Selection Trial (MOST), have compared atrial or dual-chamber pacing with ventricular pacing in patients with SND (5–8,14). These randomized controlled trials

Table 1. Consensus Recommendations for Device and Mode Selection Apply to Situations Where the Clinical Decision for Pacing has Already Been Made

	Class I	Class IIa	Class IIb	Class III
Sinus Node Dysfunction	1. Dual-chamber pacing (DDD) or single-chamber atrial pacing (AAI) is recommended over single-chamber ventricular pacing (VVI) in patients with SND and intact AV conduction (Level of Evidence: A) 2. Dual-chamber pacing is recommended over single-chamber atrial pacing in patients with SND (Level of Evidence: B)	1. Rate adaptive pacing can be useful in patients with significant symptomatic chronotropic incompetence and its need should be reevaluated during follow-up (Level of Evidence: C) 2. In patients with SND and intact AV conduction, programming dual-chamber pacemakers to minimize ventricular pacing can be useful for prevention of atrial fibrillation (AF) (Level of Evidence: B)	1. AAI pacing may be considered in selected patients with normal AV and ventricular conduction (Level of Evidence B) 2. Single-chamber VVI pacing may be considered in instances where frequent pacing is not expected or the patient has significant comorbidities that are likely to influence survival and clinical outcomes (Level of Evidence: C)	1. Dual-chamber pacing or single-chamber atrial pacing should not be used in patients in permanent or longstanding persistent AF in whom efforts to restore or maintain sinus rhythm are not planned (Level of Evidence: C)
AV Node Disease	1. Dual-chamber pacing is recommended in patients with AV block (Level of Evidence: C) 2. Single-chamber ventricular pacing is recommended as an acceptable alternative to dual-chamber pacing in patients with AV block who have specific clinical situations that limit the benefits of dual-chamber pacing. These include, but are not limited to, sedentary patients, those with significant medical comorbidities likely to impact clinical outcomes, and those in whom technical issues, such as vascular access limitations, preclude or increase the risk of placing an atrial lead (Level of Evidence: B) 3. Dual-chamber pacing is recommended over single-chamber ventricular pacing in adult patients with AV block who have documented pacemaker syndrome (Level of Evidence: B)	1. Single-lead, dual-chamber VDD pacing can be useful in patients with normal sinus node function and AV block (e.g., the younger patient with congenital AV block) (Level of Evidence: C) 2. VVI pacing can be useful in patients following AV junction ablation, or in whom AV junction ablation is planned, for rate control of AF due to the high rate of progression to permanent AF (Level of evidence B)		1. Dual-chamber pacing should not be used in patients with AV block in permanent or longstanding persistent AF in whom efforts to restore or maintain sinus rhythm are not planned (Level of Evidence: C)
Hypersensitive Carotid Sinus Syndrome		1. Dual-chamber or single-chamber ventricular pacing can be useful for patients with hypersensitive carotid sinus syndrome (Level of Evidence: C)		1. Single-chamber AAI pacing is not recommended for patients with hypersensitive carotid sinus syndrome (Level of Evidence: C)
Neurocardiogenic Syncope		1. Dual-chamber pacing can be useful for neurocardiogenic syncope (Level of Evidence: C)		1. Single-chamber AAI pacing is not recommended for neurocardiogenic syncope (Level of Evidence: C)
Long QT	1. Dual-chamber or atrial pacing compared to ventricular pacing is recommended for symptomatic or high-risk patients with congenital long QT syndrome (Level of Evidence: C)			
Hypertrophic Cardiomyopathy		1. Dual-chamber pacing can be useful for patients with medically refractory, symptomatic hypertrophic cardiomyopathy with significant resting or provoked left ventricular outflow obstruction (Level of Evidence: C)		1. Single-chamber (VVI or AAI) pacing is not recommended for patients with medically refractory, symptomatic hypertrophic cardiomyopathy (Level of Evidence: C)

included mostly elderly patients (mean age 72–76 years), many of whom had several comorbidities. PASE and CTOPP included a general pacemaker population with 42% having SND. The vast majority of patients in these studies, randomized to atrial-based pacing, received dual-chamber devices. These trials are summarized in Table 2 and Figure 1. When interpreting the results of these trials, some limitations should be considered. The crossover from one arm of the study to the other (typically VVI to DDD) was variable, ranging from less than 5% over 3 years in CTOPP, which required reoperation and addition of an atrial lead, to 37.6% over 3 years in MOST, which was accomplished simply by reprogramming the pulse generator to the DDD mode (5–8,14). In addition, the percentage of atrial and ventricular pacing was not reported in the Danish study, CTOPP, or PASE (5,6,14). A summary of the effects of pacing mode on important clinical endpoints in these clinical trials is presented below.

1.1. AF

Atrial or dual-chamber pacing compared to ventricular pacing significantly reduced AF in the Danish, CTOPP, and MOST study populations with relative risk reductions of 46%, 18%, and 21% respectively (Table 2) (6–8,14). In CTOPP, a general pacemaker population, the number needed to treat to prevent any AF over 10 years was 9 patients, and in MOST the number needed to treat to prevent permanent AF over 3 years was 9 patients (17). A meta-analysis of these clinical trials (that also pooled data from the United Kingdom Pacing and Cardiovascular Events, UK-PACE, a trial that included only patients with AV block [22]) showed a highly significant 20% relative risk reduction (hazard ratio [HR] 0.80, 95% confidence interval [CI] 0.72–0.89, p = 0.00003) in AF with atrial or dual-chamber pacing compared to ventricular pacing (Figure 2) (9). Device diagnostics in atrial and dual-chamber pacemakers permit detection of episodes of AF that may not have been previously identified, thus facilitating a decision about the appropriateness of antithrombotic therapy based on risk for stroke (23,24). Although not the primary endpoint of the above randomized trials, prevention of AF is an important clinical outcome for clinicians to consider when making decisions about permanent pacing in patients with SND. This consideration is based upon the association of AF with an impaired quality of life and increased morbidity related to stroke and other clinical outcomes, as well as the cost of therapies to control AF and prevent or treat these problems (see Recommendations Table 1) (25).

1.2. Stroke/Thromboembolism

Although the Danish study showed a 53% relative reduction in the risk of systemic thromboembolism with AAI compared to VVI pacing, none of the other studies could replicate this finding (Table 2). However, the meta-analysis of the pooled data reported a significant reduction in the risk of stroke with atrial-based pacing (HR 0.81, 95% CI 0.67–0.99, p = 0.035; Figure 3) (9). Such an effect is consistent with the reduction in AF observed with atrial or dual-chamber pacing.

1.3. Heart Failure

Compared with ventricular pacing (VVI), atrial pacing (AAI) improved the heart failure status of patients enrolled in the Danish study (Table 2) (14). In MOST, heart failure occurred in 10.3% of the dual-chamber (DDDR) group and 12.3% of the ventricular pacing (VVIR) group (HR 0.82, 95% CI 0.63–1.06, p = 0.13) (8). However, after an adjusted analysis to address some imbalances in clinical characteristics between the two groups, hospitalization for heart failure was significantly lower with dual-chamber pacing than ventricular pacing (HR 0.73, 95% CI 0.56–0.95, p = 0.02). In addition, during follow-up in MOST, patients with dual-chamber pacing had a significantly lower heart failure score than patients with ventricular pacing (p <0.001) (8). However, PASE, CTOPP, and the afore-mentioned meta-analysis failed to show a significant reduction in heart failure by atrial or dual-chamber pacing (6–9).

1.4. Mortality

Except for the Danish study (14), none of these randomized clinical trials showed a significant difference in cardiovascular mortality between atrial or dual-chamber pacing and ventricular pacing (Table 2) (6,8,10). Likewise, the meta-analysis of the pooled data demonstrated no significant reduction in mortality with atrial-based pacing compared to ventricular pacing (Figure 1) (9).

1.5. Quality of Life and Functional Status

PASE, CTOPP, and MOST examined the effect of pacing mode on the quality of life and functional status (5,26,27). CTOPP showed no significant effect of pacing mode on the quality of life. However, an improvement in exercise capacity, as assessed by the distance walked in 6 minutes, was observed in the atrial or dual-chamber pacing subgroup with a high degree of pacing (26,28,29). In patients with SND enrolled in PASE, dual-chamber pacing was associated with improved quality of life and cardiovascular functional status compared to ventricular pacing (5). In MOST, dual-chamber pacing resulted in a significant improvement in some subscales of quality of life as assessed by the SF-36 instrument, specifically role physical, role emotional, and vitality (27).

1.6. Pacemaker Syndrome

Pacemaker syndrome is the occurrence of overt symptoms, such as fatigue, chest discomfort, dyspnea, cough, confusion, presyncope, or syncope due to adverse hemodynamics that result from loss of AV synchrony and occurrence of ventriculoatrial conduction or atrial contraction against closed AV valves in patients with an implanted pacemaker (30). Although pacemaker syndrome may occur with any mode of pacing, it is most common with ventricular pacing in the VVI mode in patients who are in sinus rhythm. One randomized clinical trial compared 16 different symptoms and hemodynamic parameters among 40 patients in sinus rhythm who were randomly programmed to the VVI mode or the DDD mode. Patients were blinded to the mode of pacing. Twelve of sixteen symptoms were significantly worse in the VVI mode, with a mean symptom score of 29.0 ± 26.1 in

Table 2. Major Randomized Controlled Trials*

Characteristics	Danish Study (14)	PASE (5)	CTOPP (6,7)	MOST (8)	DANPACE (10)	UKPACE (22)
Patient population	SSS	SSS plus AVB	SSS plus AVB	SSS	SSS	AVB
Patients with SSS/AVB	220/0	175/232	1,028/1,540	2,010/0	1,415/0	0/2,021
Mean or median follow-up (yr)	5.5	1.5	3.5 6.4 (extended CTOPP)	2.8	5.4	3.0
Pacing modes	AAI vs. VVI	DDDR vs. VVIR	DDD/AAI vs. VVI(R)	DDDR vs. VVIR	AAIR vs. DDDR	DDD(R) vs. VVI(R)
Primary endpoint	Composite of mortality, thromboembolism and AF	Health-related quality of life as measured by the SF-36	Stroke or CV mortality	All-cause mortality or nonfatal stroke	All-cause mortality	All-cause mortality
Secondary endpoints	CV mortality, HF, and AVB	All-cause mortality, nonfatal stroke, AF, and pacemaker syndrome	All-cause mortality, AF, HF hospitalization	Composite of all-cause mortality, first stroke, first HF; all-cause mortality; CV mortality; AF; pacemaker syndrome; health-related quality of life; Minnesota Living with HF score	Incidence of paroxysmal and chronic AF, stroke, HF, need for pacemaker reoperation	AF; HF; composite of stroke, transient ischemic attack, or other thromboembolism
Atrial fibrillation	24% AAI vs. 35% VVI RRR 46%, p = 0.012	19% VVIR vs. 17% DDDR, p = 0.80	Annual rate 6.6% VVI vs. 5.3% DDD/AAI, RRR 18%, p = 0.05 Extended CTOPP: Annual rate 5.7% VVI vs. 4.5% DDD/AAI, RRR 20.1%, p = 0.009	27.1% VVIR vs. 21.4% DDDR, RRR 21%, p = 0.008	28.4% AAIR vs. 23.0% DDDR, RRR 27%, p = 0.024	Annual rate 3.0% VVI/VVIR vs. 2.8% DDD/DDDR, p = 0.74
Stroke/thromboembolism	12% AAI vs. 23% VVI RRR 53%, p = 0.023		Annual rate 1.1% VVI vs. 1.0% DDD/AAI, p = NS (Extended CTOPP: Remained NS)	4.9% VVIR vs. 4.0% DDDR, RRR 18%, p = 0.36	5.5% AAIR vs. 4.8% DDDR, RRR 13%, p = 0.59	Annual rate 2.1% VVI/VVIR vs. 1.7% DDD/DDDR, p = 0.20
Heart failure or hospitalization for heart failure			Annual rate 3.5% VVI vs. 3.1% DDD/AAI, RRR 7.9%, p = 0.52	12.3% VVIR vs. 10.3% DDDR, RRR 18%, p = 0.13		Annual rate 3.2% VVI/VVIR vs. 3.3% DDD/DDDR, p = 0.80
Mortality, all-cause	35% AAI vs. 50% VVI RRR 34%, p = 0.045	17% VVI vs. 16% DDDR, p = 0.95	Annual rate 6.6% VVI vs. 6.3% DDD/AAI, RRR .9%, p = 0.92 (Extended CTOPP: Remained NS)	20.5% VVIR vs. 19.7% DDDR, RRR 3%, p = 0.78	29.6% AAIR vs. 27.3% DDDR, RRR 6%, p = 0.53	Annual rate 7.2% VVI/VVIR vs. 7.4% DDD/DDDR, p = 0.56
Cardiovascular mortality	17% AAI vs. 34% VVI RRR 53%, p = 0.0065			9.2% VVIR vs. 8.5% DDDR, RRR 7%, p = 0.61		Annual rate 3.9% VVI/VVIR vs. 4.5% DDD/DDDR, p = 0.07

*Outcomes for AF, stroke/thromboembolism, heart failure, mortality, and CV mortality are listed as overall absolute event rates or mean annual event rates (when specified).

AF = atrial fibrillation; AVB = AV block; CV = cardiovascular; HF = heart failure; NS = not significant; RRR = relative risk reduction; SSS = sick sinus syndrome.
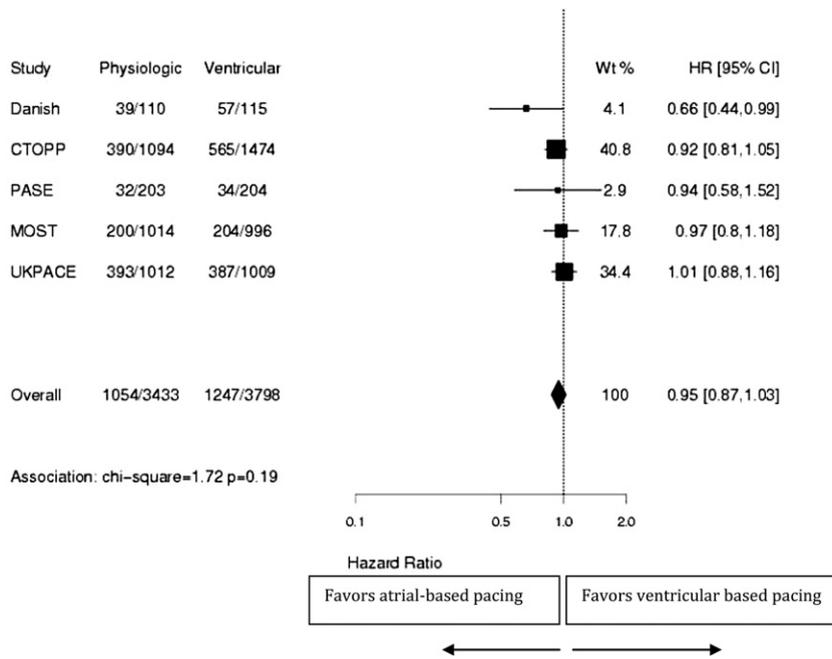
Figure 1. Effect of pacing mode on all-cause mortality expressed as the hazard ratio (HR) and 95% confidence interval (CI). An HR <1.0 is shown to the left of the center line and favors atrial-based pacing. CIs that cross 1.0 signify a statistically nonsignificant effect. Reprinted with permission from Healey et al. (9).

the VVI group compared with 7.3 ± 12.4 in the DDD or DDI group (p <0.001). Importantly, pacemaker syndrome was clinically recognized in 83% of patients paced in the VVI mode; 65% of all patients experienced development or exacerbation of moderate to severe symptoms in the VVI mode compared with the dual-chamber pacing mode (31). Some of these symptoms may have been dependent on the underlying baseline or sensor-

driven ventricular rate among patients programmed in the VVI mode (32). In some patients, pacemaker syndrome can be prevented by programming backup VVI pacing at a lower ventricular rate.

Many small early crossover studies of dual-chamber vs. VVI pacing, which evaluated quality of life and functional capacity, consistently showed a marked benefit and prefer-

Figure 2. Effect of pacing mode on atrial fibrillation expressed as the HR and 95% CI. An HR < 1.0 is shown to the left of the center line and favors atrial-based pacing. CIs that cross 1.0 signify a statistically nonsignificant effect. Reprinted with permission from Healey et al. (9).
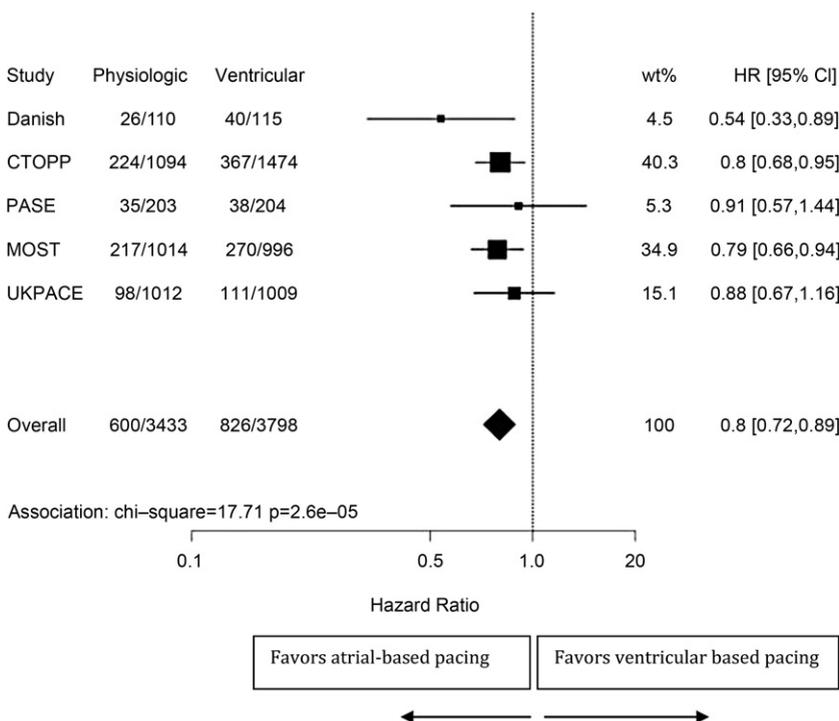
Figure 3. Effect of pacing mode on stroke expressed as the HR and 95% CI. An HR < 1.0 is shown to the left of the center line and favors atrial-based pacing. CIs that cross 1.0 signify a statistically nonsignificant effect. Reprinted with permission from Healey et al. (9).
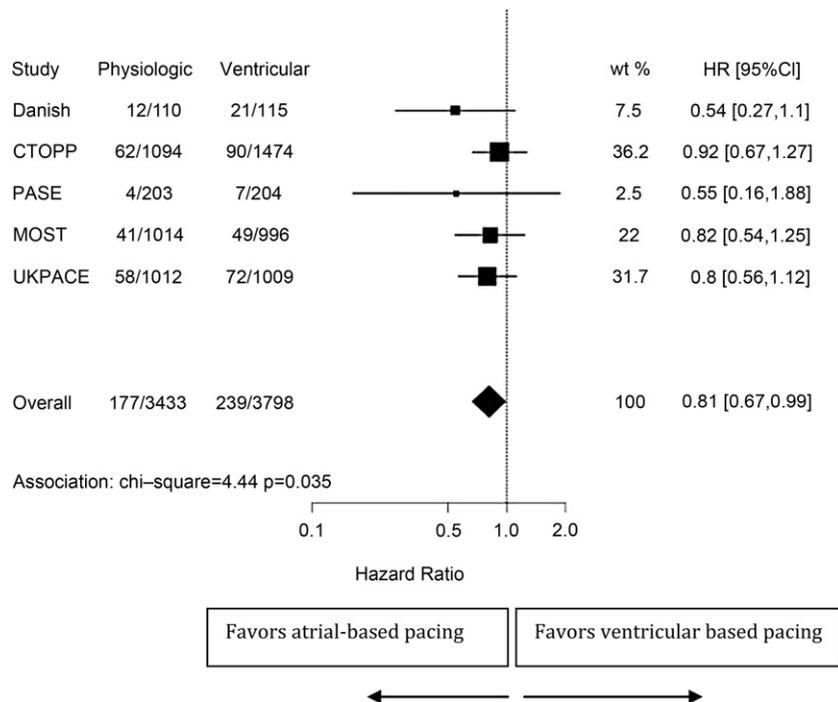
ence for DDD pacing compared to VVI pacing. In the PASE trial, 26% of the patients randomized to VVIR pacing needed to crossover to dual-chamber pacing due to severe pacemaker syndrome (33). A significant improvement in the quality of life was observed in these patients with reestablishment of AV synchrony. In MOST, 38% of patients in the ventricular pacing group had their pacemakers reprogrammed to the dual-chamber pacing mode for symptoms believed to be due to pacemaker syndrome (8). Of the 996 patients randomized to VVIR pacing, 182 (18.3%) developed severe pacemaker syndrome during follow-up that improved with reprogramming the device to DDDR pacing (33). A systematic review of the literature conducted by the Cochrane Collaboration reported a significant reduction in the symptoms of pacemaker syndrome associated with the use of dual-chamber pacing, compared to ventricular pacing, for both parallel and crossover design studies (34). A limitation of this analysis is the inclusion of patients with both SND and AV block indications for pacing. It is important to emphasize that no baseline parameter or data obtained at pacemaker implantation can be used to reliably predict the occurrence of clinically significant pacemaker syndrome (35,36). Although a blood pressure drop of ≥20 mm Hg associated with symptoms has been used as a definition of pacemaker syndrome, a drop in systolic blood pressure during ventricular pacing at implantation did not predict development of pacemaker syndrome during follow-up in MOST (33).

1.7. Deleterious Effects of Right Ventricular Pacing

Several studies have reported deleterious effects of right ventricular pacing, including an increased risk of developing heart failure and an increased burden of AF (18,37–40). Right ventricular apical pacing may cause ventricular dys-

function by creating ventricular dyssynchrony due to an abnormal activation sequence (39–42). In 50 patients with SND randomized to AAIR or DDDR pacing, dyssynchrony was more pronounced in the DDDR group than in the AAIR group at 12 months (p <0.05), reflecting a significant increase in dyssynchrony in the DDDR group without change in the AAIR group. Left ventricular ejection fraction decreased significantly in the DDDR group from baseline to 12 months (63.1 ± 8% vs. 59.3 ± 8%, p <0.05), while left ventricular ejection fraction remained unchanged in the AAIR group (61.5 ± 11% vs. 62.3 ± 7%, p = NS), thus supporting the concept that some degree of ventricular pacing may promote structural remodeling in the ventricle (43).

In a clinical trial of 225 patients randomized to atrial single-chamber pacing vs. ventricular single-chamber pacing, ventricular pacing was associated with a higher risk of heart failure (44). In a post-hoc analysis from MOST, a high cumulative percentage of ventricular pacing in 1,339 patients with a QRS <120 ms was found to be associated with an increased risk of heart failure hospitalization and AF (37). As indicated by the results of the Danish Multicenter Randomized Trial on Single Lead Atrial Pacing versus Dual-Chamber Pacing in Sick Sinus Syndrome (DANPACE) trial, most patients with SND have normal left ventricular function and tolerate some degree of right ventricular pacing without developing heart failure during long-term follow-up (10). Although not a study of the pacemaker population, the Dual-Chamber and VVI Implantable Defibrillator (DAVID) trial demonstrated that right ventricular pacing increased the combined endpoint of death or hospitalization for heart failure in patients with standard indications for implantable cardioverter defibrillator (ICD) therapy and left ventricular dysfunction but no indication for cardiac pacing (38). From the above studies, the percentage of right

ventricular pacing that has been implicated as potentially resulting in a higher risk of heart failure or AF is >40–50% (37,45–47).

Thus, there is strong evidence that a high proportion of right ventricular pacing, particularly in patients with some degree of left ventricular systolic dysfunction, is detrimental, and every attempt should be made to minimize it. The detrimental effects of right ventricular pacing may be minimal in patients without significant structural heart disease but are likely amplified in patients with clinical heart failure, a high percentage of right ventricular apical pacing, and evidence of left ventricular systolic dysfunction. Minimizing right ventricular pacing may be achieved effectively by programming longer AV delays (e.g., 220–250 ms) or implanting pacemakers that have specific algorithms for minimizing ventricular pacing (17,48). Such algorithms have been shown to substantially reduce the percentage of ventricular pacing in both patients with SND and AV block indications for pacing (49). Algorithms that reduce the cumulative percentage of ventricular pacing also have been reported to lower the burden of AF and the development of persistent AF during follow-up (13,48). In a retrospective study of 102 patients older than 75 years with SND, dual-chamber pacemakers with an algorithm to minimize ventricular pacing were associated with a fewer number of heart failure episodes and a lower risk of mortality than conventional dual-chamber devices (50). The optimal programming algorithm for minimizing ventricular pacing and optimizing clinical outcomes is unknown. Use of these algorithms may be inappropriate in patients with a long baseline PR interval or in whom atrial pacing results in a long PR interval (>250 ms) (51). Programming to minimize unnecessary right ventricular pacing may include turning off rate response in patients with single-chamber ventricular devices or turning off the rate responsive AV delay in patients with dual-chamber devices if these features are not deemed beneficial for a specific patient.

1.8. Is There a Role for Single-Chamber Atrial Pacing in SND?

The recently published DANPACE trial supports the preferential choice of a dual-chamber pacing system to an AAI pacing system for patients with SND and preserved AV conduction (see Recommendations Table 1) (10). Reasons for preferring DDD pacing to AAI pacing are the relatively high risk of AV conduction disease at baseline (up to 20%), the progressive risk of developing AV block during follow-up, and the risk of a significant complication associated with an operative revision from single-chamber atrial to dual-chamber pacing necessitated by the development of AV block in this population (8,10). In DANPACE, 1,415 patients with SND were randomized to DDDR pacing or AAIR pacing (10). The criteria for enrollment into DANPACE included a PR interval ≤220 ms if aged 18–70 years or <260 ms if aged >70 years, and a QRS duration <120 ms. Exclusion criteria included AV block or bundle branch block. After a mean follow-up of 5.4 years, no difference was observed with respect to the primary endpoint—death from any cause—between the two treatment arms. AF occurred more commonly with AAIR pacing than with DDDR pacing (HR 1.27,

p =0.02), and the risk of pacemaker reoperation in the AAIR group was twice as high when compared with the DDDR group. A total of 9.3% of patients (1.7% per year) randomized to AAIR pacing needed an operative revision to a dual-chamber pacing system during the study period despite careful patient selection. The risk of developing AV block over 34.2 months of follow-up after implantation of an AAI pacemaker in candidates considered "suitable" for this pacing mode was 8.4%, and this risk is predicted to increase over a longer duration of follow-up (15,16,19,20). No differences between the two treatment arms were observed with respect to stroke or the development of heart failure. Considering the risk of AV block with single-lead atrial pacing, together with the documentation that atrial pacing has no beneficial effect on long-term clinical outcomes compared with dual-chamber pacing, plus the incremental complications related to an operative revision to a dual-chamber pacing system, dual-chamber pacing is preferable to atrial pacing in SND.

Previous studies have indicated that frequent ventricular pacing even in an AV synchronous pacing mode increases AF (13). It was therefore an unexpected finding in the DANPACE trial that AF was significantly less common with DDDR pacing than with AAIR pacing. The use of moderately prolonged and individualized AV intervals in the DDDR group in the DANPACE trial may help explain this finding. Programming of a moderately prolonged AV interval results in minimal ventricular pacing when the patients have normal intrinsic AV conduction and prevents very prolonged AV conduction, which also has been associated with AF (51,52). Furthermore, very short AV intervals truncating the atrial emptying may also be associated with atrial dilatation and should be avoided. In addition, a recent meta-analysis of four clinical trials suggests that a high proportion of atrial pacing may increase the risk for AF (53). Although the DANPACE trial suggests that the use of AAIR pacing or pacing modes mimicking AAI would not significantly reduce AF compared to DDDR pacing with the pacemaker programmed with a moderately prolonged and individualized AV interval, the need to minimize atrial pacing by eliminating rate adaptive programming unless deemed clinically essential must be considered. It is also important to emphasize that some algorithms that result in excessive prolongation of the AV interval may be detrimental under certain clinical circumstances. and thus the use of these algorithms must be individualized (13,54). These algorithms may result in exaggerated AV delays resulting in pacemaker syndrome as a consequence of atrial contraction early in diastole (17). Timing cycles in the Managed Ventricular Pacing (MVP) mode are ventricular based and under some circumstances (eg. ventricular premature beat), noncompetitive atrial pacing will extend the V-A interval resulting in an extension of the next atrial pacing interval. The relative bradycardia or the occurrence of short–long–short ventricular sequences have been reported to cause ventricular proarrhythmia (55–57).

Early clinical trials reported a relatively low rate of progression to high-grade AV block in patients selected for AAI pacing (15,16). Since DANPACE included predominantly elderly patients, an AAI pacing system might be considered in the younger patient (i.e., <70 years at time of first implant) with SND and no evidence of AV or ventricular

conduction abnormality who may expect a number of pacing system revisions over decades of follow-up (see Recommendations Table 1) However, later development of AV block cannot be predicted.

1.9. Single-Chamber Ventricular Pacing in SND

None of the randomized trials of dual-chamber pacing vs. single-chamber ventricular pacing have reported a substantial benefit of the dual-chamber pacing mode on survival or stroke (6,8,10). Backup VVI pacing may be considered in the patient with normal ventricular function not expected to require frequent pacing. Backup VVI pacing may also be considered in the sedentary patient who is not likely to require frequent pacing, the patient with significant comorbidities that will influence survival and other clinical outcomes, as well as in patients in whom venous access is an issue. Dual-chamber pacing is not beneficial, and single-chamber ventricular pacing is indicated in patients with permanent AF or longstanding persistent AF if no attempt to restore sinus rhythm is planned (see Recommendations Table 1).

1.10. Rate Adaptive Programming

Chronotropic incompetence is common in patients with SND and may evolve as part of the natural history of the disease, particularly if AV nodal drugs or other negatively chronotropic medications are required to manage atrial tachyarrhythmias. All contemporary pacemakers have sensor systems and are able to provide rate adaptive pacing. Rate adaptive pacing was used predominantly, but not exclusively, in all of the randomized trials that included patients with SND (5–8,10). Although some clinical trials have reported a benefit of rate adaptive pacing on exercise tolerance over the short term, the long-term benefit is the subject of debate. One trial evaluated whether dual-chamber rate adaptive pacing improved quality of life compared with dual-chamber pacing alone (12). A total of 872 patients with moderate chronotropic incompetence were included and randomized into the two arms and followed for 1 year. Moderate chronotropic incompetence was defined as a blunted heart rate response not exceeding 80% of maximum predicted heart rate (220 − age) at peak exercise having completed at least two stages of exercise testing using a modified Bruce protocol. No difference between the two treatment arms was observed with respect to the primary endpoint—quality of life. Patients with rate modulation had a higher peak exercise heart rate after 6 months, but total exercise time was not increased with rate modulation. Furthermore, more hospitalizations for heart failure were observed in the group treated with rate adaptive pacing compared to the group without rate adaptive pacing (7.3% vs. 3.5%, p <0.01). Based on these data and the concern that more atrial pacing may increase the risk of AF (53) rate adaptive programming is recommended only for patients with evidence of significant symptomatic chronotropic incompetence and demonstrated improvement following programming the rate adaptive feature. The need for rate adaptive pacing should be reassessed as part of routine follow-up since chronotropic incompetence may evolve over time (see Recommendations Table 1).

2. Pacemaker Device and Mode Selection for AV Block

Expert Consensus Recommendations (see Table 1 for a summary of consensus recommendations)

CLASS I

1. Dual-chamber pacing is recommended in patients with AV block (Level of Evidence: C) (22).
2. Single-chamber ventricular pacing is recommended as an acceptable alternative to dual-chamber pacing in patients with AV block who have specific clinical situations that limit the benefits of dual-chamber pacing. These include, but are not limited to, sedentary patients, those with significant medical comorbidities likely to impact clinical outcomes, and those in whom technical issues, such as vascular access limitations, preclude or increase the risk of placing an atrial lead (Level of Evidence: B) (22).
3. Dual-chamber pacing is recommended over single-chamber ventricular pacing in adult patients with AV block who have documented pacemaker syndrome (Level of Evidence: B) (31–34,61).

CLASS IIa

1. Single-lead, dual-chamber VDD pacing can be useful in patients with normal sinus node function and AV block (e.g., the younger patient with congenital AV block) (Level of Evidence: C) (58,59).
2. VVI pacing can be useful in patients following AV junction ablation, or in whom AV junction ablation is planned, for rate control of AF due to the high rate of progression to permanent AF (Level of Evidence: B) (86–89).

CLASS III

1. Dual-chamber pacing should not be used in patients with AV block in permanent or longstanding persistent AF in whom efforts to restore or maintain sinus rhythm are not planned (Level of Evidence: C) (1).

Pacemakers with ventricular pacing capabilities are indicated in patients with AV conduction disturbances that include various degrees of intermittent or permanent AV block and selected patients with bifascicular block who have documented or presumed intermittent AV block (1). Although a patient may present with complete heart block, AV conduction may resume and the need for pacing may be intermittent over time (49). Nevertheless, recent clinical data show that a number of patients with intermittent AV conduction abnormalities progress to complete heart block over longer-term follow-up (17,60). Patients with AV conduction disease and left ventricular dysfunction and some patients who will be paced in the ventricle most of the time may benefit from cardiac resynchronization therapy. As stated in the introduction, indications for cardiac resynchronization therapy have been published previously, and guideline updates related to these indications are also in progress (1–3). Thus, specific recommendations for cardiac resynchronization therapy are not addressed in this document.

The minimum requirement for pacing in AV conduction disease is to prevent symptoms secondary to bradycardia.

Ideally, pacing should restore AV synchrony without adversely affecting ventricular synchrony. In patients with normal sinus node function, VDD pacing restores both AV synchrony and chronotropic competence. Single-chamber rate adaptive ventricular pacing also restores chronotropic competence, but not AV synchrony. AV synchrony contributes significantly to cardiac output, especially at rest and during lower levels of exercise. It increases stroke volume by as much as 50% and may decrease left atrial pressure by up to 25% (32,61). Patients with diastolic dysfunction, such as those with significant left ventricular hypertrophy, who depend on optimized preload, likely derive the most benefit from AV synchrony (62,63).

As discussed previously, ventricular pacing can cause adverse hemodynamic effects due to ventriculoatrial conduction or atrial contraction against closed AV valves, resulting in pacemaker syndrome (30). Shortly after the introduction of dual-chamber pacemakers, several randomized controlled short-term studies reported that dual-chamber pacing resulted in improved symptom scores and less pacemaker syndrome compared with ventricular pacing (30,32,64). Based on these studies, dual-chamber pacemakers were widely adopted in preference to single-chamber pacemakers for the treatment of patients with AV conduction disease.

The optimal pacing mode for patients with AV conduction disease has been the subject of debate. Three major randomized clinical trials (PASE, CTOPP, and UKPACE) have compared dual-chamber pacing to single-chamber ventricular pacing in patients with AV block (5–7,22). These randomized controlled trials included mostly elderly patients (mean age 73–80 years) and many with comorbidities. PASE and CTOPP also included patients with SND, 49% and 51% had AV block as the primary indication for pacing, respectively. Only UKPACE was limited to patients paced for AV conduction disease. UKPACE (22) enrolled 2,021 elderly patients (mean age 80 ± 6 years) and randomized them to dual- or single-chamber ventricular pacing. The ventricular pacing cohort was also randomized to fixed-rate ventricular pacing or rate adaptive pacing. At entry, 20% of patients were asymptomatic, and 38% had intermittent AV block. For the 65% of patients in whom data were available, the percent of ventricular paced beats was significantly lower for single-chamber vs. dual-chamber pacemakers (93% vs. 99%, p $<$0.001). Neither CTOPP nor PASE was powered to specifically assess clinical outcomes in the subgroup of patients with an AV block indication for pacing, and neither showed a significant advantage of dual- or single-chamber pacing for most outcomes measured. The effects of pacing on important clinical outcomes in patients with AV block as a result of these clinical trials are summarized below.

2.1. AF

Atrial or dual-chamber pacing compared to single-chamber ventricular pacing in the CTOPP population overall significantly reduced the risk of AF (6,7). The incidence of AF is lower in patients with an AV block indication for pacing compared to those with a SND indication for pacing (21). In CTOPP patients with an AV block indication for pacing were less likely to progress to permanent AF compared to those with a SND indication for pacing (65). In UKPACE, which

included only patients with AV conduction system disease, the annual event rates for developing AF were similar in the dual-chamber and ventricular pacing groups (2.8%/yr and 3.0%/yr, respectively) (Figure 2) (22).

2.2. Stroke/Thromboembolism

Dual-chamber pacing, compared with single-chamber ventricular chamber pacing, did not reduce the risk of stroke or systemic thromboembolism in either CTOPP or UKPACE (Figure 3) (6,7,22).

2.3. Heart Failure

Dual-chamber pacing, compared with single-chamber ventricular chamber pacing, did not reduce the risk of heart failure in either CTOPP or UKPACE (6,22).

2.4. Mortality

Dual-chamber pacing, compared with single-chamber ventricular chamber pacing, did not reduce the risk of death from all causes or from cardiovascular causes in either CTOPP or UKPACE (Figure 1) (6,22).

2.5. Exercise Capacity

Shortly after the introduction of dual-chamber pacemakers, short-term studies reported that dual-chamber pacing resulted in improved exercise tolerance compared with fixed-rate ventricular pacing (66). However, few studies comparing dual-chamber and rate adaptive ventricular pacing have shown similar benefit. Sulke et al. (67) performed a crossover study of 22 patients implanted with dual-chamber rate adaptive pacemakers for high-grade AV block. These authors reported improved exercise time, functional status, and symptoms with DDDR compared with VVIR pacing, as well as a strong patient preference for the DDDR pacing mode (67). In contrast, most crossover studies reported no significant increase in exercise tolerance when dual-chamber pacing was compared with the VVIR pacing (68–74). In CTOPP, an improvement in exercise capacity as assessed by the distance walked in 6 minutes was observed in a subgroup of patients randomized to atrial or dual-chamber pacing who had a high degree of pacing (29).

2.6. Quality of Life

Small, randomized crossover studies have reported significant differences in quality of life, with most individual patients preferring dual-chamber to single-chamber pacing (Table 3) (31,67–84). These studies included patients who were capable of exercising, and many had been paced in the dual-chamber mode at the time of study enrollment. Patients who were recruited after a period of dual-chamber pacing, or patients who were randomized to dual-chamber pacing first, were more likely to request early crossover from single-chamber to dual-chamber pacing. In one study, patients with no reported symptoms attributed to single-chamber ventricular pacing were revised to dual-chamber pacing at the time of generator change. Despite their being asymptomatic before crossover, their symptom scores improved after initiation of dual-chamber pacing (78).

Table 3. Comparison of Symptom Score and Patient Preference in Randomized Crossover Trials of Pacing Mode in Patients With AV Conduction Disease: Single- vs. Dual-Chamber Pacemakers

Study	n	Age	Pacing Indication	Symptoms	Patient Preference
Studies comparing physiological pacing with fixed-rate VVI pacing					
Perrins 1983 (75)	13	65 (32–87) years	AV block	Symptoms and exercise tolerance improved with physiological (VDD) pacing compared with VVI	More patients preferred VDD
Heldman 1990 (31)	40	Not stated	Not stated	Symptoms worse in VVI mode compared with dual-chamber pacing	65% had moderate or severe symptoms and 18% mild symptoms in VVI compared with DDD
Sulke 1992 (78)	16	41–84 years	AV block	Fewer symptoms in DDD compared with VVI	69% preferred DDD, VVI least acceptable in 50%
Avery 1994 (69)	13	>75 years	AV block	Fewer symptoms and increased exercise tolerance with dual-chamber physiological pacing compared with ventricular pacing	Physiological dual-chamber pacing preferred
Channon 1994 (70)	16	77–88 years	AV block	Fewer symptoms and improved exercise ability with DDD compared with VVI pacing	3 patients requested early reprogramming from VVI; 11 of 16 preferred DDD
Studies comparing physiological pacing with rate adaptive VVIR pacing					
Sulke 1991 (67)	22	18–81 years	High-grade AV block and chronotropic incompetence	Perceived general well-being, exercise capacity, functional status, and symptoms were significantly worse in the VVIR than in dual-chamber rate responsive modes	5 in VVIR requested early reprogramming DDDR preferred to VVIR
Oldroyd 1991 (73)	10	23–74 years	AV block	No difference in symptoms and maximal exercise performance between DDD and VVIR pacing	1 patient requested early crossover
Lau 1994 (79)	33	66 ± 1 years	15 AV block	Fewer symptoms, better stamina, and improved quality of life with DDDR	DDDR preferred over DDD and VVIR
Lukl 1994 (80)	21	68 ± 8 years	13 AV block	Symptoms and quality of life improved with DDD compared with VVIR pacing	Majority preferred DDD
Hargreaves 1995 (72)	20	80.5 ± 1 years	AV block	Symptoms reduced with DDD pacing compared with VVIR or VVI; exercise performance worse with VVI compared with DDD or VVIR	11 preferred DDD
Deharo 1996 (71)	18	70 ± 6.5 years	AV block	No significant difference in quality-of-life or cardiopulmonary performance, but trend toward increased sense of well-being with DDD compared with VVIR mode	3 disliked VVIR
Kamalvand 1997 (68)	48	64 years (mean)	Atrial arrhythmias and heart block	Perceived well-being better with DDDR with mode switching compared with conventional DDDR or VVIR	DDDR preferred over VVIR
Höijer 2002 (82)	19	75.5 ± 7.3 years	12 AV bock	Quality of life was better, with less dyspnea and improved general activity, with DDDR compared with VVIR mode	7 in VVIR requested early crossover; 11 preferred VVIR
Ouali 2010 (81)	30	76.5 ± 4.3 years	Complete Heart block	Improved quality of life with DDD pacing compared with VVIR; Pacemaker syndrome 30% VVI vs. 0% DDD, $p < 0.05$	18 preferred DDD; 0 preferred VVI

Although it is clear that the majority of patients who have already experienced pacing, either dual-chamber or ventricular, prefer dual, neither PASE (5) nor CTOPP (26) reported significant differences in quality of life between single- and dual-chamber pacing in patients with AV block. A detailed analysis of quality of life in these two randomized studies of pacing mode confirmed that pacing clearly improved quality of life over no pacing, but it did not show a difference between dual- and single-chamber pacing (5,26). These data suggest that the effect of pacing mode on quality of life depends on various factors, including the order of testing, the patient population, and the follow-up duration. For example, pacing mode may be more important in younger, active patients with few comorbidities than in patients whose quality of life may be strongly influenced by comorbidities, such as the patients enrolled in the PASE study.

2.7. Pacemaker Syndrome

Previous studies, including a meta-analysis of patients with SND and AV block, reported a significant reduction in pacemaker syndrome with dual-chamber pacing compared to single-chamber ventricular pacing (see Recommendations Table 1 and Table 3) (33,34,67–74). However, as indicated previously, crossover to dual-chamber pacing is heavily influenced by whether this can be accomplished by reprogramming alone in the presence of a dual-chamber pacemaker or by a surgical intervention. For example, in PASE, all patients received a dual-chamber pacemaker. and 26% of patients randomized to ventricular pacing were considered to have pacemaker syndrome sufficiently severe to necessitate reprogramming the pacemaker from the VVI to DDD mode (5). About half of the patients who had pacemaker syndrome and reprogramming to the DDD mode had AV block (5). Functional status, assessed by SF-36, improved after crossover in all patients (5). In contrast, in CTOPP, only 7% of patients who were implanted with single-chamber pacemakers and followed over 6 years underwent reoperation for revision to a dual-chamber pacing system (7). This apparent difference in incidence may reflect variability or the reliability of the diagnosis. It may also reflect the preference of patients and/or physicians to consider a pacing system revision only for severe symptoms if this requires a reoperation.

2.8. Pacing Mode after AV Junction Ablation

Catheter ablation of the AV node to produce complete heart block combined with permanent pacing is a recognized treatment to control the heart rate and alleviate symptoms in patients with medically refractory AF. Although this procedure is most often utilized in patients with persistent or permanent AF, AV junction ablation and pacing is also an accepted treatment for patients with drug-refractory paroxysmal AF (85). However, 16–35% of patients develop permanent AF within the first 6 months after AV junction ablation (86–89), and this rate continues to increase during long-term follow-up (86,88,89). The progression of AF has been attributed to the cessation of antiarrhythmic drug therapy; however, even with continued antiarrhythmic drug therapy the incidence of permanent AF is high after AV junction ablation

(39,90). This high incidence of permanent AF may be due to the unfavorable neurohumoral or hemodynamic consequences of ablation and/or the impact of right ventricular pacing (39). Based on the high rate of progression to persistent or permanent AF following AV junction ablation, single-chamber ventricular pacing is an appropriate mode of pacing for the majority of patients undergoing this procedure (see Recommendations Table 1).

2.9. Potential Deleterious Effects of Ventricular Pacing in AV Block

Most randomized controlled trials did not report the percent of ventricular pacing in patients with AV block (5–7,22). Because they were not performed with pacemakers that included algorithms to minimize right ventricular pacing, it is likely that the proportion of right ventricular pacing was high. Although algorithms to minimize ventricular pacing are most effective in patients with intact AV conduction (13,91,92), they have also been used in patients with intermittent AV block (49,60). One such algorithm allowed a 60% relative reduction in ventricular pacing in patients with AV block over the short term (48). Cumulative ventricular pacing can be as low as 28% in patients with intermittent AV block (93). However, there is no documentation that minimizing ventricular pacing is beneficial in patients with AV block. Moreover, no sufficiently large trial has evaluated the safety of such algorithms in patients with AV block. Case reports have indicated that the use of algorithms allowing intermittent AV block may have deleterious effects in some patients with AV block (13,55–57). Furthermore, a considerable number of patients with intermittent AV block progress to develop complete heart block over longer-term follow-up (60).

2.10. Single-Lead, Dual-Chamber VDD Pacemakers

In contrast to commonly used dual- and single-chamber pacemakers, single-lead, AV pacemakers (VDD) constitute less than 1% of implanted pacemakers in the United States and 5% in Canada (94). The single ventricular lead contains an additional floating bipole for atrial sensing that permits VDD pacing. These systems can restore AV synchrony in patients with normal sinus node function without an additional atrial lead. Thus, they may reduce procedure time and some complications associated with dual-chamber implants. They are used infrequently because the atrial sensing ability of the lead has tended to degrade over time, and implanters are concerned about the potential need for atrial pacing if SND develops (95–96). However, a VDD pacing system can have a potential role in the management of the younger patient, such as the patient with congenital heart block who might expect multiple system revisions over decades of follow-up (see Recommendations Table 1).

2.11. Factors Influencing Choice of DDD over VVI

Several factors may influence the choice of dual-chamber vs. single-chamber ventricular pacing. It should first be noted that patients might present with evidence for both SND and

AV block. SND is common in patients with AV block, occurring in about 30% (8,10). All of the randomized clinical trials compared outcomes in AV block in an elderly population (Table 2). Data on younger patients are limited. Among the consensus panel, dual-chamber pacing is preferred for the younger or more physically active patient in whom there is a strong desire to preserve AV synchrony and chronotropic response driven by the sinus node rather than by an imperfect activity sensor (see Recommendations Table 1) (30,61,97). There is also a preference for dual-chamber pacing in patients with any degree of systolic dysfunction and/or diastolic dysfunction in whom the maintenance of AV synchrony is more important for preserving optimal hemodynamics than heart rate alone (98–101). The atrial arrhythmia detection features in dual-chamber pacemakers also permit detection of atrial tachyarrhythmias that may result in therapeutic interventions, including therapy for stroke prevention (23–24). Dual-chamber pacing is not beneficial, and single-chamber ventricular pacing is indicated in patients with permanent AF or longstanding persistent AF if no attempt to restore sinus rhythm is planned (see Recommendations Table 1).

3. Other Indications

The writing committee did not address pacing mode for every indication identified in the current Device-Based Therapy of Cardiac Rhythm Abnormalities (1) as there are limited to no data on pacing mode for some less frequent indications (e.g., following cardiac transplantation, sarcoidosis, and muscular dystrophy). Consensus recommendations on pacemaker device and mode selection are provided for the following conditions **where a clinical decision for pacing has already been made:** hypersensitive carotid sinus syndrome, neurocardiogenic syncope, long QT syndrome, and hypertrophic cardiomyopathy.

3.1. Pacemaker Device and Mode Selection for Hypersensitive Carotid Sinus Syndrome

Expert Consensus Recommendations (see Table 1)

CLASS IIa

1. **Dual-chamber or single-chamber ventricular pacing can be useful for patients with hypersensitive carotid sinus syndrome (Level of Evidence: B) (102–106).**

CLASS III

2. **Single-chamber AAI pacing is not recommended for patients with hypersensitive carotid sinus syndrome (Level of Evidence: C) (102).**

Hypersensitive carotid sinus syndrome is defined as syncope or presyncope resulting from an exaggerated reflex in response to carotid sinus stimulation. There are two components of the reflex: the cardioinhibitory component, which is likely due to excess parasympathetic tone, causing slowing of the sinus rate with prolongation of the PR interval or even complete or high-grade AV block, and the vasodepressor component, which is due to inhibition of sympathetic discharge leading to vasodilatation and hypotension, independent of heart rate changes. The response to carotid massage

may not necessarily reproduce the clinical events that may occur in a variety of positions and under a variety of conditions. Moreover, even in a single individual, there is no reason to suspect that hypersensitive carotid response is a reproducible phenomenon.

No large randomized clinical trials of pacing mode have been conducted in this syndrome. Nevertheless, the impact of pacing mode in patients with syncope and hypersensitive carotid sinus syndrome has been evaluated in a few studies. AAI pacing alone has been shown to be ineffective in this syndrome (102), presumably due to concomitant AV block during carotid sinus activation. In a 17-year prospective study of 89 patients with hypersensitive carotid sinus syndrome, in which males outnumbered females 4.5:1 (age range at symptom onset 37–88 years, average 63 years), not one case of recurrent syncope occurred after single-chamber VVI pacemaker implantation (103). In a prospective randomized study of pacing vs. no pacing therapy performed in 60 patients with carotid sinus syndrome, syncope recurred in 16 (57%) of the no-pacing group and in only 3 (9%) of the pacing group (p = 0.0002), while 18 of 32 (56%) of the paced group received VVI devices and the remainder received DDD devices (104). Data from two studies of patients with hypersensitive carotid sinus syndrome reported that VVI pacing in this age group has been associated with a high (30–50%) incidence of intolerance, driven primarily by pacemaker syndrome (105,106). As indicated previously, preimplantation testing to predict pacemaker syndrome and intolerance to VVI pacing to aid in mode selection is imperfect (33).

A recent prospectively designed, double-blind study has been conducted to assess pacing mode on clinical outcomes in patients with carotid sinus syndrome (107). In this small crossover study, comparisons were made between VVI vs. DDDR vs. DDDR with rate drop response in patients with carotid sinus syndrome without evidence of concomitant SND or AV block. The primary endpoints of syncope or presyncope were significantly reduced after pacemaker implantation in all three groups, and no significant differences in the primary outcomes were demonstrated among the three pacing modalities. SF-36 scores revealed some minor benefits of DDDR pacing vs. baseline in the categories, but no pacing mode was found to be superior. The development of pacemaker syndrome was not seen in any group. Despite the physiological hemodynamic advantage of AV synchrony, the superiority of DDD pacing was not observed in this study. Sudden bradycardia response algorithms are designed to identify preemptively the onset of a reflex-mediated cardioinhibitory event and initiate a high-rate pacing intervention that putatively intercedes and aborts the episode. The results from this small randomized study suggest no clear advantage to this manner of pacing. Patients with pure vasodepressor syncope related to carotid sinus hypersensitivity were not enrolled in this study. It remains unclear whether this group derives benefit from the sudden bradycardia/rate-drop response algorithms.

Based on our knowledge of the pathophysiology of hypersensitive carotid sinus syndrome, there is a potential benefit of dual-chamber pacing to minimize the impact of the vasodepressor response and prevent pacemaker syndrome.

However, ventricular pacing seems to be effective in preventing syncope (see Recommendations Table 1).

3.2. Neurocardiogenic Syncope

Expert Consensus Recommendations (Table 1)

CLASS IIa

1. **Dual-chamber pacing can be useful for neurocardiogenic syncope (Level of Evidence: C) (109–114).**

CLASS III

1. **Single-chamber AAI pacing is not recommended for neurocardiogenic syncope (Level of Evidence: C).**

Similar to hypersensitive carotid sinus syndrome, patients with neurocardiogenic syncope may experience a cardioinhibitory response, a vasodepressor response, or both. Bradycardia usually accompanies neurocardiogenic syncope during tilt table testing and may be more often recorded during clinical episodes. Data supporting the use of pacemakers for neurocardiogenic syncope are scant (108), and there is a large placebo effect associated with pacing (109–112). Early studies published between 1980 and 1994 suggested that pacing is useful in patients with predominantly cardioinhibitory vasovagal responses and that pacing eliminated symptoms in 25% of these patients and prevented abrupt cardiovascular collapses (113). However, recent randomized trials have failed to confirm a substantial impact of pacing for prevention of syncope in neurocardiogenic syncope (109,114). The VPS II trial showed a trend in the direction of a benefit from pacing (110). This study may have been underpowered to detect a physiological response to pacing, as the design did not consider the strength of a placebo effect as a component of pacemaker benefit. Other studies evaluating the role of pacing in the treatment of this condition are ongoing (115).

In the clinical context, patients with neurocardiogenic syncope, particularly those with profound episodes of asystole (e.g., pauses >10 seconds), may benefit from cardiac pacing. Some patients with neurocardiogenic syncope have underlying sinus bradycardia and associated high vagal tone. Furthermore, the premonitory rate drop prior to syncope can be rather prolonged, with a total duration of the cardioinhibitory reflex lasting 85 seconds (range 47–116 seconds) (116). An atrial (AAI) pacemaker should not be used in an individual who may have episodic transient AV block due to augmented parasympathetic activation. If the clinical decision has been made to implant a pacemaker, a dual-chamber pacemaker should be selected to preserve AV synchrony, minimize ventricular pacing, and provide rate modulation in response to a sudden drop in heart rate (see Recommendations Table 1). VVI pacing has not been tested in this context.

3.3. Long QT Syndrome

Expert Consensus Recommendations (Table 1)

CLASS I

1. **Dual-chamber or atrial pacing compared to ventricular pacing is recommended for symptomatic or high-risk patients with congenital long QT syndrome (Level of Evidence: C) (117–119).**

The long QT interval syndrome can lead to episodic bradycardia-dependent torsades de pointes ventricular tachycardia (VT) causing presyncope, syncope, or cardiac arrest. While a pacemaker will not treat ventricular fibrillation that might develop in patients with long QT syndrome, it may be beneficial in patients who have recurrent episodic torsades de pointes due to bradycardia. Indeed, no studies have compared pacing therapy to ICD therapy for prevention of syncope or sudden cardiac arrest in the setting of long QT syndrome. It is recognized that ICD therapy might be recommended in symptomatic or high-risk long QT syndrome patients, and the above recommendations that apply specifically to pacemaker mode selection may not be applicable to all patients receiving ICDs. For instance, a single-chamber ICD may be preferred in some situations, especially in children and adolescents, to minimize lead complications and maximize device longevity.

Unfortunately, the literature regarding the benefits of pacing and selection of pacing mode in this syndrome is very limited. In one study of eight patients, pacing was instituted in three who were unsuccessfully treated with both beta-blockers and left cardiothoracic sympathectomy, and in two who proved refractory or intolerant to beta-blockers. After pacing using DDD, AAI, or VVI devices (70–85 bpm), there was no change in the corrected QT interval, but the measured QT interval decreased significantly. In long-term follow-up, all patients were alive and syncope-free. One patient with an AAI pacemaker developed dizziness due to AV block but remained asymptomatic after DDDR pacing (117).

From an international prospective study of long QT syndrome patients, 30 patients were identified who had undergone permanent pacemaker implantation (AAI, VVI, or DDD) for the management of recurrent syncope (118). Pacing reduced the rate of recurrent syncopal events in high-risk long QT syndrome patients, but pacing did not provide complete protection with recurrent syncope or ventricular arrhythmias occurring in 9 patients. The effect of pacing on repolarization was evaluated in 10 patients in whom the demand atrial pacing rate was faster than the intrinsic rate, and a significant reduction in QT interval with a nonsignificant reduction in corrected QT interval was noted. Another study suggested that combined beta-blocker therapy and pacing (DDD, AAI, or VVI) at a rate designed to normalize the QT interval appeared effective for symptomatic patients with long QT syndrome, although one sudden death occurred in a patient who had discontinued beta-blocker therapy (119).

Atrial pacing alone may be effective as it prevents bradycardia that causes torsades de pointes VT, and since most of these individuals have normal AV conduction, they do not require ventricular pacing. No randomized studies have compared the efficacy of a specific pacing mode for long QT syndrome. A dual-chamber pacemaker in this population may help detect episodes of VT with device monitoring that might impact patient management. It is possible that ventricular pacing in this population may lead to an increased risk of abnormal ventricular repolarization that could increase the risk for torsades de pointes VT (120). Based on these considerations, dual-chamber pacing might be preferred for patients with long QT syndrome and syncope secondary to pause-dependent VT (see Recommendations Table 1).

Table 4.   Perioperative Complications for DDD and VVI Pacing Systems

Type of Complication	CTOPP			UKPACE			MOST	PACE
	Dual (n = 1,084)	Ventricular (n = 1,474)	p Value	Dual (n = 1,012)	Ventricular (n = 1,009)	p Value	Dual	Dual
Any	9.0%	3.8%		7.8%	3.5%	<0.001	4.8%	6.1%
Pneumothorax	1.8%	1.4%	<0.001	—	—	—	1.5%	2%
Hemorrhage	0.2%	0.4%	0.42	—	—	—	—	—
Inadequate pacing	1.3%	0.3%	0.32	—	—	—	—	—
Inadequate sensing	2.2%	0.5%	0.002	—	—	—	—	—
Device malfunctioning	0.2%	0.1%	<0.001	—	—	—	—	—
Lead dislodgement	4.2%	1.4%	0.4	4.2%	2.5%	0.04	Atrial 1.9%, ventricular 1.1%	Atrial 0.5%, ventricular 1.7%

3.4. Hypertrophic Cardiomyopathy

Expert Consensus Recommendations (Table 1)

CLASS IIA

1. **Dual-chamber pacing can be useful for patients with medically refractory, symptomatic hypertrophic cardiomyopathy with significant resting or provoked left ventricular outflow obstruction (Level of Evidence: C) (121–124).**

CLASS III

1. **Single-chamber (VVI or AAI) pacing is not recommended for patients with medically refractory, symptomatic hypertrophic cardiomyopathy (Level of Evidence: C) (124).**

Hypertrophic obstructive cardiomyopathy is associated with diastolic dysfunction and obstruction to aortic outflow. Data are limited, and there is considerable controversy regarding the potential benefit of pacing in this setting. The concept that dual-chamber pacing may improve symptoms, reduce the left ventricular outflow tract gradient, and potentially reduce the risk of episodic AF is not supported by strong clinical evidence, although initial trials suggested benefit (121–123).

The M-PATHY Trial was a prospective, multicenter trial assessing pacing in 48 patients with symptomatic drug-refractory hypertrophic obstructive cardiomyopathy who were randomized to DDD pacing or pacing backup (AAI-30) in a double-blind, crossover study design followed by an uncontrolled and unblinded 6-month pacing trial (124). No benefit of pacing was seen for subjective or objective measures of symptoms or exercise capacity. After unblinded pacing, functional class and quality-of-life score were improved compared with baseline, but peak oxygen consumption was unchanged. Outflow gradient decreased in 57% of patients but showed no change or was increased in 43%. These data indicated that pacing is not a primary treatment for obstructive hypertrophic cardiomyopathy, and there was a substantial placebo effect from pacing (124). A placebo effect was also suggested in another small double-blind trial that randomized DDD pacing to backup AAI pacing for 3 months, as subjective symptomatic improvement occurred with implantation of a pacemaker even without any hemodynamic benefit (125).

In the absence of symptomatic AV block or SND in patients with hypertrophic cardiomyopathy, ventricular pac-

ing offers no benefit and could be detrimental. AAI pacing is not useful as the goal of pacing therapy is to maintain AV synchrony and create ventricular preexcitation. Thus, for the medically refractory patient in whom the clinical decision has been made to implant a pacemaker, dual-chamber pacing is recommended (see Recommendations Table 1).

4. Complications Related to Pacing

4.1. Implant Complications

Table 4 summarizes implant-related complications for dual-chamber and ventricular pacing. The overall complication rate was higher for dual-chamber pacing systems, compared to single-chamber ventricular pacing systems, as reported by the CTOPP and UKPACE Investigators (6,22). About half of these complications were atrial lead dislodgements that required surgical correction, and half were atrial sensing or pacing problems that did not require reoperation. In UKPACE, patients in the dual-chamber group were more likely to need a therapeutic intervention (8.8% vs. 5.6%, p <0.001) and to undergo a repeat procedure prior to hospital discharge (4.2% vs. 2.5%, p = 0.04) than those in the single-chamber group.

4.2. Complications Secondary to Pacing System Modifications

Although clinicians may favor starting with a single-chamber device in most patients with the intent to upgrade the device to a dual-chamber device if a patient develops AV block (with AAI pacemakers) or pacemaker syndrome (with VVI pacemakers), upgrading a device can be technically challenging and is associated with an increased risk of complications. The higher rate of initial implant complications for dual-chamber pacemakers is offset by the subsequent need to insert an atrial lead in some patients with single-chamber pacemakers during follow-up. In CTOPP, this upgrade rate was 4.3% in the first 3 years, and during long-term follow-up the rate of upgrade to a dual-chamber pacing system remained <1%/year (6,7). In one retrospective study of 44 patients who underwent upgrade from a single-chamber to a dual-chamber device, 20 patients (45%) experienced one or more complications. This led the authors to conclude that, compared with single- or dual-chamber implantation, pacemaker upgrades take longer

and have higher complication rates (126). The REPLACE Registry prospectively assessed procedure-related complications associated with pacemaker or ICD generator replacements over 6 months of follow-up. In the group of patients who also underwent a planned transvenous lead addition, the rate of major complications was 15.3% (95% CI 12.7–18.1). The authors concluded that pacemaker generator replacements with addition of a transvenous lead are associated with an appreciable complication risk (127).

5. Cost and Cost-Effectiveness of Dual- Versus Single-Chamber Pacemakers

Initial hospitalization costs are higher for dual- vs. single-chamber pacemakers, primarily because of the more expensive pulse generator and additional lead and the potential for higher rates of complications associated with dual-chamber pacemakers that are largely driven by atrial lead dislodgement. The reported differential initial cost between the two systems is in the range of $2,200–$2,600 (128,129). Indeed, several studies have assessed the economic implications of implanting a ventricular or dual-chamber pacemaker in patients with SND and AV block. Instead of just examining the absolute difference in cost between the two systems, these studies present cost-effectiveness analyses that also take into account differences in effectiveness between the two systems and, in some cases, adjust the results for quality of life. Indeed, such analyses are affected by many factors, including whether all important and relevant costs and effects are included, the perspective from which the costs and benefits are to be considered, whether direct and indirect costs are accounted for, the length of follow-up, and the method used to adjust the results for time. Differences in any of these factors may lead to different results.

In one analysis conducted by the Italian government, the incremental cost-effectiveness ratio of implanting a dual vs. a ventricular device was 260 Euros/quality-adjusted life year (QALY) (approximately US $330/QALY). Importantly, device replacement rates due to pacemaker syndrome had the biggest impact on the final results. Thus, the higher initial costs of the dual-chamber device implants appeared to be offset by a reduction in costs associated with repeat procedures and treatment of AF (130). Another study conducted in the United Kingdom examined the health and economic consequences of implanting a dual-chamber vs. a ventricular pacemaker for SND or AV block. That study demonstrated that the additional health benefits from dual-chamber pacing are achieved at a mean net cost of £43 per patient, resulting in a cost-effectiveness ratio of £477/QALY (approximately US $739/QALY). Therefore, although implanting a dual-chamber device increases the cost of the initial procedure, this is expected to be counterbalanced by a reduction in costs associated with repeat procedures and the management of AF (131).

In CTOPP, the incremental cost-effectiveness of physiological pacing was estimated from the viewpoint of a provincial government health care payer. The incremental cost-effectiveness of dual-chamber pacemakers was CAN $297,600 per life year gained (approximately US $290,482) and CAN $74,000 per AF event avoided (approximately US $72,230) (129). Based on only mortality and prevention of AF (and not considering

pacemaker syndrome and quality of life), physiological pacing did not appear to be economically attractive in the short term; however, long-term studies incorporating all nonfatal cardiac events, pacemaker syndrome, and quality of life may provide a more accurate assessment of the cost-effectiveness of physiological pacing (129).

Using a Markov model, a cost-effectiveness analysis of MOST showed that during the first 4 years, dual-chamber pacemakers increased quality-adjusted life expectancy by 0.013 year per subject with an incremental cost-effectiveness ratio of $53,000/QALY gained. Over a lifetime, dual-chamber pacing was projected to increase quality-adjusted life expectancy by 0.14 year with an incremental cost-effectiveness ratio of about $6,800/QALY gained. Thus, this analysis demonstrated that for patients with SND, dual-chamber pacing increases quality-adjusted life expectancy at a cost that is generally considered acceptable (128).

Although not specifically examined in these cost–benefit analyses, it is anticipated that battery technology as well as device programming will also impact on cost-effectiveness. Regardless of whether single- or dual-chamber devices are selected, programming should be optimized to enhance battery longevity and reduce cost.

6. Values and Preferences

Similar to guideline documents, this consensus document uses a grading system that separates the quality of evidence from the strength of recommendations. In this document, we have already considered factors that impact on the quality of life and functional status, such as pacemaker syndrome, right ventricular pacing, and AF while noting how these factors may influence mode selection. We recognize that in addition to the quality of the evidence, several other factors might affect the class of recommendations. These factors are not represented in our official recommendations as the current class of recommendations focuses largely on scientific evidence. Alternate grading systems may consider the balance between desirable and undesirable effects of a therapy, patient and physician values, and preferences in the provision of clinical care, as well as cost of therapy for determining the strength of recommendations (132,133).

In arriving at our recommendations, we considered factors such as the desirable effect of AV sequential pacing to prevent AF and the undesirable effects of ventricular pacing to cause pacemaker syndrome or promote AF. We considered the values and preferences of patients to avoid AF or pacemaker syndrome. We also present examples where patient conditions influence decision of pacing mode. For instance, a young active patient who has SND and normal AV and ventricular conduction may elect an AAI pacemaker to minimize hardware and reduce the risk of complications. Or a sedentary patient with prostate carcinoma and SND who has syncope with prolonged pauses and subclavian venous stenosis with limited venous access may accept single-chamber backup pacing rather than undergo a more complex procedure to allow insertion of a second lead.

In summary, guideline documents and consensus statements should be used to assist health care providers in clinical decision-making by describing generally accepted approaches for patient management based on review of the literature and a consensus from experts. However, as in all such documents, "the ultimate judgment regarding care of a particular patient must be made by the health care provider and the patient in light of all of the circumstances presented by that patient" (1). It is acknowledged that there will be circumstances in which deviations from guidelines or consensus recommendations are appropriate.

7. Conclusions

Patients with SND may derive benefit from atrial or dual-chamber pacing compared with ventricular pacing with regard to the risks of AF, stroke, pacemaker syndrome, and improved quality of life. Over the long term, dual-chamber pacing may be cost-effective. In patients with AV block, although dual-chamber pacing compared to ventricular pacing has equivalent effects on major cardiovascular outcomes including mortality, stroke, heart failure, and AF, it can reduce the incidence of pacemaker syndrome and improve some indexes of quality of life. For less common indications for pacing, the recommendations to consider dual-chamber pacing are based on small clinical studies. It is unlikely that large randomized trials will ever be conducted in these unique clinical subgroups. While implant complications are more frequent for dual-chamber than single-chamber pacemakers, the higher risk of complications for dual-chamber pacemakers is offset over time by the need to reoperate on a number of patients with single-chamber pacemakers for AV block or pacemaker syndrome. Estimates of the cost-effectiveness of dual-chamber pacemakers vary widely and should not be the dominant factor determining pacing device and mode selection.

Abbreviations

ACCF = American College of Cardiology Foundation
AF = atrial fibrillation
AHA = American Heart Association
AV = atrioventricular
CI = confidence interval
HR = hazard ratio
HRS = Heart Rhythm Society
ICD = implantable cardioverter defibrillator
QALY = quality-adjusted life year
SND = sinus node dysfunction
VT = ventricular tachycardia

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a = $0
b = <$10,000
c = >$10,000 to <$25,000
d = >$25,000 to <$50,000
e = >$50,000 to <$100,000
f = >$100,000

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a = $0
b = <$10,000
c = >$10,001 to ≤$25,000
d = >$25,001 to ≤$50,000
e = >$50,001 to ≤100,000
f = >$100,001

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Key Words: ACCF Expert Consensus Document ■ AV block ■ pacemaker mode ■ sinus node disease.