In the August 1, 1996, issue of Circulation, Connolly et al. presented their evaluation of current data concerning the use of DDD versus VVI pacing in patients with preserved sinus rhythm. They described a dilemma of DDD/VVI pacing in the following terms: “There are reasons to believe that dual-chamber pacing improves patient tolerance of pacing and reduces morbidity and mortality . . . However, . . . this technology is not widely used in most countries.” In summary they noted, “There are theoretical reasons why dual-chamber pacing might reduce mortality . . . Whether these theoretical expectations and physiological observations are indeed associated with a reduction in major clinical outcomes requires careful and prospective evaluation.”

There is some concern that the Connolly article may lead the cardiology community to question what most pacing experts already believe to be the superiority of dual-chamber pacing.

There is no question that careful and prospective evaluation may be very useful in confirming the theoretical and physiological observations that many in the pacing community have come to accept as fact. There are several points to be made in support of this argument.

Ventricular pacing is the mode most frequently used worldwide. This fact certainly cannot be construed as evidence of the superiority or equality of ventricular pacing or of atrial-based pacing (AAI, AAIIR, VDD, DDD, DDDR). Most likely this situation reflects the limited selection of pacemakers available in some countries owing to financial constraints, as well as the limited experience of pacemaker implanters with atrial leads and atrial-based pacing. An alternative explanation of why some physicians might be unwilling to adopt a more expensive new technology is that there is a lack of hard evidence from large-scale randomized trials. Certainly, reliable evidence from prospective randomized trials makes it easier to justify more expensive new technology. However, the United States and other countries with excellent healthcare standards have adopted the more expensive pacemaker technology on the basis of what is believed to be its clinical superiority.

There is a significant body of retrospective literature regarding the lower morbidity and mortality of atrial-based pacing over ventricular pacing. Connolly et al make the statement that data from any observational study regarding morbidity and mortality cannot be conclusive because they are nonrandomized, and data from a randomized study “raises concern.” Although this statement certainly appears valid, it should not lead the cardiology community away from atrial-based pacing devices. Despite all of the flaws of the retrospective literature regarding the superiority of atrial-based pacing, there is certainly a consistent trend common to all of these studies. One must now wait for the prospective studies to draw definitive conclusions but not abandon the current bias toward atrial-based pacing simply because the prospective data are limited.

Andersen et al. were the first to publish prospective data regarding patients with sinus node dysfunction. They have now followed up 225 patients randomized with either AAI or VVI pacing for 8 years. When they initially published the data, they were able to show a significantly higher incidence of paroxysmal and chronic atrial fibrillation (AF) and thromboembolism in the VVI-paced patients. In very recently published data with follow-up for 8 years, they have now been able to show a significantly higher incidence of congestive heart failure (CHF) and total and cardiovascular mortality in the VVI group of patients as well.

Also available in abstracts only are recent data from several additional prospective studies in which >300 patients were randomized to either dual-chamber or ventricular pacing mode and followed up for 2 years. In these studies, patients exhibited significantly fewer episodes of AF during dual-chamber pacing than during ventricular pacing. It should be noted that the rate of AF in randomized studies was comparable with data from outcomes studies.

In the largest outcomes study (retrospective analysis of 38,459 randomly selected pacemaker patients from the Medicare national hospital database), mortality in patients with dual-chamber devices was significantly lower than in patients with ventricular pacing. Notwithstanding the fact that dual-chamber pacing was used more frequently than ventricular pacing in cardiac patients with CHF, valvular diseases, and hypertension, the incidences of AF, stroke, and CHF were significantly higher during ventricular
pacing. Furthermore, dual-chamber pacing did reduce hospitalizations for AF and stroke.

Also subject to criticism but frequently quoted are quality-of-life comparisons between different pacing modes. In most studies that have evaluated quality of life, patients randomized to VVI/VVIR and DDD/DDDR preferred the dual-chamber pacing mode.

Definite end points of morbidity and mortality aside, it is also important to remember the significance of pacemaker syndrome. Although pacemaker syndrome can occur with any pacing mode, it is most common with ventricular pacing modes. These observations from non-randomized studies may be related in part to a reporting bias, because pacemaker syndrome is defined as symptoms due to lack of AV synchrony. In clinical practice, it is likely that some physicians may not attribute typical symptoms in a dual-chamber–paced patient to pacemaker syndrome. However, numerous studies designed randomly to evaluate the incidence of pacemaker syndrome have recognized this adverse hemodynamic effect in 75% to 83% of patients paced in ventricular modes, with 65% of these patients experiencing significant symptoms and 29% to 42% demonstrating absolute intolerance to ventricular pacing. A similar intolerance of ventricular pacing has been demonstrated more recently in 2 randomized, prospective studies.

Economic considerations are always an issue when a more expensive technology is being considered. It should be recognized that “economics is a societal concern, whereas randomization must be justified according to its effect on the individual.” Economic considerations related to dual-chamber pacing have recently been evaluated. One investigator has shown that in the long run, there is a significant cost benefit to implanting DDD pacemakers in patients with preserved sinus rhythm. In addition, meta-analysis of existing retrospective studies has also demonstrated a significant incremental cost associated with single-chamber ventricular pacing.

Critical appraisal of the current data (multiple large outcomes studies and small prospective randomized studies) leads us to believe that there is strong evidence to suggest that atrial-based pacing is superior to ventricular pacing in terms of hemodynamic and electrophysiological profiles, morbidity, and mortality, and consequently in long-term cost benefit as well as patient preference. There are limited subsets of patients for whom ventricular pacing is the mode of choice. Certainly for chronic AF, this would be the only reasonable pacing mode. In addition, there are some patients with significantly limited life expectancy or infirm patients for whom the benefits of dual-chamber pacing may not be demonstrable. However, this is certainly a specific subset of the total pacing population.

It is erroneous to construe the lack of large randomized studies as equivalent to the lack of any data supporting atrial-based pacing. On the contrary, we believe that the existing data from small randomized and large nonrandomized studies, particularly the high incidence of iatrogenic events in ventricularly paced patients, give some pause to the urgency of planning of large randomized trials. This is particularly true for a physician already using predominantly atrial-based pacing. Ethical considerations may allow these studies to be performed in centers not yet using atrial-based pacing for whatever reason.

Controversies remaining over atrial-based versus ventricular-based pacing (VVI, VVIR) may be resolved through ongoing prospective trials. Recently, one of us discussed in detail the obstacles to conducting large-scale clinical trials for pacemaker mode selection. Only a study in which all patients receive dual-chamber systems regardless of presentation has the ability to discern whether atrial-based pacing is superior to ventricular pacing. It is essential that randomization must be justified according to its effect on the individual. Ethical considerations may contraindicate the use of atrial-based pacing in selected indications; recommendations similar to those proposed by us in this paper and previously are made.

Note Added in Proof
Since this article was accepted for publication, new ACC/AHA guidelines for the implantation of cardiac pacemakers have been published in Circulation (1998;97:1325–1335). Three levels of supporting evidence of recommendations are defined. Level A includes evidence with data from multiple, randomized clinical trials. Level B includes data derived from a limited number of trials involving a comparatively small number of patients or from well-designed data analysis of nonrandomized studies or observational data registries. Evidence based on consensus of expert opinion was assigned C. According to these criteria, the superiority of DDD pacing versus VVI would be ranked at level B. In the flow chart and table of guidelines for choice of an atrial-based pacemaker in selected indications, recommendations similar to those proposed by us in this paper and previously are made.

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