Pacing for Atrioventricular Block

TO THE EDITOR: The report by Toff and colleagues on the United Kingdom Pacing and Cardiovascular Events (UKPACE) trial (July 14 issue), 1 evaluating cardiovascular end points in elderly patients with atrioventricular block, showed that the use of dual-chamber pacing to maintain atrioventricular synchrony conferred no survival advantage over the use of single-chamber pacing. These results may be considered along with those of recent trials involving patients with atrial fibrillation that showed a lack of mortality benefit associated with a strategy that maintains atrioventricular synchrony by restoring sinus rhythm. 2 Perhaps the consequences of atrioventricular synchrony deserve closer inspection.

As Ellenbogen and Wood mention in the accompanying editorial, 3 atrioventricular pacing increases stroke volume and systolic blood pressure, as compared with ventricular pacing. These effects are probably more pronounced in elderly persons because of reduced aortic compliance and an increased incidence of diastolic dysfunction. Did the different pacing strategies lead to a meaningful difference in blood-pressure control or medication requirements? The harmful effects of higher blood pressure in the dual-chamber group may have offset any benefit from this pacing mode. In addition, how was baseline hypertension ascertained? A prevalence of 33 percent is about half what one would expect for an elderly population.

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TO THE EDITOR: A well-designed study, the UKPACE trial showed that among elderly patients with atrioventricular block, the pacing mode did not influence either the rate of death from all causes or secondary outcomes. In our opinion, this may underestimate the benefits of dual-chamber pacing. The UKPACE trial did not examine the effect of the pacing mode on the quality of life. Evidence indicates that VVIR pacing (ventricular pacing, ventricular sensing, inhibition response, rate-adaptive), as compared with DDDR pacing (atrial and ventricular pacing, atrial and ventricular sensing, dual response, rate-adaptive) can significantly influence the quality of life and the development of pacemaker syndrome. 1

Furthermore, as has been found with right ventricular pacing, evidence is emerging that right atrial pacing can be detrimental, resulting in interatrial dyssynchrony, delayed left atrial contraction, and reduced left ventricular filling. Studies support avoiding right atrial pacing, with the use of either the VDD mode 2 or bialtrial pacing. 3 Programming

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in the UKPACE trial encouraged right atrial pacing (DDDR, 60 to 125 beats per minute; rate-responsive atrioventricular delay, 75 to 150 msec), and the resulting effects on interatrial conduction and left ventricular filling may have reduced the benefit of atrioventricular dual-chamber (DDD) pacing.

Therefore, we believe that it would be premature to withhold dual-chamber pacing completely from the elderly population. Future studies to address the effects of pacing mode on the quality of life and to minimize right ventricular pacing could answer these important questions.

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THE AUTHORS REPLY: We agree with Drs. Fauchier and Babuty that a prospective evaluation of single-lead VDD pacing would be of interest. Single-lead VDD pacing is regarded as an acceptable alternative to dual-chamber pacing in atrioventricular block,1 but there are few comparative data.2

Dr. Amato raises the possibility that deleterious effects of higher systolic blood pressure due to improved hemodynamic function might offset any benefit of dual-chamber pacing. Blood pressure was not recorded during follow-up, so we cannot test this hypothesis on the basis of our data. The rate of use of beta-blockers during follow-up was higher in the dual-chamber group than in the single-chamber group (6.5 percent vs. 3.2 percent at 10 months), but there was little difference in the use of diuretics (50.1 percent vs. 49.9 percent), angiotensin-converting–enzyme inhibitors (21.3 percent vs. 21.6 percent), or calcium-channel blockers (16.9 percent vs. 12.5 percent). The reported prevalence of hypertension at baseline was determined on the basis of direct questioning of the patients and review of case notes, and it relates to a previously established diagnosis of hypertension. The actual prevalence is probably higher, since population screening data suggest that only 50 to 75 percent of elderly patients with hypertension are aware of having it.3

We agree with Dr. Heist and colleagues, and with the editorialists, Drs. Ellenbogen and Wood, that the quality of life is an important consideration. This was, in fact, assessed as a secondary outcome in UKPACE with the use of patients’ responses to the Medical Outcomes Study 36-item Short-Form General Health Survey and the EuroQol EQ-5D questionnaire.4 Spatial constraints precluded the inclusion of these data. We previously reported the low incidence of suspected pacemaker syndrome (2.7 percent) in our study and the lack of evidence to suggest the presence of a subclinical form.5

Heist and colleagues suggest that our recommended pacemaker settings, which investigators were free to change on clinical grounds, might have reduced the benefits of dual-chamber pacing by encouraging right atrial pacing. The median proportion of atrial beats that were paced in the dual-chamber group, obtained from pacemaker interrogation at 1, 10, and 36 months, was 15.0 percent, 20.0 percent, and 24.0 percent, respectively. Although we support the principle that unnecessary pacing (of the atrium or ventricle) should be minimized, the trial design was pragmatic, and the implementation of the pacing modes under investigation was intended to reflect standard clinical practice.

We believe that the data support our conclusion that for elderly patients with atrioventricular block, the choice between single-chamber or dual-chamber pacing is unlikely to influence the risk of death from all causes or of cardiovascular events in the early years after pacemaker implantation.

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for the UKPACE Trial Investigators
Progressive Multifocal Leukoencephalopathy, Natalizumab, and Multiple Sclerosis

TO THE EDITOR: According to the established definition of multiple sclerosis, the condition in the patient described by Kleinschmidt-DeMasters and Tyler (July 28 issue) should not have been diagnosed as multiple sclerosis. Apart from the unusual clinical findings, no oligoclonal bands were detected in two separate examinations of the cerebrospinal fluid, and repeated magnetic resonance imaging (MRI) scans obtained over the course of several years showed new and enlarging, but never enhancing, lesions. The most convincing argument against a diagnosis of multiple sclerosis is the neuropathology: no lesions that are characteristic for multiple sclerosis were detected. The patient described by Langer-Gould et al. in another article in the same issue may also raise concern about the diagnosis of at least “typical” multiple sclerosis. One to two oligoclonal bands in the cerebrospinal fluid would have to be considered negative, and repeated MRI scans would not show enhancing lesions. Therefore, it does not seem appropriate to conclude that patients with multiple sclerosis may be at risk for progressive multifocal leukoencephalopathy (PML) owing to treatment with natalizumab and interferon beta-1a. Is it possible to misdiagnose subclinical nonfatal cases of PML as multiple sclerosis in patients who are not obviously immunosuppressed? Further investigations of JC virus infections should extend our knowledge of this scenario.

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