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Permalink
https://escholarship.org/uc/item/0c5869qz

Journal
New England Journal of Medicine, 338(16)

ISSN
0028-4793

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Publication Date
1998-04-16

DOI
10.1056/nejm199804163381602

Peer reviewed
QUALITY OF LIFE AND CLINICAL OUTCOMES IN ELDERLY PATIENTS TREATED WITH VENTRICULAR PACING AS COMPARED WITH DUAL-CHAMBER PACING

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ABSTRACT

Background Standard clinical practice permits the use of either single-chamber ventricular pacemakers or dual-chamber pacemakers for most patients who require cardiac pacing. Ventricular pacemakers are less expensive, but dual-chamber pacemakers are believed to be more physiologic. However, it is not known whether either type of pacemaker results in superior clinical outcomes.

Methods The Pacemaker Selection in the Elderly study was a 30-month, single-blind, randomized, controlled comparison of ventricular pacing and dual-chamber pacing in 407 patients 65 years of age or older in 29 centers. Patients received a dual-chamber pacemaker that had been randomly programmed to either ventricular pacing or dual-chamber pacing. The primary end point was health-related quality of life as measured by the 36-item Medical Outcomes Study Short-Form General Health Survey.

Results The average age of the patients was 76 years (range, 65 to 96), and 60 percent were men. Quality of life improved significantly after pacemaker implantation (P<0.001), but there were no differences between the two pacing modes in either the quality of life or prespecified clinical outcomes (including cardiovascular events or death). However, 53 patients assigned to ventricular pacing (26 percent) were crossed over to dual-chamber pacing because of symptoms related to the pacemaker syndrome. Patients with sinus-node dysfunction, but not those with atrioventricular block, had moderately better quality of life and cardiovascular functional status with dual-chamber pacing than with ventricular pacing. Trends of borderline statistical significance in clinical end points favoring dual-chamber pacing were observed in patients with sinus-node dysfunction, but not in those with atrioventricular block.

Conclusions The implantation of a permanent pacemaker improves health-related quality of life. The quality-of-life benefits associated with dual-chamber pacing as compared with ventricular pacing are observed principally in the subgroup of patients with sinus-node dysfunction. (N Engl J Med 1998;338:1097-1104.)

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METHODS

The study was a single-blind, randomized, controlled comparison of ventricular pacing and dual-chamber pacing involving 29 centers. On the basis of statistical-power calculations, 400 patients were required in order to have a power of more than 80 percent to detect a clinically meaningful difference in the quality...
of life between treatment groups. Blocked randomization lists were produced centrally for each site. Patient recruitment began February 26, 1993, and ended September 30, 1994, when 407 patients had been enrolled. The patients were followed and clinical end points were assessed until the initiation of the close-out procedure, which began June 1, 1995, and ended August 31, 1995. After the close-out procedure was completed, the patients’ quality of life was assessed by telephone interviews through June 30, 1996. The average follow-up for clinical end points was 580 days (range, 216 to 996).

All patients were 65 years of age or older, were in sinus rhythm, required a permanent pacemaker for the prevention or treatment of bradycardia,4 and gave written informed consent for research participation. Intermediates dual-chamber rate-adaptive pacemakers (models 294-03, 293-03, 294-03R, and 294-05) were implanted. Patients were excluded from the study if they could not participate in the quality-of-life assessments, had clinically overt congestive heart failure at the time of implantation, had had atrial fibrillation without any documented sinus mechanism for more than six months, had serious noncardiac illness, or had inadequate atrial-capture or sensing thresholds.

Implantation and Programming

Once both atrial and ventricular leads had been positioned, a randomization envelope was opened. The pacemaker was programmed to ventricular or dual-chamber pacing before implantation. Randomization was stratified according to clinical site. Initial programming in both groups required the use of rate adaptation, which allows a sensor-based increase in the heart rate proportional to a patient’s activity. Therefore, the formal mode designations for the study were DDDR (atrial and ventricular pacing, atrial and ventricular sensing, dual response, rate-adaptive) for dual-chamber pacemakers and VVIR (ventricular pacing, ventricular sensing, inhibition response, rate-adaptive) for ventricular pacemakers.5 For both groups, a lower rate limit of at least 50 beats per minute was required, and an upper limit of less than 130 beats per minute was suggested. Programming of all other features was left to the discretion of the investigators.

Patient Monitoring

Follow-up visits and health-status assessments took place 3, 9, and 18 months after enrollment and at the end of the study. The assessment of health status before randomization was performed at the local clinical site, before the pacemaker mode was assigned. Subsequent assessments were made by telephone from the coordinating center by two experienced telephone interviewers who were unaware of the patients’ mode assignments. The first interviewer conducted 98 percent of the 9-month interviews, whereas the second interviewer conducted 98 percent of the 9-month interviews and 99 percent of the 18-month interviews.

Multidimensional health-related quality of life was assessed with the 36-item Medical Outcomes Study Short-Form General Health Survey (SF-36),6 which includes one multi-item scale measuring eight health-related aspects: physical function, social function, physical role, emotional role, mental health, energy, pain, and general health perceptions. The score on each of the eight health concepts ranges from 0 (worst) to 100 (best). For example, the average physical-function score for a healthy 70-year-old person is 69, whereas the average score for a patient of similar age but with congestive heart failure is 48.7 Disease-specific cardiovascular functional status was measured with the Specific Activity Scale.8 The score on this four-point scale ranges from 1 (best) to 4 (worst). We validated the SF-36 by comparing subgroups of study patients with diagnoses known to affect quality of life, such as heart failure or angina, and those without such diagnoses.

End Points

The primary end point was health-related quality of life as measured by the SF-36. In addition, we compared the following prespecified secondary clinical end points between groups: death from all causes; first nonfatal stroke or death; first hospitalization for heart failure; first nonfatal stroke, or death; development of atrial fibrillation; and development of the pacemaker syndrome. All the components of the composite end points were chosen on the basis of data in the pacing literature suggesting the potential for improvement with atrial-based pacing.9 The pacemaker syndrome (which is related to a sustained loss of synchrony between atrioventricular contraction) was defined as the presence of left-sided or right-sided heart failure in association with ventricular pacing or of symptomatic hypotension with a drop in blood pressure of 20 mm Hg or more during ventricular pacing. We also analyzed prespecified subgroups of patients with a diagnosis at implantation of sinus-node dysfunction or atrioventricular block.

Statistical Analysis

Base-line characteristics were compared between treatment groups with use of Wilcoxon’s rank-sum test for continuous measures and Fisher’s exact test for categorical variables. We used Wilcoxon’s signed-rank tests for paired data to assess changes that occurred after randomization in all patients and changes that occurred after crossover to dual-chamber pacing in patients with ventricular pacing. All analyses were based on the intention to treat. Scores for the SF-36 subscales were compared between modes at each period with a multiple linear regression analysis, with adjustment for sex, quartile of age, and base-line score for the specific subscale. Scores for the Specific Activity Scale were compared between treatment groups with an ordinal logistic regression adjusted for sex, quartile of age, and base-line score for the specific patient. In addition, longitudinal mode-related differences were analyzed with generalized estimating equations.10 For scores for the SF-36 subscales, a repeated-measures linear regression was used. For the scores for the Specific Activity Scale, the general-estimating-equation analogue of a binomial model was used. The design of the study necessarily permitted reprogramming from ventricular to dual-chamber pacing if severe pacemaker syndrome developed in patients assigned to ventricular pacing. In each such patient, scores for the SF-36 and Specific Activity Scale were assessed before crossover, and these scores were carried forward for subsequent statistical analyses of quality of life. The length of time to the occurrence of the clinical end points in each group was compared visually with use of Kaplan–Meier curves11 and inferentially with use of the Cox proportional-hazards method12 adjusted for sex and quartile of age. For all analyses, the P values were two-tailed, and a P value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Base-Line Characteristics

The average age of the patients was 76 (range, 65 to 96), and 60 percent were men. Over 70 percent of the overall population was in New York Heart Association class I or II. Twenty-nine percent of the patients had a history of supraventricular tachycardia, including atrial fibrillation, and 27 percent had a history of heart failure. Cerebrovascular disease was present at base line in 13 percent. The ejection fraction was known in the case of 254 patients (62 percent) and was normal in 56 percent of these. Antiarrhythmic therapy was in use in 17 percent of patients. There were no significant differences in any of the base-line characteristics between groups (Table 1).

Indications for and Characteristics of the Pacemakers

The indications for the implantation of a permanent pacemaker included atrioventricular block in...
201 patients (49 percent, of whom 119 patients, or 59 percent, had third-degree block), sinus-node dysfunction in 175 patients (43 percent), and other diagnoses in 31 (8 percent). Ventriculoatrial (retrograde) conduction at the time of implantation was present in 29 percent. There were no important differences in capture and sensing thresholds between groups at the time of implantation (Table 2).

Pacemaker Syndrome

During the course of the trial, pacemaker syndrome severe enough to warrant reprogramming from ventricular to dual-chamber pacing was diagnosed in 53 patients assigned to ventricular pacing (26 percent), in 45 percent of whom sinus-node dysfunction was the reason for implantation. Cross-over from ventricular to dual-chamber pacing occurred early: 44 percent of the 53 crossovers occurred within one month after implantation, and 77 percent within six months (Fig. 1). Although multiple symptoms were recorded in each patient, the clinical manifestations were fatigue in all patients, dyspnea or effort intolerance in 67 percent, orthopnea or paroxysmal nocturnal dyspnea in 24 percent, presyncope in 33 percent, and a feeling of fullness in the neck in 20 percent. After crossover, the patients had improvement in SF-36 scores, including scores for physical function (27, P = 0.03) and emotional role (+27, P = 0.01).

Other Changes in Assigned Mode

Four patients (2 percent) who were initially assigned to dual-chamber pacing had their pacemakers reprogrammed to single-chamber ventricular pacing during the course of the study because chronic atrial fibrillation or supraventricular tachycardia developed (P < 0.001 for the comparison with the crossover rate in the ventricular-pacing group).

Validation of SF-36

Patients with a history of heart failure at base line were compared with those without such a history. There was a 13-point difference in scores for the physical-function subscale of SF-36 (44 vs. 57, P < 0.001) and a 13-point difference in scores for the physical-role subscale (25 vs. 38, P = 0.004). Patients with a base-line history of angina were compared with those without angina. There was a 10-point difference in scores for the physical-function subscale (47 vs. 57, P = 0.001) and a 14-point difference in scores for the physical-role subscale (25 vs. 39, P = 0.002).

Quality of Life

In the overall group, there was significant improvement in health-related quality of life between base line (before implantation) and three months after implantation, as measured by several SF-36 subscales (social function, P < 0.001; physical role,
P<0.001; emotional role, P<0.001; mental health, P<0.001; energy, P<0.001). In contrast, there were no significant differences in scores between the ventricular-pacing group and the dual-chamber–pacing group in any of the SF-36 subscales at 3 months or 18 months. After nine months of follow-up, there was a significant difference favoring dual-chamber pacing only in scores for the mental health subscale (P=0.03) (Table 3). Longitudinal analyses, however, detected a borderline improvement in scores on the emotional-role subscale in patients assigned to dual-chamber pacing (P=0.04). There were no significant differences in cardiovascular functional status between groups, as assessed by the Specific Activity Scale, at either the three-month or the nine-month assessment. However, there was a significant difference favoring dual-chamber pacing at the 18-month visit (Table 4), and longitudinal analysis demonstrated a significant difference favoring dual-chamber pacing (P=0.045).

Clinical Events

There were no significant differences between the ventricular-pacing group and the dual-chamber–pacing group in the rates of death from all causes, stroke or death, stroke or death or hospitalization for heart failure, and the development of atrial fibrillation (Table 5).

Analysis of Prespecified Subgroups

Sinus-Node Dysfunction

Among the patients who received pacemakers because of sinus-node dysfunction, there were significant differences favoring dual-chamber pacing at three months in scores on the physical-role subscale (P=0.02), social-function subscale (P=0.03), and emotional-role subscale (P=0.002) of SF-36. Although in the later assessments there were no significant differences between treatment groups at each time point, longitudinal analyses demonstrated better scores on the emotional-role subscale (P=0.001) and social-function subscale (P=0.02) in the patients assigned to dual-chamber pacing. Longitudinal analysis of scores on the Specific Activity Scale demonstrated a significant difference favoring dual-chamber pacing (P=0.02). Furthermore, there were trends of borderline significance in clinical end points favoring dual-chamber pacing (Table 5).

Atrioventricular Block

Among the patients with atrioventricular block at implantation, there were no significant differences between groups in any of the SF-36 subscales, in longitudinal analyses of the Specific Activity Scale, or in any of the prespecified clinical end points (Table 5).

DISCUSSION

Industry sources estimate that nearly 190,000 pacemakers will be implanted in patients in the United States in 1998, a substantial increase since 1989, when 110,500 devices were implanted.13 Although dual-chamber pacemakers have been in common use for nearly two decades, the effect of the type of pacemaker on the long-term health-related quality of life of elderly pacemaker recipients has not been adequately studied.

Over 70 percent of pacemaker recipients are at least 70 years old,14 and there are sound physiologic reasons to expect that maintenance of atrioventricular synchrony with a dual-chamber pacemaker might
be desirable in elderly patients.\textsuperscript{15,16} However, dual-chamber pacemakers are more expensive and more difficult to implant and monitor than single-chamber ventricular pacemakers, and dual-chamber pacemakers carry a risk of complications in two leads, not just one.\textsuperscript{17} In the present cohort, pacemaker placement led to dramatic improvements in health-related quality of life. This uncontrolled observation is consistent with the reported low rate of recurrence of symptoms after pacemaker implantation.\textsuperscript{18} However, when patients with ventricular pacing were compared with patients with dual-chamber pacing, there were no convincing differences in general health-related quality of life. Analysis of two pre-specified subgroups — patients with sinus-node dysfunction and those with atrioventricular block at implantation — did reveal a favorable response to dual-chamber pacing in patients with sinus-node dysfunction. Nonetheless, these differences are considerably smaller than were previously thought. In contrast to the pattern observed with respect to general quality of life in the overall group, the Specific Activity Scale, an instrument that specifically measures the physical limitations associated with cardio-

### Table 3. Quality of Life Before and After Pacemaker Implantation, According to the Scores on the SF-36.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base Line</th>
<th>3 Months</th>
<th>9 Months</th>
<th>18 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VVIR (n = 204)</td>
<td>DDDR (n = 203)</td>
<td>P VALUE</td>
<td>VVIR (n = 167)</td>
</tr>
<tr>
<td>Percentage of eligible patients evaluated</td>
<td>100</td>
<td>100</td>
<td>85</td>
<td>81</td>
</tr>
<tr>
<td>Subscale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical function</td>
<td>52.9</td>
<td>54.4</td>
<td>0.55</td>
<td>53.9</td>
</tr>
<tr>
<td>Social function</td>
<td>61.3</td>
<td>63.4</td>
<td>0.45</td>
<td>70.0</td>
</tr>
<tr>
<td>Emotional role</td>
<td>33.4</td>
<td>35.9</td>
<td>0.54</td>
<td>53.6</td>
</tr>
<tr>
<td>Mental health</td>
<td>70.6</td>
<td>67.2</td>
<td>0.41</td>
<td>83.8</td>
</tr>
<tr>
<td>Energy</td>
<td>73.0</td>
<td>71.9</td>
<td>0.59</td>
<td>77.0</td>
</tr>
<tr>
<td>Pain</td>
<td>43.9</td>
<td>42.3</td>
<td>0.52</td>
<td>53.0</td>
</tr>
<tr>
<td>Health perception</td>
<td>67.3</td>
<td>66.1</td>
<td>0.67</td>
<td>69.7</td>
</tr>
<tr>
<td></td>
<td>60.3</td>
<td>60.3</td>
<td>0.97</td>
<td>62.3</td>
</tr>
</tbody>
</table>

*The numbers of patients are the numbers eligible for evaluation. VVIR denotes rate-adaptive single-chamber ventricular pacing, and DDDR rate-adaptive dual-chamber pacing. Patients who died were excluded from the analysis, and patients who enrolled too late for the 18-month interview were not included in the analysis at 18 months.

### Table 4. Cardiovascular Functional Status Before and After Pacemaker Implantation, According to the Scores on the Specific Activity Scale.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base Line</th>
<th>3 Months</th>
<th>9 Months</th>
<th>18 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VVIR (n = 204)</td>
<td>DDDR (n = 203)</td>
<td>P VALUE</td>
<td>VVIR (n = 167)</td>
</tr>
<tr>
<td>Percentage of eligible patients evaluated</td>
<td>100</td>
<td>100</td>
<td>81</td>
<td>80</td>
</tr>
<tr>
<td>Score on Specific Activity Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (best)</td>
<td>37</td>
<td>39</td>
<td>41</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
<td>20</td>
<td>22</td>
<td>27</td>
</tr>
<tr>
<td>3</td>
<td>37</td>
<td>38</td>
<td>34</td>
<td>27</td>
</tr>
<tr>
<td>4 (worst)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>P value</td>
<td>0.71</td>
<td>0.22</td>
<td>0.23</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*The numbers of patients are the numbers eligible for evaluation. VVIR denotes rate-adaptive single-chamber ventricular pacing, and DDDR rate-adaptive dual-chamber pacing. Patients who died were excluded from the analysis, and patients who enrolled too late for the 18-month interview were not included in the analysis at 18 months. P values and proportions shown are from an unadjusted chi-square test for trend.
vascular disease, detected differences favoring dual-chamber pacing that increased over time and were significant in longitudinal analyses.

Prior studies have suggested a measurably superior quality of life in patients with dual-chamber pacing, and on the basis of these studies we expected dual-chamber pacing to have a greater benefit than we actually found. There are important methodologic differences that may account for our divergent results. Some studies have used a short-term crossover design or measured quality of life with nonstandard instruments that have not been validated. We measured quality of life with a standard instrument and validated it against known disease states within the study population. Follow-up in crossover studies is short, and the long-term effects of any given pacemaker mode cannot be assessed. Blinding in crossover studies may be difficult, and investigator bias may occur. Our use of a long-term, parallel study design with quality-of-life interviewers who were unaware of patients’ treatment assignments obviated many of these problems and may account for our unexpected results.

The apparently divergent results of a generic instrument (SF-36) and a cardiovascular disease–specific instrument (the Specific Activity Scale) assessing quality of life in the overall group emphasize the complexities inherent in measuring this variable in the elderly. Although it is clear from our results that dual-chamber pacing is associated with long-term improvements in cardiovascular function, the importance of aging and of the development of other conditions may overwhelm the moderate improvements in cardiovascular functional class and minimize the long-term effect on general quality of life.

The pacemaker syndrome most often mimics left-sided or right-sided congestive heart failure with or without associated left ventricular systolic dysfunction, or it may present with autonomic dysfunction, hypotension, and associated symptoms. The syndrome is related to the loss of synchronous atrioventricular conduction. The reported incidence of the pacemaker syndrome varies widely, from 1.7 percent to 83 percent. Our results mandate a cautious interpretation of the crossover statistics. Crossovers occurred when symptoms of possible pacemaker syndrome reached a clinical threshold for reprogramming to dual-chamber pacing. Consequently, it is not surprising that we report an intermediate incidence of reprogramming to a dual-chamber mode. Nevertheless, over 70 percent of patients who were assigned to ventricular pacing and were alive at the end of the study were still in their assigned mode. Thus, on the basis of quality-of-life considerations alone, many patients who receive dual-chamber pacemakers might fare just as well with ventricular systems. However, more investigative effort should be focused on finding simple ways in which to identify preoperatively the minority of patients who will prove intolerant to ventricular pacing.

The literature on cardiac pacing is replete with retrospective analyses associating dual-chamber or atrial pacing with improved clinical outcomes. However, all these retrospective studies are flawed because pacemaker selection was not random and because clinicians selected the more expensive forms of technology for younger, less sick patients. In a late follow-up of a prospective study of patients with sinus-node dysfunction, Andersen et al. reported that atrial pacing reduced embolic events, atrial fibrillation, and mortality. We found that there was no significant mode-related difference in either the incidence of atrial fibrillation or any of the other prespecified clinical end points in the overall group. However, analyses of subgroups of patients with sinus-node dysfunction revealed trends similar to the findings reported by Andersen et al.

Patients with atrioventricular block did not demonstrate any clear benefit from dual-chamber pacing. This finding in patients with atrioventricular block is consistent with

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**TABLE 5. Analysis of the End Points in the Group as a Whole and Among Patients With Sinus-Node Dysfunction or Atrioventricular Block at Implantation.**

<table>
<thead>
<tr>
<th>Prespecified End Point</th>
<th>Overall Population</th>
<th>Sinus-Node Dysfunction</th>
<th>Atrioventricular Block</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VVIR (n = 204)</td>
<td>DDDR (n = 203)</td>
<td>VVIR (n = 95)</td>
</tr>
<tr>
<td></td>
<td>no. (%)</td>
<td>P VALUE</td>
<td>no. (%)</td>
</tr>
<tr>
<td>Death from all causes</td>
<td>34 (17)</td>
<td>32 (16)</td>
<td>17 (20)</td>
</tr>
<tr>
<td>Stroke or death from any cause</td>
<td>39 (19)</td>
<td>35 (17)</td>
<td>19 (22)</td>
</tr>
<tr>
<td>Stroke or hospitalization for heart failure or death from any cause</td>
<td>56 (27)</td>
<td>44 (22)</td>
<td>26 (31)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>38 (19)</td>
<td>35 (17)</td>
<td>24 (28)</td>
</tr>
</tbody>
</table>

*VVIR denotes rate-adaptive single-chamber ventricular pacing, and DDDR rate-adaptive dual-chamber pacing.*
the reported failure to find a clear difference in exercise duration in patients with atrioventricular block with rate-adaptive pacing, ventricular pacing, or dual-chamber pacing.27,30

The design of the study did not permit maintenance of an accurate registry to compare the screened and enrolled populations. However, the demographic and clinical characteristics of the participants were very similar to those of recipients of dual-chamber pacemakers in the Medicare data bank.26 Frequent ventricular pacing might be associated with the development of the pacemaker syndrome.31 However, the pacemakers used in this trial did not have accurate internal event counters, and the frequency of paced ventricular events is unknown. The use of rate adaptation may obscure differences between dual-chamber and ventricular pacing. The importance of this possibility cannot be assessed, since our study did not include a comparison group with simple ventricular-demand pacing. The difference in clinical events between groups may have been reduced by the crossover rate. The study was designed with good statistical power to detect clinically relevant differences in health-related quality of life. However, the statistical design still permitted a 20 percent likelihood of a false negative result. Finally, there was only limited statistical power to address differences in clinical events.

In the study, health-related quality of life improved dramatically after pacemaker implantation; however, general quality-of-life benefits associated with dual-chamber pacing as opposed to ventricular pacing were detectable only in the subgroup of patients with sinus-node dysfunction. These benefits were moderate. The interpretation of the quality-of-life results must be tempered by the rather high crossover rates from ventricular pacing to dual-chamber pacing and by strong trends toward clinical benefit in patients assigned to dual-chamber pacing, particularly in those with sinus-node dysfunction.

Funded by a grant from Intermedics, Freeport, Tex.

We are indebted to John Garcia and Richard Sanders for their support; to the study coordinators, Kimberly Vitale, R.N., and Carolina Dedosantos, for their dedicated assistance; to Elaine Abrams, quality-of-life interviewer, for her attention to detail; and to Lori Maritens for secretarial assistance.

APPENDIX

Other principal investigators of the Pacemaker Selection in the Elderly trial are as follows: J. Zimmerman, Hackensack Medical Center, Hackensack, N.J.; J. Kirchhofer, Baystate Medical Center, Springfield, Mass.; J. Brinker, Johns Hopkins Hospital, Baltimore; J. Hayes, Marshall Clinic, Marshfield, Wis.; N. Tulio, St. Joseph’s Hospital and Medical Center, Patterson, N.J.; S. Greenberg, St. Francis Hospital, Roslyn, N.Y.; H. Wein er, Delaware Cardiology Research Foundation, Newark, Del.; C. Love, Ohio State University, Cleveland; C. Dennis, Deborah Heart and Lung Center, Browns Mills, N.J.; R. Henry, Christ Hospital, Cincinnati; J. Herre, Cardiology Consultants, Norfolk, Va.; O. Randall, Howard University Hospital, Washington, D.C.; D. Bush, Francis Scott Key Medical Cen ter, Baltimore; C. Ulyse, University of Pennsylvania Medical Center, Phil adelphia; L. Beaunegard, Cooper Hospital, Camden, N.J.; T. Frichling, Fairfax Hospital, Fairfax, Va.; C. Schugert, Beth Israel Deaconess Medical Center, Boston; and J. Langberg, Emory University, Atlanta.

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Volume 338 Number 16 • 1103
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