To the Editor: Alternate- and multiple-site atrial pacing (AP) have been proposed as methods to prevent atrial fibrillation (AF) (1,2). However, changes in atrial activation by alternate- or multiple-site(s) AP might adversely affect atrial mechanical function and cardiac performance via atrioventricular (AV) mechanical coupling, especially during rapid atrial overdrive pacing. The aim of this study was to investigate the effect of mechanical coupling, especially during rapid atrial overdrive pacing. The study population included 12 patients without structural heart disease (6 men, mean age: 43 ± 14 years) after successful radiofrequency catheter ablation of paroxysmal supraventricular tachycardia. The study protocol was approved by our institutional research board. A quadripolar electrode catheter and a decapolar catheter were positioned in the RA appendage (RAA) or at high intra-atrial septum (IAS) and in coronary sinus, respectively, for pacing of RAA, IAS, coronary sinus ostium (CSO), and distal coronary sinus (DCS). An additional electrode catheter was positioned at right ventricular apex for ventricular pacing. Atrial volume and pressure were estimated using a 7-F custom-designed five-electrode combination pressure-conductance catheter (Millar Instruments, Houston, Texas) positioned within the RA as described previously (3,4). A fluid-filled catheter in the femoral artery was used to measure arterial pulse pressure (PP) as an index of global cardiac performance.

Before recording hemodynamic variables, at least 3 min of stable continuous capture at pacing site (at 3× threshold output with pulse duration of 2 ms) was performed to achieve steady-state conditions. Then RA pressure, RA conductance, and PP were measured during AV pacing from RAA, IAS, DCS, RAA + CSO, and RAA + DCS, respectively, at AV intervals of 0, 50, 100, and 150 ms using drive cycle lengths of 350 and 500 ms in random order. Intravenous 0.9% saline infusion at a constant rate of 100 ml/h was administered throughout the procedure to maintain ventricular preload and blood resistivity.

The RA pump and reservoir function were determined by using pressure-volume plane analysis, assuming that that measured conductance was proportionate to chamber volume (3,4). The “A” loop area and “V” loop area as quantified via planimetry represent the active work performed by the atrium during atrial contraction and the extent of atrial filling during ventricular

### Improved Atrial Mechanical Efficiency During Alternate- and Multiple-Site Atrial Pacing Compared With Conventional Right Atrial Appendage Pacing: Implications for Selective Site Pacing to Prevent Atrial Fibrillation

<table>
<thead>
<tr>
<th>Coronary Artery</th>
<th>n</th>
<th>Agreement (%)</th>
<th>Kappa</th>
<th>Agreement (%)</th>
<th>Kappa</th>
<th>Agreement (%)</th>
<th>Kappa</th>
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<tr>
<td>LAD</td>
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<td>93.3</td>
<td>0.85</td>
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<td>0.64</td>
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<tr>
<td>RCA</td>
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<td>95.6</td>
<td>0.88</td>
<td>95.6</td>
<td>0.91</td>
<td>92.4</td>
<td>0.82</td>
</tr>
<tr>
<td>Per segment</td>
<td>685</td>
<td>93.1</td>
<td>0.85</td>
<td>97.7</td>
<td>0.93</td>
<td>94.2</td>
<td>0.82</td>
</tr>
<tr>
<td>Per artery</td>
<td>180</td>
<td>93.3</td>
<td>0.86</td>
<td>97.2</td>
<td>0.94</td>
<td>91.7</td>
<td>0.83</td>
</tr>
<tr>
<td>Per patient</td>
<td>45</td>
<td>95.6</td>
<td>0.85</td>
<td>95.6</td>
<td>0.89</td>
<td>97.8</td>
<td>0.93</td>
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LM = left main coronary artery; RCA = right coronary artery.

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systole, respectively (5). Hemodynamic variables including PP, RA pressure, maximal RA conductance, and “A” and “V” loop area were averaged over three to six cardiac cycles. Optimal AV interval was determined as programmed AV delay resulting in maximal PP.

Continuous variables are expressed as mean ± 1 SD. Statistical comparisons were performed using repeated two-way analysis of variance. Adjustments for pairwise comparisons were made using Student-Neuman-Keuls test. Values of p < 0.05 were considered significant.

Because changes in RA mechanical work at optimal AV interval during different AP sites at 350 ms and 500 ms are similar, only data from AP at 500 ms were presented. The atrial pressure-dimension “A” loop areas were significantly larger during DCS pacing than during AP at other sites and were significantly smaller during IAS or RAA + CSO pacing than during RAA pacing (p < 0.05) (Fig. 1A). However, there were no significant differences in the “V” loop area between the different AP sites (Fig. 1B).

As compared to sinus rhythm (96 ± 8 ms), AP at RAA (126 ± 7 ms) and DCS (122 ± 7 ms) significantly increased P-wave duration (p < 0.05), but not during IAS (98 ± 9 ms), RAA + CSO (102 ± 10 ms), or RAA + DCS (99 ± 10 ms) pacing (p > 0.05). Furthermore, P-wave durations were significantly reduced during IAS, RAA + CSO, and RAA + DCS pacing compared with RAA pacing (p < 0.05).

As shown in Figure 2, there were no significant differences in PP, RA pressure, and maximal RA conductance during different AP sites at different AV intervals between 350 ms and 500 ms. As compared to AP at 350 ms, PPs were higher (Fig. 2A) and RA pressures were lower (Fig. 2B) during AP at 500 ms at the corresponding sites of AP and AV interval, but there was no difference in the RA conductance (Fig. 2C).

Although alternate- and multiple-site APs have been increasingly applied to prevent AF (1,2), clinical data on the effects of AP sites on atrial mechanical function are limited. Previous studies suggested that AP lead location alters atrial and ventricular hemodynamics (4,6). The present results confirm and extend these previous findings and further indicate that AP site has important, albeit subtle, effects on atrial function independent of cycle length and AV delay.

To optimized atrial mechanical function, preferred AP sites should increase atrial efficiency by maximizing the proportion of work for ventricular filling. We observed significantly reduced “A” loop area with no change in global cardiac performance during IAS and RAA + CSO compared to RAA and DCS pacing at optimal AV delay. In contrast, “V” loop area was not affected by the AP site. These findings suggest that RAA + CSO and IAS pacing improved atrial mechanical pump efficiency without significantly altering atrial reservoir function.

Recent studies showed that alternative pacing at IAS (1) or dual-site RA pacing at RAA + CSO (2) might prevent AF. In concordance with these findings, the present results suggest that optimized atrial lead placement at RAA + CSO or IAS may reduce or slow the progression of pro-arrhythmic substrate by reducing atrial activation time and improving atrial mechanical efficiency during atrial overdrive pacing. Although the mechanism remains unclear, pacing at RAA + CSO or IAS may improve atrial mechanical efficacy by synchronization of atrial activation via stimulation at the level of Bachmaan’s bundle and the coronary sinus (7). The relative importance of this mechanism compared to changes in electrophysiologic properties related to alternate-or multiple-site atrial pacing is unknown.

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Figure 2. Changes in mean arterial pulse pressure (A), mean right atrial (RA) pressure (B), and mean maximal RA conductance (C) during pacing at various atrial sites and atrioventricular (AV) intervals using drive cycle length (CL) of 350 ms and 500 ms. Max = optimal AV interval. Other abbreviations as in Figure 1.
Letters to the Editor

Cardiac Rehabilitation, Exercise Training, and Psychosocial Risk Factors

The recent review by Rozanski et al. (1) outlined the important role of behavioral and psychosocial risk factors in the pathogenesis and expression of cardiovascular (CV) diseases, particularly coronary artery disease (CAD). Although the investigators briefly mentioned the potential for exercise training to improve prognosis in patients with depression, as well as the role of adding psychosocial intervention to standard cardiac rehabilitation programs to reduce subsequent major CAD events (1,2), they mainly emphasized the role of behavioral and psychopharmacologic interventions.

Formal phase II cardiac rehabilitation and exercise training programs, however, are known to produce marked benefits on exercise capacity, plasma lipids, obesity indices, inflammation, metabolic syndrome, autonomic function, blood viscosity and rheology, measures of ventricular repolarization dispersion, subsequent hospitalization costs, as well as major CV morbidity and mortality (3–5). In addition to producing over 50% reductions in the prevalence of depressive symptoms (6–9), we have also demonstrated that formal cardiac rehabilitation programs, with general but without specific psychosocial intervention, also produced nearly 50% reductions in depressive symptoms (6–9), we have also demonstrated that formal cardiac rehabilitation programs, with general but without specific psychosocial intervention, also produced nearly 50% reductions in depressive symptoms. However, we also believe that greater physician input is needed to improve referral, attendance, and completion of the readily available and proven, yet greatly underutilized, cardiac rehabilitation and exercise training programs to enhance psychosocial and behavioral adaptation and the secondary prevention of CAD.

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REPLY

We agree with Drs. Lavie and Milani that exercise is a well-established intervention for the secondary prevention of coronary heart disease (CHD), and is a major component of cardiac rehabilitation programs (1,2). We also are aware that cardiac rehabilitation services are seriously underutilized. For example, according to a recent position paper from the American Heart Association (3) only 10% to 20% of eligible patients actually participate in cardiac rehabilitation. A meta-analysis (4) reported results from 32 studies with 16,804 patients eligible for cardiac rehabilitation and reported that only 25% to 31% of eligible men and 11% to 20% of eligible women participated. It is evident that many physicians do not refer patients to cardiac rehabilitation, and this reluctance is especially true for women and minorities (5).

As alluded to by Drs. Lavie and Milani, exercise cannot only induce beneficial physiological adaptations, but can also improve psychological functioning. For example, in a recent randomized trial, exercise training decreased depressive symptoms as effectively as antidepressant medication in patients with clinical depression (6,7). Other work by Thayer et al. (8) has demonstrated that even short bursts of exercise activity can effectively increase energy or decrease tension for two-hour periods. Recent data also emphasize the beneficial effects of...