Effect of P-Wave Timing During Supraventricular Tachycardia on the Hemodynamic and Sympathetic Neural Response

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Background—Previous studies have shown the importance of the timing of atrial and ventricular systole on the hemodynamic response during supraventricular tachycardia (SVT). However, the reflex changes in autonomic tone during SVT remain poorly understood.

Methods and Results—Eleven patients with permanent dual-chamber pacemakers were enrolled in the study. Arterial blood pressure (BP), central venous pressure (CVP), and peripheral muscle sympathetic nerve activity (SNA) were recorded during DDD pacing at a rate of 175 bpm (cycle length 343 ms) with an atrioventricular (AV) interval of 30, 200 and 110 ms, simulating tachycardia with near-simultaneous atrial and ventricular systole, short-RP tachycardia (RP<PR), and long-RP tachycardia (RP>PR). Each pacing run was performed for 3 minutes separated by a 5-minute recovery period. All patients demonstrated an abrupt fall in BP, an increase in CVP, and an increase in SNA regardless of the AV interval. The decreases in SBP, DBP, and MAP and the increase in CVP were significantly less during long-RP tachycardia (AV interval 110 ms) than during the other 2 pacing modes (P<0.05), and the increase in SNA in 7 of the 11 patients was significantly greater during closely coupled atrial and ventricular systole than during long-RP tachycardia (P<0.05).

Conclusions—These data suggest that the superior maintenance of hemodynamic stability during long-RP tachycardia is accompanied by reduced sympathoexcitation, which is primarily mediated by the arterial baroreceptors, with a modest cardiopulmonary vasodepressor effect. (Circulation. 2001;103:96-101.)

Key Words: pacing ■ nervous system, autonomic

Supraventricular tachycardia (SVT) may result in disabling symptoms such as palpitations and shortness of breath, or it may be scarcely noticed. Hemodynamic tolerance of SVT is dependent on heart rate, ventricular performance, loading conditions, atrioventricular (AV) coupling, and autonomic nervous system–regulatory mechanisms. Previous studies have shown the importance of the timing of atrial and ventricular systole on blood pressure (BP), central venous pressure (CVP) and cardiac output.1–5 These studies demonstrated a greater fall in BP and cardiac output with closely coupled atrial and ventricular systole. However, the reflex changes in autonomic tone during tachycardia, in particular during simultaneous atrial and ventricular contractions, remain poorly understood. Although the fall in BP during SVT unloads extracardiac baroreceptors, resulting in a reflex increase in sympathetic nerve activity (SNA), the increase in cardiac filling pressures activates cardiac mechanoreceptors, leading to a reflex withdrawal of sympathetic tone. Furthermore, an atrial vasodepressor reflex triggered by the atrial contraction against closed AV valves has been suggested but remains unproved.6

The purpose of the present study was to examine the effect of atrial timing during simulated tachycardia on the hemodynamic and sympathetic neural responses. Two hypotheses were tested: (1) superior arterial BP maintenance during long-RP tachycardia (RP>PR) produces a reduced sympathoexcitation relative to short-RP tachycardia (RP<PR) and tachycardia with near-simultaneous atrial and ventricular systole and (2) tachycardia with near-simultaneous atrial and ventricular systole produces a vasodepressor effect that may be mediated by atrial receptors. Rapid dual-chamber pacing with varying AV intervals was performed to simulate SVT with almost simultaneous atrial and ventricular systole and short-RP and long-RP tachycardia. Arterial BP, CVP, and...
peripheral muscle SNA were continuously recorded during these interventions.

Methods

Study Patients
The study was performed at the Dallas Veterans Affairs Medical Center and Parkland Memorial Hospital. Both institutional review boards approved the study. Informed consent was obtained from all patients, and all procedures were in accordance with institutional guidelines. All patients with a dual-chamber pacemaker (Medtronic pacemaker models 7088 and 7960) were screened for the study. Patients were excluded if they had neuropathy, NYHA class III or IV congestive heart failure, recent myocardial infarction, or unstable angina. All patients had an echocardiogram performed within 6 months of the study to determine left ventricular function and chamber sizes. A total of 12 patients were enrolled. One patient developed atrial fibrillation soon after the first pacing sequence and therefore was excluded. The data for the remaining 11 patients form the material of this study.

Measurements
Patients were studied in the drug-free postabsorptive state after informed consent was obtained. Efferent postganglionic muscle SNA was recorded from the right peroneal nerve as previously described. Briefly, a sterile microelectrode was inserted into a fascicle of the peroneal nerve near the fibular head. The nerve signals were amplified, filtered (700 to 2000 Hz), rectified, and discriminated. Raw nerve signals were integrated to produce a mean voltage display for quantitative analysis. The SNA was quantified as the total activity derived from the sum of the area of the SNA bursts for a given time period. Finger arterial BP was continuously monitored and recorded according to the Penaz volume-clamp method with a finger cuff (Ohmeda Monitoring System). CVP was continuously recorded with a catheter placed in the superior vena cava via the right antecubital vein. Heart rate was derived from continuous ECG recorded of ≥2 leads.

Experimental Protocol
After adequate CVP, BP, and SNA recordings were obtained, the following protocol was performed. The order of the 3 pacing runs (with different AV intervals) was randomized:

1. Baseline measurements for a period of 5 minutes.
2. Dual-chamber pacing (DDD) at a rate of 175 bpm (cycle length 343 ms) with an AV interval of 30 ms (simulating tachycardia with near-simultaneous atrial and ventricular systole).
3. Recovery for 5 minutes.
4. Dual-chamber pacing (DDD) at a rate of 175 bpm (cycle length 343 ms) with an AV interval of 200 ms for 3 minutes (simulating short-RP tachycardia).
5. Recovery for 5 minutes.
6. Dual-chamber pacing (DDD) at a rate of 175 bpm (cycle length 343 ms) with an AV interval of 110 ms for 3 minutes (simulating long-RP tachycardia).
7. Recovery for 5 minutes.

SNA, BP, and CVP were measured continuously during the study. Data were analyzed during the last minutes of recovery and pacing with each AV interval. Pacing was always done at maximum output, and capture was confirmed through analysis of the 12-lead ECG. In addition to the hemodynamic and autonomic measurements, arterial baroreflex-SNA gain was calculated during each pacing mode. The gain was estimated from the initial changes in diastolic BP (DBP) and SNA at the nadir of arterial BP in the first 20 seconds of each pacing run (gain = ΔSNA/ΔDBP).

Data Analysis
All data sets passed a test for normality with a Smirnov-Kolmogorov test; therefore, the following parametric tests were used. A 1-way ANOVA with repeated measures design was used for all comparisons between the 3 AV intervals for baseline data and the hemodynamic changes during pacing. When a significant main effect was obtained, the specific differences were determined through the application of a least significant difference post hoc test. Correlation analyses were performed by determination of the Pearson linear correlation coefficients, and a forward progression stepwise regression model was used to assess the relative contribution of changes in hemodynamic variables to the SNA responses. For all tests, statistical significance was set a priori at an α level of 0.05.

Results

Clinical Characteristics
All subjects were men with a mean age of 63 ± 10 years. Left ventricular function was normal in 7 patients, mildly depressed in 2, and moderately depressed in 2. The clinical characteristics of all subjects, including the indications for pacing, are summarized in Table 1.

Hemodynamic Response
Hemodynamic data were obtained for all 11 patients. The results of dual-chamber pacing at baseline and during each AV interval are shown in Table 2. All values shown are at steady state. At the onset of pacing, all patients demonstrated an abrupt fall in BP regardless of the AV interval. After 30 to 60 seconds, BP gradually recovered and reached a new baseline below the resting state (Figure 1). The average changes in SBP, DBP, and mean arterial BP (MAP) are summarized in Figure 2. The decreases in SBP, DBP, and MAP were all significantly less during long-RP tachycardia (AV interval 110 ms) than during the other 2 pacing modes (P < 0.05). An abrupt increase in CVP was noted at the onset of pacing regardless of the AV interval, with a gradual decrease to a new baseline above the resting state. The changes in CVP during pacing are summarized in Figure 2. Similar to arterial BPs, the increase in CVP during long-RP tachycardia (AV interval 110 ms) was significantly less than during the other 2 pacing modes (P < 0.05). When pacing was terminated, both arterial BP and CVP returned to prepacing levels within 30 seconds. For all pacing conditions, the

<table>
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<th>TABLE 1. Patient Characteristics</th>
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AVB indicates atrioventricular block; SSS, sick sinus syndrome; and LVEF, left ventricular ejection fraction.
change in MAP correlated inversely with the change in CVP ($r^2 = 0.88$, $P<0.001$).

**SNA Determination**

SNA was obtained in 7 patients. In the remaining 4, the data were discarded because of decreased signal-to-noise ratio or loss of recording site during the study. SNA rose abruptly in all patients with the onset of pacing and reached a steady state after 30 to 60 seconds (Figure 1). The percent change in SNA from baseline with near-simultaneous atrial and ventricular systole or short-RP and long-RP tachycardia was 39±6%, 52±6%, and 18±9%, respectively ($P<0.05$). A summary of the changes in SNA during pacing with different AV intervals is provided in Figure 2. The increase in SNA was significantly less during long-RP tachycardia (AV interval 110 ms) than during the other 2 pacing modes ($P<0.05$). There was no statistical difference between short-RP tachycardia and near-simultaneous atrial and ventricular pacing ($P=0.21$). However, this was limited by a low statistical power (0.69). SNA returned to prepacing baseline levels within 1 minute of termination of pacing. There was no statistical significance between SNA at baseline and that at 1 minute after pacing ($P<0.001$).

The relative roles of arterial BP and CVP in the SNA responses were assessed with a stepwise regression model. In the first step of the forward regression model, $\Delta DBP$ was entered with an $r^2$ value of 0.77 ($P<0.001$). In the second step, $\Delta CVP$ was entered and the $r^2$ value was increased to 0.89 ($P<0.001$). The slope estimates for the regression model were $-3.3$ for $\Delta DBP$ and $-0.8$ for $\Delta CVP$.

**Baroreflex Gain**

Arterial baroreflex-SNA gain estimates tended to be greater during long-RP tachycardia (1.4±0.7%/mm Hg) than during short-RP tachycardia (1.1±0.7%/mm Hg) and during tachycardia with near-simultaneous atrial and ventricular systole.

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**TABLE 2. Hemodynamic and SNA Responses to Pacing With Each AV Interval**

<table>
<thead>
<tr>
<th></th>
<th>Near Simultaneous A&amp;V (AV=30 ms)</th>
<th>Short RP (AV=200 ms)</th>
<th>Long RP (AV=110 ms)</th>
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<tr>
<td></td>
<td>Baseline</td>
<td>Pacing</td>
<td>Baseline</td>
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<tr>
<td>SBP, mm Hg</td>
<td>159±7</td>
<td>108±12</td>
<td>155±8</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>87±8</td>
<td>75±7</td>
<td>86±8</td>
</tr>
<tr>
<td>MBP, mm Hg</td>
<td>111±8</td>
<td>86±9</td>
<td>109±7</td>
</tr>
<tr>
<td>CVP, mm Hg</td>
<td>13±2</td>
<td>20±2</td>
<td>13±2</td>
</tr>
<tr>
<td>SNA, %</td>
<td>100</td>
<td>139±11</td>
<td>100</td>
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</tbody>
</table>

A&V indicates atrial and ventricular systole. n=11 (7 with SNA).

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**Figure 1.** Sample tracings of integrated sympathetic neurogram, arterial BP, CVP, and ECG during baseline (prepacing) and during minute 3 of rapid pacing (175 bpm) with either near-simultaneous atrial and ventricular systole (A&V), short-RP tachycardia, or long-RP tachycardia. In this individual, it is apparent that long-RP tachycardia produced a higher arterial BP, lower CVP, and less increase in SNA.
Hemodynamic Changes During SVT

The hemodynamic effects of SVT have been reported previously in detail.\(^4\),\(^5\),\(^11\),\(^12\) In summary, tachycardias, regardless of their mechanisms or cause, result in decreased diastolic filling, stroke volume, and cardiac output. The results are a decrease in BP and pulse pressure, which is directly related to the tachycardia rate, cardiac function, and AV synchrony. At any given rate, the timing of atrial systole has been shown to alter the hemodynamic response.\(^1\),\(^11\) Several authors have shown that closely coupled atrial and ventricular systole results in increases in atrial pressures, A-wave magnitude, and pulmonary pressure and decreases in cardiac index and BP.\(^4\),\(^12\),\(^13\) The first combined electrophysiological and hemodynamic study that assessed the hemodynamic consequences of SVT in which patients served as their own control was reported by Goldreyer et al.\(^13\) Eight patients with AV nodal reentrant tachycardia were studied at baseline and during induced tachycardia. Right atrial and pulmonary artery pressures increased during SVT, whereas cardiac index and BP decreased. In addition, the authors observed large atrial waves during tachycardia, presumably due to atrial contraction against closed tricuspid valves. Subsequently, several authors\(^11\),\(^14\) demonstrated that patients with AV nodal reentrant tachycardia had significantly higher mean and peak right atrial pressures during tachycardia than did patients with circus movement tachycardia. Furthermore, Sganzerla et al\(^3\) found a lesser degree of hypotension and a faster recovery of BP in patients with atypical AV nodal reentrant tachycardia compared with patients with typical AV nodal reentrant tachycardia. They attributed these findings to the temporal relationship between atrial and ventricular systole.

Our findings are consistent with these previous studies. We found that long-RP tachycardia was associated with the least drop in BP, whereas tachycardias with closely coupled atrial and ventricular systole (AV intervals 30 and 200 ms) resulted in a greater decrease in BP. Similarly, the increase in CVP was least with long-RP tachycardia and greatest with the other tachycardias. Therefore, in the present study, the autonomic responses to simulated SVT, as discussed later, are relevant to the previous experimental and clinical studies of hemodynamic function.

Autonomic Changes During SVT

During SVT, the fall in BP reduces the stretch on the arterial baroreceptors, resulting in a decrease in the afferent nerve traffic to the vasomotor centers. This in turn augments sympathetic efferent tone and withdraws vagal efferent tone.\(^15\),\(^16\) Previously, the evidence for activation of the sympathetic tone was indirect and only qualitative as suggested by (1) BP recovery during sustained tachycardia and (2) a brisk overshoot of the BP after tachycardia termination.\(^17\),\(^18\) Although the fall in BP during tachycardia leads to a reflex increase in sympathetic activity through extracardiac baroreceptors,\(^15\),\(^16\) the increase in cardiac filling pressures may result in opposite effects.\(^17\),\(^18\) The increase in filling pressure activates the cardiac mechanoreceptors, leading to reflex withdrawal of sympathetic tone. We have previously shown in humans that arterial baroreflex control predominates in mediation of sympathoexcitation during ventricular tachycardia\(^19\) and that baroreflex gain predicts BP recovery during sustained ventricular tachycardia.\(^20\) However, the relative roles of cardiopulmonary and arterial baroreceptors in the control of SNA and arterial BP during SVT and the effect of AV coupling on these responses remain unknown. Leitch et al\(^12\) explored the mechanism of syncope in 22 patients with SVT. The authors found that the tachycardia cycle length tended to be longer in patients with syncope than in patients without syncope and that the former group had a propensity toward vasodepressor syncope. They postulated that the slower
tachycardia rate might be related to inappropriate stimulation of left ventricular stretch receptors by the reduced left ventricular volume and increased adrenergic tone, similar to what is seen with vasovagal syncope. In that study, the tachycardia rate was used as a surrogate for sympathetic activity.

In the present study, we directly measured SNA responses to address the role of arterial and cardiopulmonary baroreceptors in the control of SNA when AV coupling is altered. We found a significant increase in sympathetic activity during rapid pacing with all 3 AV intervals. This was associated with a decrease in BP and an increase in CVP. The increase in sympathetic tone despite an increase in filling pressures suggests that the sympathetic response is mainly mediated by the arterial baroreceptors and that the contribution of the cardiopulmonary baroreceptors is minimal. This was further demonstrated by the presence of a greater increase in sympathetic activity during closely coupled atrial and ventricular systole compared with long-RP tachycardias despite higher cardiac filling pressures. Nevertheless, a greater role of cardiopulmonary baroreceptors in the decrease in SNA may be implied by these data because of the large decrease in arterial BP. A 20- to 30-mm Hg decrease in MAP alone would be expected to produce a much greater increase in SNA than the 40% to 60% increase that we observed. Previous studies have shown that 15- to 20-mm Hg changes in MAP produced by nitroprusside infusion, lower body negative pressure, or ventricular pacing will elicit increases in SNA of ≥100% to 200%. We previously showed a prominent role of arterial baroreceptor control of SNA during ventricular pacing in which the decreases in MAP were modest. The lack of a greater increase in SNA in the present study in which the decrease in MAP averaged >20 mm Hg may imply a greater cardiopulmonary baroreflex sympathoinhibition, or it may reflect an impairment in the arterial baroreflex control of SNA in these patients.

Is There an Atrial Vasodepressor Response?
The presence of an atrial vasodepressor response triggered by large atrial waves during simultaneous atrial and ventricular contractions has been suggested but remains unproved. This reflex has been implied as a potential cause of hypotension during ventricular pacing. Erlebacher et al. found that the presence of cannon A waves during ventricular pacing was associated with a relative decrease in systemic vascular resistance with a significant decrease in BP. The authors concluded that the hypotension was primarily due to a vasodepressor reflex initiated by left atrial cannon A waves.

During SVT, the A and V waves tend to be fused, giving rise to large atrial waves. These waves tend to be larger with closely coupled atrial and ventricular systole and are usually associated with a higher CVP and a lower BP. The present study was not designed to assess the presence of an atrial vasodepressor reflex. However, we have seen a greater increase in SNA during pacing with closely coupled atrial and ventricular systole compared with long-RP tachycardia, suggesting the predominance of arterially mediated sympathoexcitation. On the other hand, the difference between nearly simultaneous atrial and ventricular systole and short-RP tachycardia was not significant (P=0.21), although it was limited by a relatively low statistical power (0.69). The lack of differences in CVP between the conditions also limits the conclusions that can be made regarding an atrial vasodepressor effect. The stepwise regression model does provide some suggestion that there was a very modest vasodepressor effect; however, we cannot discern whether this was mediated specifically by atrial receptors. Our findings of a lesser arterial baroreflex-SNA gain during closely coupled atrial and ventricular systole compared with long-RP tachycardia also suggest a modest vasodepressor effect of the increased cardiac filling yet do not confirm or negate the presence of an atrial vasodepressor response.

Conclusions
Our data suggest that arterial baroreflex control predominates in mediation of sympathoexcitation during rapid AV sequential pacing regardless of the AV interval, with only modest contribution of the cardiopulmonary baroreceptors. In addition, we found a greater hemodynamic response with long-RP tachycardia compared with pacing with closely coupled atrial and ventricular systole. Finally, the existence of an atrial vasodepressor reflex was suggested by a reduced baroreflex-SNA gain during simultaneous atrial and ventricular pacing, but the importance of this effect appeared to be minimal.

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