Appraisal of Sinus Node Artery Disease

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SUMMARY
The relationship of depressed sinus node function to coronary artery disease (CAD) was evaluated. The sinus node artery (SNA) was easily identified in all of 80 unselected normal coronary arteriograms. Angiographic disease of, or significant obstruction proximal to, the SNA was seen in 21% of 80 unselected CAD patients. Heart rate and sinoatrial recovery times (SART) were obtained in 50 consecutive unmedicated patients prior to arteriography. There was no difference between the SART of 23 CAD patients free of SNA involvement (1092 msec ± 55 SEM) and 18 normals (1070 ± 40 msec). Nine patients with SNA involvement had shorter SART (941 ± 52 msec) than normals (P < 0.05) or other CAD patients (NS).

Similar results were obtained for heart rate. No patient with SNA involvement had a prolonged SART or sick sinus syndrome (SSS). Six of the 50 patients studied were symptomatic with SSS. Five of these SSS patients had CAD but none had angiographic evidence of SNA involvement. Obstructions involving the SNA were common in CAD but were not associated with altered heart rate or SART. Patients with SSS exhibited no angiographic evidence of SNA involvement. Therefore, it is unlikely that SSS is related to CAD of the SNA.

SINUS BRADYCARDIA and the sick sinus syndrome (SSS) are among a variety of supraventricular rhythm disturbances reported in the presence of coronary artery disease (CAD). Obstructive disease of the sinus node artery (SNA) is thought to produce sinus node dysfunction by causing anoxia, fibrotic or degenerative changes or loss of central artery oscillations. However, a role for obstructive disease of the SNA in the pathogenesis of SSS remains to be established. The purpose of this study is to examine whether relationships exist between depressed sinus node function, angiographically demonstrable CAD and obstruction of the SNA.

Methods

Angiographic Evaluations
Coronary arteriography was performed by either the Judkins or Sones technique, utilizing a Picker image intensifier with 35 mm film at 60 frames/sec. Films were reviewed on a Tagamor projector. All patients included in the study had high quality angiograms.

Angiographic identification of the SNA was based upon the anatomic descriptions of James, and Kennel and Titus. The SNA was best defined in the right anterior oblique projection, as illustrated in figure 1. Criteria for identification of the SNA were: 1) a large vessel originating proximally from the right or circumflex coronary artery and extending to the region at the junction of the right atrium and superior vena cava, and 2) a distal branching system consistent with encirclement of the superior vena cava. James has described the SNA in 106 autopsies, using the injection-and-corrosion method. He found the SNA, with few exceptions, to be the largest and most constant of the atrial arteries, almost always originating from the proximal few centimeters of the right or circumflex artery. He demonstrated constant presence of the SNA in the node and at the junction of the superior vena cava and right atrium. The SNA encircled the superior vena cava in a clockwise or counterclockwise manner, or bifurcated to encircle the superior vena cava as two branches, but encirclement of the superior vena cava was constant. Kennel and Titus correlated radiographic evaluation of 39 postmortem specimens with injection of color-coded contrast material and histologic evaluation. In most specimens the SNA was easily identified radiographically, and confirmed by radio-opaque markers at the expected location of the node. Their radiographs closely resemble our angiograms (fig. 1) and they reported good correlation between postmortem and antemortem angiograms in five patients.

Significant CAD was defined for the purposes of this investigation as the presence of arterial narrowing greater than 50%. Disease of the arterial supply to the sinus node was diagnosed in the presence of: 1) greater than 50% narrowing proximal to the region of the SNA (all such patients with > 50% narrowing actually had stenoses ≥ 70%), or 2) major diminution in caliber, usually with ghost-like appearance of an SNA originating from a diseased area of the parent artery. Precise estimates of SNA stenosis were impossible because of the small size of that vessel. SNA disease without parent artery disease or absence of an identifiable SNA were not encountered.

Eighty unselected coronary arteriograms from patients with otherwise normal coronary arteries, who had been studied because of the suspicion of CAD, were retrospectively reviewed to establish our ability to visualize the SNA. Eighty arteriograms from patients with definite angiographic evidence of CAD were retrospectively reviewed to determine the incidence of angiographic disease of the SNA.

There was independent agreement of at least two observers regarding SNA location and disease in these 160 arteriograms.

Atrial pacing was performed prospectively in 50 patients undergoing diagnostic cardiac catheterization, including coronary arteriography, mostly for evaluation of chest pain

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suggestive of angina pectoris. There was independent agreement among three observers regarding the arteriograms obtained from these patients. Coronary arteriography was performed in only six patients thought to be symptomatic due to SSS because few patients with this syndrome presented anginal symptoms justifying that procedure.

SSS is diagnosed in our laboratory by recording one of the following rhythm disturbances during a symptomatic episode: 1) asystole, or 2) sinus or junctional bradycardia less than 35 beats/min, or 3) sinus bradycardia less than 60 beats/min during a stress characteristically associated with tachycardia, such as pulmonary edema or hypovolemic shock, or 4) bradycardia alternating with supraventricular tachycardia. However, most patients with sinus node dysfunction have only rare and unpredictable near-syncope. Our criteria for diagnosing SSS therefore include patients with the following triad: 1) episodic symptoms of circulatory insufficiency; 2) sinus bradycardia less than 60 beats/min; and 3) second degree sinoatrial block during a monitored period or a prolonged sinoatrial recovery time (SART). SSS is not diagnosed if the abnormalities described above occur while receiving cardioactive medication. The criteria above only detect sinus dysfunction and do not imply a need for pacemaker therapy.

Evaluation with Atrial Pacing

Patients were studied in the postabsorptive state with no premedication until completion of electrophysiologic testing. Informed written consent was obtained from all patients. Patients were excluded from study 1) if they received cardioactive medications within the week prior to catheterization; 2) if there was clinical or laboratory evidence of heart disease other than CAD; or 3) if they had ever undergone cardiac surgery.

Atrial pacing was performed prior to insertion of arterial catheters or angiography. After recording resting heart rate, SARTs were recorded subsequent to 30-60 sec of pacing. SARTs were taken as the maximal interval from the last paced P wave to the next spontaneous P wave, regardless of P wave morphology. Standard ECG leads I, II and III were recorded at 0.1-20 Hz with an Electronics for Medicine VFT-7 amplifier and DR12 recorder at a paper speed of 100 mm/sec. Pacing was performed at 1½ diastolic threshold, at rates approximating 100, 120, 140 and 150 beats/min, unless angina supervened, with at least 30 sec between paced periods. Stimulation was provided by either a Grass S58 stimulator with isolation unit or a battery powered Medtronic 5880A pacemaker via a bipolar catheter with ring electrodes 1 mm wide and 1 cm apart, positioned at the mid to high right atrium.

SARTs corrected for cycle length (CL) were computed in two manners: by subtraction of the basic unpaced cycle length (SART–CL) and by dividing by the unpaced cycle length (SART/CL). The response of SART to atropine was not determined because it interfered with appraisal of the ensuing ventriculograms. Results were expressed as averages ± the standard error of the mean (SEM) and statistical comparisons were made with an unpaired t-test, using a Hewlett-Packard Model HP-65 computer.

Results

The SNA was identified easily in all of the 80 unselected normal coronary arteriograms. It originated from the right coronary artery in 61% and the
circumflex in 39%. One patient had an SNA originating from both the left and right coronary arteries. Angiographic disease of the SNA, or significant obstruction proximal to the SNA was present in 21% of 80 patients with CAD. SNA involvement was diagnosed because of significant stenosis of the main right or circumflex coronary artery proximal to the SNA origin in all but three patients. The latter three patients had ghost-like SNAs originating from diseased areas of the parent artery. When proximal stenosis was present, it involved the right coronary artery in 50%, the left main artery in 12%, the circumflex artery in 29% and both the left main and circumflex in 9%. Collaterals to the region of the sinus node were often observed in the presence of SNA involvement.

There was no difference between the SART of 23 CAD patients free of SNA involvement (1092 ± 55 msec) and 18 patients with normal coronary arteries (1070 ± 40 msec). Similar results were obtained when SARTs were corrected for cycle length. These values closely compare with SART obtained from larger series of normals using identical methodology.16 A vagal influence on SART from ischemic disease of the inferior wall was discounted by comparing SARTs of those 17 patients whose CAD involved dominant vessels supplying the inferior wall (1041 ± 65 msec) and normals. There remained no difference in SARTs.

Nine patients had significant disease of, or proximal to, the SNA. The manner of SNA involvement is detailed in table 1. Six of these patients had significant stenoses of both right and circumflex coronary arteries and eight also had significant left anterior descending stenoses. No patient with SNA involvement had SSS or a prolonged SART (range 660–1200 msec). Their SARTs (941 ± 52 msec), in fact, were slightly shorter than normals (P < 0.05) or those CAD patients without SNA involvement (NS). SARTs from these three groups of patients are compared in figure 2.

There was no significant difference in heart rate between patients with SNA involvement (82.4 ± 5.4 beats/min) and CAD patients without SNA involvement (74.4 ± 3.4 beats/min) or those with normal coronary arteries (74.4 ± 2.8 beats/min). Figure 3 compares heart rates of the three groups of patients. The faster heart rates among patients with SNA involvement do not completely explain their shorter SARTs. SARTs of those with SNA involvement, when corrected for heart rate (SART-CL = 192 ± 31 msec; SART/CL = 1.26 ± 0.04) were shorter than corrected SARTs of CAD patients without SNA involvement (248 ± 25 msec; 1.29 ± 0.02) or normals (243 ± 28 msec; 1.30 ± 0.04), although the differences were not significant.

Six of the 50 patients prospectively studied were symptomatic with SSS and underwent coronary arteriography for evaluation of symptoms suggesting CAD (table 2). Three of our SSS patients were symp-

### Table 1

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Heart rate (beats/min)</th>
<th>SART (msec)</th>
<th>Sinus node artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>115</td>
<td>660</td>
<td>Ghost-like, origin at site of 100% RCA occlusion</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>97</td>
<td>820</td>
<td>Ghost-like, distal to 100% RCA occlusion</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>95</td>
<td>860</td>
<td>Distal to 50%, left main stenosis and 70% circumflex stenosis</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>72</td>
<td>900</td>
<td>Distal to 90%, CIRC stenosis</td>
</tr>
<tr>
<td>5</td>
<td>56</td>
<td>75</td>
<td>930</td>
<td>Distal to 100%, RCA occlusion</td>
</tr>
<tr>
<td>6</td>
<td>41</td>
<td>73</td>
<td>1020</td>
<td>Pulsatile flow, at site of 100% RCA occlusion</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>74</td>
<td>1020</td>
<td>Significant stenosis at origin from. diseased circumflex (fig. 1)</td>
</tr>
<tr>
<td>8</td>
<td>36</td>
<td>66</td>
<td>1060</td>
<td>Distal to 95%, RCA stenosis</td>
</tr>
<tr>
<td>9</td>
<td>42</td>
<td>75</td>
<td>1200</td>
<td>Ghost-like, origin at lesion proximal to 95% RCA stenosis</td>
</tr>
</tbody>
</table>

Abbreviations: CIRC = circumflex artery; RCA = right coronary artery; SART = sinoatrial recovery times.

![Figure 2](https://example.com/figure2.png)

**Figure 2.**

Sinoatrial recovery times in 50 patients undergoing coronary arteriography. Patients with angiographic disease of, or obstruction proximal to, the sinus node artery (stippled middle bar) did not have prolonged recovery times when compared to those with normal coronary arteriograms or those whose coronary artery obstructive disease did not involve the sinus node artery. CAD = coronary artery disease; SEM = standard error of the mean; SNA = sinus node artery.

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Using the methodology described above, SARTs longer than 1250 msec are considered abnormal. SSS was diagnosed in another three patients because of the triad of episodic symptoms of circulatory insufficiency, sinus bradycardia and prolonged SART. One patient had light-headed spells, a sinus rate of 36 per minute and a SART of 1570 msec. A second had spells of almost complete loss of consciousness, a sinus rate of 39 per minute and a SART of 1740 msec. None of the SSS patients had documented tachyarrhythmias. None had prolonged return cycles after programmed extrastimuli.

Five of the six SSS patients had CAD but none had disease of, or obstruction proximal to, the SNA. The patient with normal coronary arteries became asystolic with coronary injection only of that artery from which the SNA did not arise.

Discussion

The etiology of SSS is uncertain despite evidence suggesting degeneration of the sinus node or autonomic dysfunction. Most reports of SSS include a large percentage of patients with CAD. A role for arteriosclerotic disease of the sinus node might thus be inferred. However, arteriosclerosis as a cause of SSS remains unproven.

Four lines of evidence suggest that CAD may not be important in the pathogenesis of SSS. 1) Patients with SSS are generally of advanced age, but a high incidence of CAD might be expected on that basis alone, independent of but merely coexistent with SSS. 2) Significant narrowing of the SNA has not been found consistently in the limited number of pathologic studies of SSS to date. 3) The SNA appears to be relatively free of the senile effects of aging despite degeneration of the node. 4) Asystole

Table 2

Patients with Sick Sinus Syndrome

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Symptoms</th>
<th>Arrhythmias</th>
<th>HR (beats/min)</th>
<th>SART (msec)</th>
<th>Significant coronary stenosis</th>
<th>SNA involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>Lightheadedness,</td>
<td>SB (36)</td>
<td>53</td>
<td>1570</td>
<td>LAD</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>Angina, episodes</td>
<td>SB (39)</td>
<td>55</td>
<td>1740</td>
<td>RCA</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>62</td>
<td>Syncope, angina</td>
<td>SB (&lt;35),</td>
<td>&lt;35</td>
<td>&gt;5000*</td>
<td>Diagonal branch</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Syncope, angina</td>
<td>junctional rhythm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>Angina, episodes</td>
<td>SA arrest &gt;15 sec</td>
<td>73</td>
<td>1155</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>59</td>
<td>Angina</td>
<td>SB (40) with</td>
<td>48</td>
<td>1470</td>
<td>LAD</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>postoperative</td>
<td>hypoglycemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>42</td>
<td>Angina</td>
<td>SB (44)</td>
<td>59</td>
<td>1480</td>
<td>LAD, CIRC, RCA</td>
<td>None</td>
</tr>
</tbody>
</table>

*SART were recorded after pressure recordings and after bradycardia necessitated administration of 2 mg atropine. Therefore, this patient was not included in statistical comparisons.

Abbreviations: CIRC = circumflex artery; HR = heart rate at time of study; LAD = left anterior descending artery; RCA = right coronary artery; SART = sinoatrial recovery time; SB = sinus bradycardia (beats/ min indicated); SNA = sinus node artery.

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implies a failure of pacemakers throughout the heart. There is evidence for such diffuse disease in SSS, but this is not consistent with the largely focal nature of CAD.

Our study suggests that CAD as defined by angiography does not correlate well with SSS or disordered sinus node function. Patients with CAD appear not to differ in sinus node function from those with normal coronaries, as estimated by heart rate and the response to atrial overdrive suppression. Significant obstructions involving the SNA were often seen in our patients with CAD, but were not associated with altered heart rate, abnormal SART, or a clinical picture of SSS.

Prolonged sinoatrial conduction times in the absence of prolonged SART, or prolonged SART only after atropine administration, are very unusual and do not detract from the usefulness of SART as a marker of SSS. Heart rate and SART by themselves, of course, do not necessarily define sinus node function and normal SART may be recorded in bona fide SSS (e.g., patient 4, table 2). Our patients with SNA involvement did not undergo systematic monitoring and exercise testing. It is uncommon for a period of electrocardiographic monitoring to include a symptomatic episode. Monitoring is therefore of low yield in detecting cryptic forms of SSS. Thus, SNA involvement does not preclude SSS, despite the normal heart rate and SART in our series. However, our patients symptomatic with SSS invariably exhibited no angiographic evidence of SNA involvement. This does not exclude small vessel disease but only disease of those vessels which can be visualized by arteriography and are considered significant at this time in the detection of clinical CAD.

Anginal pain was encountered only once at the rates and durations of atrial pacing used in this study. SART was not recorded during this episode of angina. It is possible that the ischemia which exists during angina is required to produce the abnormalities of heart rate and overdrive suppression typical of SSS. Certainly SNA occlusion can cause sinus arrest, usually with transient atrial standstill or fibrillation. However, patients with SSS and associated CAD do not show a consistent relationship between anginal episodes and rhythm disturbances, although sinus bradycardia precipitating angina has been described.

Normal sinus node generator function in the presence of arteriosclerotic involvement of the SNA could be explained by the extensive collateral supply to the sinus node. Billette et al. have shown that collateral vessels must be occluded to obtain reduction in heart rate from ligation of the SNA of the dog.

The results of this study raise doubts concerning a cause and effect relationship between arteriosclerotic disease of the SNA and SSS. Thus, when bradycardia or asystole occur in patients with chronic CAD, sinus node malfunction cannot be assumed to be caused by SNA disease.

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