Therapeutic Effects of Permanent Pacemaker in Patients With Sinus Node Dysfunction

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Abstract

Background: The electrocardiography (ECG) pattern of sinus node dysfunction (SND) does not always correlate with the symptoms. Objectives: The aim of this study was to find variables associated with therapeutic effects of permanent pacemaker in patients with sinus node dysfunction and abnormal electrophysiological findings. Methods: In this prospective study, 69 patients with symptomatic sinus node dysfunction and permanent pacemaker were selected from the Rajaie heart center in Tehran and Heshmat heart center in Rasht, Iran, between 2006 and 2015. Results: From a total of 69 patients enrolled in this study, 34 cases (49.3%) were females and the mean age of the patients was 63.2 ± 9 years. Patients with the tachycardia-bradycardia syndrome were excluded from the study. The most frequent symptoms were weakness in 55 cases (79%) and dizziness in 52 (75%), and the least common symptoms were dyspnea in 27 cases (39%) and syncope in 9 cases (13%). There was no association between the type of symptoms and response to pacemaker. A non-invasive electrophysiological study (EPS) showed that 47 (68%) of the patients had CSNRT more than 783 ms. The mean age of the aforementioned patients was 66 ± 5.43 years. There was a significant relationship between CSNRT more than 783 ms and symptom improvement 6 months after permanent pacemaker implantation (P = 0.000). Patients with exercise intolerance had better response to pacemaker compared to the patients with resting symptoms (P = 0.001). Mean age of the patients with CSNRT > 783 ms was significantly higher than those with CSNRT < 780 ms (66 ± 5.43 years versus 56 ± 11.50 years respectively, P = 0.001). Repolarization abnormalities did not correlate with persistence of clinical symptoms (P = 0.42). Conclusions: Pacemaker implantation can improve symptoms in sinus node dysfunction with corrected sinus node recovery time more than 783 ms. Symptoms related to the vagal nervous system can be the cause of persistence of clinical symptoms after pacemaker implantation.

Keywords: Sinus Node Dysfunction, Permanent Pacemaker

1. Background

The electrocardiography (ECG) pattern of sinus node dysfunction (SND) does not always correlate with the symptoms. There may be overlap between SND and hyper-vagotonia (1).

Disorders of sinus node functions are an important cause of cardiac syncope. Symptoms such as syncope may be related to vagal reaction, heart block, and significant pause. When electrophysiological studies demonstrate the likelihood of existence of heart block, pacemaker may be useful. Pacemaker clearly can help to prevent syncope especially in patients that the cause of syncope was transient bradycardia. Long-term management of patients with syncope of undetermined origin by an electrophysiologic study was usually successful in preventing recurrent syncope (2).

Tachycardia-bradycardia syndrome is the most frequently encountered form of symptomatic SND and it is associated with the highest incidence of syncope (3). An electrophysiologic study is rarely needed in this group because most of the patients with the tachycardia-bradycardia syndrome are symptomatic clinically.

Syncope is an uncommon symptom in patients with isolated sinus bradycardia. When these patients are symptomatic it is usually fatigue or dyspnea on exertion. Persistent sinus bradycardia associated with syncope can occur in both SND and in the vasovagal syncope, but the recommendations are different (4).

The frequency and clinical significance of sinus pauses have been studied. Sinus pauses greater than or equal to 2 seconds were found in 82 (2.6%) of 3259 consecutive
24-hour holter monitoring. The length of pause correlated poorly with symptoms and did not predict death. Most pauses were asymptomatic and did not predict death. Pacemaker did not have any benefit in asymptomatic people and failed to prevent dizziness, presyncope and syncope in one-third of patients in whom such symptoms were felt to be secondary to the pauses (5).

Other studies have demonstrated pauses > 2 seconds in 11% of normal and in one third of trained athletes (6, 7). Despite the limitation of retrospective studies, these data suggest that most sinus pauses even sinus pause greater than 3 seconds need not to be treated.

The use of invasive electrophysiologic studies has been decreasing as clinicians have recognized its limitation and the importance of the clinical history. Nevertheless, these studies have provided important information about normal and abnormal sinus node function.

It may be important to test sinus node function in these patients with truly unclear causes of symptoms to avoid unnecessary implantation of a pacemaker, perhaps the most useful measures of their overall sinus node function are a combination of the response to the exercise stress test (EST) and sinus node recovery time (SNRT).

2. Objectives

The aim of this study was to evaluate clinical course of patients with SND, abnormal exercise stress test, and non-specific symptoms.

3. Methods

In this prospective study, 69 patients who were candidates for permanent pacemaker were selected from Rajaie Heart Center in Tehran and Heshmat heart center in Rasht, Iran, from 2006 to 2015.

Demographic characteristics including age and sex and attributable symptoms such as syncope, dizziness, dyspnea, echocardiography, EST, results of electrophysiological study (EPS), and ECG before implantation of permanent pacemaker (PPM) were recorded in a previously prepared questionnaire. Patients with the tachycardia-bradycardia syndrome were excluded from the study. The most frequent symptom was weakness 55 (79%) and syncope was the least common 9 (13%). The frequency of patient’s symptoms before PPM has been shown in Table 2. We could not find a significant association between the type of symptoms and corrected sinus node recovery time (CSNRT) or clinical response to pacemaker (Table 2).

3.1. Statistical Analysis

Statistical analysis was performed using SPSS 22 for Windows (SPSS Inc, Chicago, Illinois). Data were expressed as mean values ± standard deviation for interval and count (%) for categorical variables. To evaluate the distribution of data, one-sample Kolmogorov-Smirnov test was used. Qualitative data were compared with the chi-square test. Mann-Whitney U test was used to compare quantitative variables. Variables that had any relationship with improvement of symptoms after 6 months were entered into a multivariable logistic regression model. P value less than 0.05 was considered statistically significant.

4. Results

From a total of 69 studied patients, 34 cases (49.3%) were females and the mean age of the patients was 63.2 ± 9 years. Baselines characteristics of the patients have been shown in Table 1. Patients with the tachycardia-bradycardia syndrome were excluded from the study. The most frequent symptom was weakness 55 (79%) and syncope was the least common 9 (13%). The frequency of patient’s symptoms before PPM has been shown in Table 2. We could not find a significant association between the type of symptoms and corrected sinus node recovery time (CSNRT) or clinical response to pacemaker (Table 2).

The area under the curve (AUC) in the ROC for CSNRT was 0.870 (95% CI, 0.772 - 0.969, P < 0.0001) (Figure 1). The curve indicated that a sensitivity of 94% (95% CI, 82.25 - 99.36), a specificity of 71% (95% CI, 51.33 - 86.7), PPV of 81% (95% CI, 67.2 - 91.8) and NPV of 90% (95% CI, 70.8 - 98.8) were obtained with a CSNRT of 783 ms. An electrophysiologic study (EPS) showed that 47 (68%) of the patients had CSNRT more than 783 ms. The mean age of aforementioned
patients was $66 \pm 5.43$. There was a significant relationship between CSNRT more than 783 ms and symptom improvement 6 months after PPM implantation ($P = 0.000$). Patients with exercise intolerance had better response to pacemaker compared to the patients with dominant resting symptom ($P = 0.002$). Presence of nocturnal AV Wenckebach block in holter monitoring was more prevalent in patients with CSNRT < 783 and absence of response to pacemaker ($P = 0.02$). Mean age of patients with CSNRT > 783 ms was significantly higher than those with CSNRT < 780 ms ($66 \pm 5.43$ years versus $56 \pm 11.50$ years respectively, $P = 0.001$). Repolarization abnormalities (memory T-wave) after PPM implantation and patient’s sex did not correlate with improvement of clinical symptoms (Table 3).

### Table 1. Baseline and Demographic Data of All Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>63.2 ± 9</td>
</tr>
<tr>
<td>Sex, F</td>
<td>34 (49.3)</td>
</tr>
<tr>
<td>Improvement of symptoms 6 months later</td>
<td>40 (57)</td>
</tr>
<tr>
<td>CSNRT &gt; 783</td>
<td>47 (68)</td>
</tr>
<tr>
<td>Baseline LVEF</td>
<td>54 ± 10</td>
</tr>
<tr>
<td>Memory T-wave change</td>
<td>12 (17.4)</td>
</tr>
</tbody>
</table>

Abbreviations: CSNRT, corrected sinus node recovery time; LVEF, left ventricular ejection fraction. Values are expressed as mean ± SD or No. (%).

### Table 2. Frequency of Different Symptoms in Two Groups of Patients With CSNRT Less Than 783 and More Than 783 ms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency in Patients With CSNRT &lt; 783</th>
<th>Frequency in Patients With CSNRT &gt; 783</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>16 (72.7)</td>
<td>39 (83)</td>
<td>0.32</td>
</tr>
<tr>
<td>Dizziness</td>
<td>15 (68)</td>
<td>37 (80.4)</td>
<td>0.26</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>7 (31.8)</td>
<td>20 (42.6)</td>
<td>0.39</td>
</tr>
<tr>
<td>Syncope</td>
<td>4 (18)</td>
<td>5 (10.6)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Abbreviation: CSNRT, corrected sinus node recovery time.

### Figure 1. ROC of the Corrected Sinus Node Recovery Time (AUC: 0.870; 95% CI, 0.772-0.969)

### Table 3. Multivariate Analysis of the Relationship of Different Variables With Improvement of Symptoms

<table>
<thead>
<tr>
<th>Variable</th>
<th>P Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.011</td>
<td>1.047 1.413</td>
</tr>
<tr>
<td>Exercise intolerance</td>
<td>0.002</td>
<td>2.353 40.971</td>
</tr>
<tr>
<td>Wenckebach nocturnal AV block</td>
<td>0.02</td>
<td>1.02 4.995</td>
</tr>
<tr>
<td>Gender</td>
<td>0.15</td>
<td>0.009 2.057</td>
</tr>
<tr>
<td>RV pacing 2 months later</td>
<td>0.59</td>
<td>0.919 1.160</td>
</tr>
<tr>
<td>Memory T-wave</td>
<td>0.34</td>
<td>0.002 7.948</td>
</tr>
</tbody>
</table>

### 5. Discussion

The electrocardiographic pattern of SND does not always correlate with the symptoms. Dizziness, weakness, dyspnea and lightheadedness are nonspecific symptoms that may occur due to different diseases. A variety of interventions may be necessary to evaluate more carefully the presence and degree of abnormalities of SND. Some patients have SND and their symptoms do not have any relation to SND. Our study groups were followed for 6 months for evaluation of improvement after applied treatment.

Some times a good history can prove the presence of SND. It may be important to test sinus node function in those with truly unclear causes of symptoms to avoid an unnecessary implantation of a pacemaker. Also, it is necessary to follow those with an abnormal EPS and suspicious symptoms after PPM implantation. In the present study, the frequency of improved symptoms in all of the patients after pacemaker implantation was nearly 57%.

It is commonly accepted that a permanent pacemaker reduces syncopal attacks in patients with SND, but this has not been documented. In fact, the natural history of syncopal attack appears to be variable and unpredictable (8, 9).
Syncope occurs in those with the tachycardia-bradycardia syndrome and this group was not a subgroup of this study. Syncope in patients with other presentation of SND, such as sinus bradycardia occurs due to vasovagal reflex not SND. So, therapeutic efficacy of PPM in patients with syncope and suspicious SND (sinus pause and bradycardia) can be evaluated only in large randomized clinical trial.

Permanent pacemakers may abolish syncope because of failure of intrinsic sinus node automaticity as well as carotid sinus hypersensitivity whereas there is no definitive demonstration of their efficacy in the prevention of associated vasovagal syncope (10).

It should be noted that pacing that is successful in treating bradycardia-induced symptoms may not be efficacious in preventing syncope due to decrease in peripheral resistance, a common final pathway for the vasovagal mechanism. We implanted DDR pacemakers, which seems to represent the best mode of stimulation in patients with syncopal attacks and/or chronotropic incompetence.

The beneficial effect of dual-chamber pacing in our patients appears to be related to the increase in a heart rate and very likely to the preservation of atrioventricular synchrony. In previous noncontrolled studies (11-13), permanent pacemakers were reported to reduce symptoms in patients with SND. Improvements in sign and symptoms were associated with an increase in a heart rate. These results suggest that patients with SND generally call for medical attention when they are symptomatic for bradycardia-related symptoms such as syncope, dizziness, and easy fatigue; during this time, the heart rate appears to be low. Subsequently, in the vast majority of these patients, heart rate increases spontaneously and symptoms diminish. In the present study, patients with less impairment in sinus node function (CSNRT < 783 ms) and evidence of vagal activity (nocturnal Wenckebach AV block and more symptoms in resting state) benefit less from implanted pacemaker. Park et al. defined hypervagotonic SND if the normal electrophysiologic properties of the sinus node were normalized after the administration of atropine (0.04 mg/kg). The aforementioned investigation showed that hypervagotonic SND has a benign course and most of the patients can be managed safely without implanting a pacemaker (1). Atropine injection was not performed in our patients. So, we are not sure that two groups of patients have the same underlying pathophysiology. Memory T-wave as an indirect indicator of ventricular pacing was present in 17% of the patients. We could not find any association between memory T-wave and absence of response to pacemaker.

5.1. Study Limitations

The reported symptoms are subjective that some older patients may not be able to describe it accurately. Sample size was small; therefore, for further evaluations a large randomized clinical trial is needed.

5.2. Conclusions

Pacemaker implantation is effective in old patients with SND and corrected sinus node recovery time more than 783 ms. Symptoms related to the vagal nervous system can be the cause of persistence of clinical symptoms after pacemaker implantation.

References