Ischemic Stroke After Cardiac Pacemaker Implantation in Sick Sinus Syndrome

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The risk of embolic stroke during sick sinus syndrome before cardiac pacemaker insertion is substantial, but stroke after pacemaker insertion has not been well studied. We observed 10 sick sinus syndrome patients who developed an ischemic stroke 4 days to 112 months after pacemaker insertion. Nine patients represented 6% of the 156 ischemic stroke patients observed during a 30-month period. Eight had a ventricular-demand pacemaker, one had a dual-chamber pacemaker, and one had an atrial-inhibited pacemaker. Six patients were in atrial fibrillation at stroke onset, but none had atrial fibrillation when the pacemaker was inserted. Six patients were taking aspirin, and one was anticoagulated when stroke occurred. Stroke in sick sinus syndrome after pacemaker insertion is not rare, and pacing does not appear to be protective. Sick sinus syndrome patients who convert to atrial fibrillation or who have a ventricular-demand pacemaker might represent high-risk groups for stroke. (Stroke 1988;19:712–715)

Sick sinus syndrome (SSS), a common cardiac rhythm disorder in the elderly, now constitutes the most common indication for permanent cardiac pacemaker insertion.1 Patients with SSS typically experience syncope, light-headedness, and palpitations. Implantation of a permanent cardiac pacemaker substantially improves these symptoms, although long-term survival might not be altered.2,3 In addition, patients with SSS are at high risk for cardioembolic stroke.2,4 The annual stroke incidence rate in nonpaced SSS patients might approach 8–10%.4,5 Stroke may occur after pacemaker implantation, and neither the impact of pacemaker therapy on the substantial baseline stroke risk in SSS nor the role of prophylactic antithrombotic therapy has yet been clarified.5 We have encountered 10 SSS patients who developed ischemic stroke at varying intervals after pacemaker insertion. A careful analysis of these patients might help to elucidate risk factors for stroke development after pacemaker insertion and lead to the consideration of treatment trials.

Subjects and Methods

Patients with stroke after permanent pacemaker insertion for SSS were evaluated within 1 week after stroke onset. Preparing criteria for SSS included a sinus rate of <50 beats/min while awake without β-blockade or a sinus arrest of ≥2 seconds with or without supraventricular tachyarrhythmias. We excluded patients with documented atrial fibrillation (AF) before pacemaker insertion. Patients manifesting intracerebral hemorrhage on computed tomography (CT scanning) were excluded, as were patients with ischemic symptoms lasting <24 hours. Nine patients were seen by the neurology service at Worcester Memorial Hospital over a 30-month period during which time 156 patients with a completed ischemic stroke were evaluated. None of the other non-SSS stroke patients had pacemakers at the time of stroke onset. The cardiac rhythm at stroke presentation was evaluated by a standard 12-lead electrocardiogram (ECG) on the day of admission and/or prolonged ECG monitoring. One additional patient was evaluated by the neurology service at the Boston University School of Medicine.

Results

The patients ranged in age from 69 to 90 years old; six were women, and four were men. Strokes occurred from 4 days to 112 months after pacemaker insertion, although most strokes occurred at least 44 months after pacemaker insertion (Table 1). Stroke in SSS patients after permanent cardiac pacemaker insertion represented a relatively common occurrence as 6% of ischemic stroke patients seen during a 30-month period at a community teaching hospital had both conditions. Eight patients had ventricular-demand pacemakers, while one patient had an atrial-inhibited pacemaker and one had a dual-chamber, atrial-ventricular sequential pacemaker. Five patients had developed sustained AF at the time of stroke admission, and one patient manifested paroxysmal AF. All six patients with AF had a ventricular-demand pacemaker. Hypertension was present in seven patients, but no other commonly recognized stroke risk factor was seen in more than one patient. Six of the 10 patients underwent carotid noninvasive studies or cerebral angiography, and only one had significant disease ipsilateral to the symptomatic vascular territory. Another patient had a dilated cardiomyopathy associated with AF. Six patients were taking aspirin (325–975 mg/day) when their strokes occurred, and one patient was on long-term warfarin therapy with a prothrombin time of 17 seconds; control time was 12 seconds.
<table>
<thead>
<tr>
<th>Case/age/sex</th>
<th>Clinical stroke localization</th>
<th>Rhythm before pacemaker</th>
<th>Antithrombotic therapy</th>
<th>Associated disorders</th>
<th>Pacer type</th>
<th>Pacemaker insertion to stroke (time)</th>
<th>Anticoagulation, Ancillary studies during stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/69/M</td>
<td>L carotid</td>
<td>Bradycardia</td>
<td>Aspirin</td>
<td>Cardiomyopathy, hypertension, hypertension, hypothyroidism</td>
<td>VVI</td>
<td>93 months</td>
<td>Carotid noninvasives: unremarkable; CT: (Day 1) normal</td>
</tr>
<tr>
<td>2/90/F</td>
<td>R carotid</td>
<td>Bradycardia</td>
<td>Aspirin</td>
<td>Dementia</td>
<td>VVI</td>
<td>68 months</td>
<td>CT: R parietal infarct</td>
</tr>
<tr>
<td>3/77/F</td>
<td>R basilar</td>
<td>Bradycardia</td>
<td>Aspirin</td>
<td>None</td>
<td>DDD</td>
<td>24 days</td>
<td>CT: R MCA territory infarct</td>
</tr>
<tr>
<td>4/77/M</td>
<td>L carotid</td>
<td>Bradycardia</td>
<td>Aspirin</td>
<td>None</td>
<td>VVI</td>
<td>5 months</td>
<td>Carotid noninvasives: unremarkable; CT: (Day 1) normal</td>
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<tr>
<td>5/79/F</td>
<td>L basilar</td>
<td>Bradycardia</td>
<td>Aspirin</td>
<td>Polycythemia vera</td>
<td>VVI</td>
<td>44 months</td>
<td>CT: left frontal infarct</td>
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<tr>
<td>6/79/F</td>
<td>L carotid</td>
<td>Tachybradycardia</td>
<td>Aspirin</td>
<td>None</td>
<td>VVI</td>
<td>48 months</td>
<td>CT: L MCA territory infarct</td>
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<tr>
<td>7/81/F</td>
<td>L carotid</td>
<td>Bradycardia</td>
<td>Aspirin</td>
<td>None</td>
<td>VVI</td>
<td>4 weeks</td>
<td>CT: L MCA territory infarct</td>
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<td>8/79/M</td>
<td>R carotid</td>
<td>Bradycardia</td>
<td>Aspirin</td>
<td>Hypertension, coronary artery disease</td>
<td>VVI</td>
<td>47 months</td>
<td>Angiography: 30% L carotid stenosis, 30% R carotid stenosis; CT: normal</td>
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<tr>
<td>9/77/F</td>
<td>R carotid</td>
<td>Bradycardia</td>
<td>Warfarin</td>
<td>Hypertension</td>
<td>VVI</td>
<td>4 weeks</td>
<td>Carotid noninvasives: unremarkable; CT: R MCA territory infarct</td>
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<tr>
<td>10/69/F</td>
<td>R carotid</td>
<td>Tachybradycardia</td>
<td>Aspirin</td>
<td>Diabetes mellitus, old lacunar stroke, hypertension</td>
<td>AAI</td>
<td>64 months</td>
<td>Carotid noninvasives: unremarkable; CT: R MCA territory infarct</td>
</tr>
</tbody>
</table>

M, male; F, female; L, left; R, right; VVI, ventricular-inhibited pacer; VVI, atrial-inhibited pacer; MCA, middle cerebral artery; CT, computed tomography.
Illustrative Cases

Case 3. A 77-year-old woman with coronary artery disease presented for evaluation of syncope. While in the emergency room, sustained ventricular tachycardia developed, which required electrical cardioversion. Afterward, her ECG demonstrated sinus bradycardia with left bundle branch block. Serial creatine phosphokinase determinations showed no elevations. Telemetry revealed that she had episodic sinus bradycardia of 30–35 beats/min associated with presyncope. An atrial-ventricular cardiac pacemaker was inserted, and the patient was discharged on 600 mg tocainide t.i.d. Three weeks after pacemaker insertion, she suddenly developed left-sided weakness and slurred speech. General physical examination was remarkable only for the presence of a grade 2/6 systolic ejection murmur. Neurologic examination disclosed that she was obtunded but arousable. Her speech was dysarthric, and there was a left extensor plantar response. ECG demonstrated synchronous atrioventricular pacing. CT scan of her head disclosed an area of infarction in the territory of the right middle cerebral artery. During the next 4 weeks, there was no improvement in her left hemiparesis.

Case 7. An 81-year-old woman presented with the acute onset of difficulty with word finding. She had no other neurologic symptoms. Four years earlier, she had received a ventricular-demand pacemaker for tachybradyarrhythmias associated with syncope. Her medical history involved only hypertension. Medications on the day of admission included 75 mg metoprolol b.i.d., 0.25 mg digoxin daily, and 325 mg aspirin daily. On general physical examination, she was noted to have diffuse lung rales. The cardiac rhythm was irregularly irregular, and a grade 2/6 systolic ejection murmur was noted. Neurologic examination demonstrated the patient to be alert and cooperative with good spontaneous speech, repetition, comprehension, naming, and reading abilities. She had difficulty with calculations and writing. Right–left confusion and finger agnosia were also present. The remainder of the neurologic examination was unremarkable. A head CT scan on the day of admission showed only mild cerebral atrophy, and a carotid noninvasive battery demonstrated minimal proximal internal carotid artery stenosis bilaterally. ECG revealed AF with a rapid ventricular response (120 beats/min). She was placed on intravenous heparin sodium and then switched to oral warfarin. The neurologic examination returned to normal 6 days after admission.

Discussion

The stroke risk in SSS before cardiac pacemaker insertion is substantial and probably remains so after pacemaker insertion. We encountered 10 SSS patients who developed ischemic stroke 4 days to 112 months after pacemaker implantation. Nine of these patients represented 6% of the ischemic, completed stroke patients seen at one hospital during a 30-month period. The precise stroke risk after cardiac pacemaker insertion remains uncertain, but strokes have been observed in 4.5–23% of paced SSS patients who are followed for 2–3 years. It has been suggested that atrial pacing or atrial-ventricular sequential pacing might be better than ventricular-demand pacing in reducing the risk of subsequent embolic episodes. Studies comparing the stroke risk after various modes of cardiac pacing have been limited and have offered only trends, not significant proof, that atrial or atrial-ventricular sequential pacing is more effective than ventricular-demand pacing in reducing the stroke risk after pacemaker insertion. In our population, eight of 10 SSS patients with ischemic stroke had ventricular-demand pacemakers. This observation is of uncertain significance because most patients (85%) in our population receive this type of cardiac pacemaker. A large, carefully controlled and monitored cohort of SSS patients who receive different types of pacemakers should be studied to determine whether pacing mode influences stroke risk.

Five patients with stroke after cardiac pacemaker insertion had also developed sustained AF, and one patient manifested paroxysmal AF. All of these patients had received a ventricular-demand pacemaker. AF is a well-recognized risk factor for the development of cardioembolic stroke with an annual incidence approaching 5%. The development of AF in paced SSS patients might identify a subpopulation at increased risk for stroke. This potential association should be assessed by follow-up of a cohort of paced SSS patients. AF frequently develops in paced SSS patients with an observed prevalence of 25–30% 2–3 years after pacemaker insertion. The pacing mode used appears to influence the rate of AF development. Markzwit et al. calculated an annual incidence of AF development of 10% in patients receiving a ventricular-demand pacemaker compared with 3.3% with atrial and 2.9% with atrial-ventricular sequential pacemakers. The reduced risk for AF development with atrial or atrial-ventricular sequential pacing might be associated with a diminished risk for stroke.

The patients in our study presumably had cardioembolic strokes. This can only remain an assumption as the clinical diagnosis of cardioembolic stroke is difficult. As many as one third of patients so labeled might have another pathogenetic mechanism for their cerebral ischemic event. Six of our patients underwent either a carotid noninvasive battery or cerebral angiography, and in only one patient (Case 5, Table 1) did these studies demonstrate hemodynamically significant disease in an appropriate vessel. This patient had bihemispheric cerebral infarctions and the abrupt onset of stroke symptoms, which are two signs suggestive of cardioembolic stroke. Seven patients had a history of hypertension, but none had clinical or CT evidence of a small-vessel, lacunar stroke. Other stroke risk factors such as diabetes mellitus, coronary artery
disease, and polycythemia were seen only rarely. We conclude that most of our patients had cardioembolic strokes.

The use of antithrombotic agents to potentially reduce stroke risk before or after pacemaker insertion in SSS patients has not been carefully assessed. Six of our patients were receiving platelet antiaggregant therapy with aspirin when their stroke occurred, and one patient was receiving an oral anticoagulant. Platelet antiaggregant therapy with aspirin might not provide protection against stroke development in SSS, although this medication may reduce the extent of neurological damage. The role of anticoagulants in reducing stroke risk has not been assessed, but Radford and Julian suggest their use after pacemaker insertion in SSS patients. Clinical trials are underway to assess the efficacy of antithrombotic medications in reducing stroke risk in chronic AF patients, and similar trials, perhaps including a subgroup treated with aspirin, might be necessary in paced SSS patients.

In summary, patients with SSS are at risk for cardioembolic stroke, often occurring in the setting of paroxysmal or sustained atrial fibrillation. Our observations suggest that ventricular-demand pacemakers do not offer protection from this risk and that the role of antithrombotic medications needs further clarification.

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References


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