

# Diagnosis and Treatment of Sick Sinus Syndrome

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**Sick sinus syndrome comprises a variety of conditions involving sinus node dysfunction and commonly affects elderly persons. While the syndrome can have many causes, it usually is idiopathic. Patients may experience syncope, pre-syncope, palpitations, or dizziness; however, they often are asymptomatic or have subtle or nonspecific symptoms. Sick sinus syndrome has multiple manifestations on electrocardiogram, including sinus bradycardia, sinus arrest, sinoatrial block, and alternating patterns of bradycardia and tachycardia (bradycardia-tachycardia syndrome). Diagnosis of sick sinus syndrome can be difficult because of its nonspecific symptoms and elusive findings on electrocardiogram or Holter monitor. The mainstay of treatment is atrial or dual-chamber pacemaker placement, which generally provides effective relief of symptoms and lowers the incidence of atrial fibrillation, thromboembolic events, heart failure, and mortality, compared with ventricular pacemakers. (Am Fam Physician 2003;67:1725-32,1738. Copyright©2003 American Academy of Family Physicians)**

 A patient information handout on sick sinus syndrome, written by the authors of this article, is provided on page 1738.

**S**ick sinus syndrome is a generalized abnormality of cardiac impulse formation that may be caused by an intrinsic disease of the sinus node that makes it unable to perform its pacemaking function, or by extrinsic causes.<sup>1</sup> Abnormalities encompassed in this syndrome include sinus bradycardia, sinus arrest or exit block, combinations of sinoatrial and atrioventricular nodal conduction disturbances, and atrial tachyarrhythmias. Sick sinus syndrome is not a disease with a single etiology and pathogenesis but, rather, a collection of conditions in which the electrocardiogram (ECG) indicates sinus node dysfunction.<sup>2</sup>

Sick sinus syndrome is characterized by sinus node dysfunction with an atrial rate inappropriate for physiologic requirements. Although the condition is most common in the elderly, it can occur in persons of all ages, including neonates.<sup>3</sup> The mean age of patients with this condition is 68 years, and both sexes are affected approximately equally.<sup>4</sup> The syndrome occurs in one of every 600 cardiac patients older than 65 years and may account for 50 percent or more of permanent pacemaker placements in the United States.<sup>5</sup>

## Etiology

Most cases of sick sinus syndrome are idiopathic, and the cause can be multifactorial (Table 1).<sup>3</sup> Degenerative fibrosis of nodal tissue is the most common cause of intrinsic changes in the sinoatrial node that lead to sick sinus syndrome. Certain conditions can cause these intrinsic changes.<sup>3,5,6</sup> There also are extrinsic causes of sinus node dysfunction and conditions that can cause this problem in children (Table 1).<sup>3</sup>

Coronary artery disease may coexist with sick sinus syndrome in a significant number of patients, although it is not considered a major cause of the syndrome. It is unclear whether inflammation, sinus node ischemia, or local autonomic neural effects lead to the development of sick sinus syndrome in patients with myocardial infarction. Sinus node dysfunction usually is temporary when it follows an acute myocardial infarction. Uncommonly, chronic ischemia may cause fibrosis and lead to symptoms of sick sinus syndrome for months to years after myocardial infarction.

## Clinical Manifestations

Patients with sick sinus syndrome often are asymptomatic or have symptoms that are

TABLE 1

**Causes of Sick Sinus Syndrome**

<b>Intrinsic causes</b>	<b>Extrinsic causes</b>
Amyloidosis	Cholinesterase deficiency (suggested)
Arteritis	Hyperkalemia
Cardiomyopathies	Hypoxia
Chagas' disease	Pharmacologic agents
Collagen vascular disease	Digitalis
Diphtheria	Calcium channel blockers
Familial sinoatrial node disorders	Beta blockers
Fatty replacement	Sympatholytic agents
Friedreich's ataxia	Antiarrhythmics
Hemochromatosis	Toxins
Idiopathic degenerative fibrotic infiltration*	<b>Pediatric causes</b>
Ischemia/infarction	Congenital abnormalities
Leukemia	Sinoatrial nodal artery deficiency
Metastatic disease	
Muscular dystrophy	
Myocarditis	
Pericarditis	
Rheumatic heart disease	
Sarcoidosis	
Surgical injury	

\*—Most common intrinsic cause.

Adapted with permission from Wahls SA. Sick sinus syndrome. *Am Fam Physician* 1985;31:118.

TABLE 2

**Symptoms of Sick Sinus Syndrome**

<b>Central nervous system</b>	<b>Cardiovascular system</b>	<b>Other</b>
Dementia	Angina pectoris	Digestive disturbances
Irritability	Arterial thromboemboli	Dizziness
Lethargy	Cerebrovascular accident	Errors in judgment
Lightheadedness	Congestive heart failure	Facial flushing
Memory loss	Palpitations	Fatigue
Nocturnal wakefulness		Oliguria
Syncope or pre-syncope		

Adapted with permission from Wahls SA. Sick sinus syndrome. *Am Fam Physician* 1985;31:123.

mild and nonspecific<sup>7</sup> (Table 2).<sup>3</sup> Symptoms are related to the decreased cardiac output that occurs with the bradyarrhythmias or tachyarrhythmias.<sup>3</sup> Most of the symptoms are caused by decreased cerebral perfusion, and 50 percent of patients have syncope or pre-syncope.<sup>5</sup>

Symptoms, which may have been present for months or years, can include syncope, palpitations, and dizziness, as well as symptoms caused by the worsening of conditions such as congestive heart failure, angina pectoris, and cerebral vascular accident.<sup>8</sup> Peripheral thromboembolism and stroke, which can occur in the presence of bradycardia-tachycardia syndrome (alternating bradyarrhythmias and tachyarrhythmias), may be related to dysrhythmia-induced emboli.<sup>3</sup> A slow heart rate in the presence of fever, left ventricular failure, or pulmonary edema may be suggestive of sick sinus syndrome.<sup>2,9</sup> Associated tachycardia may cause flushing of the face, pounding of the heart, and retrosternal pressure.<sup>10</sup> Other symptoms include irritability, nocturnal wakefulness, memory loss, errors in judgment, lethargy, lightheadedness, and fatigue<sup>2,11</sup> (Table 2).<sup>3</sup> More subtle symptoms include mild digestive disturbances, periodic oliguria or edema, and mild intermittent dyspnea.<sup>2</sup>

**ECG Manifestations**

Sick sinus syndrome can produce a variety of ECG manifestations consisting of atrial bradyarrhythmias, atrial tachyarrhythmias, and alternating bradyarrhythmias and tachyarrhythmias<sup>7</sup> (Table 3).<sup>3</sup> Supraventricular bradyarrhythmias may include sinus bradycardia, sinus arrest with or without junctional escape, sinoatrial exit block, ectopic atrial bradycardia, and atrial fibrillation with slow ventricular response. The sinus bradycardia that occurs in patients with sick sinus syndrome is inappropriate and not caused by medications.<sup>2,5</sup> The sinoatrial exit block that occurs in patients with sick sinus syndrome may demonstrate a

**TABLE 3**  
**Arrhythmias Associated**  
**with Sick Sinus Syndrome**

**Atrial bradyarrhythmias**

Sinus bradycardia  
 Sinus arrest (with or without junctional escape)  
 Sinoatrial exit block  
   Mobitz type I block (Wenckebach block)  
   Mobitz type II block  
 Ectopic atrial bradycardia  
 Atrial fibrillation with slow ventricular response  
 Greater-than 3-second pause following carotid massage  
 Long pause following cardioversion of atrial tachyarrhythmias

**Atrial tachyarrhythmias**

Atrial fibrillation  
 Atrial flutter  
 Atrial tachycardia  
 Paroxysmal supraventricular tachycardia

**Ventricular (escape) tachyarrhythmia**

**Alternating bradycardias and tachycardias**

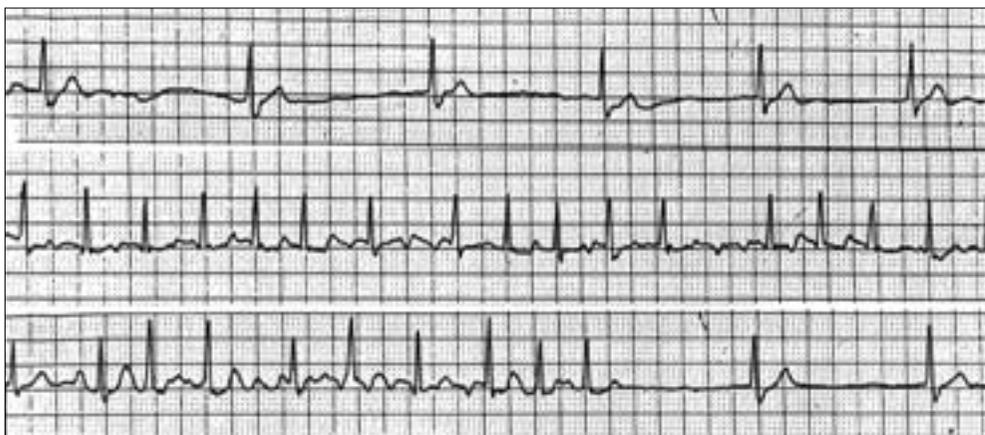
Bradycardia-tachycardia syndrome

*Adapted with permission from Wahls SA. Sick sinus syndrome. Am Fam Physician 1985;31:120.*

*The treatment of choice for symptomatic bradyarrhythmias in patients with sick sinus syndrome is the placement of a pacemaker.*

Mobitz type I block (Wenckebach block) and a Mobitz type II block.<sup>2</sup> The ECG may reveal a long pause following cardioversion of atrial tachyarrhythmias, and a greater-than three-second pause following carotid massage.<sup>5</sup> Sixty percent of patients have tachyarrhythmias.<sup>8</sup>

Supraventricular tachyarrhythmias that occur in patients with sick sinus syndrome include paroxysmal supraventricular tachycardia, atrial flutter, atrial fibrillation, and atrial tachycardia.<sup>2,3</sup> Atrial fibrillation is the most common tachydysrhythmia in these patients.<sup>12</sup> Rarely, a ventricular escape tachyarrhythmia may be seen on ECG.<sup>8</sup> Sinus node re-entrant rhythm is another ECG manifestation.<sup>5</sup> Bradycardia-tachycardia syndrome may be seen on ECG or cardiac rhythm strip (Figure 1); this syndrome is more common in older patients with advanced sick sinus syndrome.<sup>3</sup>



**FIGURE 1.** Electrocardiogram exhibiting alternating patterns of bradycardia and tachycardia as seen in patients with sick sinus syndrome.

TABLE 4

## Indications for Permanent Pacemaker Implantation in Sick Sinus Syndrome

### Class I\*

1. SSS with documented symptomatic bradycardia, including frequent sinus pauses that produce symptoms. In some patients, bradycardia is iatrogenic and will occur as a consequence of essential long-term drug therapy of a type and dosage for which there are no acceptable alternatives.
2. Symptomatic chronotropic incompetence

### Class IIa

1. SSS occurring spontaneously or as a result of necessary drug therapy, with heart rate less than 40 bpm when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented.

### Class IIb

1. In minimally symptomatic patients, chronic heart rate less than 30 bpm while awake

### Class III

1. SSS in asymptomatic patients, including those in whom substantial sinus bradycardia (heart rate less than 40 bpm) is a consequence of long-term drug treatment
2. SSS in patients with symptoms suggestive of bradycardia that are clearly documented as not associated with a slow heart rate
3. SSS with symptomatic bradycardia caused by nonessential drug therapy

SSS = sick sinus syndrome; bpm = beats per minute.

\*—Class I represents conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective. Class II represents conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Class IIa represents conditions in which the weight of evidence/opinion is in favor of usefulness/efficacy. Class IIb represents conditions in which the usefulness/efficacy is less well established by evidence/opinion. Class III represents conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

Information from Gregoratos G, Cheitlin MD, Conill A, Epstein AE, Fellows C, Ferguson TB Jr, et al. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). *J Am Coll Cardiol* 1998;31:1178, 1182.

## Diagnosis

The diagnosis of sick sinus syndrome may be difficult because of the slow and erratic course of the syndrome. The condition often goes undetected in the early stages because only sinus bradycardia may be present at its origin.<sup>9</sup> Some symptoms of patients with sick sinus syndrome (e.g., fatigue, irritability, memory loss, lightheadedness, palpitations, cognitive defects) are present in several other disorders that occur in elderly patients and may be misdiagnosed as those of senile dementia.<sup>5</sup>

Symptoms of sick sinus syndrome may be variable, intermittent, and difficult to associate

with ECG changes.<sup>2</sup> If the patient is asymptomatic when ECG or ambulatory monitoring is performed, the dysrhythmias of the syndrome are often not present.<sup>5</sup> Furthermore, there is no definitive way to distinguish patients with atrial fibrillation associated with sick sinus syndrome from patients with atrial fibrillation and normal sinus function; this distinction is clinically important because treating atrial fibrillation with cardioversion or medications can have catastrophic consequences if the sinus node is inadequate.

One manifestation of serious sinus node dysfunction in patients with atrial fibrillation is a slow ventricular rate in the absence of medications such as propranolol (Inderal) or digitalis.<sup>2</sup> Bradycardia may be misattributed to digoxin treatment in a patient with congestive heart failure. Cardioactive drugs, such as digoxin, quinidine (Quinaglute), and procainamide (Pronestyl), as well as hyperkalemia, can cause periodic sinus arrest or sinoatrial exit block.

Functional sinus bradycardia, enhanced vagal drive, gastrointestinal and neurologic conditions, and other causes of syncope can produce symptoms similar to those of sick sinus syndrome and must be included in the differential diagnosis of the syndrome. Sinus node dysfunction can occur perioperatively because of increased vagal tone caused by anesthesia or surgical intervention.<sup>13</sup> All of these possibilities must be excluded before the diagnosis of sick sinus syndrome can be made.<sup>9</sup>

The diagnosis requires not only documentation of sinus node dysfunction but also correlation with the associated symptoms of sick sinus syndrome. The most common method of diagnosis is Holter monitoring. During monitoring, patients must keep a precise diary of their activities and symptoms, so that these factors can be correlated with the ECG changes.<sup>3</sup>

If two 24-hour periods of Holter monitoring fail to reveal the dysrhythmias of sick sinus syndrome, but the symptoms are severe and intermittent, it is likely that the sinus node

*Symptoms associated with sick sinus syndrome may be worsened in patients who are receiving digitalis, verapamil, beta blockers, sympatholytic agents such as clonidine and methyldopa, and antiarrhythmic agents.*

dysfunction is severe but intermittent. In these cases, patients can carry a pocket-sized device for transmitting ECG readings via telephone when they are having symptoms. For this procedure to be successful, the arrhythmia must last for at least one minute. Another approach is to have patients activate a recording device to monitor the events of cardiac dysrhythmias when they are having symptoms.<sup>2</sup>

There are several other methods of diagnosing sick sinus syndrome. Isometric hand-grip exercises or Valsalva's maneuvers normally increase the heart rate, but this effect may be minimal or absent in patients with this syndrome. If carotid massage produces abrupt sinus arrest of three seconds' duration, sinus node dysfunction may be suspected.<sup>8</sup> These measures and monitoring cardiac response to such agents as atropine and isoproterenol (Isuprel) should only be attempted while a patient is undergoing careful ECG monitoring.<sup>3</sup>

Exercise testing may be useful in determining the response of the sinus node to physiologic demands. At an equal level of oxygen consumption, some patients with sick sinus syndrome have a decreased heart rate response to exercise compared with healthy patients.<sup>5</sup> Intracardiac electrophysiologic tests (atrial overdrive pacing and premature atrial stimulation) can be used to elicit intrinsic sinus node disease or to document the effects of cardioactive drugs<sup>2,3</sup>; however, electrophysiologic testing is no longer routinely recommended for diagnostic purposes because of its poor sensitivity and specificity.<sup>14</sup> The risks and benefits of these diagnostic modalities must be considered and discussed with the patient before they are used.

### **Treatment**

Pacemaker therapy is warranted in many patients with sick sinus syndrome. *Table 4*<sup>15</sup> lists practice guidelines from the American College of Cardiology/American Heart Association task force on permanent pacemaker placement in patients with this condition.<sup>15</sup> It is essential

to document symptoms concurrent with the dysrhythmia when evaluating whether pacemaker placement will be beneficial.

The treatment of choice for symptomatic bradyarrhythmias in patients with sick sinus syndrome is the placement of a pacemaker.<sup>1,3</sup> Artificial pacemakers are well tolerated in elderly patients.<sup>2</sup> In all patients with this syndrome, except those with chronic atrial fibrillation, atrial-based pacemakers are recommended<sup>1,16</sup> (*Figure 2*).<sup>16</sup>

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### **Optimal Pacemaker Mode Recommendation in Sick Sinus Syndrome**

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FIGURE 2.

*Patients with sick sinus syndrome who have bradycardia-tachycardia syndrome or chronic atrial fibrillation are at risk for embolic stroke.*

Table 5<sup>14,17</sup> lists the international codes describing pacemakers and implanted devices. Patients who have sick sinus syndrome with right bundle branch block have an increased risk of developing symptomatic high-degree atrioventricular block and should be treated with a dual-chamber pacemaker. Patients with no signs of atrioventricular conduction abnormalities should be treated with an atrial-based pacemaker.<sup>18</sup> Pacing with a dual-chamber demand pacemaker with automatic mode-switching function is appropriate in patients with sick sinus syndrome who have intermittent tachyarrhythmic components. Pacing with a rate-responsive single-chamber ventricular demand pacemaker should be used in patients with the syndrome and chronic atrial fibrillation.<sup>7</sup>

Complications, including myocardial perforation, pneumothorax, wound hematoma, venous thrombosis, pacemaker lead failure, and infection, can occur with permanent endocardial pacemaker therapy, but they are uncommon.<sup>19</sup>

When tachyarrhythmias are a problem in a patient with sick sinus syndrome, a pacemaker may decrease the risk of complete heart block or asystole associated with pharmacotherapy.<sup>3</sup> Digitalis can cause bradyarrhythmias in patients with sick sinus syndrome and should only be used in conjunction with a pacemaker in the management of supraventricular tachyarrhythmias.<sup>5</sup> Severe sinus bradycardia, sinoatrial arrest, or sinoatrial exit block occasionally occurs with the use of beta-blocker medications in patients with this condition.<sup>2</sup>

Symptoms associated with this syndrome may be worsened in patients who are receiving digitalis, verapamil (Calan), beta blockers, sympatholytic agents such as clonidine (Catapres) and methyldopa (Aldomet), and antiarrhythmic agents.<sup>3,5</sup> Therefore, the use of negative chronotropic drugs should be cautiously considered.<sup>7</sup> The effects of procainamide and quinidine are unpredictable. In certain patients with sick sinus syndrome and episodes of heart failure, oral theophylline therapy and dual-chamber pacemakers have been shown to reduce the occurrence of heart failure.<sup>20</sup> In the absence of pacing, cardioversion may be dangerous because of the likelihood of prolonged sinus arrest.<sup>3</sup>

Patients with sick sinus syndrome who have bradycardia-tachycardia syndrome or chronic atrial fibrillation (especially in association with congestive heart failure, large left atria, or mitral valve disease) are at risk for embolic stroke. Although the risk-to-benefit ratio for anticoagulation is not well defined in these patients, warfarin (Coumadin) has been shown to decrease the number of strokes and embolic events in patients with sick sinus syndrome who have paroxysmal and chronic atrial fibrillation.<sup>5,11</sup>

## Prognosis

Randomized controlled trials<sup>4,21</sup> have examined morbidity and mortality in patients with sick sinus syndrome using various pacing modes. Compared with ventricu-

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lar pacing, atrial pacing is associated with a lower incidence of thromboembolic complications, atrial fibrillation, heart failure, cardiovascular mortality, and total morbidity.<sup>1,18</sup> In a retrospective study,<sup>22</sup> patients with sick sinus syndrome who had pacemaker therapy were followed for 12 years; at eight years, mortality among those with ventricular pacing was 59 percent compared with 29 percent among those with atrial pacing. This discrepancy may well be a result of the physiologic or anatomic disorder (e.g., fibrosis of conductive tissue) leading to the requirement for the particular pacemaker rather than the type of pacemaker used.

Patients who have sick sinus syndrome with only sinus bradycardia have a better prognosis. One study<sup>3</sup> indicated that mortality rates in these patients may not be different from mortality rates in the normal population. Researchers conducting one literature review<sup>22</sup> concluded that patients with this syndrome who require atrial or dual-chamber pacing have a mortality rate of 3.6 percent (plus or minus 1.8 percent) per year. There is

*Compared with ventricular pacing, atrial pacing is associated with a lower incidence of thromboembolic complications, atrial fibrillation, heart failure, cardiovascular mortality, and total morbidity.*

a high prevalence of cardiovascular disease in patients with sick sinus syndrome who die within the first few years of pacemaker implantation.<sup>2</sup>

Recent improvements in rate-responsive pacemaker engineering have led to improvements in maximum heart rate, exercise tolerance, functional status, suppression of dysrhythmias, and sense of well-being in patients.<sup>16</sup> The achievement of near-physiologic rate responsiveness and atrioventricular synchrony, as well as decreased mortality and morbidity, has led to a better prognosis in patients with sick sinus syndrome.<sup>19</sup>

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TABLE 5

**International Codes Describing Pacemakers and Implanted Devices**

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### REFERENCES

1. Mangrum JM, DiMarco JP. The evaluation and management of bradycardia. *N Engl J Med* 2000; 342:703-9.
2. Bigger JT Jr, Reiffel JA. Sick sinus syndrome. *Annu Rev Med* 1979;30:91-118.
3. Wahls SA. Sick sinus syndrome. *Am Fam Physician* 1985;31:117-24.
4. Lamas GA, Lee K, Sweeney M, Leon A, Yee R, Ellenbogen K, et al. The mode selection trial (MOST) in sinus node dysfunction: design, rationale, and baseline characteristics of the first 1000 patients. *Am Heart J* 2000;140:541-51.
5. Rodriguez RD, Schocken DD. Update on sick sinus syndrome, a cardiac disorder of aging. *Geriatrics* 1990;45:26-30.
6. Tierney LM, McPhee SJ, Papadakis MA. Heart conduction disturbances: sick sinus syndrome. In: Papadakis MA, Tierney LM, McPhee SJ. *Current medical diagnosis & treatment*, 2000. 39th ed. New York, N.Y.: Lange Medical Books/McGraw-Hill, 2000:412.
7. Fuster V, Alexander RW, O'Rourke RA, eds. *Hurst's The heart*. 10th ed. New York, N.Y.: McGraw-Hill Medical Publishing Division, 2001.
8. Bower PJ. Sick sinus syndrome. *Arch Intern Med* 1978;138:133-7.
9. Ferrer MI. The sick sinus syndrome. *Hosp Pract* 1980;15:79-89.
10. Kaplan BM. The tachycardia-bradycardia syndrome. *Med Clin North Am* 1976;60:81-99.
11. Colquhoun M. When should you suspect sick sinus syndrome? *Practitioner* 1999;243:422-5.
12. Atlee JL. Perioperative cardiac dysrhythmias: diagnosis and management. *Anesthesiology* 1997;86:1397-424.
13. Hollenberg SM, Dellinger RP. Noncardiac surgery: postoperative arrhythmias. *Crit Care Med* 2000; 28(10 suppl):N145-50.
14. The Merck manual of diagnosis and therapy. 17th ed. Whitehouse Station, N.J.: Merck, 1999:1719.
15. Gregoratos G, Cheitlin MD, Conill A, Epstein AE, Fellows C, Ferguson TB Jr, et al. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). *J Am Coll Cardiol* 1998; 31:1175-209.
16. Alagona P Jr. Advances in pacing for the patient with sick sinus syndrome. *Curr Opin Cardiol* 1997; 12:3-11.
17. Bernstein AD, Camm AJ, Fletcher RD, Gold RD, Rickards AF, Smyth NP, et al. The NASPE/BPEG generic pacemaker code for antibradyarrhythmia and adaptive-rate pacing and antitachyarrhythmia devices. *Pacing Clin Electrophysiol* 1987;10: 794-9.
18. Andersen HR, Nielsen JC, Thomsen PE, Thuesen L, Mortensen PT, Vesterlund T, et al. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. *Lancet* 1997;350:1210-6.
19. Kiviniemi MS, Pirnes MA, Eranen HJ, Kettunen RV, Hartikainen JE. Complications related to permanent pacemaker therapy. *Pacing Clin Electrophysiol* 1999;22:711-20.
20. Alboni P, Menozzi C, Brignole M, Paparella N, Gaggioli G, Lolli G, et al. Effects of permanent pacemaker and oral theophylline in sick sinus syndrome. The THEOPACE study: a randomized controlled trial. *Circulation* 1997;96:260-6.
21. Tang CY, Kerr CR, Connolly SJ. Clinical trials of pacing mode selection. *Cardiol Clin* 2000;18:1-23.
22. McComb JM, Gribbin GM. Effect of pacing mode on morbidity and mortality: update of clinical pacing trials. *Am J Cardiol* 1999;83(5B):211-3D.