The Incidence of Coronary Artery Disease in Patients with Symptomatic Bradyarrhythmias

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SUMMARY

Symptomatic bradyarrhythmia occurs most often in aged patients. Most of these patients have multiple coronary risk factors and present with angina-like symptoms. The coexistence of CAD not only has major effects on their prognosis but also influences the long-term care. This study was designed to evaluate the incidence of coexistent CAD in patients with symptomatic bradyarrhythmias and its relationship to conventional coronary risk factors in Chinese people.

From May 1996 to April 1998, we prospectively studied all consecutive patients admitted to our institution for symptomatic bradyarrhythmias requiring permanent pacemaker implantation. Coronary angiographies were performed non-selectively at the same session of pacemaker implantation. Based on the presence or absence of CAD, patients were divided into two groups for analysis. Multivariate logistic regression analysis was performed to determine independent predictors of CAD including sex, age, diabetes mellitus (DM), hypertension, hypercholesterolemia, and smoking. The odds-ratio (OR) and 95% confidence interval (CI) were determined.

A total of 113 patients [68 males and 45 females, mean age 70.4±8.2 years old (range 45-86)] were included in our study. The diagnosis was sick sinus syndrome in 69 patients (61%) and atrioventricular block in 44 patients (39%). The incidence of CAD based on coronary angiography was 20%. The nodal-related artery was seldom involved among patients with coexistent CAD and symptomatic bradyarrhythmias (9%), and most patients had significant stenosis over LAD (74%). The baseline characteristics and presenting symptoms were not different statistically between patients with or without CAD. Hypercholesterolemia (OR 6.6, 95% CI 2.0-22.2, $p=0.002$) and DM (OR 4.7, 95% CI 1.3-17.2, $p=0.020$) were the two most significant independent predictors of CAD.

In our patients with symptomatic bradyarrhythmias requiring permanent cardiac pacing, the incidence of CAD was 20% as determined by coronary angiography (CAG). Hypercholesterolemia and DM were the two most significant independent predictors for CAD in these patients. The nodal artery was seldom involved in patients with coexistent CAD and symptomatic bradyarrhythmias. (Jpn Heart J 2001; 42: 417-423)

Key words: Coronary artery disease, Permanent pacemaker, Bradyarrhythmia

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SYMPTOMATIC bradyarrhythmia occurs most often in aged people. Most of these patients have many underlying systemic diseases and multiple coronary risk factors. Permanent pacemaker implantation has been a standard treatment for these patients. However, in the previous reports, a small portion of these patients had coexistent coronary artery disease (CAD).¹⁻³⁾

The presence of CAD among patients with symptomatic bradyarrhythmia has several important clinical implications. First of all, CAD is a possible cause of these patients' dysrhythmia. According to the previous reports, one-third of patients with sick sinus syndrome and 15% of patients with chronic atrioventricular block could be attributed to the underlying CAD.^{2,3)} Second, coexistent CAD is a major prognostic determinant in these patients.⁶⁻⁸⁾ Though most patients had major improvement of their clinical symptoms after pacemaker implantation, those with coexistent CAD had worse prognosis in the long-term follow up. Finally, since permanent cardiac pacing is inevitable in most patients with symptomatic bradyarrhythmia, there will be some major drawbacks among patients with coexistent CAD. The distorted electrocardiography of a pacemaker-dependent patient makes it invalid for the diagnosis of myocardial ischemia or infarction. Increased or fixed heart rate, a loss of atrioventricular synchrony, and abnormal contraction and relaxation patterns of the left ventricle after cardiac pacing may aggravate the myocardial ischemia.^{4,5)} Hence, in patients with symptomatic bradyarrhythmia demanding permanent pacemaker implantation, early diagnosis of coexistent CAD is mandatory for adequate pacemaker-mode selection and better patient care.

Most previous studies either confined their objectives to the etiologic role of CAD in bradyarrhythmias or were merely statistical results of follow-up data. Most of their diagnostic methods for CAD were based upon clinical findings and lacked hard evidence such as coronary angiography. Furthermore, there are no studies in Oriental people. The objective of this study was to evaluate the incidence of CAD among Chinese patients who suffered from symptomatic bradyarrhythmias and its association with conventional coronary risk factors.

MATERIALS AND METHODS

Patients: From May 1996 to April 1998, all consecutive patients admitted to our institution for pacemaker implantation due to symptomatic bradyarrhythmia were studied prospectively. The diagnosis of bradyarrhythmias, which included sick sinus syndrome (SSS) and atrioventricular dysfunction (AVD), should be established by 12-lead surface ECG, 24-hour ambulatory ECG or electrophysiological study. Coronary angiography had been performed non-selectively. Patients were excluded due to young age (age <45 years old), impaired renal function (serum

creatinine >3.0 mg/dl), or because informed consent for coronary angiography was not obtained.

Interpretation of coronary angiography: Coronary angiography was performed during the same session as pacemaker implantation. A total of 3-4 views of left coronary artery and two views of right coronary artery were done. The coronary angiography was reviewed by two independent experienced cardiologists unaware of the patient's general data. Luminal stenosis was calculated as the percentage of diameter reduction in diseased segment compared to the proximal disease-free reference segment. More than 75% stenosis in either one of three major coronary arteries including the left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA) or their first-order branches was considered as significant for CAD. The sinus nodal artery (SNA) and atrio-ventricular nodal artery (AVNA) were identified. Significant flow compromise was defined as more than 75% stenosis in the nodal artery or its feeding artery proximal to the origin.

Symptoms of bradyarrhythmia: The medical records were carefully reviewed and symptoms retrieved. Low cardiac output was defined as upright dizziness, fainting, lethargy, or decreased workload. The presentations of cardiac congestion included dyspnea on exertion, paroxysmal nocturnal dyspnea, or frank pulmonary edema. Presentations of angina included chest tightness with typical or atypical characteristics. Syncope was defined as transient loss of consciousness with spontaneous recovery and without neurological sequelae. Subjective sensation of an irregular heart rhythm was considered to be a symptom of palpitations. Central nervous system (CNS) symptoms included transient ischemic attack (TIA) or cerebral infarction with evidence of focal neurological sequelae.

Evaluation of coronary risk factors: Conventional coronary risk factors including sex, age, diabetes mellitus (DM), hypertension, hypercholesterolemia, and smoking were recorded. The presence of DM and hypertension were determined by history taking or medical record. A fasting total serum cholesterol level above 200 mg/dl on two sequential blood tests was considered as hypercholesterolemia. Our definition of smoking risk factor requires at least 10 years exposure to tobacco with at least 10 cigarettes per day.

Statistical analysis: The patients were divided into two groups based on their coronary angiographic findings. All parametric data are expressed as the mean ($\pm$ SD of the measured variables. Intergroup differences in means were checked by two-sided unpaired Student's *t*-test. The categorical variables were measured by the chi-square test with or without Yate's correction as needed. Multivariate logistic regression analysis was performed to determine independent predictors of CAD including sex, age (dichotomized at 70 years old), DM, hypertension, hypercholesterolemia, and smoking. The odds-ratios and 95% confidence inter-

vals of independent factors were calculated. A *p* value of less than 0.05 was considered significant.

RESULTS

During the study period, 215 patients were admitted to our institution for pacemaker implantation due to symptomatic bradyarrhythmia. There were 72 patients who did not undergo coronary angiography due to young age (25 patients), impaired renal function (18 patients) or did not provide informed consent (29 patients). Among the 143 patients who had received coronary angiography, 30 were excluded due to recent myocardial infarction (15 patients), bradyarrhythmia after coronary bypass surgery (3 patients), inadequate angiography (6 patients), and incomplete medical records (6 patients).

A total of 113 patients (68 males, 45 females) were eligible for further analysis. The mean age was 70.4 ± 8.2 years old (range 45-86). The diagnoses were SSS in 69 patients (61%) and AVD in 44 patients (39%). Twenty-three patients (20% of total study population) had evidence of CAD by coronary angiography. For patients with SSS, the incidence was 17% (12 in 69); and for patients with AVD, 25% (11 in 44). There were no significant differences in baseline characteristics and presenting symptoms between patients with or without CAD (Table I). The three most frequent complaints for patients with abnormal CAG were low cardiac output (61%), angina (61%) and syncope (52%). For patients with normal CAG, they were syncope (60%), low cardiac output (58%), and angina (40%). Angina was a common shared complaint in both groups of patients.

Table I. Demographic Data and Presenting Symptoms

	Abnormal CAG (<i>n</i> =23)	Normal CAG (<i>n</i> =90)	<i>p</i> value
Age (years)	70.6 $\pm$ 6.2	70.3 $\pm$ 8.7	0.869
Male	14 (61%)	54 (60%)	0.939
Diagnosis			0.327
Sick sinus syndrome	12 (52%)	57 (63%)	
Atria-ventricular block	11 (48%)	33 (37%)	
Symptoms			
Low cardiac output	14 (61%)	52 (58%)	0.788
Angina	14 (61%)	36 (40%)	0.072
Syncope	12 (52%)	54 (60%)	0.497
Palpitation	1 (7%)	13 (14%)	0.190
Cardiac congestion	3 (13%)	11 (12%)	0.915
CNS symptoms	0 (0%)	2 (2%)	0.471

Regarding coronary risk factors, patients with abnormal CAG had significantly higher percentages of hypercholesterolemia (52% vs 24%, $p=0.010$; Table II) and DM (30% vs 11%, $p=0.021$; Table II). Multivariate logistic regression analysis of conventional coronary risk factors revealed hypercholesterolemia and DM were the two most significant independent predictors of CAD (Table III). The odds-ratio was 6.6 (95% CI 2.0-22.2) for hypercholesterolemia and 4.7 (95% CI 1.3-17.2) for DM.

We further divided patients with CAD into 2 subgroups based on their diagnoses of bradyarrhythmia. The findings of their coronary angiographies are presented in Table IV. Both subgroups had similar distributions with respect to the coronary arteries involved. Most patients had significant stenosis over LAD (74%). The nodal-artery insufficiency was quite infrequent among our patients

Table II. Distribution of Conventional Coronary Risk Factors

	Abnormal CAG ($n=23$)	Normal CAG ($n=90$)	p value
Hypercholesterolemia	12 (52%)	22 (24%)	0.010
Diabetes mellitus	7 (30%)	10 (11%)	0.021
Age	15 (65%)	53 (59%)	0.580
Hypertension	13 (57%)	41 (46%)	0.347
Smoking	7 (30%)	28 (31%)	0.950
Male sex	14 (61%)	54 (60%)	0.939

Table III. Multivariate analysis of Coronary Risk Factors

	OR	95% CI	p value
Hypercholesterolemia	6.6	2.0-22.2	0.002
Diabetes mellitus	4.7	1.3-17.2	0.020
Age	2.5	0.7-8.0	0.120
Hypertension	2.0	0.7-5.7	0.206
Smoking	1.5	0.4-5.8	0.557
Male sex	1.3	0.4-4.6	0.703

Table IV. Distribution of Involved Coronary Arteries in Different Diagnosis

	Sick sinus syndrome ($n=12$)	AV block ($n=11$)	p value
LAD	9 (75%)	8 (73%)	0.901
LCX	4 (33%)	5 (46%)	0.552
RCA	4 (33%)	2 (18%)	0.408
SN artery	1 (8%)	2 (18%)	0.484
AVN artery	3 (25%)	1 (9%)	0.315

(9%). Only one patient in the SSS group had sinus nodal artery involvement and one patient in the AV block group had atrioventricular nodal artery involvement.

DISCUSSION

To our knowledge, this is the first human study concerning the incidence of CAD in Asian patients receiving permanent pacemaker implantation for symptomatic bradyarrhythmia. The results have revealed that 20% of patients with symptomatic bradyarrhythmias had coexistent CAD. In previous reports, Rubenstein, *et al* found that 20 of their 56 patients with sick sinus syndromes had coronary artery disease based on either historical or electrocardiographic evidence;¹⁾ Shaw, *et al* reported that 12 of their 25 patients with sick sinus syndromes had abnormal postmortem CAG.²⁾ The CAD incidence in the present study was lower compared to those of previous reports. However, we excluded patients with documented myocardial infarction or status post coronary bypass surgery. In addition, evidence of fixed coronary artery stenosis was used for the diagnosis of ischemic heart disease in this study. These factors may contribute to the lower incidence of ischemic heart disease in the present.

Nearly half of our study patients complained of chest tightness with either typical or atypical characteristics. The patients were senile, and most of them acquired one additional coronary risk factor. Furthermore, considering the major prognostic role of CAD in patients undergoing permanent cardiac pacing, these patients dictate an aggressive evaluation for ischemic heart disease. However, patients with bradyarrhythmia are usually not suitable for conventional noninvasive evaluation for coronary artery disease, and the left bundle-branch-block ECG pattern after right ventricular pacing is invalid for the diagnosis of CAD. On the other hand, routine CAG is costly and low yielding in non-selective patients. Our study revealed that hypercholesterolemia and DM were the two most significant independent coronary risk factors in these patients. These two factors may be used as clinical markers in selecting patients undergoing further CAG.

The distribution of diseased vessels in our patients was not different between the two different bradyarrhythmia diagnoses. LAD was the most frequent vessel involved. Sinus nodal artery insufficiency was noted in one patient among 12 patients diagnosed with sick sinus syndrome. Atrioventricular nodal artery insufficiency was noted in one patient among 11 patients with the diagnosis of high degree atrioventricular block. In a previous report, Jordan, *et al* found significant sinoatrial conduction time (SACT) prolongation in patients with sinus nodal artery insufficiency and suggested a pathogenetic role of CAD in the development of sinus nodal dysfunction.⁹⁾ However, Shaw, *et al* reported only 4 of 25 patients with chronic sinoatrial disorder had angiographic evidence of more than

75% stenosis obstructing the sinus nodal artery.²⁾ Our data also disclosed that a nodal related artery was seldom involved in patients with symptomatic bradyarrhythmia and coexistent CAD. Although our study population was small and confined to Asian people, the results suggest that CAD is not a major cause of symptomatic bradyarrhythmia.

In conclusion, coexistent CAD was noted in a small portion (20%) of our patients receiving permanent pacemaker implantation for symptomatic bradyarrhythmia. Among the conventional coronary risk factors, DM and hypercholesterolemia were the two statistically significant independent predictors and may act as important markers for the judgment of further coronary artery evaluation. The nodal artery was seldom involved among patients with bradyarrhythmia and coexistent CAD, suggesting that CAD is not a major cause of symptomatic bradyarrhythmia.

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