Evaluating the Prevalence of Silent Coronary Artery Disease in Asymptomatic Patients With Spinal Cord Injury

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SUMMARY

To evaluate the prevalence of coronary artery disease (CAD) in patients with spinal cord injury (SCI), 47 clinically asymptomatic SCI patients received thallium-201 myocardial perfusion single photon emission computed tomography (Tl-201 SPECT) after dipyridamole administration for the diagnosis of CAD. There were 4 groups as follows; group 1: 13 patients with quadriplegia and complete SCI, group 2: 11 patients with quadriplegia and incomplete SCI, group 3: 11 patients with paraplegia and complete SCI, and group 4: 12 patients with paraplegia and incomplete SCI. There were no significant differences in sex distribution, ages, SCI duration, or CAD risk factors among the SCI patients in the 4 groups. All Tl-201 SPECT images were interpreted by the agreement of 2 experienced nuclear medicine physicians without prior knowledge of the patients' histories. A total of 30 of 47 (63.8%) SCI patients had abnormal Tl-201 SPECT findings. Among the 4 groups of SCI patients, those in groups 1 and 4 had the significantly highest and lowest prevalences of abnormal Tl-201 SPECT findings, respectively. We concluded that combined quadriplegia and complete SCI is an important CAD risk factor in SCI patients based on the objective evidence of intravenous dipyridamole cardiac stress testing with Tl-201 SPECT. (Int Heart J 2006; 47: 325-330)

Key words: Spinal cord injury, Thallium-201 myocardial perfusion single photon emission computed tomography

There is a cluster of multiple risk factors for coronary artery disease (CAD) among individuals with spinal cord injury (SCI), but there is little information available on the prevalence of CAD in this population. SCI patients tend to have an increased percentage of body fat and have sedentary life styles. These individuals may not have symptoms despite significant CAD, partially due to their reduced level of activity. SCI patients often undergo rehabilitation programs, exercise training, metabolic testing, and surgical procedures without having their...
cardiac status assessed, which may pose a significant potential, unpredictable risk. The usefulness of intravenous dipyridamole cardiac stress testing with thallium-201 myocardial perfusion single photon emission computed tomography (TI-201 SPECT) for the diagnosis of CAD has been supported by numerous clinical trials in evaluating the efficacy and safety of the method in physically normal or impaired individuals.2-6 Therefore, in this study, we performed TI-201 SPECT in clinically asymptomatic SCI patients without known heart disease to evaluate the prevalence of CAD in this population.

**METHODS**

**Patients:** Forty-seven clinically asymptomatic SCI patients were included in this study. Group 1 consisted of 13 patients with quadriplegia and complete SCI (4 females and 9 males, ages, 45.5 ± 6.5 years old, SCI duration, 15.3 ± 1.6 years), group 2; 11 patients with quadriplegia and incomplete SCI (3 females and 8 males, ages, 44.1 ± 5.9 years old, SCI duration, 16.0 ± 2.1 years), group 3; 11 patients with paraplegia and complete SCI (3 females and 8 males, ages, 46.4 ± 7.0 years old, SCI duration, 16.2 ± 2.0 years), and group 4; 12 patients with paraplegia and incomplete SCI (8 females and 16 males, ages, 45.6 ± 6.8 years old, SCI duration, 15.9 ± 1.7 years). The sex distribution, age distribution, and duration of SCI were not significantly different among the 4 groups (Table I). None of the 47 SCI patients had known underlying CAD, hemodynamically significant aortic stenosis, clinical congestive heart failure, hemodynamic and/or electrical instability, or significant underlying lung disease or asthma. To obtain a more homogeneous patient population, we excluded other physically handicapped patients with other types of neuromuscular disorders.

**TI-201 SPECT:** Medications containing caffeine or theophylline were discontinued within 48 hours of the procedure. Beverages containing these substances
were withheld within 12 hours of the procedure. While the patient was supine, an intravenous line with normal saline solution was inserted in an upper extremity vein. A baseline electrocardiogram (ECG), heart rate, and blood pressure were recorded. Intravenous dipyridamole was infused at a rate of 0.142 mg/kg of body weight per minute for 4 minutes. During and after the dipyridamole infusion, ECG monitoring and vital signs were recorded every 60 seconds. Side effects were monitored throughout the course of the study. Aminophylline was readily available, and if necessary, patients were injected intravenously with 2 mg/kg of the drug to stop the action of dipyridamole and reverse any adverse side effects. A dose of 2.5-3 mCi of TI-201 was then injected intravenously as a bolus. Stress TI-201 SPECT imaging was started before 5 minutes after TI-201 injection. After a 3 to 4 hour rest, a resting TI-201 SPECT image was obtained. Acquisition parameters were identical for both the stress and resting studies. TI-201 SPECT imaging was performed on a dual-headed gamma camera equipped with a low-energy, high-resolution collimator. Images were acquired using a step-and-shoot circular orbit over a 180° arc, starting at the 45° right anterior oblique projection and ending at the 45° left posterior oblique projection, for a total 32 projections at 40 seconds/projection. One energy window was used consisting of a 20% window centered on the 70-keV peak. All projection images were acquired into 64 × 64 image matrices, corrected for nonuniformity and center of rotation and quality controlled for patient or organ movement. The 20-segment model evaluation consisted of 3 short slices (1 apical, 1 midventricular, and 1 basal slice), 1 vertical long-axis slice, and 1 horizontal long-axis slice (midlevel). The evaluation was performed with a linearly thermal color scale. All selected short-axis slices were further divided into 6 evenly spaced regions (anterior, anteroseptal, inferoseptal, inferior, inferolateral, anterolateral) covering a 60-degree angle of the circumference. From the vertical and horizontal long-axis slices, 2 segments were defined to evaluate the apex. Hence, the thallium uptake in each segment was evaluated via a previously recommended 5-point scale for TI-201 SPECT images: 0-normal; 1-mildly decreased; 2-moderately decreased; 3-severely decreased; and 4-absent. All TI-201 SPECT images were interpreted by the agreement of 2 experienced nuclear medicine physicians without prior knowledge of the patient histories. The TI-201 SPECT images were considered abnormal if more than 2 segments had a stress score of at least 2.7,8)

**Coronary artery disease risk factor assessment:** The recently updated recommendations of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults9) were used in this study. The NCEP advised that the following be considered risk factors for CAD: age for men at least 45 years old, family history of premature CAD (myocardial infarction or sudden death before age 55 in a first-degree relative),
current cigarette smoking, hypertension (blood pressure greater than or equal to 140/90 mmHg or taking antihypertensive medication), high density lipoprotein (HDL) cholesterol less than 35 mg/dL, and diabetes mellitus.\(^9\) Low density lipoprotein (LDL) cholesterol was the primary risk factor, with levels above 130 mg/dL representing increased risk, and, as such, is also a risk factor. HDL cholesterol greater than 60 mg/dL was established as a negative risk factor for CAD.

**Statistical analyses:** The chi-square or Fisher exact test was used to evaluate the difference of the prevalence of abnormal Tl-201 myocardial SPECT findings among the SCI patients in the 4 groups. The same 2 tests were also used to compare the normal and abnormal Tl-201 SPECT groups with respect to positive CAD risk factors: older age, family history of CAD, current cigarette smoking, hypertension, elevated LDL cholesterol, decreased HDL cholesterol, and diabetes mellitus. If the *P* value was < 0.05, the difference was considered to be significant.

### RESULTS

In this study, no patient had any severe adverse reaction to dipyridamole. There were no significant differences in the sex distribution, ages, SCI duration, or CAD risk factors among the 4 groups of SCI patients. In addition, there were no significant differences in CAD risk factors between SCI patients with normal and abnormal Tl-201 SPECT findings (Table II). A total of 30 of 47 (63.8%) SCI patients had abnormal Tl-201 SPECT findings. Eleven of 13 (84.6%) patients in group 1, 7 of 11 (63.6%) in group 2, 6 of 11 (54.5%) in group 3, and 6 of 12 (50.0%) in group 4 had abnormal Tl-201 SPECT findings (Table I). However, there was a significant difference in the prevalence of abnormal Tl-201 SPECT findings between groups 1 and 4 among the 4 groups of SCI patients (*P* < 0.05).

<table>
<thead>
<tr>
<th>Tl-201 SPECT</th>
<th>Normal</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean &gt; 45 years)</td>
<td>6/17</td>
<td>13/30</td>
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<tr>
<td>Family history of CAD</td>
<td>4/17</td>
<td>6/30</td>
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<tr>
<td>Smoking</td>
<td>6/17</td>
<td>13/30</td>
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<tr>
<td>Hypertension</td>
<td>5/17</td>
<td>9/30</td>
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<tr>
<td>HDL cholesterol (&lt; 35 mg/dL)</td>
<td>4/17</td>
<td>7/30</td>
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<tr>
<td>LDL cholesterol (&gt; 130 mg/dL)</td>
<td>5/17</td>
<td>11/30</td>
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<tr>
<td>Diabetes mellitus</td>
<td>3/17</td>
<td>5/30</td>
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</table>
DISCUSSION

In SCI patients, marked skeletal muscle atrophy, increased adipose tissue, and a sedentary lifestyle may contribute to carbohydrate abnormalities such as impaired glucose tolerance or diabetes mellitus, all of which are well known risk factors for CAD. Furthermore, possibly in large measure a consequence of reduced cardiovascular fitness, reduced serum high density lipoprotein (HDL) cholesterol has been reported in patients with SCI. Therefore, CAD became the leading cause of mortality among SCI subjects who are 30 years postinjury or who are more than 60 years of age. Persons with SCI die at a younger age than the able-bodied population.

Because SCI patients may have a clustering of risk factors for CAD, it may be prudent to screen the individuals before all nonemergency surgical procedures, exercise training, or testing, as well as other procedures or maneuvers that may potentially stress the cardiovascular system. A survey of the literature concerning arm ergometry exercise stress testing with Tl-201 myocardial perfusion imaging has demonstrated a high prevalence of latent myocardial ischemia or infarction in 20 asymptomatic subjects with paraplegia. In another report, intravenous dipyridamole cardiac stress testing with Tl-201 SPECT was considered to be a safe and effective noninvasive method for the detection of myocardial ischemia or infarction in 6 clinically asymptomatic subjects with quadriplegia. Their findings are compatible with our results: a total of 30 of 47 (63.8\%) clinically asymptomatic SCI patients with paraplegia or quadriplegia had abnormal Tl-201 SPECT findings. In addition, increased CAD risk was found in SCI patients with a higher level (quadriplegia) and severity of SCI (complete). Therefore, in this study, group 1 SCI patients had the significantly highest prevalence of abnormal Tl-201 SPECT findings. However, there were no significant differences in the sex distribution, ages, SCI duration, or CAD risk factors among the 4 groups of SCI patients.

In the present study, no patient had any severe adverse reaction to dipyridamole. Therefore, we believe that intravenous dipyridamole Tl-201 SPECT myocardial perfusion imaging is a safe and reliable noninvasive method with which to assess silent CAD in clinically asymptomatic SCI patients. We found that combined quadriplegia and complete SCI is an important CAD risk factor in SCI patients based on the objective evidence obtained from intravenous dipyridamole cardiac stress testing with Tl-201 SPECT.

There are limitations in this study that should be considered. First, the case number was not sufficiently large to perform multivariate analyses between the Tl-201 SPECT findings and many clinical variables that are or are not related to SCI. In addition, we believe that further studies with a larger case number and
longer follow-up are necessary to confirm our preliminary findings and to explain why the prevalence of silent myocardial ischemia detected by dipyridamole cardiac stress testing with TI-201 SPECT is very high in SCI patients.

REFERENCES