Clinical characteristics associated with myocardial infarction, arrhythmias, and sudden death in patients with vasospastic angina

MOTOOMI NAKAMURA, M.D., AKIRA TAKESHITA, M.D., AND YOSHIKI NOSE, M.D.*

ABSTRACT A total of 349 patients with vasospastic angina were followed in eight centers in Japan for a period of 3.4 ± 0.1 years (mean ± SE). Ninety-eight percent of patients were treated with calcium blockers. Twenty-one episodes of myocardial infarction occurred in 18 patients (5%), including two fatal myocardial infarctions. The rate of myocardial infarction was higher (p < .01) in patients with a fixed stenosis of 90% or greater than in patients with a fixed stenosis of less than 90% or normal coronary arteries. Myocardial infarctions occurred predominantly during hospital stays or at a time when the frequency of vasospastic angina increased. There were five sudden deaths (2%). Only one patient suffering sudden death had a fixed stenosis of 75% or greater. Serious arrhythmias were noted in 49 patients (14%). The risk of arrhythmias did not depend on the presence of a fixed stenosis of 75% or greater. These results suggest that cardiac events are rather infrequent in Japanese patients with vasospastic angina who are receiving treatment with calcium blockers and that the presence of a severe fixed stenosis markedly increases the risk of myocardial infarction but not the risk of arrhythmias. Circulation 75, No. 6, 1110–1116, 1987.

SEVERAL STUDIES have examined the long-term prognosis of more than 100 patients with vasospastic angina.1–4 Myocardial infarction and cardiac death have been reported to occur in approximately 10% to 20% of patients over several years of follow-up.1–4 These studies have identified two important risk factors: the presence of atherosclerotic coronary artery disease, in particular multivessel disease, and acceleration of the tempo of vasospastic angina.1–4

A few aspects of these studies should be noted in considering clinical implications of their results. First, they apparently included a large number of patients who were not treated with calcium blockers.3, 4 It has been suggested that treatment with calcium blockers may reduce the rate of cardiac events in patients with vasospastic angina.3, 5 Since these drugs are currently widely used in the treatment of vasospastic angina,6 the long-term prognosis of today’s patient with vasospastic angina might be different from that reported in previous studies.1–4 Second, a large portion of the patients in the previous studies had significant atherosclerotic coronary artery disease.1–4 Thus, the results of previous studies may not be applicable to patients with insignificant atherosclerotic disease. It is known that myocardial infarction or sudden death may occur in patients with vasospastic angina with no or insignificant atherosclerotic coronary artery disease.7, 8

We report the results of a follow-up study of 349 patients with vasospastic angina treated in eight centers in Japan. This study differs from previous studies in several aspects. First, 98% of our patients were treated with calcium blockers. Second, about 70% of our patients had no or insignificant atherosclerotic coronary artery disease. The rates of cardiac complications were considerably lower in our patients than in patients reported in previous studies.1–4

Methods

Patients. This study was a part of a national cooperative study (1981–1983) that aimed to characterize the clinical features and causes of vasospastic angina in Japan. A total of 349 patients in whom vasospastic angina was diagnosed between 1980 and 1983 in eight cardiovascular centers were registered and followed until 1985. The average duration of the follow-up
study was 3.4 ± 0.1 years (mean ± SE). There were 308 male and 41 female patients and their ages ranged from 28 to 83 years (average 54 ± 0.5).

The diagnosis of vasospastic angina was made when at least one of the following criteria was met: (1) recurrent resting angina associated with ST segment elevation of at least 2 mm, with or without effort angina, and (2) coronary vasospasm demonstrated by coronary angiography during spontaneous angina or angina provoked by ergonovine maleate, hyperventilation, or the cold pressor test. Electrocardiograms recorded during spontaneous or provoked anginal attacks showed ST segment elevation in 256 patients and ST segment depression in 48 patients. No significant ST change was recorded during provoked coronary vasospasm in 45 patients. Coronary vasospasm was documented by coronary angiography in all patients who had no ST changes or ST depression. One hundred eighty-eight patients had resting angina and 161 patients had resting and effort angina. Twenty-seven patients had a history of myocardial infarction.

Coronary angiographic examinations at rest were performed in all patients. Coronary angiograms were read by at least two experienced coronary angiographers at each institution. Moreover, a third of the cine films of coronary angiograms were exchanged between pair institutions and the severity of coronary stenosis on these films as assessed independently by the angiographers at two institutions did not differ. In 308 patients, coronary angiography was repeated after sublingual (0.3 mg) or intravenous (200 µg by bolus followed by 20 µg/min) nitroglycerin to assess the severity of a fixed or atherosclerotic coronary stenosis, since coronary vasospasm might be present at rest in patients with vasospastic angina. A fixed coronary artery stenosis of 75% or greater was present in 101 of 308 patients. Eight of 101 patients with a fixed coronary stenosis had single-vessel disease and 21 patients had multivessel disease. A fixed coronary stenosis of 75% or greater was present in the left anterior descending coronary artery (LAD) in 83 patients, in the right coronary artery (RCA) in 20 patients, and in the left circumflex coronary artery (LCX) in 27 patients. Among those who did not undergo coronary angiographic examination after nitroglycerin (41 patients), a luminal narrowing of 75% or greater was present in 18 patients.

Coronary vasospasm was demonstrated in 246 patients, during spontaneous angina in 49 patients, and during provoked angina in 197 patients. Coronary vasospasm was considered present when a luminal narrowing of 75% or greater developed in a coronary artery with no or insignificant (less than 75%) luminal narrowing at rest or when a total or nearly total occlusion developed in a coronary artery with a luminal narrowing between 75% and 90%. If there was an artery with luminal narrowing of greater than 90% at rest, coronary vasospasm was considered present when it developed in other coronary arteries with luminal narrowing of less than 90% at rest.

The location of myocardial ischemia was assessed by the location of ST segment elevation on electrocardiograms. In those who did not have ST segment elevation, the ischemic region was assumed to be in the anterior, lateral, or inferior wall when coronary vasospasm was in the LAD, LCX, or RCA, respectively. Anterior, lateral, or inferior ischemia was present in 161, 14, and 144 patients, respectively. The remaining 30 patients had either coronary vasospasm in multiple vessels or ST segment elevation in multiple regions.

**Cardiac complications**

*Cardiac death.* Sudden death, defined as death within 1 hr after collapse, and death associated with acute myocardial infarction were considered cardiac deaths.

*Myocardial infarction.* Myocardial infarction was diagnosed by the development of new Q waves and/or elevation of levels of cardiac enzymes. The location of myocardial infarction was determined by the location of new Q waves, akinetic or dyskinetic motion of the left ventricular wall evident on two-dimensional echocardiograms, or a persistent perfusion defect demonstrated by thallium-201 scintigrams. It was assumed that worsening angina was present before myocardial infarction when there was a history of an abrupt increase in the frequency and/or duration of anginal attacks before myocardial infarction.

**Arrhythmias.** Tachy- or bradyarrhythmias documented on electrocardiograms during anginal attacks were registered. Tachyarrhythmias included sustained or nonsustained ventricular tachycardia and/or ventricular fibrillation, and bradyarrhythmias included second- or third-degree atrioventricular block.

**Treatment.** Three hundred forty-one patients were treated with calcium blockers with or without other antianginal drugs. Calcium blockers given to these patients included diltiazem, nifedipine, and nicardipine. Other antianginal drugs used included nitrates, ß-blockers, and nicorandil. The effectiveness of drug treatment in the control of anginal attacks was considered to be good when the frequency of anginal attacks was reduced to less than 25% of that before treatment. Nine patients underwent coronary bypass surgery.

**Statistical analysis.** The distribution of characteristics in patients with and without complications was compared by the chi-square test. A p < .05 was considered indicative of a significant difference.

**Results**

**Incidence of cardiac complications (table 1).** Eleven patients died during the period of the follow-up study. Death was sudden in five and in two it occurred after acute myocardial infarction. Four patients died from noncardiac causes.

Eighteen patients had at least one myocardial infarction after entry into the study. Among these, one patient had two infarctions and one patient had three. One patient had one myocardial infarction before and one after entry to the study.

Ventricular tachyarrhythmias and/or bradyarrhythmias were recorded in 49 patients. Twenty-three patients had ventricular tachycardia and/or ventricular fibrillation and 23 patients had second- or third-degree atrioventricular block. Three patients had ventricular

**TABLE 1**  
Rates of cardiac complications during the follow-up study

<table>
<thead>
<tr>
<th>Complication</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden death</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>Myocardial infarction*</td>
<td>18 (5%)</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td></td>
</tr>
<tr>
<td>VT and/or VF</td>
<td>23</td>
</tr>
<tr>
<td>2 and/or 3 degree AVB</td>
<td>23 (14%)</td>
</tr>
<tr>
<td>VT/VF and AVB</td>
<td>3</td>
</tr>
</tbody>
</table>

\*Two patients had multiple infarctions. A total of 21 myocardial infarction occurred in 18 patients. Two were fatal.
tachycardia as well as third-degree atrioventricular block.

Severity of coronary artery disease (table 2)

Sudden death. Only one of five patients suffering sudden death had a fixed coronary artery stenosis of 75% that was evident on the coronary angiogram obtained after nitroglycerin.

Myocardial infarction. Sixteen of 18 patients with myocardial infarction underwent coronary angiographic examination after nitroglycerin. Eleven of these 16 patients had a fixed coronary stenosis of 75% or greater, including a fixed stenosis of 90% or greater in nine patients. Two patients who died from acute myocardial infarction had a fixed coronary stenosis of 90%. Ten of 11 patients with a fixed coronary stenosis had a single lesion, in the LAD in nine patients and in the LCX in one. One patient had lesions in the LAD and the RCA. In two patients who did not undergo coronary angiography after nitroglycerin, the examination before nitroglycerin showed a luminal narrowing of greater than 90%.

The incidence of myocardial infarction in patients with fixed coronary artery stenoses of 75% or greater (11 of 101 patients) was higher (p < .01) than that in patients with no or insignificant stenoses of less than 75% (five of 207 patients). The incidence of myocardial infarction was particularly high in patients with a fixed coronary artery stenosis of 90% or greater (nine of 59 patients).

Fourteen myocardial infarctions occurred in 11 patients with a fixed stenosis of 75% or greater. In 12 of these 14, the infarcted region coincided with the region supplied by the coronary artery with a fixed stenosis. On two occasions, myocardial infarction occurred in the region supplied by a coronary artery appearing normal on the coronary angiogram, even though there were fixed stenoses of greater than 75% in other coronary arteries. In two patients who did not undergo coronary angiography after nitroglycerin, myocardial infarction occurred in the region supplied by a coronary artery with luminal narrowing of greater than 75%.

Arrhythmias. Forty-eight of 49 patients who had ventricular tachyarrhythmias and/or bradyarrhythmias underwent coronary angiography after nitroglycerin. A fixed coronary artery stenosis of 75% or greater was present in seven of 23 patients with ventricular tachyarrhythmias and in three of 22 patients with bradyarrhythmias. None of three patients who had ventricular tachycardia and third-degree atrioventricular block had a fixed coronary stenosis of 75% or greater.

The incidence of arrhythmias in patients with a fixed coronary artery stenosis of 75% or greater (10 of 101 patients) was less (p < .05) than that in patients with no or insignificant fixed stenosis of less than 75% (39 of 207 patients).

Overall rate of cardiac complications. The overall rate of cardiac complications was similar in patients with fixed coronary stenoses greater than 75% (22%), patients with fixed stenoses less than 75% (23%), and those with normal coronary arteries (23%).

Other features of cardiac complications

Sudden death. Four of five patients suffering sudden death had ST segment elevation during anginal attacks. In one patient an electrocardiogram could not be recorded during spontaneous anginal attacks. No arrhythmias had been recorded during anginal attacks in the five patients suffering sudden death.

Myocardial infarction. Electrocardiograms recorded during anginal attacks showed ST segment elevation in 15 of 18 patients with myocardial infarction. In five patients, ventricular tachycardia was recorded during anginal attacks.

Myocardial infarction occurred during a hospital stay in 10 patients. Eight patients had 11 myocardial infarctions during the follow-up period after discharge from hospital.

Worsening angina pectoris was present before 13 of 21 episodes of myocardial infarction. An increase in the frequency of angina pectoris was noted in 13 patients, a longer duration of anginal attacks in eight patients, and an increased severity of anginal pain in six patients.

The development of new Q waves was noted after 12 myocardial infarctions; nine were non-Q wave infarctions.

The location of myocardial infarction was in the anterior or anteroseptal region in 14 cases, in the infe-

### TABLE 2

<table>
<thead>
<tr>
<th>Coronal angiographic findings in patients with and without complications</th>
<th>Fixed stenosis &gt;75%</th>
<th>Fixed stenosis &lt;75%</th>
<th>Normal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No complication</td>
<td>79</td>
<td>112</td>
<td>48</td>
<td>239</td>
</tr>
<tr>
<td>Sudden death</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonfatal</td>
<td>9</td>
<td>3</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>Fatal</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VT and/or VF</td>
<td>7</td>
<td>12</td>
<td>4</td>
<td>23</td>
</tr>
<tr>
<td>2- and/or 3-degree AVB</td>
<td>3</td>
<td>14</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>VT/VF + AVB</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>101</td>
<td>145</td>
<td>62</td>
<td>308</td>
</tr>
</tbody>
</table>

Abbreviations are as in table 1.
rior region in four cases, and in the lateral region in two cases. The location could not be determined in one case. All inferior myocardial infarctions occurred in patients without a fixed coronary stenosis of 75% or greater. Ten of 14 anterior or anteroseptal myocardial infarctions and two lateral infarctions were associated with a fixed coronary stenosis of 75% or greater.

**Arrhythmias.** Forty-seven of 49 patients had ST segment elevation and two patients had ST segment depression during anginal attacks. Ventricular tachyarhythmias were associated with anterior ischemia in 13 patients and with inferior ischemia in eight patients. The remaining two patients with ventricular tachyarhythmias had myocardial ischemia in the anterior and inferior wall. Bradyarrhythmias were associated with inferior ischemia in 19 patients, with inferior as well as anterior ischemia in two patients, and with anterior ischemia in one patient. Combined ventricular tachyarhythmias and bradyarrhythmias occurred in two patients with inferior ischemia and in one patient with inferior as well as anterior ischemia.

**Effects of treatment (table 3).** At the end of the follow-up study, angina pectoris remained well controlled in 328 patients. Calcium blockers had been discontinued in 27 patients.

Eighteen myocardial infarctions occurred in 15 patients while they were on calcium blockers. Sixteen of 18 myocardial infarctions occurred in patients in whom angina pectoris was not well controlled by treatment with calcium blockers.

Three patients had myocardial infarctions while they were not on calcium blockers. In two of these patients, myocardial infarction occurred a few days after calcium blockers were discontinued. Angina pectoris was well controlled in these two patients before the discontinuation of drug therapy. Twenty-seven patients had had a documented myocardial infarction before their entry to this study. In 25 of the 27 patients, the infarction had occurred shortly after the onset of angina pectoris before they sought medical treatment.

Sudden death occurred in three patients while they were on calcium blockers. Angina pectoris appeared well controlled in at least two patients before their deaths. One patient suffered sudden death within a week after the discontinuation of a calcium blocker. The clinical status of two patients before sudden death is not known.

**Discussion**

In this study the rate of cardiac death or myocardial infarction was low in patients with vasospastic angina. Myocardial infarction occurred predominantly in patients with a severe fixed coronary stenosis at a time when vasospastic angina was accelerated. On the other hand, the rate of serious arrhythmias was less in patients with a fixed stenosis compared with the rate in those without a fixed stenosis. It also appears that the risk of sudden death did not depend on the presence of a fixed coronary stenosis. The following discussion will focus on these results compared with the results of previous studies.

**Rate of cardiac complications.** Cardiac death and myocardial infarction occurred in 2% and 5% of our patients with vasospastic angina during an average 3.4 years of follow-up study. We must be cautious in comparing the results of this study with those of others since the methods of selection of patients and populations differed. However, the rates of cardiac death and myocardial infarction in our patients were considerably less than those in previous studies, which have reported a rate of cardiac death ranging from 8% to 11% and a rate of myocardial infarction from 13% to 23% over a comparable duration of follow-up.1-4

There are two important differences between this and previous studies that may have contributed to the differences in the rates of cardiac complications. First, our patients had less severe coronary atherosclerotic disease than those included in previous studies. Less than 35% of our patients had a fixed coronary stenosis of 75% or greater, whereas a stenosis greater than 75% or 70% was present in 80% and 60% of the patients studied by Mark et al.4 and Waters et al.,3 respectively. Severi et al.1 considered a stenosis greater than 50% significant, and such a stenosis was present in 92% of their patients who underwent coronary angiography.1 A stenosis greater than 50% was present in 54% of our patients. Second, about 98% of our patients were treat-

---

**TABLE 3**

<table>
<thead>
<tr>
<th>Cardiac events and the status of vasospastic angina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Myocardial infarction (n) Sudden death (n)</td>
</tr>
<tr>
<td>With calcium blockers</td>
</tr>
<tr>
<td>Angina controlled 18</td>
</tr>
<tr>
<td>Angina uncontrolled 16</td>
</tr>
<tr>
<td>Without calcium blockers</td>
</tr>
<tr>
<td>Angina controlled 3</td>
</tr>
<tr>
<td>Angina uncontrolled 2</td>
</tr>
</tbody>
</table>

Angina pectoris was considered to be controlled when the frequency was reduced to less than 25% of that before treatment.

A: The clinical status before sudden death is not known for two patients suffering sudden death.

B: These two myocardial infarctions were recurrent.

C: Cardiac events occurred shortly after the discontinuation of a calcium blocker. Patients were not on other drugs.

Vol. 75, No. 6, June 1987
ed with calcium blockers, whereas previous studies apparently included large numbers of patients who were not treated with these drugs.3, 4

Previous studies have suggested that the presence of severe fixed coronary artery disease, in particular multivessel disease, increases the risk of cardiac complications.1, 3 Also, Schroeder et al.5 have shown a significant reduction in the rate of cardiac complications as a result of treatment with calcium blockers.5 Thus, we believe that less severe coronary atherosclerotic disease and a higher rate of treatment with calcium blockers may have contributed to the lower rate of cardiac complications in our patients compared with the rate in patients in previous studies.1-4 However, this study was not designed to test the efficacy of calcium blockers over the long term in patients with vasospastic angina. We therefore do not know how much treatment with calcium blockers contributed to the lower rate of cardiac complications in our patients. Nevertheless, the results of this study indicate that in Japan the rate of cardiac complications is low in patients with vasospastic angina who are under treatment with calcium blockers.

Fixed coronary stenosis and cardiac complications. This study differs from previous studies in that the severity of coronary atherosclerotic disease was assessed based on findings of coronary angiography in patients who had received nitroglycerin. This difference is important since, in patients with vasospastic angina, luminal narrowing of a coronary artery at rest may be caused by coronary vasospasm as well as atherosclerotic disease.9 The magnitude of coronary vasospasm must have been much less after nitroglycerin than at rest. Coronary angiography after nitroglycerin was performed in 88% of the total group and in 94% of patients with cardiac complications; the significance of a fixed coronary stenosis as a risk factor for cardiac complications was examined in those who underwent this examination.

The results indicate that myocardial infarction occurred predominantly in patients with a severe fixed coronary stenosis. A fixed stenosis of 75% or greater was present in 69% of patients with myocardial infarction, whereas it was present in 33% of the total group. Moreover, nine of 16 patients with myocardial infarction had a fixed stenosis of 90% or greater. The rate of myocardial infarction in patients with a fixed stenosis of 90% or greater (nine of 59 patients, 15%) was higher than that in patients with a fixed stenosis between 90% and 75% (two of 42 patients, 5%) (p < .01) or that in patients with a stenosis less than 75% or normal coronary arteries (five of 207 patients, 2%) (p < .01).

To our knowledge, this is the first study that has demonstrated that the risk of myocardial infarction in patients with vasospastic angina depends on the magnitude of a luminal narrowing caused by atherosclerotic disease. Previously studies have suggested that the presence of multivessel disease increases the risk of myocardial infarction,1, 3 but multivessel disease was present in only 20% of our patients with a significant fixed stenosis so that the significance of multivessel disease as a risk factor could not be evaluated.

In contrast to myocardial infarction, the incidence of arrhythmias was less (p < .05) in patients with a fixed coronary stenosis (10%) than in those without it (19%). However, this finding may have resulted from the fact that the majority of patients who had bradyarrhythmias had no or insignificant coronary artery disease. The incidence of ventricular tachyarrhythmias in patients with (7%) and those without a fixed coronary stenosis (6%) did not differ significantly. The rate of bradyarrhythmias was less (p < .05) in patients with a fixed stenosis (3%) than in those without a fixed stenosis (9%). However, the latter finding may be accounted for by the fact that bradyarrhythmias were almost exclusively associated with inferior myocardial ischemia. Only 20 of 144 patients who had inferior myocardial ischemia had a fixed stenosis of 75% or greater. Thus, we believe that our results are inconclusive with respect to whether the risk of arrhythmias is significantly altered by the absence or presence of a fixed coronary stenosis. Previous studies have reported that the incidence of arrhythmias in patients with and those without a fixed coronary stenosis did not differ.10-12

The rate of cardiac death was low (2%) in our patients, which makes it difficult to know the risk factors for cardiac death. However, only one patient suffering sudden death had a fixed stenosis of 75% and another four patients had a stenosis of 50% or less. Thus, it appears that sudden death may occur in patients without a severe fixed stenosis. These results are not unexpected since the cause of sudden death is presumably arrhythmias and arrhythmias often occur in the absence of a severe fixed stenosis. Millar et al.7 found no difference in the incidence of fixed stenosis in the coronary artery supplying the ischemic region in patients suffering sudden death and that in survivors. The absence of a correlation between fatal arrhythmias and coronary anatomy has also been reported by Maseri et al.12 Millar et al.7 have reported that nearly 80% of patients suffering sudden death have had ventricular tachyarrhythmias. However, ventricular tachyarrhythmias were documented in none of our patients suffering sudden death.
Finally, it should be noted that the presence of fixed coronary artery disease did not influence the overall rate of cardiac complications, including sudden death, myocardial infarction, and arrhythmias. The overall rate of cardiac complications was similar in patients with fixed coronary stenosis greater than 75%, those with fixed stenosis less than 75%, and those with normal coronary arteries.

Vasospastic activity and the effect of treatment. Previous studies have reported that the risk of myocardial infarction is particularly high in a “hot phase” during the first hospital stay or shortly after discharge.1-4,7 A similar trend was observed in this study. Ten patients had myocardial infarction during their hospital stays, and thus presumably during the hot phase. Eleven myocardial infarctions occurred in eight patients after they were discharged from the hospital. Angina pectoris in the latter patients had been under control as a result of therapy with calcium blockers, but there was an abrupt worsening of angina before nine of these 11 myocardial infarctions despite the fact that drug therapy had been continued. These results suggest that the risk of myocardial infarction is high when the tempo of vasospastic angina is accelerated. It should be noted that two of the myocardial infarctions that occurred in the hospital were in patients in whom calcium blockers had been temporarily stopped.

The significance of acceleration of vasospastic angina as a risk factor for sudden death cannot be evaluated in our patients since the number of sudden deaths was small and the status of angina pectoris before death was unknown in two patients. However, it is notable that two patients suffered sudden death while vasospastic angina appeared to be well controlled by calcium blockers. It has been observed that serious arrhythmias may occur during painless ST segment elevation.13 It also should be noted that one patient died when angina pectoris recurred shortly after treatment with a calcium blocker was discontinued.

Site of coronary vasospasm and myocardial ischemia. Bradyarrhythmias were almost exclusively associated with inferior myocardial ischemia or vasospasm in the RCA. These results were expected since a reflex increase in vagal tone occurs more frequently in association with inferior myocardial ischemia than in association with anterior myocardial ischemia14,15 and the atioventricular nodal artery arises from the RCA in 90% of patients.16 On the other hand, the incidence of ventricular tachyarrhythmias was similar in patients with anterior and inferior myocardial ischemia.

Anterior myocardial infarction was more frequent than inferior myocardial infarction. It is likely that this result reflects the prevalence of a fixed coronary stenosis in the LAD.

Clinical implications. A limitation of this study was that it was a retrospective and uncontrolled one and patients were not treated in the same manner. However, despite these limitations, several clinical implications of our results merit emphasis. First, the presence of a severe fixed stenosis of greater than 90% markedly increased the risk of myocardial infarction. It may be suggested that coronary angiography be required in patients with vasospastic angina to evaluate the risk of myocardial infarction. Second, in many cases myocardial infarction occurred in the presence of newly developed or accelerated vasospastic angina. We believe that patients with newly diagnosed or worsening vasospastic angina should be intensively treated to suppress vasospastic activity by the prompt initiation of therapy with an increase in the dose of antivasospastic drugs. This therapy may require a combination of calcium blockers or calcium blockers with nitrates or nicorandil. Third, the incidence of sudden death was low, but it occurred in patients with insignificant atherosclerotic coronary artery disease even when vasospastic angina appeared to be under control. A complete suppression of vasospastic activity, including painless ischemic attacks, may be the only way to prevent sudden death. Calcium blockers can be discontinued in many patients without recurrence of anginal attacks.17-19 However, the discontinuation of calcium blockers should be attempted with caution, particularly in patients with recent acceleration of vasospastic angina, since myocardial infarction and sudden death occurred in three of our patients shortly after calcium blockers were discontinued.

Study participants
Cooperating institutions and principal investigators were: Tokyo Women’s Medical College (Dr. Kohichiro Hirosawa), Kurume Medical College (Dr. Hironori Toshima), Jichi Medical College (Dr. Saichi Hosoda), Nippon Medical College (Dr. Koichi Hayakawa), Toranomon Hospital (Dr. Hiroshi Yamaguchi), Osaka University, Faculty of Medicine (Dr. Michitoshi Inoue), and National Cardiovascular Center (Dr. Katsuhiko Hiramoto).

We thank Drs. T. Matsuguchi, H. Ootsubo, and Y. Watanabe for their help and suggestions and Ms. K. Yoshida for secretarial assistance.

References
2. Waters DD, Szlachcic J, Miller D, Theroux P: Clinical characteristics of patients with variant angina complicated by myocardial infarction or death within one month. Am J Cardiol 49: 658, 1982
3. Waters DD, Miller DD, Szlachcic J, Bouchard A, Methe M, Kreeft

Vol. 75, No. 6, June 1987
Clinical characteristics associated with myocardial infarction, arrhythmias, and sudden death in patients with vasospastic angina.
M Nakamura, A Takeshita and Y Nose

Circulation. 1987;75:1110-1116
doi: 10.1161/01.CIR.75.6.1110

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1987 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/75/6/1110

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/