Relationship between Coronary Risk Factor and Arteriographic Feature of Coronary Atherosclerosis

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Coronary arteriography was performed in 1,029 consecutive patients with ischemic heart disease and the relationship between the arteriographic features of coronary atherosclerosis and coronary risk factors was analyzed by case control studies. Patients were divided into four groups according to coronary arteriographic findings.

Patients with normal or near normal coronary arteriograms (Group I) showed a high prevalence of smoking habit and a higher value of serum uric acid compared with the control group, so smoking and hyperuricemia were considered to be the risk factors for coronary atherosclerosis in patients of group.

Four selected variables: smoking, hyperuricemia, hypertension and hyperlipidemia, were identified to be risk factors for the patients with minor plaques in the coronary arteries (Group II).

As in Group I, smoking and hyperuricemia had a close relationship to solitary tight plaque in a branch of the coronary artery (Group III).

Multiple tight stenoses in the coronary arteries (Group IV) correlated closely with smoking, hyperuricemia, hypertension, hyperlipidemia and diabetes mellitus.

Thus, there were many strong risk factors for patients with diffuse, extended coronary atherosclerosis (Group II and Group IV), while only two factors, smoking and hyperuricemia, were considered to be risk factors for the patients with near normal coronary arteries ies or a solitary plaque in a branch of the coronary artery.

These findings suggest that the role of the coronary risk factors on the pathogenesis of coronary atherosclerosis is not uniform but variable depending on the morphologic variability of the coronary atherosclerosis and on the pathophysiology of the ischemic heart disease.

CORONARY arteriography has been widely used in clinical situations to evaluate the severity of coronary atherosclerosis.

It is a some of valuable information in elucidating the pathophysiology of ischemic heart disease. There is a close relationship between coronary atherosclerosis and coronary artery disease, and the arteriographic

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442  Japanese Circulation Journal  Vol. 54, April 1990
features of coronary atherosclerosis in patients with ischemic heart disease are very diverse. For example, patients with variant form of angina often show entirely normal coronary arteriograms, while patients with unstable angina sometimes show multiple and diffuse extended tight plaques in all three coronary branches.

Many risk factors for coronary artery disease have been identified, but the relationship between those factors and the arteriographic characteristics of coronary atherosclerosis has not been well defined.

In this study, we tried to analyze the relationship between the coronary risk factor and the arteriographic features of coronary atherosclerosis.

METHODS

Patients: Between 1973 and 1987, 1,029 consecutive patients with ischemic heart disease underwent coronary arteriography in our cardiac catheterization laboratory in order to evaluate the severity of their coronary atherosclerosis. The subjects included 644 patients with previous myocardial infarction and 385 patients with angina pectoris (88 with effort angina, 184 with rest angina and 113 with effort and rest angina). They were 892 men and 137 women and ages ranged from 25 to 75 years (mean 55). For case control studies, 1,029 age and sex matched healthy people having neither a history of cardiac symptoms nor electrocardiographic abnormalities were recruited.

Coronary arteriography (Fig. 1): Patients were divided into four groups according to coronary arteriographic findings.

Group I: 110 patients with entirely normal or near normal coronary arteriograms (near normal group).

Group II: 99 patients with multiple minor plaques and less than 50% narrowing (diffuse minor group).

Group III: 72 patients with a solitary tight stenosis and more than 75% narrowing (solitary tight group).
TABLE 1  RELATIONSHIP BETWEEN CORONARY RISK FACTORS AND CORONARY ARTERIOGRAPHIC FEATURES: UNIVARIATE ANALYSIS(1)

<table>
<thead>
<tr>
<th></th>
<th>GROUP I</th>
<th>GROUP II</th>
<th>GROUP III</th>
<th>GROUP IV</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum total cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>181±4.1</td>
<td>192±4.25</td>
<td>184±45.4</td>
<td>204±49.8</td>
<td>199±49.7</td>
</tr>
<tr>
<td>Control</td>
<td>182±33.5</td>
<td>175±29.7</td>
<td>180±36.8</td>
<td>185±34.3</td>
<td>184±34.1</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>5.74±1.89</td>
<td>5.65±1.40</td>
<td>5.92±1.55</td>
<td>5.96±1.58</td>
<td>5.91±1.54</td>
</tr>
<tr>
<td>Control</td>
<td>4.97±1.34</td>
<td>4.99±1.39</td>
<td>5.12±1.26</td>
<td>5.24±1.27</td>
<td>5.18±1.29</td>
</tr>
<tr>
<td>% Obesity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.

*: p<0.05    **: p<0.01    ***: p<0.001
NS: not significant

Group IV: 748 patients with multiple tight stenoses (diffuse tight group).

The percentage of luminal narrowing was recorded according to the American Heart Association's reporting system.

Coronary risk factors: The following six variables were selected as coronary risk factors.

1. Hypertension: a definite history of high blood pressure or blood pressure on admission more than 160/95 mmHg.
2. Smoking: the number of cigarettes per day if the patient smokes.
3. Hyperlipidemia: the value of serum total cholesterol (mg/dl) examined on the day of admission.

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TABLE II  RELATIONSHIP BETWEEN CORONARY RISK FACTORS AND CORONARY ARTERIOGRAPHIC FEATURES: UNIVARIATE ANALYSIS(2)

<table>
<thead>
<tr>
<th></th>
<th>GROUP I</th>
<th>GROUP II</th>
<th>GROUP III</th>
<th>GROUP IV</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(−) vs (+)</td>
<td>1.4(NS)</td>
<td>3.0(1.6−5.6)</td>
<td>1.4(NS)</td>
<td>2.2(1.8−2.7)</td>
<td>2.1(1.7−2.5)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(−) vs (+)</td>
<td>0.6(NS)</td>
<td>3.1(1.3−7.8)</td>
<td>2.3(NS)</td>
<td>3.2(2.4−4.3)</td>
<td>2.7(2.1−3.5)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(−) vs under 20/day</td>
<td>1.8(1.1−3.5)</td>
<td>3.9(1.8−8.2)</td>
<td>2.5(1.1−5.4)</td>
<td>2.8(2.2−3.7)</td>
<td>2.7(2.2−3.4)</td>
</tr>
<tr>
<td>(−) vs over 21/day</td>
<td>3.1(1.6−6.1)</td>
<td>7.7(3.4−17.3)</td>
<td>5.5(2.2−13.7)</td>
<td>5.0(3.8−6.7)</td>
<td>4.9(3.9−6.3)</td>
</tr>
</tbody>
</table>

Values are expressed as relative risks.
(−), 95% confidence interval; NS, not significant.

TABLE III  RELATIONSHIP BETWEEN CORONARY RISK FACTORS AND CORONARY ARTERIOGRAPHIC FEATURES: MULTIVARIATE ANALYSIS (LOGISTIC REGRESSION MODEL)

<table>
<thead>
<tr>
<th></th>
<th>GROUP I</th>
<th>GROUP II</th>
<th>GROUP III</th>
<th>GROUP IV</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum total cholesterol</td>
<td>0.29</td>
<td>2.30*</td>
<td>0.40</td>
<td>4.35***</td>
<td>4.42***</td>
</tr>
<tr>
<td>Serum uric acid</td>
<td>3.75**</td>
<td>1.99*</td>
<td>2.59*</td>
<td>5.49***</td>
<td>7.19***</td>
</tr>
<tr>
<td>% Obesity</td>
<td>−1.87</td>
<td>−0.95</td>
<td>−2.04*</td>
<td>−5.75***</td>
<td>−6.31***</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(−) vs (+)</td>
<td>0.42</td>
<td>2.58**</td>
<td>−0.39</td>
<td>5.75***</td>
<td>6.04***</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(−) vs (+)</td>
<td>0.17</td>
<td>1.36</td>
<td>1.71</td>
<td>4.35***</td>
<td>4.35***</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(−) vs under 20/day</td>
<td>2.37**</td>
<td>2.76**</td>
<td>0.64</td>
<td>5.35***</td>
<td>6.71***</td>
</tr>
<tr>
<td>(−) vs over 21/day</td>
<td>3.08***</td>
<td>3.13**</td>
<td>2.65*</td>
<td>7.54***</td>
<td>9.53***</td>
</tr>
</tbody>
</table>

Values are expressed as t values of regression coefficients.
*,p<0.05; **,p<0.01; *** ,p<0.001

4 diabetes mellitus: the presence of diabetes mellitus checked by oral glucose tolerance test.
5 hyperuricemia: the value of serum uric acid (mg/dl) examined on the day of admission.
6 % obesity: actual body weight on admission (kg) / ideal body weight (kg) multiplied by 100 (%).

Statistical analyses: The relationships between these variables and the coronary arteriographic findings were analyzed by case control studies. The univariate analyses were based on t-test and the comparison of the relative risk. The multivariate analysis was based on a logistic regression model. A p value less than 5% was considered significant.

RESULTS

(1) Arteriographic features and pathophysiology of ischemic heart disease (Fig. 2): A higher proportion of myocardial infarction was noted in patients with tight plaques (Group III and Group IV) than in patients with minor plaques (Group I and Group II). The majority of angina in patients in Group I and Group II was rest angina, suggesting that coronary vasospasm played a major role in the pathophysiology of the patients in these groups. All patients with effort angina were included in Group III or Group IV.

(2) Relationship between coronary risk factors and coronary arteriographic features (Univariate analysis; Table I and Table II): Patients in Group I had higher values of
serum uric acid (p < 0.001), and high relative risks of smoking compared with the control group. Other variables like hyperlipidemia, hypertension and diabetes mellitus were not significant risk factors. Patients in Group II had higher values of serum total cholesterol (p < 0.001) and serum uric acid (p < 0.001) compared with the control group. Significantly high relative risks of hypertension, diabetes mellitus and smoking were also noted in Group II patients. Patients in Group III had higher values of serum uric acid (p < 0.01) and lower values of % obesity (p < 0.05). High relative risks of smoking were noted compared with the control group. Hyperlipidemia, hypertension and diabetes mellitus were not significant risk factors. Patients in Group IV had higher values of serum total cholesterol (p < 0.001) and serum uric acid (p < 0.001), and lower values of % obesity (p < 0.001). High relative risks of hypertension, diabetes mellitus and smoking were noted compared with the control group.

(3) Relationship between coronary risk factors and coronary arteriographic features (Multivariate analysis; Table III): Using six variables, the logistic regression model was formulated in each group to discriminate between the subject group and the control group.

In group I, serum uric acid and smoking showed significantly high t values of regression coefficients. Therefore, hyperuricemia and smoking were considered to be risk factors for the patients in this group. Other variables like serum total cholesterol, % obesity, hypertension and diabetes mellitus did not show significant t values. In Group II, serum total cholesterol, serum uric acid, hypertension and smoking showed significantly high t values of regression coefficients. In Group III, serum uric acid and smoking showed high t values of regression coefficients and % obesity showed a significantly low t value of the regression coefficients. In Group IV, all variables except % obesity showed high t values of regression coefficients and % obesity showed a low t value of regression coefficients.

DISCUSSION

Many coronary risk factors have been identified in numerous epidemiological studies. The management of these factors is one of the important therapeutic modalities for the primary and secondary prevention of coronary heart disease. However, the arteriographic features of coronary atherosclerosis are very diverse, ranging from normal coronary arteries to severe multivessel disease. The factors relating this variability to coronary atherosclerosis and the pathophysiology of ischemic heart disease are still poorly understood.

This study clarified that so called coronary risk factors are strongly correlated with the morphologic characteristics of coronary atherosclerosis. However, depending on the characteristics of the arteriographic features, the degree to which each factor contributes to the pathogenesis of the coronary atherosclerosis varies. For patients with entirely normal or near normal coronary arteriograms as in Group I (near normal group), smoking and hyperuricemia are considered to be definite risk factors. For patients with single tight plaque as in Group III (solitary tight group), smoking and hyperuricemia were considered to be contributing factors. Neither hyperlipidemia, nor hypertension, nor diabetes mellitus could be identified as risk factors for these patients. For the patients with multiple minor plaques as in Group II (diffuse minor group) and for patients with multiple tight plaques as in Group IV (diffuse tight group), hyperlipidemia, hypertension and diabetes mellitus were considered to be definite risk factors as well as smoking and hyperuricemia. The stronger the correlation with these factors, the more diffuse and extensive are the plaques detected by coronary arteriography.

These findings suggest that the role of coronary risk factors in the pathogenesis of coronary atherosclerosis is not uniform but variable depending on the variability of the coronary atherosclerosis and on the pathophysiology of the ischemic heart disease. Smoking and hyperuricemia are strongly correlated with all types of coronary atherosclerosis, whatever the arteriographic features of the coronary artery. This implies that these two factors may play a much more important role in the pathogenesis of the coronary atherosclerosis and in the pathophysiology of the coronary
heart disease than previously reported.7-11

Limitations of this study: Obesity has been considered to be a major coronary risk factor. In this study, obesity was not determined to be an independent positive risk factor but was a significant negative risk factor in some cases. Restriction of calories intake during hospitalization might modify the role of obesity in the pathogenesis of atherosclerosis. Further studies should be needed.

REFERENCES


