Variant Angina Pectoris

Role of Coronary Spasm in the Development of Fixed Coronary Obstructions

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Background. It has been suggested that recurring coronary artery spasm may lead to the development of fixed atherosclerotic coronary obstructions.

Methods and Results. We studied 10 patients with typical Prinzmetal’s variant angina in whom the disease remained active for years and in whom occlusive coronary spasm occurred reproducibly at the same arterial site during repeat coronary arteriography (25±12 months after initial angiography). At initial evaluation, four patients had significant (≥50% fixed coronary diameter reduction) one-vessel coronary artery disease, and six had nonsignificant disease. Spasm developed at stenotic sites (20–65% diameter reduction) in nine patients and at an angiographically normal site in one patient. Progression of coronary disease was assessed in 62 segments: 10 spastic (of which nine were stenotic) and 52 nonspastic (eight stenotic and 44 angiographically normal), using computerized arteriography. Mean diameters (millimeters) of spastic segments, nonspastic stenoses, and angiographically normal nonspastic segments were not significantly different at first and second arteriograms (1.52±0.14 versus 1.43±0.21, 1.32±0.17 versus 1.12±0.23, and 2.40±0.12 versus 2.42±0.12, respectively). Stenosis progression (from 65% diameter reduction to total occlusion) occurred in one patient at a spastic site and in two at nonspastic sites (from 34% to 65% and from 84% to 100%). Complicated stenoses suggestive of plaque fissuring were not observed during the study.

Conclusions. In patients with chronic Prinzmetal’s variant angina without myocardial infarction, stenosis progression was not frequently observed at spastic sites despite the recurrence of focal coronary spasm over relatively long periods of time. (Circulation 1992;85:619–626)

Coronary thrombosis is the most common cause of acute myocardial infarction,1–3 and it has been also documented in patients with unstable angina pectoris.4–6 Plaque fissuring,7,8 endothelial damage9,10 (by both promoting a displacement of the thrombotic-thrombolytic equilibrium toward thrombosis and favoring coronary vasoconstriction), and coronary artery spasm11–14 have been proposed as likely triggers of occlusive coronary thrombosis.

Although intimal tearing is the most common event initiating major coronary thrombosis,15 its cause and mechanisms remain unknown. Circumstantial evidence12,13 has implicated coronary artery spasm in the transition from stable coronary artery disease to acute coronary syndromes. It has been suggested that in patients with unstable angina pectoris, plaque disruption and thrombus formation may be the result of one or more episodes of coronary spasm.12 Moreover, it has been hypothesized that in patients with Prinzmetal’s variant angina, coronary artery spasm could lead to the development of organic coronary stenosis.16,17

We studied the relation between coronary spasm and the development of fixed obstructive coronary lesions in patients with Prinzmetal’s variant angina in whom the disease remained active for years and in whom repeat coronary arteriography, at a mean of 25 months after the initial angiographic assessment, showed coronary artery spasm occurring consistently at the same arterial site.

Methods

Patients

Ten patients (eight men, two women; aged 40–63 years) with active Prinzmetal’s variant angina were included in the study. All had typical clinical features of variant angina, including angina at rest (usually nocturnal or in the early morning) associated with ST
Table 1. Clinical and Angiographic Characteristics of 10 Patients with Prinzmetal's Variant Angina Pectoris

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>CAD risk factors</th>
<th>Cholesterol (mg/dl)</th>
<th>ST † (leads)</th>
<th>Coronary arteriography at initial evaluation (% diameter reduction)</th>
<th>“Hot phases”</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>M</td>
<td>Smoking</td>
<td>180</td>
<td>V₇-V₃</td>
<td>LAD prox, 34%; mid, 37%*; RCA, 39%</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>M</td>
<td>Diabetes</td>
<td>158</td>
<td>V₇-V₃</td>
<td>LAD prox, 56%*</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>M</td>
<td>0</td>
<td>218</td>
<td>V₇-V₆</td>
<td>LAD prox, 40%; RCA prox, 22%; mid, 20%; Cx prox, 37%; mid, 44%</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>M</td>
<td>0</td>
<td>248</td>
<td>V₇-V₃</td>
<td>LAD prox, 30%*</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>52</td>
<td>M</td>
<td>Smoking</td>
<td>188</td>
<td>V₇-V₆</td>
<td>LAD prox, 51%*</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>54</td>
<td>M</td>
<td>Smoking</td>
<td>184</td>
<td>II, III, aVF</td>
<td>RCA mid, 12%*</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>48</td>
<td>F</td>
<td>0</td>
<td>240</td>
<td>V₃-V₅</td>
<td>LAD prox, 48%; mid, 43%</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>M</td>
<td>Smoking</td>
<td>192</td>
<td>V₇-V₅</td>
<td>LAD mid, 65%*</td>
<td></td>
<td>2†</td>
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<tr>
<td>9</td>
<td>42</td>
<td>M</td>
<td>Smoking</td>
<td>259</td>
<td>V₇-V₆</td>
<td>LAD prox, 41%; Cx mid, 84%</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>10</td>
<td>48</td>
<td>F</td>
<td>Smoking</td>
<td>188</td>
<td>V₇-V₅</td>
<td>LAD prox, 35%*</td>
<td></td>
<td>5</td>
</tr>
</tbody>
</table>

M, male; F, female; CAD, coronary artery disease; LAD, left anterior descending coronary artery; prox, proximal third; mid, middle third; RCA, right coronary artery; Cx, circumflex coronary artery.

*Spastic segment.
†Infarction developed during second “hot phase.”

Segment elevation and a preserved exercise capacity (all patients had negative results on exercise testing, with the exception of patient 9, who had angina and 0.1 mV of ST segment depression at a high work load). None of the patients had electrocardiographic or angiographic evidence of previous myocardial infarction.

In every patient, the vasospastic disease remained active for years and coronary artery spasm occurred reproducibly at the same arterial site, as assessed by repeat coronary arteriography. Ambulatory electrocardiographic monitoring showed numerous episodes of ST segment elevation in eight of the 10 patients during initial clinical characterization and subsequently in all 10 at the time of recurrence of symptoms. In individual patients, ST segment shifts tended to recur in the same electrocardiographic leads. Focal occlusive coronary artery spasm was angiographically documented at initial presentation in all patients. Spasm was provoked by ergonovine in nine patients and by hyperventilation in one.

During follow-up, “hot phases” (periods of disease activity with recurrence of symptoms and of ischemic ST segment shifts) that ranged from 4 days to several weeks were observed in all patients (Table 1). During periods of increased disease activity, an increase in the dose of the patients’ antianginal medication was required to significantly reduce or abolish symptoms and ischemic ST segment changes. Once symptoms were controlled, the dose was gradually reduced and patients returned to their baseline dosage. This strategy was usually effective in controlling relapses. Except for the necessity to increase dosage during hot phases, individual patients remained largely on the same medication throughout the follow-up. Baseline medication consisted of sustained release isosorbide dinitrate (20–60 mg/day) or isosorbide mononitrate (20–60 mg/day) in association with calcium antagonists. Patients 2 and 4 received verapamil (240–480 mg/day), and patients 6 through 10 received diltiazem (180–480 mg/day) throughout the study. Patients 1 and 3 were treated with verapamil (240–480 mg/day) during the first 20 and 12 months of follow-up, respectively, but received diltiazem thereafter. Patient 5 was treated with nifedipine (40–60 mg/day) during the initial 8 months and with diltiazem (180–360 mg/day) thereafter.

In individual patients, ST segment elevation occurred repeatedly in the same electrocardiographic leads (Table 1). Owing to recurrence of symptoms, coronary arteriography was repeated in all patients at a mean of 25±12 months (range, 8–52 months) after the initial angiographic evaluation to assess stenosis progression. In all patients (with the exception of patient 8, in whom the spastic coronary artery was found to be occluded during the second angiogram), ergonovine consistently caused occlusive spasm at the same site documented at initial evaluation. Coronary artery spasm occurred at the site of significant coronary stenoses (≥50% diameter reduction) in three patients, of nonsignificant stenoses (20–49% diameter reduction) in six, and at an angiographically normal segment in one (Table 1). None of the patients had systemic hypertension, but patient 2 had diabetes mellitus, and patients 1, 5, 6, 8, and 9 were smokers. Cholesterol levels ranged from 158 to 259 mg/dl at entry and from 173 to 267 mg/dl at outset (Table 1). Clinical and angiographic characteristics of all the patients are summarized in Table 1.

Study Protocol

Coronary arteriography. All patients gave written informed consent for both cardiac catheterization and tests of coronary spasm. After admission, patients were scheduled for angiography when the activity of their disease was considered to be mark-
edly reduced (fewer than two anginal episodes or ST segment shifts in the preceding 24 hours, as assessed by symptoms and continuous electrocardiographic monitoring). Sublingual nitrates were allowed for relief of angina at any time, but calcium antagonists and oral nitrates were gradually reduced over 72 hours and discontinued at least 12 hours before angiography in patients 2, 4, 5, 6, 9, and 10.

Perpendicular views of the left and right coronary arteries, suitable for computerized quantitative analysis, were obtained at baseline angiography, during spasm, and after administration of nitrates. These views were carefully recorded and duplicated as closely as possible during the follow-up study. Angiographically normal segments (reference segments), proximal and juxtaposed to the diseased segments, were used to determine percent stenosis. Significant stenoses (≥50% fixed coronary lumen diameter reduction) were found in four patients (at spastic sites in three) (Table 1); all four patients had one-vessel disease. For the purpose of the study, all coronary stenoses ≥20% diameter reduction were considered for analysis.

Ergonovine, administered during repeat coronary angiography, caused occlusive spasm and ST segment elevation in all patients with the exception of patient 8, in whom the spastic artery was occluded, as mentioned above. Spasm was rapidly relieved by administration of 1–2 mg of intracoronary isosorbide dinitrate in all patients.

Quantitative analysis. The severity of significant and nonsignificant coronary stenoses was assessed by two independent observers blinded to the patient’s identity and clinical characteristics. Quantitative assessment of stenosis severity was carried out using a validated computer-assisted system, as described elsewhere.18,19 Coronary luminal diameters were measured by an automated edge contour detection system (Coronary Angiography Analysis System [CAAS]; Pie Data Medical).20 The size of the stem of the Judkins coronary catheter was used for calibration to determine absolute measurement in millimeters, and correction was made for radiographic pincushion distortion. End-diastolic frames were selected for analysis by one investigator (J.C.K.) and analyzed by two independent observers who were unaware of the patient’s identity or clinical characteristics.

Single-plane orthogonal views of the coronary arteries were obtained in all patients. For each coronary segment, diameter values represent the average of measurements carried out in orthogonal views. For the purpose of the study, all measurements were carried out in views obtained after intracoronary administration of nitrates (1–2 mg isosorbide dinitrate), in an attempt to eliminate the influence of coronary vasomotor tone on stenosis diameter. Measurements were made in the angiographic view at end diastole in which the lesion appeared most severe. Because accuracy of computerized measurements is particularly high in vessels with diameter >1 mm, the three major coronary arteries were arbitrarily divided in thirds, and only proximal and mid-third segments were considered for analysis. For the purpose of the study, 52 nonspastic control segments (5.2±0.8 per patient; range, 4–6; in proximal or mid-third locations) were identified and analyzed in addition to all 10 spastic segments (one per patient). Of the 52 control segments, eight showed stenosis ranging from 20% to 84%, whereas the remaining 44 were angiographically normal.

Coronary arteriograms were analyzed by two independent observers and blindly reanalyzed months later to assess the reproducibility of the method. No significant difference in the variances between analyses was found (p=0.8). Intraobserver reproducibility of measurements was 98%.

Qualitative analysis. Qualitative analysis of coronary stenoses was also carried out by the same two independent observers. Stenoses were morphologically classified as concentric, eccentric, or complicated on the basis of analysis in every lesion in two orthogonal projections. Concentric stenoses were those that produced symmetric narrowing of a coronary artery. The borders of these lesions were smooth and their appearance was identical, or almost identical, in orthogonal projections. Eccentric stenoses were asymmetric narrowings of a coronary artery with a smooth outline. Complicated lesions were defined as asymmetric stenoses with irregular borders, overhanging edges (type II of Ambrose et al.21,22), an “abrupt proximal face,”23 or a “sawtooth” component.23 Discrepancies regarding stenosis classification, which arose in two stenoses, were solved by consensus of the two observers. The reproducibility of the morphological classification was determined by repeat evaluation of all films without knowledge of the first reading. Ninety-eight percent of stenoses were classified in the same way.

Stenosis progression. A progression in stenosis severity was defined as an increase of ≥20% in a preexisting stenosis of ≥50%, an increase of ≥30% in a stenosis <50%, or any increase in lesion severity that resulted in total coronary occlusion. New coronary stenoses were defined as stenoses ≥20% that developed at a site that was previously angiographically normal. Repeat angiography was carried out at a mean of 25±12 months (range, 8–52 months) after the initial coronary arteriogram.

Data Analysis

Coronary lumen diameter data are presented as mean±SEM. Differences between proportions were analyzed by Yates’ corrected χ2 test. Paired and unpaired Student’s t tests were used to analyze continuous data. A value of p<0.05 was considered significant.

Results

A total of 62 coronary segments (10 spastic and 52 nonspastic) were found suitable for computerized analysis at initial evaluation and at follow-up angiography. At initial evaluation, of the 10 spastic segments, three showed fixed significant stenoses, six showed nonsignif-
significant stenoses (range, 30–48%), and one was angiographically normal (Table 1). Of the 52 control nonspastic segments, 44 were angiographically normal, whereas eight showed coronary stenoses.

Coronary Stenosis Progression

Stenosis progression was observed in three of the 10 patients; in two it occurred at the site of nonspastic coronary stenoses and in one at the spastic site. On average, diameter (mean ± SEM) of the 17 coronary stenoses was not significantly different when the first and second angiograms were compared (1.37 ± 0.10 mm versus 1.23 ± 0.15 mm; p = 0.2). The mean diameter of angiographically normal coronary segments did not change in the interval between the first and second angiograms (2.40 ± 0.12 mm and 2.42 ± 0.12 mm, respectively) (Table 2).

Spastic segments. Quantitative analysis carried out at 10 spastic sites, of which three were significant stenoses (one concentric and two eccentric), six were nonsignificant stenoses, and one was an angiographically normal segment, revealed that mean coronary diameters were not significantly different during initial evaluation and follow-up evaluation (1.52 ± 0.14 mm and 1.43 ± 0.21 mm, respectively; p = 0.5) (Table 2). Individual analysis of the nine spastic stenoses showed that only one of these, which was concentric and with 65% diameter reduction at initial evaluation, progressed to total occlusion (associated with acute myocardial infarction; see Table 1), whereas the remaining eight either remained unchanged (seven lesions) or regressed (one lesion; from 56% to 30% diameter reduction) (Figures 1 and 2).

Nonspastic segments. Fifty-two nonspastic sites were assessed: Eight showed coronary stenoses (one significant concentric and seven nonsignificant) and 44 were angiographically normal segments (Tables 1 and 2). Mean diameters of stenotic segments and angiographically normal coronary segments were not significantly different during the first and second coronary arteriograms (1.32 ± 0.17 mm versus 1.12 ± 0.23 mm; p = 0.6, and 2.40 ± 0.12 mm versus 2.42 ± 0.12 mm; p = 0.85, respectively) (Table 2). Two nonspastic stenoses progressed in two patients (Figures 1 and 2): one from 34% to 65% diameter reduction and the other from 84% to 100% (crescendo angina but no myocardial

| TABLE 2. Absolute Coronary Diameters and Percentage Diameter Reduction of Nonspastic Normal Segments, Nonspastic Stenoses, and Spastic Segments |
|---|---|---|
| Normal segments (n=44) (mm) | Stenosis (%) | Normal segments (n=44) (mm) | Stenosis (%) |
| First angiogram | 2.40±0.12 | 1.32±0.17 | 40.6±7 | 1.52±0.14 | 41.8±4 |
| Second angiogram | 2.42±0.12 | 1.12±0.23 | 49.7±8 | 1.43±0.21 | 43.8±7 |

Values are mean±SEM for absolute coronary diameters; mean±SD for percentage diameter reduction.
infarction developed in association with the coronary occlusion in this patient).

**Stenosis Morphology and Development of New Coronary Lesions**

Compared with that observed during the initial angiogram, stenosis morphology remained unchanged in 14 of the 17 stenoses, whereas three stenoses (all of them located in nonspastic segments) changed their geometric configuration but without a significant increase of stenosis severity: Two concentric stenoses became eccentric, and one eccentric developed irregular borders.

Neither complicated stenoses suggestive of plaque fissuring or rupture nor new angiographic lesions developed at the site of spastic or nonspastic coronary segments during the study (Figure 1).

**Discussion**

The results of this study indicate that in patients with active Prinzmetal’s variant angina, stenosis progression or the development of fixed coronary stenosis are not frequent at spastic sites. Complicated stenoses, suggestive of plaque fissuring and thrombosis, are not commonly seen at angiography in these patients despite the occurrence of repeated episodes of focal occlusive spasm over long periods of time. Our findings also suggest that in patients with Prinzmetal’s variant angina, myocardial infarction is unlikely to be related to plaque rupture or stenosis progression.

**Coronary Artery Spasm and Stenosis Progression**

In our patients, the incidence of stenosis progression was similar in spastic and nonspastic coronary segments. Although spasm occurred often at the same arterial site over a relatively long period of time, it did not result in the development of new coronary stenoses or in a more frequent or larger progression of the preexistent ones compared with nonspastic segments.

**Mechanical injury to the endothelium.** Mechanical injury to the endothelium by spasm has been proposed as a contributing factor for atherogenesis. Joris and Majno showed in an in vitro experiment involving electron microscopy that when vascular constriction is induced by dripping L-norepinephrine over rat muscular arteries, endothelial damage occurs, which is expressed as patchy endothelial denudation and adhesions between cells on opposite sides of intimal folds. These findings were suggested to be responsible for the endothelial alterations that might induce platelet aggregation and the local release of vasoconstrictor substances that might perpetuate spasm. Gertz et al observed in experimental animals that platelet deposition and thrombosis developed at the site of partial arterial constriction (arteries partially ligated with suture threads) associated with marked endothelial damage in every case. Based on these observations, these authors suggested that coronary vasospasm may result in endothelial damage, thrombus formation, and arterial occlusion at the spastic site. Thus, in their view, spasm alone might contribute to the initiation of atherogenesis as a consequence of endothelial damage. Although relevant, extrapolation of these experimental observations to Prinzmetal’s variant angina is probably not straightforward. Recently, Shimokawa et al observed the development of local atheromatous changes and a focal hyperreactive response to histamine in the coronary arteries of miniature swine subjected to balloon-induced endothelial denudation and subsequently fed a high cholesterol diet. In this model, mechanical endothelial damage led to both atherosclerotic disease and focal coronary hyperreactivity. However, these studies did not address the question of whether spasm triggered by stimuli other than mechanical denudation might be responsible for both the endothelial injury and the development of coronary atheroma.

**Coronary spasm and progression of atherosclerosis.** Marzilli et al observed a rapid angiographic progression of coronary artery disease (at the spastic site) in a patient with Prinzmetal’s variant angina who had angiographically normal coronary arteries, and suggested that coronary artery spasm could precede the development of coronary atherosclerosis. Unfortunately, despite the interest of this observation, these authors did not carry out longitudinal studies aimed at exploring the issue further. Long-term follow-up studies in patients with Prinzmetal’s variant angina have shown that acute myocardial infarction may develop in 2–19% of patients who have angiographically normal coronary arteries or nonsignificant coronary stenoses. However, in these studies, the question of a potential role for spasm in the development of organic coronary stenosis was not addressed; therefore, stenosis progression was not systematically and objectively investigated.

Recently, Corrado et al reported intimal proliferation of smooth muscle cells superimposed on the fibrous cap of atheromatous plaques in two patients.
with angina at rest who died suddenly after episodes of ST segment elevation. These authors and others suggested that in patients with variant angina, coronary artery spasm might be associated with the development of coronary atherosclerosis. Their findings, however, do not necessarily indicate a cause–effect relation because the histological lesions observed in their patients could have been “innocent bystanders” indicative of the presence of an atherosclerotic process but not necessarily responsible for the coronary hyperreactivity that causes spasm in variant angina patients. Although coronary atherosclerosis is a common finding in the general population (and almost universal in patients with typical angina pectoris), coronary artery spasm is a rare condition. It is therefore unlikely that the mere presence of atherosclerotic plaques or of endothelial dysfunction alone cause coronary spasm, although they may play a modulatory role in the response of the hyperreactive coronary segments.

Coronary artery spasm has been also suggested as a possible cause of accelerated restenosis after coronary angioplasty. However, restenosis after coronary angioplasty is frequent in patients with no preexisting evidence of vasospastic angina. Moreover, it has been shown that treatment with calcium antagonists does not affect the rate of restenosis after angioplasty.

Nonatherosclerotic Lesions in Variant Angina

Studies in patients with typical Prinzmetal’s variant angina pectoris have shown that histopathological alterations of the coronary arteries other than atherosclerosis and endothelial damage may be responsible for variant angina. Highly cellular and edematous fibroelastic endarteritis and medial sclerosis were reported by Gueronprez et al, whereas Dhurandar et al and Petitier et al observed the presence of intimal fibrous dysplasia similar to that seen in cases of nonatherosclerotic renal, femoral, vertebral, and carotid artery fibrous dysplasia in the coronary arteries of patients with the typical syndrome of variant angina. However, it has been suggested recently that these lesions may also be an early expression of progressing atherosclerosis. Forman et al found an increased number of mast cells in the adventitia of the spastic coronary artery of an individual with classic variant angina (who died suddenly) compared with coronary vessels of control patients.

Although it is conceivable that a particular phase in the evolution of coronary atherosclerosis could favor the development of the local coronary hyperreactivity characteristic of patients with Prinzmetal’s variant angina and that, at least in some patients, coronary artery spasm might result from still unknown biological processes involved in atherogenesis, there is no objective evidence at present to support the notion that spasm can cause endothelial damage or the development of atherosclerosis.

Coronary Spasm and Plaque Evolution

In patients with angina pectoris, the majority of coronary thrombi large enough to be detected by angiography are associated with fissures in the caps of the atherosclerotic plaques. These fissures allow blood to penetrate into the arterial wall, contributing to thrombus formation within the intima and coronary lumen. The anatomic result of this process, which appears to be responsible for acute myocardial infarction, unstable angina, and sudden coronary death, can be recognized at angiography and observed during coronary angioscopy. Although intimal disruption is the most common event initiating major coronary thrombosis, its cause and mechanisms still remain speculative. Alpert has recently suggested, although based on circumstantial evidence, that disruption of coronary atherosclerotic plaques in individuals with unstable coronary syndromes might be the result of one or more episodes of coronary vasospasm.

In our patients with Prinzmetal’s variant angina, and despite the presence of repeated episodes of coronary spasm occurring consistently at the same arterial site over a relatively long period of time, spastic segments were not associated with the angiographic development of complicated lesions suggestive of plaque fissuring or with a greater incidence of stenosis progression than nonspastic segments. This is in agreement with the fact that plaque fissuring was not found at autopsy in patients with documented variant angina who died after an acute infarction, as reported by several investigators.

Study Limitations

Because we included in this study only patients with a form of variant angina that remained chronically active over the years, our results do not allow us to rule out a potential role for coronary spasm in the genesis of plaque fissuring in acutely evolving coronary syndromes. It is conceivable that plaque fissuring could develop in some patients as a result of acute forms of spasm, which may in turn cause infarction or unstable angina but do not tend to recur chronically. Therefore, such patients will not come to our attention under the diagnosis of variant angina. Moreover, it is also possible that spasm could cause disruption of plaques more fragile than those present in our patients.

The fact that only patients with chronically active variant angina but no patients with infarction were included in this relatively small series could have biased the study against a causal role of spasm in plaque rupture. However, our observations are in agreement with findings in studies in which patients with infarction were included. In these studies, plaque fissuring was not observed as the cause of infarction. In some cases, no atheromatous lesions or histological alterations were found, whereas in others, uncomplicated atheromatous plaques were.
thrombosis,25 and persisting postmortem coronary spasm27,33 were reported.

The small number of patients in our study, although justifiable by the rarity of the syndrome of variant angina pectoris, may limit extrapolation of results to other types of angina patients. Also, the study interval in some of our cases may have been too short to expect progression of coronary artery disease, particularly in the absence of hypercholesterolemia.

Conclusions

Our findings suggest that in patients with chronic Prinzmetal's variant angina, coronary artery spasm plays a minor contributory role, if any, in coronary stenosis progression. Our observations also suggest that the mechanism by which coronary artery spasm may result in myocardial infarction in patients with variant angina is likely to be a prolonged spastic obliteration of the coronary lumen with associated coronary thrombosis and platelet aggregation.

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References


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