ORIGINAL ARTICLES

Percutaneous Transluminal Coronary Angioplasty in Patients with Variant Angina

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SUMMARY Among the first 83 patients treated with percutaneous transluminal coronary angioplasty (PTCA) at our institution, typical variant angina was recognized beforehand in five cases and was discovered within 4 months of PTCA in six others. All patients had a 65–95% proximal left anterior descending coronary artery stenosis and only one had a coronary lesion >50% in other coronary arteries. Before PTCA, all patients were premedicated with calcium-antagonist drugs. Thirteen of 15 PTCA, including three of four repeat PTCA, were technically successful. However, variant angina recurred after successful PTCA in three of the five patients in whom it was documented beforehand and in an additional two of two patients with variant angina before a successful repeat PTCA. Overall, among the nine patients with variant angina after successful PTCA, five had restenosis at the site of PTCA and two others developed severe lesions adjacent to the site of PTCA within 4 months of the procedure. The three patients without restenosis have been treated with calcium-antagonist drugs from soon after PTCA and have remained angina-free.

These results suggest that PTCA is technically feasible in patients with variant angina who have organic lesions, but symptoms due to coronary spasm usually persist or recur, often with restenosis.

A SPECTRUM of coronary arteriographic findings are seen in patients with variant angina, ranging from normal arteries to severe multivessel disease.1–3 Variant angina can usually be controlled with calcium-antagonist drugs.4, 5 Although patients with organic lesions often do well after bypass surgery,6–7 the results are poorer than in other subsets of coronary disease,8, 9 and variant angina may occur after surgery in spite of patent grafts.10

Variant angina is caused by coronary spasm, but the cause of spontaneous coronary spasm is unclear. However, coronary spasm in variant angina is intimately associated with organic lesions if they are present; thus, of 69 adequately documented cases with organic lesions collected by MacAlpin,1 spasm occurred at the stenosis in 62. If the organic stenoses were not present, would spasm still have occurred? MacAlpin11 reasoned that coronary vasomotion within the normal physiologic range could theoretically obstruct a pliable vessel at the site of a severe organic stenosis. Under these conditions, eliminating the organic stenosis would theoretically prevent intermittent vasoconstrictive occlusion of the artery. These considerations suggest that reduction of the severity of the organic stenosis in patients with variant angina might relieve symptoms. Therefore, we considered percutaneous transluminal coronary angioplasty (PTCA) as a treatment for some patients with variant angina.

Among the first 83 patients treated with PTCA at our institution, typical variant angina was recognized before the procedure in five cases and was discovered within 4 months after PTCA in six others. In this report we describe the clinical evolution of these patients and discuss the implications of our findings.

Methods

Patients

For this study, the diagnosis of variant angina was made in patients who met the following criteria: burning or squeezing retrosternal chest pain at rest; sublingual nitroglycerin relieving the pain in less than 5 minutes; ST elevation of at least 0.2 mV not present on the baseline ECG but documented during pain and disappearing with relief of pain; and no subsequent evidence of myocardial necrosis. Variant angina was also diagnosed when these events were provoked by ergonovine.

Between March 1980 and April 1981, 83 patients were treated with PTCA at the Montreal Heart Institute. Generally accepted guidelines12, 13 were used in patient selection. The diagnosis of variant angina was made before referral for PTCA in only one of the 11 patients in this study. In three others, variant angina was detected during hospitalization before PTCA and in six the diagnosis was made within the 4 months after PTCA. The final patient had episodes of variant angina during the week after PTCA; variant angina had been documented at another hospital, but this fact was uncovered only after PTCA.

Patient Management

Candidates for PTCA underwent a graded treadmill exercise test with monitoring of 15 electrocardiographic leads and thallium-201 studies according to
previously described techniques,14 except if the patients were thought to have unstable angina. Efforts were made to record a 12-lead ECG during spontaneous episodes of angina at rest. In patients with suspected or documented variant angina, an ergonovine test was performed, usually in the coronary care unit using a protocol described in detail elsewhere,15 but occasionally during coronary arteriography.

Patients not known to have variant angina were treated with diltiazem, 90 or 120 mg, on the evening before and the morning of PTCA; patients with known variant angina received 90 or 120 mg of diltiazem, 20–40 mg of nifedipine and 60 mg of isosorbide dinitrate orally 2 hours before PTCA. All patients were treated with sulfinpyrazone, 200 mg four times daily, beginning 3 days before and continuing for 6 months after PTCA.

Coronary arteriography was performed by a percutaneous transfemoral approach using preformed polyethylene catheters;16 craniocaudal and caudocranial, sagittally angulated views of the left coronary artery were routinely filmed. All organic lesions were refilmed in multiple views after nitroglycerin administration. The PTCA technique we use is similar to that of Gründzig et al.17 The pressure gradient across the stenosis was measured before and after each balloon inflation except in patients 2 and 11, in whom a Simpson catheter17 was used. A USCI inflation device was used for balloon inflation; the inflation medium was contrast material warmed and diluted to 30% of the usual concentration. The number of balloon inflations varied depending on the residual gradient across the stenosis and the appearance of the lesion during control angiography filmed in at least three views. The first inflation was to 4 atmospheres for 5–10 seconds. With successive inflations the pressure was increased by 1-atmosphere increments to 5 or 6 atmospheres without increasing duration. If further inflations were required, the highest pressure was repeated and the duration was increased incrementally to a maximum of 25 seconds. During PTCA, nitroglycerin was infused intravenously at 10–30 μg/min in all cases. Boluses of intracoronary nitroglycerin were added if waxing and waning of the distal coronary artery pressure was noted or if partial coronary spasm was suspected because of the angiographic appearance of the artery.

For 24 hours after PTCA, all patients underwent continuous electrocardiographic monitoring. Graded treadmill exercise testing with 15 ECG leads was repeated at 1, 3 and 6 months after PTCA, including thallium-201 studies at the 1- and 6-month tests. Coronary arteriography was performed 6 months after PTCA in all cases. As described below, coronary arteriography was repeated sooner in some patients with suspected restenosis or variant angina. The treatment of variant angina after PTCA varied from patient to patient, influenced by the results of treatment in the earlier cases. As previously noted, all patients received calcium antagonists and long-acting nitrates before PTCA. Before the initial PTCA, no patient had been treated with a calcium antagonist for longer than 1 week. Calcium antagonists and nitrates were not given after the first PTCA, except to patient 3, but were restarted when variant angina recurred. Patients who underwent a second PTCA were treated with calcium antagonists for at least 6 months thereafter, irrespective of their clinical status.

All angiographic documents were interpreted independently by an experienced cardiovascular radiologist. Coronary artery stenoses are defined according to the criteria of the Coronary Artery Surgery Study:18 the estimated percentage of obstruction is derived from the angiographic view showing the greatest reduction in diameter for the vessel in question. All measurements were made after the administration of nitroglycerin and all comparisons between pre-PTCA and post-PTCA films were made using the same view.

Illustrative Case Summaries

Patient 1

A 43-year-old postman was referred for PTCA because of rest and effort angina of 2 months’ duration. Physical examination and the baseline ECG were normal. Coronary arteriography revealed a 70% proximal left anterior descending coronary artery (LAD) stenosis (fig. 1A) with otherwise normal arteries and a normal left ventriculogram. During the first 24 hours in the hospital, four episodes of rest angina occurred with ST elevation in leads V1 to V4, rapidly relieved by nitroglycerin. An exercise test was stopped at 6 minutes at a heart rate of 102 beats/min because of angina and ST elevation; the corresponding thallium scan revealed a large anterior zone of hypoperfusion that was absent from the resting scan. An ergonovine test was positive at a dose of 0.025 mg, with ST elevation in leads I, aV1, and V4 to V6.

Treatment with nifedipine, diltiazem and long-acting nitrates eliminated the spontaneous attacks of variant angina, and an ergonovine test during this treatment was negative to the maximal dose of 0.4 mg. Because of the patient’s reluctance to continue medical treatment, PTCA was performed, reducing the LAD stenosis from 70% to 35% (fig. 1B) and the gradient from 38 to 13 mm Hg. Coronary spasm did not occur during the procedure. Three days later, all medication was discontinued and angina did not recur. An ergonovine test was negative to the maximal dose.

The patient was discharged without cardiac medication and remained asymptomatic for 2 months. At 2 months, coronary arteriography was repeated and showed no change; however, an ergonovine test done during angiography induced angina. ST elevation and severe coronary spasm localized to the site of the residual lesion (fig. 1C). Rest angina recurred 1 week later, with several episodes per day. Nifedipine and diltiazem were represcribed. During the next 3 months, only three episodes of rest angina and no effort angina occurred. Thereafter, typical effort angina appeared.

Coronary arteriography 6 months after PTCA demonstrated a restenosis graded at 70% (fig. 1D). PTCA was repeated without difficulty, leaving a residual stenosis of 25%. Nifedipine and diltiazem were conti-
ued after the second PTCA, and the patient had neither rest nor effort angina. Coronary arteriography 6 months after the second PTCA showed a partial restenosis graded at 50%; ergonovine administration during arteriography induced focal coronary spasm less intense than that after the first PTCA.

**Patient 6**

A 36-year-old engineer was referred for PTCA because of effort angina of 3 months’ duration in spite of medical treatment. Two months previously he had been hospitalized because of rest angina. An 85% proximal isolated LAD stenosis (fig. 2A) with otherwise normal arteries and a normal left ventriculogram were found. Rest angina occurred infrequently and an ECG was never recorded during an episode. An ergonovine test was not done.

PTCA was performed without incident, reducing the stenosis from 85% to 30% (fig. 2B) and decreasing the gradient from 60 to 10 mm Hg. Angina disappeared completely, but 6 weeks later rest and effort angina recurred abruptly. An ergonovine test induced angina and ST elevation in leads V₁ to V₃ at a dose of 0.2 mg. At repeat coronary arteriography, a restenosis graded at 85% was seen at the site of PTCA (fig. 2C). Thus, PTCA was repeated, reducing the stenosis to 30% (fig. 2D) and reducing the gradient from 40 to 10 mm Hg.

The patient was discharged with no antianginal medication. No effort angina was noted, but he complained of rest angina, particularly in the early morning hours. During rest angina, ECGs revealed either ST elevation in V₁ and V₃ or ST depression in V₄ to V₆. At coronary arteriography, a 60% restenosis was observed (fig. 2E). Ergonovine administration during arteriography induced angina, ST elevation in leads V₁ to

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**Figure 1.** Left coronary arteriograms in the left anterior oblique view from patient 1. (A) Before the first percutaneous transluminal coronary angioplasty (PTCA). The arteriogram reveals a 70% proximal left anterior descending coronary artery (LAD) stenosis. (B) Immediately after the first PTCA. The 70% LAD stenosis has been successfully dilated, leaving a residual 35% stenosis. (C) After ergonovine administration 2 months after the first PTCA. The LAD is completely obstructed at the site of the previous stenosis (arrow). Angina and ST elevation in the anterior ECG leads coincided with the occurrence of coronary spasm. Before ergonovine and after nitroglycerin administration, the LAD appeared as in panel B. (D) Six months after the first PTCA, arteriography reveals a 70% LAD restenosis at the site of the original lesion.
Figure 2. Left coronary arteriogram in the right anterior oblique view from patient 6. (A) Before the first percutaneous transluminal coronary angioplasty (PTCA). The arteriogram reveals an 85% proximal left anterior descending coronary artery (LAD) stenosis. (B) Immediately after the first PTCA. The LAD stenosis is reduced to 30%. (C) Six weeks after the first PTCA. The proximal LAD stenosis graded at 85% has recurred at the site of PTCA. (D) After the second PTCA. The 85% LAD stenosis has again been reduced to 30%. (E) Two months after the second PTCA. An LAD restenosis graded at 60% is seen at the site of the previous PTCA. (F) After ergonovine administration 2 months after the second PTCA. Angina and ST elevation in leads V1 to V3 accompanied the severe coronary spasm observed in this illustration at the site of PTCA. Coronary spasm disappeared promptly after nitroglycerin administration and repeat arteriograms were similar to panel E.
V₃ and coronary spasm at the site of restenosis (fig. 2F). Nine months later, infrequent episodes of rest angina occurred despite treatment with diltiazem, 120 mg three times daily.

Results

Table 1 is a summary of the clinical and angiographic data before and after PTCA for the 11 patients in this study. Table 2 is a summary of the clinical outcomes.

Before PTCA

All 11 study patients had rest angina; 10 of the 11 also had effort angina before PTCA. The mean duration of rest angina was 3.9 months (range 1–8 months) and of effort angina was 3 months (range 1–6 months). The clinical syndrome of variant angina was documented before PTCA in five patients (nos. 1–5). In three of these five, transient ST elevation was present on an ECG recorded during rest angina. In the other two, ergonovine administration induced angina and ST elevation.

Only one of the six patients in whom variant angina was diagnosed after PTCA (patient 11) had an ECG recorded during an episode of rest angina and only one (patient 10) had an ergonovine test beforehand; the procedure was normal in both patients.

Each patient had a proximal LAD stenosis graded at 65–95%. No patient had an additional coronary lesion >50% elsewhere except for patient 9, who had a 60% distal right coronary artery stenosis. ST elevation was localized to the anterior ECG leads in all 11 cases, in the territory of the LAD stenosis. Each of the four patients (nos. 1, 6, 7 and 9) who had spontaneous or provoked spasm during arteriography had focal spasm at the site of the LAD lesion.

After PTCA

Patients 1–5 had variant angina documented before PTCA; patients 1–4 had a successful PTCA. In patient 5, the lesion could not be crossed. Variant angina recurred after PTCA in three of the four successful cases (patients 1, 2 and 4). Restenosis was documented in two (patients 1 and 4); a second PTCA was successful in one (patient 1); the other (patient 4) received medical therapy. In the third patient (no. 2), variant angina recurred during the week after PTCA; treatment with calcium antagonists eliminated all symptoms, and repeat coronary arteriography at 6 months demonstrated no restenosis.

PTCA was also successful in patients 6–11, in whom variant angina was not diagnosed before PTCA. Variant angina was demonstrated after PTCA by an ECG recorded during rest angina in three, patients 6, 9 and 11, and by ST elevation during an ergonovine test in patients 7, 8 and 10. In spite of the initially successful result in these six patients, three (nos. 6, 10 and 11) developed restenosis and two others (nos. 7 and 9) developed severe lesions adjacent to the site of PTCA within 4 months of the procedure. In patient 8, variant angina was detected soon after PTCA, treatment with calcium antagonist drugs eliminated all symptoms and repeat arteriography at 6 months demonstrated no restenosis or new lesions.

Overall, coronary artery spasm did not occur during 14 of the 15 PTCA’s in the 11 study patients, including repeat PTCA’s for restenosis in patients 1, 6 and 10. Patient 9 was the only patient who developed complications during PTCA. His first PTCA was successful, reducing the LAD stenosis from 65% to 25% and the gradient from 30 to 15 mm Hg, but 3½ months later, rest angina recurred, with ST elevation in leads aV₃ and V₃ to V₆. Arteriography revealed no change in the LAD at the site of PTCA, but a new 75% stenosis had developed in the mid-LAD since the previous arteriogram. PTCA reduced this lesion to 40%, but during the procedure coronary spasm developed that completely occluded the LAD at the site of the initial PTCA and required intracoronary nitroglycerin for relief. Six hours later the patient had an acute anterior transmural infarction.

Patients 1, 6 and 10 had a technically successful repeat PTCA, but variant angina persisted after this procedure in patients 6 and 10 and patient 1 continued to have a positive response to ergonovine, but remained angina-free on calcium-antagonist drugs.

Discussion

This study indicates that PTCA is technically feasible in patients with variant angina and a coexisting organic coronary stenosis. All of our patients were premedicated with at least one calcium-antagonist drug, and during PTCA, all received an infusion of i.v. nitroglycerin. Coronary spasm occurred in only one patient during PTCA, and although this patient subsequently developed a myocardial infarction, the incidence of complications in these patients does not appear to be much higher than that in other patients who undergo PTCA. PTCA has not been recommended for patients with coronary spasm. Spasm during PTCA has, in a few cases, been associated with infarction or has been an indication for urgent bypass surgery. Coronary spasm during PTCA is a distinct clinical entity, analogous to catheter-induced spasm during coronary arteriography, but unrelated to the spontaneous or ergonovine-induced spasm that occurs in variant angina. In each of the patients in this study, variant angina was documented either before or 3 days to 4 months after PTCA, and was thus independent of PTCA-related coronary spasm. The possibility that PTCA caused vessel injury and subsequent spasm seems unlikely because an asymptomatic interval of at least 4 weeks followed PTCA in seven of the nine patients with variant angina after PTCA.

The syndrome of variant angina is characterized by frequent spontaneous exacerbations and remissions, making the effect of any treatment difficult to evaluate; however, our results indicate that PTCA alone is inadequate treatment for variant angina. Variant angina recurred after a successful first PTCA in three of four cases and after a successful repeat PTCA
in two of two additional patients. The data from this study are insufficient to determine whether the combination of PTCA with appropriate medical treatment improves the prognosis of selected patients with variant angina compared with medical treatment alone. The incidence of restenosis after successful PTCA has not been accurately defined, but is probably 15–20% in the first 6 months. In contrast, seven of the 10 successfully dilated patients in this study developed either restenosis or a new severe lesion adjacent to the site of PTCA within 6 months. These results raise the possibility that multiple episodes of focal coronary spasm could have caused restenosis in these patients. The fact that the three patients who did not develop restenosis had been treated with calcium antagonists soon after PTCA and had remained angina-free adds further support to this hypothesis. Few data are available defining the rate of progression of coronary obstructive disease in patients with variant angina compared with other coronary patients. Recently, Marzilli et al. speculated that a cause of atherosclerotic lesions in all patients with ischemic heart disease might be coronary spasm. The evidence supporting this contention is scanty. Nevertheless, it is attractive to postulate that the cause of restenosis in PTCA patients with variant angina could be repetitive coronary spasm.

A high incidence of variant angina, often undiagnosed, is present in patients referred to our institution for PTCA. The selection criteria for PTCA, severe angina in spite of medical treatment, a proximal, isolated, noncalcified stenosis of a single vessel without

<p>| Table 1. Clinical and Angiographic Data of Patients Before and After Percutaneous Transluminal Coronary Angioplasty |
|-----------|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Pt</th>
<th>Duration of angina (months)</th>
<th>ECG during</th>
<th>PTCA</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>43</td>
<td>M</td>
<td>Rest</td>
<td>Rest angina</td>
<td>Ergonovine test</td>
<td>% LAD stenosis</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>F</td>
<td>Effort</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 35</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>M</td>
<td>2</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>4</td>
<td>43</td>
<td>M</td>
<td>3</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>F</td>
<td>5</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>6</td>
<td>36</td>
<td>M</td>
<td>1</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>7</td>
<td>51</td>
<td>M</td>
<td>2</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>8</td>
<td>52</td>
<td>M</td>
<td>4</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>9</td>
<td>69</td>
<td>M</td>
<td>1</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>10</td>
<td>41</td>
<td>M</td>
<td>6</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>11</td>
<td>59</td>
<td>F</td>
<td>4</td>
<td>ST</td>
<td>Not done</td>
<td>70 → 30</td>
</tr>
<tr>
<td>Mean</td>
<td>3.9</td>
<td>3.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Appearance of a LAD stenosis at a site other than that of PTCA. Abbreviations: PTCA = percutaneous transluminal coronary angioplasty; LAD = left anterior descending coronary artery; ST = ST-segment depression; Th pos = positive thallium exercise scan without ST changes; LM = left main coronary artery; CABG = coronary artery bypass grafting; CA = calcium-antagonist drug, either nifedipine or diltiazem; MI = myocardial infarction.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Clinical Evolution of Study Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlined numbers refer to patients with variant angina diagnosed before their initial PTCA. Restenosis group includes 2 patients whose new lesions were not at PTCA site but in adjacent segments. See text for details. Abbreviations: PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass grafting; MI = myocardial infarction.</td>
</tr>
</tbody>
</table>
complete occlusion but with well-preserved left ventricular function, are biased in favor of patients with variant angina. In one survey,26 30 of 500 patients undergoing coronary arteriography because of intractable symptoms had one-vessel disease ideal for PTCA; in contrast, 28 of the 124 variant angina patients treated at our institution during the past 5 years, excluding the patients in this study, were PTCA candidates using the same angiographic criteria.

Thus, the possibility of variant angina should be considered in patients with angina at rest referred for PTCA and in patients with restenosis after PTCA. In our experience, the results of PTCA are excellent in patients with rest angina who do not have variant angina. However, patients with variant angina may not benefit from PTCA, and they should be treated with calcium antagonists whether PTCA is performed or not. Diagnostic procedures such as exercise testing14,27 or ergonovine administration15 may be required in many cases to confirm variant angina.

References

21. Waters DD, Szlachcic J, Miller D, Théroux P: Clinical characteristics of patients with variant angina complicated by myocardial infarction or death within one month. Am J Cardiol 49: 658, 1982

Table 1. (Continued)

<table>
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<tr>
<th>After PTCA</th>
<th>ECG during</th>
<th>Angina Rest</th>
<th>Effort</th>
<th>Rest angina</th>
<th>Exercise test</th>
<th>Ergonovine test</th>
<th>% LAD stenosis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>No ECG</td>
<td>No ECG</td>
<td>No ECG</td>
<td>ST</td>
<td>ST</td>
<td>35 → 75</td>
<td>Repeat PTCA → asymptomatic on CA</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>↑ ST</td>
<td>↑ ST</td>
<td>↑ ST</td>
<td>ST</td>
<td>ST</td>
<td>85</td>
<td>Repeat PTCA → repeat restenosis + variant angina</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>No ECG</td>
<td>↓ ST</td>
<td>↓ ST</td>
<td>Not done</td>
<td>ST</td>
<td>50</td>
<td>New 75% LM stenosis → CABG</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>No ECG</td>
<td>No ECG</td>
<td>No ECG</td>
<td>↓ ST</td>
<td>↑ ST</td>
<td>75 → 30</td>
<td>Repeat PTCA → variant angina → CA → asymptomatic</td>
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<tr>
<td>Yes</td>
<td>No</td>
<td>↑ ST</td>
<td>↓ ST</td>
<td>↑ ST</td>
<td>No ECG</td>
<td>ST</td>
<td>75 → 30</td>
<td>Repeat PTCA → variant angina → CA → asymptomatic</td>
</tr>
</tbody>
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Failure of Thromboxane A<sub>2</sub> Blockade to Prevent Attacks of Vasospastic Angina

S. Chierchia, M.D., R. de Caterina, M.D., F. Crea, M.D., C. Patrono, M.D., and A. Maseri, M.D.

SUMMARY Thromboxane A<sub>2</sub> (TxA<sub>2</sub>), released by aggregating platelets, has been proposed as a potential mediator of coronary vasospasm. We studied six patients with variant angina, a clinical syndrome due to coronary vasospasm, and one patient with frequent recurrent episodes of transient ST-segment depression at rest in whom the spasm was demonstrated angiographically. All patients underwent continuous ECG monitoring for 2 days before and 2 days after a single, low, i.v. dose of aspirin (2 mg/kg), which reduced TxB<sub>2</sub> (the stable metabolite of TxA<sub>2</sub>) to less than 3% of the control values. There were 129 transient ischemic episodes during control and 146 after aspirin, when platelet TxB<sub>2</sub> was reduced to negligible levels. The duration, severity and incidence of symptomatic episodes were not significantly affected by TxA<sub>2</sub> blockade. We conclude that platelet TxA<sub>2</sub> is probably not responsible for the initiation of coronary vasospasm.

THROMBOXANE A<sub>2</sub> (TxA<sub>2</sub>), a derivative of arachidonic acid, is mainly produced by platelets and actively released during platelet release reaction. TxA<sub>2</sub> is a powerful constrictr of vascular smooth muscle and may be a cause of coronary vasospasm. Increased levels of thromboxane B<sub>2</sub> (TxB<sub>2</sub>), the stable nonenzymatic metabolite of TxA<sub>2</sub>, have been found in the peripheral blood of patients with variant angina, a widely recognized hallmark of vasospastic ischemia. Whether high levels of TxA<sub>2</sub> play a primary role in precipitating coronary vasospasm or merely represent an epiphenomenon of transient myocardial ischemia, however, is still uncertain.

The present study was aimed at assessing the effects of a single, low, i.v. dose of aspirin, which blocks the release of platelet TxA<sub>2</sub>, on the number, severity and duration of episodes of transient acute ischemia caused by coronary vasospasm.

Material and Methods

We studied seven consecutive male patients, ages 39–60 years (mean 52 years), who had frequent episodes of angina at rest. Transient ST-segment elevation was documented in six patients by serial 12-lead ECGs recorded in the coronary care unit during several anginal episodes; ST-segment depression was consistently observed in one patient (BU), in whom spasm was demonstrated angiographically. Every patient underwent continuous ECG monitoring/recording in the coronary care unit to assess objectively the frequency of ischemic episodes even if asymptomatic. The ECG lead showing the most evident ST-segment changes during the episode was selected for this purpose. All seven patients had 10 or more episodes of transient myocardial ischemia per day documented by typical transient ischemic changes.

Coronary arteriography, performed in all patients by the Judkins technique, showed variable degrees of atherosclerotic disease, from normal coronary arteries (one patient) to three-vessel disease (one patient). During angiography, a transient vasospasm of the left circumflex coronary artery in one patient and the right coronary artery in another occurred spontaneously. In one, the spasm completely occluded the vessel and was accompanied by ST-segment elevation in the inferior leads; in the other (BU), the spasm was not occlusive, markedly delayed distal filling and was accompanied by ST-segment depression in the inferolateral leads. In both patients, the spasm was promptly relieved by intracoronary nitrates. We no longer consider it essential to perform provocative tests in patients with electrocardiographically proved variant angina, particularly when the stress test is negative (three patients) or positive at a rather high work load only (four patients).
Percutaneous transluminal coronary angioplasty in patients with variant angina.
P R David, D D Waters, J M Scholl, J Crépeau, J Szlachcic, J Lespérance, G Hudon and M G Bourassa

Circulation. 1982;66:695-702
doi: 10.1161/01.CIR.66.4.695

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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