Relation of basal coronary tone and vasospastic activity in patients with variant angina

Yukio Ozaki, David Keane, Patrick W Serruys

Abstract

Objective—To examine the vasoconstrictor response to ergonovine and the vasodilator response to isosorbide dinitrate in spastic and non-spastic coronary segments from 31 patients undergoing serial angiographic follow up of variant angina.

Methods—Coronary angiograms and ergonovine provocation tests were repeated at an interval of 45 (SD 15) months apart. While all 31 patients showed a positive response to ergonovine initially, vasospastic responsiveness persisted in only 16 patients at follow up (group 1) and not in the other 15 patients in whom symptoms of variant angina had resolved (group 2). Mean luminal diameter of 170 normal or near normal entire coronary segments (American Heart Association classification) were measured (a) at baseline, (b) after the administration of ergonovine, and (c) after the administration of isosorbide dinitrate, during both the initial and follow up angiograms using a computer based quantitative angiography analysis system (CAAS II).

Results—In vasospastic patients (initial and follow up angiograms in group 1, and initial angiogram in group 2), basal tone was significantly higher in spastic segments compared to adjacent segments or segments in non-spastic vessels. The diagnostic sensitivity and specificity at 20% increase in basal coronary tone for the prediction of vasospasm were 77% and 73%, respectively.

Conclusions—Coronary artery tone may change in proportion to the activity of variant angina over several years. Contrary to some previous reports, the estimation of basal coronary tone may be useful in the assessment of vasospastic activity in patients with variant angina.

Keywords: coronary spasm, variant angina, ergonovine provocation test, quantitative coronary angiography

Coronary vasospasticity plays an integral role in the genesis of variant angina, some types of acute myocardial infarction, and restenosis after balloon angioplasty.1-9 The proposed mechanism of vasospasm includes hypersensitivity to endothelium derived factors, platelet derived vasoactive substances, and autonomic nervous tone.10-13 Basal coronary tone is felt to be related to the regulation of vascular smooth muscle tension by local endothelium derived factors, humoral factors, and parasympathetic nervous tone.14-16 Thus similar factors may play a role in both vasospasm and the mediation of basal coronary tone. Despite the common mediators, previous clinical studies attempting to determine whether basal coronary tone is increased in patients with vasospastic angina have yielded conflicting evidence17-22 and the chronological interaction of basal coronary tone and vasospastic activity over several years is unknown.

To examine the role of coronary tone, its chronological changes, and its relation to vasospastic anginal attacks, we compared basal coronary tone and vasospastic activity during both initial and follow up angiographic studies in 31 patients. We measured changes in mean luminal diameter of each entire spastic segment, segments adjacent to the spastic segment, and segments in non-spastic vessels at baseline, after administration of ergonovine and after administration of isosorbide dinitrate, using computer based quantitative coronary angiography.

Methods

PATIENT SELECTION

Thirty one patients who met the following criteria of variant angina were included in the study: (1) chest pain at rest associated with ST segment changes of more than 0.2 mV on ECG; (2) pain relief immediately following the administration of glyceryl trinitrate; (3) no subsequent evidence of myocardial infarction; and (4) ergonovine provoked coronary spasm associated with chest pain and ischaemic ECG changes. Coronary spasm was defined as a transient total or nearly total occlusion reversible with isosorbide dinitrate, or as a transient but significant (> 50%) narrowing reversible with isosorbide dinitrate in normal or nearly normal segments.2-24

The disease activity of vasospastic angina was assessed by anginal symptoms, 12-lead ECG during symptoms, and ambulatory in-hospital electrocardiographic monitoring, or Holter monitoring out of hospital. Of the 31 patients who had symptoms of variant angina at the time of the initial angiographic study, 16
had persistent symptoms of vaso- spasms of angina
with ischaemic electrocardiographic changes during
the follow up period, and vaspasm was reproduced at
the same coronary site at the follow up angio-gram (group 1), while in 15 patients symptoms of variant angina
had resolved completely and neither ischaemic ST-segment
changes nor positive response to ergonovine was demonstrated during follow up (group 2).

Table 1 shows the clinical and electrocardiographic characteristics of the two groups.

There were no significant differences in age, gender, duration of follow up, coronary risk
factors, or location of ischaemic ST-segment
changes on ECG. One patient of each group
with ST elevation in both anterior and inferior
leads had spasm in the right coronary and left
anterior descending coronary arteries.

It has been reported that the response to an
ergonovine provocation test is of value in the
prediction of spontaneous activity of vaso-
spastic angina.²⁵⁻²⁶ We therefore performed follow
up angiography and ergonovine provocation
testing when progression of coronary athero-
sclerosis was suspected, frequency of anginal attacks increased, or vaspasm activity was
thought to have resolved, and it may no longer
have been necessary to continue long term
drug treatment. In patients who had a negative
response to ergonovine at the follow up test
(group 2) the treatment dose was tapered or
discontinued after the follow up angiogram.
At angiographic follow up, coronary spasm was
observed at the same coronary arterial site in
group 1, while no spasm was reproduced at
follow up in group 2.

STUDY PROTOCOL

The study was approved by the hospital's ethics
committee and informed written consent
was obtained from each patient before examination.
All patients were admitted to the coronary care
unit before the study. Sublingual glyceryl trinitrate was given as
required, but calcium antagonists and oral
nitrates were gradually tapered, and calcium
antagonists were discontinued for 36 h and
oral nitrates was discontinued for 24 h before
the study. Coronary angiography was
performed in the morning (from 8:30 to 11:00
am) by the Sones technique at Anjo Kosei
Hospital in Japan.

After baseline angiograms suitable for quan-
titative analysis of the right and left coronary
arteries had been obtained, 0.2 mg ergonovine
maleate was given intravenously by a rapid
bolus injection. Radiographic projections were
identical during the sequential angiographic
studies. Heart rate and aortic pressure were
monitored continuously, and 12-lead ECGs
were recorded at 30 s intervals. Whenever
chest pain or significant ST segment changes
were observed, selective coronary angiograms
were immediately performed. In patients of
group 2 at follow up, unresponsiveness to
ergonovine was confirmed by the administra-
tion of a further rapid bolus of up to 0.4 mg
ergonovine. In group 1 at both tests and group
2 at the initial test, all coronary spasms were
observed after the first administrated dose of
ergonovine (0.2 mg).

Coronary vaspasm was relieved by isosor-
dibide dinitrate, given as one or two intracor-
only boluses to a total of 5 mg. To exclude the
possibility of persistent spasm, we gave a dose
(5 mg) of intracoronary isosorbide dinitrate
which was previously shown to achieve maximum coronary vaso-
dilatation in patients with vaso- spastic angina
(3 mg).²⁷⁻²⁸

The follow up angiography and provocation
tests were performed in the same angiographic
projection as the initial angiogram after view-
ing the initial angiographic records and cine-
film. The response to ergonovine and isosorbide dinitrate and the severity of fixed
stenosis after the administration of isosorbide
dinitrate were quantified in matched views
between the initial and follow up angiograms
using a quantitative angiographic analysis
system.

QUANTITATIVE CORONARY ANGIOGRAPHIC

The new version of the computer based
Coronary Angiography Analysis System
(CAAS II)²⁹ was used to perform the quantita-
tive analysis in a core angiographic laboratory
(Cardialysis, Rotterdam, The Netherlands). In
the CAAS analysis, which has been described
elsewhere previously,²⁹⁻³³ the entire cineframe
of size 18 × 24 mm is digitised at a resolution
of 1329 × 1772 pixels. Correction for pin-
cushion distortion is performed before anal-
ysis. Boundaries of a selected coronary segment
are detected automatically. The absolute
diameter of the stenosis (in mm) is determined
using the guiding catheter as a scaling device.
To standardise the method of analysis of the
initial and follow up angiograms, the following
measures were taken: all study frames selected
for analysis were end diastolic to min-
imise motion artefact; and arterial segments
were measured between the same identifiable
branch points at baseline, after the administra-
tion of ergonovine, and after the administra-
tion of isosorbide dinitrate. Changes in the
mean luminal diameter of each entire coronary
segment as well as the minimum luminal
diameter of each analysed coronary segment
were studied.

ANALYSED SEGMENTS

In group 1, the 16 spastic segments studied
were located in the right coronary artery

---

<table>
<thead>
<tr>
<th>Table 1 Baseline characteristics of 31 patients with vaso- spasms of angina in groups 1 and 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Age, years (SD)</td>
</tr>
<tr>
<td>Male/female</td>
</tr>
<tr>
<td>Follow up period, months (SD)</td>
</tr>
<tr>
<td>Coronary risk factors (No of patients)</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Site of ST elevation</td>
</tr>
<tr>
<td>Anterior</td>
</tr>
<tr>
<td>Inferior</td>
</tr>
<tr>
<td>Both</td>
</tr>
</tbody>
</table>
Basal coronary tone and vasospastic activity in variant angina

(RCA) in eight patients, left anterior descending coronary artery (LAD) in two patients, and left circumflex coronary artery (LCX) in six patients. In group 2, the 16 spastic segments were located in the RCA in eight patients, the LAD in six patients, and the LCX in two patients. The three major coronary arteries were divided according to the classification of the American Heart Association (AHA) committee report. The proximal and distal segments of each coronary artery were analysed. The proximal segment of the RCA was taken as AHA segments 1 and 2, the distal segment of the RCA was AHA segment 3, the proximal segment of the LAD was AHA segment 6, the distal segment was AHA segment 7, the proximal segment of the LCX was AHA segment 11, and the distal segment was AHA segment 13.

For the purpose of this study only angiographically normal or nearly normal segments were selected. Of a total of 93 major coronary arteries in both groups, four vessels in each group with a significant stenosis (>50% diameter stenosis) were excluded from analysis. Sixteen spastic AHA segments, 16 AHA segments adjacent to spastic segments (adjacent segment), and 56 segments in non-spastic vessels were estimated in group 1; 16 spastic AHA segments, 16 segments adjacent to spastic segments, and 50 segments in non-spastic vessels were assessed in group 2.

ESTIMATION OF BASAL CORONARY TONE AND VASOCONSTRICTION
Basal coronary tone and vasoconstriction were determined from the change in the mean luminal diameter of each entire AHA coronary segment at baseline, after the administration of ergonovine, and after the administration of isosorbide dinitrate. To express the degree of basal coronary artery tone and the degree of vasoconstriction, the per cent dilatation after administration of isosorbide dinitrate and per cent vasoconstriction after administration of ergonovine were used as follows:

\[
\text{Basal coronary tone (dilatation after isosorbide dinitrate)} (\%) = \left( \frac{\text{Mean luminal diameter after isosorbide dinitrate} - \text{Baseline mean luminal diameter}}{\text{Baseline mean luminal diameter}} \right) \times 100
\]

Constriction after ergonovine (\%) = \left( \frac{\text{Baseline mean luminal diameter} - \text{mean luminal diameter after ergonovine}}{\text{Baseline mean luminal diameter}} \right) \times 100

Table 2. Mean diameter of coronary artery segment and response to ergonovine during initial and follow up angiograms in groups 1 and 2. Values are means (SEM)

<table>
<thead>
<tr>
<th>Segment Type</th>
<th>Initial Angiogram</th>
<th>Follow up Angiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (mm)</td>
<td>After ergonovine (mm)</td>
</tr>
<tr>
<td><strong>Group 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spastic</td>
<td>2.14 (0.10)</td>
<td>1.56 (0.08)</td>
</tr>
<tr>
<td>Adjacent to spastic</td>
<td>2.28 (0.09)</td>
<td>1.90 (0.09)</td>
</tr>
<tr>
<td>Non-spastic</td>
<td>2.61 (0.07)</td>
<td>2.00 (0.07)</td>
</tr>
<tr>
<td><strong>Group 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spastic</td>
<td>2.07 (0.12)</td>
<td>1.46 (0.09)</td>
</tr>
<tr>
<td>Non-spastic</td>
<td>2.22 (0.10)</td>
<td>1.94 (0.10)</td>
</tr>
</tbody>
</table>

**DIAGNOSTIC PREDICTIVE VALUES OF BASAL TONE FOR VASOSPASM IN CORONARY ARTERY**

The diagnostic sensitivity and specificity were defined as follows:

\[
\text{Diagnostic sensitivity} (%) = \frac{\text{True positive}}{\text{True positive + false negative}} \times 100
\]

\[
\text{Diagnostic specificity} (%) = \frac{\text{True negative}}{\text{True negative + false positive}} \times 100
\]

While the true positive value indicates the number of spastic segments in spastic vessel which show basal coronary tone above a value of coronary tone, the false negative value indicates the number of spastic segments in spastic vessel which show basal coronary tone below the same value. While the true negative value indicates the number of non-spastic segments in non-spastic vessel which show basal coronary tone below a value of coronary tone, the false positive value indicates the number of non-spastic segments in the non-spastic vessel which show basal coronary tone above the same value.

**STATISTICAL ANALYSIS**

All values are expressed as mean (SEM). The paired Student t test was used to compare the chronological changes at the same segment in the same patients. The unpaired Student t test was used to compare different segments or different patient groups. Differences between proportions were analysed by the χ² test with correction. A P value of less than 0.05 was considered significant.

**Results**

**RESPONSE TO ERGONOVINE AT THE SPASTIC SITE**

Coronary spasm was observed at the same site in group 1, while no spasm was reproduced at follow up in group 2. In group 1, the absolute reduction in the minimum luminal diameter in the spastic segment was 1.21 (SEM 0.09) mm with a reduction in minimum diameter of 70 (5%) during the initial angiogram and 1.05 (0.09) mm [68 (5%) reduction] at follow up; in group 2, the reduction in minimum luminal diameter 1.04 (0.09) mm [69 (5%) reduction] during the initial angiogram and 0.32 (0.07) mm [15 (3%) reduction] at follow up.
Table 3  Mean diameter of coronary artery segment and response to isosorbide dinitrate during initial and follow up angiograms in groups 1 and 2. Values are means (SEM)

<table>
<thead>
<tr>
<th></th>
<th>Initial angiogram</th>
<th>Follow up angiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (mm)</td>
<td>After isosorbide</td>
</tr>
<tr>
<td>Group 1</td>
<td></td>
<td>dinitrate (mm)</td>
</tr>
<tr>
<td>Spastic segment</td>
<td>2.14 (0.10)</td>
<td>2.84 (0.14)</td>
</tr>
<tr>
<td>Adjacent to spastic segment</td>
<td>2.28 (0.09)</td>
<td>2.78 (0.10)</td>
</tr>
<tr>
<td>Segment of non-spastic vessel</td>
<td>2.61 (0.07)</td>
<td>3.02 (0.07)</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spastic segment</td>
<td>2.07 (0.12)</td>
<td>2.80 (0.18)</td>
</tr>
<tr>
<td>Adjacent to spastic segment</td>
<td>2.22 (0.10)</td>
<td>2.73 (0.16)</td>
</tr>
<tr>
<td>Segment of non-spastic vessel</td>
<td>2.52 (0.07)</td>
<td>2.87 (0.08)</td>
</tr>
</tbody>
</table>

Adjacent to spastic segment, segments either proximal or distal to the spastic segment.

**VASOMOTOR BEHAVIOUR OF THE SEGMENTS AT THE INITIAL AND FOLLOW UP TESTS**

Table 2 shows the average values of mean luminal diameter of each spastic segment, of the adjacent segments, and of segments of non-spastic vessels at baseline and after administration of ergonovine, and the per cent vasoconstriction, in groups 1 and 2. Table 3 gives the average value of the mean luminal diameter at baseline and after administration of isosorbide dinitrate, and the per cent dilatation (basal coronary tone) in groups 1 and 2.

Figure 1 Group 1: Vasomotor responses to ergonovine (constriction) and isosorbide dinitrate (basal tone) in spastic segments (black bar), adjacent segment (hatched bar), and segments in non-spastic vessels (white bar) of patients in group 1 at the initial and follow up angiograms. Vasoconstriction and basal coronary tone in the three segments were similar between the initial and follow up tests. Error bar indicates 1 SEM.

![Figure 1](http://heart.bmj.com/)

Figure 2 Group 2: Vasomotor responses to ergonovine (constriction) and isosorbide dinitrate (basal tone) in spastic segments (black bar), adjacent segments (hatched bar), and segments in non-spastic vessels (white bar) of patients in group 2 at the initial and follow up angiograms. Vasoconstriction and basal coronary tone in the spastic segments decreased significantly from the initial to the follow up tests. Basal tone of the adjacent segments also decreased from the initial to the follow up test, while vasoconstriction of the adjacent segments was unchanged (NS). Segments in non-spastic vessels showed similar vasoconstriction and basal coronary tone at both tests (NS). Error bar indicates 1 SEM.

![Figure 2](http://heart.bmj.com/)
spastic vessels. Although vasoconstriction in the adjacent segments was not significantly different from the vasoconstriction in segments of non-spastic vessels, basal tone in the adjacent segment was greater than that of segments in non-spastic vessels during both the initial and follow up tests.

**Group 2**

Figure 2 shows the vasoconstriction and basal coronary tone in group 2. During the initial test, vasoconstriction of the spastic segments was greater than in the adjacent segments or in segments in non-spastic vessels. During the initial test, vasoconstriction was comparable in adjacent segment and non-spastic segments, while basal coronary tone in the spastic segment was greater than in the adjacent segments and in the segments of non-spastic vessels. Furthermore, during the initial test, basal tone in the adjacent segments was greater than in the segments of non-spastic vessels. At follow up, no difference was observed in either vasoconstriction or basal tone among previously spastic and adjacent segments and segments in non-spastic vessels. Both vasoconstriction and basal coronary tone of the spastic segments decreased significantly from the initial to the follow up angiograms. Basal tone of the adjacent segments also decreased significantly from the initial to the follow up angiograms. Vasoconstriction of the adjacent segment was similar during the initial and follow up angiograms. We found no difference in vasoconstriction and basal tone of segments in non-spastic vessels between the initial and follow up angiograms.

**Predictive Value of Basal Tone for the Presence of Vasospasm**

Figure 3 shows distribution curves of the sensitivity and specificity of basal coronary tone for the prediction of vasospasm in coronary artery. The sensitivity and specificity were calculated from all 48 spastic segments in spastic vessels and all 162 non-spastic segments in non-spastic vessels in the initial and follow up angiograms of group 1 and the initial angiogram of group 2. At 20% increase in basal tone, which is the nearest rounded number to the crossing point of two distribution curves, the sensitivity was 77% and the specificity 73%.

**Discussion**

The specific findings of this study are as follows: (1) neither basal coronary tone nor vasoconstriction changed over time in patients with persistent variant angina, while in patients in whom symptoms of variant angina resolved, both vasoconstriction and basal coronary tone of previously spastic segments were restored to normal; (2) vasoconstriction in adjacent segments and segments in non-spastic vessels was equivalent both in patients with active disease and in patients with inactive disease; (3) in patients with active disease, basal tone in spastic segments was greater than in adjacent segments or segments in non-spastic vessels; (4) adjacent segments only showed increased basal coronary tone compared to segments in non-spastic vessels during the period of disease activity.

**Discordant Findings of Previous Studies**

Previous studies have provided conflicting evidence on whether basal coronary tone is increased in spastic segments. Hill et al reported that basal coronary tone in the spastic site, estimated after the administration of 0.4 mg of sublingual glyceryl trinitrate, was greater than in non-spastic sites in 17 patients with variant angina. Hoshino et al reported that coronary artery tone assessed after the administration of 5 mg intracoronary isosorbide dinitrate was greater in the entire coronary tree in 30 patients with variant angina than in 35 patients without coronary spasm. Hackett et al, however, found that basal coronary tone, analysed after the administration of 2 mg intracoronary isosorbide dinitrate, was not different at spastic sites than at non-spastic sites in six patients with variant angina. Kaski et al also found that basal coronary tone of segments in non-spastic vessels, estimated after the administration of 1 to 2 mg intracoronary isosorbide dinitrate, was not different between 13 patients with variant angina and 41 patients without coronary spasm. Kuga et al found that basal coronary tone was increased in 15 patients with variant angina but not in five others after the administration of 0.26 mg intravenous glyceryl trinitrate.

The conflicting results of previous studies may relate to differences in patient selection and the methods employed, including (1) use of nitrates, (2) selection of angiographic segments, and (3) disease activity.

**Use of Nitrates**

Although in all previous studies basal coronary tone was determined by the magnitude of vasodilator response to organic nitrates, there are differences in the dose and route of administration of nitrates (intracoronary or sublingual) in previous studies. In 1982, Lablanche et al found that maximum vasodilatation was achieved in patients with variant angina by 3 mg of intracoronary isosorbide dinitrate.
However, we have found that further vasodilatation may be achieved in some patients by doubling the dose of isosorbide dinitrate from 2.5 mg to 5.0 mg. With the aim of achieving maximal vasodilatation in all our study population we estimated coronary artery diameter after the intracoronary administration of 5 mg isosorbide dinitrate. While Feldman et al. reported that 0.4 mg of sublingual glycercy l trinitrate evoked maximum coronary vasodilatation, Jost et al. recently found that 0.8 mg was necessary to achieve maximum vasodilatation. Varying dosages and routes of administration of isosorbide dinitrate or glycercy l trinitrate as detailed above may have contributed to the different degree of vasomotor responses observed in previous studies.

Selection of angiographic segments

The degree of vasodilatation following the administration of nitrates will not necessarily be identical at all points within a coronary segment (as evidenced by the difference in our results between changes at the spastic point and changes in the entire AHA segment with spasm). In some studies the vasomotor responses were measured at specific points of bifurcation, while we feel that change in the mean luminal diameter of each entire AHA coronary segment is of greater relevance for the assessment of coronary tone. Such differences in the selection of quantitative angiographic sites may add to the discrepancies of the results of previous studies.

Disease activity

The results of our study indicate that basal coronary tone changes in relation to changes in activity of vasospastic disease. Kuga et al. recently reported that basal coronary artery tone was increased at the spastic site when spasm was provoked by a low dose of ergonovine, whereas basal tone was not increased at those spastic sites that required a higher dose of ergonovine to induce spasm. Previtali et al. indicated that a low dose of ergonovine was required in patients with a high degree of vasospastic ana ina, while in patients with low level of disease activity a high dose of ergonovine was necessary to provoke spasm. Thus the inverse relation between the dose of ergonovine required to provoke spasm and the degree of basal coronary tone may indirectly support our findings. Given the close relation between disease activity and vasomotor response, it is conceivable that differences in the state of disease activity in the patients of previous studies may have contributed to the discrepancies of their results.

PATHOPHYSIOLOGICAL ROLE OF BASAL CORONARY TONE IN VASOSPASM

Experimental studies have indicated that various endothelium dependent vasoactive factors which modulate vascular smooth muscle contraction may play an important role. Waters et al. and Kasiki et al. have shown that coronary spasm may be induced by several stimuli such as ergonovine, histamine, hyperventilation, and exercise in the same patient with variant angina and have suggested that vasospasm is caused by a variety of non-specific stimuli. Basal coronary artery tone is thought to be mediated by a balance of various stimuli such as the parasympathetic nervous system, humoral factors, and local endothelial dependent vasoactive factors. Given the above similarities in mediation of coronary spasm and mediation of coronary tone, the demonstration of a close relation between coronary vasospastic disease and basal coronary vessel tone is not surprising. It could be hypothesised that basal coronary tone may express a "threshold" for vasospastic activity. Increased tone not in only spastic segments but also in adjacent segments may reflect a low "threshold" for vasospasm during high activity of the disease.

CONCLUSIONS

Coronary artery tone may change in proportion to the activity of vasospastic disease over time. While vasoconstrictor response to ergonovine is increased in spastic segments only, basal tone of both spastic and adjacent segments is augmented during periods of active disease and is restored to normal during disease inactivity. The high diagnostic sensitivity and specificity of basal tone for prediction of spasm in coronary arteries indicates that the estimation of basal coronary tone may be useful in the assessment of vasospastic activity in patients with variant angina.

We gratefully acknowledge the dedication and contribution of Dr Fumimaro Takatsu, Dr Yukio Shiga, Dr Masato Watarasi, Dr Seiji Shimizu, Dr Anssui Nishiyama, Mr Takesi Suba, and all the staff of the catheterisation laboratory at Anjo Kosei Hospital, Japan. In addition we are grateful to the staff of the Core Angiographic Laboratory, Cardialysis, in Rotterdam for their quantitative analysis of the coronary angiograms. We thank Eric Boersma MSc for his statistical advice. Dr Yukio Ozaki is a recipient of a grant from Takeda Medical Research (Tatsa Ito) Foundation, Osaka, Japan. Dr David Keane is a recipient of a travel grant from the Peel Medical Research Trust, London, UK.

5. Waters DD, Szalacie J, Miller D, Theroux P. Clinical characteristics of patients with variant angina complicated by myocardial infarction or death within 1 month. Am J Cardiol 1989;64:658-64.
Relation of basal coronary tone and vasospastic activity in patients with variant angina.

Y. Ozaki, D. Keane and P. W. Serruys

*Heart* 1996 75: 267-273
doi: 10.1136/hrt.75.3.267

Updated information and services can be found at:
http://heart.bmj.com/content/75/3/267

**Email alerting service**

*These include:*

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/