Coronary blood flow reserve and wall motion recovery in patients undergoing angioplasty for myocardial infarction


Service des Explorations Fonctionnelles, Fédération de Cardiologie et Institut National de la Santé et de la Recherche Médicale, U400, Service de Médecine Nucléaire, France; *St Louis University, St Louis, MO, U.S.A.

Aims The aim of this study was to evaluate the relationship between coronary flow reserve and the recovery of wall motion contractility in patients with recent myocardial infarction.

Methods and Results Nineteen patients (55 ± 8 years) undergoing balloon angioplasty for recent myocardial infarction were studied. After angioplasty, coronary flow reserve was lower in the infarct-related artery than in a reference artery, 2.2 ± 0.6 and 2.8 ± 0.7, respectively, P<0.05. There was no immediate correlation between coronary blood flow reserve measured after angioplasty and wall motion index. There was a negative correlation between coronary flow reserve and the number of necrotic segments (r = -0.43; P=0.006). At the 4 month control angiogram, there was a significant increase in both left ventricular ejection fraction (59 ± 14% vs 51 ± 13%; P<0.05) and wall motion index (−0.63 ± 1.2 vs −1.94 ± 0.9 units SD, P=0.005). In patients in whom wall motion improved (>1 unit SD), the immediate coronary flow reserve was higher (P<0.05) than in patients without improved wall motion. In this group, the increase in wall motion index was correlated to the coronary blood flow reserve (r=0.55; P<0.02).

Conclusion These data show that after myocardial infarction, coronary flow reserve is associated with myocardial viability.

Key Words: Myocardial infarction, occlusion, coronary flow reserve, wall motion contractility.

See page 248 for the Editorial comment on this article

Introduction

Previous studies have suggested that the measurement of coronary blood flow reserve in the infarct-related coronary artery may help to assess myocardial viability and consequently predict further myocardial function recovery after myocardial infarction\[1,2\]. One of the hypotheses supporting such a relationship is that the microcirculation is altered in the infarct zone proportional to tissue necrosis. In patients with viable myocardium, coronary flow reserve would be preserved and thus prior revascularization procedures could help define the reversibility of wall motion dysfunction, especially in patients with large areas of hypo or akinesia.

The use of Doppler-tipped angioplasty guide wires allows direct assessment of coronary flow reserve in the setting of angioplasty\[3\]. Recently, our laboratory and others have shown that elective angioplasty of infarct-related coronary artery occlusions leads to left ventricular wall motion recovery if the artery remains patent at follow-up\[4,5\]. In this study population, it was also shown that myocardial viability, as assessed by thallium scintigraphy, was predictive of future myocardial recovery. In the present study, we hypothesize that coronary flow reserve after angioplasty of infarct-related coronary artery lesions will be related to myocardial viability and may predict left ventricular wall motion recovery. Consequently, the purpose of this study was to compare coronary flow reserve after angioplasty of the infarct-related coronary artery, with wall motion recovery at follow-up.


Correspondence: Dr Dubois-Randé, Service de Cardiologie, Hôpital Henri Mondor, 94010, Créteil, France.
Methods

Patient selection

Twenty two consecutive patients with the diagnosis of a
first myocardial infarction who underwent coronary angiography 6 to 8 days after myocardial infarction were
included in this study. Study inclusion criteria were (1)
diagnosis of a first acute myocardial infarction with
characteristic electrocardiographic ST segment elevation
and confirmation by creatinine kinase MB isoenzyme
elevation; (2) occlusion of a clearly identified infarct-
related coronary artery; (3) left ventricular dysfunction
of the infarct area; (4) suitability for coronary angi-
oplasty revascularization; (5) agreement for a control
angiogram 4 months after angioplasty. An interval of 2
to 3 weeks after myocardial infarction was selected to
evaluate wall motion contractility and coronary flow
reserve, to permit resolution of the effects of stunned
myocardium.

Study protocol

All patients underwent an initial diagnostic angio-
graphic study within 6 to 8 days after myocardial
infarction. Patients with the inclusion criteria were
referred for an elective coronary angioplasty 2 and 3
weeks after diagnostic angiography, and a quantitative
evaluation of global and regional left ventricular func-
tion. The infarct-related artery was identified by the
electrocardiographic ST segment elevation change
during the acute stage of infarction, the site of regional wall
motion abnormalities and the coronary angiogram.

All patients received aspirin (250 mg daily)
and beta-blockers (atenolol 50mg daily) as tolerated.
Angiotensin-converting enzyme inhibitor (captopril 75–
150 mg daily) was given within the first week of infarc-
tion if the angiographic ejection fraction was ≤40%.
Other medications were continued after angioplasty.
The same dosages were maintained constant until the
4 month follow-up angiogram. Patients with stent im-
plantation received ticlopidine and aspirin for 1 month
after angioplasty. The study was approved by the ethical
committee of our hospital.

Assessment of myocardial viability

Before angioplasty, all patients underwent stress redistribution–reinjection Thallium 201 single photon
emission computed tomography [Elscint large field of
view single head gamma-camera (Apex SP6) was used] as previously described.[6] Beta-blocking agents were
stopped 48 h prior to the test and reintroduced immedi-
ately after the evaluation. Stress was achieved either by
bicycle exercising (n=19) or by dipyridamole infusion
(0.56 mg . kg⁻¹) (n=3). Four hours after thallium injec-
tion thirty 40 s redistribution images were acquired
using the same rotation protocol (180° clockwise
rotation). Thirty seven MBq (1 mCi) of 201Tl were
reinjected and thirty 30 s reinjection images were
acquired, 20 min after reinjection. The reconstructed
tomographic data (64 × 64 matrix, Hamming/Hann fil-
ter) were displayed in three planes. Sixteen myocardial
regions were defined. A four-point grading system was
used as described by van-Eck-Smit[7] (0=no visible
uptake, 1=severe defect, 2=moderate defect, 3=normal
uptake). Reversibility was defined as an improvement by
one or more grade of the initial uptake on the redistri-
bution or the reinjection images. Segments were then
classified as normal (post-stress 201Tl uptake equal to
3), necrotic (initial uptake of 0 or 1) or viable (moderate
irreversible defects or reversible defects (whatever their
stress thallium uptake).

Angioplasty technique and measurement of
coronary blood flow reserve

Coronary angioplasty was performed using standard
balloon techniques with a Doppler-tipped guidewire to
cross the coronary occlusion. Stent implantation was
performed if there was a residual stenosis (>35%),
timal dissection or evidence of intraluminal thrombus.
Quantitative computer-assisted angiographic measure-
ments performed in at least two projections of the
dilated lesion were obtained[8]

Coronary blood flow velocity was measured with a
0.014-inch Doppler-tipped guidewire (12 MHZ-
Flowire, Cardiometrics, Inc., Mountain View, CA). The
Doppler guidewire was positioned 2 cm distal to the
coronary lesion. Doppler data were obtained prior to
angioplasty and after coronary angioplasty was com-
pleted. The average peak velocity was measured at
baseline and again after bolus intracoronary adenosine
(12–24 μg). Coronary vasodilatory reserve was calcu-
lated as the ratio of peak hyperaemia average peak
velocity to baseline average peak velocity. To avoid
post-ischaemic hyperaemic effects, coronary flow reserve
was measured 10 min after angioplasty. Before proceed-
ting to the target vessel, coronary flow reserve was also
measured in an adjacent angiographically normal coro-
nary reference vessel supplying a territory without wall
motion abnormalities. This coronary flow reserve
measurement provided a relative coronary reserve value,
defined as the ratio of the coronary reserve of the
target vessel to the coronary reserve of a non-stenotic
reference vessel of the same patient. Aortic blood
pressure, measured through the guiding catheter, was
continuously recorded throughout the procedure.

Evaluation of global and regional left
ventricular function

Global left ventricular function was evaluated on two
orthogonal contrast ventriculograms (30° right anterior

Eur Heart J, Vol. 20, issue 4, February 1999
oblique and 60° left anterior oblique positions). The left ventricular contours were manually traced by one blinded observer and then digitized (computer system developed by T.S.I., Paris, France). End-diastolic and end-systolic volumes and left ventricular ejection fraction were calculated according to the area–length method[9]. Segmental wall motion was expressed as radial shortening fraction [(end-diastolic radius minus end-systolic radius)/end-diastolic radius] of 13 anatomical wall segments by the centre gravity method in the right anterior oblique projection[5]. The segments 1 to 6 were denoted anterior and 7 to 13 inferior. The normal range was determined for ejection fraction and for each radial segment studied using ventriculograms performed in 40 subjects with atypical chest pain who had no evidence of coronary artery disease or other cardiovascular pathology. To compare values for regional anterior or posterior wall motion with normal values and with values at follow-up angiography, a standardized motion index expressed in units of standard deviation from the normal mean was calculated [% shortening of a patient’s segment n (1–13) – mean of the same normal segment)/standard deviation of the normal segment]. The wall motion for an individual segment was considered to be normal if the value lay within two standard deviations of the equivalent mean value in the control population. Regional wall function was considered to be hypokinetic if the wall motion of at least three segments lay ≥ two standard deviations below the normal range. For a given territory (segments from 1 to 6 or from 7 to 13), an average of the most three hypokinetic segments was calculated and served for statistical comparisons. The method of analysis has been described in detail elsewhere[5].

Follow-up evaluations

After successful angioplasty, a 4-month follow-up coronary angiogram, left ventricular angiography and re-evaluation of the coronary flow reserve were performed. Restenosis was defined by quantitative coronary angiography as the recurrence of ≥50% diameter narrowing in a coronary segment that had previously been dilated.

Statistical analysis

Data are presented as mean ± standard deviation. Paired data were compared by the Wilcoxon paired test. Comparisons between groups were made with a Mann–Whitney U test. Differences between proportions were assessed by chi-square analysis. Correlations were obtained by the linear regression method. Data in figures are expressed as mean ± standard error of the mean. A value of $P<0.05$ was considered to indicate statistical significance.

<table>
<thead>
<tr>
<th>Table 1 Baseline characteristics of the study population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
</tr>
<tr>
<td>Infarct location</td>
</tr>
<tr>
<td>Anterior infarction</td>
</tr>
<tr>
<td>Inferior infarction</td>
</tr>
<tr>
<td>Thrombotic agent</td>
</tr>
<tr>
<td>Streptokinase</td>
</tr>
<tr>
<td>Recombinant tissular plasminogen activator</td>
</tr>
<tr>
<td>Creatinine kinase (peak: Units l$^{-1}$)</td>
</tr>
<tr>
<td>Interval between infarction and angioplasty (days)</td>
</tr>
<tr>
<td>Single- vessel disease</td>
</tr>
<tr>
<td>Multivessel disease</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
</tr>
<tr>
<td>Anterior infarction (%)</td>
</tr>
<tr>
<td>Inferior infarction (%)</td>
</tr>
<tr>
<td>Coronary artery having angioplasty</td>
</tr>
<tr>
<td>Left anterior descending artery</td>
</tr>
<tr>
<td>Right coronary artery</td>
</tr>
<tr>
<td>Left circumflex artery</td>
</tr>
<tr>
<td>Treatment</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
</tr>
</tbody>
</table>

Reproducibility of intra-observer measurements of coronary blood flow reserve showed that the mean difference for two analyses of coronary flow reserve was 2.2%.

Results

Patient characteristics

The study group consisted of 22 patients (19 men and 3 women) with a mean age of 55 ± 8 years (Table 1). All had received thrombolytic treatment at time of admission. Ten had anterior wall infarction and 12 inferior wall infarction. The occlusion was located with equal frequency in the left anterior descending coronary artery and the right coronary artery and less often in the left circumflex artery. The time between acute myocardial infarction and angioplasty of the infarct-related vessel was 16 ± 4 days. The mean left ventricular ejection fraction was 51 ± 13%. Ejection fraction was lower in patients with anterior infarction (42 ± 13%) than with inferior infarction (57 ± 7%, $P<0.01$). Initial ejection fraction was negatively correlated to the number of necrotic segments ($r^2 = 0.65; P<0.0001$).

Immediate outcome

Angioplasty was successful in 19 patients (86%). Nine patients had a stent implantation. Mean luminal diameter after angioplasty was 2.27 ± 0.63 mm (reference
vessel segment diameter: 2·78 ± 0·42 mm) with a residual stenosis of 19·5 ± 12% (Table 2). There was no major in-hospital complications.

Four-months follow-up

Follow-up was available in all patients who had a successful angioplasty. One patient suffered sudden death during follow-up. Fifteen of the 18 remaining patients were asymptomatic at follow-up. None had recurrent angina or myocardial infarction. At follow-up angiography, only one patient had an occluded coronary artery (balloon dilatation) and five had a restenosis (two within a stent).

Coronary blood flow reserve (Table 2)

Before angioplasty (after the guidewire crossed the occlusion), the artery was patent in 17/19 patients (TIMI 3 in 12 and TIMI 2 in 5). Target coronary flow reserve was 1·3 ± 0·7. Baseline average peak velocity was lower than in the reference artery (n=15, 8·2 ± 7·5 vs 15·8 ± 6·8 cm . s⁻¹, respectively, P<0·05).

After angioplasty, haemodynamic conditions were unchanged. Coronary flow reserve improved but remained lower in the infarct-related artery than in the reference artery, 2·2 ± 0·6 vs 2·8 ± 0·7, respectively, (P<0·05). There was no correlation between coronary blood flow reserve and wall motion index measured at the time of angioplasty.

At 4 month follow-up, haemodynamics were unchanged from the initial measurements except for a decrease in end-diastolic pressure (13 ± 5 mmHg vs 18 ± 7 mmHg, P=0·02). In 12 patients with no restenosis or reocclusion, there was no significant difference in the coronary flow reserve or the relative coronary flow reserve (Fig. 1). Individual data are shown in Fig. 2. In six patients with restenosis (including the one with the occlusion), a successful reangioplasty was performed. Coronary blood flow reserve after angioplasty remaining unchanged compared with values found initially (Fig. 1).

Coronary blood flow reserve after angioplasty and changes in left ventricular function

Left ventricular functional analysis was done in patients with and without restenosis. The patient who had an occluded artery at follow-up was excluded. Left ventricular ejection fraction increased from 51 ± 13% to 59 ± 14% (P<0·05) at follow-up. The wall motion index increased from −2·02 ± 0·9 to −0·64 ± 1·2 units of standard deviation (P=0·005). Six patients failed to increase their left ventricular wall motion >1 unit. Only one of these six patients had restenosis. In patients in whom wall motion improved (>1 unit SD), the target coronary flow reserve and the relative coronary flow reserve measured initially was higher (Fig. 3). The increase in wall motion index was correlated both to the initial coronary flow reserve (Fig. 4) and to the relative coronary reserve after angioplasty (r=0·53; P=0·027 and r=0·51; P<0·05, respectively).
Coronary flow reserve and myocardial viability

At follow-up, although there was no relationship between the number of viable myocardial segments and improvement in global ejection fraction, there was a positive correlation between the number of viable myocardial segments and improvement in the infarct zone wall motion ($r = 0.5; P < 0.05$). There was a negative correlation between the post angioplasty coronary flow reserve and the number of necrotic segments ($r = -0.43; P = 0.006$).

Discussion

This study shows that in patients with myocardial infarction coronary blood flow reserve after angioplasty is inversely correlated with the extent of myocardial infarction and directly correlated with the improvement in wall motion contractility during the recovery period.

Abnormalities of coronary flow reserve have been well documented in the setting of myocardial infarction. In the acute phase of myocardial infarction, complex alterations of coronary circulation occur. Histologically, extracellular and intracellular oedema is

---

**Coronary flow reserve and myocardial viability**

At follow-up, although there was no relationship between the number of viable myocardial segments and improvement in global ejection fraction, there was a positive correlation between the number of viable myocardial segments and improvement in the infarct zone wall motion ($r = 0.5; P < 0.05$). There was a negative correlation between the post angioplasty coronary flow reserve and the number of necrotic segments ($r = -0.43; P = 0.006$).

**Discussion**

This study shows that in patients with myocardial infarction coronary blood flow reserve after angioplasty is inversely correlated with the extent of myocardial infarction and directly correlated with the improvement in wall motion contractility during the recovery period.

Abnormalities of coronary flow reserve have been well documented in the setting of myocardial infarction. In the acute phase of myocardial infarction, complex alterations of coronary circulation occur. Histologically, extracellular and intracellular oedema is
invariably present. The vascular endothelium is damaged and the capillaries are congested with blood cells\cite{10}. Experimental studies have shown that the ‘no reflow’ injury phenomenon is limited to infarcted tissue. In contrast, coronary flow reserve in viable myocardium is transiently diminished but improves within 1 week of reperfusion\cite{10}. Additionally, it has been shown that coronary flow reserve may be preserved in stunned myocardium\cite{11}. Recent experimental animal and human studies have reported similar findings using myocardial contrast echocardiography to explore the coronary microcirculation\cite{12}. During the reperfusion period, this technique demonstrated substantial myocardial viability when post-reflow coronary hyperaemia was still present\cite{13}.

**Myocardial viability and recovery time**

In the present study, the relationship between coronary flow reserve and myocardial viability was addressed more than 15 days after myocardial infarction in patients with occluded coronary arteries. At this point in time, coronary flow reserve reflects the damage in microvessels due to the extent of the infarcted zone (i.e. necrotic tissue) rather than the alterations of the microvascular bed during the acute phase of infarction or the effects of myocardial stunning.

The current data and several previous studies support the proposed hypothesis. Picano et al. demonstrated that in patients with recent, as well as previous myocardial infarction, the dipyridamole-induced improvement in the contractile function of identified viable segments corresponded to regions with thallium-201 uptake and recovery of function after coronary revascularization\cite{1}. Similarly, Marzullo et al. have
shown that persistant coronary flow reserve induced after dipyridamole provided prognostic information on myocardial viability\cite{2,14,19}.

**Coronary flow velocity reserve and myocardial viability**

The physiological consequences of coronary angioplasty on coronary circulation have been widely investigated\cite{3,16,17}. Before angioplasty, as expected, baseline flow velocity and coronary flow reserve were markedly diminished compared to a normal reference artery. However, because of the critical and subtotal stenosis and a potential functioning collateral circulation, coronary flow reserve is not a reliable predictor of myocardial perfusion reserve before angioplasty. Post angioplasty conditions were used for all subsequent analyses\cite{18}.

In agreement with previous studies, this study demonstrated no relationship between coronary flow reserve and the level of myocardial wall motion dysfunction, whereas coronary reserve was negatively correlated to the number of necrotic myocardial segments. However and most importantly, coronary flow reserve was significantly related to the recovery of regional wall motion contractility. Another important finding of the present study is that the coronary reserve after elective angioplasty in patients with recent myocardial infarction improved and remains stable over the follow-up period despite important recovery of myocardial function. Indeed, although a slight increase in coronary blood flow reserve was observed in the infarct-related artery at follow-up, it did not reach a significant level. However, this increase also occurred in the reference artery and a constant relative coronary flow reserve was ultimately reached. These findings suggest that coronary flow reserve measurement early after myocardial infarction is linked more to myocardial viability than to contractility. The slight increase in coronary flow reserve observed both in the infarct-related artery and in the reference artery may be due, in part, to the change in load conditions since, despite similar haemodynamic conditions during coronary flow reserve measurements throughout the study, a decrease in end-diastolic pressure occurred during the follow-up period in these patients.

Recently, it has been demonstrated that elective revascularization of occluded coronary arteries with viable myocardium after myocardial infarction improves left ventricular function and lessens ventricular remodelling if the artery remains patent during the follow-up\cite{5,19,20}. Previous studies have suggested that infarct-related lesions have a greater tendency to recur after successful angioplasty, thus hampering the potential beneficial effects on left ventricular function and survival\cite{21}. Interestingly, in the present study, the number of reocclusions at follow-up was particularly low and contrasts with the 43% reocclusion rate previously reported\cite{5}. This difference between the two studies may be attributed to stenting used when the immediate angioplasty result was not acceptable. Although these results are in concert with other recent studies\cite{22}, the present study was not designed to further explore this point.

**Limitations**

The technical limitations of Doppler flow velocity have been described in detail elsewhere\cite{4}. The present study is limited by the small population studied. The weak correlation found between coronary flow reserve and wall motion recovery would probably increase with a larger patient population. The fact that only postangioplasty coronary blood flow reserve can be used limits the clinical relevance of coronary blood low reserve measurements reached following recanalization. Nevertheless and in agreement with others\cite{23}, the value of coronary flow reserve after myocardial infarction in the present study falls within a wide range, probably rendering the use of the initial absolute coronary flow reserve difficult as an accurate sharply defined index of myocardial viability. However, a value above 1.75 is associated with an improved wall motion index, whereas it is unlikely for values below this cut-off. Relative coronary flow reserve was used to normalize the absolute coronary flow reserve values for each individual patient, but it does not change the results significantly. Additionally, although the absolute coronary flow reserve was correlated to the number of necrotic segments, no significant relationship was observed with the number of viable segments. This finding may be explained by the fact that although thallium imaging is accurate in defining necrotic tissue it may have underestimated viable segments\cite{24}.

**Clinical implications**

Despite several limitations, the current results provide insight into the physiology of acute myocardial infarction and demonstrate a link between the extent of myocardial infarction and coronary flow reserve. These data also suggest that in clinical practice a higher coronary flow reserve will be associated with greater myocardial functional recovery and perhaps improved long-term prognosis.

**References**


