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Impact of microvascular integrity and local viability on left ventricular remodelling after reperfused acute myocardial infarction

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Infarct size, location, and transmural, as well as the patency of the infarct related artery and the presence of collateral flow, are involved in the process of left ventricular remodelling after acute myocardial infarction.¹⁻⁴ Coronary reflow has beneficial effects in preventing left ventricular dysfunction and dilatation, thus improving the outcome in large populations of patients who have had an infarct.⁵⁻⁷ However, a substantial population of patients with reperfused acute myocardial infarction still manifests persistent left ventricular dysfunction along with significant dilatation, which worsens morbidity and mortality.² Recently the concept has emerged that the ischaemia-reperfusion induced injury of the microvasculature may have an important role in left ventricular remodelling.⁸⁻⁹ Early prediction of left ventricular remodelling after reperfused acute myocardial infarction remains challenging on an individual basis.

As a consequence of reperfusion injury, the no reflow phenomenon may involve a combination of capillary obstruction and microvascular dysfunction responsible for prolonged ischaemia and myocardial cell death.¹⁰⁻¹¹ We recently reported that, during the early convalescent period of reperfused myocardial infarction, subsequent improvement of myocardial blood volume is associated with pre-existent recruitable microvascular function in the infarct related artery and local tissue viability in patients with persistent myocardial wall dysfunction.¹² To clarify the relations between left ventricular remodelling, microvascular function, myocardial blood volume, and local tissue viability after reperfused acute myocardial infarction, we assessed left ventricular remodelling and studied its relation to coronary flow reserve (CFR) in the infarct related artery (CFR_{IRA}) on day 1 and myocardial blood volume on day 8 in patients after an infarct with and without local viability.

Objective: To assess left ventricular remodelling in patients with reperfused acute myocardial infarction and to study its relation to microvascular damage.

Patients: 25 patients successfully treated by primary percutaneous coronary angioplasty for acute myocardial infarction.

Setting: University hospital

Methods: Indexed end diastolic (EDVi) and end systolic (ESVi) volumes were assessed on admission and repeated at days 1 and 8. Coronary flow reserve (CFR) was assessed in the infarct related artery on day 1. Myocardial blood volume was assessed on admission and at day 8 by myocardial contrast echocardiography. In patients who manifested persistent myocardial dysfunction at hospital discharge (n = 21), local inotropic reserve was assessed by dobutamine echocardiography at day 7.

Results: On admission, patients with and without local viability had similar EDVi and ESVi (EDVi 67 (9) and 73 (14) ml/m², respectively; ESVi 34 (8) and 40 (11) ml/m², respectively; NS). EDVi increased to 97 (22) ml/m² in patients without local viability (p < 0.01 v admission) but remained unchanged at 70 (11) ml/m² in patients with viable myocardium (NS v admission). For pooled patient data, the percentage change in EDVi correlated with CFR (r = 0.76, p < 0.0001) and myocardial blood volume in the infarct territory (r = 0.80, p < 0.0001).

Conclusion: Left ventricular dilatation may preferably occur in patients without local viability and is correlated with early CFR and extent of myocardial blood volume in the infarct territory.

METHODS

Screened population

The screened population comprised 30 consecutive patients successfully treated (residual stenosis < 30%, TIMI (thrombolysis in myocardial infarction) grade 3 flow) by direct angioplasty < 8 hours after the onset of acute myocardial infarction. To be included, patients had to have a coronary occlusion deemed suitable for balloon angioplasty and stent placement, single vessel disease, and a large myocardial infarction on left ventricular cineangiograms assessed before angioplasty (that is, involving > 25% of myocardial segments). Patients with cardiogenic shock, prior myocardial infarction, and a history of diabetes mellitus or severe left ventricular hypertrophy were excluded. Informed consent was obtained for all patients.

Study protocol

Primary angioplasty was performed using standard techniques. The collateral flow to the infarct related artery was graded before angioplasty according to the usual angiographic classification.¹³ Stenting was systematically performed to optimise coronary blood flow. Left ventricular angiogram was systematically performed. After the angioplasty was completed, myocardial contrast echocardiography was performed in the catheterisation laboratory. Repeat left ventricular and coronary angiograms were performed in all patients on day 1 and a mean (SD) of 8 (2) days after the onset of symptoms.

Abbreviations: CFR, coronary flow reserve; CFR_{IRA}, coronary flow reserve in the infarct related artery; EDVi, indexed end diastolic volume; ESVi, indexed end systolic volume; TIMI, thrombolysis in myocardial infarction

Table 1 Clinical and angiographic characteristics of the study population

	Viability present (n=18)	Viability absent (n=7)	p Value*
Age (years)	55 (12)	62 (8)	0.09
Men	17	5	NS
LDL cholesterol (mmol/l)	3.5 (0.8)	3.7 (1.1)	NS
Glucose (mmol/l)	5.4 (0.6)	6.2 (0.7)	0.07
Current smoking	13	2	<0.05
Anterior AMI	8	3	NS
Admission SBP (mm Hg)	124 (18)	115 (18)	NS
Admission HR (beats/min)	89 (12)	94 (12)	0.07
Collateral (Rentrop 2 and 3)	3	1	NS
Time to TIMI 3 (minutes)	258 (108)	273 (102)	NS
Residual stenosis (%)	8 (3)	9 (4)	NS
Admission EF (%)	46 (5)	47 (2)	NS

Data are numbers or mean (SD). AMI, acute myocardial infarction; EF, ejection fraction; HR, heart rate; LDL, low density lipoprotein; SBP, systolic blood pressure; TIMI, thrombolysis in myocardial infarction.

In all patients, CFR and myocardial contrast echocardiography measurements were scheduled on day 1 and on day 8, respectively. Dobutamine echocardiography was performed 7 (1) days after myocardial infarction onset in patients in whom there was evidence of persistent myocardial wall dysfunction ($n = 21$). Assessment of left ventricular ejection fraction and volumes was available in 60% of the patients at a mean range of 4 (1.5) months after inclusion (5 of the 7 patients without local viability and 10 of the 15 patients with local viability).

Left ventricular angiography

Global and regional left ventricular wall motion were analysed off line by two independent operators blinded to patients' data (CAAS II, Pie Medical, Maastricht, Netherlands). The average measurements were used for analysis. Indexed end diastolic (EDVi) and end systolic (ESVi) volumes and left ventricular ejection fraction were calculated according to the area-length method. To assess the impact of microvascular integrity on left ventricular remodelling, we defined a 25% variation of EDVi at discharge relative to the baseline value as a cut off value for presence or absence of left ventricular remodelling.³ Segmental wall motion was calculated by a modification of the centreline method.¹⁴ The regional wall motion score was calculated as the average wall motion score in SD/chord from normal values in a control population in the same segment.¹⁵ One hundred equidistant chords were drawn perpendicular to the centreline, and the left ventricular contour was divided in to 20 segments whose motion was calculated by averaging the motion of consecutive sets of five chords.¹⁶ We defined a 20% variation of regional wall motion score at discharge relative to baseline value as a cut off for the presence or absence of segmental contractile recovery.¹⁷ The mean interobserver variability of measurements of ejection fraction, ventricular volumes, and regional wall motion score was < 5%.

Myocardial viability

In the absence of subsequent segmental myocardial contraction, dobutamine echocardiography was used to assess local viability in the infarct territory. The presence of inotropic reserve was defined as an improvement of myocardial thickening in ≥ 2 adjacent segments located in the infarct area and a > 20% decrease in wall motion score index during dobutamine infusion.¹⁸ Dobutamine echocardiography was performed on a Sequoia (Acuson, Mountain View, California, USA) equipped with harmonic technology (2–3.5 MHz) using a standardised, previously described technique.¹²

Coronary flow reserve

CFR was measured (in duplicate with < 15% variations) using a 0.014 inch Doppler guidewire (FloWire, Jomed, Helsingborg, Sweden), and coronary hyperaemia was induced with the intracoronary injection of adenosine. The CFR was first

measured in the reference vessel followed by the CFR_{IRA} after the tip of the guide wire was placed at least 2 cm distal to the site of the occlusion.¹⁹ Relative CFR was computed as the ratio of CFR_{IRA} to the CFR of the reference vessel.

Myocardial contrast echocardiography

Myocardial contrast echocardiography was performed by repeating an intracoronary bolus of 3 ml sonicated ioxaglate (Hexabrix-360, Guerbet, Villepinte, France) on the Sequoia. Gain settings were kept constant throughout the procedure. Two apical echocardiographic views were stored on optical disks for subsequent analysis. Echocardiographic images with the best delineation between contrast enhanced and non-enhanced myocardium were selected to determine the risk area, defined as the area showing no contrast enhancement before coronary reopening. The extent of the no reflow area (percentage of left ventricular surface area) was defined as the ratio of the area with residual contrast defect after coronary opening to the total area of the left ventricular myocardium. Quantitative videodensitometric analysis (NIH Image, National Institutes of Health, Bethesda, Maryland, USA) was performed for the assessment of contrast intensity in the entire risk area. The peak intensity ratio was determined as the ratio of contrast peak intensity in the risk area to the baseline contrast intensity in the remote wall. In accordance with previous reports,²⁰ the interobserver variability for the magnitude of echocardiographic measurements was 7.2% for the peak intensity ratio and 6.4% for areas of residual contrast defect.

Statistical analysis

Data are presented as mean (SD). Two way analysis of variance with repeated measures were used to assess differences in continuous variables between patients with and those without local viability, as well as between patients with and those without left ventricular remodelling. Paired and unpaired Student's *t* tests were used when appropriate. Logarithmic regression analysis was used to analyse the relation between left ventricular remodelling at follow up and both CFR and myocardial blood volume.

RESULTS

Study population

Of the 30 initial subjects, 25 patients satisfied the study criteria. All patients were successfully treated (residual stenosis < 30%, TIMI 3 flow) by primary angioplasty < 8 hours after the onset of symptoms. All of them received angiotensin converting enzyme inhibitors early. Five patients could not be included because myocardial dysfunction involved < 25/100 chords ($n = 2$) and because of prior myocardial infarction ($n = 1$), diabetes mellitus ($n = 1$), and cardiogenic shock ($n = 1$).

Figure 1 Serial changes in indexed end diastolic (EDVi) and end systolic (ESVi) volumes are depicted for patients with (open bars) and without (solid bars) local viability. EDVi and ESVi increased relative to baseline at day 8 and at four months' follow up among patients without local viability. Both remained unchanged among patients with viable myocardium.

Myocardial viability

Among the 25 patients enrolled in the study, 18 had local viability. Segmental left ventricular function recovered almost fully in four of them. Fourteen had significant inotropic reserve. When the study population was broken down according to presence ($n = 18$) or absence ($n = 7$) of local viability, there were no differences between the two groups with regard to infarct territory, peak creatine kinase concentration, and troponin I concentration, nor in mean time elapsed from pain onset to achievement of TIMI 3 (table 1). On dobutamine echocardiography, the wall motion score was improved during dobutamine infusion in 4.2 (2.8) segments in patients with inotropic reserve and in 1.2 (1.8) segments in those without inotropic reserve ($p = 0.02$).

Relation between left ventricular remodelling, myocardial blood volume, and microvascular function

Although EDVi and ESVi were similar between patients with and those without local viability on admission (fig 1),

Figure 2 Relation between changes in EDVi assessed at day 8 and (1) coronary flow reserve in the infarct related artery (CFR_{RA}) assessed at day 1 (top) and (2) myocardial blood volume assessed by myocardial contrast echocardiography at day 8 (bottom). The early determination of CFR_{RA} was highly correlated with the degree of left ventricular dilatation at the day 8 follow up, as was myocardial blood volume assessed in the infarct territory.

substantial myocardial dilatation was observed at day 8 among patients without local viability ($p < 0.01$ v patients with local viability for both EDVi and ESVi). At four months' follow up, EDVi was still higher among patients without local viability ($p < 0.01$ v patients with local viability).

Left ventricular remodelling was observed at day 8 in all patients without inotropic reserve and in one patient with viable myocardial wall dysfunction. The region at risk was similar in patients with and those without left ventricular remodelling, as were the mean time elapsed from pain onset to achievement of TIMI 3 in the infarct related artery and the mean ejection fraction on admission (table 2). In contrast, CFR at day 1 and peak intensity ratio at day 8 were severely depressed in patients with left ventricular remodelling relative to those with no change in EDVi at the day 8 follow up

Table 2 Characteristics of patients with and without early left ventricular remodelling

	Remodelling absent (n=17)	Remodelling present (n=8)	p Value
Age (years)	56 (12)	61 (8)	NS
Men	16	6	NS
Anterior AMI	8	3	NS
Time to TIMI 3 (minutes)	256 (109)	267 (104)	NS
Region at risk	34.5 (10.0)	35.9 (10.6)	NS
Day 1 CFR	2.4 (0.6)	1.4 (0.4)	<0.0001
Day 1 relative CFR	0.9 (0.2)	0.7 (0.2)	<0.001
Day 8 peak intensity ratio	3.0 (0.9)	1.3 (0.8)	<0.0001
Day 8 residual contrast defect ratio	5.4 (2.2)	20.2 (7.1)	<0.01
Day 8 EF (%)	49 (8)	46 (8)	NS

Data are numbers or mean (SD). Region at risk and residual contrast defect ratio are expressed as percentages of left ventricular area. CFR, coronary flow reserve.

Figure 3 Relation between changes in EDVi assessed at four months' follow up and (1) CFR_{IRA} assessed at day 1 (top) and (2) myocardial blood volume assessed by myocardial contrast echocardiography at day 8. The early determination of CFR_{IRA} and myocardial blood volume in the infarct territory predicted left ventricular remodelling at four months' follow up.

($p < 0.0001$ for both) (table 2). Additionally, areas of no reflow were higher among patients with left ventricular remodelling ($p < 0.01$ v patients without remodelling).

For pooled patient data, the change in EDVi at day 8 was correlated with CFR_{IRA} ($r = 0.76$, $p < 0.0001$) (fig 2) and peak intensity ratio as assessed by myocardial contrast echocardiography ($r = 0.80$, $p < 0.0001$) (fig 3).

At four months' follow up, EDVi and ESVi remained significantly higher among patients without local viability than among those with local viability ($p < 0.001$ for both, fig 1). The left ventricular ejection fraction was statistically higher in patients with local viability at hospital discharge (51 (9) v 42 (5)% in patients without local viability). Our data show that mean EDVi remained unchanged at four months' follow up relative to day 8 in both groups, suggesting that a decrease in ESVi at four months among patients with local viability was primarily responsible for the differences in ejection fraction. Interestingly, the change in EDVi at four months and both CFR_{IRA} and peak intensity ratio remained highly correlated indicating that the extent of microvascular damage measured during the early convalescent period after reperfused acute myocardial infarction may be able to predict left ventricular remodelling at later follow up.

DISCUSSION

The present study supports and extends the conclusions of previous reports concerning the relation that exists between early left ventricular remodelling after reperfused acute myocardial infarction and microvascular damage induced by ischaemia-reperfusion injury.^{2 7-9 21} Ito and colleagues⁸ showed that the presence of no-reflow was associated with more frequent left ventricular dilatation at a mean of 25 days after myocardial infarction onset. More recently, Gerber and colleagues⁹ emphasised the role of microvascular obstruction

in increased postinfarct left ventricular remodelling through decreased systolic myocardial deformation in regions of microvessel damage. As opposed to thrombolysis, which was shown to attenuate left ventricular remodelling, the direct effects of primary angioplasty of an acutely occluded infarct related artery on left ventricular dilatation remain uncertain in humans.²¹ Our data clearly indicate that early left ventricular remodelling may preferably occur in patients with major microvascular damage, independently of infarct size and left ventricular ejection fraction. Additionally, our results indicate that the extent of ischaemia-reperfusion induced microvascular damage assessed within the first days after reperfused acute myocardial infarction may be able to predict left ventricular remodelling at later follow up (four months).

Ischaemia-reperfusion induced microvascular damage and left ventricular remodelling

Since a combination of microvascular obstruction (downstream microembolism of platelets, de novo thrombosis, and neutrophil capillary plugging) and stunning (endothelial dysfunction) is involved in the no reflow phenomenon,^{10 11} we sought to study the integrity of the microvasculature characterised by both the extent of microvascular obstruction on myocardial contrast echocardiography (capillary blood volume) and its functional response to hyperaemia (capillary vasodilatation and recruitment). Recent studies have reported that microvascular obstruction is a dynamic process that gradually increases over the first days after coronary reflow. However, microvascular damage may also regress within the first days after acute myocardial infarction with subsequent recovery of myocardial function.^{20 22} Since microvascular obstruction is thought to vary during the first days after coronary reflow, the accuracy of the exclusive analysis of myocardial blood volume early after reperfused acute myocardial infarction for differentiation between patients with and those without microvascular damage at follow up remains questionable on an individual basis.

Recently, our group reported that subsequent improvement of myocardial perfusion was preceded by the recovery of recruitable microvascular function in the infarct related artery and was associated with local tissue viability after reperfused acute myocardial infarction.¹² Our data indicate that a clear relation exists between the extent of early and late left ventricular dilatation and both microvascular function assessed on day 1 and myocardial blood volume as measured on day 8. Accordingly, the relation between myocardial perfusion at the tissue level and left ventricular remodelling provides mechanistic insights relevant to cardiac remodelling following direct angioplasty. The relation between ventricular remodelling and coronary reperfusion has so far been reported especially after thrombolysis.^{2 6 7 21} The present data may therefore have important clinical implications, since they suggest that the early determination (from day 1) of the CFR in the infarct related artery may therefore be useful to predict individually early and left ventricular dilatation after reperfused acute myocardial infarction.

The beneficial effects of myocardial reperfusion on left ventricular remodelling may be partly independent of its direct effect on infarct size reduction. This concept is known as the "open artery hypothesis". Although the restoration of adequate reflow in the epicardial coronary artery is not constantly associated with prompt reperfusion at the tissue level, it is unknown whether the benefits of reperfusion on left ventricular remodelling result from reduced injury to the microvasculature. However, preliminary clinical observations suggest that patients in whom reperfusion failed or was not attempted have more severe microvascular injury and worse left ventricular remodelling. Our data show that the persistence of myocardial wall dysfunction in the first days after reperfused acute myocardial infarction may be variably

associated with subsequent left ventricular dilatation. Indeed, the presence of tissue viability in the infarct area may have beneficial effects in preventing left ventricular dilatation independently on infarct size and myocardial function. This may be related to preserved mechanical properties in viable and dysfunctional tissue as opposed to scar myocardium, as recently mentioned.⁹ The present data suggest that the preservation of microvascular function early after reperfused acute myocardial infarction is associated with the complete benefit of myocardial reperfusion at the muscle level (that is, myocardial blood volume, myocardial salvage, and limitation of remodelling) and finally with the presence of viable myocardium despite wall dysfunction at rest (myocardial stunning).

Study limitations

CFR was determined through the use of an intracoronary Doppler guidewire and therefore cannot be used routinely. Other promising approaches such as magnetic resonance imaging, positron emission tomography, and transthoracic Doppler echocardiography have the potential for the non-invasive assessment of CFR.^{23–25} CFR depends on factors other than microvasculature integrity, such as haemodynamics and residual stenosis. There was no difference in residual stenosis, heart rate, and systolic blood pressure between the groups at initial angiography and during follow up, and the use of relative CFR helped to control for individual variations in haemodynamics. Because of the relatively small population of patients included in the present study, the territory of myocardial infarction, one of the main factors involved in the phenomenon of left ventricular remodelling, could not be characterised as an independent predictor of ventricular remodelling.

Conclusion

Subsequent left ventricular dilatation is associated with impaired microvasculature during the early convalescent period after reperfused acute myocardial infarction. The presence of altered microvascular function is therefore associated with altered perfusion at the tissue level at follow up and with non-viable myocardium. The present study helps clarify the relation between microvascular integrity and left ventricular remodelling after reperfused acute myocardial infarction and may therefore have important clinical implications.

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REFERENCES

- Eaton LW, Weiss JL, Bulkley BH, *et al.* Regional cardiac dilatation after acute myocardial infarction: recognition by two-dimensional echocardiography. *N Engl J Med* 1979;**300**:57–62.
- McKay RG, Pfeffer MA, Pasternak RC, *et al.* Left ventricular remodeling after myocardial infarction: a corollary to infarct expansion. *Circulation* 1986;**74**:693–702.
- Meizlish JL, Berger HJ, Plankey M, *et al.* Functional left ventricular aneurysm formation after acute anterior transmural myocardial infarction: incidence, natural history, and prognostic implications. *N Engl J Med* 1984;**311**:1001–6.
- Pfeffer MA, Braunwald E. Ventricular remodeling after myocardial infarction: experimental observations and clinical implications. *Circulation* 1990;**81**:1161–72.
- Touchstone DA, Beller GA, Nygaard TW, *et al.* Effects of successful intravenous reperfusion therapy on regional myocardial function and geometry in humans: a tomographic assessment using two-dimensional echocardiography. *J Am Coll Cardiol* 1989;**13**:1506–13.
- Marino P, Zanolla L, Zardini P. Effect of streptokinase on left ventricular modeling and function after myocardial infarction: the GISSI (Gruppo Italiano per lo studio della streptochinasi nell'infarto miocardico) trial. *J Am Coll Cardiol* 1989;**14**:1149–58.
- Erlebacher JA, Weiss JL, Weisfeldt ML, *et al.* Early dilation of the infarct segment in acute transmural myocardial infarction: role of infarct expansion in acute left ventricular enlargement. *J Am Coll Cardiol* 1984;**4**:201–8.
- Ito H, Maruyama A, Iwakura K, *et al.* Clinical implications of the 'no reflow' phenomenon: a predictor of complications and left ventricular remodeling in reperfused anterior wall myocardial infarction. *Circulation* 1996;**93**:223–8.
- Gerber BL, Rochitte CE, Melin JA, *et al.* Microvascular obstruction and left ventricular remodeling early after acute myocardial infarction. *Circulation* 2000;**101**:2734–41.
- Bolli R, Triana JF, Jeroudi MO. Prolonged impairment of coronary vasodilation after reversible ischemia: evidence for microvascular "stunning". *Circ Res* 1990;**67**:332–43.
- Ito H, Tomooka T, Sakai N, *et al.* Lack of myocardial perfusion immediately after successful thrombolysis: a predictor of poor recovery of left ventricular function in anterior myocardial infarction. *Circulation* 1992;**85**:1699–705.
- Garot P, Pascal O, Simon M, *et al.* Time course and relation to local viability of microvascular function and volume after reperfused acute myocardial infarction. *Am J Cardiol* 2002;**89**:1341–6.
- Rentrop KP, Feit F, Sherman W, *et al.* Serial angiographic assessment of coronary artery obstruction and collateral flow in acute myocardial infarction. Report from the second Mount Sinai-New York University reperfusion trial. *Circulation* 1989;**80**:1166–75.
- Sheehan FH, Bolson EL, Dodge HT, *et al.* Advantages and applications of the centerline method for characterizing regional ventricular function. *Circulation* 1986;**74**:293–305.
- Monin JL, Garot J, Scherrer-Crosbie M, *et al.* Prediction of functional recovery of viable myocardium after delayed revascularization in postinfarction patients: accuracy of dobutamine stress echocardiography and influence of long-term vessel patency. *J Am Coll Cardiol* 1999;**34**:1012–9.
- Sheehan FH, Dodge HT, Mathey DG, *et al.* Measurement of abnormalities in the timing and extent of motion from frame-by-frame analysis of contrast left ventriculograms. *Comput Cardiol* 1983:35–9.
- Cohen MV, Yang XM, Neumann T, *et al.* Favorable remodeling enhances recovery of regional myocardial function in the weeks after infarction in ischemically preconditioned hearts. *Circulation* 2000;**102**:579–83.
- Cigarroa CG, deFilippi CR, Brickner ME, *et al.* Dobutamine stress echocardiography identifies hibernating myocardium and predicts recovery of left ventricular function after coronary revascularization. *Circulation* 1993;**88**:430–6.
- Kern MJ. Coronary physiology revisited: practical insights from the cardiac catheterization laboratory. *Circulation* 2000;**101**:1344–51.
- Ito H, Iwakura K, Oh H, *et al.* Temporal changes in myocardial perfusion patterns in patients with reperfused anterior wall myocardial infarction: their relation to myocardial viability. *Circulation* 1995;**91**:656–62.
- Sutton MG, Sharpe N. Left ventricular remodeling after myocardial infarction: pathophysiology and therapy. *Circulation* 2000;**101**:2981–8.
- Brochet E, Czifrom D, Karila-Cohen D, *et al.* Early changes in myocardial perfusion patterns after myocardial infarction: relation with contractile reserve and functional recovery. *J Am Coll Cardiol* 1998;**32**:2011–7.
- Hozumi T, Yoshida K, Ogata Y, *et al.* Noninvasive assessment of significant left anterior descending coronary artery stenosis by coronary flow velocity reserve with transthoracic color Doppler echocardiography. *Circulation* 1998;**97**:1557–62.
- Al-Saadi N, Nagel E, Gross M, *et al.* Improvement of myocardial perfusion reserve early after coronary intervention: assessment with cardiac magnetic resonance imaging. *J Am Coll Cardiol* 2000;**36**:1557–64.
- Jeremy RW, Links JM, Becker LC. Progressive failure of coronary flow during reperfusion of myocardial infarction: documentation of the no reflow phenomenon with positron emission tomography. *J Am Coll Cardiol* 1990;**16**:695–704.