CARDIOVASCULAR MEDICINE

Usefulness of myocardial parametric imaging to evaluate myocardial viability in experimental and in clinical studies

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Objective: To evaluate whether myocardial parametric imaging (MPI) is superior to visual assessment for the evaluation of myocardial viability.

Methods and results: Myocardial contrast echocardiography (MCE) was assessed in 11 pigs before, during, and after left anterior descending coronary artery occlusion and in 32 patients with ischaemic heart disease by using intravenous SonoVue administration. In experimental studies perfusion defect area assessment by MPI was compared with visually guided perfusion defect planimetry. Histological assessment of necrotic tissue was the standard reference. In clinical studies viability was assessed on a segmental level by (1) visual analysis of myocardial opacification; (2) quantitative estimation of myocardial blood flow in regions of interest; and (3) MPI. Functional recovery between three and six months after revascularisation was the standard reference. In experimental studies, compared with visually guided perfusion defect planimetry, planimetric assessment of infarct size by MPI correlated more significantly with histology ($r^2 = 0.92$ versus $r^2 = 0.56$) and had a lower intraobserver variability (4% v 15%, $p < 0.05$). In clinical studies, MPI had higher specificity (66% v 43%, $p < 0.05$) than visual MCE and good accuracy (81%) for viability detection. It was less time consuming (3.4 (1.6) v 9.2 (2.4) minutes per image, $p < 0.05$) than quantitative blood flow estimation by regions of interest and increased the agreement between observers interpreting myocardial perfusion ($\kappa = 0.87$ v $\kappa = 0.75$, $p < 0.05$).

Conclusion: MPI is useful for the evaluation of myocardial viability both in animals and in patients. It is less time consuming than quantification analysis by regions of interest and less observer dependent than visual analysis. Thus, strategies incorporating this technique may be valuable for the evaluation of myocardial viability in clinical routine.

Myocardial contrast echocardiography (MCE) has provided new insight into the assessment of myocardial viability in acute ischaemic syndromes^{1,2} and in stable ischaemic heart disease.^{3,4} However, clinical assessment of myocardial viability by MCE is based on visual interpretation of MCE images or on quantitative computer assisted processing. Visual interpretation of myocardial perfusion is subjective and requires experienced investigators.^{3–7} Quantitative analysis of myocardial perfusion by using replenishment kinetics to fit exponential curves is, on the other hand, time consuming and provides low spatial resolution. Myocardial parametric imaging (MPI) is a new method that provides automated colour coded quantification of myocardial blood flow and parametric imaging according to the relative degree of perfusion.^{8–9} Myocardial parametric quantification to detect inducible ischaemia has been shown to be feasible.^{8,9} However, the value of MPI for myocardial viability assessment has not been reported. The purpose of this study was to assess the value of MPI for viability detection in the experimental setting of acute infarction and in patients with stable ischaemic heart disease.

METHODS

Experimental studies

Experimental protocol

The experimental protocol was approved by the German Animal Research Committee and carried out as described previously.^{1,2} Briefly, 11 farm pigs (15–25 kg) were anaesthetised with α chloralose (25 mg/kg/h). The heart was

exposed through a sternotomy and an occluder was placed between the first and second diagonal branch of the left anterior descending coronary artery (LAD) for 45 minutes followed by two hours of reperfusion.

Myocardial contrast echocardiography

Real time MCE was performed with an ATL HDI 5000 (Philips Medical Systems, Bothell, Washington, USA) in short axis sections at baseline, during occlusion, and after two hours of reperfusion.² Ultrasound images were recorded in colour coded harmonic power pulse inversion mode. The mechanical index was set between 0.14–0.18 and the dynamic range was set at low. SonoVue (Bracco, Byk-Gulden, Konstanz, Germany) was applied as a continuous intravenous infusion (60 ml/h). When the myocardium of the left ventricle was fully opacified a brief pulse of higher mechanical index (fast low angle shot (FLASH)) was transmitted to clear the myocardium of microbubbles. After immediate return to low power imaging, replenishment was visualised over 10–15 cardiac cycles. The risk area was identified as the area of severely reduced or absent myocardial opacification during LAD occlusion and determined by visual and MPI guided planimetry. Similarly, perfusion defects at two hours of reperfusion were determined by planimetry as the area of severely reduced or absent

Abbreviations: FLASH, fast low angle shot; LAD, left anterior descending coronary artery; MCE, myocardial contrast echocardiography; MPI, myocardial parametric imaging

myocardial opacification 10–15 cardiac cycles after FLASH and expressed as a percentage of the risk area (perfusion defect size to risk area ratio).

Histology

The LAD was occluded again at the end of the experiment and Monastral blue dye (Sigma, St Louis, Missouri, USA) was injected into the left atrium to outline the area at risk as previously described.² Myocardial tissue was then immersed in a solution of 1.3% 2,3,5-triphenyltetrazolium chloride (Sigma) for 20 minutes, staining viable myocardium red. The risk area by histology was expressed as a percentage of the total left ventricle. The infarct size was expressed as a percentage of the risk area and was correlated with the perfusion defect size to risk area ratio estimated by MCE by linear regression analysis and Bland-Altman statistics.

Clinical studies

Patient population

The study population consisted of 34 consecutive patients with impaired left ventricular function (ejection fraction $\leq 40\%$) caused by ischaemic heart disease who were scheduled for revascularisation. Two patients were excluded because of extremely poor echographic windows. The study was approved by the local ethics committee and all patients signed an informed consent form before their enrolment in the study. MCE studies were performed within two weeks before revascularisation.

Two dimensional echocardiography

Images were recorded in standard apical views with an ATL HDI 5000. Regional function was assessed according to the 16 segment left ventricular model of the American Society of Echocardiography and graded 1 (normal), 2 (hypokinesia), 3 (akinesia), or 4 (dyskinesia). Ejection fraction was quantified by the biplane Simpson's method.¹⁰ Follow up echocardiograms were obtained at 3–6 months of follow up and recovery of regional function was defined as an improvement of ≥ 1 grade in wall motion. Functional recovery was the standard reference for myocardial viability.^{3–4 11}

Real time MCE

Perfusion images were recorded similarly to experimental studies with the use of low power imaging.^{4–7} Boluses of SonoVue (1.0 to 1.5 ml per bolus) were injected slowly to optimise visualisation of the left ventricle.

Visual analysis

Two independent observers analysed the images. Afterwards, a third independent observer verified the variability of the two first observers. Differences in opinion were resolved by consensus of all three. Normally, it takes about 5–6 cycles at rest to completely replenish the ultrasound beam in systole after microbubble destruction.^{4 7} Therefore, for visual assessment of myocardial viability, readers interpreted inter-FLASH sequences concentrating on myocardial opacification in the first 5–6 end systolic frames after FLASH. Segmental opacification was graded on a semiquantitative scale, as previously described^{4–7}: 3, homogeneous; 2, mildly reduced; and 1, severely reduced or absent. Segments with homogeneous or mildly reduced opacification were judged to be viable, whereas regions with severely reduced or absent opacification were judged to be non-viable.⁴ To prevent the effects of attenuation and lateral dropout from affecting interpretation, contrast defects were considered to be present only when the segment under question was entirely visualised from epicardium to endocardium. A slight oblique orientation of the four and two chamber views was obtained when obvious attenuation artefacts in the lateral or anterior

basal segments were seen. If a contrast defect was limited to the anterior or lateral basal segment the defect was attributed to attenuation.

Quantitative analysis of regions of interest

For quantitative analysis regions of interest were placed from epicardium to endocardium in 16 myocardial segments. Contrast intensity after FLASH was measured at end systole.¹² Plots of contrast intensity versus time were constructed and fitted to an exponential function ($y = A*(1 - e^{-\beta t})$).¹³ The plateau of signal intensity (A) and the slope of maximum signal intensity rise (β) were measured and the product of $A*\beta$ was calculated. Receiver operating characteristics of flow parameters were analysed to select the best cut off value for viability detection.

Parametric imaging

Parametric quantification was assessed off line by commercially available software (Q-Lab, Philips Medical Systems). To generate parametric images, end systolic frames after FLASH were automatically selected by ECG and an assisted border detection algorithm was used to define the endocardial and epicardial borders. The exponential curve function $y = A*(1 - e^{-\beta t})$ was fitted to the intensity vector from each pixel position, and A and β values were automatically tabulated. The mean parameters within the myocardial border were calculated and the parameter values from each pixel were colour coded according to the mean values. Parametric images of blood volume (A images), velocity (β images), and flow ($A*\beta$ images) were generated for each pixel in the myocardium. A median filter was used to reduce noise caused by poor curve fits to noisy intensity vectors. Gradations of colour were applied linearly with fixed break-points at the mean (green), two thirds of the mean (yellow), and one third of the mean (red) corresponding to normal, mildly reduced, severely reduced, and absent myocardial opacification by visual criteria.

Methodological approach to compare parametric imaging with standard methods for the assessment of myocardial viability

Experimental studies

MPI codes regions with the lowest myocardial blood flow (one third or less of the mean) as red or dark red. We hypothesised that these segments correspond to the area at risk during coronary occlusion and to tissue necrosis at two hours after reperfusion. By this approach we sought to compare MPI guided versus visually guided planimetry for perfusion defect area assessment. Histological analysis of necrotic tissue was the standard reference.

Clinical studies

In clinical studies myocardial viability by MPI was assessed qualitatively on a segmental level. We hypothesised that segments coded red or dark red would have a low probability of recovering contractile function after revascularisation (non-viable segments). Thus, segments predominantly coded red or dark red were classified as non-viable and segments predominantly coded yellow or green were identified as viable. By this approach we sought to compare the accuracy of visual analysis versus quantitative estimation of blood flow by regions of interest and versus MPI. Functional recovery at 3–6 months of follow up was the standard reference. We also assumed that by this approach the reproducibility and accuracy of MCE to detect viable myocardium could be increased. The time spent assessing myocardial perfusion by each of the three methods was measured for 20 representative images.

Figure 1 Parametric quantification of myocardial blood flow ($A^*\beta$) allowed objective delineation of the risk area during left anterior descending coronary artery (LAD) occlusion and determination of dynamics of infarct size during reperfusion. Gradations of colour were applied linearly with fixed breakpoints at the mean (green), two thirds of the mean (yellow), and one third of the mean (red) corresponding to normal, mildly reduced, severely reduced, and absent myocardial opacification by visual criteria.

Statistical analysis

Data are presented as mean (SD). Agreement between observers was assessed by κ statistics.¹⁴ Visually guided planimetry of the perfusion defect area was compared with MPI and with standard techniques by linear regression analysis and Bland-Altman statistics.¹⁵ Receiver operating characteristics were used to assess the diagnostic value of quantitative MCE parameters. Differences in diagnostic value were evaluated by the McNemar χ^2 test.⁴⁻⁷ Differences were considered significant at $p < 0.05$.

RESULTS

Experimental studies

Determination of perfusion defect size to risk area ratio

MPI allowed objective risk area delineation during LAD occlusion and infarct size determination during reperfusion (fig 1). MPI of myocardial blood flow ($A^*\beta$ images) correlated significantly more closely with histological perfusion defect size to risk area ratio ($r^2 = 0.92$, $p < 0.0001$) than with MPI of A images ($r^2 = 0.66$, $p < 0.01$), with MPI of β images ($r^2 = 0.63$, $p < 0.01$), and with visually guided planimetry ($r^2 = 0.56$, $p < 0.01$) (fig 2).

Interobserver and intraobserver variabilities

Interobserver (6% v 18%, $p < 0.05$) and intraobserver (4% v 15%, $p < 0.05$) variabilities were lower when the perfusion

defect size to risk area ratio was determined by MPI than by visually guided planimetry.

Clinical studies

Viability detection by parametric imaging in humans

Parametric quantification of myocardial blood volume (A images) yielded significantly higher specificity (66% v 43%, $p < 0.05$) than did visual assessment. Table 1 lists clinical characteristics of patients undergoing revascularisation. Visual analysis was feasible in 457 (89%) of 512 available segments and quantification analysis by time intensity curves and by MPI was feasible in 421 (82%) segments. Selecting cut off values of $A = 0.95$ dB for myocardial blood volume and $A^*\beta = 0.28$ dB/s for blood flow failed to significantly improve the diagnostic characteristics of visual assessment (tables 2 and 3, fig 3). However, parametric quantification of blood volume (A images) yielded significantly higher specificity (66% v 43%, $p < 0.05$) for viability detection than did visual assessment and provided good accuracy of 81% (table 2). Of segments judged to be viable according to predefined criteria by MPI, 179 were coded green (normal perfusion) and 119 were coded yellow (patchy perfused). Of 179 segments coded green, 150 (84%) had recovered function, whereas of 119 segments showing patchy perfusion by MPI 102 (86%) had recovered resting wall motion at follow up (table 3). MPI of myocardial blood flow ($A^*\beta$ images) underestimated myocardial viability resulting in

Figure 2 Parametric quantification of myocardial blood flow (MPI; $A^* \beta$) correlated more significantly with histological assessment of perfusion defect size to risk area ratio (B) than with visually guided planimetry of perfusion defects (A). (C, D) Bland-Altman plots showing less deviation from standard techniques ($Ratio_{Histol}$) with parametric quantification ($Ratio_{MPI}$) than with visually guided planimetry ($Ratio_{Visual}$). TTC, 2,3,5-triphenyltetrazolium chloride.

lower sensitivity (72%). Figure 4 shows a patient with an akinetic apex six months after revascularisation. MCE before revascularisation detected the non-viable tissue of the apex, indicated by severely reduced opacification. MPI of myocardial blood volume (A image) accurately and objectively identified non-viable tissue in the same region, coded as red.

Table 1 Demographic and clinical characteristics of 32 patients

Age (years)	65 (8)
Men	30 (94%)
Single vessel disease	3 (9%)
Multivessel disease	29 (91%)
CABG	27 (84%)
PCI	5 (16%)
EF before revascularisation (%)	31 (6)
EF after revascularisation (%)	39 (8)
Improved HF symptoms after 6 months	23 (72%)
Hypertension	29 (91%)
Diabetes	14 (44%)
Increased cholesterol*	29 (91%)
Family history of CAD	17 (53%)
Tobacco use	21 (66%)

Data are mean (SD) or number (%).

*Low density lipoprotein >3.11 mmol/l.

CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; EF, ejection fraction; HF, heart failure; PCI, percutaneous coronary intervention.

MPI of velocity (β images) and flow ($A^* \beta$ images) underestimated myocardial viability in the lateral wall.

Interobserver and intraobserver variabilities and assessment time

Agreement was significantly higher between observers interpreting MCE images by MPI than by visual analysis (95% ($\kappa = 0.87$) v 82% ($\kappa = 0.75$), $p < 0.05$). Analysis time was similar for MPI and visual analysis (3.4 (1.6) v 2.7 (1.7) minutes per image, not significant) but was significantly longer for quantitative analysis of regions of interest (3.4 (1.6) v 9.2 (2.4) minutes per image, $p < 0.05$).

DISCUSSION

MPI is less time consuming than offline processing by regions of interest, is less operator dependent than visual analysis, and provides high spatial resolution. MPI correlates more closely with standard techniques for viability assessment in experimental studies and has better specificity for viability detection in humans.

Experimental studies

Linka *et al*⁸ first introduced parametric analysis of contrast images by peak intensity and peak rate of rise of intensity. This approach was based on the use of triggered imaging modalities and requires background subtraction of individual frames obtained during increasing trigger intervals to select contrast specific signals. High power imaging modalities

Table 2 Prediction of myocardial viability by visual assessment, quantitative myocardial contrast echocardiography (MCE), and myocardial parametric imaging (MPI)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Visual assessment	86	43	77	57	73
MCE A values (cut off = 0.95 dB)	86	56	80	65	76
MCE A* β values (cut off = 0.28 dB/s)	82	53	79	59	73
MPI of A images	88	66*	85	73	81
MPI of A* β images	72†	62	73	61	68

* $p < 0.05$ visual assessment versus MPI of A images; † $p < 0.05$ MPI of A versus A* β images.
NPV, negative predictive value; PPV, positive predictive value.

require end systolic triggering over several seconds. Stable imaging conditions to prevent patient and observer related motion artefacts are therefore mandatory.¹⁶ Such artefacts can be more easily recognised and avoided with newer real time techniques. Furthermore, as tissue non-linearity can be ignored in low power imaging,¹⁷ real time MCE renders baseline subtraction unnecessary. We have previously shown the potential of real time MCE to assess the dynamics of post-ischaemic microvascular dysfunction^{2 18} and the usefulness of first harmonic Fourier algorithms to display myocardial perfusion in a parametric format, which allows an objective evaluation of real time MCE in animal studies.¹⁹ In the present study we used simple, commercially available software to quantify tissue viability in the experimental setting of myocardial infarction. Visual MCE confirmed ischaemia during LAD occlusion and reappearance of a major perfusion defect two hours after reperfusion. Visual assessment of risk area and infarct size corresponded with standard histological techniques. We have previously reported an $r^2 = 0.86$ for visually guided planimetry in pigs receiving soluble P selectin to reduce myocardial ischaemia-reperfusion injury.² In the present study no cardioprotective agents were applied so that the perfusion defect size was larger. This may have influenced the variability in visually guided perfusion defect planimetry, resulting in a lower $r^2 = 0.56$. Nevertheless, visually guided planimetry was still significantly related to histological findings ($p < 0.01$). As the variability for perfusion defect assessment by MPI was significantly lower, the correlation coefficient between MPI and histological analysis remained high ($r^2 = 0.92$). Thus, perfusion assessment by MPI had higher reproducibility, was less time consuming, and was more closely related to standard histological measurements. Reperfusion of infarcted tissue

results in acute microvascular obstruction and vasoconstriction causing a decrease in both blood velocity and volume.² Thus, parametric quantification of A* β images incorporating information of both blood volume and velocity offered better correlation of perfusion defect size assessment than parametric imaging of blood volume or velocity alone (A or β images). Reperfusion injury occurs in a substantial number of patients with acute coronary syndromes despite the application of aggressive reperfusion treatments. Consequences are impaired reperfusion at the microcirculatory level, contractile dysfunction, and poorer clinical outcomes.²⁰ New pharmacological approaches are aimed at preserving endothelial function and inhibiting leucocyte mediated inflammation and vasodilatation.¹⁻² Since real time MCE and particularly parametric quantification can assess the patterns of myocardial reperfusion, MPI may become a valuable and practical tool to assess the effectiveness of new

Table 3 Contingency table comparing visual assessment, quantitative MCE, and MPI for detection of functional recovery by segments

Wall motion (follow up)	Recovery	Non-recovery	κ	Agreement
Visual			0.31	73%
Viable	272	79		
Non-viable	46	60		
MCE A values			0.43	76%
Viable	245	60		
Non-viable	41	75		
A* β values			0.36	73%
Viable	234	64		
Non-viable	51	72		
MPI A images			0.56	81%
Viable	252	46		
Green	150	29		
Yellow	102	17		
Non-viable	33	90		
MPI A* β images			0.34	68%
Viable	179	65		
Non-viable	69	108

Figure 3 Receiver operating characteristic analysis of myocardial blood volume (area under the curve (AUC) 0.72) and flow (AUC 0.69) by regions of interest provides good sensitivities (86% and 82%) but low specificities (56% and 53%) for detection of myocardial viability.

Figure 4 (A) Myocardial contrast echocardiography (MCE) before revascularisation accurately detected non-viable tissue in the apical regions in a patient with an akinetic apex six months after revascularisation. (B) MPI of myocardial blood volume (A image) also correctly and objectively delineated non-viable myocardium in the apical regions, coded as red. However, MPI of (C) myocardial blood velocity (β image) and (D) flow ($A \cdot \beta$ image) underestimated the presence of myocardial viability in the lateral wall).

pharmacological or mechanic approaches in acute ischaemic syndromes.

Clinical studies

In patients with ischaemic heart disease revascularisation is associated with improved left ventricular function and better clinical outcomes when viability is present.²¹ We and others previously evaluated the role of MCE in detecting myocardial viability in stable ischaemic heart disease by using intravenous contrast administration.^{3–4} However, to the best of our knowledge, no investigation of the value of MPI for viability assessment in humans has been reported. Having shown the usefulness of MPI to assess myocardial tissue viability in experimental studies we sought to determine the potential of parametric quantification to improve the diagnostic accuracy of visual MCE for viability detection in patients with ischaemic heart disease. Assessment of tissue perfusion by both triggered and real time techniques suffers from several restrictions, including inhomogeneous distribution of regional contrast opacification, attenuation, contrast drop out in basal segments, and blooming.²² These limitations reduce the specificity of MCE to detect myocardial viability by visual criteria.^{3–4, 23–24} We and others have previously shown that complex and time consuming quantification of regional myocardial blood flow parameters including normalisation of regional myocardial blood volume to normal myocardium are necessary to improve the specificity of the technique.^{3–4} Chronic ischaemic heart disease is associated with myocardial fibrosis and increased collagen content causing decreases

in capillary density and particularly of blood volume.³ Thus, it is not surprising that parametric quantification of blood volume provided the best specificity for viability detection in accord with previous clinical studies.⁴ Myocardial parametric quantification provides automatic calculation of contrast replenishment kinetics in multiple pixels of the myocardium, which are then colour coded on a linear scale according to a normal value adjusted to the entire myocardium. This is the first study to show that, by parametric quantification of blood volume, heterogeneity of contrast distribution can be reduced and the specificity of the technique for viability detection can be significantly improved from 43% to 66%. However, the sensitivity of MPI to detect viability was comparable with visual assessment (88% *v* 86%) and the increase in accuracy was not significant by McNemar χ^2 test (81% *v* 73%). As parametric imaging has lower observer variability and requires less experience for the interpretation of myocardial perfusion this method may be of particular interest to novice interpreters.

Limitations

In accord with previous studies, we chose recovery of contractile function after revascularisation as the standard reference for assessment of myocardial viability^{4–11} because myocardial viability is an important clinical goal. However, it should be recognised that microvascular integrity in the mid and epicardial layer may be clinically important in other ways such as protection against left ventricular remodelling even in the absence of functional recovery.²⁵ Furthermore, we slowly injected boluses of contrast agent in the clinical studies, where delivery of microbubbles is not constant and may confound calculations of the peak rate of rise of contrast intensity. The use of continuous infusion may have provided more accurate results for estimation of myocardial blood flow. However, we and others have shown that calculation of replenishment kinetics is still feasible by slow bolus injections during optimal myocardial opacification,^{4–6, 26} which may therefore be a more practical approach in routine clinical settings. Parametric imaging has a relatively high false negative rate, resulting in a moderate negative predictive value of 73% for viability assessment by myocardial blood volume. However, this was not lower than the negative predictive value achieved by visual assessment in the present and in previous studies with the same technique.⁴ Owing to the relatively low specificity and moderate negative predictive value of the technique for prediction of recovery of resting wall motion we have previously suggested that MCE should be combined with low dose dobutamine stress echocardiography for detection of myocardial viability to guide clinical decision making in regard to such patients.⁴

Conclusion

Observer variability is lower with MPI than with visual assessment and MPI is less time consuming than myocardial blood flow quantification of regions of interest. MPI correlates more strongly with standard techniques for the assessment of myocardial viability in experimental studies and has better specificity than visual analysis for viability detection in humans. Thus, methods that incorporate myocardial parametric quantification may be useful for the evaluation of myocardial viability both in animals and in patients and can be applied in a busy clinical laboratory with the use of commercially available software and contrast agents.

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REFERENCES

- 1 Galiuto L, DeMaria AN, del Balzo U, et al. Ischemia-reperfusion injury at the microvascular level: treatment by endothelin A-selective antagonist and evaluation by myocardial contrast echocardiography. *Circulation* 2000;**102**:3111–6.
- 2 Hansen A, Kumar A, Wolf D, et al. Evaluation of cardioprotective effects of recombinant soluble P-selectin glycoprotein ligand-Ig in myocardial ischemia-reperfusion injury by real-time myocardial contrast echocardiography. *J Am Coll Cardiol* 2004;**44**:887–91.
- 3 Shimoni S, Frangogiannis NG, Aggeli CJ, et al. Identification of hibernating myocardium with quantitative intravenous myocardial contrast echocardiography: comparison with dobutamine echocardiography and thallium-201 scintigraphy. *Circulation* 2003;**107**:538–44.
- 4 Korosoglou G, Hansen A, Hoffend J, et al. Comparison of real-time myocardial contrast echocardiography for the assessment of myocardial viability with 18 F-fluorodeoxyglucose positron emission tomography and dobutamine stress echocardiography. *Am J Cardiol* 2004;**94**:31–7.
- 5 Korosoglou G, Labadze N, Giannitis E, et al. Usefulness of real-time myocardial perfusion imaging to evaluate tissue level reperfusion in patients with non-ST-elevation myocardial infarction. *Am J Cardiol* 2005;**95**:1033–8.
- 6 Korosoglou G, Labadze N, Hansen A, et al. Usefulness of real-time myocardial perfusion imaging in the evaluation of patients with first time chest pain. *Am J Cardiol* 2004;**94**:1225–31.
- 7 Korosoglou G, Dubart AE, DaSilva KGC, et al. Real-time myocardial perfusion imaging for pharmacologic stress testing: added value to single-photon emission computed tomography. *Am Heart J* (in press).
- 8 Linka AZ, Sklenar J, Wei K, et al. Assessment of transmural distribution of myocardial perfusion with contrast echocardiography. *Circulation* 1998;**98**:1912–20.
- 9 Yu EH, Skyba DM, Leong-Poi H, et al. Incremental value of parametric quantitative assessment of myocardial perfusion by triggered low-power myocardial contrast echocardiography. *J Am Coll Cardiol* 2004;**43**:1807–13.
- 10 Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantification of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1989;**2**:358–67.
- 11 Pagano D, Bonser RS, Townend JN, et al. Predictive value of dobutamine echocardiography and positron emission tomography in identifying hibernating myocardium in patients with postischemic heart failure. *Heart* 1998;**79**:281–8.
- 12 Iwanaga S, Ewing SG, Hussein WK, et al. Changes in contractility and afterload have only slight effects on subendocardial systolic flow impediment. *Am J Physiol* 1995;**269**:H1202–12.
- 13 Wei K, Jayaweera AR, Firoozan S, et al. Quantification of myocardial blood flow with ultrasound-induced destruction of microbubbles administered as a constant venous infusion. *Circulation* 1998;**97**:473–83.
- 14 Kramer MS, Feinstein AR. Clinical biostatistics: the biostatistics of concordance. *Clin Pharmacol Ther* 1981;**29**:111–23.
- 15 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*, 1986;i, 307–10.
- 16 Becher H, Burns PN. Contrast agents for echocardiography: principles and instrumentation. In: *Handbook of contrast echocardiography*. Heidelberg: Springer Verlag, 2000:184.
- 17 Murthy TH, Li P, Lovicchio E, et al. Real-time myocardial blood flow imaging in normal human beings with the use of myocardial contrast echocardiography. *J Am Soc Echocardiogr* 2001;**14**:698–705.
- 18 Bekereditjan R, Hansen A, Filusch A, et al. Cyclic variation of myocardial signal intensity in real-time myocardial perfusion imaging. *J Am Soc Echocardiogr* 2002;**15**:1425–31.
- 19 Hansen A, Bekereditjan R, Korosoglou G, et al. Fourier phase analysis can be used to objectively analyze real-time myocardial contrast echocardiograms. *Int J Cardiovasc Imaging* 2004;**20**:241–8.
- 20 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.
- 21 Gioia G, Powers J, Heo J, et al. Prognostic value of rest-redistribution tomographic thallium-201 imaging in ischaemic cardiomyopathy. *Am J Cardiol* 1995;**75**:759–62.
- 22 Schlosser T, Pohl C, Kuntz-Hehner S, et al. Echoscintigraphy: a new imaging modality for the reduction of color blooming and acoustic shadowing in contrast sonography. *Ultrasound Med Biol* 2003;**29**:985–91.
- 23 Sabia PJ, Powers ER, Jayaweera AR, et al. An association between collateral blood flow and myocardial viability in patients with recent myocardial infarction. *N Engl J Med* 1992;**327**:1825–31.
- 24 Ragosta M, Camarano G, Kaul S, et al. Microvascular integrity indicates myocellular viability in patients with recent myocardial infarction: new insights using myocardial contrast echocardiography. *Circulation* 1994;**89**:2562–9.
- 25 Pagley PR, Beller GA, Watson DD, et al. Improved outcome after coronary bypass surgery in patients with ischemic cardiomyopathy and residual myocardial viability. *Circulation* 1997;**96**:793–800.
- 26 Lindner JR, Villanueva FS, Dent JM, et al. Assessment of resting perfusion with myocardial contrast echocardiography: theoretical and practical considerations. *Am Heart J* 2000;**139**:231–40.

IMAGES IN CARDIOLOGY

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Post-infarct rupture of the membranous ventricular septum complicated by left atrial dissection

A 56-year old man developed a cardiogenic shock 24 hours after a postero-inferior myocardial infarction. The coronary angiogram revealed a dominant right coronary artery occluded at the origin of its third segment. Transoesophageal echocardiography showed a complex basal ventricular septal rupture at the level of the membranous septum (panels A and B). The rupture was accompanied by an extensive haemorrhage into the muscular ventricular

septum and into the interatrial septum, creating a left atrial dissection (panel C).

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(A, B) Two dimensional transoesophageal echocardiography showing rupture of the membranous ventricular septum with extensive haemorrhage into its muscular portion and the interatrial septum. (C) Four chamber view with special emphasis on the left atrial wall dissection. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; VSR, ventricular septal rupture.