Concordance between dobutamine Doppler tissue imaging echocardiography and rest reinjection thallium-201 tomography in dysfunctional hypoperfused myocardium

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Abstract

Objective—To evaluate the efficiency of the new technique colour Doppler tissue imaging (DTI) by studying the concordance between dobutamine DTI, standard grey scale echocardiography (SE), and rest-reinjection TI-201 tomography (TI) in dysfunctional myocardium.

Patients—23 patients with chronic wall motion abnormalities and proven coronary artery disease (> 70% diameter stenosis of at least one major coronary artery at angiogram).

Methods—The contractile reserve and the resting perfusion characteristics of dysfunctional myocardial segments were assessed with low dose dobutamine SE and/or DTI (2.5 up to 20 μg/kg/min) and TI on a semiquantitative basis. The DTI or SE data were separately compared with TI, on the basis of a 13 segment ventricular model. The resulting score of combined DTI and SE was also compared with TI. Finally the results obtained from DTI were compared with SE.

Results—A total of 142 severely hypokinetic or akinetic segments were visualised. The viability study was feasible in 127 segments as TI and showed a better agreement than DTI or SE alone for the assessment of myocardial viable segments evidenced by TI.

Conclusions—DTI is a helpful adjunct to SE, when using low dose dobutamine. This combination revealed as many viable segments as TI and showed a better agreement than DTI or SE alone for the assessment of myocardial viable segments evidenced by TI.

Keywords: colour Doppler tissue imaging; hibernating myocardium; thallium 201 single photon emission computed tomography; stress echocardiography

Stress echocardiography is currently performed to detect hibernating myocardium in patients suffering from chronic coronary artery disease. Other techniques such as thallium-201 reinfusion tomography (TI) and positron emission tomography might offer a good prediction of contractility recovery after myocardial reperfusion or revascularisation. High concordance between stress echocardiography or TI and positron emission tomography was observed in studies involving small series of patients. Two previous studies comparing standard echocardiography (SE) and TI paradoxically showed discordances in the specificity for recovery of function.

Doppler tissue imaging (DTI) was introduced with the hope to give a quantitative echocardiographic approach to myocardial wall velocities and to minimise the subjectivity of SE assessment of ventricular function. A visual semiquantitative evaluation of dobutamine on DTI colour images versus grey scale echocardiography has been recently reported, but no reference method was used.

To test the efficiency of this new technique we undertook a study to evaluate the concordance between dobutamine DTI, SE, and TI chosen as a reference method in consecutive patients not selected for their echogenicity suffering from chronic coronary artery disease and dysfunctional myocardium.

Methods

Patients

Twenty three consecutive patients (three women, mean (SD) age 56 (11) years) with chronic coronary artery disease and resting regional left ventricular dysfunction were included in the study. Informed consent was obtained from all patients. The assessment of both myocardial perfusion and contraction was required in the patients involved in this study for the strategy of revascularisation. TI rather than echocardiography detection improvement in function after revascularisation was chosen as a reference because most interventions were not planned for the patients included in our study. Mean ejection fraction measured by radionuclide ventriculography was 39 (11)% (range 10–56%). All patients had a coronary angiogram which exhibited the presence of significant coronary artery stenosis (> 70% diameter stenosis of at least one major epicardial artery). The study population comprised patients with single (n = 11), two vessel (n = 5), and three vessel (n = 7) coronary artery disease.
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artery disease. The lesions were located on the left anterior descending coronary artery in 21 patients, the left circumflex coronary artery in seven patients, and the right coronary artery in 13 patients. The exclusion criterion was a recent myocardial infarction (less than three weeks). A previous myocardial infarction, clinical manifestation of cardiac heart failure, and chronic angina pectoris were present in 12, seven, and 12 patients, respectively.

ECHOCARDIOGRAPHIC EQUIPMENT AND EXAMINATION

The equipment consisted of a wide angle, phased array two dimensional scanner and a colour Doppler flow and tissue imaging system (Acuson 128 XP 10; Acuson Inc, Mountain View, California, USA). The modifications to obtain only information on tissue have been previously described.\(^{12-14}\) The Doppler principle has been validated on rotating tissue models with excellent correlations between Doppler measured velocity and the applied actual speed. Whereas flows, even laminar, have high velocity and weak signal intensity, the reverse occurs for tissues which are phenomena of low velocity and high intensity. Thus, gain amplification used before the quadrature Doppler signal demodulation was reduced in order to avoid the display of intracavitary flows signals, and high pass filters used to reject high intensity tissue Doppler echoes were bypassed with tissue signal directly input into the autocorrelator. Changes in lines and their number of bursts have also been made to increase the frame rate and the sensitivity to low velocities since, as a rule, wall velocities range from 2 mm/s up to 20 cm/s. Temporal resolution of images varies with the frame rate. Velocity maps are the most usual modality. The colour scale reflects the amplitude and direction of velocity. According to the Doppler principle, velocities are positive when approaching toward the transducer (red coded), whereas those away from the transducer are negative (blue coded). The brightest shades correspond to the highest velocities on the colour scale. Velocity scale should be chosen in order to avoid aliasing. The velocity scales usually ranged between 9 and 13 cm/s. Images were recorded on video, and colour DTI images were digitised online and stored on optical disc and were then reoriented into short axis images perpendicular to the long axis of the left ventricle.

SEGMENTATION OF THE LEFT VENTRICLE

A 13 segment ventricular model derived from the 16 segment model was used for the analysis of both isotopic and echographic images.\(^3\) The segments included the basal, mid, and apical segments of the anterior, septal, lateral, and inferoposterior walls. The apical portion of the left ventricle accounted for the 13th segment.

ECHOCARDIOGRAPHIC ANALYSIS

The images were interpreted by one experienced investigator who was blinded to all other data. The DTI analysis was blinded to the SE interpretation. SE studies were interpreted by reviewing the videorecording (cineloop) whereas DTI images were usually analysed on early mid-systolic frames (fig 1). Frame by frame analysis of the cineloops was used to select the brightest colours corresponding to peak systolic velocity for individual segments. On the one hand the DTI or SE results were separately compared with TI. On the other hand the resulting scores of combined DTI and SE were compared with TI. Data obtained from DTI were compared with SE. Wall motion and velocities were semi-quantified by use of a six grade scoring system. With SE: hyperkinesia = 0; normal = 1; mild hypokinesia = 2; severe hypokinesia = 3; akinesis = 4; and dyskinesia = 5.
With DTI: white = 0; yellow or green (wall motion toward or away from the transducer, respectively) = 1; orange or turquoise = 2; red or dark blue = 3; dark or poorly coloured with red or blue = 4; paradoxal colouration = 5. A change from grade 3, 4, or 5 to grade 2, 1, or 0 was considered positive for the viability evaluation.

**TI-201 SPECT ANALYSIS**

Rest-reinjection TI-201 SPECT studies were analysed for the interpretation of myocardial viability by an experienced nuclear physician blinded to the clinical, echocardiographic, and angiographic data (fig 2). For this purpose, the TI-201 uptake was scored visually using a 13 segment analysis and a five point intensity score for each segment: 0 = normal; 1 = mildly reduced; 2 = moderately reduced; 3 = severely reduced; 4 = absent tracer uptake.21

**STATISTICAL ANALYSIS**

A $\chi^2$ test was used to study the relation between echographic and scintigraphic data. Significance was set at $p < 0.05$. Sensitivity, specificity, accuracy, and positive and negative predictive values were obtained from each echocardiographic evaluation with TI-201 SPECT considered as the reference. The agreement between DTI, SE, and TI-201 SPECT was expressed with the $\kappa$ value. Inter- and intraobserver interpretative variabilities for echocardiography were tested over 116 segments by two observers for the former and within three weeks' time by one observer for the latter. They were expressed by the percent agreement and the $\kappa$ value. As described by Landis and Koch, $\kappa = 0$–0.2 suggests slight agreement, $\kappa = 0.21$–0.40 suggests fair agreement, $\kappa = 0.41$–0.60 suggests moderate agreement, $\kappa = 0.61$–0.80 suggests substantial agreement, and $\kappa = 0.81$–1.0 suggests almost perfect agreement.22

**Results**

Of 299 left ventricular segments, 142 (47%) severely hypokinetic ($n = 87$) or akinetic ($n = 55$) segments were analysed. Datasets were available in 127 segments (feasibility 89%) and 121 segments (feasibility 85%) for DTI and SE, respectively. The difficulties encountered to analyse the viability with DTI essentially occurred for the mid-lateral ($n = 4$) and the anterior ($n = 7$) segments on the apical four and two chamber views.
Table 1. Operating characteristics and concordance between standard echocardiography (SE), Doppler tissue imaging (DTI), and thallium-201 tomography (TI) in dysfunctional hypoperfused myocardium.

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ANALYSIS OF THE CONCORDANCE BETWEEN THE THREE TECHNIQUES

Table 1 shows overall results in terms of diagnostic accuracy between SE and TI, between DTI and TI, between combined DTI and SE versus TI, and between DTI and SE. Correspondence in terms of number of segments is detailed in table 2. DTI was at least as accurate as SE for viability detection and seemed more sensitive than SE when TI-201 SPECT was considered as the reference. When DTI and SE were combined, the agreement between echocardiography and TI increased notably. DTI tended to reveal more viable segments than SE but the difference did not reach significance (50 vs 50, NS). TI more often revealed viable segments than SE (80 vs 50, p < 0.001) or DTI (84 vs 61, p < 0.001), but not more than the resulting score of both DTI and SE (84 vs 78, NS). When the study concentrated on the mid-anterior and the mid-inferior segments, the agreement between dobutamine echocardiography and TI was moderate for SE ($\kappa = 0.52$) and substantial for DTI ($\kappa = 0.76$) (table 3).

INTER- AND INTRAOBSERVER VARIABILITIES FOR ECHOCARDIOGRAPHY (116 SEGMENTS)

Intraindividual agreement was 85% for DTI and SE for the evaluation of the colour of each segment or wall motion analysis, respectively, and 85% for colour changes induced by dobutamine ($\kappa = 0.7$) versus 79% for wall motion changes ($\kappa = 0.51$). The interindividual study revealed 89% agreement for colour analysis of each segment with DTI and 52% agreement for the evaluation of contractility with SE. The percent agreement and the $\kappa$ value for detecting the changes of colour or segmental thickening from baseline to low doses of dobutamine were also better for DTI than for SE. The agreement was substantial for DTI (86% agreement, $\kappa = 0.74$) and moderate for SE (79% agreement, $\kappa = 0.52$).

Discussion

The present study shows that an evaluation of TI suspected myocardial hibernation can be more accurately achieved using relatively low doses of dobutamine with the combination of DTI and dobutamine SE than with SE alone. In contrast with DTI or SE alone, the combination of both methods revealed as many viable segments as TI.

DTI has been introduced since 1992 with the hope of quantifying the regional velocity of myocardium. The quantification of the velocity from either two dimensional or time motion images still necessitates complex time consuming analysis of data from digitised images. Our study shows that a semiquantitative DTI echocardiography analysis can reveal TI suspected hibernating myocardium with an accuracy of 70% when considered alone and 80% when the data are associated with SE in patients not selected on the basis of their echogenicity. The $\kappa$ value for the overall analysis ranges from 0.4–0.57, which represents a moderate agreement between both techniques and notably raised the analysis of the mid-anterior and mid-inferior myocardial segments.

Although earlier investigations comparing dobutamine echocardiography with perfusion scintigraphy and involving a small number of patients showed comparable results, differences in specificity for recovery of function have been reported. Hibernating myocardium is defined by its ability to recover function with restoration of adequate perfusion. The evidence of regional recovery of contractility, however, depends on a number of factors including the interobserver and intraobserver interpretative variabilities for the assessment of wall motion (when echocardiography is the imaging technique chosen for later analysis), the technique used for myocardial protection during surgery, the perioperative myocardial infarction in otherwise viable segments, the adequacy of revascularisation, and the speed of recovery ("embalmed myocardium"). Recovery of contractility is mainly assessed by standard rest grey scale echocardiography, a method which cannot usually provide evidence of small islands of viable tissue or viable subepicardial layers, or viable tissue tethered to scar tissue.

Piérard and colleagues were the first to use low dose dobutamine echocardiography to identify reversible dysfunction after reperfused acute myocardial infarction. Dobutamine echocardiography has been compared to positron emission tomography in 17 patients. Both techniques were found to be concordant in 79%. Gerber and colleagues studied the ability...
of hibernating myocardium to respond to an inotropic stimulus.\textsuperscript{27} Segments with hibernating myocardium do not improve their function in all cases with dobutamine, especially in patients with severe and globally reduced left ventricular function. These results were confirmed by Pagano and colleagues.\textsuperscript{28} They are probably explained by both the loss of contractility and the limitation of residual coronary flow reserve encountered in hibernation.

Because the results obtained with DTI appear to be closer to TI than the visual assessment of endocardial excursion and myocardial thickening from standard two dimensional images, it raises the hypothesis that colour coded myocardial velocity by DTI not only detects the contraction performance of the myocardium but also its perfusion characteristics (figs 1 and 2). Another interpretation may be that DTI evaluates the transmural wall motion velocities just as TI assesses the transmural myocardial perfusion, whereas SE analysis focuses on the subendocardial layers. In our experience, the tethering effect seems to be minimised by DTI, thus enhancing the detection of suspected viable segments.

A previous visual echocardiographic evaluation of colours had shown encouraging results for the application of DTI to stress echo.\textsuperscript{29} As our data show, a detailed interpretation of DTI images is affected by a lower intra- and interobserver variabilities than SE evaluation of the regional contractility. The interindividual $\kappa$ value was substantial for DTI and moderate for SE. This difference probably reflects the difficulties encountered when distinguishing between mild and severe hypokinesia on SE, whereas the differences between colours—for example, orange and red or turquoise and dark blue—were easier to single out. The poor agreement observed with SE evaluation of wall motion was counterbalanced by a better agreement than dobutamine SE alone. Quantitative studies with either manual or automatic detection of myocardial velocities had the most improvement in wall motion and predicts recovery of left ventricular function after coronary revascularisation had the most improvement in wall motion and predicts recovery of left ventricular function after coronary revascularisation.

Our study suggests that the refinements obtained from DTI increase the ability of echocardiography to detect the presence of myocardial hibernation myocardium detected by TI in patients suffering from chronic coronary artery disease. When associated with SE, DTI provided evidence for as many viable segments as TI-201 tomography with a better agreement than dobutamine SE alone. Quantitative studies with either manual or automatic detection of myocardial velocities are needed to evaluate the threshold of velocity variations which would predict functional recovery after revascularisation.

CONCLUSIONS

Our study suggests that the refinements obtained from DTI increase the ability of echocardiography to detect the presence of myocardial hibernation myocardium detected by TI in patients suffering from chronic coronary artery disease. When associated with SE, DTI provided evidence for as many viable segments as TI-201 tomography with a better agreement than dobutamine SE alone. Quantitative studies with either manual or automatic detection of myocardial velocities are needed to evaluate the threshold of velocity variations which would predict functional recovery after revascularisation.

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