Functional diagnosis of coronary stenosis using tissue tracking provides best sensitivity and specificity for left circumflex disease: experience from the MYDISE (myocardial Doppler in stress echocardiography) study

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**KEYWORDS**
Coronary artery disease; Tissue Doppler; Dobutamine stress echocardiography; Tissue tracking

**Abstract**

**Aims**
To evaluate the diagnostic capacity of quantitative analysis of segmental longitudinal myocardial displacement images (tissue tracking, TT) during dobutamine stress echocardiography for the detection of patients with coronary artery disease (CAD).

**Methods and results**
TT-generated colour-coded maps of systolic segmental longitudinal displacement were obtained by post-processing of echocardiographic data from 105 patients with CAD and 90 low risk individuals selected from MYDISE database. Quantitative analysis of the distribution pattern of segmental displacement during dobutamine stress was most successful when a ratio of basal (high amplitude) to apical (low amplitude) colour-coded displacement bands (B/A ratio) was employed. Applied in four different left ventricular sectors, the B/A ratio provided a significant discrimination of patients with CAD ($p < 0.05$ in the anterior and $p < 0.001$ in the inferior wall) as assessed by receiver operating characteristic analysis. The procedure was most sensitive when applied in inferior wall for the detection of left circumflex coronary artery disease, the B/A ratio of 0.8 giving the best combination of sensitivity (77 ± 8%) and specificity (77 ± 5%) values.
Conclusion
Quantification of dobutamine stress echocardiography using TT is an efficient diagnostic approach and a valuable additional modality in functional cardiac imaging for the initial identification of patients suspected for CAD.

Introduction

Colour tissue Doppler imaging and the analysis of the systolic and diastolic longitudinal motion of the heart is increasingly becoming a useful research and clinical tool for quantification of regional myocardial function both at rest and during stress. Although colour tissue Doppler software has a number of modalities including tissue displacement and strain imaging, the analysis of myocardial velocity has hitherto been by far the most commonly applied, mainly because of the relative ease of computation as well as acceptable reproducibility of the procedure. However, tissue velocity measurement ordinarily depends on the Doppler data sampling from a single, selected point in the myocardium and may be subject to an artifactual influence of "tethering" and "translational" motion of the heart. On the other hand, the myocardial tissue displacement imaging—tissue tracking—provides the information about the longitudinal motion of the heart based on the Doppler data extracted from multiple sampling points within the entire projected left ventricular wall and is not subjected to the same artifactual influence. The obtained information is presented in the form of several colour bands representing graded displacement from base to apex along a given left ventricular wall. The assessment of the longitudinal myocardial function can then be inferred from the distribution of these colour bands. The tissue tracking modality thus offers the possibility of rapidly gaining a supplementary information on myocardial function and efforts have been made to utilize the imaging capability of the technique qualitatively in various clinical situations including dilated cardiomyopathy, left bundle branch block, and acute and chronic myocardial ischemia. However, the quantification of the distribution of the segmental longitudinal displacement and its significance during dobutamine stress has not yet been sufficiently studied. Given the limitations of velocity measurements in defining the exact location of the disease in the presence of coronary artery disease (CAD) and the possibility that the quantitative analysis of the segmental longitudinal displacement distribution described by tissue tracking may provide a convenient and rapid approach for the evaluation of regional functional impairment during stress echocardiographic procedure, it appears important to evaluate the diagnostic capacity of such an analysis for the detection of significant coronary artery lesions.

In this study, we have post-processed the digitally stored dobutamine stress echocardiographic images extracted from the database of the recently published multicentre MYDISE study in order to obtain longitudinal segmental displacement colour maps using TT and, subsequently, to test the capacity of the modality for the identification of patients with significant coronary stenoses.

Methods

Study population and image acquisition

Tissue tracking was feasible in 195 out of totally 289 patients who, according to the inclusion criteria, were included in the MYDISE study even if grey-scale images were suboptimal or incomplete. The control group included 90 individuals (aged 55 ± 12 years, equal numbers of men and women) of whom 60 were patients referred for assessment of atypical chest pain and were found to have normal coronary angiograms within 3 months of the stress echocardiography. Exercise ECG was normal in all but six of these patients in whom mild ST segment abnormalities were recorded. However, all six had normal perfusion scintigrams. Perfusion scintigraphy was performed in 22% of the subjects in this subgroup and was normal in all cases. The second subgroup of controls included 30 healthy volunteers with a normal exercise ECG and a low pre-test probability of developing coronary artery disease (8.9 ± 8.0% over 10 years). All of the controls also had normal 2D echo and normal echocardiographic stress results. Among the rest 105 patients, 1-, 2-, and 3-vessel disease was revealed by elective coronary angiography. Mean age in this group was 61 ± 9 years. Exclusion criteria in the patient group were atrial fibrillation, previous myocardial infarction (electrocardiographic...
Q wave or akinetic segments on the resting echocardiographic images, previous revascularisation, unstable angina, complete bundle branch block, significant heart valve disease, uncontrollable hypertension, contraindication to dobutamine or atropine and possible pregnancy. Coronary angiography and dobutamine stress echo were performed according to the standard procedures. Resting and maximal stress echocardiographic images were obtained using a Vingmed System FiVe equipment (GE Vingmed Ultrasound, Horten, Norway). The acquired cine loops were transferred to a Macintosh computer for storage in the EchoPac programme (GE Vingmed Ultrasound, Horten, Norway) and on magneto-optical disks for post-processing. Full details of subject characteristics and methodology are given in the MYDISE study. In this study only images stored at a frame rate of more than 90 Hz were calculated. Images so stored provide better reproducibility and more homogeneous TT profile.

Colour maps of myocardial long axis displacement (tissue tracking)

Colour tissue Doppler cine loops acquired in apical view were processed using EchoPac software. After defining the beginning and the end of systole using velocity profile from the base of the left ventricular myocardium and ECG signal, colour-coded maps of the systolic segmental longitudinal displacement were obtained using TT algorithm (Fig. 1). Totally eight coding colour bands were used which means that if all colours were represented, the AV-plane longitudinal displacement exceeded 12 mm. The bands coding for high amplitude (8 to \( \geq 12 \) mm) displacement (pink, light and deep blue) represented the basal while the bands coding low amplitude (\( > 0 \) to 4 mm) displacement (yellow and red) represented the apical region of a given left ventricular wall. In healthy individuals, there is a gradual reduction of displacement from base towards the apex. The

Figure 1  Principles of tissue tracking. Starting with colour tissue Doppler imaging (left upper panel), the beginning and the end of systole is defined using ECG signal and velocity profile from the base of left ventricular myocardium. The integrals of tissue velocity from base to apex are then achieved (right panel) to give systolic longitudinal displacement profile along the longitudinal axis of the imaged left ventricular myocardium. The individual displacement values are grouped in increasing order of magnitude according to a scale with steps equal to 2 mm of displacement each and coded by different colour bands. The colour map thus obtained is superimposed on 2D image giving a typical tissue tracking picture (left lower panel). Totally eight colours are used and the upper limit of the tracking scale is chosen according to wall motion status, normally \( > 12 \) mm.
reason behind selecting three basal bands is because of the fact that frequencies of occurrence of high amplitude bands vary from patient to patient, the highest amplitude colour bands (pink with > 12 mm or light blue with > 10 mm displacement) being sometimes absent altogether, particularly during maximal dobutamine stress. Similarly, since the most common colour bands that cover the apical area are actually yellow (2–4 mm displacement) and/or red (0–2 mm displacement), these two bands in combination were used as the apical component of the B/A ratio.

Data analysis

Quantification of TT colour band distribution
Initially, the extent of the myocardium covered by each individual band was calculated as a percentage of the total length of the left ventricular myocardium both at rest and during maximal stress. The change in size of the colour bands from rest to stress was then assessed both in controls and in patients with CAD. The distribution pattern of colour bands was analysed in controls as well as in patients using the ratio (B/A ratio) of the basal (pink + light blue + deep blue) to apical bands (red + yellow).

Receiver operating characteristic (ROC) analysis
The capacity of the TT-derived B/A ratio as a diagnostic tool for the identification of patients with different anatomic location of coronary stenoses was determined by evaluation of the relation between true positive and false positive rates at several B/A ratio thresholds in different left ventricular walls (septal, anterior and inferior) corresponding to the respective coronary territory using receiver operating characteristic curves based on boundary conditions restricting their theoretical shape. For the ROC analysis, the patients were clustered from the entire database and grouped according to left anterior descending (LAD), left circumflex (LCX) and right coronary artery (RCA) stenoses, irrespective of whether they suffered from single, double or triple vessel disease. To determine whether the B/A ratio provided a significant amount of diagnostic information regarding the occurrence of coronary artery stenoses of 50%, the Z statistic based on the slope (m) ± SD of the respective ROC curve was compared with m = 1.0, indicative of an uninformative test using standard tables for normal distribution. The difference between the diagnostic abilities of B/A ratios in different left ventricular wall to detect a specific type of coronary artery stenosis was assessed by calculating the area (A) under the respective ROC curve as a percentage of the entire probabilistic area; the area under the identity line between true positive and false positive rate equal to 50% of the entire probabilistic area being indicative of totally uninformative test. The Z statistic for a difference between the areas under the respective hyperbolic ROC curves was then calculated.

General statistics
One-way ANOVA followed by Scheffe’s test was performed to compare each individual band between the patients with different types of stenotic coronary lesions. Unpaired t tests were performed for comparisons of differences in the size of colour bands from rest to stress between patients and controls. A significance level was at p value < 0.05. All values are given as means ± SD unless otherwise stated.

Results
The overall prevalence of CAD in the study population was 54%. Single vessel disease was present in 40%, double vessel disease in 32%, and triple vessel disease in 28% of the patients.

Segmental longitudinal displacement

Single vessel disease
Isolated LAD stenoses were present in 25 patients, isolated LCX stenoses in 12 patients and isolated RCA stenoses in 5 patients.

Septal wall
No statistically significant differences in the distribution of the segmental longitudinal displacement were observed at rest or peak stress between patients with different localisation of the single vessel stenoses.

Anterior wall
The distribution of the segmental displacement at rest in the patients with LCX disease differed from that observed in the patients with LAD lesions. Thus, the green bands, corresponding to a moderate amplitude displacement, occupied in these patients a greater (p < 0.05) area of the anterior left ventricular wall (15.7 ± 17.3% vs. 9.2 ± 11.3% in the patients with LAD disease). The differences disappeared, however, at peak stress.

Lateral wall
A different distribution of the segmental displacement was observed at rest in patients with LCX...
disease in whom the orange band coding for a moderate amplitude displacement occupied a larger ($p < 0.05$) area of the lateral left ventricular wall ($20.0 \pm 16.4\%$) than in patients with LAD stenoses ($12.0 \pm 8.6\%$), but the differences vanished at peak stress.

**Inferior wall**  
No statistically significant differences in any of the segmental displacements were observed between patients with different localisation of the single vessel stenoses at rest or at peak stress.

**Double vessel disease**  
LAD and LCX stenoses were found in 14 patients, stenoses in LAD and right coronary artery (RCA) in 11 patients and LCX and RCA disease in 9 patients.

**Septal wall**  
No significant differences were observed at rest between the patients with different localisation of stenotic lesions. However, at peak stress, the area occupied by light blue band coding for a high amplitude displacement was lower ($p < 0.05$) in the patients with LCX and RCA stenoses ($1.0 \pm 2.3\%$) than in the patients with LAD and LCX disease ($8.9 \pm 7.9\%$). At the same time, the patients with LCX and RCA stenoses presented wider ($p < 0.05$) yellow band coding for a moderate to low amplitude displacement ($28.7 \pm 24.5\%$) than the patients with LAD and LCX disease ($10.8 \pm 8.0\%$).

**Anterior wall**  
No statistically significant differences were observed at rest. At peak stress, the yellow band coding for a moderate to low displacement was wider ($p < 0.05$) in the patients with LAD and RCA disease ($45.3 \pm 15.9\%$) than in the patients with LCX and RCA stenoses ($13.0 \pm 16.7\%$) while the low amplitude displacement band (red) was narrower ($33.0 \pm 10.2\%$ vs. $67.0 \pm 24.8\%$ in the patients with LCX and RCA disease; $p < 0.05$).

**Lateral wall**  
No statistically significant differences appeared at rest. At peak stress, the area covered by deep blue band coding for a high amplitude displacement was significantly smaller in the patients with LCX and RCA disease ($p < 0.05$) than in the patients with LAD and RCA stenoses ($1.0 \pm 2.3\%$ vs. $8.1 \pm 7.9\%$, respectively).

**Inferior wall**  
At rest, the area occupied by a high amplitude displacement bands (deep blue) was significantly smaller ($p < 0.05$) in the patients with LCX and RCA disease than in the patients with LAD and LCX lesions ($8.8 \pm 11.9\%$ vs. $14.3 \pm 9.4\%$). These differences disappeared at peak stress.

**Triple vessel disease**  
Triple vessel disease was present in 29 patients.

**Septal wall**  
At peak stress, the high amplitude displacement bands (pink) were marginally altered ($p = 0.05$) while the light blue bands decreased significantly ($p < 0.05$). The moderate to low displacement bands (orange and yellow) increased significantly ($p < 0.05$ and $p < 0.01$, respectively) compared with the resting distribution of these bands.

**Anterior and lateral wall**  
No statistically significant changes have been observed in these two walls between the distribution of the segmental displacement at rest and peak stress.

**Inferior wall**  
The length of the high amplitude displacement deep blue bands decreased ($p < 0.05$), while the low amplitude displacement yellow bands increased ($p < 0.01$) from rest to peak stress.

**Change in segmental longitudinal displacement from rest to peak stress**  
The changes in the colour band length from rest to peak stress in patients with single vessel disease did not differ significantly from the corresponding changes in the control population. However, regional changes involving different colour bands were seen in patients with both double and triple vessel disease (Table 1).

**ROC analysis**  
The TT-derived B/A ratio in control population was 0.84 (95% confidence interval 0.65 – 1.04) in the septal wall and 1.1 (95% confidence interval 0.78 – 1.47) in the inferior wall. The B/A ratio provided a significant discrimination of patients with coronary artery disease in all myocardial walls except for the anterior wall in which the slope of the ROC curve did not differ from the slope of uninformative test ($m = 1.0$). The discriminating capacity of the B/A ratio was highest in the inferior wall ($p < 0.001$) whereas in the septal wall, the provided diagnostic information was somewhat lower ($p < 0.01$ for LAD + RCA...
Tissue tracking in diagnosis of coronary artery disease

The TT method has been developed to provide a rapid, “at a glance” understanding of the segmental longitudinal systolic shortening, which is expected to be of value for the efficient evaluation of patients with chest pain by stress echocardiography. The diagnostic decision using TT is usually based in these cases on a visual interpretation of the display of the colour bands and takes an advantage of the superior capability of the human eye to recognise promptly many simultaneous changes in size, colour and synchrony. However, visual interpretation is a subjective individual process and therefore a subject to a considerable inter-individual variation. In order to achieve a more objective quantification of the segmental longitudinal displacement and, at the same time, to act in a way similar to that of visual discrimination, we introduced and tested the B/A ratio as a diagnostic variable. This variable takes into account simultaneous changes in the display of the high and low amplitude displacement colour bands, changes of which are the most conspicuous during stress echocardiography. The B/A ratio does not include middle amplitude displacement colour bands (green and orange, i.e. 4–6 mm of displacement) and we are very much aware of the limitation that this imposes upon such a diagnostic approach. However, changes in the middle amplitude displacement bands during stress echocardiography are usually more variable and less apparent and a quantification method considering possible changes in all colour-coded bands would certainly require more analytical processing, thereby losing an advantage of being simple and fast. The B/A ratio is easy to calculate and performs sufficiently well as a diagnostic instrument without compromising the important feature of the method, i.e. its simplicity and rapidity.

The present results demonstrate that the B/A ratio at peak dobutamine stress performs diagnostically better than the analysis of differences in disease and \( p < 0.05 \) for LAD disease). The procedure appeared to be most sensitive for the detection of LCX disease, the cut point at the B/A ratio of 0.8 in the inferior wall providing the best combination of sensitivity and specificity values (77 ± 8% and 77 ± 5%, respectively; Fig. 2). RCA disease, too, was detected best in the inferior wall but the sensitivity (65 ± 8%) and specificity (62 ± 5%) values obtained with the optimal cut point at a B/A ratio value of 1.0 were somewhat lower (\( p < 0.05 \)). LAD disease was detected most efficiently in septal wall, the optimal cut point value of the B/A ratio equal to 0.7 giving sensitivity of 55 ± 7% and specificity of 62 ± 6%.

**Discussion**

Tissue tracking is one of the modalities provided by colour tissue Doppler software and offers a possibility of a colour-coded display of the distribution of the longitudinal myocardial displacement along a particular left ventricular wall during systole. In this study, the diagnostic capacity of TT for the detection of CAD was evaluated by off-line analysis of digitised tissue Doppler images of 195 patients from the recently published MYDISE study.\(^3\) The presence of CAD was verified angiographically but since both the patients and also several of the control subjects were preselected on clinical grounds, a selection bias could not be avoided. Selection bias is known to influence true and false positive rates causing a systematic overestimation of diagnostic sensitivity and underestimation of diagnostic specificity,\(^16\) and this probably may have occurred to some extent in the MYDISE study.\(^3\) The evaluation of the diagnostic ability of the methods in the present study was, however, performed employing the hyperbolic ROC curve based on boundary conditions, which is statistically insensitive to selection bias.\(^17,19\) Consequently, the data presented here are not expected to be significantly distorted.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Left ventricular sector (wall)</th>
<th>Coding colour band</th>
<th>% Change (m ± SD)</th>
<th>( p )</th>
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</thead>
<tbody>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Patients</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Double vessel</td>
<td>Lateral</td>
<td>Pink</td>
<td>1.93 ± 6.4</td>
<td>-0.8 ± 6.9</td>
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<tr>
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<td>Inferior</td>
<td>Red</td>
<td>5.6 ± 18.0</td>
<td>-3.8 ± 16.0</td>
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<tr>
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<td>Deep blue</td>
<td>5.0 ± 8.0</td>
<td>1.5 ± 8.0</td>
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<tr>
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<td>Anterior</td>
<td>Orange</td>
<td>-2.6 ± 13.0</td>
<td>2.6 ± 10.0</td>
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<tr>
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<td>Pink</td>
<td>1.93 ± 6.0</td>
<td>-0.7 ± 4.0</td>
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<tr>
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<td>Green</td>
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<td>1.8 ± 11.0</td>
</tr>
<tr>
<td>Triple vessel</td>
<td>Inferior</td>
<td>Red</td>
<td>6.0 ± 18.0</td>
<td>-6.0 ± 18.0</td>
</tr>
</tbody>
</table>
the extension of the individual colour bands coding for the segmental displacement. Thus, the differences in the extension of individual colour bands in different left ventricular walls in patients with different types of single vessel disease, even if some were present at rest, vanished at peak stress whereas the B/A ratio provided a clear discrimination between LAD, RCA and LCX stenoses. In the patients with double vessel disease, the individual colour band differences were not related to the affected coronary territory and the differences occurring in the inferior wall at rest disappeared at peak stress. Only in the patients with triple vessel disease, some of the high amplitude displacement bands decreased and some of the low amplitude displacement bands increased at peak stress. Hence, the analysis of the individual colour bands at peak dobutamine stress in patients with CAD but with anatomically preserved myocardial integrity, as was the case with the studied MYDISE population,\(^3\) does not appear to be an efficient or easy way to a proper diagnosis. This is not surprising since the motion of the AV-plane during systole decreases successively as it proceeds toward the apex and the individual segmental movements are not isolated but interconnected with each other. The diagnostic ability of the changes in the colour band length from rest to peak stress appears to be limited, too. The percentage band length change in our patients with single vessel disease did not differ from that in the controls whereas some regional changes occurred in the patients with double and triple vessel disease. A modest increase in displacement from rest to peak stress was also reported recently by Cain et al.\(^{14}\) Our present results are in agreement with these data.

In the present study, the TT-derived B/A ratio provided a statistically significant discrimination of patients with CAD. However, the ability of the method to detect coronary stenoses varied depending on the anatomic location of the stenotic lesions as evidenced by differences in the distribution of colour bands within different patient groups as well as by varying sensitivity and specificity figures from the ROC analysis (60–77%). At first glance, the diagnostic performance of TT in this study seems to be poorer than that reported from the MYDISE study.\(^3\) However, it should be defining true positive rate (TPR) at increasing false positive rate are described by a slope $m$.\(^{17}\) The individual data points represent the actual true positive (TPR observed) and corresponding false positive rates ± SD at the tested B/A ratio cut off values. The optimal cut points values are indicated (bold style) in each ROC curve.

Figure 2  ROC curve based on data from B/A ratio measurements. (A) ROC curve for B/A ratio in septal wall for the detection of LAD stenoses, (B) ROC curve for the B/A ratio in inferior wall in the detection of RCA stenoses and (C) ROC curve for the B/A ratio in inferior wall in the detection of LCX stenoses. The fitted curves
kept in mind that the higher sensitivity and specificity values reported from the MYDISE study were obtained first after adjusting for heart rate, gender and age and hence, cannot be directly compared with unadjusted data from tissue tracking. As a matter of fact, the currently presented ROC curves follow quite well the unadjusted ROC curves from the MYDISE study with the exception for the ROC curve for tissue tracking in the inferior wall in patients with LCX disease (Fig. 3). The latter curve follows instead a trajectory in-between the corresponding adjusted and unadjusted ROC curve from the MYDISE study, thus clearly demonstrating a considerable diagnostic efficiency of TT, particularly in the detection of LCX stenoses. However, it is important to realise in this context that the diagnostic information provided during dobutamine stress by segmental myocardial displacement is different and thereby complementary to the information obtained from myocardial velocity imaging, rather than being mutually exclusive. During stress, myocardial velocity is affected not only by increased inotropic interference but probably also by the increased contribution of the radial fibres of the heart to the contractile process. Accordingly, stress induced changes in myocardial velocity will reflect both the changes in heart rate and stroke volume while changes in displacement are connected to alterations in stroke volume only. Therefore, velocity measurements and displacement data may vary in the same population.

Considering the validity of the present results it is important to emphasise that the current optimal...
B/A ratio cut points and the corresponding sensitivity and specificity values were obtained in a moderately high prevalence population of patients with anatomically preserved myocardial integrity and cannot be automatically extrapolated to the populations of CAD patients with other disease profile. Recently, a superior diagnostic performance of tissue tracking was reported by Cain et al. and the method appears to perform very well in the evaluation of patients undergoing cardiac resynchronisation therapy. However, in the population studied by Cain et al., 33% of the patients presented myocardial scarring on 2D echocardiography and the patients subjected to cardiac resynchronisation suffered from an obvious contractile disorder. Hence, changes in the TT colour bands observed in these studies were certainly more dramatic and, consequently, the reported accuracy figures cannot be directly compared with the results obtained in our study population, which was much more homogeneous in terms of anatomical myocardial integrity resulting in less pronounced changes in the colour band distribution at peak stress.

In conclusion, tested in a middle high prevalence population of patients with anatomically preserved myocardial integrity, the quantitative analysis of the systolic segmental longitudinal displacement using TT is an efficient diagnostic method for the detection of CAD during dobutamine stress providing the best sensitivity and specificity for LCX disease. The approach has the advantage of being fast and objective, performing at the same time with a diagnostic accuracy comparable to that of other diagnostic tests. The method thus offers a valuable methodological addition for the initial identification of patients suspected for CAD.

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References


