Predictors of Viability in Patients with Negative Low-dose Dobutamine Stress Echocardiography

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Abstract
Background: Low-dose dobutamine stress echocardiography is specific for predicting reversible contractility dysfunction, but its sensitivity is lower than ideal.

Objective: We sought to explore the predictors of myocardial contractile recovery following revascularization, in patients with no viability by low-dose dobutamine stress echocardiography.

Methods: We prospectively enrolled 30 consecutive patients with significant coronary stenosis/occlusion amenable for revascularization, regional wall motion abnormality in the distribution of the affected artery and absence of viability by low-dose dobutamine stress echocardiography. They underwent resting $^{99m}$Tc-sestamibi imaging study, and then underwent successful coronary revascularization. Follow-up echocardiography was performed 3 months later. Patients were classified into 2 groups: group 1: with evidence of myocardial contractile recovery after revascularization at follow-up echocardiography and group 2: with no such evidence of recovery. The two groups were compared with respect to patients' clinical, echocardiographic and scintigraphic data.

Results: The mean age was 52.3 ± 5.9 years, with 97% being males. The percentage of total $^{99m}$Tc-sestamibi uptake was significantly higher in group 1 as compared to group 2 (p < 0.01), and it was the strongest independent predictor of myocardial contractile recovery at 3-month follow-up by multivariate regression analysis. Receiver operating characteristics curve revealed that a cutoff value of the percentage of total $^{99m}$Tc-sestamibi uptake of 72% best predicted myocardial contractile recovery, with a sensitivity of 100% and specificity of 95.7%.

Conclusion: In patients with no viability by low-dose dobutamine stress echocardiography, the percentage of total $^{99m}$Tc-sestamibi uptake independently predicted myocardial contractile recovery following coronary revascularization. (Arq Bras Cardiol 2011;96(3):188-195)

Keywords: Predictors; viability; revascularization; dobutamine stress echocardiography.

Introduction
With the enormous progress in the field of myocardial revascularization over the last two decades, predicting the presence of viable myocardium has acquired paramount clinical importance, particularly in patients considered for interventional treatment. Myocardial viability represents the impairment of contractile function that is potentially reversible if blood supply is adequately restored. Presumably, improving blood supply to dysfunctional, but viable regions, results in subsequent improvement in regional and global left ventricular function, heart failure symptoms, functional capacity and long-term survival. Thus, an important consideration is whether hypokinetic or akinetic myocardial areas represent viable myocardium with critically endangered blood supply, or irreversibly damaged necrotic scar tissue. This scenario was supported by the results of several studies, wherein only patients with severe left ventricular dysfunction who harbored viable myocardium, benefited from revascularization.

Pharmacological stress echocardiography has gained wide acceptance for the identification of viable myocardium, chiefly because of its feasibility, safety, diagnostic accuracy and prognostic power. Low-dose dobutamine stress echocardiography (DSE) has emerged as an attractive and increasingly used method to identify viable myocardium through its ability to elicit a beta adrenoreceptor-mediated increase in myocardial contractility. Dobutamine-responsive wall motion was found to be specific for predicting reversible contractility dysfunction, but its sensitivity is lower than ideal. In a prospective study design, we sought to explore the predictors of contractile recovery after revascularization, in patients with absence of viability by low-dose DSE.

Methods
Patient selection
Prospectively, we enrolled 30 consecutive patients referred from our catheterization labs with significant coronary
steno\(s\)/occlusion, during the period from November 2006 to October 2008. Patients were considered eligible for inclusion if they had regional wall motion abnormality in the anatomical distribution of the affected arteries as explained later, affected arteries amenable for revascularization, and absence of viability by low-dose DSE. Significant coronary stenosis was defined as at least 70% luminal obstruction of at least one sizable coronary artery (measuring 2.5 mm or more in diameter), seen in 2 different projections. Total coronary occlusion was defined as 100% luminal obstruction with Thrombolysis In Myocardial Infarction (TIMI) grade 0 forward flow distal to the site of obstruction. We excluded patients with recent myocardial infarction or unstable angina during the past 4 weeks, significant stenosis of the left main coronary artery (defined as at least 50% luminal obstruction), decompensated heart failure, protruding fresh left ventricular thrombus, significant valvular or congenital heart disease, any myocardial disease apart from ischemia, left ventricular ejection fraction > 40%, bundle branch block, contraindication to dobutamine (for example: history of complex ventricular arrhythmias, uncontrolled hypertension with blood pressure > 180/110), and patients with limited life expectancy due to coexistent disease (for example: malignancy). Before inclusion, an informed written consent was obtained from each patient after full explanation of the study protocol, the type of data collected, the way of data processing and the scope of data collection. The study protocol was reviewed and approved by the local institutional human research committee in our center according to the ethical guidelines of the 1964 Declaration of Helsinki, as revised in 2002.

Definitions of risk factors

The presence of hypertension was defined as a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg, previously recorded by repeated non-invasive office measurements, which lead to life-style modification or antihypertensive drug therapy. The presence of diabetes mellitus was defined as a fasting plasma glucose ≥ 126 mg/dl, and/or a 2-hour postload glucose ≥ 200 mg/dl, or specific anti-diabetic drug therapy. Dyslipidemia was defined by a low-density lipoprotein cholesterol > 100 mg/dl, and/or serum triglycerides > 150 mg/dl, and/or a high-density lipoprotein cholesterol < 40 mg/dl in men and < 50 mg/dl in women.

Baseline echocardiographic assessment

Assessment of regional and global left ventricular systolic function was performed in all patients by transthoracic echocardiography within 48 hours of admission. Doppler echocardiography was performed using a Hewlett Packard Sonos 5500 cardiac ultrasound machine (Hewlett Packard, Andover, Massachusetts, USA) equipped with harmonic imaging capabilities. A 2.5 MHz phased array probe was used to obtain standard 2D, M-mode and Doppler images. Patients were examined in the left lateral recumbent position using standard parasternal and apical views. Global left ventricular systolic function was assessed in apical 4-chamber and 2-chamber views using the biplane modified Simpson’s method. Regional wall motion was assessed according to the standard 16-segment model recommended by the American Society of Echocardiography. Individual segments were then sub-grouped based on the known vascular distribution into left anterior descending territory, left circumflex territory, right coronary artery territory, and overlap segments.

Regional wall motion was visually assessed for each segment individually, considering both endocardial excursion and systolic thickening, and each segment was graded according to the semiquantitative scoring system described by Knudsen et al. Segments with poorly defined endocardial borders for 50% or more of their length were considered non-visualized and assigned a score of 0. Wall thickening was assessed at a distance of at least 1 cm from the adjacent segment to minimize the effect of tethering. Wall motion in a vascular territory was considered abnormal if wall thickening was abnormal in at least two contiguous non-overlap segments. Wall motion score index (WMSI) was derived by dividing the sum of individual segment scores by the number of interpretable segments.

Stress echocardiographic protocol

All patients underwent low-dose DSE as follows: dobutamine (Dobutrex™, Lilly, Eli and Company, Indianapolis, USA) was infused intravenously starting at 5 µg/kg/minute, increased up to 20 µg/kg/minute, in 3-minute stages. Examinations were standardized and performed by the same operator. Standard views were recorded at baseline, during each stage of the infusion protocol, as well as during recovery. Images were digitized in cine-loop format and saved for subsequent playback and analysis. Views were analyzed by a single expert echocardiographer (Z.A.) employing the software program of the echocardiography machine. Analysis of viability was performed during all stages of the protocol. Visual assessment of wall motion and thickening was performed as before. Global left ventricular systolic function and wall motion score index were evaluated at rest and at the end of each stage. The presence of viability was defined by improvement in regional wall motion score by at least one grade in at least two contiguous non-overlap segments along with at least 20% reduction in global WMSI compared with baseline evaluation. The stress test was performed with the patients on their full anti-ischemic and anti-failure medications. All patients were receiving beta-blockers, angiotensin converting enzyme inhibitors, statins and aspirin.

99mTc-sestamibi imaging protocol

Patients underwent resting 99mTc-sestamibi imaging study with the administration of trimetazidine, using the standard imaging technique, within 4 days of coronary angiography, provided that no ischemic events were recorded during the time from the coronary angiography to 99mTc-sestamibi imaging. Trimetazidine (Vastarel™, Servier, France) was administered by the oral route the day before the study (60 mg divided in 3 equal doses 8 hours apart), and 1 hour before performing the study (60 mg in a single dose). Injection of 25-30 mCi of radioactive tracer was administered 45-60 minutes before image acquisition. Images were acquired using a rotating single-head gamma camera (GE Starcam 4000i, UK) equipped with low-energy all-purpose collimators. Energy windows of 20% were respectively centered on the 140-keV peaks of 99mTc-sestamibi.
Thirty-two images were obtained over 180° extending from the 45° right anterior oblique to the 45° left posterior oblique projections. All studies were subjected to quality-control checks and corrections when necessary for camera non-uniformity, center-of-rotation offsets, patient motion, and “upward creep”.

**99mTc-sestamibi image analysis**

Two experienced nuclear cardiologists blinded to the clinical, echocardiographic and angiographic data, analyzed the 99mTc-sestamibi images. The vascular assignment of myocardial segments to the vascular distribution of major coronary arteries was performed according to the 17 segments scoring system11. The percentage of 99mTc-sestamibi uptake was assessed for each segment individually. The mean value of percent 99mTc-sestamibi uptake was calculated for all left ventricular segments (total 99mTc-sestamibi uptake), as well as separately, for each individual vascular territory.

**Coronary revascularization**

All patients underwent coronary revascularization either by percutaneous coronary angioplasty, or by surgical bypass grafting according to the decision of the attending physician. Revascularization was performed within 2 weeks of the index coronary angiography, provided that no ischemic events were recorded during the time from the coronary angiography to revascularization. The decision was based on the clinical presentation, coronary anatomy and evidence of ischemia.

**Echocardiographic follow-up**

Follow-up echocardiographic re-assessment was performed 3 months after revascularization to evaluate regional and global left ventricular systolic function as described before. All evaluations were performed offline by the same echocardiographer (Z.A.) who was blinded to whether the images were obtained before or after revascularization. The occurrence of myocardial contractile recovery was defined by improvement in regional wall motion score by at least one grade in at least two contiguous non-overlap segments along with at least 20% reduction in global WMSI compared with baseline evaluation10. During follow-up, patients were questioned regarding the occurrence of new myocardial infarction or congestive heart failure by means of clinical visits, telephone calls, hospital chart reviews, or personal communication with the referring physician.

**Statistical analysis**

All continuous variables were presented as mean ± SD, if they were normally distributed. Data were tested for normal distribution using the Kolmogorov-Smirnov test. Categorical variables were described with absolute and relative (percentage) frequencies. According to the above definition of myocardial contractile recovery, patients were classified into 2 groups: group 1 with evidence of actual myocardial contractile recovery after revascularization at follow-up echocardiography, and group 2 with no such evidence of recovery. The two groups were compared with respect to patients’ clinical characteristics, echocardiographic, scintigraphic and angiographic data, using the unpaired t test for normally distributed continuous variables, and the Pearson chi-square test for categorical variables. Multivariate regression analysis was performed to identify the independent predictors of myocardial contractile recovery after revascularization, in which the dependent variable was the outcome variable of interest, whereas factors entered into the model included the mean value of percent 99mTc-sestamibi uptake by all left ventricular segments (total 99mTc-sestamibi uptake), as well as that assessed separately, for each individual vascular territory, the mean resting left ventricular ejection fraction and WMSI before revascularization. Eventually, we generated a receiver-operating characteristics (ROCs) curve to identify the cutoff value of the percentage of total 99mTc-sestamibi uptake that best predicted myocardial contractile recovery after revascularization. The optimal cutoff value was defined as the value giving the largest area under the curve (AUC). Finally, twenty cases were randomly selected for analysis of intra-observer variability. Assessment of variability was performed using linear regression analysis. All analyses were 2-sided and a probability value of P < 0.05 was considered statistically significant. Analyses were performed with the SPSS, version 12.0 statistical package (SPSS Inc., Chicago, IL, USA).

**Results**

**Baseline demographic characteristics**

Of a total of 61 patients with significant coronary stenosis/occlusion amenable for revascularization and regional wall motion abnormality in the anatomical distribution of the affected arteries, during the study period, 31 had evidence of viability by low-dose DSE, while 30 had no such evidence of viability. All patients with positive viability by low-dose DSE underwent coronary revascularization. According to the aforementioned definition of myocardial contractile recovery at the 3-month follow-up echocardiography, there were 27 patients (87.1%) with evidence of myocardial contractile recovery after revascularization, and 4 (12.9%) with no such evidence of recovery. A total of 30 consecutive patients with no evidence of viability by low-dose DSE were included in the current study, who underwent coronary revascularization for significant coronary stenosis/occlusion. All patients completed the 3-month follow-up period, and no patient reported any clinical events during the period from revascularization to the follow-up echocardiography evaluation. According to the aforementioned definition of myocardial contractile recovery at follow-up echocardiography, there were 7 patients (23.3%) with evidence of myocardial contractile recovery after revascularization (group 1), and 23 (76.7%) with no such evidence of recovery (group 2). Of the total cohort (61 patients), low-dose DSE predicted myocardial contractile recovery following revascularization with a sensitivity of 79.4% and a specificity of 85.2%11.

Revascularization was successful and complete in all patients. All patients in group 1 were revascularized by surgical bypass grafting, while in group 2, 5 patients (21.7%) were treated with percutaneous coronary angioplasty and 18 (78.3%) were treated by surgical bypass grafting (p > 0.05). The demographic characteristics of the entire cohort as well as of the 2 individual groups are shown in Table 1. The mean age was 52.3 ± 5.9 years, with 97% of them being males. Diabetes mellitus was
found more frequently in group 2 as compared to group 1 (69.6% versus 28.6% respectively, \( p < 0.05 \)). Otherwise, no statistically significant differences were found between the two groups regarding any of the demographic characteristics.

**Echocardiographic data**

Table 2 shows the DSE data of the entire study cohort as well as the 2 individual groups. At baseline, the mean left ventricular ejection fraction of the entire study cohort was 24 ± 4%, while the mean WMSI was 2.7 ± 0.15. No statistically significant differences were found between the two groups regarding any of the DSE data (Table 2). At the 6-month follow-up, the mean left ventricular ejection fraction was 24 ± 4% versus 24 ± 4%, while the mean WMSI was 2.3 ± 0.07 versus 2.6 ± 0.24, in group 1 as compared to group 2, respectively, (\( p < 0.05 \) for both).

The DSE protocol was well tolerated by all patients with no major side effects during or after the test.

**Table 1 - Baseline clinical characteristics of the whole cohort and the 2 individual groups**

<table>
<thead>
<tr>
<th></th>
<th>Total cohort (n = 30)</th>
<th>Group 1 (n = 7)</th>
<th>Group 2 (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.3 ± 5.9</td>
<td>52.3 ± 3.7</td>
<td>52.3 ± 6.6</td>
</tr>
<tr>
<td>Male gender</td>
<td>29 (97)</td>
<td>6 (85.7)</td>
<td>18 (78.3)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18 (60)</td>
<td>2 (28.6)</td>
<td>16 (69.6) *</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18 (60)</td>
<td>4 (57.1)</td>
<td>14 (60.9)</td>
</tr>
<tr>
<td>Smoking</td>
<td>25 (83.3)</td>
<td>5 (71.4)</td>
<td>20 (86.9)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>7 (23.3)</td>
<td>2 (28.6)</td>
<td>5 (21.7)</td>
</tr>
</tbody>
</table>

Continuous variables are presented as mean ± SD, while categorical variables are presented as numbers (percentage). IHD indicates ischemic heart disease. * indicates \( p < 0.05 \).

**Table 2 - Echocardiographic data of the whole cohort and the 2 individual groups**

<table>
<thead>
<tr>
<th></th>
<th>Total cohort (n = 30)</th>
<th>Group 1 (n = 7)</th>
<th>Group 2 (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV EF (%) at baseline</td>
<td>24 ± 4</td>
<td>24 ± 3</td>
<td>24 ± 4</td>
</tr>
<tr>
<td>WMSI at baseline</td>
<td>2.7 ± 0.16</td>
<td>2.7 ± 0.06</td>
<td>2.6 ± 0.25</td>
</tr>
<tr>
<td>LV EF (%) at low-dose dobutamine</td>
<td>24 ± 4</td>
<td>24 ± 4</td>
<td>24 ± 4</td>
</tr>
<tr>
<td>SBP at baseline</td>
<td>119 ± 14</td>
<td>115 ± 16</td>
<td>123 ± 12</td>
</tr>
<tr>
<td>SBP at low-dose dobutamine</td>
<td>125 ± 14</td>
<td>122 ± 14</td>
<td>128 ± 14</td>
</tr>
<tr>
<td>DBP at baseline</td>
<td>86 ± 8</td>
<td>88 ± 9</td>
<td>83 ± 7</td>
</tr>
<tr>
<td>DBP at low-dose dobutamine</td>
<td>82 ± 6</td>
<td>84 ± 6</td>
<td>79 ± 6</td>
</tr>
<tr>
<td>HR at baseline</td>
<td>71 ± 9</td>
<td>73 ± 10</td>
<td>69 ± 9</td>
</tr>
<tr>
<td>HR at low-dose dobutamine</td>
<td>77 ± 9</td>
<td>79 ± 10</td>
<td>75 ± 9</td>
</tr>
</tbody>
</table>

All variables are presented as mean ± SD. LV EF - indicates left ventricular ejection fraction; WMSI - wall motion score index; SBP - systolic blood pressure; DBP - diastolic blood pressure; HR - heart rate.

**Scintigraphic data**

Table 3 shows \(^{99m}\)Tc-sestamibi scintigraphy data of the entire study cohort as well as the 2 individual groups. The percentage of total \(^{99m}\)Tc-sestamibi uptake was significantly higher in group 1 as compared to group 2 (78 ± 9% versus 64 ± 9% respectively, \( p < 0.01 \)). Similarly, the percentage of \(^{99m}\)Tc-sestamibi uptake by segments in the left anterior descending coronary territory, was significantly higher in group 1 as compared to group 2 (90 ± 12% versus 78 ± 19% respectively, \( p < 0.01 \)).

**Independent predictors of contractile recovery**

The multivariate regression analysis showed that the percentage of total \(^{99m}\)Tc-sestamibi uptake, and the uptake by segments in the left anterior descending coronary territory, independently predicted myocardial contractile recovery at 3-month follow-up after revascularization, with the former being the strongest independent predictor (Table 4).

**Cutoff value for prediction of myocardial contractile recovery**

The receiver operating characteristics (ROCs) curve revealed that a cutoff value of the percentage of total \(^{99m}\)Tc-sestamibi uptake of 72%, best predicted myocardial contractile

**Table 3 - Scintigraphic data of the two individual study groups**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=7)</th>
<th>Group 2 (N=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% total (^{99m})Tc-sestamibi uptake</td>
<td>77.6 ± 2.6</td>
<td>64.4 ± 8.9 *</td>
</tr>
<tr>
<td>% (^{99m})Tc-sestamibi uptake by LAD segments</td>
<td>90 ± 12.4</td>
<td>78.2 ± 19 *</td>
</tr>
<tr>
<td>% (^{99m})Tc-sestamibi uptake by LCx segments</td>
<td>86 ± 5.9</td>
<td>89.2 ± 14.3</td>
</tr>
<tr>
<td>% (^{99m})Tc-sestamibi uptake by RCA segments</td>
<td>62.1 ± 17.8</td>
<td>48.7 ± 20.7</td>
</tr>
</tbody>
</table>

All variables are presented as mean ± SD. LAD indicates left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery. * indicates \( p < 0.05 \).

**Table 4 - Multivariate linear regression model demonstrating the independent predictors of myocardial contractile recovery following revascularization at 3-month follow-up**

<table>
<thead>
<tr>
<th></th>
<th>B Coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% total (^{99m})Tc-sestamibi uptake</td>
<td>2.5</td>
<td>0.003</td>
</tr>
<tr>
<td>% (^{99m})Tc-sestamibi uptake by LAD segments</td>
<td>1.6</td>
<td>0.042</td>
</tr>
<tr>
<td>% (^{99m})Tc-sestamibi uptake by LCx segments</td>
<td>0.4</td>
<td>0.626</td>
</tr>
<tr>
<td>% (^{99m})Tc-sestamibi uptake by RCA segments</td>
<td>-0.02</td>
<td>0.959</td>
</tr>
<tr>
<td>LV EF (%) at baseline</td>
<td>-0.08</td>
<td>0.276</td>
</tr>
<tr>
<td>WMSI at baseline</td>
<td>-0.2</td>
<td>0.290</td>
</tr>
</tbody>
</table>

LAD - indicates left anterior descending artery; LCx - left circumflex artery; RCA - right coronary artery; LV EF - left ventricular ejection fraction; WMSI - wall motion score index.
recovery at 3 months following revascularization, with an area under the curve (AUC) =0.957 (95% confidence interval 0.812 to 0.994, p < 0.001). Using this 72% cutoff value, the percentage of total $^{99m}$Tc-sestamibi uptake had a sensitivity of 100%, specificity of 95.7%, for predicting myocardial contractile recovery following revascularization (Figure 1).

The analysis of intra-observer variability revealed a close correlation between repeated assessments of regional wall motion by the single operator, with a correlation coefficient $r$ =0.92.

Discussion

Assessment of myocardial viability is one of the most challenging areas of modern cardiology. The gold standard for the presence of viability is improvement in global and/or regional contractility following myocardial revascularization. Nevertheless, triaging a patient for revascularization depends on the ‘expected’ ensuing recovery of contractile function in the compromised area. In this regard, the ability of low-dose dobutamine to elicite a contractile response in dysfunctional, but viable myocardial segments supplied by occluded/critically stenosed arteries has been a controversial issue. Some previous studies reported the limited ability of even very low doses of dobutamine to unmask the presence of viable myocardium in the setting of severe coronary stenosis or total occlusion, where coronary flow reserve is exhausted and resting myocardial perfusion is severely reduced. A meta-analysis of six studies (287 patients) that used DSE to predict improvement in the left ventricular systolic function following revascularization showed a weighted mean sensitivity and specificity of 57 and 73%, with a PPV and NPV of 63 and 68%, respectively.

Complex structural changes occur in viable dysfunctional myocardium at both cardiomyocyte and extracellular matrix levels, which include ultrastructural abnormalities seen by electron microscopy. Moreover, indirect markers of apoptosis have been recently demonstrated in more severely compromised hibernating cardiac myocytes. Additionally, reduced gap junction area in hibernating myocardium might interfere with local coordination of myocyte contraction. Other pathophysiological alterations in dysfunctional—viable—myocardium include energy depletion and reduced calcium responsiveness. Overall, they may hamper the contractile response to low-dose dobutamine, with a subsequent large proportion of false negative results to DSE, and a resultant suboptimal sensitivity.

The issue of predicting myocardial contractile recovery following revascularization has long been controversial. Previously reported studies in literature have not provided consistent data to determine the specific predictors of potential contractile recovery. Some reports highlighted the importance of coronary collaterals to the infarct-related artery territory as a predictor of the presence of underlying myocardial viability and the potential myocardial contractile recovery following revascularization. Generally speaking, it is always recommended to search for viable myocardium before revascularization of an occluded coronary artery; however, there is no practical, yet sensitive, method for assessing myocardial viability in the cath lab.

To the best of the authors’ knowledge, the current study was the first in literature to report that the percentage of total $^{99m}$Tc-sestamibi uptake and the percentage of uptake by segments in the left anterior descending coronary territory, independently predicted ‘actual’ myocardial contractile recovery at the 3-month follow-up following revascularization, in a very specific group of patients with absence of viability by low-dose DSE. Additionally, a cutoff value of 72%, of the former, predicted contractile recovery, with an excellent sensitivity and specificity. Nevertheless, the current study does not compare the two methods (low-dose DSE and $^{99m}$Tc-sestamibi imaging) and an alleged superiority of $^{99m}$Tc-sestamibi imaging over low-dose DSE cannot be advocated. Furthermore, even when resting systolic function does not recover following revascularization, the presence of partial viability is likely to be beneficial for contractile reserve, exercise tolerance, prevention of remodeling and survival; revascularization can still be beneficial in this group of patients.

In the current study, we employed a protocol of resting $^{99m}$Tc-sestamibi imaging after oral administration of trimetazidine. A robust body of evidence indicates that resting $^{99m}$Tc-sestamibi may be a good marker for viability. Both trimetazidine and $^{99m}$Tc-sestamibi share the same intracellular target: the mitochondrion. As metabolic reserve does exist in the hibernating state, trimetazidine might exploit this reserve by increasing mitochondrial metabolism. One study demonstrated that trimetazidine was associated with an increase in $^{99m}$Tc-sestamibi uptake in infarcted, but viable myocardial areas and stated that this increase was probably related to improvement in mitochondrial oxidative metabolism, which is essential for $^{99m}$Tc-sestamibi retention. They concluded that coupling trimetazidine administration to
99mTc-sestamibi perfusion scintigraphy may represent a better means of detecting viable myocardium27.

Our results suggested that the absence of diabetes mellitus also predicted the presence of viability, though it was not an independent predictor at the multivariate regression analysis. A previous study by Auerbach et al28 reported that, apart from anginal symptoms, no statistically significant association was found between the presence of viability (detected by positron emission tomography) and any of the clinical characteristics, including diabetes28. Inconsistent findings would reflect the heterogeneous nature of the underlying disease process, the lack of uniformity in patient selection and study protocols among different studies.

Limitations of the study

Our findings were based on a single-center study with a relatively small sample size, a fact that makes it difficult to generalize our results to all patients undergoing risk stratification for predicting contractile recovery after revascularization. Multicenter studies using the same protocol and examining a larger number of patients are needed. Additionally, the number of patients who recovered adequate contractility was very small; therefore the results of the current study should be considered with caution. Moreover, the follow-up period of 3 months might have been inadequate to allow recovery of some dyssynergic, but viable segments, which would otherwise translate to a better myocardial contractile recovery rate. Delayed recovery can further occur in a substantial number of segments up to a median of 14 months following revascularization, a fact that warrants repeated assessment after longer periods of follow-up. The fact that all patients were receiving beta blockers before DSE examination may have contributed to a substantial proportion of false negative results, since it is known that this drug interferes with the sensitivity of DSE. A possible limitation of the current study is that it does not provide a direct comparison between DSE and 99mTc-sestamibi perfusion scintigraphy. Given that magnetic resonance imaging is considered the gold standard for detection of viability, the fact that the patients did not undergo this modality may constitute another limitation. Another limitation of the study is the lack of quantitative methods for measuring systolic thickening; instead, the operator adopted visual assessment only. Nevertheless, the problem of intra-observer variability can be minimized by stronger adherence to common and new methodological standards. Finally, follow-up coronary angiography was not performed, therefore, restenosis or reocclusion cannot be definitely excluded, something that would hazard the initially achieved contractile recovery. However, no patient reported any clinical events during the period from revascularization to follow-up echocardiographic evaluation.

Conclusion

Our data suggest that myocardial contractile recovery after revascularization in patients with no evidence of viability by low-dose DSE could be independently predicted by the percentage of total 99mTc-sestamibi uptake and the uptake by segments in the left anterior descending coronary territory. A cutoff value of the percentage of total 99mTc-sestamibi uptake of 72% best predicted myocardial contractile recovery at 3 months following revascularization.

Clinical implications

Patients with ischemic left ventricular dysfunction whose coronary arteries are amenable for revascularization and who have no evidence of viability by low-dose DSE, may still have a “glimpse of hope” in gaining significant myocardial contractile recovery following revascularization, if they have an ‘ample’ percentage of total left ventricular 99mTc-sestamibi uptake, especially in the absence of diabetes mellitus. The other way around is also true, however: due to the relatively low specificity of perfusion scintigraphy to detect viability, DSE can be performed in patients with positive viability by perfusion scintigraphy. Yet, the routine use of both modalities together in all patients cannot be advocated, as it would not be cost-effective.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any post-graduation program.

References


