Comparative Study of 18 F-Fluorodeoxyglucose Imaging with a Dual-Head Coincidence Gamma Camera with Dobutamine Stress Echocardiography for the Assessment of Myocardial Viability

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Objective
To compare Dual-Head Coincidence Gamma Camera (DCD-AC) with Dobutamine Stress Echocardiography (DSE) in viability assessment, using functional recovery as the gold standard.

Methods
Twenty-one patients were prospectively studied, with coronary artery disease and severe left ventricular dysfunction undergoing DSE and DCD-AC at baseline and DSE three months after myocardial revascularization (MR).

Results
From 290 segments analyzed, 83% were akinetic, 15% hypokinetic and 2% dyskinetic at rest. DSE identified 68% of these segments as non-viable. DCD-AC identified 56% of these segments as normal (dysfunctional segments with preserved metabolism and perfusion), 30% as viable (preserved metabolism and reduced perfusion) and 14% as non-viable (absent perfusion and metabolism). Among DSE non-viable segments, DCD-AC classified 80% as normal or viable and 19.9% as non-viable (p<0.001). In hypokinetic segments viability and normal segments were detected in a higher proportion by both methods (p<0.001). DSE sensitivity and specificity were 48.3% and 78.1% respectively. DCD-AC sensitivity and specificity was 92.2% and 20.0%. DCD-AC identifies a higher incidence of function improvement in normal segments than in viable and non-viable.

Conclusion
DCD-AC classified as normal or viable most of the non-viable DSE segments. In assessment of functional recovery, three months after MR, DCD-AC showed a high sensitivity but low specificity.

Key words
stunned myocardium, 18 F-fluorodeoxyglucose, echocardiography, myocardial revascularization.
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Arquivos Brasileiros de Cardiologia – Axle, long axle, long vertical axle and long horizontal axle.

with transmission attenuation correction were divided into short
filtered back projection by using a Butterworth convolution filter
matrix. Transaxial tomography images were reconstructed through
(Vértex Plus MCD/AC).

cameras and use of ultra-high energy collimators, was initially
used, but with limited image quality. With the event of scintillation

Definition of myocardial viability involves recovery of segmental
myocardial contractility with proper restoring revascularization of
compromised segment. Therefore, different identification methods
of myocardial viability must be compared with contractility recovery
after surgical or percutaneous myocardial revascularization.

So, such work compared myocardial viability detection through
capitation of FDG, through AC and DSE, in patients with severe
left ventricular dysfunction. Functional recovery three months after
MR was used as gold standard.

Methods

Twenty-one patients (20 men, mean of age of 58.6±10 years
old) with multi-arterial coronary disease and severe left ventricular
dysfunction, defined by LVFE <0.40, echocardiography at rest (Simp-
son method), submitted to MR, were prospectively studied. The
study was carried out in patients with indication of MR and results
from AC and DSE were not used for procedure definition. All patients
were under sinus rhythm and were ill-taken from at least one myo-
cardial infarction, with more than 15 days from the beginning of
the study. Thirteen patients showed angina due to exercise and
did not show angina. Eight showed stable heart failure (class
≥ III New York Heart Association). Nine were diabetic and 15
hypertensive. Beta-blockers administration was interrupted on the
day of DSE. The mean of LVFE was 0.32±5.9. There were no
patients with significant valve disease or left ventricular aneurysm.

The study was previously approved by the Ethics Committee in Research and information on free and clear consent was provided
by all patients.

Myocardial viability was assessed by DSE, as by AC, before
surgery. Regional and global contractility were assessed through
echocardiography, at rest and under stress by dobutamine.

Myocardial contractility recovery was analyzed three months after
myocardial revascularization, through transthoracic echocardiography
at rest and through dobutamine stress echocardiography.

For assessment purposes, left ventricle was divided into 17
segments, according to standards by American Heart Association.

With fasting patients, 50 g of glucose were administrated 50
minutes prior to FDG endovenous administration (2.22 MBq/Kg) and
insulin administration. Images were acquired by using dual-head coinci-
dence gamma camera operated through coincidence mode, with
correction attenuation (Vértex Plus MCD/AC ADAC Laboratories).

For perfusion study, Setamibi-[Tc-99m] (MIBI) (555 MBq) was
utilized. Images were acquired with dual-head coincidence gamma
camera, equipped with low energy and high resolution collimator
(Vértex Plus MCD/AC).

Images were obtained in 48 projections with 180° 64x64
matrix. Transaxial tomography images were reconstructed through
filtered back projection by using a Butterworth convolution filter
with Autospect plus software (Philips Medical System). Images
with transmission attenuation correction were divided into short
axle, long axle, long vertical axle and long horizontal axle.

Segments were qualitatively classified in accordance to MIBI
or FDG uptake: normal = 0, discreet reduction = 1, moderate
reduction = 2, important reduction = 3 and absent = 4.

Every myocardial was classified as normal, if perfusion was
shown normal or discreetly reduced; as viable, if FDG uptake was
relatively increased in a perfusion defect (perfusion-metabolism
disagreement); and as non-viable, if there was reduced perfusion
and FDG uptake (absence of perfusion-metabolism).

Segment contraction was assessed through transthoracic e-
chocardiography (HP Sonos 5500 and ATL HDI 5000, Philips Me-
dical System), according to recommendations from American E-
chocardiography Society. Myocardial contraction was assessed as
normal = 1, hypokinetic = 2, akinetic = 3 and dyskinetic = 4.

Dobutamine infusion started from 5 µg/kg/min, then increasing to
10 and 20 µg/kg/min, every 3 minutes.

In pre-surgery DSE, segments were classified as: 1) normal,
in the presence of preserved contraction at rest, with hyperdynamic
response to dobutamine infusion; 2) viable, hypokinetic or akinetic
segments with improvement of at least one point in contraction
score due to dobutamine infusion; e 3) non-viable, segments with
reduced contraction at rest and absence of improvement due to
dobutamine infusion. Segments classified as normal were excluded
from the analysis. Only segments with contraction changes at
rest were considered.

In DSE, carried out three months after MR, segments were
classified according to echocardiographic assessment compared to
pre-operative period contractility, in: 1) functional recovery segments,
which means segments that showed contractility improvement in
relation to pre-operative period; 2) contractile reserve, segments
without contraction improvement at rest, but with improvement due
to dobutamine infusion; 3) absence of improvement; and, finally,
4) worsening of contraction in relation to pre-operative period. Thickening
assessment, instead of contractility, was carried out at cipol region,
due to abnormal movement at post-operative period.

Quantitative data were described as mean ± 1 standard devia-
tion and qualitative data as proportions.

Chi-square test was used for comparisons between proportions,
and the t-test of Student, was used for the analysis of quantitative
variables. In the presence of two or more categories in at least
one of the variable, residue analysis was applied for identification
of more relevant proportions. The level described of p<0.05 was
regarded as significant.

Results

Clinical characteristics of patients are shown in table I. All patie-
tnts were ill-taken by previous myocardial infarction. Time interval
between the infarction and their inclusion in the study was longer
than 15 days. All patients had stable coronary artery disease. All
patients showed significant obstruction in anterior descending artery
and, at least, another artery with lesion higher than 75%.

All patients underwent anterior descending artery revasculari-
zation, being internal thoracic artery used in 20 patients. Three
patients showed signs of left ventricular failure, one showed pul-
monary complication, one patient showed transitory renal failure
and another patient showed transitory atrioventricular block. Four-
teen patients did not show any complication.
Twenty patients had improvement in their functional level and none of them showed angina.

From a total of 357 segments, 51 were excluded for showing normal contractility at rest, 12 because they were not submitted to revascularization and four due to improper echocardiography analysis. From 290 assessed segments, 83% were akinetic, 15%, hypokinetic and 2% dyskinetic.

DSE classified 94 (32%) segments as viable and 196 (68%), as non-viable. On the other hand, AC classified 162 (56%) segments as normal, 87 (30%), as viable and 41 (14%), as non-viable segments (fig. 1).

Among segments classified as viable through DSE, there was a greater incidence of normal and viable segments through AC (p<0.05) and, among segments classified as non-viable through DSE, there was a greater incidence of non-viable segments through AC (p<0.05).

According to contractility at rest, hypokinetic segments showed a greater incidence of viable segments through DSE and normal and viable segments through AC (p<0.001). A larger number of non-viable segments occurred among akinetic segments through both methods (p<0.006) (fig. 2).

Regional contraction recovery, either at rest or under dobutamine, was detected in 116 (43%) segments. DSE identified 90 segments as viable, from which 56 recovered their contraction.

AC identified 231 segments as normal or viable, from which only 107 recovered their contractility (fig. 3).

**Discussion**

Contractile reserve detection through DSE needs a preserved contractile system and, therefore, a greater quantity of functioning myocytes, whereas AC assesses the perfusion and metabolism of glucose.

In this work, myocardial viability detection through DSE and DCD-AC was compared. Data obtained showed differences between the two methods, regarding sensitivity and specificity. DSE showed lower sensitivity, but its specificity was satisfactory, whereas AC showed high sensitivity, but reduced specificity. Results from DSE can be explained by to many factors. Studied population showed at least one previous myocardial infarction, multilateral coronary disease and a high proportion of akinetic segments (83% from dysfunction segments). Akinetic segments showed a larger quantity of fibrosis, dedifferentiation and loss of contractile elements. Those segments require a longer time to recover from post-MR myocardial contraction, and the three-month assessment may be underestimated the total number of those segments. Previous studies in patients with severe left ventricular dysfunction showed a lower prevalence of akinetic segments, which reflected the important ventricular dysfunction level among the assessed population.

Hypokinetic segments were mostly classified as viable, through DSE, and normal or viable, through DCD-AC. Obviously, those segments have preserved myocardial cells and sufficient contractile apparatus to allow for myocardial contraction. Some of those regions were considered as non-viable due to a discreet improvement of segment contraction, which was not sufficient to change the contractility score during dobutamine infusion.

A significant number of segments show a normal or viable pattern through DCD-AC, without showing post-MR contraction.

**Table I - Data expressed through mean ± SD or number of patients.**

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
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<tbody>
<tr>
<td>Age (years old)</td>
<td>58.61±10.5</td>
</tr>
<tr>
<td>Sex (male/female)</td>
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</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>21</td>
</tr>
<tr>
<td>Angina, NYHA I</td>
<td>5</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
</tr>
<tr>
<td>Ill-taken vessels 1 vessel</td>
<td>0</td>
</tr>
<tr>
<td>2 vessels</td>
<td>6</td>
</tr>
<tr>
<td>3 vessels</td>
<td>12</td>
</tr>
<tr>
<td>Trunk</td>
<td>3</td>
</tr>
<tr>
<td>Infarction location</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>12</td>
</tr>
<tr>
<td>Inferior</td>
<td>6</td>
</tr>
<tr>
<td>Anterior and inferior</td>
<td>1</td>
</tr>
<tr>
<td>Non-Q</td>
<td>2</td>
</tr>
</tbody>
</table>

| Hypokinetic              |  |
| Viable                   |  |
| Non-viable               |  |
| Akinetic                 |  |
| Viable                   |  |
| Non-viable               |  |

**Fig. 1 - Number of normal, viable, and non-viable segments through DCD-AC, divided according to DSE viability (p<0.001). DSE = dobutamine stress echocardiography. DCD-AC = dual-head coincidence gamma camera and attenuation correction programs.**

**Fig. 2 - Number of normal, viable, and non-viable segments through DCD-AC, divided according to DSE viability and contractility detection (p<0.001). DSE = dobutamine stress echocardiography. DCD-AC = dual-head coincidence gamma camera and attenuation correction programs.**
improvement. Those findings can be explained by the following reasons: 1) hypokinetic segments were considered as non-viable due to discreet or absence of myocardial contraction improvement, during dobutamine infusion, which was insufficient to allow for a change of the echocardiographic score; 2) presence of viable tissues islands, intertwined by a significant quantity of fibrotic tissue, which did not allow for post-MR contractility improvement; and 3) hibernating myocardium, with preserved FDG uptake and that does not show response to inotropic stimulation, can have other changes of cell functions involved.

One hundred and sixteen segments recovered their contractile function. DCD-AC showed good sensitivity, but reduced specificity, and DSE showed lower sensitivity and specificity than the literature. Those differences can be attributed to the great quantity of akinetic segments and to the short time interval for functional recovery. A significant number of truly viable segments was classified as non-viable through DSE and showed FDG uptake. That fact can be explained by the severity of changes in cardiomyocytes (damage and loss of myofibrils and increase of interstitial fibrosis), ill-taken explained by the severity of changes in cardiomyocytes (damage and loss of myofibrils and increase of interstitial fibrosis), ill-taken.

Contractility assessment, three months after MR, may have underestimated the number of segments with functional recovery. Bax et al. studied 26 patients, before and after MR. Contractile function was early (three months) and tardively (14 months) reassessed, after MR. Only 32% of hibernating segments showed improvement of contractile function at early assessment, with an additional improvement of 61%, tardively. Pagano et al. carried out the control study after six months of MR, mentioning that a longer period would be necessary.

Accuracy of both techniques was compared with functional recovery after MR. Despite such gold standard being imperfect, when placing excessive importance on sub-endocardium, it is the most suitable for clinical assessment. That gold standard does not assess remodeling, arrhythmias and prevention from new infarctions.

Myocardial contraction assessment, under dobutamine infusion, allows for identification of segments that show contraction recovery only under inotropic stimulus.

This study made use of assessment per segment, which is suitable for validation and comparison between different techniques. However, some studies use the improvement of fraction of ejection, measured at rest, as an indication of myocardial viability. The measurement of global left ventricular fraction of ejection has the influence of hypercontractile myocardial segments, which compensate for viable segments with contraction reduction. Improvement in viable segment contraction with revascularization allows for hypercontractile segments take over normal contraction, without modifying global fraction of ejection.

Due to the remarkable attenuation effect through positron annihilation energy transmission, attenuation correction program, through transmission method, is necessary to reach validation of positron emission tomography with dedicated equipment.

This is the first study assessing Ac use in MR submitted patients, by using regional contractility recovery analysis as myocardial viability gold standard. This study allows for the analysis of results from this new technology in clinical practice.

Left ventricle was divided into 17 segments. Such model provides the best harmony with anatomical data and has the best adjustment with usually employed methods in echocardiography and in nuclear cardiology.

DSE interpretation is visual, therefore a dependent operator. Contractility division in four categories gathers, in the same category, segments with small contractility differences. As the contractility assessment is subjective, the division into a larger number of categories could lead to misinterpretation. The 17-segment model used may have caused some discrepancy in left ventricular division between different techniques.

Only lower doses of dobutamine were used. The utilization of high doses allows for identifying biphasic response, which has greater sensitivity. In post-operative assessment, the use of high doses would allow for the identification of ischemic segments, occasioned by failure in revascularization. Even in lower doses of dobutamine, a high incidence of ventricular arrhythmias and hypotension took place.

Functional recovery was assessed three months after surgical procedure. Akinetic segments may require a longer time for contractility recovery, but the necessary time is still unknown. A serial mode analysis would allow for a better information on the necessary time for myocardial functional recovery.

Both methods use in this study identified a greater proportion of viable and normal segments among hypokinetic segments. Most DSE non-viable segments were classified as normal or viable through AC.

In post-three-moth functional recovery, AC showed high sensitivity, but reduced specificity, whereas DSE showed low sensitivity and good specificity.

Acknowledgements

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