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The predictive value of ^{201}Tl rest-redistribution and ^{18}F-fluorodeoxyglucose SPECT for wall motion recovery after recent reperfused myocardial infarction

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^{201}Tl and ^{18}F-FDG are useful for acute myocardial infarction (MI) assessment. The goal of this study was to compare their predictive value for wall motion recovery in the culprit area after a recent reperfused MI using SPECT technique. ***Methods:*** Forty-one patients (mean age: 56 ± 12 years) were included, 81% of them male; all were studied within 1–24 days post MI. They underwent angioplasty in 27 cases (12 primary); bypass grafting in 10 cases and successful thrombolysis in 4. SPECT ^{201}Tl injected at rest and redistribution (R-R) and also ^{18}F-FDG, were performed on different days. Processed tomograms were interpreted blinded to clinical or angiographic data. Segmental wall motion assessed with echocardiography at baseline was compared with the 3 month follow up. ***Results:*** Sensitivity [Confidence Interval] for ^{201}Tl R-R was 74.6% [60.5–84.5], for FDG it was 82.1% [70.8–90.4]; specificities were 73% [64.3–80.5] and 54.8% [45.6–63.7], respectively. ^{18}F-FDG tended to be more sensitive than ^{201}Tl R-R, but the latter was more specific ($p < 0.0004$). Both ^{201}Tl R-R and ^{18}F-FDG presented high negative predictive value (p: ns). ***Conclusion:*** In recent MI, SPECT ^{201}Tl R-R is a valuable and widely available technique for viability detection, with similar sensitivity and significant better specificity than SPECT ^{18}F-FDG.

Key words: ^{201}Tl, ^{18}F-FDG, myocardial infarction, viability, SPECT

INTRODUCTION

MYOCARDIAL INFARCTION (MI) due to coronary artery disease (CAD) is the main cause of death in most developed countries. After MI, it is important to clearly assess residual ischemia and ventricular mass with potential recovery. These viable zones could have a significant impact on ventricular function, future cardiac events, survival, and even on myocardial remodeling. It is also important to correctly identify its size and recognize candidates for eventual revascularization. The ability to detect viable zones posterior to an acute or recent MI offers the patient different therapeutic approaches. During the initial period the vessel can be opened by thrombolysis, percutaneous transluminal coronary angioplasty (PTCA) using a balloon, with or without a stent, as well as coronary artery bypass grafting (CABG). However, after a recent MI, noninvasive methods able to detect viable tissue could have a role in decision selection.

Different imaging modalities have been used to recognize viability. Currently, the most commonly employed are ^{201}Tl protocols [such as rest-redistribution (R-R) or reinjection], quantitative ^{99m}Tc-sestamibi, and dobutamine echocardiography.[1–4] Studies with PET are less easily available, even though ^{18}F-fluorodeoxyglucose (FDG) and ^{13}N-ammonia are considered the gold standard for

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myocardial metabolism and flow. These procedures are valuable in the chronic manifestations of CAD mainly reflecting hibernating myocardium; nonetheless, in the early post-MI phase, especially after revascularization there is probably significant tissue extension with stunning phenomenon. In old MI or ischemic cardiomyopathy with severe contractile dysfunction, there is the presence of necrotic, ischemic, stunned, hibernated and normal tissue.[5–9]

FDG SPECT technique is as reliable as FDG performed with PET dedicated systems for myocardial evaluation.[10–12] Regardless of the imaging modality and the revascularization method employed, clinically, the improvement in regional contractile function some months post-revascularization is the most accepted gold standard for myocardial viability.

The purpose of this study was to compare the predictive value of FDG SPECT with ^{201}Tl R-R in the assessment of viability after recent MI. Echocardiography was employed to evaluate regional wall motion recovery in segments with basal abnormal contraction. The clinical relevance in this setting of patients with early revascularization could be to recognize those cases with considerable areas of myocardium still viable in spite of the fact that the procedure might have appeared successful. A control angiography is routinely not performed in these patients and a noninvasive method could be of great help.

MATERIALS AND METHODS

Population

Forty-one patients were studied prospectively after acute MI, at a mean of 8.9 days after symptoms onset [range: 1–24 d; 68% < 10 d and 98% < 15 d post MI]. The mean age was 56 ± 12 years, and 81% were males. The diagnosis of MI was established clinically with EKG and cardiac enzymes. Their history included: type II diabetes in 6 cases, old MI in 4, and coronary revascularization in other territories in 2 cases. After MI, successful thrombolysis was performed as the only revascularization method in 4 cases, PTCA with or without stent in 27, and bypass surgery in 10. These procedures were performed in 18 patients prior to the radionuclide scan and in 23 after it. Mean left ventricular ejection fraction, estimated visually through ECHO or ventriculogram, was 44% ± 10.0 (severely depressed in 4 patients, moderately in 5 and mildly in 4).

All patients had an angiogram. CAD was demonstrated using the standard technique with a Siemens Pandoros 1200 angiographer angioskop-D, model 9023375, Elema, Switzerland. The MI corresponded to the left anterior descending artery (LAD) in 24 cases, right coronary artery (RCA) in 12, and circumflex artery (CX) in 5. Thirty-four percent of the patients had multivessel disease (6 with 3-vessel and 8 with 2-vessel disease); and significant arterial stenosis was considered as ≥ 50%.

Inclusion Criteria:

- Confirmed MI in the prior 25 days period.
- Demonstrated CAD by angiogram.
- Signed informed consent.
- Abnormal segmental baseline echocardiography.
- Presence of 3-month follow up echocardiography.
- ^{201}Tl SPECT performed within 24 h of FDG SPECT.
- Blood glucose level <160 mg/d*l* prior to FDG injection.

Exclusion Criteria:

- Recent unsuccessful thrombolysis as the only revascularization procedure.
- Normal segmental baseline echocardiography.
- Unstable hemodynamic condition.
- Pregnancy.
- Absence of signed informed consent.

Table 1 ^{201}Tl R-R patterns and wall motion recovery in hypo or akinetic segments of the culprit territory

^{201}Tl R-R	Echocardiographic wall motion		Total
	Improvement	No improvement	
Normal	34	28	62
Viable	16	6	22
Non viable	17	92	109
Total	67	126	193

Table 2 Comparison of ^{201}Tl R-R and FDG in the prediction of segmental wall motion recovery after recent MI and revascularization procedures

	^{201}Tl R-R	FDG/^{201}Tl	p
Sensitivity	74.6 [60.5–84.5]	82.1 [70.1–90.4]	ns
Specificity	73.0 [64.3–80.5]	54.8 [45.6–63.7]	< 0.00038
Positive predictive value (PPV)	59.5 [48.2–70.1]	49.1 [39.6–58.7]	ns
Negative predictive value (NPV)	84.4 [76.2–90.6]	85.2 [75.6–92.1]	ns
LR positive	2.77	1.81	
LR negative	0.34	0.32	

LR: Likelihood Ratio, [CI]: Confidence Interval
ns: not significant

Table 3 FDG /^{201}Tl patterns and wall motion recovery in hypo or akinetic segments in the culprit territory

FDG/ ^{201}Tl rest	Echocardiographic wall motion		Total
	Improvement	No improvement	
Normal	31	26	57
Mismatch	24	31	55
Match	12	69	81
Total	67	126	193

Table 4a Concordance between ^{201}Tl Rest-Red and FDG for viability assignment in segments with wall motion improvement

		FDG	
		Viable	Non-viable
^{201}Tl Rest-Red	Viable	***48***	2
	Non-viable	7	***10***

Concordance: 86.6%; kappa: 0.61

Red: Redistribution

Table 4b Concordance between ^{201}Tl Rest-Red and FDG for viability assignment in segments with no wall motion improvement

		FDG	
		Viable	Non-viable
^{201}Tl Rest-Red	Viable	***32***	2
	Non-viable	25	***67***

Concordance: 78.6%; kappa: 0.72

Red: Redistribution

Echocardiography

All patients had a baseline and a 3-month follow-up echocardiography performed with a Hewlett-Packard echocardiography system Sonos 5500 or 2500, Andover, Massachusetts, USA. The tests were interpreted independently, and then, jointly, to assess wall motion changes by 2 blinded observers using a segmental model and a score ranging from 1–4.[13,14] They were classified as normal, hypokinetic, akinetic or dyskinetic. In the 3-month control exam, the same score was used to register recovery.

Radionuclide Studies Protocol

^{201}Tl acquisition parameters were the same in all patients. FDG and ^{201}Tl processing were also similar. Interpretation was performed using myocardial slices in all studies by 3 independent blinded observers.

^{201}Tl rest-redistribution SPECT

1. SPECT ^{201}Tl was performed with 148 MBq injected at rest.
2. Images were acquired 10 min after injection at rest and at 3–4 h after redistribution.
3. 180° acquisition from 45° right anterior oblique; 32 steps of 40 sec duration; 64 × 64 matrix; low-energy and high resolution collimator with a dual Genesys ADAC camera, Milipitas, San Jose, California, USA or a Starcam General Electric gamma camera, Milwaukee, WI, USA.

FDG SPECT

1. In non-diabetic patients: the preparation required:
   - Low fat diet for 24 h and fasting for at least 4 h prior to injection.
   - 250 mg of acipimox and 350 mg of acetyl salicilic acid (to block unpleasant effects of acipimox) were given between 3 h and 1½ h prior to FDG injection, respectively.
   - 75-g carbohydrate meal was given 1½ h prior to FDG injection.
2. In diabetic patients: the same protocol was utilized but fasting was not required.
3. Glucotest was performed in all patients prior to FDG injection in order to fulfill the inclusion criteria. Mean glucose value of the group was 111.6 ± 37 mg/dl.
4. FDG was administrated using doses between 96–533 MBq, with a mean of 280 MBq.
5. FDG SPECT was performed with the dual Genesys, ADAC, Milipitas, San Jose, California, USA.
6. 511 keV collimators were used to acquire under the same conditions of ^{201}Tl but with a different frame duration (range: 40–60 sec according to dose).

Analysis and Interpretation

A 17 segmental model was employed for all echocardiograms and radionuclide studies.[13] Discrepancies were resolved by consensus. ^{201}Tl R-R were interpreted as normal, or with reversible or fixed perfusion defects. Normal segments and those with reversible defects with ^{201}Tl were considered viable as well as low or moderate fixed defects (>50% of maximal, uptake in left ventricle, according to semiquantitative analysis). All severe fixed defects were considered non viable. FDG uptake was related to the corresponding ^{201}Tl rest perfusion status and interpreted as match, mismatch or normal. All mismatches (classical or reverse; see definition below) and normal segments were considered viable. FDG ^{201}Tl matches in segments with severe perfusion defects (< 50%) were considered non viable.

Viable and non-viable segments were then correlated with the 3-month wall motion recovery by echocardiography. The final analysis included only culprit lesion segments with baseline abnormal wall motion (193 abnormal segments out of 345 in the areas subtended by the infarct related artery).

Sensitivity, specificity, predictive values and likelihood ratios for positive and negative studies (LR positive and LR negative), with their respective 95% confidence

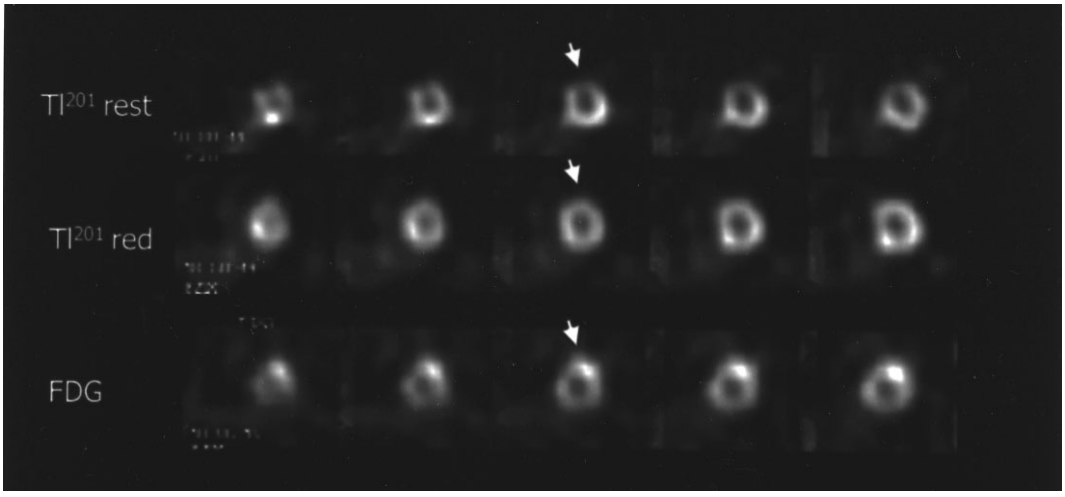

Fig. 1 Fifty-year-old female with a recent anterior MI (90% proximal LAD stenosis); treated with PTCA and stent ten days post MI. FDG was performed at day 11 post MI. **^{201}Tl Rest:** anteroapical perfusion defect at rest (*first row*); **^{201}Tl Red:** the defect showed important improvement in the redistribution images (*second row*); **FDG:** significant hypermetabolism in anteroapical segment (*third row*). Anterior and apical wall motion recovery was observed in the follow-up echocardiogram at 3 months.

intervals [CI], were calculated for both tracers. These values were obtained considering the segments with abnormal basal wall motion at echocardiography. Fisher test for small samples and the McNemar test were used (considering 0.05 as significant). Concordance analysis was also performed between ^{201}Tl R-R and FDG applying kappa test.

RESULTS

A. ^{201}Tl R-R

The analysis of ^{201}Tl R-R studies demonstrated 84 normal or viable segments and 109 non-viable as observed in Table 1.

Sensitivity for detecting viability was 74.6% and specificity 73.0%. Positive and negative predictive values and likelihood ratios are shown in Table 2.

B. FDG

The analysis of FDG studies related to rest perfusion ^{201}Tl demonstrated 55 segments with mismatch and 81 with match, as also seen in Table 3. Two-thirds of the 24 segments with wall motion improvement presented classical mismatch (greater metabolic glucose activity than perfusion) and one-third presented the opposite or reverse mismatch.

Sensitivity for viability detection was 82.1% and specificity 54.8%. Positive and negative predictive values and likelihood ratios are also shown in Table 2.

C. Comparison of ^{201}Tl R-R and FDG

There were no statistical differences in sensitivity, or negative and positive predictive values for ^{201}Tl R-R compared to FDG. However, specificity was significantly higher for ^{201}Tl R-R than FDG ($p < 0.001$). Positive likelihood ratio was also higher than ^{201}Tl R-R and FDG (Table 2).

Concordance of 86.6% was observed for segments with wall motion improvement while for those segments with no improvement, the concordance observed was 78.6% (Tables 4a and 4b).

DISCUSSION

In patients with recent MI, viability detection has been less extensively studied than in chronic CAD. It is known that, in the acute setting, stunned myocardium is relevant. There are some reports suggesting that the value of FDG in that condition could be lower than during the chronic period. A recent work (Bax et al.) in patients with chronic CAD, compared the value of FDG SPECT with ^{201}Tl R-R and low dose dobutamine echography (LDDE) concluding that the two latter techniques associated are similar to the former, in spite of the low specificity of ^{201}Tl R-R and the low sensitivity of LDDE for predicting the improvement of left ventricular function post-revascularization.[15] Dangas et al.[16] recently compared quantitative ^{99m}Tc-sestamibi, LDDE and FDG in asymptomatic patients early after infarction. They observed very little additional value of FDG over sestamibi for viability detection 3–10 d post Q-wave MI. We agree with them that this could be due to abnormal myocardial metabolism of glucose in that period. Schwaiger et al.[8] studied a group of post-MI patients within 72 h of the symptoms onset with ^{13}N ammonia and FDG, showing a high incidence of residual viability in segments with

reduced flow and impaired function. Czernin et al.[17] studied also patients with recent MI with ^{13}N ammonia and FDG (21–170 h after onset) and reported a variation of diminished segmental blood flow in quantitative serial studies with diminished or normal FDG uptake. They believed that preserved oxidative metabolism in segments with mismatch could be a prerequisite for survival of ischemic segments.

Diverse SPECT protocols are available for viability evaluation.[1,18–21] ^{201}Tl and dobutamine echocardiography have similar post-MI sensitivity with LDDE appearing to be more specific and having a better predictive value.[1,22] Pierard et al.[23] who compared PET FDG and dobutamine echo in patients with MI after thrombolytic therapy, describing that early recovery of perfusion in the area at risk is associated with a good functional outcome, whereas a high glucose/perfusion ratio indicates jeopardized myocardium that frequently loses viability.

In this study, FDG had similar sensitivity compared with ^{201}Tl R-R for detecting myocardial viability in patients with recent MI. Beanlands et al.[7] found that in patients with recent occlusion rest/stress/reinjection, ^{201}Tl protocol was 89% sensitive and 54% specific in predicting wall motion recovery, considering diverse revascularization procedures. Bax et al.[15] described ^{201}Tl R-R specificity of 57% in chronic CAD. We obtained better specificity with ^{201}Tl R-R, and their data were similar to ours with FDG. However, we do not have a clear explanation for our comparative FDG lower specificity in this acute setting. FDG may be taken up by leucocytes around the inflammatory process in acute MI, decreasing its specificity even more.

Concerning our echographic control of the abnormal myocardial segments performed at 3 m after revascularization, this limit was selected due to the known asynchronic recovery between motion frequently observed; metabolism recovery could be even more delayed.[25,26] Post-PTCA restenosis may also occur later even though stents have significantly reduced this complication.[27–29]

Other important factors to be mentioned were related to the time elapsed after the MI; it has been observed that there is more FDG uptake (glycolitic activity) in hypoperfused segments with shorter post-MI periods[30] and also that coronary flow reserve in an infarct-related artery correlates with the extent of viability.[31] Uren et al.,[32] demonstrated after acute MI a severely abnormal vasodilator response involving not only resistance vessels in infarcted myocardium, but also in tissue perfused by normal coronary vessels. However, the interpretation of this parameter involving microvasculature is complex.

On the other hand, the finding that all flow/metabolism mismatches were considered viable in this study was also supported by the data of others (reverse mismatch has been associated with viability and could be due to a mixture of fibrotic and ischemic myocardium in multivessel disease).[33–35] Stunned myocardium could also be involved in the phenomenon. This needs to be confirmed with more data, but these results showed that reverse mismatch segments have a viable behavior after revascularization. In early post MI stages it is possible that radionuclide techniques are less affected by stunning than echocardiograhic ones, and it has been demonstrated than they could be more accurate to define MI extent.[36]

Regarding the selected protocol, there are several reports recommending acipimox (a nicotinic acid derivative) as simpler and effective compared to euglycemic hyperinsulinemic clamp, even in diabetics.[37–40]

Finally, echocardiography also offers a valuable alternative for viability assessment after MI. LDDE and contrast technique have been employed and there are some works comparing them with ^{201}Tl or sestamibi viability protocols in recent MI.[41–44] Recently, Hillis et al.[45] reported a comparison between real time intravenous contrast and LDDE in 37 patients studied early post MI (2–3 days); 88% of their group was submitted to PTCA prior to echo (control at 51 ± 19 days). LDDE was superior for prediction of functional recovery in akinetic segments, but both tests together improved the predictive accuracy; Sensitivity was 86% for contrast and 71% for LDDE and specificities 44% and 82% respectively. For LAD their results were superior to those for RCA or CX using contrast method. They conclude that their results were similar in accuracy to reported results with conventional nuclear SPECT techniques.

Regarding limitations, it could be mentioned that a) follow-up coronary angiography was not performed in this study to assess the patency of revascularized territories and b) our sample, representing a prospective clinical study, was not perfectly homogeneous (patients with different ventricular functions were included).

CONCLUSION

In recent MI, SPECT ^{201}Tl R-R is a valuable and widely available technique similar to SPECT FDG to predict wall motion recovery after revascularization. It has similar sensitivity and significantly better specificity than SPECT ^{18}F-FDG. The lower specificity of FDG in the acute setting should be taken into account if such studies are performed in that group of patients.

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