A comparison of the clinical relevance of thallium-201 and technetium-99m-methoxyisobutyl-isonitrile for the evaluation of myocardial blood flow

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Summary

Thallium-201 is at present the radiotracer of choice for the clinical evaluation of myocardial blood flow. Although different technetium-99m-isonitrile agents have been synthesised recently, only ^{99m}Tc-methoxyisobutyl-isonitrile (^{99m}Tc-MIBI) has proved to hold promise for clinical implementation. The myocardial distribution of ^{201}Tl and ^{99m}Tc-MIBI was compared in a group of 20 patients, who underwent both ^{201}Tl single photon emission computed tomography and ^{99m}Tc-MIBI study as well as coronary angiography. The sensitivity for predicting a lesion ranged from 25% to 88% in different areas of the heart and was comparable for the two radiopharmaceuticals. The specificity was $>$ 80% for all regions except the inferior region where a specificity of 58% obtained by ^{99m}Tc-MIBI was better than the low specificity of 17% obtained with ^{201}Tl ($P <$ 0,008).

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Thallium-201 is at present the radiotracer of choice for the clinical evaluation of myocardial blood flow. This radionuclide has, however, certain disadvantages — sub-optimal physical characteristics and only a limited dose of 111 - 148 MBq (3 - 4 mCi) can be administered. Owing to these factors, research focus shifted to the evaluation of myocardial perfusion agents labelled with technetium-99m. Although different ^{99m}Tc-isonitrile agents have recently been synthesised,[1-3] only ^{99m}Tc-methoxyisobutyl-isonitrile (^{99m}Tc-MIBI) has proved to hold promise for clinical implementation. The kinetics and biodistribution of this agent have been studied in animal models as well as in man,[4-6] and its clinical usefulness in evaluating myocardial perfusion is under investigation.[7-10]

Recent comparisons between ^{201}Tl and ^{99m}Tc-MIBI have shown a good correlation between the agents in planar imaging as well as with single photon emission computed tomography (SPECT).[6,7,9-11] Although most of these investigations included comparisons between the two radionuclide modalities, angiographic data have not always been readily available. In the single report where this was done, a detailed comparison of the distribution of the two radiotracers in the myocardium was not included. A study was therefore undertaken to compare the myocardial distribution of ^{201}Tl and ^{99m}Tc-MIBI in patients with normal to mildly reduced left ventricular function, using SPECT techniques. Data obtained from coronary angiography were used as reference.

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Patients and methods

There were 20 patients (14 men) in the study group (mean age 56 ± 7 years). They underwent both ^{201}Tl SPECT and coronary angiography as part of their clinical evaluation. Patients were referred for ^{201}Tl scanning before angiography if the available clinical information was not conclusive or after angiography if results of an angiogram indicated a partially occluded coronary artery of doubtful significance. Only patients with highly relevant indications for ^{201}Tl scanning were thus included. All patients gave written consent for enrolment in the study. All studies were performed within 2 months before or after coronary angiography while the ^{201}Tl and ^{99m}Tc-MIBI scans were performed within 2 - 3 weeks.

Acquisition of data

Patients were exercised on a motor-driven treadmill according to the Bruce protocol.[12] ECG, heart rate and blood pressure were recorded at rest and during each minute of exercise. Exercise was performed to a symptom-limited maximum end-point with termination by fatigue, angina, dyspnoea, hypotension or ventricular arrhythmias. At peak exercise 74 - 111 MBq (2 - 3 mCi) ^{201}Tl was administered. Exercise was terminated approximately 60 seconds later and SPECT was then performed within 5 minutes, using a General Electric Starcam 400 ACT gamma camera. SPECT images were taken in 32 steps over 180° of rotation. The 40 seconds per projection resulted in a total acquisition time of 21 minutes. Redistribution images were taken approximately 3 hours later.

Studies with ^{99m}Tc-MIBI were done according to the same exercise protocol with the same end-point criteria. At peak exercise 555 - 740 MBq ^{99m}Tc-MIBI (Cardiolite; Du Pont de Nemours) was administered, the patient then continued exercising for another 2 minutes, and the abovementioned data acquisition protocol followed 60 minutes later. The resolution of the images was increased from a 64 × 64 to a 128 × 128 matrix. The tracer distribution at rest was determined the next day using the same protocol but excluding the treadmill exercise.

Data processing

Pre-processing of the data was performed using a Hanning filter with a cut-off frequency of 0,7/cm followed by back projection with a ramp filter. Orthogonal reconstructions of the vertical long axis, horizontal long axis and short axis of the heart were obtained. On these three sets of images the anterior, lateral, inferior, septal and apical areas of the heart could be distinguished. The three sets of reconstructions were displayed on a computer screen and the five territories of the heart were visually assessed by two to three experienced observers. A territory was classified as positive for coronary artery disease when consensus was reached between the observers that a reduction in radioactivity existed on the stress images. A reversible defect was classified as an area where redistribution of the ^{201}Tl occurred or where ^{99m}Tc-MIBI uptake was present at the resting study with reduced uptake during the stress study. These results were also compared with the results from coronary angiograms.

The assignment of vascular territories on the radionuclide images was chosen arbitrarily according to the same criteria used by others,[9] namely the left anterior descending (LAD) artery perfused the anterior wall and septal areas, the left circumflex (LCX) artery, the lateral wall and the right coronary (RCA) artery the inferior wall. Since these boundaries were not fixed, the results obtained when comparing the angiographic information with the radionuclide information could suffer a systematic error, but this effect is cancelled when the two radionuclide procedures are correlated. For the same reason, the apical area was not included in the comparison of the radionuclide methods with the angiographic results, but was included when the two radionuclide methods were compared.

Coronary angiography

Coronary angiography was performed in multiple projections employing the transcutaneous femoral Seldinger technique. Contrast left ventriculograms were also obtained in the 30° right anterior oblique projection in all patients. Coronary artery obstructions of more than 50% in at least two projections were regarded as significant. It was assumed that obstructions of this order should have a high possibility of a corresponding defect on the stress images of the radionuclide studies.

Statistical analyses

The sensitivity, specificity and positive and negative predictive values for relating coronary occlusions in the three main coronary vessels to reduced uptake in the assigned territorial areas of the stress images were used for comparing the two radionuclide methods. A scoring analysis on both the stress and redistribution images was also performed (a value of 2 represented a fixed defect or scarred tissue, 1 a transient defect or ischaemic tissue and 0 no defect or normal tissue). The results of the scoring were subjected to a sign test. P values of $< 0{,}05$ were considered significant.

Results

Coronary angiography showed significant stenosis in 16 of the 20 patients. Two of the 4 patients without significant stenosis had stenotic areas of 40% in both the LAD and LCX. One patient with a bridge on the LAD resulting in a 80% stenosis during systole was regarded as normal for the purpose of this investigation while the 4th patient had only diffuse low-grade atheroma. Only 1 of these patients could be classified as normal on ^{99m}Tc-MIBI imaging, while none was classified as normal by ^{201}Tl imaging.

The 16 patients with significant coronary artery disease could be classified as follows: 10 patients with single-vessel disease and 6 patients with two-vessel disease. Ten LAD arteries were involved, 4 LCX arteries and 8 RCA arteries. Only 1 of these patients was classified as normal by the ^{201}Tl scan while 2 were normal with the ^{99m}Tc-MIBI investigation.

The sensitivity for predicting a lesion > 50% in a specific artery by evaluating the abovementioned areas of the myocardium ranged from 25% to 88% (Fig. 1). The lowest sensitivity (25%) was obtained with both ^{201}Tl and ^{99m}Tc-MIBI in evaluating the lateral region of the heart, followed by higher sensitivities of 50% and 70% for ^{99m}Tc-MIBI and ^{201}Tl, respectively, in the anterior region. The sensitivity was > 70% for both radionuclides when the inferior and septal regions were evaluated.

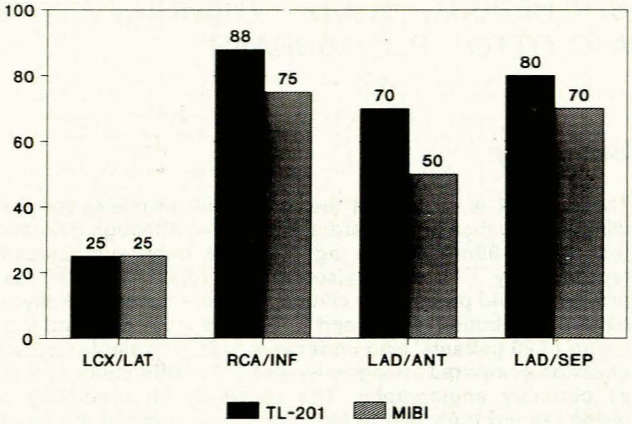

Fig. 1. A comparison of the sensitivity of ^{201}Tl and ^{99m}Tc-MIBI scanning for the detection of lesions > 50% in the main coronary arteries supplying the different myocardial regions (LCX/LAT = correspondence between left circumflex artery and lateral region: RCA/INF = correspondence between right coronary artery and inferior region: LAD/ANT = correspondence between left anterior descending artery and anterior region; LAD/SEPT = correspondence between left anterior descending artery and septal region).

The specificity was > 80% for all regions except the inferior region where the specificity of 58% obtained by ^{99m}Tc-MIBI scanning was better than the low specificity of 17% obtained with ^{201}Tl scanning (Fig. 2). According to the sign test, there was a significant difference in the interpretation of the inferior region when using the two radionuclide tracers ($P < 0{,}008$).

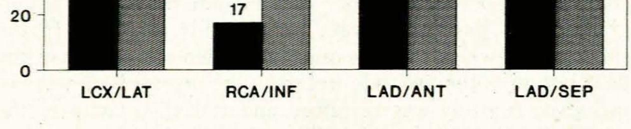

Fig. 2. A comparison of the specificity of ^{201}Tl and ^{99m}Tc-MIBI scanning for the detection of lesions > 50% in the main coronary arteries supplying the different myocardial regions (see Fig. 1 for legend).

The negative predictive values of the two tracers were similar (Fig. 3) except for the anterior region where ^{201}Tl was slightly better at 75% (compared with 67% for ^{99m}Tc-MIBI) and the inferior region where ^{99m}Tc-MIBI was better at 78% (compared with 67% for ^{201}Tl). The positive predictive values (Fig. 4) were also > 80% except in the inferior region where ^{99m}Tc-MIBI scanning yielded a better value than ^{201}Tl scanning (55% and 41%, respectively).

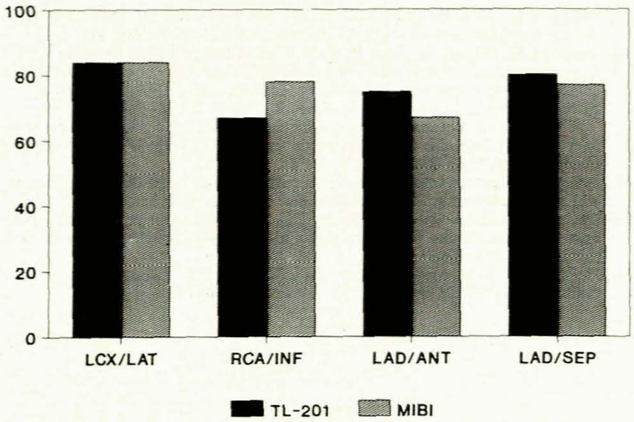

Fig. 3. A comparison of the negative predictive value of ^{201}Tl and ^{99m}Tc-MIBI scanning for the detection of lesions > 50% in the main coronary arteries supplying the different myocardial regions (see Fig. 1 for legend).

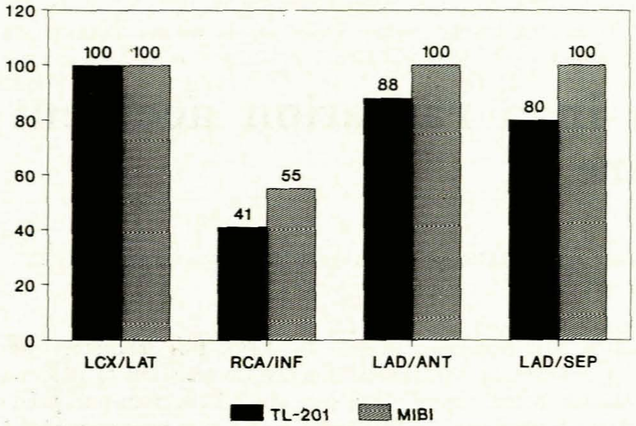

Fig. 4. A comparison of the positive predictive value of ^{201}Tl and ^{99m}Tc-MIBI scanning for the detection of lesions > 50% in the main coronary arteries supplying the different myocardial regions (see Fig. 1 for legend).

Discussion

In this study the myocardial distribution of ^{201}Tl and ^{99m}Tc-MIBI was compared in patients with normal to mildly reduced left ventricular function using SPECT techniques. Although several studies have been conducted previously[6-11] yielding information on the same subject, the results of this study either confirm these findings in a new way or contradict the results.

A number of investigations have been carried out comparing the sensitivity and specificity of ^{99m}Tc-MIBI with ^{201}Tl scanning for the detection of CAD.[8,9] Taillefer *et al.*[7,10] found a good correlation between the two radiopharmaceuticals both on a segment by segment basis as well as on a patient by patient basis using planar imaging. According to their findings, ^{201}Tl imaging was slightly superior in detecting LAD disease.[7] Planar imaging was also used in a multicentre comparative study reported by Wackers *et al.*[6] Since their population group was not representative of the general population, they decided to use the terms 'detection rate of coronary artery disease' and 'identification of absence of coronary disease' instead of sensitivity and specificity. They reported good agreement between the two radiopharmaceuticals with more abnormal myocardial segments on the ^{201}Tl images. According to their results the 'sensitivity' for detecting LCX occlusions was relatively low, with low 'specificities' for the LAD and RCA arteries.

In the report by West *et al.*[8] no comparison was made with ^{201}Tl, but detailed information was given on sensitivities and specificities calculated by shifting their confidence criteria. They obtained the best results for the RCA with a 73% sensitivity and 82% specificity, followed by the LCX and LAD. The report by Kiat *et al.*[9] compared ^{201}Tl with ^{99m}Tc-MIBI scanning on a segmental basis, but no detailed information on the different segments was given.

In general, our results indicated a high sensitivity for relating a filling defect to a specific coronary artery. Scanning with ^{201}Tl was slightly more sensitive than ^{99m}Tc-MIBI for all coronary arteries. The low sensitivity for detecting LCX occlusions is in agreement with the work by Wackers *et al.*,[6] but it cannot be concluded that this will generally be the case. In our study, only 1 out of 4 patients with LCX disease could be detected. The high negative predictive value for this vessel indicates that it cannot be concluded that the sensitivity for detecting LCX occlusions will be as low as 25%. The 3 patients with LCX occlusions who were not detected by either ^{201}Tl or ^{99m}Tc-MIBI scanning also had LAD occlusions. Since septal uptake was used as a reference, the reduced perfusion due to the LAD lesion caused the uptake in the lateral wall to appear spuriously high, therefore resulting in a normal interpretation with respect to the septum.

The more conservative approach in the interpretation of the images is reflected by the somewhat higher specificities than those reported elsewhere.[13] This was obtained at the cost of a lower sensitivity than the values reported by De Pasquale *et al.*[13] The lower specificities in the RCA territory, however, reflects the same tendency as reported by Wackers *et al.*[6]

In our hands ^{99m}Tc-MIBI scanning was, in general, more specific than ^{201}Tl. This is especially evident in the RCA region where the low sensitivity of 17% was increased to 58% with the use of ^{99m}Tc-MIBI. This was the only region where a significant difference between the two radiopharmaceuticals could be shown. Previous reports have also indicated that the inferior region of the heart is subject to false-positive results. Although the reason for the false-positive results in the inferior wall is still unclear,[14] our results indicate that the use of ^{99m}Tc-MIBI may reduce this problem.

The results of this study could have been influenced by several factors. In accordance with the study by Wackers *et al.*,[6] some of the patients in this study were enrolled because of the results of their ^{201}Tl scans. Furthermore, the image interpreters had vast experience with ^{201}Tl imaging, while ^{99m}Tc-MIBI experience was limited to the patients included in the study.

In conclusion, the higher specificity of ^{99m}Tc-MIBI (at the cost of the higher sensitivity of ^{201}Tl) reported in this study, might be advantageous to patients in our clinic, since the number of patients referred for invasive investigation could be reduced.

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