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Combined Thallium-201 and Dynamic Iodine-123 Iodophenylpentadecanoic Acid Single-Photon Emission Computed Tomography in Patients after Acute Myocardial Infarction with Effective Reperfusion

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Summary

Background: Considerable derangements of energy metabolism are to be expected during ischemia and reperfusion. In ischemic myocardium, the oxidative degradation of carbohydrates is shifted toward the anaerobic production of lactate and the oxidation of fatty acids is suppressed.

Hypothesis: The aim of this study was to examine the uptake and metabolism of iodine-123 (^{123}I) iodophenylpentadecanoic acid (IPPA) in stunned myocardium.

Methods: In 15 patients, SPECT with ^{201}Tl and ^{123}I IPPA as well as echocardiography with low-dose dobutamine stimulation were performed 12 ± 5 days after myocardial infarction with reperfusion. Follow-up echocardiography was carried out 24 ± 8 days later for documentation of functional improvement. Uptake of ^{201}Tl and ^{123}I IPPA were obtained in five left ventricular segments, and dynamic SPECT imaging was used for calculation of the fast and the slow components of the biexponential myocardial ^{123}I IPPA clearance.

Results: Wall motion improved in 14 of 26 dysfunctional segments (54%). Stunned segments were characterized by a reduced ^{123}I IPPA extraction, a shorter half-life of the fast, and a longer half-life of the slow clearance component. All parameters of the combined ^{201}Tl/^{123}I IPPA study predicted functional recovery with similar accuracies (area under the receiver operator characteristic curves between 0.68 and 0.76; p = NS). Analysis of ^{201}Tl uptake alone could not predict functional recovery in this study.

Conclusions: Stunned myocardium is characterized by a disturbance of fatty acid metabolism. For prediction of functional improvement, ^{123}I IPPA imaging added significant diagnostic information.

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Introduction

Considerable derangements of energy metabolism are to be expected during ischemia and reperfusion. In ischemic myocardium, the oxidative degradation of carbohydrates is shifted toward the anaerobic production of lactate and the oxidation of fatty acids is suppressed.[1] Longer lasting ischemia leads to an augmented turnover in the cardiac triacylglycerol pool and a net breakdown of membrane-bound phospholipids. In oxygen-deprived tissue, several fatty acid-containing metabolites accumulate, some of which are thought to be responsible for deleterious effects on the damaged myocardium.[2,3] The derangement of fatty acid metabolism persists after restoration of blood flow.[4–6]

The effects of coronary stenoses on energy balance can be examined noninvasively with radiopharmaceuticals.[7] The aim of this study was to assess fatty acid metabolism in stunned myocardium. The examinations were performed with iodine-123 (^{123}I) iodophenylpentadecanoic acid, (^{123}I IPPA) which is taken up by cardiomyocytes analogous to palmitic acid, is partially integrated into the intracellular lipid pools,[8,9] and undergoes beta-oxidation. The initial uptake and the myocardial elimination of ^{123}I IPPA were studied in patients after myocardial infarction with effective reperfusion and correlated with wall motion obtained from echocardiography. Since any disturbance of fatty acid metabolism is a sensitive parameter of myocardial damage,[10–14] it was assumed that stunned myocardium would be characterized by a typical alteration of ^{123}I IPPA kinetics.

Patients and Methods

Patients

Fifteen patients (12 men, 3 women; age 54.7 ± 12.5 years, range 34–79 years) after a first acute myocardial infarction with effective reperfusion within 6 h were prospectively enrolled. The diagnosis of acute myocardial infarction was based

on history as well as enzymatic and electrocardiographic (ECG) criteria. Infarction was anterior in 10 patients, posterior in 4, and lateral in 1.

Percutaneous transluminal coronary angioplasty (PTCA) was carried out immediately after hospitalization in 9 patients (with stenting in 6) and thrombolytic therapy was performed in 5. One patient with anterior infarction initially received thrombolytic therapy; in addition, the left anterior descending (LAD) artery was treated with PTCA (without stenting) on Day 7 after infarction (remaining stenosis, 20%). Data from coronary angiography were available in 11 patients, in 10 of whom PTCA had been performed. In one patient with coronary triple-vessel disease (LAD 50%, left circumflex [LCx] 60%, right coronary artery [RCA] 80%) no revascularization was carried out. All 11 patients suffered from significant coronary artery disease (> 50% diameter stenosis). Single-vessel disease was diagnosed in eight patients (LAD, n = 5; LCx, n = 1; RCA, n = 2), double-vessel disease in two (LAD and RCA), and triple-vessel disease in one (see above). Percent stenosis of coronary lesions was assessed visually without knowledge of the scintigraphic and echocardiographic data.

The infarct-related vessel was occluded in all patients in whom PTCA was performed. Percutaneous transluminal coronary angioplasty resulted in TIMI-3 flow in all cases; the remaining stenosis was between 20 and 90% (mean 31 ± 23%).

Study Protocol

After inclusion into this study, echocardiography at rest and with low-dose dobutamine stimulation (5 and 10 μg/kg body weight) as well as myocardial single-photon emission computed tomography (SPECT) studies with ^{201}Tl and ^{123}I IPPA were carried out in every patient (4–19 days after infarction; mean 12 ± 5 days). Echocardiography at rest was repeated 24 ± 8 days (15–42 days) later for documentation of wall motion recovery (stunned myocardium).

Scintigraphic Studies

All patients were continued on their current cardiac medications without interruption and were studied after an overnight fast. Scintigraphy comprised 15 ^{123}I IPPA SPECT acquisitions within 90 min p.i. and a ^{201}Tl study after injection at rest (n = 3) or following the stress-4 h redistribution-reinjection protocol (12 patients). The three patients studied at rest did not differ from the rest of the group with regard to symptoms, scintigraphic, or angiographic findings.

Thallium-201 at a dose of 95–105 MBq was injected during the last 30 s of submaximal bicycle exercise (initial workload 50 W, increase by 25 W every 2 min) in 12 patients and imaging was started 5 min later. A second scan was obtained 4 h p.i. and a third the next day after reinjection of 50–60 MBq ^{201}Tl. In three patients, ^{201}Tl was injected at rest and imaging was started 10 min later.

Iodine-123 IPPA imaging was performed after completion of the ^{201}Tl study (i.e., after the reinjection study in 12 patients and after the rest study in 3). For assessment of spillover of ^{201}Tl emissions into the ^{123}I window, one SPECT acquisition with the photopeak centered at 159 keV and a window of 10% was carried out prior to IPPA injection in every patient. This first SPECT acquisition was subtracted from the following acquisitions in order to correct for spillover of ^{201}Tl emissions. The registered spillover was 4 ± 2% (range: 1.3–10.4%) of maximal ^{123}I IPPA activity. Thallium-201 activity was assumed to be stable during the ^{123}I IPPA acquisitions. Iodine-123 IPPA was injected at rest at a dose of 200–350 MBq and 15 SPECT acquisitions were obtained until 90 min p.i. Starting 1 min p.i., the first seven SPECT acquisitions were registered without interscan delay. For the remaining eight studies, SPECT was started every 7 min (i.e., interscan delay of 4 min).

Data Acquisition

Single-photon emission computed tomography imaging was carried out using an Elscint Apex-415 camera equipped with a low-energy, medium resolution, medium sensitivity collimator (APC-3). For each SPECT acquisition, 30 projection images with the heart in the center of rotation were recorded on a 180° circular orbit from right anterior oblique (RAO) 60 to left posterior oblique 60 and stored in a 64 × 64 matrix. For the ^{201}Tl studies, a 15% window centered on the 69 keV peak was used, acquisition time was 20 min (40 s per projection). For the ^{123}I IPPA acquisitions, a 10% window centered on the 159 keV peak was chosen, acquisition time was 180 s. About 1.2 million counts were recorded during one IPPA SPECT rotation.

Prior to this study, computer simulations were performed to examine whether quantitative analysis of ^{123}I IPPA SPECT with an acquisition time as short as 180 s yields reliable data. The results of these simulations show that left ventricular count rates can be assessed accurately with the regions of interest used in this study.[15] Similar dynamic SPECT protocols have been used by Hansen *et al.*[16] and Matsunari *et al.*[17]

Image and Data Analysis

From the raw data, horizontal and vertical long-axis as well as short-axis slices were reconstructed (Ramp and Metz filter). For quantitative analysis, a circumferential profile technique was used. An operator-defined circular region of interest was drawn around the left ventricular activity of each short-axis slice. The region of interest was then automatically subdivided into 60 sectors, each subtending an arc of 6°, and mean activity in each sector was registered and displayed in a polar diagram. Myocardial activity was obtained in five segments corresponding to the apical, anterior, septal, inferior, and lateral wall (Fig. 1). The maximum segmental activity was assigned a value of 100% without correction or normalization relative to a normal data base, and activity in the remaining segments was standardized to this value.

By definition, the maximum segmental ^{201}Tl uptake in either the redistribution or the reinjection study served as an index of myocardial viability (maximal ^{201}Tl uptake). Segments with a maximal ^{201}Tl uptake < 50% were regarded as nonvi-

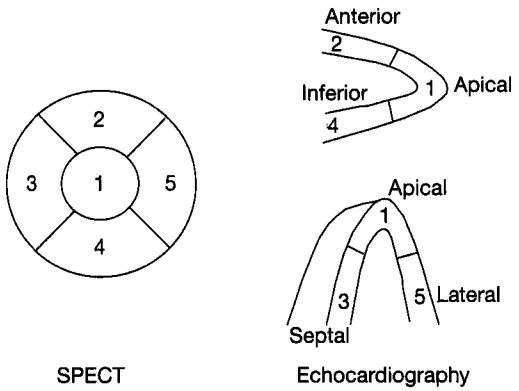

FIG. 1 Segments used for analysis in single-photon emission computed tomography (SPECT) studies and echocardiography.

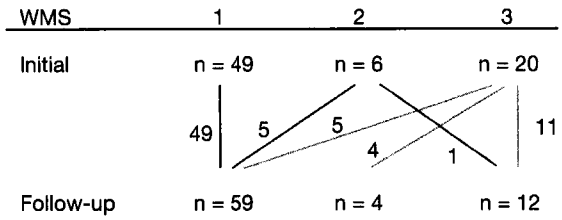

FIG. 2 Changes of wall motion scores (WMS) during follow-up in the 75 segments (1 = normokinesia, 2 = hypokinesia, 3 = akinesia).

able. The difference between maximal ^{201}Tl uptake and the corresponding exercise value defined the extent of exercise-induced ischemia. A relevant ischemia was diagnosed in segments in which this value exceeded 10 percent points. Segments with a loss of thallium activity of more than 10 percent points between the exercise and the 4 h redistribution study were regarded as showing reverse redistribution.

The initial uptake of ^{123}I IPPA in the myocardium depends on regional fatty acid extration and regional myocardial blood flow.[18, 19] Initial ^{123}I IPPA uptake is therefore not a pure parameter of fatty acid metabolism. For characterization of ^{123}I IPPA extraction, initial ^{123}I IPPA uptake has to be corrected for flow. In this study, this correction was achieved by calculating an "extraction index" as the ratio between initial ^{123}I IPPA uptake and perfusion at rest (IPPA ratio).[20] Perfusion at rest was defined as the ^{201}Tl uptake in either the rest (n = 3) or the reinjection (n = 12) study. Since ^{123}I IPPA is rapidly metabolized, information about ^{123}I IPPA extraction can only be obtained in the early phase after injection. To improve count statistics, the 2., 3., and 4. ^{123}I IPPA SPECT studies were added together and polar diagrams were calculated as described above. This combined image set was used for calculation of the IPPA ratio and the mismatch value (see below) only.

As a second parameter, the numerical difference between initial ^{123}I IPPA uptake and maximal ^{201}Tl uptake was calculated (mismatch value).

For analysis of myocardial fatty acid turnover time, activity curves were generated from all 15 polar diagrams of the dynamic SPECT acquisitions. The fast (initial) and the slow (late) clearance component were visually identified for each segment on a semilogarithmic plot and the respective half-lives were obtained using a least squares minimization criterion.

Echocardiography

Two-dimensional echocardiographic analysis of regional wall motion was performed with a Sonotron Vingmed CFM 750 (Kranzbuehler/GE Ultrasound Europe, Solingen, Germany) equipped with a 3.25 MHz transducer. Parasternal long-axis and short-axis and apical two-chamber and four-chamber views were analyzed by an experienced echocardiographer blinded to the scintigraphic and angiographic data. Regional wall motion was scored in five left ventricular segments (apical, anterior, septal, inferior, and lateral) (Fig. 1) on a semiquantitative scale from 1 to 4 in increments of 1.0 (normal wall motion = 1, hypokinesia = 2, akinesia = 3, dyskinesia = 4).

Statistics

All data are given as arithmetic mean ± 1 standard deviation or as median (range). Differences between groups were examined using the nonparametric Kruskal-Wallis test. In cases where the Kruskal-Wallis test revealed a significant difference, subgroups were further tested using the Wilcoxon-Mann-Whitney test. Differences within groups were tested using the nonparametric Wilcoxon signed-ranks test. Receiver operator characteristic analysis including maximum likelihood estimation of binormal ROC curves was performed using the ROCKIT 0.9B software.[21] Statistical significance was assumed for $p < 0.05$.

Results

In all, 75 segments were analyzed. In 14 of 26 dysfunctional segments (54%), an improvement of wall motion during follow-up was registered; 1 segment (4%) showed a deterioration. The frequencies and changes of wall motion scores are summarized in Figure 2. Wall motion abnormalities were registered in infarct-related regions only. According to maximal ^{201}Tl uptake, all 75 segments were viable. Minimal segmental ^{201}Tl uptake was 52.3%. Nine segments were classified as ischemic, six revealed the reverse redistribution pattern. Tables I

TABLE I Wall motion scores (WMS) in control and ischemic myocardium and in segments with reverse redistribution as defined by thallium-201 single-photon emission computed tomography

	WMS (initial)	WMS (follow-up)	Change in WMS
Control	1.48 ± 0.81	1.32 ± 0.70	0.24 ± 0.59
Ischemia	2.00 ± 1.00	1.44 ± 0.88	0.56 ± 0.88
Rev. red.	2.33 ± 1.03 [a]	1.83 ± 0.98	0.50 ± 0.84

[a] Significantly different from control segments ($p < 0.05$).
Abbreviation: Rev. red. = reverse redistribution.

TABLE II Thallium-201 and I-123-IPPA uptake (%) in control and ischemic myocardium and in segments with reverse redistribution as defined by ^{201}Tl single-photon emission computed tomography. Results of 60 segments of 12 patients examined according to the stress 4 h redistribution —24 h redistribution — reinjection protocol. Solid lines represent differences between groups ($p < 0.05$). The results of 15 segments of three patients examined at rest only are displayed in parentheses (NS vs. control segments)

	Tl-uptake (exercise)	Tl-uptake (4h red.)	Tl-uptake (reinjection)	Tl-uptake (rest)	Max. Tl-uptake	IPPA-uptake	Mismatch-value	IPPA ratio
Control	85.9 ± 14.6	86.4 ± 13.1	87.8 ± 12.3		88.4 ± 12.6	87.1 ± 13.5	1.32 ± 7.1	1.02 ± 0.09
				(89.1 ± 10.5)		(87.0 ± 14.0)	(2.59 ± 9.2)	(0.98 ± 0.13)
Ischemia	68.9 ± 17.6[a]	75.3 ± 17.4	82.1 ± 16.9		84.7 ± 15.6[a]	77.6 ± 17.0	7.04 ± 5.9	0.96 ± 0.05
Rev. red.	81.8 ± 13.1[a]	67.9 ± 14.4[a]	78.8 ± 11.1		85.4 ± 12.9[a]	72.8 ± 15.6	12.6 ± 5.2	0.93 ± 0.17

[a] Significantly different from I-123-IPPA uptake in the respective group ($p < 0.05$).
Abbreviations: Tl = thallium, IPPA = iodophenylpentadecanoic acid, NS = not significant, Rev. red. = reverse redistribution.

and II summarize wall motion scores and segmental ^{201}Tl and ^{123}I IPPA uptake.

Analysis of Thallium-201 and Iodine-123 IPPA Uptake

1. Iodine-123 IPPA extraction: In 16 segments with an IPPA ratio < 0.95 (i.e., lower ^{123}I IPPA and higher ^{201}Tl uptake), the improvement in wall motion score was 0.5 ± 0.7 compared with 0.17 ± 0.5 ($p < 0.05$) in segments with an IPPA ratio of ≥ 0.95. The ROC curve of the IPPA ratio for prediction of wall motion recovery is shown in Figure 3; sensitivity and specificity for prediction of wall motion recovery using an IPPA ratio of 0.95 as the threshold were 42.9 and 83.6%, respectively.

2. Mismatch between ^{123}I IPPA and maximal ^{201}Tl uptake: The mismatch values were increased (i.e., reduced IPPA uptake compared with maximal ^{201}Tl uptake) in segments with functional improvement during follow-up compared with those without (6.9 ± 8.2 vs. 2.3 ± 7.7 percent points; $p < 0.05$). Defining any mismatch value of 5 percent points or more as predictive for functional recovery, sensitivity, and specificity were 71.4 and 72.1%, respectively. The ROC curve is shown in Figure 3, a patient example is displayed in Figure 4. The mismatch values were also increased in segments with exercise-induced ischemia and reverse redistribution (Table II).

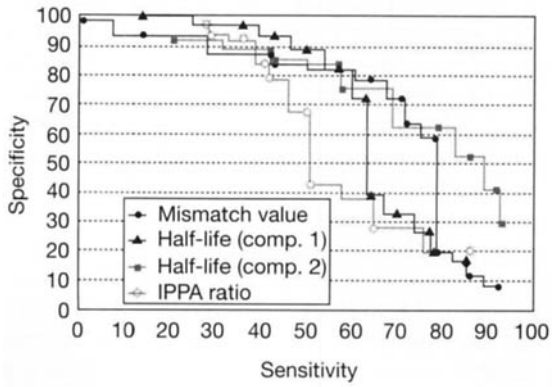

FIG. 3 Receiver operator characteristic curves of the scintigraphic parameters for prediction of functional improvement during follow-up.

Analysis of Myocardial Iodine-123 IPPA Kinetics

In 26 viable segments with normal wall motion, normal ^{201}Tl uptake (> 80%), and without evidence of ischemia or reverse redistribution, the half-lives of the fast and the slow clearance components of the myocardial ^{123}I IPPA clearance were 19.6 (range, 6.5–57.5) min and 96.8 (range, 62.0–2035) min, respectively.

Segments with functional improvement were characterized by a shorter half-life of the fast and a longer half-life of the slow clearance component (Table III). The ROC curves of the two clearance components for prediction of functional recovery are displayed in Figure 3. Defining any fast half-life shorter than 12 min as predictive for functional recovery, sensitivity and specificity were 64.3 and 72.1%, respectively. The corre-

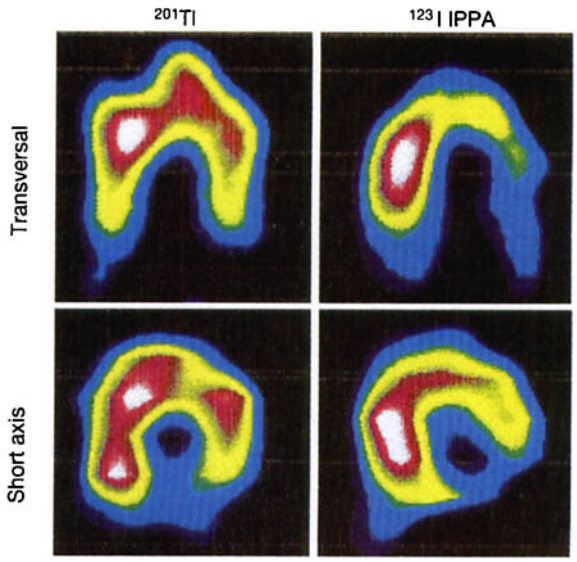

FIG. 4 Long-axis and short-axis slices from a 53-year-old patient obtained 13 days after inferolateral infarction with recombinant tissue plasminogen activator lysis. Iodine-123 IPPA uptake is reduced as compared to thallium-201 uptake (reinjection image) in the lateral and apical wall. Functional improvement was noted in the mismatch areas at follow-up.

TABLE III Elimination half-lives of the early and late I-123 IPPA clearance components given as median (minimum, maximum). For analysis of the effects of exercise-induced ischemia, segments with reverse redistribution were excluded

	Elimination half-life (min)	
	Early clearance component	Late cleareance component
Functional improvement (n = 14)	8.9 (4.9–36.8) [a]	192 (87–2257) [a]
No functional improvement (n= 61)	16.7 (6.1–57.5)	107 (48–2035)
No ischemia (n = 45)	16.0 (4.9–57.5) [b]	107 (62–2257)
Ischemia (n = 9)	10.8 (4.9–22.6)	171 (59–514)
No reverse redistribution (n = 54)	14.4 (4.9–57.5)	114 (59–2257)
Reverse redistribution (n = 6)	9.5 (6.4–45.1)	152 (48–760)

[a] Significantly different from segments without functional improvement ($p < 0.05$).
[b] Significantly different from segments with exercise-induced ischemia ($p < 0.05$).
Abbreviations as in Table II.

sponding values for any slow half-life longer than 180 min were 57.1 and 83.6%, respectively. In 18 segments with a slow half-life longer than 180 min, wall motion improved by 0.44 ± 0.51 points compared with 0.11 ± 0.31 points ($p < 0.05$) in 57 segments with shorter half-lives. A patient example is shown in Figure 5.

Segmental ^{123}I IPPA uptake correlated with the elimination half-life of the fast ($r = 0.42$; $p < 0.001$) and the slow ($r = -0.40$; $p < 0.001$) clearance component of the respective segment. Both clearance components did not correlate with each other.

Diagnostic Performance for Prediction of Functional Improvement

The area under the ROC curve (AUC) characterizes the diagnostic performance of the test applied. The AUC was not different for the four ^{123}I IPPA parameters tested in this study (IPPA ratio, 0.72; mismatch value, 0.69; fast clearance component, 0.68; slow clearance component, 0.76; p = NS).

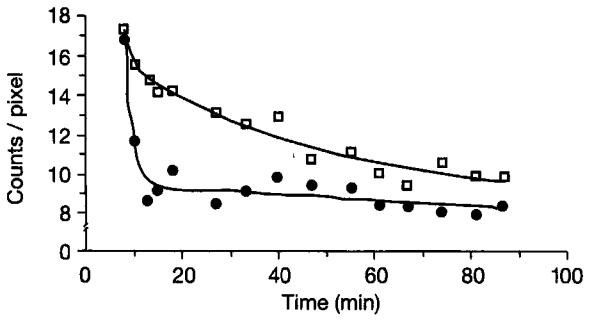

FIG. 5 A 38-year-old patient presenting with anterior infarction. Time acitivity curves of the septal (stunned, solid circles) and lateral (reference, open boxes) regions show a biexponential clearance with the fast clearance component followed by the slow component at 12 min p.i. Compared with the control region, the half-life of the first clearance component is shortened in the stunned septum whereas that of the second component is prolonged.

A high ^{201}Tl uptake alone did not contain diagnostic information for prediction of functional recovery (AUC 0.24; $p < 0.05$ vs. IPPA ratio, mismatch value, fast, and slow clearance component). In 14 segments with functional improvement during follow-up maximum, ^{201}Tl uptake was 75.4 ± 13.5% compared with 87.8 ± 10.9% in 12 dysfunctional segments without improvement ($p < 0.05$).

Low-Dose Dobutamine Echocardiography

Of 26 dysfunctional segments, 10 showed inotropic reserve during low-dose dobutamine stimulation. All of these segments were characterized by an improvement of wall motion during follow-up. Of the 16 segments without inotropic reserve, wall motion did not recover in 12. Consequently, low-dose dobutamine echocardiography was 71.4% sensitive and 100% specific for prediction of functional improvement.

Discussion

The effects of ischemia and reperfusion on myocardial fatty acid metabolism have been extensively analyzed in previous studies. Controversial results have been obtained in reperfused myocardium showing either a rapid normalization of fatty acid turnover[5] or a longer lasting reduction of fatty acid oxidation.[6, 22, 23] The extraction of palmitate was unaffected by ischemia and reperfusion in animal experiments,[22, 24] whereas ^{123}I IPPA influx into ischemic tissue was reduced in patients.[18] In this study, stunned myocardium was characterized by a reduced ^{123}I IPPA extraction and a characteristic disturbance of ^{123}I IPPA turnover.

Different labeled fatty acids are available for scintigraphy. During the last years, β-methyl-p-(^{123}I)-iodophenylpentadecanoic acid (^{123}I BMIPP), which is retained in the myocytes without major degradation has been widely used. Myocardial ^{123}I-BMIPP retention is affected by alterations in fatty acid turnover and correlates with the cellular ATP content probably due to adenosine triphosphatase (ATP)-dependent activation of fatty acids with coenzyme A.[25]

Iodine-123 IPPA, in contrast, undergoes beta-oxidation. Determination of ^{123}I IPPA uptake permits the assessment of fatty acid extraction, and the analysis of time activity curves gives direct insight into cardiac lipid turnover. For SPECT, the rapidly changing tissue concentrations of ^{123}I IPPA are a disadvantage at the same time since SPECT relies on a stable tracer distribution to avoid the problem of inconsistent data.[26, 27]

Interpretation of the Results

The finding of a reduced extraction of ^{123}I IPPA in stunned myocardium has not been reported previously. This result is in some contrast to animal experiments in which the extraction of palmitic acid was unaffected by ischemia and reperfusion.[22, 24] The discrepancy between the animal experiments and this study is most probably explained by the different species, different tracers, and different experimental conditions.

The shorter half-life of the first ^{123}I IPPA clearance component in stunned myocardium compared with control segments is difficult to interpret. The fast component of the bi-exponential clearance curve is commonly believed to represent beta oxidation.[10, 28] The results of this study consequently suggest an increased beta oxidation in stunned myocardium. Even if experimental studies are compatible with a partial decoupling of the respiratory chain with preferential oxidation of fatty acids in stunned segments,[5, 29] beta oxidation has been consistently reported as depressed in animal experiments.[4, 23] One possible explanation (besides a true increase of beta oxidation) includes the rapid back-diffusion of unmetabolized ^{123}I IPPA from cardiomyocytes into the blood after the initial uptake, thus contributing to a rapid decline of tissue ^{123}I IPPA activity.[30] Back-diffusion has been described for ^{123}I BMIPP and palmitic acid and may contribute to as much as 50% of all activity in the effluent.[17, 31]

The longer half-life of the second ^{123}I IPPA clearance component reflects the integration and delayed turnover of long chain fatty acids in the intracellular esterified lipid pools during reperfusion. A similar prolongation of the second clearance component has been described in ischemic myocardium.[32]

All parameters of the combined ^{201}Tl/^{123}I IPPA study had similar diagnostic accuracies for prediction of functional improvement and were superior to analysis of ^{201}Tl uptake alone. Nevertheless, there was a tendency for the IPPA ratio to perform less well in the clinical situation since, with acceptable specificity, sensitivity was unacceptably low. The poor capacity of ^{201}Tl uptake for prediction of functional recovery in this study is not surprising since all segments were viable and an efficient stratification in a subgroup of viable segments cannot be expected.

Theoretically, analysis of myocardial ^{123}I IPPA clearance alone would be sufficient for detection of metabolically compromised, stunned segments. In clinical practice, however, a viability study will be obtained in most cases and any mismatch between viability and fatty acid uptake may be easily appreciated. Since the calculation of elimination half-lives was not superior to the mismatch value or the IPPA ratio, the potential advantage of ^{123}I IPPA over ^{123}I BMIPP in directly tracking the different routes of fatty acid metabolism could not be translated into a clear diagnostic benefit.

In comparison with the scintigraphic parameters, the diagnostic accuracy of low-dose dobutamine echocardiography for prediction of functional recovery was higher in this study. However, low-dose dobutamine echocardiography was not completely independent from echocardiography at rest used as the reference method for assessment of functional recovery. It remains to be established whether these results can be reproduced using an independent reference method and studying patients with more advanced coronary artery disease. In a study by Franken *et al.*, the diagnostic yield of low-dose dobutamine echocardiography was lower than combined technetium-99m (^{99m}Tc) sestamibi and ^{123}I BMIPP imaging.[33]

Limitations of This Study

The acquisition time for the dynamic SPECT protocol was a compromise between the demand for good count statistics and the demand for rapid imaging aiming at the exact registration of the two clearance components. However, despite this limitation, the calculated half-lives in normal myocardium are in good agreement with the respective values reported in the literature.[28, 32]

For assessment of ^{123}I IPPA extraction, initial ^{123}I IPPA uptake has to be corrected for perfusion at rest. Data from ^{201}Tl SPECT were used for this purpose. However, in most patients a separate ^{201}Tl study at rest could not be obtained and the reinjection image was used instead. We are aware of the problems associated with this approach. Using the 4 h redistribution image for estimation of IPPA extraction (instead of the reinjection image) did not alter the results (data not shown). Furthermore, we were able to reproduce the finding of a reduced ^{123}I IPPA extraction in stunned myocardium in a recent study using ^{123}I IPPA and ^{99m}Tc sestamibi at rest.[34]

Since the time interval between infarction/reperfusion and imaging was relatively long and follow-up was relatively short, the full extent of myocardial stunning was probably greater than documented here. However, the main interest has been to characterize fatty acid metabolism in stunned segments and not to identify the full extent of stunning in patients after myocardial infarction and reperfusion. It is probable that some of the dysfunctional segments with high ^{201}Tl uptake would have shown functional improvement at later follow-up.

The time interval between infarction and scintigrapic imaging depended on availability of ^{123}I IPPA and was therefore variable. As a consequence, patients have been examined in different pathophysiologic states. However, responses after ischemic events show considerable interindividual variation per se, and the effect of any standardization of acquisition dates does not necessarily result in a uniform pathophysiology. The results of this study show that stratification by pathophysiologic states (i.e., by state of fatty acid metabolism) is possible and yields additional clinical information independent from the time interval between infarction and imaging.

Conclusion

Stunned myocardium could be characterized by a reduced net extraction of ^{123}I IPPA and a delayed turnover in the esterified intracellular lipid pools. Iodine-123 IPPA imaging added significant information to ^{201}Tl imaging for prediction of functional recovery but, in this study, its clinical value was borderline when compared with echocardiography.

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