Quantitation of Thallium-201 Myocardial Washout by Serial Rest Myocardial Imaging

Michihiro NARITA*, Tadashi KURIHARA*, Masahisa USAMI*, Minoru HONDA**, Tadashi OGAWA** and Keisuke KANAO**

Abstract For quantitative analysis of myocardial thallium-201 clearance, we performed rest serial myocardial imaging in 5 normal volunteers and 20 patients with coronary artery disease. We studied the sequential change of myocardial thallium concentration by using myocardial thallium uptake indices and calculated the half life of the washout of myocardial thallium. Myocardial images obtained in 2 projections were divided into 6 segments and they were classified into 53 normally perfused segments, 41 infarct segments and 26 ischemic segments (defects were observed in 15 of them at the initial myocardial image) on the basis of coronary angiography, radionuclide angiography and ECG findings. Mean half life of the washout of myocardial thallium in normally perfused myocardium (5.9 ± 1.0 hours in coronary artery disease and 5.6 ± 0.7 hours in normal volunteers) was not different from that of infarcted myocardium (5.7 ± 1.1 hours). On the contrary, the washout rate in ischemic myocardium was very slow and the mean half life of the washout was 13.1 ± 4.2 hours, and prolonged thallium washout rate was observed in 25 of 26 ischemic segments irrespective of the presence or absence of the defects at the initial myocardial images.

In conclusion, the examination of myocardial washout curves can differentiate between 3 different conditions of myocardium and is useful for the detection of ischemic myocardium.

Thallium-201 (TI) myocardial imaging has become an important diagnostic tool in evaluation of patients with coronary artery disease (CAD), because TI distributes into myocardium in proportion to regional blood flow following intravenous injection1,2). Thus, the defects appearing in TI myocardial imaging at rest represent myocardial ischemia as well as myocardial scar. But in cases with extensive myocardial ischemia, especially when both myocardial infarction and underperfusion exist in an image, the infarcted area appears as the defect, but the underperfused area, which contains more TI than the infarcted area, may be interpreted as normal. On the other hand, recent clinical studies3-5) have demonstrated that initial defects due to underperfusion disappeared on delayed images, while those due to scar persisted. Besides, animal experiments on the mechanism and time course of myocardial TI redistribution have demonstrated that the modes of redistribution were different between normally perfused and ischemic myocardium, and a factor determining the redistribution was flow-independent6). These findings suggest that the quantitative analysis of TI redistribution could differentiate the ischemic myocardium from the infarcted or normally perfused myocardium, even if ischemic myocardium does not appear as defect. Therefore, we have investigated the myocardial washout rates of TI by the rest serial myocardial imagings, and we have tested its possible application to distinguish among ischemic myocardium, infarction and normally perfused myocardium.
Materials and Methods

Patients
Twenty patients with angiographically documented CAD (≥75%, luminal narrowing of at least one coronary artery) without evidence of acute myocardial ischemia and 5 healthy volunteers were selected for the study. CAD group consisted of 18 males and 2 females, and the mean age was 58.7 years (range 44–88 years). Fourteen patients of CAD had history of previous myocardial infarction. Clinical findings of CAD group were listed in Table 1. Volunteer group consisted of 4 males and a female, and the mean age was 25 years (20–33 years).

Study Protocol
A Pho/Gamma HP scintillation camera equipped with 15000 parallel hole high resolution collimator was used and it was interfaced to a minicomputer (Scintipac 230).

Rest Serial Myocardial Imaging. A rest 12-lead ECG was obtained at the time of the study in each patient. Two millicuries of Tl were injected intravenously and the first myocardial imaging was started after 5 minutes. The repeated myocardial images were obtained at 1 hour, 2 hours and 4 hours after Tl injection in patients with CAD. In healthy volunteers, myocardial imagings at 30 minutes, 1 hour, 1.5 hours, 2 hours and 4 hours after Tl injection were performed.

Myocardial images were recorded with a patient supine in anterior and 45-degree left anterior oblique (LAO) views in patients with CAD, and in LAO view in healthy volunteers. A total of 400,000 counts requiring 5 to 8 minutes for collection were obtained in each projection. In addition to the conventional scintiphoto imaging on Polaroid films, all Tl studies were stored in a computer.

For the quantitative analysis of myocardial images, background was subtracted by using bi-linear interpolative method7) and images were divided into 6 segments as shown in Fig. 1, and

<table>
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<th>Location of MI (ECG)</th>
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Abbreviations: AL; anterolateral, Ap; apical, Inf; inferior, PL; posterolateral Ant; anterior, H; hypokinesis, A; akinesis, N; normal wall motion in angiography and no perfusion defect in Tl imaging, T; transient defect, P; persistent defect, 3vd; triple vessel disease
Quantitation of Thallium-201 Myocardial Washout by Serial Rest Myocardial Imaging

Myocardial Segments

Anterior View

LAO View

Antero-lat

Septal

Postero-lat

Inferior

Apex

Fig. 1 Myocardial images in anterior and LAO projections were divided into 3 segments each. Blood supply of the myocardial segments were estimated as follows; anterolateral (Antero-lat) and septal segments represent left anterior descending coronary artery (LAD) vascular area, posterolateral segment (Posterolat) represents circumflex coronary artery, inferior segment (Inf) represents right coronary artery (RCA) vascular area and apical segment represents LAD or RCA vascular area.

myocardial Tl uptake indices were calculated sequentially in each segment. Half life of the washout of myocardial Tl was calculated as follows: Tl uptake indices were plotted against time in each segment. The index reached to the maximum within 60 minutes, and then decreased gradually. An approximately straight line was obtained by drawing a line from the maximal point to the following successive points. The half life of the washout was defined as the time from the injection of Tl to the half maximal point on the linear line.

Radionuclide Angiography. One week after the rest Tl study, angiography was performed at equilibrium state after red blood cells were labeled with 20 mCi of technetium-99m in vivo in all patients with CAD. Angiography was obtained at anterior and 45-degree left anterior oblique views by ECG gated method as we reported before.

Left ventricular margin at end-diastole and end-systole were detected automatically (isocount method) and they were superimposed for the interpretation of left ventricular wall motion. Left ventricular margin, both at anterior and LAO views, was divided into 3 portions in a similar method as myocardial images (Fig. 1), and in each segment regional wall motion was assessed by inspection and classified into normal, hypokinesis, akinesis and dyskinesis. For the interpretation of septal wall motion, we referred to the first pass radionuclide angiograms which had been obtained at 45-degree left anterior oblique position before equilibrium study.

Results

Normal Volunteers

Serial rest myocardial images which were recorded in LAO views did not show any perfusion abnormality in every case. Table 2 and Fig. 2 shows the sequential changes of myocardial Tl uptake indices. The myocardial Tl uptake indices reached to the maximum at 30 minutes after Tl injection, and then Tl uptake indices decreased linearly with time. The mean half life of the washout of myocardial Tl was 5.6 ± 0.7 hours.

Coronary Artery Disease

Satisfactory myocardial images and angiograms were obtained in all patients studied.

Out of total 120 segments, wall motion abnor-

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<th>Table 2</th>
<th>Sequential changes of myocardial Tl uptake indices</th>
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<td>Initial</td>
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<tr>
<td>Normal Volunteers</td>
<td>2.18 ± 0.38</td>
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<tr>
<td>Normally Perfused</td>
<td>2.11 ± 0.40</td>
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<tr>
<td>Infarcted</td>
<td>1.27 ± 0.35</td>
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<tr>
<td>Ischemic</td>
<td>1.30 ± 0.45</td>
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<tr>
<td>Mean ± SD</td>
<td>T 1/2: mean half life of washout of Tl</td>
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malities were observed in 67 segments, while defects were observed in 56 myocardial segments at rest initial images (Table 1).

The zones of myocardium supplied by each of the 3 major coronary arteries were matched to the corresponding zones on the TI image and angio-gram (Fig. 1)\(^\text{(1)}\).

Fig. 3 illustrated a patient with anterior myocardial infarction (Patient no. 7 in Table 1). Angiography showed anterolateral and apical akinesia. The initial TI image revealed anterolateral and apical defects and these defects did not change with time. Half life of the washout of myocardial TI was 5.9 hours in the inferior segment (normally perfused area) and 5.6 hours in the anterolateral segment (infarction area).

Fig. 4 and Fig. 5 represented a case of triple vessel disease with inferior infarction (Patient no. 18 in Table 1). Angiograms showed inferior, anterolateral, apical and septal hypokinesis, but posterolateral wall motion was preserved normally in spite of circumflex stenosis. Rest initial imaged showed inferior and septal defects. In the inferior segment the defect persisted, but in the septal segment the defect has filled in gradually. The anterolateral segment, which appeared to be ischemic on the basis of left ventricular wall motion abnormality, did not show any perfusion abnormality.

**Fig. 2** Sequential changes of myocardial TI uptake indices in 5 normal volunteers. The TI uptake indices reached to the maximum at 30 minutes after TI injection and then TI uptake indices declined linearly with time. The mean half life of the washout of myocardial TI (t 1/2) was 5.6 ± 0.7 hours.
But half life of the washout of TI in the anterolateral segment as well as in the septal segment, was significantly prolonged comparing with those in the inferior segment (infarction) and the posterolateral segment (normally perfused area).

On the basis of coronary angiography, radiouclide angiography and ECG findings, myocardial segments were divided into 3 conditions. The first was infarct segments characterized by pathologic Q waves, coronary stenosis and wall motion abnormality. And 41 myocardial segments were included in this category. The second was ischemic segments and they were characterized by coronary stenosis, wall motion abnormality and the absence of pathologic Q wave. Perfusion defect at the initial TI image was not a requisite condition. Twenty six myocardial segments corresponded to the second condition. The third was normally perfused segments and they were characterized by normal left ventricular wall motion. Myocardial segments supplied by stenosed coronary artery were regarded as normally perfused segments when the left ventriculogram showed normal contraction.

**Normally Perfused Segments.** All myocardial segments included in this condition showed no perfusion abnormality on TI imaging. Among 53 segments included in this condition, 5 segments

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**Fig. 4** A case of triple vessel disease with inferior infarction (patient no. 18). Angiograms showed inferior, anterolateral apical and septal hypokinesis. Posterolateral wall motion was motion was preserved normally. ED: end-diastole, ES: end-systole

**Fig. 5** A case of triple vessel disease with inferior infarction whose angiograms were illustrated in Fig. 4. Initial rest image showed inferior and septal defects. In the septal segment the defect has filled in with time, but in the inferior segment the defect persisted. Half life of the washout of TI (T 1/2) in ischemic segments (anterolateral, septal) was prolonged compared with those in infarct (inferior) and normally perfused (posterolateral) segments.

AL: anterolateral, PL: posterolateral, IVS: septal
were supplied by stenosed coronary artery.

As shown in Table 2 and Fig. 6, myocardial Tl indices reached to the maximum at 1 hour after Tl injection, and then Tl uptake indices decreased rapidly, and the mean half life of the washout of Tl was 5.9±1.0 hours. There was no myocardial segment in which the half life exceeded 7.5 hours.

Infarction Segments. All 41 infarction segments showed perfusion defects on initial Tl images and these defects did not change with time (persistent defect). Tl uptake indices at the initial images were significantly lower than those of normally perfused segments (p<0.01). In these segments, Tl uptake indices decreased rapidly after the peak (1 hour after Tl injection) and the mean half life of the washout was 5.7±1.1 hours (Table 2, Fig. 6). In every segment, the half life was less than 7.5 hours.

Ischemic Segments. Out of 26 ischemic segments, 15 segments showed defects at their initial images and these defects filled in completely or incompletely with time (transient defect). On the contrary, 11 myocardial segments did not show perfusion defect visually through sequential Tl images. Although the initial myocardial Tl uptake indices of this condition were significantly lower than those in normally perfused segments (p<0.01), there were some overlap of Tl uptake indices between ischemic and normally perfused segments (Table 2).

In the ischemic segments, myocardial Tl uptake indices reached to the maximum at 1 hour after Tl injection, and then Tl uptake indices decreased slowly, and at 4 hours after Tl injection Tl uptake indices of ischemic segments approached to those of normally perfused segments and there was no significant difference between them. The mean half life of the washout of the ischemic segments was 13.1±4.2 hours. In all transient defective segments (15 segments), the half lives exceeded 9 hours. In other 11 ischemic segments, in which perfusion defects were not observed visually, the half lives exceeded 9 hours in 10 segments, while Tl washout rate was not prolonged in one segment (7.2 hours).

Discussion

Recent clinical studies revealed that serial rest myocardial imaging could differentiate ischemic myocardium from scar, because in ischemic myocardium initial defects were transient and filled in with time3,4. Maseri et al15 proposed that Tl redistributed itself according to myocardial cellular mass, and Gerry et al6 proved by animal experiments that an important factor of Tl redistribution was flow-independent.

For the quantitative analysis of myocardial Tl clearance, we performed rest serial myocardial imaging and studied changes of myocardial Tl concentration by using myocardial Tl uptake indices2. Myocardial Tl uptake indices in this study were derived from conventional planar images, and it is inevitable that one myocardial segment overlaps in some degree with another myocardial segment. But as we already reported, myocardial Tl uptake indices reflected myocardial Tl concentration in experimental animals and they were especially valid to quantitate sequential Tl change2.

In the present study, we obtained myocardial images at 2 projections in order to complete myocardia imaging within short time (20 minutes) and we selected anterior and LAO views to facilitate to compare with radionuclide angiography.
We classified myocardial segments into (1) ischemic, (2) infarcted and (3) normally perfused myocardium on the basis of coronary angiography, radionuclide angiography and ECG findings. Myocardial segments, in which wall motion abnormality was not observed by radionuclide angiography, were judged as normally perfused even they received blood supply from stenosed coronary artery. It is because the presence of the stenosed coronary artery does not always mean myocardial ischemia distal to it, and because it is generally accepted that wall motion abnormality is the first sign of the myocardial ischemia \(^{13}\).

Our results of myocardial TI clearance in infarcted myocardium were identical to the animal experiments by Gewirtz et al\(^{14}\), in which they studied myocardial TI clearance and they reported that TI clearance in normally perfused myocardium was not different form that in the myocardium distal to the coronary ligation. On the contrary, TI washout rates in ischemic segments were very slow compared with normally perfused and infarcted segments. These results seems to suggest that myocardial muscle mass is one of the important factors which determine myocardial TI redistribution as proposed by Maseri et al\(^{13}\). And we interpreted the differences of myocardial TI clearance in 3 different conditions of myocardium as follows; since in infarcted myocardium TI accumulated within normally perfused myocardium surrounding scar tissue, so TI clearance curves in infarcted and normally perfused myocardium are basically identical and there exist the differences in quantity of muscle mass between them. On the other hand, in ischemic myocardium initial TI concentration is low due to hypoperfusion, but myocardial mass is equal to normally perfused myocardium. Therefore, TI concentration in ischemic myocardium reaches close to that in normally perfused myocardium with time by course of the decreased intrinsic TI washout from the myocardial cells.

Beller et al\(^{15}\) reported by animal experiments that in transient ischemic myocardium, myocardial TI concentration increased till 240 minutes after coronary reperfusion, and they concluded that after transient ischemia TI accumulated in transient ischemic segments and then slow washout of myocardial TI took place. But our results were not identical to their reports, because in our cases TI accumulation in ischemic segments was slight and washout rates of myocardial TI were markedly reduced. These discrepancy seems to arise from the following reasons; in their experiments, reactive hyperemia or normal restoration of the flow following coronary reperfusion might play an important role for myocardial TI accumulation, while in our studies rest myocardial imaging was performed and coronary blood flow was stable during the study. These difference in the coronary flow change was supposed to be the reason for discrepancy in myocardial TI accumulation.

In ischemic segments, slow myocardial TI clearance was observed irrespective of the presence or absence of the defect at initial myocardial images. In other words, the absence of the cold-spot in the TI image does not always mean the absence of ischemia, because myocardial images reflect the relative difference of TI concentration. As a matter of fact, the coexistence of infarction and underperfusion might obliterate the presence of the underperfusion as shown in Fig. 5.

The magnitude of TI uptake indices at initial image could differentiate ischemic segments from normally perfused segments, but there were some overlap between those values. But neither TI uptake indices nor radionuclide angiography could differentiate ischemic segments from infarct segments. On the other hand, TI washout rates could clearly differentiate among ischemic myocardium, infarction and normally perfused myocardium.

References


要 旨

安静時経時的タリウム心筋イメージングによるタリウム流出の定量的評価

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安静時において、201TIが心筋内に分布した後の心筋TIクリアランスを定量的に評価するため、5例の従常例および20例の冠動脈疾患で、安静時心筋シンチグラムを、TI静注5分後から4時間まで経時的に撮影した。心筋内TI濃度の変化は、心筋TI摂取係数の変化として観察し、これより心筋内TIの半減期を計測した。心筋シンチグラムは、正面、左前斜位の2方向より、20分以内に撮影を終了し、心筋イメージは、各方向3区域ずつ計6区域に区分した。冠動脈疾患では、20例計120の心筋区域を、冠動脈造影所見、心電図所見、99mTcによる心アンギオからえた左室壁運動の状態をもとに、正常灌流域（53）、種塞域（41、全区域でTI注入直後の心筋イメージでdefect存在）、虚血域（26、内15区域でTI注入直後のイメージでdefect存在）に区分した。正常灌流域では、心筋内TIの半減期は平均5.9±1.0時間（疾患例では5.6±0.7時間）で、種塞域の5.7±1.1時間の有意差をみなかった。これに反し、虚血域では、心筋内TIのクリアランスは緩徐であり、半減期は平均13.1±4.2時間と有意の延長を示した。また虚血域での心筋内TIの半減期は、TI注入直後のイメージでのdefectの存否は無関係であり、虚血域26中25で半減期は9時間をこえていた。

以上より、心筋内TIクリアランスの計測は、虚血性心疾患において心筋の状態（壊死の有無、血流状態）の鑑別に有用であり、壊死のない心筋虚血の診断に有用と考えられた。

Key words: Myocardial imaging with thallium, Myocardial washout rate of TI, TI-uptake index