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Original article

Efficacy of myocardial washout of ^{99m}Tc -MIBI/Tetrofosmin for the evaluation of inflammation in patients with cardiac sarcoidosis: Comparison with ^{18}F -fluorodeoxyglucose positron emission tomography findings

Short title: Tc Washout in Cardiac Sarcoidosis

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Abstract

Objective: Both myocardial perfusion scintigraphy and ^{18}F -fluorodeoxyglucose positron emission tomography (FDG PET) are useful for the diagnosis of cardiac sarcoidosis (CS). However, the association between the washout of $^{99\text{m}}\text{Tc}$ -labeled tracer and FDG PET has not been established. This study aimed to evaluate the association between the washout of $^{99\text{m}}\text{Tc}$ -labeled tracer and FDG PET findings in patients with CS.

Methods: We retrospectively analyzed 64 patients (65.0 ± 11.2 years, 53% male) with suspected CS who underwent myocardial single-photon emission computed tomography (SPECT) with $^{99\text{m}}\text{Tc}$ -labeled tracer and FDG PET. The SPECT images were acquired at 15 min (early images) and 3 h (delayed images) after injection and scored visually using a 17-segment model with a 5-point scoring system. The washout score was defined as the difference between the early and delayed total defect scores. FDG positivity was considered as focal or focal on diffuse patterns on visual assessment, and FDG uptake was quantified by measuring the standardized uptake value (SUV) of each of the 17 segments.

Results: The washout score was significantly higher for the CS group than for the non-CS group ($3.0 [-1.0-5.0]$ vs. $0.0 [-0.5-1.0]$, $p = 0.010$). Receiver operating characteristic analysis showed that a washout score of ≥ 2 had the best accuracy for detecting CS (88% sensitivity and 56% specificity) and FDG positivity (71% sensitivity and 89% specificity). In the segment-based analysis of 833 segments from 49 patients, excluding 15 patients with diffuse FDG uptake, the median SUVs for FDG uptake for the washout scores of ≤ 0 , 1, and 2 were 2.3 (1.8–3.6), 4.2 (2.9–7.8), and 8.3 (6.5–9.4), respectively ($p < 0.001$).

Conclusions: The washout of $^{99\text{m}}\text{Tc}$ -labeled tracer can be a useful marker for the evaluation of FDG PET findings in patients with CS.

Keywords: Cardiac sarcoidosis, $^{99\text{m}}\text{Tc}$ -labeled tracer, Washout, SPECT, FDG PET

1 Introduction

2 Sarcoidosis is a systemic granulomatous disease of unknown etiology. It particularly affects the
3 hilar lymph nodes, lungs, eyes, and skin. One of the most important prognostic factors of
4 sarcoidosis is cardiac involvement, which leads to atrioventricular block, severe ventricular
5 arrhythmia, or left ventricular dysfunction (1). Early diagnosis of cardiac sarcoidosis (CS) and
6 initiation of corticosteroid therapy are essential to prevent left ventricular dysfunction and ensure
7 the best clinical outcome (2, 3). However, cardiac involvement in sarcoidosis is often difficult to
8 diagnose because only 25% of cases of CS can be diagnosed by endomyocardial biopsy (4).

9 The combination of abnormal electrocardiogram and imaging findings using
10 echocardiogram, ^{201}Tl or $^{99\text{m}}\text{Tc}$ -labeled tracer myocardial perfusion single-photon emission
11 computed tomography (SPECT), or ^{67}Ga scintigraphy have been classically used to diagnose CS
12 (5, 6). Recent studies have shown that cardiac magnetic resonance (CMR) and ^{18}F -
13 fluorodeoxyglucose positron emission tomography (FDG PET) are highly sensitive and specific
14 for the diagnosis of CS (7–9). In the guidelines for the diagnosis and treatment of CS by the
15 Japanese Circulation Society updated in 2016, late gadolinium enhancement (LGE) on CMR and
16 FDG PET was regarded as a major diagnostic criterion, although myocardial perfusion SPECT
17 was left as a minor diagnostic criterion (10).

18 $^{99\text{m}}\text{Tc}$ -labeled tracer is rapidly distributed in the myocardium after administration, but the
19 clearance is relatively slow, and redistribution is unlikely to occur. On the other hand, both
20 myocardial uptake and retention of $^{99\text{m}}\text{Tc}$ -labeled tracer were inhibited in the damaged
21 myocardium. The washout phenomenon, which releases $^{99\text{m}}\text{Tc}$ -labeled tracer outside of the
22 myocardium, reflects impaired retention of technetium resulting from mitochondrial dysfunction
23 (11, 12). The washout of $^{99\text{m}}\text{Tc}$ -labeled tracer has been reported to be associated with

mitochondrial dysfunction caused by inflammation in CS and left ventricular functional recovery after corticosteroid therapy (13, 14). The combination of myocardial perfusion and metabolic FDG imaging has been reported to be useful for evaluating the state of inflammation in CS (15, 16). However, the association between the washout of ^{99m}Tc -labeled tracer and FDG PET findings in patients with CS has not been established; thus, we aimed to evaluate it in this study.

Materials and Methods

Study design

This single-center cohort study retrospectively enrolled consecutive patients with suspected CS who underwent myocardial SPECT with ^{99m}Tc -methoxy-isobutyl-isonitrile (^{99m}Tc -MIBI) or ^{99m}Tc -tetrofosmin and FDG PET between April 2014 and March 2020 at Kobe University Hospital. CS was diagnosed according to the updated guidelines for the diagnosis and treatment of CS by the Japanese Circulation Society after comprehensive clinical and histological evaluations (10). Myocardial SPECT with ^{99m}Tc -MIBI or ^{99m}Tc -tetrofosmin and FDG PET were performed within 3 months. The following exclusion criteria were used: history of myocardial infarction, severe coronary artery stenosis ($>70\%$) detected by invasive coronary angiography or coronary computed tomography angiography, myocardial ischemia detected by stress myocardial perfusion scintigraphy, and corticosteroid therapy before SPECT or FDG PET.

The study protocol adhered to the tenets of the 1975 Declaration of Helsinki. We provided patients with an appropriate opportunity to decline consent under the opt-out method on the institutional website; the requirement for written informed consent was waived. The study was approved by the Institutional Ethical Committee of the Kobe University Graduate School of Medicine.

SPECT image acquisition

SPECT imaging was performed using a dedicated cardiac cadmium-zinc-telluride camera (D-SPECT; Spectrum Dynamics, Biosensors, Caesarea, Israel). The D-SPECT camera consisted of nine rotating pixelated detector columns of cadmium-zinc-telluride crystals. Every detector was furnished with a wide-angle square-hole tungsten collimator and rotated around its central axis during the scanning process, while focusing on the region of interest.

For each patient, 740 MBq of ^{99m}Tc -MIBI or ^{99m}Tc -tetrofosmin was intravenously injected under resting conditions. SPECT imaging data were acquired at 15 min (early imaging) and 3 h (delayed imaging) after injection. The energy window for each camera was $140 \pm 10\%$. For each projection, 16 individual electrocardiographic gated frames were acquired. Using the myocardial count rate from the pre-scan acquisition, the time per projection was set to target the recording of 2000–2500 myocardial counts.

FDG PET image acquisition

All patients fasted for at least 18 h before the examination, and a low dose (50 IU/kg) of unfractionated heparin was injected 15 min before FDG administration to suppress physiological myocardial FDG uptake. Each patient received an intravenous administration of 3.5 MBq/kg of FDG and had to be kept in a resting state before the PET images were taken. PET imaging was performed using a PET/CT scanner (GE Discovery 690 PET/CT scanner, GE Healthcare, Milwaukee, WI, USA). The FDG PET data were obtained in three-dimensional mode with a 2-minute emission in each bed position for the whole body. Subsequently, cardiac PET was performed in a 2-bed position with a 10-minute emission. CT attenuation correction was

performed.

Image analysis of SPECT and FDG PET

SPECT and FDG PET images were evaluated by two nuclear cardiologists, and all disagreements were resolved by consensus. The left ventricular myocardium was divided into 17 segments for the analysis of SPECT and FDG PET images. The SPECT images were re-oriented into short-axis, horizontal, and vertical long-axis slices using QPS software (Cedars-Sinai Medical Center, Los Angeles, CA, USA). For the SPECT images, myocardial perfusion defects were semi-quantitatively interpreted using a 17-segment model. Each segment was scored based on a five-point scale (0 = normal uptake, 1 = mildly decreased, 2 = moderately decreased, 3 = severely decreased, and 4 = absence of detectable tracer uptake). The total defect score (TDS) was calculated by adding all 17 segment scores in the early and delayed images. The washout score was calculated as the difference between the early and delayed TDSs.

FDG PET images were reviewed using dedicated software (GE Healthcare, Waukesha, WI, USA). FDG PET images were classified into four patterns: focal, focal on diffuse, diffuse, or none, according to the myocardial FDG uptake on visual assessment. Focal and focal diffuse patterns were considered FDG positive (17). FDG uptake was quantified by measuring the standardized uptake value (SUV) of each of the 17 segments on the short-axis slices. The maximum and mean SUV values in the heart were calculated. The comparison between washout score of ^{99m}Tc -labeled tracer in SPECT images and SUV of FDG uptake in PET images was performed slice by slice to co-locate each segment in the segment-based analysis. The patients with diffuse FDG uptake pattern were excluded in the segment-based analysis to avoid measuring SUV of physiological FDG uptake.

Statistical analysis

The normality of the data distribution of all continuous variables was assessed using the Shapiro-Wilk test. Continuous variables were expressed as means $\pm$ standard deviations or medians (interquartile range, IQR), as appropriate, and compared using Student's *t*-test or the Mann–Whitney U test. Categorical variables were expressed as counts and percentages and compared using the chi-squared or Fisher's exact tests. Multiple comparisons were performed using one-way repeated analysis of variance with Tukey's post hoc test or the Kruskal-Wallis test with the Steel-Dwass test, as appropriate. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the cut-off value of the washout score that best predicted CS and FDG-positive patients, using Youden's index. The DeLong test was used to compare the areas under the curve (AUC).

All statistical analyses were performed using commercially available software (JMP 14.2.0; SAS Institute, Cary, NC) and R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $p < 0.05$.

Results

Study population

Eighty-eight patients with suspected CS underwent myocardial SPECT with ^{99m}Tc -MIBI or ^{99m}Tc -tetrofosmin and FDG PET during the study period. We excluded 24 patients with a history of myocardial infarction ($n = 6$), severe coronary artery stenosis ($>70\%$) detected by invasive coronary angiography or coronary computed tomography angiography ($n = 4$), or corticosteroid therapy ($n = 14$). Thus, 64 patients (mean age 65.0 ± 11.2 years; 53% male) were studied, and

their characteristics are shown in **Table 1**. CS was diagnosed in 39 patients, including systemic sarcoidosis with cardiac involvement (n = 21) and isolated CS (n = 18). FDG PET was positive in 38 patients. The median interval between SPECT and FDG PET scans was 7 days (range, 3–14 days). SPECT images were acquired with ^{99m}Tc -MIBI (n = 28) or ^{99m}Tc -Tetrofosmin (n = 36), and there were no significant differences in patient characteristics between the two ^{99m}Tc -labeled tracers (**Table S1**). The washout score did not differ by the segments and sex.

Comparison of SPECT and FDG PET data between CS and non-CS groups

The patients were divided into two groups: CS group (n = 39) and non-CS group (n = 25) based on the diagnosis of CS (**Table 1**). Age, sex, and body mass index were similar in both groups. ~~There were more females in the FDG-positive group.~~ FDG positivity was more frequently observed in the CS group. There were no significant differences in medical history, arrhythmias, laboratory data, and echocardiographic measurements.

For the SPECT data, there were no significant differences in the early TDS (7.0 [4.0–13.0] vs. 7.0 [2.0–14.0], p = 0.98) and the delayed TDS (10.0 [6.0–16.0] vs. 9.0 [4.0–14.0], p = 0.29) between the CS and non-CS groups. The washout score was significantly higher for the CS group than for the non-CS group (3.0 [-1.0–5.0] vs. 0.0 [-0.5–1.0], p = 0.010). For the FDG PET imaging, the max SUV tended to be higher for the CS group although this was not significant. The mean SUV was similar for both groups.

ROC analyses of the SPECT data for detecting CS patients and FDG-positive patients are shown in **Figure 1**. The cut-off value of the washout score at ≥ 2 had the best accuracy for detecting CS patients (88% sensitivity and 56% specificity) (**Figure 1A**). AUC was 0.76 (95% confidence interval [CI]: 0.65–0.86) for the washout score: 0.50 (95% CI: 0.35–0.66) for early TDS and 0.58

(95% CI: 0.43–0.73) for delayed TDS. The washout score was better than both the early and delayed TDS ($p = 0.003$ and $p = 0.041$, respectively). There was no significant difference between the early and delayed TDS ($p = 0.63$). On the other hand, the cut-off value of the washout score at ≥ 2 had the best accuracy for detecting FDG-positive patients (71% sensitivity and 89% specificity) (**Figure 1B**). AUC was 0.80 (95% CI: 0.70–0.90) for the washout score: 0.61 (95% CI: 0.46–0.76) for early TDS and 0.51 (95% CI: 0.36–0.66) for delayed TDS. The washout score was better than both the early and delayed TDS ($p = 0.022$ and $p < 0.001$, respectively). There was no significant difference between the early and delayed TDS ($p = 0.52$).

Representative images are shown in **Figure 2**.

Association between ^{99m}Tc -labeled tracer washout and FDG uptake in segment-based analysis

After excluding 15 patients with diffuse FDG uptake, among 833 segments in 49 patients, the median SUVs of FDG uptake in segments with Tc washout scores of ≤ 0 , 1, and 2 were 2.3 (1.8–3.6), 4.2 (2.9–7.8), and 8.3 (6.5–9.4), respectively ($p < 0.001$) (**Figure 3A**).

Based on the initial perfusion of the ^{99m}Tc -labeled tracer and washout score, each segment was classified into the following four groups: Group A (normal initial perfusion without washout), Group B (normal initial perfusion with washout), Group C (abnormal initial perfusion without washout), and Group D (abnormal initial perfusion with washout). The median SUVs of FDG uptake were 2.3 (1.7–3.5) for Group A, 6.6 (4.8–8.8) for Group B, 2.9 (1.9–3.9) for Group C, and 4.1 (2.8–7.7) for Group D, respectively ($p < 0.001$) (**Figure 3B**).

Discussion

In the current study, we scored the early and delayed ^{99m}Tc -SPECT images of patients with suspected CS and evaluated the association between the washout of ^{99m}Tc -labeled tracer and FDG uptake. The washout score of the ^{99m}Tc -labeled tracer was significantly higher for the CS patients. FDG uptake was significantly increased as the washout score of ^{99m}Tc -labeled tracer increased in the segment-based analysis.

Washout of ^{99m}Tc -labeled tracer

^{99m}Tc -labeled tracers have been widely used for the non-invasive assessment of myocardial perfusion (18, 19). The washout phenomenon, which releases ^{99m}Tc -labeled tracer outside of the myocardium, reflects impaired retention of technetium resulting from mitochondrial dysfunction (11, 12). It is classically observed in acute myocardial infarction after percutaneous coronary intervention, indicating salvaged myocardial areas and predicting left ventricular functional recovery in the chronic state (20, 21). The washout of ^{99m}Tc -labeled tracer has also been observed in non-ischemic cardiac diseases such as left bundle branch block, hypertrophic cardiomyopathy, and dilated cardiomyopathy (22–24).

We acquired SPECT images based on myocardial counts and evaluated the washout of ^{99m}Tc -labeled tracers with visually scoring system. Time-based acquisition of SPECT image can calculate the washout rate from the myocardial counts of the early and delayed images. However, especially in acquisition of the delayed image, sufficient myocardial counts may not be obtained within the defined time due to low radiotracer activity, resulting in low-quality images. In the current study, we focused on acquiring images of sufficient quality.

Clinical significance of washout of ^{99m}Tc -labeled tracer in CS

There are two pathophysiologic phases of CS: “active phase” and “healed phase” (25). The active phase is characterized by epithelioid granulomas, which are alveolar lesions composed mainly of lymphocytes and macrophages, without central caseation. The presence of these granulomas establishes the diagnosis of CS; however, they have been reported in only 25% of patients with a clinical diagnosis of CS (4). The healed phase of CS is characterized by scar tissue that results from the fibrotic replacement of the granulomas. Although LGE on CMR has high sensitivity and specificity for the diagnosis of CS, LGE corresponds to both epithelioid granuloma and fibrosis pathologically (9). Therefore, it is difficult to evaluate the phase of disease activity using only LGE. FDG PET is known to be a useful metabolic imaging modality for evaluating active inflammation, and it has been reported that the addition of myocardial perfusion assessment is useful for determining the status of CS; perfusion defects in SPECT images in patients with CS represent areas of inflammation or scar, while abnormal FDG uptake represents only inflammation (15, 16).

In the current study, we evaluated the association between ^{99m}Tc -labeled tracer initial uptake and ^{99m}Tc -labeled tracer washout with FDG uptake. Our results showed that the washout score was significantly higher for the CS patients than for the non-CS patients. For the segment-based analysis, the segments with normal initial perfusion with washout (Group B) had significantly higher FDG uptake than the segments with normal initial perfusion without washout (Group A). Therefore, the washout of ^{99m}Tc -labeled tracer can reflect early inflammation, such that early SPECT images show no perfusion defects. On the other hand, the segments with abnormal initial perfusion without washout (Group C) had significantly lower FDG uptake than the segments with washout, regardless of whether the initial perfusion was normal or abnormal (Groups B and D). It is considered that the fixed perfusion defect areas without washout reflect

1 fibrotic replacement without active inflammation. Several studies have investigated the
2 association between the washout of ^{99m}Tc -labeled tracer in patients with CS and left ventricular
3 functional recovery after corticosteroid therapy (13, 14). These studies showed that patients with
4 the washout of ^{99m}Tc -labeled tracer showed an improvement in left ventricular function, and the
5 degree of washout decreased after corticosteroid therapy, while patients who had severe perfusion
6 defects without washout of ^{99m}Tc -labeled tracer tended to be unresponsive to corticosteroid
7 therapy. The fact that corticosteroid therapy restores left ventricular function suggests the presence
8 of myocardial inflammation, and our results are consistent with previous reports.

9 Several studies have investigated the association between FDG PET and dual myocardial
10 perfusion SPECT images using ^{201}Tl and ^{123}I -betamethyl-p-iodophenyl-pentadecanoic acid
11 (BMIPP) in patients with CS (26, 27). These studies showed that the segments with ^{201}Tl and
12 BMIPP mismatches had higher SUVs of FDG uptake than those without ^{201}Tl and BMIPP
13 mismatch. This indicates that ^{201}Tl and BMIPP mismatch may be associated with active
14 inflammation leading to ongoing myocardial damage. BMIPP images have been reported to
15 resemble delayed ^{99m}Tc -labeled tracer images (23, 28); therefore, the washout of ^{99m}Tc -labeled
16 tracer in our study can be interpreted as the same as the ^{201}Tl and BMIPP mismatch, reflecting
17 myocardial inflammation. Because the radiation dose for SPECT using ^{99m}Tc -labeled tracer is less
18 than that for SPECT using both ^{201}Tl and BMIPP, it is preferable to evaluate the washout of ^{99m}Tc -
19 labeled tracer rather than to evaluate the ^{201}Tl and BMIPP mismatches in terms of radiation
20 exposure.

21 There are few reports on the diagnostic accuracy of myocardial perfusion SPECT for
22 patients with CS (29). In our study, ROC analysis was used to evaluate the diagnostic performance
23 of ^{99m}Tc -labeled tracer perfusion SPECT images for predicting CS patients and FDG-positive

patients. The cut-off value of the washout score of ≥ 2 had the best accuracy for CS patients (88% sensitivity and 56% specificity) and FDG-positive patients (71% sensitivity and 89% specificity), and the AUC of the washout score was significantly higher than both the early and delayed TDS. Thus, evaluation of the washout score will improve the diagnostic performance of myocardial perfusion SPECT with a ^{99m}Tc -labeled tracer to evaluate myocardial inflammation. There were a few cases with ^{99m}Tc -labeled tracer washout and diffuse FDG uptake as shown in the representative images (Figure 2). The washout phenomenon could be caused by not only myocardial inflammation but also other mitochondrial injuries as mentioned above (20–24). It is obviously important to evaluate myocardial inflammation by using multimodality clinical findings with reference to ^{99m}Tc -labeled tracer washout.

Study limitations

This study has several limitations. First, this was a single-center retrospective study and may have had selection bias, even though we enrolled patients consecutively. Second, the sample size was relatively small. Third, we used both ^{99m}Tc -MIBI and ^{99m}Tc -tetrofosmin as myocardial perfusion tracers. These two perfusion tracers are pharmacokinetically almost similar, however, these are not the same according to previous animal experiments (30, 31). Although the pharmacokinetic difference between the two tracers has not been well investigated in the human heart, it might have affected the results of this study. Finally, we applied 18 hours of fasting and injection of unfractionated heparin to suppress physiological myocardial FDG uptake. However, patients were not instructed to consume a low-carbohydrate high-fat diet before examination. In the current study, the number of patients with a diffuse pattern of FDG accumulation was greater than that with no pattern (15 patients vs. 11 patients), which may have led to a relatively high SUV for the

non-CS group.

Conclusions

The washout of ^{99m}Tc -labeled tracer was frequently observed in patients with CS with abnormal FDG uptake, and the segments of the myocardium with ^{99m}Tc -labeled tracer washout had higher FDG uptake. The washout of the ^{99m}Tc -labeled tracer may be useful for evaluating inflammation in CS.

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Disclosures

None.

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- 1 retrogradely perfused guinea pig hearts. Nucl Med Biol. 2002;29:243–54.
- 2
- 3

Figure Legends

Figure 1. ROC analysis of ^{99m}Tc -labeled tracer SPECT data for predicting CS (A) and FDG positivity (B).

(A) The diagnostic accuracy of the washout score for CS was significantly higher than that of early TDS (AUC: 0.76 vs 0.50, $p = 0.003$) and delayed TDS (AUC: 0.76 vs 0.58, $p = 0.041$).

There was no significant difference between the early and delayed TDS ($p = 0.63$).

(B) The diagnostic accuracy of the washout score for FDG positivity was significantly higher than that of early TDS (AUC: 0.80 vs 0.61, $p = 0.022$) and delayed TDS (AUC: 0.80 vs 0.51, $p < 0.001$). There was no significant difference between the early and delayed TDS ($p = 0.52$).

AUC, area under the curve; CS, cardiac sarcoidosis; ROC, receiver operating characteristic; TDS, total defect score

Figure 2. Representative images of ^{99m}Tc -labeled tracer washout and FDG uptake.

(A) Focal FDG uptake with ^{99m}Tc -labeled tracer washout. ^{99m}Tc -labeled tracer perfusion in the basal lateral segment was mildly decreased in the early image and moderately decreased in the delayed image. ^{99m}Tc -labeled tracer perfusion in the mid-lateral segment was almost normal in the early image and mildly decreased in the delayed image. ^{99m}Tc -labeled tracer perfusion in the apical anterior segment was mildly decreased in the early image and moderately decreased in the delayed image. In the segments with ^{99m}Tc -labeled tracer washout, FDG uptake was increased. The early TDS, delayed TDS, and washout score were 3, 7, and 4, respectively. The max SUV and mean SUV were 13.9 and 5.2, respectively.

(B) No FDG uptake without ^{99m}Tc -labeled tracer washout. ^{99m}Tc -labeled tracer perfusion in the basal septal to inferior segments was severely decreased in the early image and had no obvious

washout in all segments of the delayed images. There was no FDG uptake in the heart. The early TDS, delayed TDS, and washout score were 15, 15, and 0, respectively. The max SUV and mean SUV were 2.0 and 1.5, respectively.

FDG, ^{18}F -fluorodeoxyglucose; SUV, standardized uptake value; TDS, total defect score.

(C) Diffuse FDG uptake with $^{99\text{m}}\text{Tc}$ -labeled tracer washout. $^{99\text{m}}\text{Tc}$ -labeled tracer perfusion in the basal inferoseptal segment was mildly decreased in the early image and moderately decreased in the delayed image. $^{99\text{m}}\text{Tc}$ -labeled tracer perfusion in the basal anteroseptal and inferior segments was almost normal in the early image and moderately decreased in the delayed image. FDG uptake was increased in the whole heart. The early TDS, delayed TDS, and washout score were 6, 11, and 5, respectively. The max SUV and mean SUV were remarkably elevated to 11.2 and 8.4, respectively.

Figure 3. Comparisons of FDG uptake among the washout score (A) and the 4 groups divided according to initial perfusion defect and washout (B) in the segment-based analysis.

(A) Median SUVs of FDG uptake associated with the Tc washout scores of ≤ 0 , 1, and 2 were 2.3 (1.8–3.6), 4.2 (2.9–7.8), and 8.3 (6.5–9.4), respectively ($p < 0.001$).

(B) Each segment was classified into one of the following 4 groups according to the $^{99\text{m}}\text{Tc}$ -labeled tracer perfusion in early images and washout in delayed images. The median SUVs of FDG uptake were 2.3 (1.7–3.5) for Group A, 6.6 (4.8–8.8) for Group B, 2.9 (1.9–3.9) for Group C, and 4.1 (2.8–7.7) for Group D, respectively ($p < 0.001$).

FDG, ^{18}F -fluorodeoxyglucose; SUV, standardized uptake value.

1 **Tables**2 **Table 1. Patient characteristics**

3

	CS (n = 39)	Non-CS (n = 25)	p value
Age, years	64.4 ± 11.2	66.0 ± 11.4	0.60
Male, n (%)	19 (49)	15 (60)	0.38
Body mass index, kg/m ²	22.6 ± 3.9	22.1 ± 4.1	0.63
Diagnosis of CS, n (%)			—
Systemic sarcoidosis with cardiac involvement, n (%)	21 (54)		
Isolated CS, n (%)	18 (46)		
Medical history			
Hypertension, n (%)	14 (36)	11 (44)	0.52
Dyslipidemia, n (%)	15 (38)	9 (36)	0.84
Diabetes mellitus, n (%)	5 (13)	4 (16)	0.72
Chronic kidney disease, n (%)	17 (44)	9 (36)	0.55
Arrhythmia			
Complete atrioventricular block, n (%)	13 (33)	5 (20)	0.24
Ventricular tachycardia, n (%)	15 (38)	9 (36)	0.84
Laboratory data			
eGFR, ml/min/1.73m ²	63.8 (47.6–74.0)	59.9 (52.4–70.0)	0.83
BNP, pg/ml	158.8 (33.6–427.3)	147.7 (77.6–352.9)	0.76

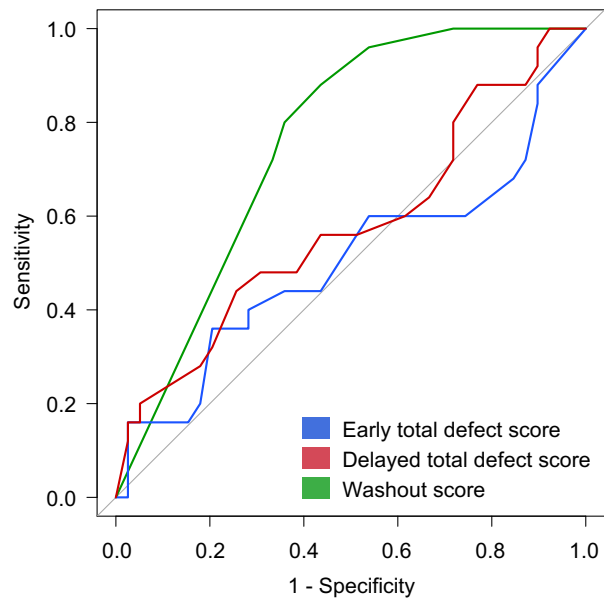
ACE, U/L	15.5 (11.0–25.4)	12.7 (6.5–14.2)	0.054
Echocardiography			
LVEF, %	45.0 ± 14.4	43.3 ± 14.3	0.64
SPECT			
Perfusion tracer			0.63
^{99m} Tc-tetrofosmin, n (%)	21 (54)	15 (60)	
^{99m} Tc-MIBI, n (%)	18 (46)	10 (40)	
Early total defect score	7.0 (4.0–13.0)	7.0 (2.0–14.0)	0.98
Delayed total defect score	10.0 (6.0–16.0)	9.0 (4.0–14.0)	0.29
Washout score	3.0 (-1.0–5.0)	0.0 (-0.5–1.0)	0.010
FDG PET			
Positive	34 (87)	4 (16)	<0.001
Patterns of FDG accumulation			<0.001
Focal, n (%)	25 (64)	2 (8)	
Focal on diffuse, n (%)	9 (23)	2 (8)	
Diffuse, n (%)	2 (5)	13 (52)	
None, n (%)	3 (8)	8 (32)	
SUV			
SUV max	6.9 (4.1–10.2)	5.2 (2.1–7.7)	0.054
SUV mean	3.4 (2.6–4.9)	3.6 (1.7–5.7)	0.59

-
- 1 Values are expressed as mean ± standard deviation, n (%), or median (interquartile range). P-
- 2 values < 0.05, are shown in **bold**.

- 1 ACE, angiotensin-converting enzyme; BNP, B-type natriuretic peptide; CS, cardiac sarcoidosis;
- 2 eGFR, estimated glomerular filtration rate; FDG PET, ¹⁸F-fluorodeoxyglucose positron emission
- 3 tomography; LVEF, left ventricular ejection fraction; MIBI, methoxy-isobutyl-isonitrile;
- 4 SPECT, single-photon emission computed tomography; SUV, standardized uptake value.

Figure 1

A



B

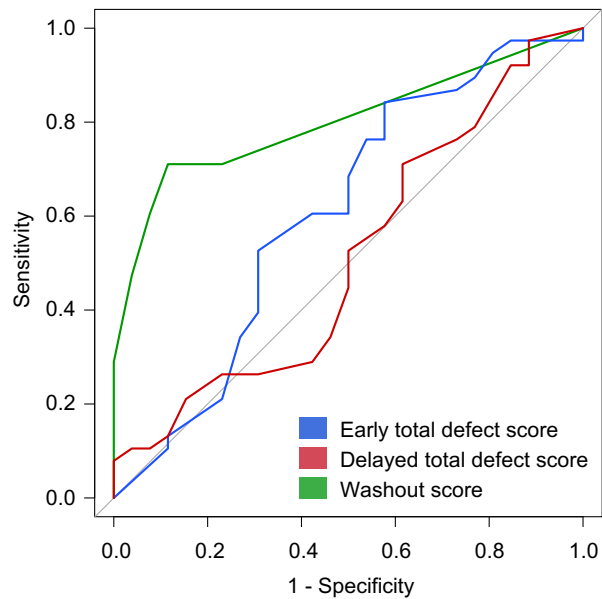


Figure 2

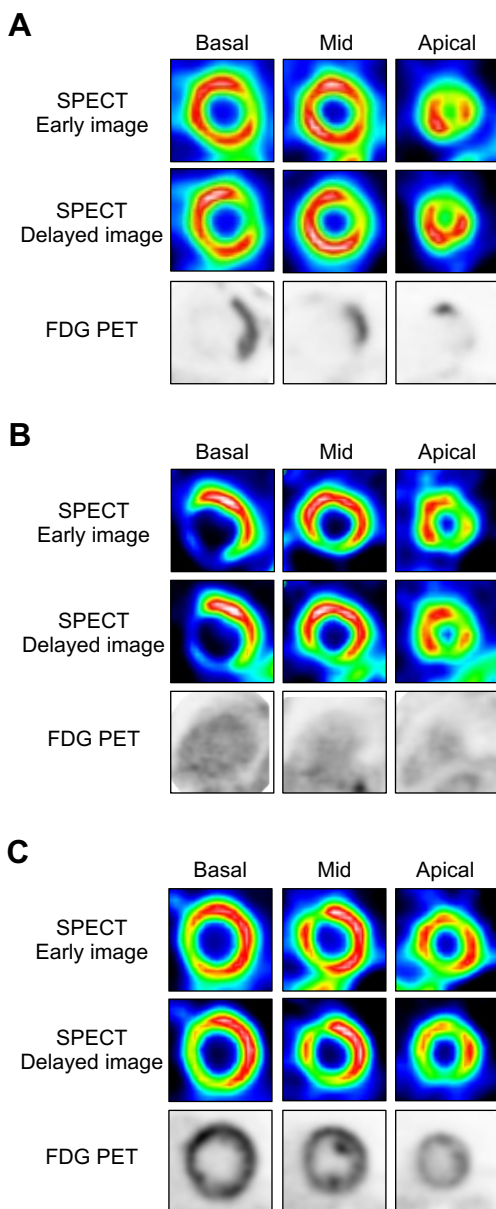
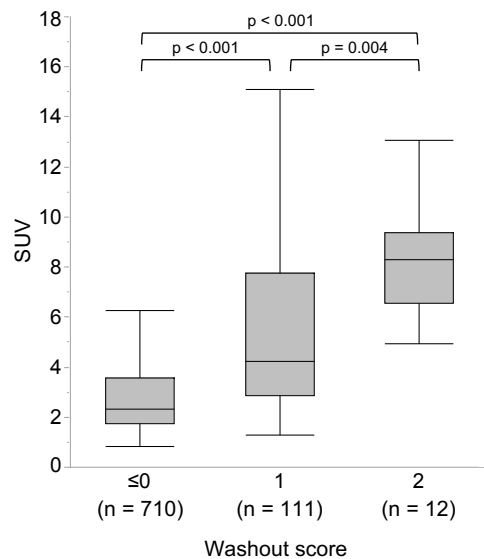


Figure 3

A



B

