



Diagnostic value of quantitative assessment of cardiac ^{18}F -fluoro-2-deoxyglucose uptake in suspected cardiac sarcoidosis

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Abstract

Objective The identification of cardiac sarcoidosis is challenging as there is no gold standard consensually admitted for its diagnosis. The aim of this study was to evaluate the diagnostic value of the assessment of cardiac dynamic ^{18}F -fluoro-2-deoxyglucose positron emission tomography (^{18}F -FDG PET/CT) and net influx constant (Ki) in patients suspected of cardiac sarcoidosis.

Methods Data obtained from 30 biopsy-proven sarcoidosis patients suspected of cardiac sarcoidosis who underwent a 50-min list-mode cardiac dynamic ^{18}F -FDG PET/CT after a 24 h high-fat and low-carbohydrate diet were analyzed. A normalized coefficient of variation of quantitative glucose influx constant, calculated as the ratio: standard deviation of the segmental Ki (min^{-1})/global Ki (min^{-1}) was determined using a validated software (Carimas[®] 2.4, Turku PET Centre). Cardiac sarcoidosis was diagnosed according to the Japanese Ministry of Health and Welfare criteria. Receiving operating curve analysis was performed to determine sensitivity and specificity of cardiac dynamic ^{18}F -FDG PET/CT analysis to diagnose cardiac sarcoidosis.

Results Six out of 30 patients (20%) were diagnosed as having cardiac sarcoidosis. Myocardial glucose metabolism was significantly heterogeneous in patients with cardiac sarcoidosis who showed significantly higher normalized coefficient of variation values compared to patients without cardiac sarcoidosis (0.513 ± 0.175 vs. 0.205 ± 0.081 ; $p = 0.0007$). Using ROC curve analysis, we found a cut-off value of 0.38 for the diagnosis of cardiac sarcoidosis with a sensitivity of 100% and a specificity of 91%.

Conclusions Our results suggest that quantitative analysis of cardiac dynamic ^{18}F -FDG PET/CT could be a useful tool for the diagnosis of cardiac sarcoidosis.

Keywords Cardiac sarcoidosis · Positron emission tomography · Dynamic acquisition · FDG · Quantitative analysis

Abbreviations

ACE	Angiotensin-converting enzyme
CRP	C-reactive protein
CS	Cardiac sarcoidosis
CT	Computed tomography
FFA	Free fatty acids
^{18}F -FDG	^{18}F -fluoro-2-deoxyglucose
^{18}F -FDG PET/CT	Cardiac dynamic ^{18}F -fluoro-2-deoxyglucose positron emission tomography
FWHM	Full width at half maximum
HFLC	High-fat and low-carbohydrate
Ki	Net influx constant
MPI	Myocardial perfusion imaging
NCOV	Normalized coefficient of variation
PET	Positron emission tomography
ROC	Receiving operating curve

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ROI	Region of interest
SUV	Standard uptake value

Introduction

Sarcoidosis is a multisystem disease of unknown etiology characterized by the formation of non-caseating granulomas in many organs [1]. Cardiac involvement in sarcoidosis is a cause of morbidity and mortality. Indeed, cardiac granulomas may lead to conduction and rhythm abnormalities, sudden death and congestive heart failure. The prognosis of sarcoidosis is commonly considered as favorable but is significantly changed by the presence of a cardiac localization [2]. Cardiac involvement is symptomatic in only 5% of patients with sarcoidosis, whereas it occurs in 27% of sarcoidosis cases, according to autopsy findings [3]. Identification of cardiac sarcoidosis (CS) is challenging and early diagnosis is needed to initiate a corticosteroid treatment, which is effective against most active clinical manifestations of CS and may improve the prognosis. However, there is no gold standard consensually admitted for the diagnosis of CS, and a lack of agreement on key aspects of patient management [4]. The 1993 guidelines of the Japanese Ministry of Health and Welfare (JMHW), revised in 2006 by the Japanese Society of Sarcoidosis and other Granulomatous Disorders [5], is frequently used as a clinical gold standard for the diagnosis of CS [6]. The Heart Rhythm Society recently published a consensus statement on the diagnosis of cardiac sarcoidosis as well [7].

^{18}F -fluoro-2-deoxyglucose (^{18}F -FDG) is known to accumulate in macrophages and reactive lymphocytes of inflammatory tissues allowing the detection of both inflammation and infection using ^{18}F -FDG PET/CT [8]. Myocardial physiological ^{18}F -FDG uptake can be suppressed using prolonged fasting, heparin load and dietary carbohydrate restriction before the examination [9, 10]. When patient preparation is performed correctly, ^{18}F -FDG PET/CT may be helpful for detecting active lesions of CS.

In most studies, a focal myocardial ^{18}F -FDG uptake using a visual analysis was considered as positive for active CS lesions. Several studies aimed to quantify the myocardial ^{18}F -FDG uptake using the standard uptake value (SUV). Tahara et al. suggested that an increased heterogeneity of myocardial ^{18}F -FDG uptake may be a characteristic feature of CS [11]. In their study, the heterogeneity of ^{18}F -FDG uptake was assessed using the coefficient of variation (COV), calculated as the ratio of the standard deviation of segmental uptake, divided by the mean left ventricular SUV, using a 17-segment model of the heart.

Qualitative or semi-quantitative analysis of the myocardial ^{18}F -FDG uptake appears helpful in this context, but does not fully benefit from the ability of dynamic ^{18}F -FDG

PET/CT to provide a quantitative assessment of the myocardial glucose metabolism, based on compartmental analysis [12]. To date, no previous study evaluated the value of quantitative analysis of the myocardial glucose metabolic rate in suspected CS. Therefore, the aim of our study was to evaluate the diagnostic value of cardiac dynamic ^{18}F -FDG PET/CT in patients suspected of CS.

Materials and methods

Study population

We retrospectively analyzed the data from 30 consecutive biopsy-proven sarcoidosis patients suspected of CS who underwent a cardiac dynamic ^{18}F -FDG PET/CT from September 2012 to June 2014 as part of clinical routine evaluation for radiological and clinical sarcoidosis suspicion of definite proven sarcoidosis at Caen University Hospital. Data from 4 patients were excluded because of non-compliance to the diet (2 cases) or because of a history of prior myocardial infarction (2 cases). Clinical evaluation, assessment of disease duration, 12-lead electrocardiogram (ECG) and transthoracic echocardiography were performed in all patients. Serum calcium, C-reactive protein (CRP), angiotensin-converting enzyme (ACE) were measured as well. In all patients, the diagnosis of sarcoidosis was established using the following criteria: consistent clinical presentation, histological evidence of non-caseous granulomas on biopsy specimens and the absence of any infection, occupational factors, or medical treatment known to cause granulomatous disease [1]. According to French regulatory rules for observational studies, our regional review committee (CPP Nord-Ouest 3) waived the requirement for additional approval.

Transthoracic echocardiography

All patients underwent echocardiography using a 1.5 MHz echo-Doppler probe with a iE33 imaging system (Phillips, Eindhoven, Netherlands) as part of routine evaluation for newly diagnosed sarcoidosis [13]. LV ejection fraction was obtained using the modified biplane Simpson's method.

Myocardial perfusion SPECT imaging

According to our institutional procedures, rest myocardial perfusion SPECT imaging (MPI) was performed in sarcoidosis patients 1 h after the injection of $^{99\text{m}}\text{Tc}$ sestamibi (7 MBq/kg). When the rest MPI was considered abnormal, MPI was repeated within 1 week after a pharmacological stress (dipyridamole, 0.56 mg/kg). MPI was analysed by an experienced reader, blinded of any clinical data, and was considered as positive for CS in case of perfusion

abnormality at rest reversible after dipyridamole, or in case of non-reversible perfusion abnormality after dipyridamole injection associated with an abnormal wall motion within the same segments.

¹⁸F-FDG PET/CT: pretest preparation

The patients received a menu indicating allowed and prohibited foods. Patients were asked to take a high-fat and low-carbohydrate (HFLC) dinner the day before the ¹⁸F-FDG PET/CT. Oral instructions were also given by a telephone call to ensure about proper understanding of the diet. A physician checked the patient compliance to diet the day of scanning. All patients fasted for at least 12 h before the examination.

Dynamic ¹⁸F-FDG PET/CT

Thirty patients underwent a cardiac dynamic PET acquisition followed by a whole body PET acquisition in 25/30 patients. Blood glucose levels were measured before the injection of the radiopharmaceutical. Patients had a plasma glucose level < 1.8 g/L at the time of injection. The heart was centered inside the scanner field of view using a CT topogram. A 50-min list-mode cardiac ¹⁸F-FDG PET/CT scan with a single bed position was immediately performed after an intravenous injection of 4 MBq/kg of ¹⁸F-FDG. All patients were kept in a resting state with the arms elevated behind the head during the acquisition. All PET acquisitions were performed on a Biograph TruePoint TrueV (Siemens Medical Solutions, Erlangen, Germany) with a 6-slice spiral CT component. CT acquisitions were achieved with the following parameters: 60mAs, 130 kV, pitch 1, collimation 6 × 2 mm. CT acquisitions were reconstructed with a slice thickness of 3 mm and an increment of 2 mm. The dynamic scan consisted of 33 frames with variable frame length (6 × 5, 6 × 10, 3 × 20, 5 × 30, 5 × 60, 8 × 300 s). PET images were reconstructed using an OSEM algorithm (4 iterations, 8 subsets) and a 5 mm FWHM Gaussian filter. Matrix size was 168 × 168 for all reconstructions. The analysis of dynamic PET data was performed using a dedicated software (Carimas 2.4, Turku PET Centre, Turku, Finland). The net influx constant (Ki) was calculated using a Patlak graphical plot method model without plasma sampling and expressed in min⁻¹ [12].

The characterization of the input function was achieved using blood time-activity curves derived from PET images. ROI were drawn in the cavity of the left ventricle to determine an arterial input function and in the cavity of the right ventricle for spillover correction. The Patlak analysis was performed over the period from 10 to 50 min after injection during steady state. We performed both global and segmental assessment of Ki. The segmental analysis was performed using a 17-segment

division of the left ventricle [14]. We estimated the heterogeneity of glucose metabolism using a normalized coefficient of variation (NCOV). The NCOV of Ki was calculated by dividing the standard deviation (SD) of Ki by the global Ki: $NCOV = SD\ Ki\ (min^{-1}) / global\ Ki\ (min^{-1})$. All analyses were performed by 2 readers (AM and DA) blinded to any clinical data.

Static ¹⁸F-FDG PET/CT

Whole body ¹⁸F-FDG PET/CT was acquired after the dynamic cardiac acquisition to assess extra-cardiac sarcoidosis involvement [15]. The whole body images were acquired from the base of skull to mid high. The duration of each bed position was set to 160 s. Static CT acquisitions parameters were the same as those used for dynamic study. Static PET images were reconstructed with a PSF reconstruction algorithm (HD; TrueX, Siemens Medical Solutions; 3 iterations and 21 subsets) without filtering (PSFallpass). Matrix size was 168 × 168 for every reconstruction. Visual analysis was performed by two experienced reader, blinded of any clinical data. Based on previous reports, none or diffuse myocardial ¹⁸F-FDG uptake was considered as normal, and a focal or focal in diffuse myocardial ¹⁸F-FDG uptake was considered as positive for CS [16].

Data analysis

CS was diagnosed according to the JMHW criteria for clinical diagnosis, revised in 2006 [5]. Data were described as median and interquartile ranges. An unpaired *t* test or Mann–Whitney test was used to examine comparisons between groups (with and without CS). Statistical significance was set at *p* value < 0.05. Receiving operating curve (ROC) analysis was performed to determine sensitivity and specificity of cardiac dynamic ¹⁸F-FDG PET/CT analysis for CS diagnosis taking the JMHW criteria as the gold standard diagnostic test. The inter- and intra-observer reproducibility of NCOV measurement from dynamic ¹⁸F-FDG PET/CT studies were assessed using linear regression and Bland–Altman plots. The intra-observer and inter-observer agreement for visual analysis of static ¹⁸F-FDG PET/CT were estimated using kappa coefficients (0.81–1 almost perfect agreement, 0.61–0.8 substantial agreement, 0.41–0.6 moderate agreement and 0.21–0.4 fair agreement). Statistical analyses were done using JMP. Graphs were carried out using Prism (GraphPad software, San Diego, CA).

Results

Population

Six out of 30 patients (20%) with sarcoidosis had cardiac involvement according to the JMHW criteria (Table 1). Histological evidence of non-caseous granuloma was obtained mainly from biopsy specimens of mediastinal lymph nodes and salivary glands (respectively 18 and 8 patients). Most patients had a pulmonary involvement (20 patients, 67%). Nine of the 30 sarcoidosis patients (all without cardiac involvement of sarcoidosis) were receiving a steroid therapy at the time of the ^{18}F -FDG PET/CT examination. There was no significant difference in age, body mass index, blood glucose level, CRP, serum calcium and ACE between sarcoidosis patients with (CS+) and without cardiac involvement (CS−). A male predominance (20/30, 67%) was observed, and CS+ had more often ECG abnormalities than CS− (100 vs. 33%, $p < 0.001$) and a lower left ventricular ejection fraction (54% [49–60] vs. 65% [60–71], $p = 0.04$). The disease duration was significantly higher in CS− than in CS+ (88.5 ± 32 vs. 41.7 ± 97.2 months, $p = 0.019$).

Dynamic ^{18}F -FDG PET/CT findings

Results of cardiac quantitative analysis of ^{18}F -FDG PET/CT are depicted in Fig. 1. Post-processing of dynamic data was not feasible in 2 patients due to the total absence of myocardial uptake, leading to a software failure. In the remaining 28 patients, the global Ki was similar between CS+ and CS− (0.010 ± 0.010 vs. 0.012 ± 0.011 , $p = \text{ns}$). The SD of the Ki was not significantly different in CS+ and CS− (0.004 ± 0.004 vs. 0.002 ± 0.002 , $p = \text{ns}$). The NCOV values were significantly greater in CS+ compared with CS− (0.513 ± 0.175 vs. 0.205 ± 0.081 ; $p = 0.0007$). Using ROC curve analysis, we found a NCOV cut-off value of 0.38 for the diagnosis of CS, with a sensitivity of 100% and a specificity of 91% (Fig. 2). Areas under the curves from ROC analysis of SD Ki and global Ki were 0.674 and 0.602, respectively. Linear regression and Bland–Altman plots demonstrated a high intra- and inter-observer reproducibility, as shown in Fig. 3.

Static ^{18}F -FDG PET/CT findings

Visual analysis of cardiac ^{18}F -FDG uptake was performed on static whole body ^{18}F -FDG PET/CT in 25 patients. In the remaining 5 patients, the cardiac visual analysis was performed using static data extracting from the dynamic cardiac acquisition (50 min). The inter-observer agreement

Table 1 Patients' characteristics

	All patients <i>n</i> = 30	CS− patients <i>n</i> = 24	CS+ patients <i>n</i> = 6	<i>P</i>
Age, years	55 [39–67]	63 [33–69]	43 [41–50]	0.14
Sex, male	20 (67%)	15 (63%)	5 (83%)	0.64
Extra-cardiac involvement				
Pulmonary	20 (67%)	18 (75%)	2 (33%)	0.02
Ophthalmologic	2 (7%)	2 (8%)	0	
Neurologic	2 (7%)	1 (4%)	1 (17%)	
Rheumatologic	1 (3%)	1 (4%)	0	
Renal	1 (3%)	1 (4%)	0	
Cutaneous	1 (3%)	1 (4%)	0	
None	3 (10%)	0	3 (50%)	
ACE, UI/L	29 [12–55]	29 [12–56]	34 [16–54]	0.56
CRP, mg/dL	3 [3–7]	3 [3–6]	6 [4–7]	0.26
Serum calcium, mmol/L	2.31 [2.25–2.40]	2.32 [2.24–2.40]	2.30 [2.28–2.34]	0.95
ECG				
Normal	16 (53%)	16 (67%)	0	<0.001
Atrioventricular block or paced rhythm	7 (23%)	2 (8%)	5 (83%)	
Bundle branch block	7 (23%)	6 (25%)	1 (17%)	
LVEF, %	62 [58–68]	65 [60–71]	54 [49–60]	0.04

Percentages do not add up to 100% due to rounding

CS+ sarcoidosis patients with cardiac involvement, CS− sarcoidosis patients without cardiac involvement, ACE angiotensin-converting enzyme, CRP C-reactive protein, LVEF left ventricular ejection fraction

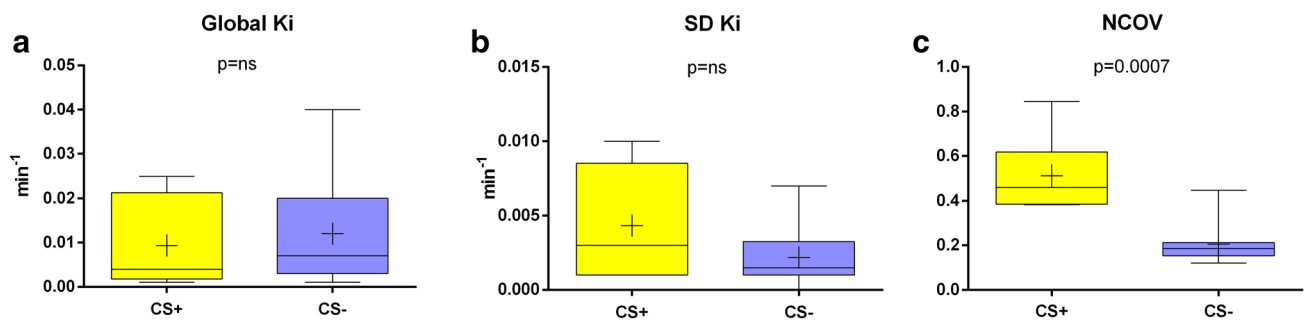


Fig. 1 Quantitative analysis of dynamic ^{18}F -FDG PET/CT. **a** Global K_i **b** $SD K_i$ **c** $NCOV$. Comparisons between groups were done using a Mann–Whitney test. Data are presented as box plots with means represented by the crosses with the 75th percentiles at the top and the 25th percentiles at the bottom of the boxes. Ranges are depicted as

whiskers. CS+ sarcoidosis patients with cardiac involvement according to the JMHW criteria, CS– sarcoidosis patients without cardiac involvement according to the JMHW criteria, K_i net influx constant, $NCOV$ normalized coefficient of variation, SD standard deviation

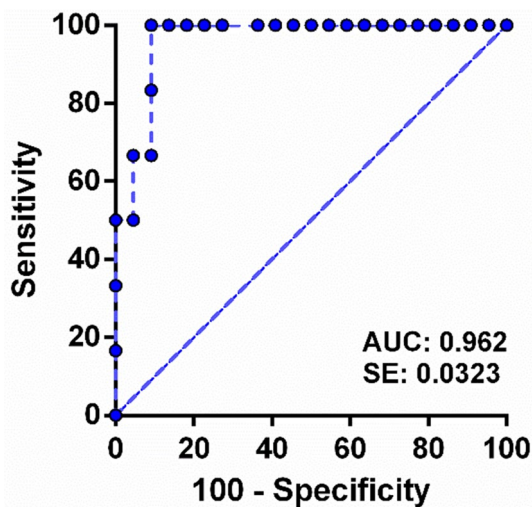


Fig. 2 ROC curves for the differential diagnosis between CS+ and CS–: using the $NCOV$, $p=1$. CS+ sarcoidosis patients with cardiac involvement according to the JMHW criteria, AUC area under the curve, CS– sarcoidosis patients without cardiac involvement according to the JMHW criteria, K_i net influx constant, $NCOV$ normalized coefficient of variation, SE standard error

was fair with a kappa of 0.383 (95% CI 0.022–0.750). The intra-observer agreement was excellent with a 0.833 (95% CI 0.525–1) kappa index. Five CS+ (83%) showed a focal uptake and 1 (17%) showed no cardiac uptake. Among the CS–, 8 (33%) and 4 (17%) showed diffuse or focal uptake patterns respectively, and 12 (50%) showed no cardiac uptake. Both sensitivity and specificity of visual cardiac analysis of the whole body ^{18}F -FDG PET/CT for CS detection were 83%. Four out of the 5 CS+ (80%), and 11/20 CS– (55%) who underwent a whole body ^{18}F -FDG PET/CT showed extra-cardiac ^{18}F -FDG uptake, particularly in mediastinal and hilar lymph nodes.

Other imaging modalities

Using transthoracic echocardiography, mean LVEF was significantly decreased in CS+ compared to CS– (54% [49–60] vs. 65% [60–71], $p=0.04$). All CS+ and 3/18 (17%) CS– exhibited abnormal MPI. The sensitivity and the specificity of MPI for diagnosing CS were 100% and 83%, respectively. Table 2 shows the diagnostic performances of each imaging modalities using the 2006 guidelines for CS from the JMHW as a gold standard.

Discussion

Our study showed that myocardial metabolism assessed by cardiac dynamic ^{18}F -FDG PET/CT was significantly heterogeneous in patients with cardiac sarcoidosis. The quantitative indexes of glucose metabolism heterogeneity were significantly increased in CS+ compared to CS–, yielding to high sensitivity and specificity for the diagnosis of cardiac sarcoidosis.

Patchy uptake on cardiac PET or late gadolinium enhancement on CMR in a pattern consistent with CS are some of the criteria used in the recently published consensus statement of the Heart Rhythm Society for the diagnosis of CS [7]. In the present work we decided not to diagnose CS according to HRS criteria because of its lack of objectiveness as no clear definition of patchy pattern is given. As a consequence, CS was diagnosed according to the JMHW criteria, revised in 2006 [5]. In our study, 20% of sarcoidosis patients had a cardiac involvement according to the JMHW criteria. This was in keeping with previous results showing a prevalence of CS of 20% in European populations [17, 18] and of 38–50% in Japanese studies [11, 19].

Tahara et al. [11] previously reported that a heterogeneous myocardial ^{18}F -FDG uptake based on SUV analysis may

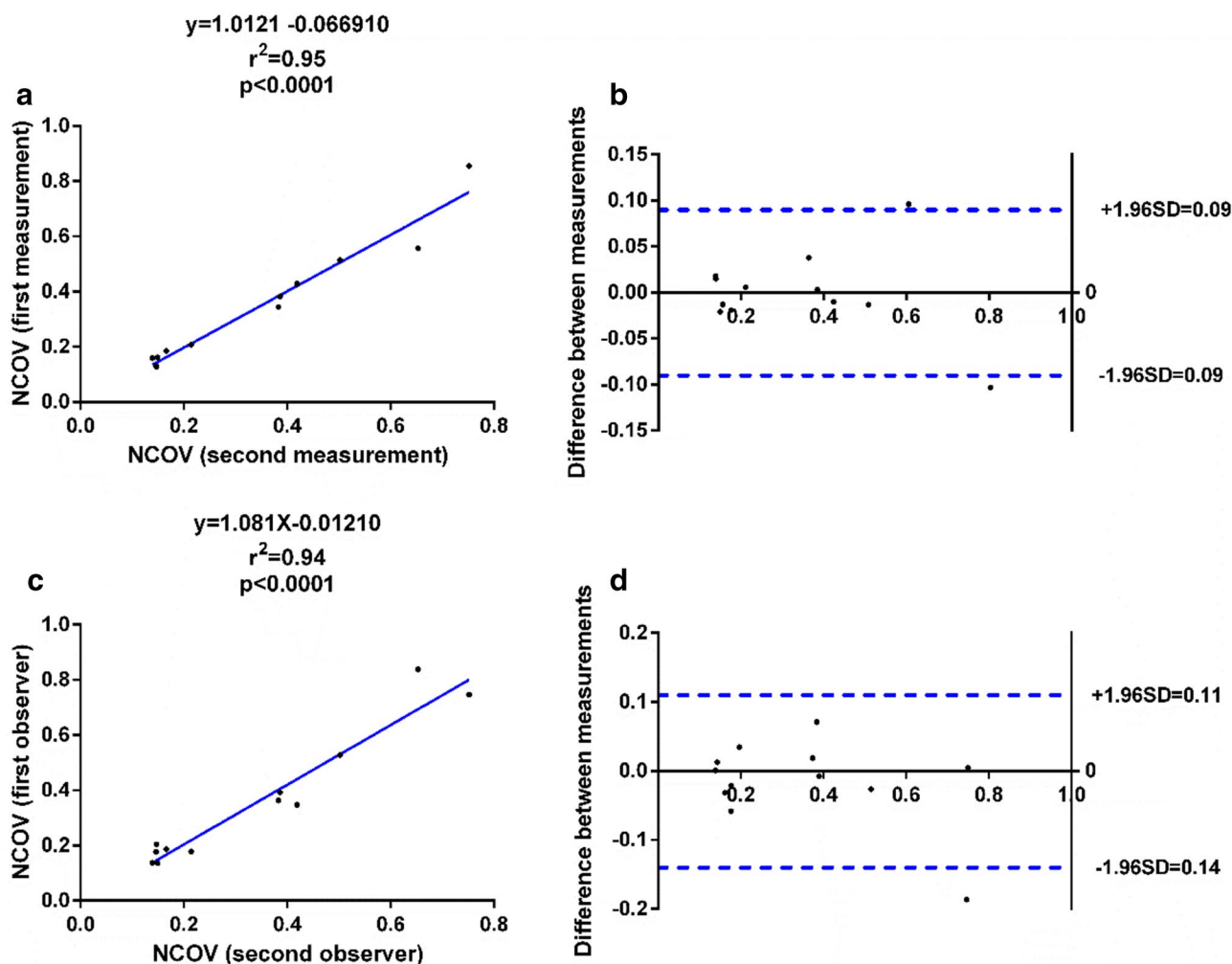


Fig. 3 Linear regression analysis (a) and Bland–Altman plots (b) for intra-observer agreement of NCOV. Linear regression analysis (c) and Bland–Altman plots (d) for inter-observer agreement of NCOV. NCOV normalized coefficient of variation of the net influx constant (Ki)

Table 2 Sensitivity, specificity and predictive values of each imaging modalities based on 2006 guidelines for diagnosis of CS from JMHW

Modality	<i>n</i>	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
Dynamic ¹⁸ F-FDG PET	28	100	91	100	75
Static ¹⁸ F-FDG PET	30	83	83	95	56
MPI	24	100	83	100	67

MPI myocardial perfusion imaging, NPV negative predictive value, PPV positive predictive value

be a useful diagnostic marker of CS. In this latter study, the coefficient of variation was calculated as the ratio of the standard deviation of segmental uptake divided by the mean left ventricular SUV, and was significantly higher in CS+

(0.25 ± 0.05) compared to CS– (0.14 ± 0.03 , $p < 0.01$) and control patients (0.14 ± 0.03 , $p < 0.01$).

The heterogeneity of myocardial glucose metabolism could be explained by two associated mechanisms: a decreased uptake in some heart regions due to myocardial fibrosis, and an increased uptake in other territories due to active granulomatous lesions. We found low NCOV values in CS–, indicating a homogenous uptake of glucose in normal heart. The high NCOV in CS+ appears as a useful marker of active myocardial inflammation to detect CS.

According to the JMHW criteria as a gold standard, we found a sensitivity of 83% with a specificity of 83% using the static ¹⁸F-FDG PET/CT for diagnosing CS. These findings are similar to previous studies reporting a sensitivity of 71–100% and a specificity of 37.5–100% [7, 9, 20]. Youssef et al. reported in a meta-analysis of 7 studies a pooled sensitivity and specificity of static ¹⁸F-FDG PET/CT of 89 and 78% respectively, compared to JMWH criteria [21].

According to MPI, the sensitivity and specificity for diagnosing CS were 100 and 83%, respectively. Previous studies reported a sensitivity of 54–100% and a specificity of 76–100% for perfusion imaging [11, 20, 22].

Quantitative analysis using the NCOV of the net influx constant Ki demonstrated an increased inter-observer reproducibility compared with the visual analysis of static ^{18}F -FDG PET/CT imaging. The main finding of our study is that the diagnostic value of cardiac dynamic ^{18}F -FDG PET/CT for CS using a NCOV cut-off value of 0.38 was better than the qualitative analysis of the cardiac ^{18}F -FDG uptake with a sensitivity and a specificity of 100 and 91% respectively. Based on the evaluation of cardiac SUVs, Tahara et al. [11] reported a comparable diagnostic value of ^{18}F -FDG PET/CT using a cut-off COV value of 0.18 for the diagnosis of CS, with a sensitivity and a specificity of 100 and 97%, respectively.

However, the semi-quantification of ^{18}F -FDG uptake using SUV suffers from some limitations. First, SUV measures the total activity in the myocardium, and includes both metabolized ^{18}F -FDG and any unmetabolized ^{18}F -FDG in the plasma, in the intracellular spaces and in the cell, including unphosphorylated ^{18}F -FDG [23]. Dynamic analysis separates these two components because the Patlak slope is determined only by metabolized ^{18}F -FDG. Secondly, SUV also depends on how long after ^{18}F -FDG injection the static acquisition is performed whereas dynamic analysis avoids this time dependence [24]. Moreover, it is well known that the ^{18}F -FDG uptake depends on blood glucose level but this parameter does not appear in the measurement of the SUV while it may be taken into account when using compartmental analysis. Finally, Patlak analysis uses the sum of all the ^{18}F -FDG available to the heart for normalization, whereas SUV approximates this integral by the injected dose divided by the body weight [25]. Quantitative analysis is time-consuming due to the addition of a 50-min dynamic acquisition, reconstruction (33 frames) and post-processing of dynamic datasets. Nevertheless, Ki derived from cardiac dynamic ^{18}F -FDG PET/CT appear to better represent myocardial glucose metabolism than does SUV.

The myocardium is able to metabolize either free fatty acids (FFA) or glucose as a substrate for metabolic energy [26]. Under fasting state, the majority of myocardial energy is obtained from oxidation of the FFA, and therefore the ^{18}F -FDG uptake is expected to be low. The performance of ^{18}F -FDG PET/CT sarcoidosis studies is closely linked to the adherence to diet which includes many prohibited foods and could lead to an improper adherence. According to our department procedures, patient's observance was insured by written and oral (phone call) instructions given to patients prior to the examination.

Additionally to the cardiac dynamic acquisition, 25 sarcoidosis patients underwent a whole body ^{18}F -FDG PET/CT

which may provide evidence of sarcoidosis and guide sites for biopsy in detecting ^{18}F -FDG uptake within mediastinal or hilar lymph nodes [15]. Figure 4 shows an example of a CS+ patient referred for a second degree atrioventricular block. Both cardiac dynamic and whole body ^{18}F -FDG PET/CT acquisitions were helpful to diagnose CS and extracardiac sarcoidosis. Additionally, ^{18}F -FDG PET/CT has the advantage of being able to image patients with implanted pacemakers or defibrillators and those with impaired renal function and might also be useful in determining the requirement for device treatment.

Limitations

We did not use the prolonged fasting [10] nor the unfractiooned heparin [20] to suppress the physiological myocardial ^{18}F -FDG uptake. Few patients received a steroid therapy at the time of examination, a situation that may affect the

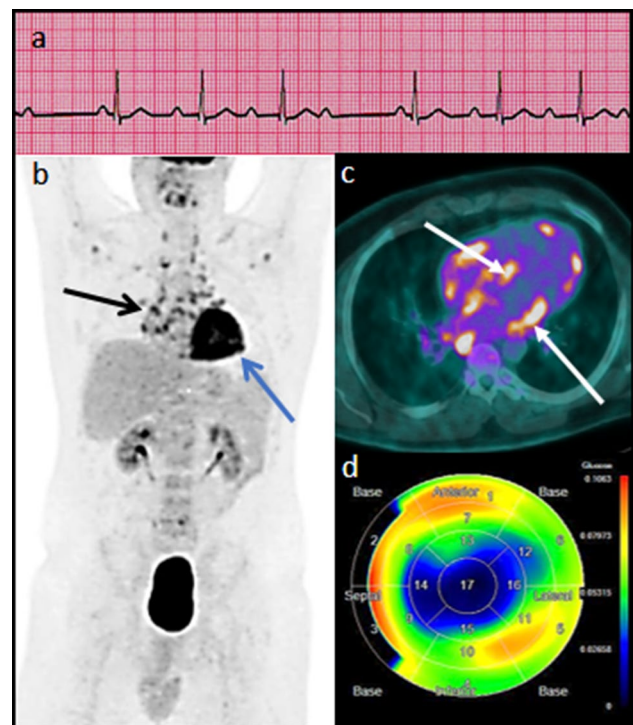


Fig. 4 Representative findings of a patient with a cardiac sarcoidosis referred for an advanced atrioventricular block. The diagnosis of sarcoidosis was biopsy-proven and an implantable cardioverter defibrillator was placed to prevent sudden death. **a** ECG showing a second degree atrioventricular block. **b** ^{18}F -FDG PET maximum intensity projection image: increased accumulation of ^{18}F -FDG is shown in the heart (blue arrow) and in several mediastinal lymph nodes (black arrow). **c** Fusion ^{18}F -FDG PET/CT axial view at cardiac level depicted focal accumulation of ^{18}F -FDG in inter-ventricular septal and lateral walls at basal level (white arrows). **d** Polar map display of the 17 LV segments assessed by cardiac dynamic ^{18}F -FDG PET/CT showed heterogeneity of the Ki with a NCOV = 0.542

sensitivity of ^{18}F -FDG PET/CT to detect CS. However, no CS+ was treated by steroid at the time of the examination.

In this study, we used the 2006 JMWH criteria for the diagnosis of CS. The use of the Japanese criteria is justified because the diagnostic yield of endomyocardial biopsy is low and has a relatively high invasiveness and complication rates [3]. Some authors have speculated that these criteria might lead to an underestimation of cardiac involvement in patients with sarcoidosis [27]. ^{18}F -FDG PET may depict early-stage sarcoidosis lesions in the heart even in patients who do not meet the diagnostic criteria. Additionally, ventricular tachycardia, which is the second clinical manifestation (23%) of CS [28], is not considered as a major criteria in the 2006 JMWH guidelines and therefore lead to a case considered as a false positive in the NCOV ROC analysis in our study.

Conclusion

In this study, heterogeneous myocardial glucose metabolism assessed using a normalized coefficient of variation (NCOV) of the net influx constant K_i derived from cardiac dynamic ^{18}F -FDG PET/CT was a highly suggestive feature of CS. Our results suggest that quantitative analysis of cardiac dynamic ^{18}F -FDG PET/CT after a HFLC diet could be a useful tool for the diagnosis of cardiac involvement in patients with sarcoidosis.

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