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Assessment of Cardiac Sarcoidosis with PET/CT

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^{18}F-FDG PET with CT is an important advanced imaging modality used to assess patients with suspected or known cardiac sarcoidosis (CS). ^{18}F-FDG PET is indicated for CS work-up in patients with extra-CS and abnormal screening results for cardiac involvement, patients under 60 y old presenting with unexplained high-grade atrioventricular heart block, and patients with suspected CS and idiopathic ventricular arrhythmias. In patients with established CS, serial ^{18}F-FDG PET can be used to assess response to immunosuppressive therapy and long-term surveillance for reactivation of myocardial inflammation in patients with low-grade or quiescent disease. Patient preparation before ^{18}F-FDG PET scanning is key in ensuring adequate suppression of physiologic myocardial ^{18}F-FDG uptake, to maximize the power of the test to detect pathology. Inadequate dietary preparation can cause diffuse or focal-on-diffuse ^{18}F-FDG uptake in the absence of active inflammation. It is important to assess resting myocardial perfusion, typically with ^{82}Rb cardiac PET. Several different patterns of abnormalities have been reported in patients with CS, including normal myocardial perfusion with focal or patchy ^{18}F-FDG uptake suggesting myocardial inflammation without scarring; the presence of a myocardial perfusion defect with abnormal ^{18}F-FDG uptake suggesting myocardial scarring with inflammation; and the presence of a myocardial perfusion defect without ^{18}F-FDG uptake indicating myocardial scarring without inflammation. Prognostically, the presence of myocardial perfusion defects and abnormal ^{18}F-FDG uptake has been shown to be an independent predictor of death or ventricular arrythmias. A high myocardial SUV_{max} in the left and right ventricles has been shown to be an independent predictor of adverse clinical outcomes. Although the diagnostic performance of ^{18}F-FDG PET has been studied, the reference standard for CS tended to rely on clinical criteria, which may be less sensitive than ^{18}F-FDG PET at detecting CS. Therefore, the diagnosis of CS should rely on a multidisciplinary team approach involving multimodality advanced imaging, including echocardiography, cardiovascular MR, and ^{18}F-FDG PET.

Key Words: cardiology; PET/CT; cardiac; FDG; PET; sarcoidosis

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Sarcoidosis is a multisystem disease characterized by the finding of nonnecrotizing granulomas in affected tissues (*1*). The prevalence of cardiac involvement in sarcoidosis patients depends on the mode of detection, being less than 10% based on clinical presentation (*2*), 20%–50% based on autopsy studies (*3*,*4*), and around 25% based on noninvasive cardiac imaging such as cardiovascular MR (CMR) (*5*). The presence of cardiac sarcoidosis (CS), particularly as the first manifestation of sarcoidosis, portends a significantly greater mortality risk than in patients without CS (*1*,*6*).

CS can affect any part of the heart but most frequently involves the myocardium (*7*). The basal left ventricular (LV) septum, the LV lateral wall, and the papillary muscles are common sites of cardiac involvement in sarcoidosis (*8*). The right ventricular free wall, although less commonly involved than the LV, can also be affected by CS (*7*,*8*). Involvement of the atria has been reported (*9*), as has been pericardial disease (*10*). Pericoronary infiltration has also been described, which may be a separate pathology from intraluminal atherosclerosis (*11*).

The granulomatous inflammation heals, with fibrosis causing scarring of the cardiac muscle, leading to LV systolic dysfunction. In CS patients, LV systolic dysfunction is an independent predictor of adverse clinical outcomes (*12*,*13*). CS patients with severe LV systolic dysfunction (ejection fraction $<$ 30%) have a 10-y survival rate of around 19%, which is nearly 4 times worse than for CS patients with a preserved LV ejection fraction (LVEF) ($>$50%) (*14*). Elevated B-type natriuretic peptide levels and active myocardial inflammation have recently been shown to be independent predictors of adverse clinical outcomes in a large contemporary cohort of 319 CS patients (*6*). Development of sustained ventricular tachycardia (VT) is also associated with a worse clinical outcome (*13*).

CS is associated with several potentially serious complications such as advanced heart failure, high-grade atrioventricular heart block, and ventricular arrythmias (*1*). Making a timely diagnosis of this condition is key to ensuring that patients are appropriately counseled and that treatment can be instigated (*1*). Although clinical guidelines recognize the

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endomyocardial biopsy finding of nonnecrotizing granulomas as a mode of diagnosis for CS, endomyocardial biopsy has a low sensitivity (≤25%) for the diagnosis of CS (*15*). This is likely due to the patchy nature of the CS disease or the localization of disease in the LV mid wall (*2*).

In clinical practice, CS should be diagnosed by a multidisciplinary team consisting of cardiologists and respiratory physicians with experience in managing CS patients, as well as nuclear medicine physicians and other specialist imaging experts to assess multimodality cardiac imaging modalities (*1*). These include echocardiography, CMR, and ^{18}F-FDG PET (*1*,*13*). The multidisciplinary team approach is also important in ensuring that every aspect of management (e.g., heart failure, arrhythmias, and immunosuppression) can be adequately addressed for each patient (*1*). The multidisciplinary team represents an important forum for the discussion and management of challenging cases to decide on the optimal therapeutic and follow-up strategies (*1*).

^{18}F-FDG PET is an important advanced imaging modality in the diagnosis and management of CS patients (*1*,*2*,*13*). It enables assessment of the severity and distribution of inflammation for both CS and extra-CS. ^{18}F-FDG PET also plays a major role in the assessment of treatment response with immunosuppressive therapy as well as ongoing surveillance of CS patients with quiescent disease. In this review, we discuss the use of ^{18}F-FDG PET/CT for the assessment of CS patients.

^{18}F-FDG AS SURROGATE FOR INFLAMMATION

Early in vivo experiments showed that ^{18}F-FDG–labeled white blood cells could track the site of inflammation in rats inoculated with a bacterial load (*16*). Contemporary ^{18}F-FDG PET/CT imaging relies on the uptake of ^{18}F-FDG in regions rich in macrophages to localize inflammation, since macrophages require a high level of exogenous glucose to fuel their metabolic activity (*17*).

INDICATIONS FOR ^{18}F-FDG PET IN CS

The joint Society of Nuclear Medicine and Molecular Imaging and American Society of Nuclear Cardiology consensus statement presented several indications for the use of ^{18}F-FDG PET to assess patients with suspected or known CS (*2*). Although ^{18}F-FDG PET alone cannot be diagnostic for CS, it forms an important part of assessment for myocardial inflammation and for extra-CS distribution and severity (*2*). Therefore, the indications for ^{18}F-FDG PET can be broadly divided into diagnostic work-up for patients with suspected CS and monitoring of disease activity levels for patients with an established CS diagnosis (*2*).

Use of ^{18}F-FDG PET/CT in Workup for Suspected CS

In patients with a histologic diagnosis of extra-CS and abnormal results on screening tests for CS, the use of ^{18}F-FDG PET/CT is indicated for the work-up of myocardial involvement (*2*). Abnormal screening results for CS include complete left or right bundle branch block or unexplained pathologic Q waves in 2 or more leads on a 12-lead electrocardiogram; a finding of regional wall motion abnormality, LV aneurysm, basal LV septal thinning, or LV systolic dysfunction (LVEF < 50%); sustained or nonsustained VT on Holter monitoring; features consistent with CS on CMR; or unexplained palpitations or syncope.

In patients younger than 60 y and presenting with an unexplained new onset of high-grade atrioventricular block (second- or third-degree), ^{18}F-FDG PET is indicated as part of the work-up for suspected CS (*2*).

^{18}F-FDG PET is also indicated as part of the work-up for suspected CS in patients with idiopathic sustained VT, excluding typical outflow tract VT, fascicular VT, or VT secondary to other structural heart disease (*2*).

Table 1 summarizes the indications of ^{18}F-FDG PET/CT in patients with suspected CS.

TABLE 1
Indications for ^{18}F-FDG PET/CT in Patients with Suspected CS

Indication	Specifics
Histologic diagnosis of extra-CS and abnormal screening tests for CS	ECG: complete left or right BBB or unexplained pathologic Q waves in ≥2 leads
	Echo: RWMA, LV aneurysm, basal LV septal thinning, or LV systolic dysfunction (LVEF < 50%)
	CMR: features consistent with CS
	Holter monitoring: sustained or nonsustained VT
	Unexplained palpitations or syncope
Younger than 60 y and presenting with unexplained new-onset high-grade AV block (second- or third-degree)	
Suspected CS with idiopathic sustained VT, excluding typical outflow tract VT, fascicular VT, or VT secondary to other structural heart disease	

ECG = electrocardiogram; BBB = bundle branch block; echo = echocardiography; RWMA = regional wall motion abnormalities; AV = atrioventricular.

Use of ^{18}F-FDG PET in Established CS

In patients with an established CS diagnosis, ^{18}F-FDG PET serves 2 main indications. First, in patients with evidence of myocardial inflammation, serial ^{18}F-FDG PET can be used to assess response to immunosuppressive therapy. Second, in patients with quiescent CS without significant myocardial inflammation, cardiac ^{18}F-FDG PET can be useful in ongoing surveillance for resurgence of active disease.

PREPARATION FOR CARDIAC ^{18}F-FDG PET

There are 2 main considerations before a patient can undergo ^{18}F-FDG PET/CT. First, it is important to rule out significant coronary artery disease since myocardial ischemia or infarction can lead to abnormal myocardial perfusion and ^{18}F-FDG uptake, which confound the presence of myocardial inflammation. It is difficult to distinguish between CS-related myocardial inflammation and myocardial infarction due to significant coronary artery disease on rest and stress perfusion imaging with ^{82}Rb cardiac PET/CT. If the patient has significant risk factors for coronary disease, coronary angiography (with CT or invasive) should be considered since an ^{18}F-FDG PET scan cannot differentiate between inflamed and ischemic myocardium. Myocardial infarction may also be detected using late gadolinium enhancement imaging by CMR, appearing as late gadolinium enhancement with a subendocardial pattern. However, in certain cases, CS can also mimic the late gadolinium enhancement pattern of myocardial infarction on CMR.

The second consideration before undertaking ^{18}F-FDG PET is the suppression of physiologic glucose uptake in the heart. The myocardium uses both fatty acids and glucose as metabolic fuel under the resting state, which makes the detection of myocardial inflammation using ^{18}F-FDG PET challenging. By implementing several patient preparation methods, the physiologic glucose uptake can be suppressed to optimize the sensitivity of ^{18}F-FDG uptake localization to detect myocardial inflammation.

There are 3 main patient preparation methods to suppress physiologic glucose uptake before an ^{18}F-FDG PET/CT scan. These include dietary preparations, prolonged fasting, and the use of intravenous heparin. These methods are usually used in combination to achieve the optimal results.

Dietary Preparation

A diet high in fat and low in carbohydrates is commonly administered before ^{18}F-FDG PET. The principle is to switch the substrate of cardiac metabolism from glucose to fatty acids and thus suppress the background physiologic myocardial glucose uptake. Several studies have shown that dietary preparation is more effective than fasting for reducing the myocardial SUV_{max} and suppressing physiologic ^{18}F-FDG uptake in the heart (*18*,*19*). However, there is currently no established consensus on the duration of dietary preparation or the constituents of the diet (*2*). Despite dietary preparations, physiologic glucose uptake with unclear etiologies may still be observed on ^{18}F-FDG PET/CT in a small proportion of patients (*20*). In our institution, we advise at least 2 meals with no carbohydrates before the scan appointment.

Prolonged Fasting

During prolonged fasting, the human body uses more fatty acid as fuel; therefore, prolonged fasting—18 h or greater—can suppress physiologic ^{18}F-FDG uptake in the heart (*20*). In practice, prolonged fasting is used after dietary preparation for minimizing physiologic ^{18}F-FDG uptake (*2*).

Intravenous Heparin

Intravenous administration of unfractionated heparin has been shown to increase fatty acid levels in the blood (*21*). Its use has been reported as an adjunct to dietary preparations and fasting before ^{18}F-FDG PET/CT scanning (*22*). It remains unclear whether intravenous heparin suppresses myocardial glucose suppression (*2*). The most common reported heparin-based protocol involves a 50 IU/kg intravenous bolus of unfractionated heparin administered about 15 min before ^{18}F-FDG (*2*).

Combined Approach

The existing literature has shown that the combination of dietary preparation and prolonged fasting has been effective in suppressing physiologic ^{18}F-FDG uptake before scanning (*20*). The joint Society of Nuclear Medicine and Molecular Imaging and American Society of Nuclear Cardiology consensus statement recommends at least 2 meals high in fat ($>$35 g) and low in carbohydrates ($<$3 g) on the day before the scan, followed by more than 12 h of fasting (*2*).

In our center, we use a similar protocol of 24 h of high-fat and no-carbohydrate dietary preparation followed by 18 h of fasting to ensure an adequate switch from glucose to fatty acid metabolism. The patient must receive robust instructions for the prescan preparation, and before beginning the scan the scan operator must confirm that the patient has adhered to the preparation.

Patients with insulin-dependent diabetes or prone to significant fluctuations in blood sugar must be carefully prepared. Type 1 diabetic patients should continue on their basal insulin regimen and minimize the use of rapid-acting insulin if tolerated and safe to do so (*2*). Some patients may require insulin per a sliding scale on the day before the scan, which should stop on the day of the scan (*2*). Type 2 diabetic patients should avoid antidiabetic medication once they start the fasting phase leading up to the scan. Type 1 diabetic patients need an individualized approach since standardized data are limited (*2*). They are put on sliding-scale rapid-acting insulin a day before the study in an inpatient setting and are offered a morning appointment.

Regular monitoring of blood sugar is advised in all diabetic patients undergoing preparation before ^{18}F-FDG PET. If clinically indicated, dietary preparation and fasting should take place on an inpatient basis. In patients who are already hospitalized and undergoing other medical therapy unrelated to ^{18}F-FDG PET scanning, adherence to dietary preparations may be challenging, since carbohydrates tend

to be present in a wide range of intravenous fluids and medications administered to the patient (*2*). In these cases, strict adherence to dietary preparations and fasting tends to be challenging. We do not routinely use intravenous heparin in our center for patient preparation.

Need for Perfusion Imaging

Myocardial perfusion imaging with ^{82}Rb or ^{13}N-ammonia provides information about the status of myocardial viability, inflammation, or scarring depending on the stage of sarcoidosis in the myocardium. Since CS is an intermittently remittent disease, perfusion imaging helps to identify perfusion defects and scarring and stage the disease. ^{18}F-FDG PET can show inflammatory activity at any given point, but it cannot assess whether the disease has been present long enough to have caused myocardial scarring or microvascular compression leading to perfusion defects. The relationship of perfusion on ^{82}Rb to inflammation on ^{18}F-FDG PET is important for diagnosis, staging, and determination of prognosis and management. Moreover, it gives information about LV function.

IMAGE ACQUISITION

Two sets of images are taken during the PET/CT scan: myocardial perfusion using either ^{13}N-ammonia or ^{82}Rb (which is our preferred tracer) and ^{18}F-FDG for cardiac and half-body coverage (*2*).

For the first set of images, patients are positioned on the scanner with a cannula in situ and arms raised above the head. A 3-lead electrocardiogram is connected because gated perfusion imaging is recommended, which enables the assessment of LV systolic function (*2*). A topogram for localization is performed, shortly followed by a low-dose CT image for attenuation correction. Before the acquisition of the PET images, the injection of ^{82}Rb chloride is given as an infusion with 1,110 MBq (1,221 MBq if the patient's weight is >100 kg), with simultaneous dynamic acquisition of the PET images for 7 min.

After perfusion images are acquired, intravenous ^{18}F-FDG is injected with an activity of 3.5 MBq/kg (up to a maximum of 280 MBq ± 10%) (*2*). This is followed by an uptake period of 75 min and image acquisition (*2*). In our center, the ^{18}F-FDG images are acquired from eyes to thighs, to enable the assessment of both CS and extra-CS disease. As before, a topogram and CT are performed before the PET acquisition; altogether the imaging takes 20–25 min. To provide a cardiac assessment with more diagnostic accuracy, a longer acquisition of the heart is performed. This can be achieved by acquiring an additional image of the heart at the end of the half-body scan or by slowing the scanner speed in the region of heart during half-body acquisition.

SCAN REPORTING

Clinical reporting of each ^{18}F-FDG PET/CT scan requires several steps. These include reviewing the indication and medical records, checking the details of the prescan patient preparation, reconstructing and coregistering the images, assessing image quality, and interpreting the images (*2*). Detailed accounts of each aspect are beyond the scope of this review, which seeks to provide the reader with an overview of the reporting process.

After the clinical indication, dietary preparation, and fasting information have been reviewed, the resting perfusion and ^{18}F-FDG images are reconstructed with application of attenuation correction (*2*). The images are displayed in 3 common cardiac planes, namely the horizontal long axis (4-chamber view), vertical long axis (2-chamber view), and short axis (*2*). The transmission and emission data are coregistered with care to avoid misregistration and false-positive perfusion defects (*2*). The ^{18}F-FDG images are assessed for the adequacy of physiologic myocardial uptake suppression. During image interpretation, the perfusion and ^{18}F-FDG images are compared side by side. Several different ^{18}F-FDG patterns can be observed during interpretation.

In our center, we routinely report SUV_{max} for sites with pathologic ^{18}F-FDG uptake detected by visual analysis. This enables an objective assessment of the severity of disease activity to help guide clinical management of immunosuppressive therapies and offers a more quantitative comparison of disease activity in serial scans over time. The availability of SUV_{max} also offers a more objective assessment of therapeutic response.

Healthy Subjects

In healthy subjects, it is expected that myocardial perfusion is normal and homogeneous (*2*). In the case of adequate suppression of physiologic ^{18}F-FDG uptake in the heart, the ^{18}F-FDG images will demonstrate no myocardial activity (*2*,*22*). In the case of inadequate suppression, there may be diffuse myocardial ^{18}F-FDG activity (*22*,*23*). Inadequate suppression relates to inadequate patient preparation; some patients who seemingly have adhered to the preparation process can also show inadequate suppression, probably because of hidden carbohydrates in many foods they consumed in the past 24 h (Fig. 1) (*2*,*22*).

Pathologic ^{18}F-FDG Uptake

Patterns of perfusion abnormality and inflammation vary depending on the disease stage at presentation. Myocardial inflammation can manifest as patchy ^{18}F-FDG uptake on an adequately or fully suppressed background with normal myocardial perfusion (*22*). This may indicate the presence of early CS, before the formation of myocardial scarring (*22*). The location and pattern of ^{18}F-FDG uptake (in the presence of normal perfusion) is also important, since focal uptake in the lateral wall may be nonspecific or even a normal variant (*2*,*22*) whereas multifocal ^{18}F-FDG is more likely to suggest CS-related pathology (*2*).

Another pathologic pattern observed in CS is the presence of focal ^{18}F-FDG uptake on a background of diffuse uptake (*2*). This focal-on-diffuse ^{18}F-FDG uptake pattern may be distinguished from inadequate patient preparation

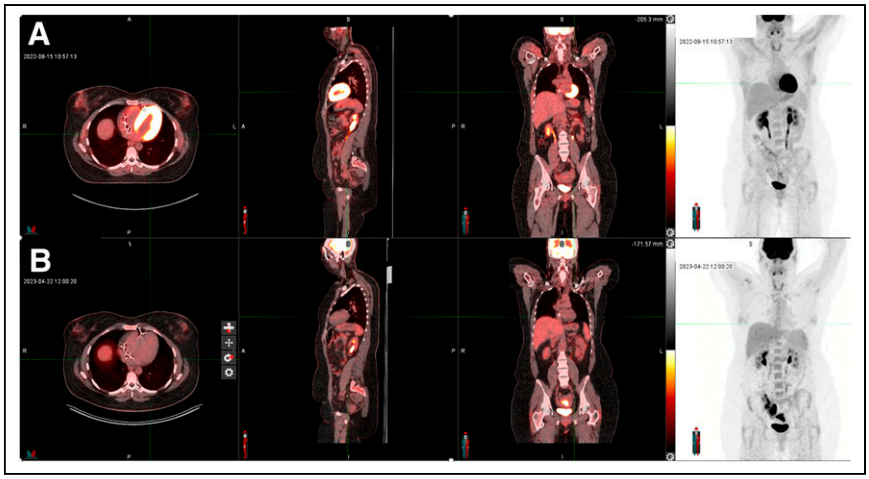

FIGURE 1. ^{18}F-FDG PET/CT images in transaxial, sagittal, and coronal planes and maximum-intensity projection images. (A) Intense ^{18}F-FDG uptake in LV myocardium due to inadequate preparation. (B) No uptake in myocardium in same patient after appropriate preparation.

by the presence of myocardial perfusion defects, often in territories corresponding to the areas of focal ^{18}F-FDG uptake (*2*,*22*). This is known as a perfusion–^{18}F-FDG mismatch pattern, whereby the perfusion defect could be due to microvascular dysfunction related to inflammation rather than to scarring (Fig. 2) (*2*,*22*).

Formation of myocardial scars in CS leads to perfusion defects in the areas of the scars (*2*,*22*). In the presence of scars, it is important to discern the relative location of the myocardial perfusion defect and ^{18}F-FDG uptake. For instance, in the case of concurrent myocardial scarring and myocardial inflammation, focal myocardial ^{18}F-FDG uptake may be present in an area different from that of the myocardial perfusion defect (*2*,*22*). Alternatively, there may be perfusion defects without any focal myocardial ^{18}F-FDG uptake, suggesting the presence of myocardial scarring but without any active inflammation (Fig. 3).

The presence of myocardial ^{18}F-FDG uptake alone does not necessarily indicate CS or CS-related disease activity (*2*). Ischemic heart disease patients may have reduced myocardial perfusion but with ^{18}F-FDG uptake in stunned or hibernating myocardium, suggesting that the myocardium is ischemic but viable (*24*). Patients with inflammatory cardiac conditions or myocarditis may also have ^{18}F-FDG uptake either in the presence or absence of perfusion defects (*25*). The absence of myocardial ^{18}F-FDG uptake does not rule out a diagnosis of CS, since the disease may simply be inactive or there has been myocardial scar formation without active inflammation (*2*).

The presence of myocardial perfusion defects in the absence of ^{18}F-FDG uptake may indicate scarring due to CS or other pathologies; hence, this is a nonspecific finding that should be interpreted within the wider clinical context of the history, biopsy result, and other cardiac imaging (*1*,*2*). These observations further emphasize that the diagnosis of CS should be based on a multidisciplinary team approach with review of the clinical picture as well as multimodality cardiac imaging (*1*).

Extra-CS

The assessment of ^{18}F-FDG uptake in extracardiac organs can enable the identification of potential sites for biopsy to offer a histologic confirmation of extra-CS (*1*). The assessment of ^{18}F-FDG uptake, along with CT imaging, can also indicate the likelihood of a radiologic diagnosis of extra-CS (*1*,*2*,*13*). The lungs, lymph nodes, liver, spleen, and skeleton are some of the common sites affected by sarcoidosis. Since the PET/CT imaging field of view ranges from eyes to thighs, it is not uncommon to also find ^{18}F-FDG uptake constituting incidental findings (*26*,*27*). For instance, ^{18}F-FDG uptake in the large intestine

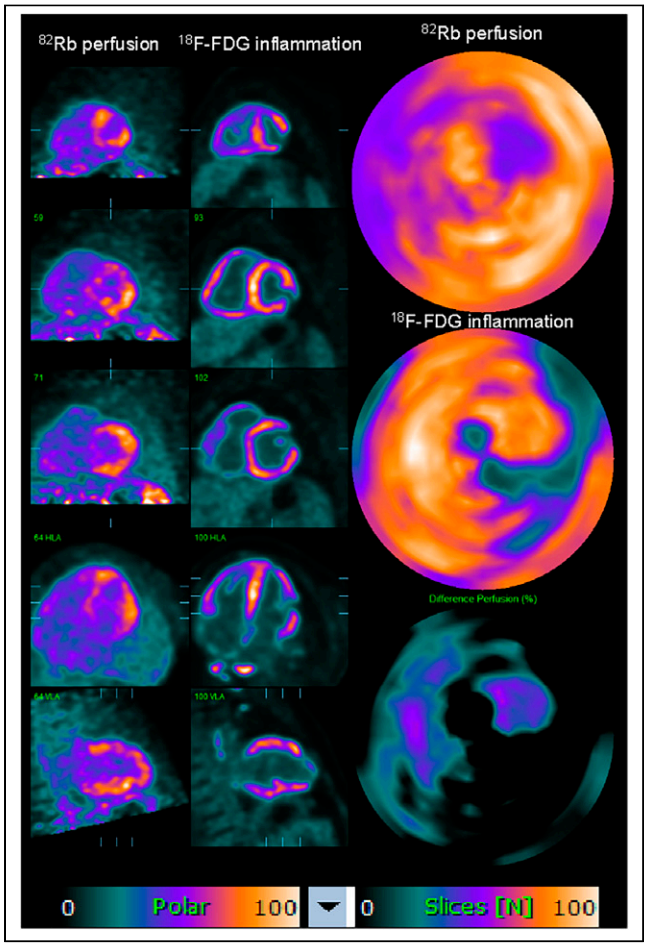

FIGURE 2. Column with resting ^{82}Rb perfusion images shows patchy perfusion in septum and in part of anterior and apical anterolateral walls. Column with ^{18}F-FDG images shows active inflammation in septum, anterior wall, and apical anterolateral wall indicative of perfusion and metabolism mismatch. Additional active inflammation demonstrated in right ventricle and papillary muscles is suggestive of biventricular involvement. Polar plots show mismatch between areas of perfusion and inflammation defects.

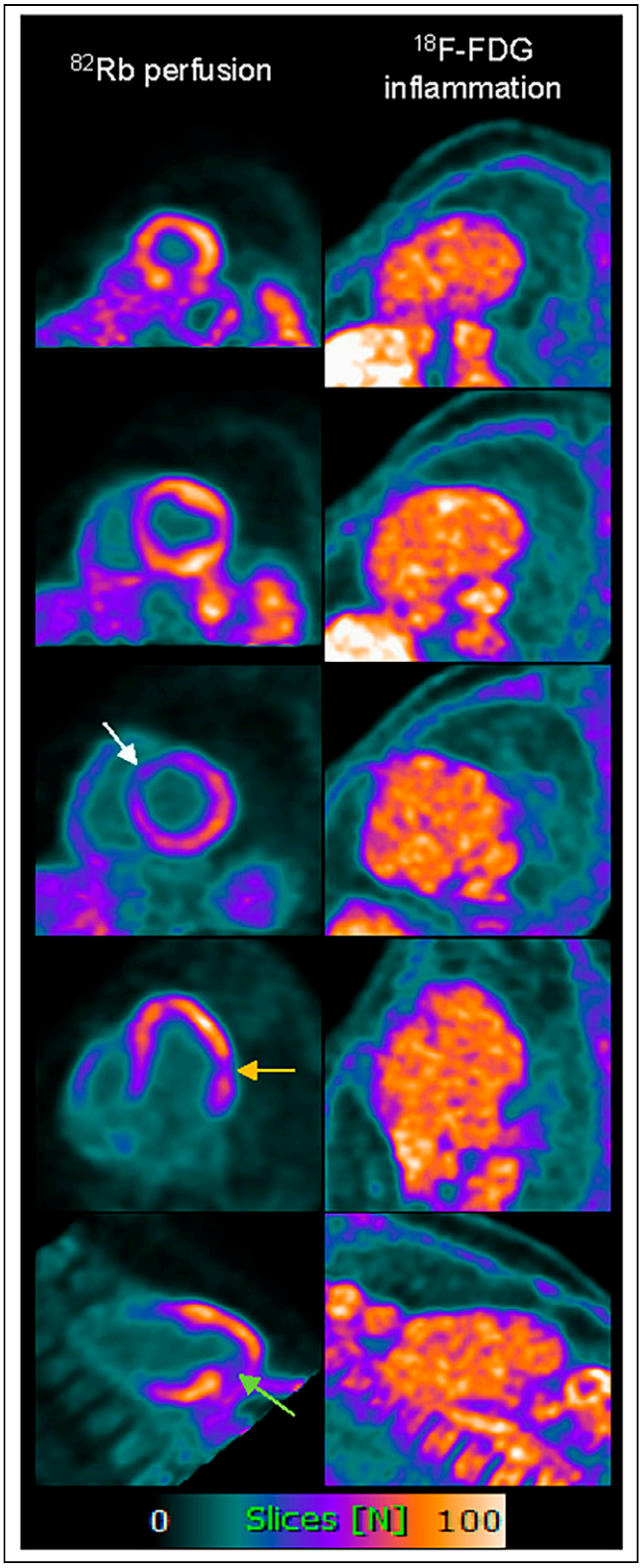

FIGURE 3. Column with ^{82}Rb perfusion images shows areas of patchy myocardial scarring in basal anteroseptum (white arrow), mid to basal lateral wall (yellow arrow), and apical inferior wall (green arrow). Column with ^{18}F-FDG shows no inflammation in myocardium but only blood-pool activity. These findings suggest that disease has left some scarring but inflammation has died out in patient with CS.

may represent inflammatory bowel disease or malignancy that warrants urgent further investigation (*26–29*).

DIAGNOSTIC VALUE OF ^{18}F-FDG PET/CT IN CS

^{18}F-FDG PET/CT should not be used in isolation to diagnose CS; the diagnosis should be based on a multidisciplinary team approach after review of the clinical information and multimodality advanced cardiac imaging data (*1*,*13*). Studies that have assessed the diagnostic performance of ^{18}F-FDG PET/CT have mostly used the Japanese Ministry of Health and Welfare criteria as the reference standard for CS diagnosis (*2*,*30*). A metaanalysis showed a pooled sensitivity of 89% and specificity of 78% for detecting clinical criteria for defining CS (*30*). The diagnostic performance values may be skewed if ^{18}F-FDG PET/CT is more sensitive than clinical criteria for detecting CS (*2*).

PROGNOSTIC VALUE OF ^{18}F-FDG PET/CT IN CS

Several retrospective studies have shown the prognostic value of abnormalities on ^{18}F-FDG PET/CT in CS patients (*31–34*). In 118 patients who had suspected CS but no significant coronary artery disease and were referred for ^{18}F-FDG PET/CT, the presence of a myocardial perfusion defect and abnormal ^{18}F-FDG uptake was associated with a hazard ratio of 3.9 for predicting composite adverse events of death or VT (*31*). This abnormal cardiac PET finding remained an independent predictor of adverse events after adjusting for LVEF and clinical criteria (*31*). The presence of focal right ventricular ^{18}F-FDG uptake was also an independent predictor for the development of composite adverse events (after correcting for LVEF and clinical criteria) (*31*).

In 197 patients who had suspected CS, were not on immunosuppressive therapy, and underwent ^{18}F-FDG PET/CT, the summed rest score in the myocardial segments with abnormal ^{18}F-FDG uptake—that is, perfusion–metabolism mismatch—was an independent predictor of a composite of death, ventricular arrhythmia, or both (*34*). However, quantitative and qualitative measurements of ^{18}F-FDG uptake were not predictors of adverse events (*34*). Furthermore, neither atrial ^{18}F-FDG uptake nor right ventricular ^{18}F-FDG uptake was a significant predictor of prognosis in this patient cohort (*34*). One limitation of these studies was that only a small percentage of patients actually had a diagnosis of CS based on international guideline criteria (either by the Heart Rhythm Society or the Japanese Ministry of Health and Welfare criteria) (*31*,*34*,*35*).

In a recently published study of 319 patients with a highly confident diagnosis of CS by the multidisciplinary team approach, the SUV_{max} on ^{18}F-FDG PET was an independent predictor of composite adverse outcomes (*6*). The adverse outcome was defined as a composite of all-cause mortality, aborted sudden cardiac death, major ventricular arrhythmic events, heart failure hospitalization, and heart transplantation (*6*). Other independent predictors of

outcomes were B-type natriuretic peptide and LVEF measured by CMR (*6*).

In our cohort of 113 newly diagnosed CS patients, active myocardial inflammation was treated with immunosuppression, and then the patients underwent repeat ^{18}F-FDG PET, ^{82}Rb, and echocardiographic imaging 6–12 mo later. Serial changes in SUV_{max}, SUV_{mean}, inflammatory extent, perfusion defect extent, metabolism–perfusion mismatch extent, global cardiac metabolic activity, and LV ejection fraction were assessed. The primary endpoint was a composite of all-cause mortality, serious ventricular arrythmias, and heart failure hospitalization. The risk of adverse events was greatest in those with a pretreatment or posttreatment perfusion deficit extent of more than 10% (*36*).

CONCLUSION

^{18}F-FDG PET/CT is an important imaging modality in the work-up for patients with suspected CS and the assessment of patients with established CS. However, patient preparation is the key to achieving meaningful results. Several features on ^{18}F-FDG PET/CT have prognostic value in CS patients and play an important role in diagnosis, in prognosis, and—importantly—in guiding patient management.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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