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Assessment of Myocarditis: Cardiac MR, PET/CT, or PET/MR?

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Abstract

Purpose of Review Diagnosis of myocarditis is challenging given its variable clinical manifestations and non-specific laboratory findings. Cardiac magnetic resonance (MR) is currently the preferred imaging modality for the diagnosis of myocarditis. ^{18}F-fluoro-deoxy-glucose (FDG) positron emission tomography/computed tomography (PET/CT), as a functional imaging tool, has a potential role in the assessment of myocarditis by detecting the underlying myocardial inflammatory activity. Data are accumulating that simultaneous cardiac PET/MR may have complementary and incremental values for the evaluation of myocarditis compared to PET/CT or cardiac MR alone. The article aims to summarize the findings in the literature and discuss future directions of cardiac PET/MR for myocarditis.

Recent Findings The Lake Louis Criteria (CLL) of cardiac MR is widely used for the diagnosis of myocarditis. It has an overall acceptable sensitivity of 67% and specificity of 91% for acute myocarditis but does not have the same accuracy for chronic myocarditis. FDG PET/CT is capable of assessing myocarditis by providing metabolic information of inflammation as increased myocardial FDG uptake. In addition to reduced radiation exposure, FDG PET performed on a hybrid PET/MR may detect more myocarditis than FDG PET/CT, because of the delayed PET acquisition time on PET/MR. Case-based observations and small clinical studies of FDG PET/MR have shown that FDG PET findings as abnormally increased myocardial uptake correlate well with the cardiac MR biomarkers. FDG PET findings may add complementary and incremental values to cardiac MR by improving the sensitivity of cardiac MR for mild or borderline myocarditis, and increasing specificity for chronic myocarditis.

Summary Preliminary data from retrospective and case-based observational studies have suggested the complementary and incremental values of simultaneous cardiac FDG PET/MR for evaluation of myocarditis, compared to PET/CT or MR alone. Well-designed studies are needed to confirm the findings and to assess the value of cardiac PET/MR for clinical management and more importantly patient's outcome in both acute and chronic myocarditis.

Keywords FDG · PET/CT · MR · PET/MR · Cardiac · Myocarditis · Inflammation

Introduction

Myocarditis is an inflammatory disease of the myocardium caused by various conditions including viral infection, autoimmune reaction, toxin exposure and drugs, or idiopathic factors [1]. The disease occurs more commonly in young subjects, particularly in young men [2, 3]. Clinical manifestations of myocarditis are very variable, being from totally asymptomatic or malaise (mild or borderline myocarditis), to severe (complicated myocarditis). The latter could present as arrhythmic events, ischemic like symptoms, heart failure, or even death [3–5]. Although underlying histopathological changes may vary among different types of myocarditis, generally, it represents an inflammatory process related to disproportional immune response against the myocardium which leads to myocardial injury, i.e., during the acute phase, membrane destruction of the myocytes induced by virus or other factors triggers immune response with infiltration of lymphocytes and macrophages through cytokine secretion [6, 7], causing high inflammatory changes including hyperemia, edema, and necrosis. In the late chronic phase, the damaged cells are

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replaced by collagen with subsequent fibrosis/scar formation in the affected myocardial regions. Prompt and accurate diagnosis of myocarditis is challenging, as the clinical symptoms, laboratory biomarkers (such as troponin, C-reactive protein), electrocardiography (ECG), and echocardiography are all nonspecific. Definite diagnosis relies on endomyocardial biopsy (EMB), but it is infrequently performed in real practice, as most patients are not appropriate candidates for EMB (uncomplicated type of myocarditis). EMB is associated with potential serious complications, and a high false-negative rate due to sampling error related to the patchy distribution nature of the disease. A postmortem study has shown only 45% sensitivity of the EMB for the diagnosis of myocarditis [8]. Thus, non-invasion imaging tools, such as ^{18}F-fluoro-deoxy-glucose (FDG) positron emission tomography/computed tomography (PET/CT) and cardiac magnetic resonance (MR), are clinically relevant in the diagnosis of myocarditis and in monitoring treatment response, by revealing the underlying pathophysiologic and morphologic/tissue changes of the disease, respectively. Both PET and MR can provide information of the entire heart regarding the distribution and pattern of the underlying inflammation, which cannot be revealed by EMB. Preliminary data have suggested that hybrid cardiac PET and MR (PET/MR) for simultaneous imaging of the heart may have complementary and incremental values for myocarditis evaluation compared to PET or MR alone, given hybrid imaging nature. This modality may be more valuable for pediatric population in terms of reduced radiation exposure compared to FDG PET/CT. This article will review the recent findings in the literature regarding cardiac PET/MR for myocarditis, and to discuss its future directions.

FDG PET/CT for Myocarditis

Brief Introduction of FDG PET/CT and Its Applications

Positron emission tomography (PET) is based on detection of the paired 511 keV photons generated from the annihilation of an electron and a positron particle released from a positron emission radioisotope, such as ^{18}F. If deoxy-glucose is labeled with ^{18}F, a positron emission isotope to form ^{18}F-fluoro-deoxy-glucose (FDG) and injected into the body for an FDG PET scan, then the signals detected by PET represent body's glucose uptake and utilization. A localizing CT is added to the PET (PET/CT) to provide anatomical colocation. FDG PET/CT is mainly used for cancer imaging, as most malignant cells show increased glucose uptake. It can also be used for infection and inflammation imaging, such as for cardiac device infection evaluation [9–12], and cardiac sarcoidosis [13], or potentially for vulnerable atherosclerotic plaque imaging [14, 15], as activated immune cells in the infected and inflammatory regions show significantly increased glucose utilization. Myocarditis is an inflammatory disease of the myocardium with infiltration of immune cells which utilize a large amount of glucose and thus can be visualized by FDG PET/CT.

Dietary Preparation for Myocarditis by FDG PET/CT

Although fatty acid is the preferred energy source for the heart, myocytes also use glucose and show FDG uptake on PET/CT, which could interfere with the detection of FDG uptake in inflammatory region of myocarditis. Thus, similar to cardiac sarcoidosis imaging, dietary preparation to suppress normal FDG uptake in myocytes is critical for FDG PET/CT detection of infiltrative myocarditis. It has been shown that a high-fat and low-carbohydrate diet can suppress physiological myocardial FDG uptake [16,17], and thus patients suspected with myocarditis should first consume a high-fat and low-carbohydrate diet 1 day before or at least for the dinner before the FDG PET/CT imaging. If a scan is scheduled in the afternoon, a continued high-fat and low-carbohydrate breakfast could improve the suppression of myocardial FDG uptake. The patient should fast for at least 4 h before the injection of FDG to ensure a low endogenous insulin level which can drive glucose into muscle including myocytes. Prolonged fasting (18 h) has also been suggested which is expected to generate more fatty acids for myocytes. This dietary preparation may be suitable for vegetarians, but its effect on suppression of myocardial FDG uptake is not completely defined [18].

Roles of FDG PET/CT in Assessing Myocarditis

There are no prospective randomized studies or well-designed retrospective studies with a large sample number for assessing the roles of FDG PET/CT in myocarditis diagnosis and management. Current evidence is limited to case-based observations which show that FDG PET/CT can detect and localize the site of myocarditis with active inflammation in acute myocarditis cases [19•,20,21]. FDG uptake in myocarditis could be focal, diffuse, or focal on diffuse depending on the underlying nature of the disease [20]. A repeated FDG PET/CT after treatment could show interval resolution of the abnormal FDG uptake, indicating its potential application in monitoring treatment response [21]. Systematic clinical studies are needed to evaluate the role of FDG PET/CT in diagnosing myocarditis and monitoring disease course. Because FDG PET/CT is not currently indicated and approved for evaluation of infection and inflammation by the Center for Medicare & Medicaid Service (CMS) in the USA, one possible strategy is to conduct a prospective clinical study, by adding an FDG PET/CT (supported by a research grant) to clinically suspected myocarditis patients before and after treatment. The PET/CT data will be blinded to the clinicians and should not affect the current standard care. At the end of the clinical care, after the patient is recovered or deceased, the FDG PET/CT can then be analyzed retrospectively for its accuracy in initial disease diagnosis and in monitoring treatment response.

Cardiac MR for Myocarditis

Cardiac MR Biomarkers of Myocarditis

Regardless of the underlying etiology of myocarditis, the pathologic cascade results in infiltration of immune cells into the myocardium. This subsequently leads to myocardial edema, hyperemia, necrosis, and eventual scar formation. These pathologic responses are well visualized by cardiac MR and are used as imaging biomarkers in the assessment of myocarditis in both acute and chronic settings. As such, cardiac MR has advanced to become the preferred modality of diagnostic assessment in clinically stable presenting patients of myocarditis [3, 22].

Global and Regional Ventricular Function

Right and left ventricular function is readily assessed with MR. Cine short axis images with steady-state free precession (SSFP) sequences demonstrate excellent distinction of the myocardium and blood pool, allowing for sensitive evaluation of acute left ventricular (LV) function and subsequent follow-up over time. Although even subtle LV dysfunction in the setting of myocarditis may be occasionally seen, global and regional wall motion abnormalities have low specificity in the diagnosis of myocarditis [23•].

Myocardial Edema

Myocarditis is associated with acute inflammatory cell injury, increased permeability of cellular membranes, and subsequently myocardial edema. The earliest investigations in the diagnostic utility of cardiac MR for myocarditis targeted identification of edema as a surrogate for active inflammation. T2-weighted sequences are sensitive to the presence of water-bound protons as a result of edema. Initial studies evaluating the use of T2 spin echo sequences to diagnose myocarditis demonstrate high sensitivity and specificity in establishing the diagnosis compared to endomyocardial biopsy [23, 24]. Although regional edema is often observed, greater diagnostic accuracy is achieved when global myocardial edema is evaluated. Normalizing the signal intensity of the myocardium to that of skeletal allows for a quantitative ratio between the two tissues. The equation for calculating the T2 ratio is as follows:

$$\text{T2 ratio} = \text{Signal intensity}_{\text{myocardium}} / \text{Signal intensity}_{\text{skeletal muscle}}$$

A value of 1.9 or greater indicates the presence of myocardial edema in the setting of myocarditis [25]. T2-weighted short tau triple inversion recovery (STIR) sequences have been validated with this technique with sensitivity of 84% and specificity of 74% in detecting myocardial edema [25, 26].

Some limitations of the T2-weighted technique include poor signal, typically when general use of body coil vs dedicated cardiac coils. The presence of concomitant skeletal inflammation can confound T2 ratio quantification. Incomplete signal suppression of slower blood flow in subendocardial blood pool may also challenge diagnostic accuracy particularly in borderline or mild myocarditis.

EGE

Inflammatory mediators are released with the onset of myocardial inflammation resulting in regional dilatation of the coronary microvasculature. This hyperemic blood flow to the involved segments effectuates increased regional uptake of the gadolinium contrast. The hyperemia and subsequent global relative enhancement of the heart is measured by normalizing myocardial signal to that of skeletal muscle, on both pre-contrast and post-contrast T1-weighted images. The ratio of early gadolinium enhancement (EGE) is calculated from the formula below:

$$\text{Early gadolinium enhancement ratio} = \text{Enhancement}_{\text{myocardium}} / \text{Enhancement}_{\text{skeletal muscle}}$$

Enhancement of the myocardium and skeletal muscle for being used for the formula above are calculated by:

$$\text{Enhancement} = \left(\text{Signal intensity}_{\text{post gadolinium}} - \text{Signal intensity}_{\text{pre gadolinium}}\right) / \text{Signal intensity}_{\text{pre gadolinium}}$$

Global relative enhancement was calculated as the mean of the relative enhancements of all slices. A signal intensity ratio greater than or equal to 4.0 is considered positive for early enhancement in the setting of myocarditis. Alternatively, since coexisting skeletal muscle hyperemia may be present, a global myocardial signal increase of 45% is also considered consistent with myocarditis. A pooled analysis of early investigations demonstrated a sensitivity of 74%, specificity of 83% and diagnostic accuracy of 78% with early enhancement for myocarditis [23].

LGE

Both animal and clinical cardiac MR studies have validated the utility of late gadolinium enhancement to assess myocardial necrosis, fibrosis, and scarring [27]. Gadolinium is an MR contrast agent that freely distributes to the extracellular space. Pathological conditions which result in expansion of the extracellular space will lead to larger volumes of gadolinium. Given that every tissue has its own T1 value, the increased concentration of gadolinium will increase the T1 signal in that tissue compartment.

Using an inversion-recovery gradient echo sequence, myocardial tissue can be imaged at multiple inversion times to determine when the net magnetization of the healthy tissue is zero (nulled). Abnormal myocardium which will have a greater concentration of gadolinium due to delayed washout will have increased signal relative to normal myocardium and subsequently demonstrates bright signal on a background of nulled tissue.

Previous studies have consistently validated the distribution of late gadolinium enhancement (LGE) with active myocarditis on histopathology, notably involving the septum or free wall of the left ventricle [25, 26, 28]. Despite the strong correlation between LGE and presence of myocarditis, reported sensitivity remains variable ranging from 27 to 95%. Subsequent pooled data reveals a sensitivity of 59% [23, 25].

MR Parametric Mapping

Newer MR techniques have been developed that reduce the limitations of classic MR sequences with use of the Lake Louise Criteria (LLC). Quantitative measurement of T1 and T2 relaxation times enables more robust tissue characterization. Multiple images at different time points are sampled at a fixed point in the cardiac cycle to generate a relaxation curve fit for the parameter in question (i.e. T1 or T2). For T1 mapping, a modified Look–Locker inversion recovery (MOLLI) sequence is run at multiple different inversion times after an initial inversion pulse. Administration of gadolinium allows for post-contrast T1 maps which can be used to create extracellular volume (ECV) fraction maps. T2 maps are also created using various echo times to fit a T2 relaxation curve.

Both T1 and T2 mapping parameters have shown superior diagnostic performance compared to LLC, significantly adding to the ability of MR to confirm or exclude the presence of myocardial inflammation. In one study, T1 mapping outpaced LLC in diagnostic accuracy (91% compared to 85%) with further improvement to 96% when supplemented with either T2-weighted imaging or LGE [29].

T2 mapping in myocarditis identifies more extensive myocardial involvement than suggested by late gadolinium enhancement, cine imaging, and T2W-STIR [30–32]. Native T2 has higher diagnostic accuracy than LLC in the detection of myocarditis in patients with chronic myocarditis and recent-onset heart failure and reduced left ventricular function [33]. These and continued investigations support that the combination of parametric mapping with components of the LLC demonstrates strong promise to amplify the diagnostic yield of MR.

Clinical Presentation

Accurate and prompt diagnosis of myocarditis remains a clinical challenge, given that the presentation of patients may range from minimal symptoms to full cardiogenic shock. This diagnostic challenge occurs both in acute and chronic presentations.

Acute Myocarditis

In the acute presentation, the cardiac MR imaging protocol focuses on assessment of global and regional function, as well as primary imaging markers of inflammation (edema on T2, hyperemia on early gadolinium enhancement (EGE), and necrosis on late gadolinium enhancement (LGE)). Additional findings such as pericardial effusion, left ventricular systolic function, or transient increase in wall thickness may support the diagnosis of active myocarditis, however have not been found to have significant sensitivity or specificity to be useful.

Individually, the selected MR biomarkers have inherent limitations in sensitivity, specificity, and accuracy in making the diagnosis of myocarditis [23, 25, 26]. However, a comprehensive multi-parametric MR approach has been developed to overcome some of these issues. The Lake Louise Criteria (LLC) is an international expert consensus cardiac MR protocol that includes assessment of the following biomarkers: (a) regional or global myocardial signal intensity increase on T2-weighted images (increased T2 ratio ≥ 2.0 for detection of edema), (b) increased global myocardial early gadolinium enhancement ratio (EGE ≥ 4.0 for hyperemia), and (c) at least one focal, non-ischemic lesion at inversion-recovery late gadolinium enhancement (LGE for necrosis) MR imaging. These criteria leverage the ability of MR to access multiple imaging biomarkers with the presence of at least 2 of the 3 yielding a sensitivity of 67% and specificity of 91% in establishing the diagnosis of myocarditis [23•].

In complicated cases, cardiac MR can be used to improve both sampling accuracy and safety of endomyocardial biopsy (EMB). In a study by Mahrholdt and colleagues, 90% of biopsy specimens performed in identified regions of LGE revealed active myocarditis by histological evaluation [28].

Patients with mild myocarditis involvement and preserved LV function typically have excellent prognosis. Follow-up MR in at least 4 weeks after the initial insult may be useful to differentiate uncomplicated courses from a complicated course with viral persistence [23•].

Chronic Myocarditis

Myocarditis months to years after the initial insult may demonstrate healed myocardium with focal areas of fibrosis but resolution of the inflammation with absent edema and hyperemia. Progression from acute to chronic myocarditis occurs in about 21% of cases, typically resulting from either direct cytotoxic effects or chronic immune-related activity [34, 35]. Myocardial fibrosis, ventricular remodeling, and ventricular dysfunction are common imaging findings at this phase of insult. MR assessment at this phase is to identify the extent of necrosis and residual scarring developed since the original injury as well as to assess the morphology and function of the heart.

The classic Lake Louis Criteria (LLC) for the diagnosis of acute myocarditis at cardiac MR does not have the same accuracy in the chronic setting [36]. It has been shown that patients with chronic myocarditis had less frequent LGE, yet demonstrated markers of inflammation including persistent myocardial edema and early gadolinium enhancement. Notably, the combination of EGE and edema parameters has a sensitivity, specificity, and diagnostic accuracy of 62%, 86%, and 72%, respectively [35]. Although the pathophysiology is not quite understood, LGE noted in chronic myocarditis does not correlate to viral persistence and suggests a continued role of EMB or hybrid FDG PET/MR in this setting.

Hybrid FDG PET/MR in Myocarditis

Technique Aspects of PET/MR

PET/MR provides simultaneous acquisition of both MR and PET data without repositioning the patient [37], which reduces movement-related mis-registration. In addition, motion correction of PET data can be performed, if necessary, by temporal and spatial co-registration, using temporally high-resolution MR [38]. Attenuation correction of PET data can be achieved using a 2-point Dixon MR sequence which is a software-based segmentation of MR data into 4 tissue classes (background, lung, fat and soft tissue) with defined attenuation coefficients [39]. The Dixon MR attenuation sequence does not differentiate soft tissue and bone which leads to underestimation of PET signals, as bone has a higher attenuation coefficient than soft tissue [39]. This Dixon MR sequence-based attenuation correction is reliable for visual evaluation of PET images but underestimates SUV (standard uptake value) of PET compared to CT-based attenuation correction [39]. This may not be an issue when using FDG PET/MR for myocarditis, as currently the diagnosis is based on visual assessment. However, quantitative analysis of PET should be performed with caution when Dixon MR attenuation sequence is used. Finally, to selectively use data from an acquired cardiac cycle, a good ECG recording is critical for most MR sequences and PET data reconstruction. Magnetic field and radio frequency pulses can significantly affect the ECG signals, and thus the ECG leads should be placed with caution and the signals should be monitored carefully to ensure accurate recoding of ECG during the scan. One of the advantages of PET/MR is potential reduction of radiation from PET, as the MR sequences are relatively long which enables simultaneous collection of high PET counts with a lower injected tracer activity [40]. This is particularly relevant for pediatric and young population, which is more sensitive to radiation and has a higher incidence of myocarditis.

On the other hand, PET/MR has a smaller inner bore than PET/CT, which limits its use in patients with large body habitus. Patients with metal implants or with renal insufficiency may not be suitable for MR with contrast. Both FDG PET and MR findings are non-specific and do not provide etiology-based diagnosis of myocarditis. In addition, in certain circumstances, FDG PET may show diffuse myocardial uptake because of incomplete suppression of physiologic uptake in the myocytes due to unsuccessful dietary preparation.

Complementary and Incremental Values of FDG PET/MR for Myocarditis

As mentioned above, cardiac MR is the preferred imaging modality for non-invasive diagnosis of myocarditis; however, the "any 2 of 3" LLC combination (T2, LGE, and EGE) of cardiac MR has its limitation. For example, the T2-weighted images tend to have a low imaging quality associated with artifact, and MR findings are not correlated to the severity of myocardial inflammation [25, 41]. FDG PET/MR thus may provide potential complementary and also incremental values for the diagnosis of myocarditis by providing both functional inflammatory information and structural changes simultaneously.

Clinical case-based observations have shown the utility of FDG PET/MR in the assessment of myocarditis [40, 42, 43], suggesting a good correlation between myocardial FDG uptake and LGE or T2 hyperintensity, indicating their complementary value. As shown in Fig. 1 [44•], (a) late gadolinium enhancement cardiac MR image obtained in short-axis view showed linear mid-wall and subepicardial LGE of the anterior wall and inferoseptum. Matched FDG PET (b) and fused FDG PET/MR (c, d) images demonstrated increased activity exactly corresponding to the pattern of injury on MR. This case

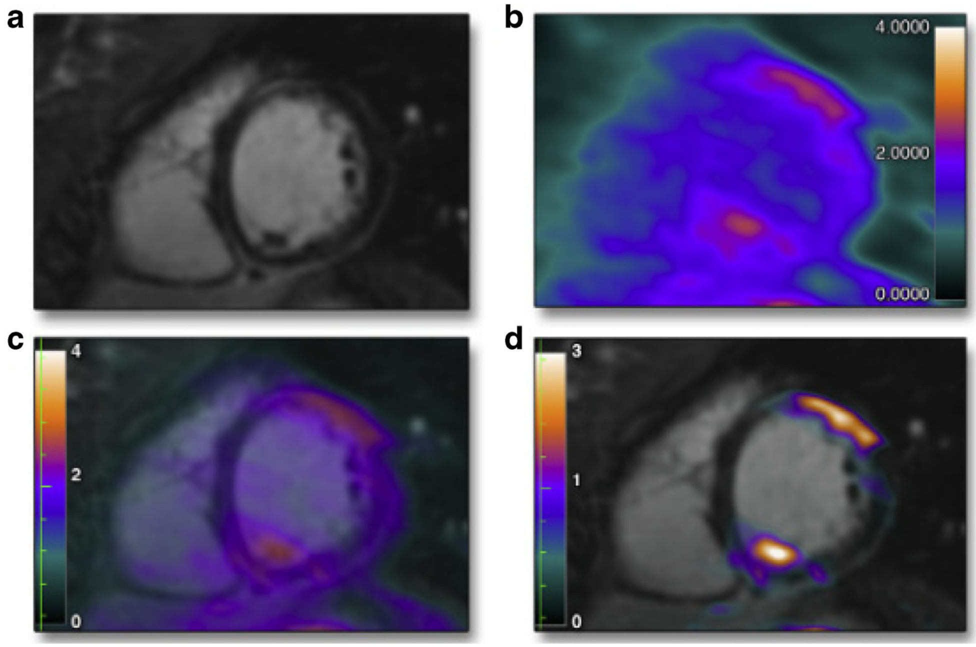

Fig. 1 An example of complementary role of FDG PET/MR for the diagnosis of acute myocarditis. Patient (25-year-old female) hospitalized for supraventricular tachycardia with history of recent viral infection. Myocardial biopsy was inconclusive. **a** Late gadolinium enhancement cardiac MR obtained in short-axis view showed linear mid-wall and subepicardial LGE of the anterior wall and inferoseptum. FDG-PET imaging (**b**) and fused FDG-PET/MR (**c**, **d**) images demonstrated increased activity exactly corresponding to the pattern of injury on MR. (Reprinted from Abgral et al., with permission from Elsevier) [44•]

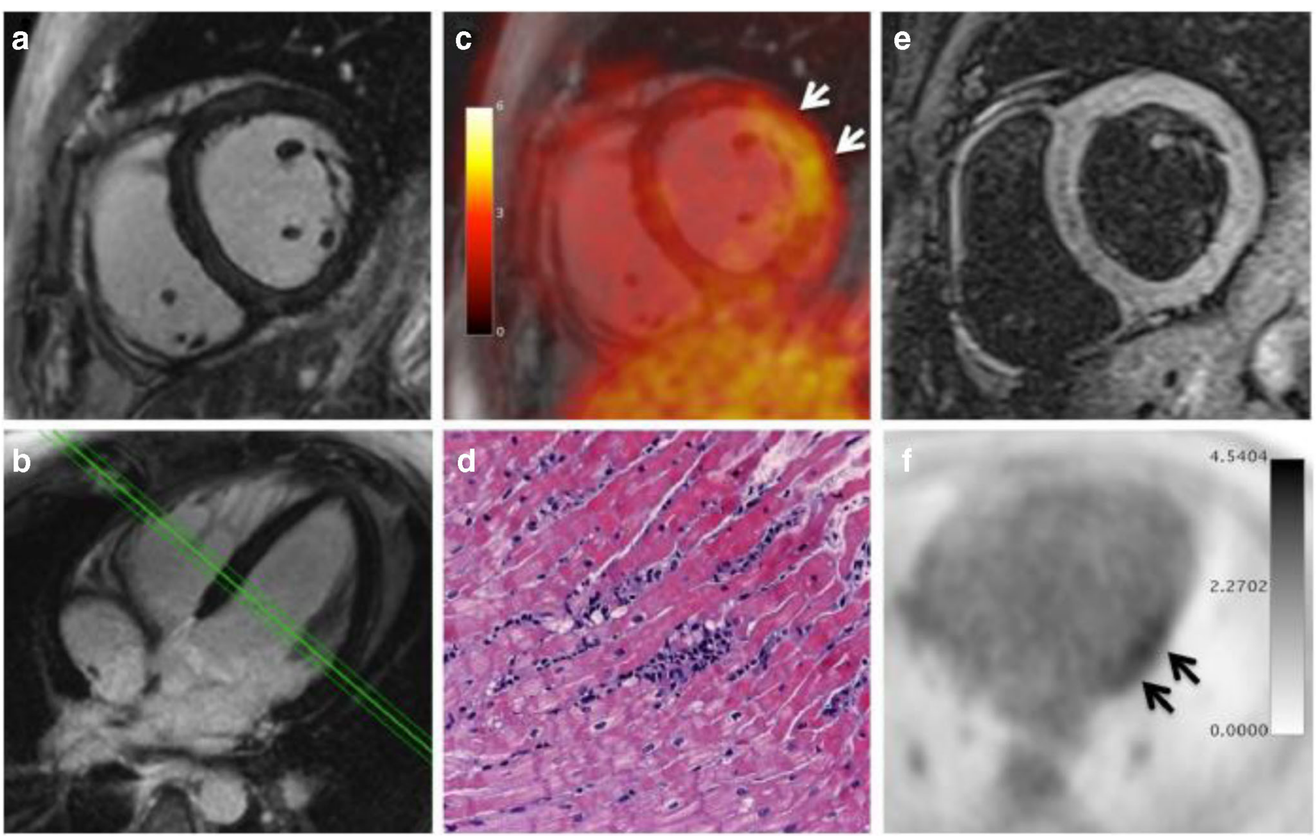

Fig. 2 An example of incremental role of hybrid FDG PET/MR for borderline myocarditis. Late gadolinium enhancement images (**a**, **b**; green line in **b** represents horizontal long axis view through the LV and RV at the level for **a**) did not reveal any signs of myocardial necrosis on the MR. FDG PET images (**c**, fused PET/MR, white arrow; **f**, PET alone, black arrow) demonstrated focal FDG uptake in the lateral wall. T2-weighted imaging (**e**) showed mild myocardial edema (T2 ratio: 2.0). Diagnosis of borderline myocarditis was confirmed by histopathological assessment after endomyocardial biopsy demonstrating sparse inflammatory infiltrates but no myocardial necrosis (**d**). (Reprinted by permission of Springer Nature: Nensa et al.) [45••]

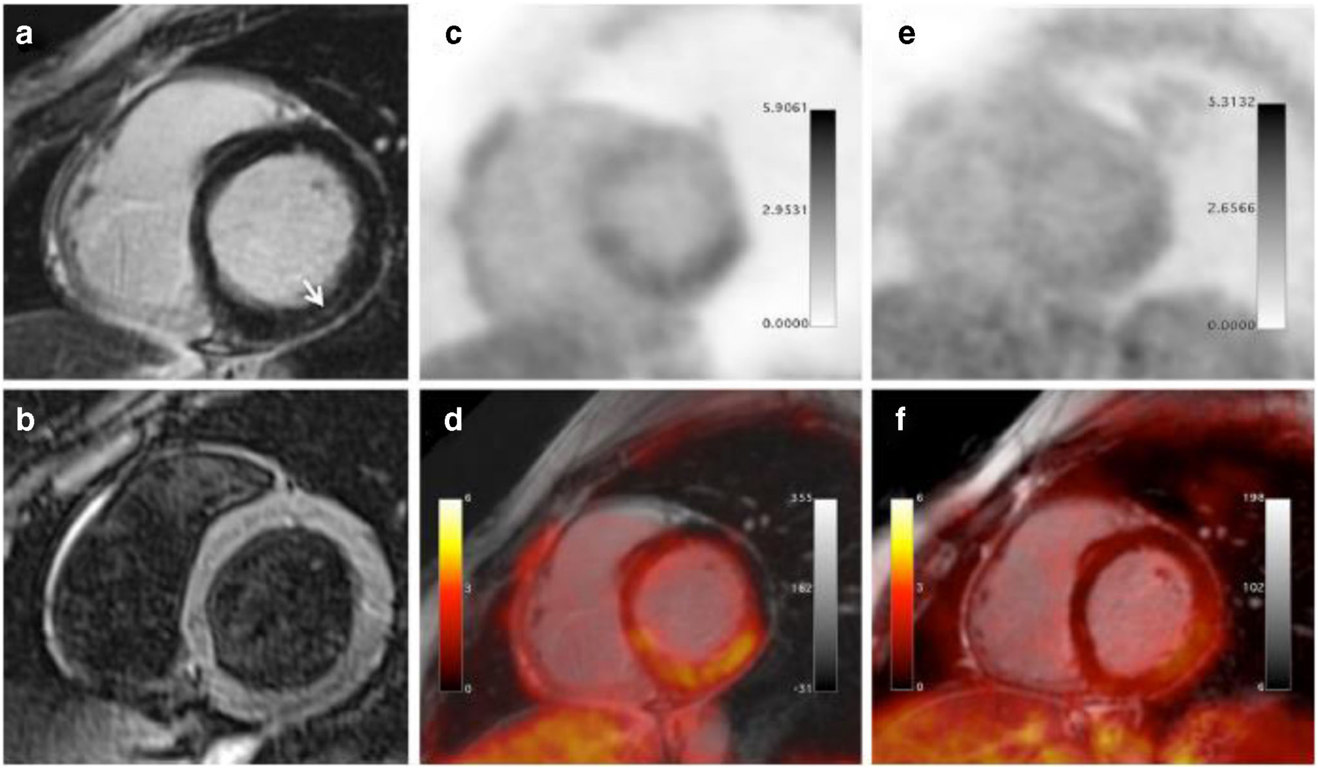

Fig. 3 An example of incremental role of FDG PET/MR for detecting active disease in chronic myocarditis. There was faint streaky late gadolinium enhancement in the inferolateral Wall (**a**). No significant increase in myocardial T2 signal was observed (**b**). PET images showed significantly increased FDG uptake in the inferior and inferoseptal wall (**c**, **d**). The patient demonstrated elevated levels of C-reactive protein, while myocardiocytolysis serum markers were negative. Endomyocardial biopsy was refused by the patient. At follow-up visit after 9 months, the patient reported significant relief from symptoms yet not completed recovery. Reexamination with PET/MR revealed clearly less but still significant FDG uptake in the inferolateral wall (**e**, **f**), while cardiac MR findings had not changed, indicating persistent inflammation in a chronic myocarditis. (Reprinted by permission of Springer Nature: Nensa et al.) [45••]

indicates the complementary role of the hybrid FDG PET/MR for myocarditis diagnosis. A recent small prospective study [45••] showed that using LGE and/or T2 as the standard of reference, FDG PET showed a sensitivity of 74% and a specificity of 97% with a diagnostic accuracy of 87%. There was overall a good agreement between increased FDG uptake on PET and MR (LGE and/or T2) [45••, 46].

Preliminary studies also show potential incremental role of FDG PET to the cardiac MR on the simultaneous FDG PET/MR. Myocardial damage in myocarditis may be often scattered, and thus undetectable with LGE. In addition, LGE may not detect mild borderline myocarditis due to the absence of relevant myocardial necrosis [47]. In these patients, FDG PET could potentially increase the sensitivity of cardiac MR by providing metabolism information. As demonstrated in Fig. 2 [45••], LGE images (a, b) did not reveal any signs of myocardial necrosis. PET images (c, f) demonstrated focal FDG uptake in the lateral wall. T2-weighted imaging (e) showed mild myocardial edema (T2 ratio: 2.0). Diagnosis of borderline myocarditis was confirmed by histopathological assessment after endomyocardial biopsy demonstrating sparse inflammatory infiltrates but no myocardial necrosis (d).

In patients with chronic myocarditis, it is often difficult to differentiate patients with residual active myocardial inflammation from myocardial scarring of other origin on late gadolinium enhancement MR. In these patients, FDG PET could improve the specificity of MR by providing metabolic information of inflammation. As shown in (Fig. 3) [45••], there was a faint streaky late gadolinium enhancement in the inferolateral wall (a). No significant increase in myocardial T2 signal was observed (b). PET images showed significantly increased FDG uptake in the inferior and inferoseptal wall (c, b). The patient demonstrated elevated levels of C-reactive protein, while myocardiocytolysis serum markers were negative. Endomyocardial biopsy was refused by the patient. Reexamination with PET/MR in 9 months revealed clearly less but still significant FDG uptake in the inferolateral wall (e, f), while MR findings had not changed. This case shows that FDG PET could be particularly useful in guiding and monitoring immunosuppressive therapy, as well as detecting recurrence after therapy. In addition, as myocarditis is often self-limited clinically, the addition of PET to MR may clarify whether the disease is still active or recovered, potentially allowing determination the duration of clinical management.

In addition, FDG PET may detect more myocarditis lesions performed on a hybrid cardiac PET/MR than on PET/CT, because of the delayed imaging acquisition of PET on PET/MR. PET is also capable of detecting pathologic extra-cardiac FDG uptake in 27% of the patients [45••].

Future Directions

Current data regarding the roles of cardiac FDG PET/MR on myocarditis are from retrospective and case-based observational studies. Systematic studies are needed to confirm the complementary and incremental values of hybrid PET/MR compared to PET and cardiac MR alone in the diagnosis of myocarditis. It would be also important to evaluate whether quantitative assessment of inflammation by FDG PET could predict the severity of myocarditis and guide clinical management, and subsequently improve patient outcome. Etiologically based diagnosis of myocarditis is critical for certain types of myocarditis for appropriate clinical management; for example, patients with giant cell and eosinophilic myocarditis or those with autoimmune disorders may benefit from immunosuppression. Data are lacking regarding the performance of FDG PET/MR in guiding endomyocardial biopsy. It also warrants further investigation regarding the reduced FDG dose with PET/MR for pediatric population.

Conclusion

The Lake Louis Criteria of cardiac Magnetic Resonance (MR) has been the preferred imaging tool for the diagnosis of myocarditis. Small retrospective and case-based observational studies have shown that FDG PET/CT could detect inflammation as increased myocardial FDG uptake in myocarditis. FDG PET may improve the performance of cardiac MR by increasing its sensitivity for mild or borderline myocarditis, and improving specificity for chronic myocarditis. Hybrid cardiac PET/MR may have complementary and incremental values for the assessment of myocarditis compared to FDG PET or cardiac MR alone. More research is needed in the application of this new PET/MR modality for myocarditis diagnosis and management.

Compliance with Ethical Standards

Conflict of Interest Wengen Chen and Jean Jeudy declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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•• Of major importance

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