Cardiac MRI and FDG PET in Cardiac Sarcoidosis: Competitors or Collaborators?

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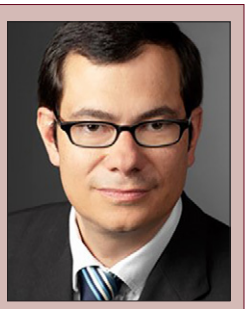

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In this issue of *Radiology: Cardiothoracic Imaging*, the article "Utility of FDG PET and Cardiac MRI in Diagnosis and Monitoring of Immunosuppressive Treatment in Cardiac Sarcoidosis" by Coulden et al (1) on a retrospective, observational study in 31 patients suspected of having cardiac sarcoidosis covers a clinically but also scientifically very interesting topic of cardiovascular imaging. Sarcoidosis itself, but even more so, cardiac involvement—cardiac sarcoidosis—is a very rare disease but may occur in up to 3%–30% of all patients with sarcoidosis. However, the mortality rate of cardiac sarcoidosis represents, as the authors emphasize, 13%–85% of all sarcoidosis-related deaths.

Cardiac sarcoidosis is a strong predictor of poor outcome, often manifesting in arrhythmia and heart failure. Therefore, it is obvious that early diagnosis of cardiac sarcoidosis and monitoring of sarcoidosis treatment is crucial, as well as the differentiation between active and chronic disease. This may help to reduce overall morbidity and mortality. However, detection and monitoring still remain challenging (2) due to the invasiveness of endomyocardial biopsy and its sampling error. Therefore, noninvasive options are favorable.

Several articles describe the usefulness of fluorine 18 fluorodeoxyglucose (FDG) PET as well as of cardiac MRI in diagnosing cardiac sarcoidosis (2–4). In a pooled meta-analysis, a sensitivity of 89% and a specificity of 78% of FDG PET for the detection of cardiac sarcoidosis have been described (2,5). On the other hand, cardiac MRI predicted outcome in patients suspected of having cardiac sarcoidosis (6), and in one of the rare comparative studies on a simultaneous PET/MRI system, cardiac MRI late gadolinium enhancement (LGE) provided a higher sensitivity of 82% and an especially higher negative predictive value of 79% for ruling out cardiac sarcoidosis as compared with FDG PET (7). In the same study, it could also be demonstrated that a combination of both methods is more than the sum of its parts and performed better than PET or cardiac MRI alone in patients with sarcoidosis.

Therefore, it has been hypothesized that especially in patients suspected of having cardiac sarcoidosis, hybrid PET/MRI systems might be beneficial (2). The well-established and very robust techniques of cardiac MRI (volumetric assessment and LGE) and FDG PET methods provide different, complementary information. On the one hand, LGE mainly visualizes irreversible myocardial damage (necrosis, scar formation, and fibrosis), but with restrictions for myocardial edema as a marker for inflammation and the acuity of the disease (8). On the other hand, FDG PET visualizes glucose metabolism and represents usually viable myocardium, and in well-prepared patients after a strict 24-hour low-carbohydrate diet, myocardial inflammation (2). Both myocardial damage and inflammation are part of the pathology of cardiac involvement in patients with sarcoidosis.

However, the question of which method is more suitable than the other in diagnosing and monitoring cardiac sarcoidosis is not solved yet. But it was not the intention of the article from Coulden et al to answer this question. They combined the best-established protocols of both methods and collected a cohort of patients with biopsy- or lung CT–proven extracardiac sarcoidosis. They included patients between August 2012 and May 2018 with suspected cardiac involvement. Patients with known cardiac disease like coronary artery disease or cardiomyopathies were excluded. Despite the fact that only 31 patients could be analyzed, it is a scientifically as well as logistically speaking very comprehensive retrospective study. Patients underwent at first visit a FDG PET/CT and a cardiac MRI examination—mostly on the same day—and at a second visit—at the earliest 3 months later—the two examinations were repeated either after immunosuppressive therapy (n = 22) or without treatment in the control group (n = 9).

The results from the cardiac MRI mainly were based on the assessment of ventricular function, LGE, and increased signal intensities on T2-weighted short-tau

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See also the article by Coulden et al in this issue. Conflicts of interest are listed at the end of this article.

inversion recovery sequences which indicate myocardial edema as an inflammation marker. The first two markers were absolutely quantified in milliliters and percentage, whereas the latter was only visually assessed by simply eyeballing. The FDG uptake after a 24-hour low-carbohydrate diet was not only described and quantified by the standard uptake value (SUV) with a cutoff of greater than 3.6, but also by the recently introduced cardiac metabolic volume. This parameter of glucose metabolism was used as a surrogate parameter for active inflammation and to monitor the degree of ongoing inflammation under therapy. The CT acquisition of the FDG PET/CT data set was only used for attenuation correction.

In the majority of patients suspected of having cardiac sarcoidosis at the first visit, the authors detected an abnormal myocardial FDG uptake and/or nonischemic LGE pattern; there were fewer instances of focally increased myocardial signal intensities on T2-weighted short-tau inversion recovery images. In the majority of patients, pathologic myocardial FDG uptake was matched by LGE, but also LGE without increased FDG uptake occurred and vice versa. This indicates, in this study, that FDG PET might be more sensitive than cardiac MRI to detect cardiac sarcoidosis, but it was not proven with endomyocardial biopsy. Therefore, the ground truth is not known.

However, the most important part of the study by Coulden et al is the results of the follow-up FDG PET and cardiac MRI examinations after immunosuppressive therapy in comparison to a small group of nontreated patients. The FDG PET myocardial inflammation markers SUV_{max}, and even more impressively, the cardiac metabolic volume, decreased significantly after therapy, and the decrease in abnormal cardiac metabolic activity was matched by an improvement in left ventricular ejection fraction (LVEF). Neither significant changes in inflammation parameters nor in functional parameters could be observed in the nontreated group of patients with clinically suspected cardiac sarcoidosis.

On the contrary, no significant volume change in LGE could be detected in both groups of patients, which is from my point of view not that surprising. It just confirms—like in other studies on myocardial infarction or myocarditis (9)—that LGE is not so much an inflammation marker, but mainly a marker for irreversibly injured myocardium. A reduction of LGE volume in patients several months after acute myocardial infarction occurs mostly as a result of tissue shrinkage, part of the normal scar formation and remodeling process. Therefore, it's not surprising that it did not resolve even after therapy. Nevertheless, it is surprising that in the study by Coulden et al SUV_{max}, size of the decrease in cardiac metabolic volume, or LGE did not predict improvement in LVEF, which is contradictory with several studies on myocarditis or even with a study on patients with sarcoidosis (6).

However, cardiac MRI alone might be able to diagnose and monitor cardiac sarcoidosis, especially the inflammatory part, with comparable results, if the latest technology of T1 and T2 mapping—like already established in patients suspected of having myocarditis—is used (9). The use of T2-weighted short-tau inversion recovery sequences and the simple visual assessment of the achieved images is critical but has a high intra- and interobserver variability, especially on focal changes of signal intensities. Therefore, the so-called edema ratio using the mean signal intensity of the myocardium divided by the mean signal intensity of skeletal muscle on the same image (eg, erector spinae muscle) has been introduced to diagnose inflammation in patients with myocarditis (9). However, the results of T2 mapping for patients with myocarditis, especially in chronic disease, were much more encouraging. Therefore, it can be assumed that this might also be the case in patients with cardiac sarcoidosis.

Furthermore, the use of cardiac MRI to detect myocardial inflammation accounts for almost 30% of all cardiac MRI examinations according to the European Society of Cardiovascular Radiology (ESCR) registry and is safe with or without the use of contrast agents (10). Furthermore, it comes with the benefit that no radiation exposure is necessary.

Therefore, by taking the results of this and several other studies into account, FDG PET/MRI holds great promise to finally answer this question with a prospective study, if cardiac MRI by using all available techniques, including T1 and T2 mapping, can compete with FDG PET in inflammation detection and therapy monitoring of patients with cardiac sarcoidosis or not.

Disclosures of Conflicts of Interest: M.G. disclosed no relevant relationships.

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