^{18}F-FDG PET/CMR in cardiac sarcoidosis: A wild card in the deck?

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Sarcoidosis is an inflammatory multi-system disorder of unknown origin, characterized by the formation of non-caseating granulomas.[1] Although more than 90% of patients present with lung, heart, skin, and lymph nodes involvement, other organs and tissues can be also affected.[2] Even if clinical manifestations of cardiac disease occur in less than 5% of cases, cardiac sarcoidosis (CS) is a potential life-threatening disease, due to ventricular arrhythmias.[3] Thus, the identification of subclinical but active CS remains crucial. However, a gold standard assessment of the disease is still lacking. Identification of non-caseating granulomas by endomyocardial biopsy can definitively establish the final diagnosis of CS. Nevertheless, the high risk related to an invasive approach does not pay back in terms of sensitivity, due to the patchy involvement of the myocardium.[4] A non-invasive advanced multi-imaging approach, including cardiac magnetic resonance imaging (CMR) and ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET), has been increasingly adopted.[5-7] In particular, CMR provides a multidimensional assessment of left ventricular wall thickness, function, as well as tissue characterization.[8] Late gadolinium enhancement (LGE) technique indeed allows the identification of myocardial injury in CS, usually occurring with a non-coronary distribution. However, LGE is not able to distinguish between active disease and chronic scar.[9] Conversely, PET is optimally suited to identify active macrophage-mediated inflammation using ^{18}F-FDG.[10] Nevertheless, even if myocardial physiological glucose uptake can be suppressed using dietary restrictions, this strategy may result ineffective potentially generating false-positive results.[11]

Recently, combined ^{18}F-FDG PET/CMR has emerged as a promising tool either with truly hybrid systems or with sequential approaches using fusion post-processing software.[12-14] Among several benefits of a combined acquisition method, the potential to provide complementary information may overcome limitations of each stand-alone technique improving the overall single modalities performance.

In the current issue of Journal of Nuclear Cardiology, Okune et al[15] investigated the role of fusion PET/CMR imaging for the identification of inflammatory phase in 74 patients with suspected CS. In particular, the Authors compared fusion ^{18}F-FDG PET/CMR results with those obtained by ^{18}F-FDG PET imaging using the 2016 Japanese Circulation Society (JCS) guidelines as reference standard for CS diagnosis. A positive finding on PET imaging was defined by ''focal'' or ''focal on diffuse'' FDG uptake pattern, whereas concomitant presence of increased ^{18}F-FDG uptake and LGE was considered as a positive result on fusion PET/CMR. PET alone and PET/CMR showed similar excellent diagnostic performance in detecting CS in the total cohort (82.4% and 87.8%, respectively). Interestingly, all cases showing focal pattern on PET imaging were considered as active CS on fusion PET/CMR image too. However, mismatch evaluations of active CS between PET and fusion PET/CMR images occurred in 27% of cases, the most showing diffuse and focal on diffuse patterns on FDG-PET images. Of note, interrater agreement of PET/CMR was excellent in both the total cohort and a subgroup of diffuse and focal on diffuse patterns (k = 0.89 and 0.86, respectively), resulting higher to that of FDG-PET alone (k = 0.57 and 0.28 respectively).

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In the study by Okune et al[15], several points deserve to be highlighted. First of all, the diagnosis of CS was made according to 2016 JCS revised criteria, which strongly rely on imaging findings. Thus, it seems a dog chasing its own tail. Furthermore, FDG-PET imaging has been performed by using two different scanners, a PET stand-alone modality and a hybrid PET/CT camera. Although no differences were observed between the two acquisition methods in terms of clinical characteristics and imaging findings, the use of different approaches may represent a limitation of the study.

Interestingly, the consistency of identifying active inflammation between T2 weighted and FDG-PET images was very low (k = 0.14). Recently, quantitative tissue characterization techniques with T1 and T2 mapping were reported to be useful for early detection of CS.[16] Therefore, it would be possible to identify myocardial inflammation by directly relating to the altered magnetization properties. Hence, the use of these promising sequences in combination with ^{18}F-FDG PET imaging may demonstrate improved accuracy for detection of inflammatory changes.[13] In addition, it may be of great interest to investigate the diagnostic value of texture analysis, a group of computational methods extracting information about relationships among adjacent pixels or voxels.[17] Those promising tools could be of added value in uncertain cases, when focal or focal on diffuse patterns are not detectable on FDG-PET images. In addition, a truly simultaneous approach by dedicated hybrid systems could overcome possible mismatch results derived from post-processing fusion images.[13]

In a recent investigation, Dweck et al[13] nicely demonstrated, in a smaller patient's population, the usefulness of this hybrid technique to simultaneously evaluate the myocardial damage, on CMR side, and disease activity status as assessed by ^{18}F-FDG PET assuring accurate identification of different disease patterns as expression of different disease stages leading to tailored therapeutic strategies.

In conclusion, combined PET/CMR is emerging as a suitable imaging modality for CS, offering the advantage of an accurate assessment of myocardial function and identification of fibrosis by CMR, as well as detection of inflammation by ^{18}F-FDG PET. Nevertheless, further large-scale and prospective studies are needed to deeply investigate its potential role for CS diagnosis as well as for prognostic stratification and treatment response.

Disclosures

Carmela Nappi, Andrea Ponsiglione, Massimo Imbriaco, and Alberto Cuocolo declare that they have no conflicts of interest.

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