

Utilizing and Interpreting FDG-PET/CT Images in Patients Referred for Assessment of Cardiac Sarcoidosis: The Devil is in the Details.

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We read with interest the article by Ohira et al. (1). The authors investigated the inter- and intraobserver agreement in FDG PET/CT interpretation for patients with suspected cardiac sarcoidosis (CS). Their retrospective study included patients from August 2009 to April 2014, which were divided into two groups with different pretest preparation protocols that aimed to suppress background myocardial FDG uptake. We would like to highlight few study limitations that would warrant the authors' consideration.

Their first 46 FDG PET/CT scans were performed between August 2009 and June 2012 with pretest preparation protocol as a fast ≥ 12 hours with pretest heparin injection (no-restriction group); while the later 54 FDG PET/CT scans performed between July 2012 to April 2014 had additional preparation of a low-carbohydrate, high fat and protein-permitted diet but without mention of length of diet preparation (low-carb group). This description suggests that the authors were not satisfied with the outcome from "12-hour fast + heparin" preparation protocol. Yet, there was not description about the duration of low-carb diet preparation before the 12-hour fasting, nor whether the non-compliant patients were identified and excluded, or if the additional low-carb diet preparation protocol improved suppression of background FDG myocardial uptake when compared to the non-restriction group. Surprisingly, even though there were 19 patients underwent more than one scan (total of 46 scans with range of 2 to 4 and median of 2 scans each): 15 patients had repeated scans to assess response to therapy, and 4 patients had repeated scans to clarify diagnosis, there were no images or discussions about whether the repeated scan were using same preparation protocol, and what was the interpretation for any discrepancy results in repeated scans..

The authors categorized cardiac FDG uptake into 5 patterns: 1) none, 2) focal, 3) focal on diffuse, 4) diffuse and 5) isolated lateral wall and/or basal uptake. They considered patterns 1, 4

and 5 as “not consistent with active CS” since “these patterns are observed in healthy subjects (2-4)”. Any patient with patterns 2 or 3 but with myocardial SUVmax values less than liver SUVmean were considered “not consistent with active CS”. Otherwise, patterns 2 and 3 were considered as “positive findings consistent with active CS”. The authors used the Guidelines of the Japanese Ministry of Health and Welfare (JMHWG), as reference standard for diagnosing CS (5). However, the authors didn’t comment on any correlation, if any, between the FDG PET/CT results and other imaging such as cardiac MRI and clinical findings. Furthermore, as JMHWG have not been clinically validated and has an imperfect diagnostic accuracy (6-8), was there any discrepancy between FDG PET/CT results and other test criteria when using JMHWG? If so, how did the authors interpret the image results?

We think there were arbitrary and subjective interpretations in Figures 1 and 2 of their paper, which we assume were the best available figures in their study. The intensity and contrast of Figures 1 and 2 are not adjusted in the same scale as evidenced by the soft tissue uptake on MIP images and myocardial uptake on the bottom images. Such discrepancy of image processing can easily lead to the subjective interpretation of patterns “focal on diffuse”, “diffuse” and “isolated lateral wall and/or basal uptake” as shown as Figure 1B, 2B and 2C. For example, we would think the “isolated lateral” and “isolated lateral and basal” shown in Figure 2B fits more into the authors “focal on diffuse” category.

And, we consider different way of interpretation of “focal on diffuse” as being active CS. First, the focal uptake in the background of diffuse uptake could be physiological papillary muscle uptake in the setting of failed suppression of physiological myocardium uptake, and papillary muscle activity has the pattern of protruding inwards, as shown in their Figure 1B. Second, a active hypermetabolic CS lesion cannot be differentiated from unsuppressed

background physiological FDG avidity in the myocardium. For the same reason, the “diffuse” pattern cannot be interpreted as “not consistent with active CS”. Rather, we believe the the “focal on diffuse” actually is “diffuse” and should be “indeterminate for CS” (9).

The lack of optimal suppression of myocardial background FDG uptake, at least in part, accounts for the intra- and inter- observer variability in the authors study. In our experience, even a 24-hour pretest low-carb diet preparation is inadequate to provide consistent myocardial suppression of physiological FDG uptake, and 72-hour diet preparation protocol had a satisfying results (9). We believe that with a modified patient preparation protocol and image categorization, the authors would have achieved even greater intra- and inter- observer agreement. Imaging of cardiac sarcoidosis remains challenging. Long-term prospective multicenter clinical trials are required to further validate the optimal PET imaging protocol.

- (1) Ohira H, Mc Ardle B, deKemp RA, Nery PB, Juneau D, Renaud JM et al. Inter- and Intra-observer agreement of FDG-PET/CT image interpretation in patients referred for assessment of Cardiac Sarcoidosis. J Nucl Med 2017 doi: 10.2967/jnumed.116.187203 [Epub ahead of print].
- (2) Morooka M, Moroi M, Uno K, Ito K, Wu J, Nakagawa T et al. Long fasting is effective in inhibiting physiological myocardial 18F-FDG uptake and for evaluating active lesions of cardiac sarcoidosis. EJNMMI Res 2014;4:1.
- (3) Bartlett ML, Bacharach SL, Voipio-Pulkki LM, Dilsizian V. Artifactual inhomogeneities in myocardial PET and SPECT scans in normal subjects. J Nucl Med 1995;36:188-95.
- (4) Gropler RJ, Siegel BA, Lee KJ, Moerlein SM, Perry DJ, Bergmann SR et al. Nonuniformity in myocardial accumulation of fluorine-18-fluorodeoxyglucose in normal fasted humans. J Nucl Med 1990;31:1749-56.
- (5) Ishida Y, Yoshinaga K, Miyagawa M, et al. Recommendations for (18)F-fluorodeoxyglucose positron emission tomography imaging for cardiac sarcoidosis: Japanese Society of Nuclear Cardiology recommendations. Ann Nucl Med. 2014;28(4):393-403..
- (6) Patel MR, Cawley PJ, Heitner JF, Klem I, Parker MA, Jaroudi WA et al. Detection of myocardial damage in patients with sarcoidosis. Circulation 2009;120:1969-77.
- (7) Youssef G, Leung E, Mylonas I, Nery P, Williams K, Wisenberg G et al. The use of 18F-FDG PET in the diagnosis of cardiac sarcoidosis: a systematic review and metaanalysis including the Ontario experience. J Nucl Med 2012;53:241-8.
- (8) Schatka I, Bengel FM. Advanced imaging of cardiac sarcoidosis. J Nucl Med 2014;55(1):99-106.
- (9) Lu Y, Grant C, Xie K, Sweiss NJ. Suppression of Myocardial 18F-FDG Uptake Through Prolonged High-Fat, High-Protein, and Very-Low-Carbohydrate Diet Before FDG-PET/CT for Evaluation of Patients With Suspected Cardiac Sarcoidosis. Clin Nucl Med 2017;42:88-94.