EDITORIAL

Does simplified quantitative analysis of ^{18}F-FDG PET in cardiac inflammatory disease work?

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The versatile substrate utilization of healthy myocardium is a persistent challenge when contemplating the use of ^{18}F-labeled fluorodeoxyglucose (^{18}F-FDG) for the depiction of cardiac inflammatory disease.[1,2] Strategies aiming at refraining from glucose utilization in the normal myocardium in a way to contrast with abnormal inflammatory processes (that exclusively rely on carbohydrates as metabolic substrate) have been advocated. The main stem of using prolonged fasting of at least 12 hour to even above 18 hour alone, fatty meals or unfractionated heparin as a means to promote hepatic release of free fatty acids, has enabled a more predictable metabolic suppression of the normal myocardium.[3-5]

The detection of sarcoidosis, a systemic inflammatory disease characterized by non-necrotizing granuloma and with cardiac involvement in 20%-50% of cases that affects survival,[6,7] has benefited from these metabolic suppression interventions. This is attested by the growing evidence supporting possible diagnosis of this condition with cardiac ^{18}F-FDG PET[8] giving at the same time sizable information on prognosis[9] and on monitoring medical treatment.[10]

Consensus is expected to promote standardized clinical scenarios, imaging preparation, acquisition, and reporting procedures so as to deliver the best level of evidence in favor of an added value of ^{18}F-FDG PET in the diagnosis and management of such conditions.[11-13] A key component lies in quantifying the extent of the inflammatory process in a manner that enables pooling of data among institutions and low variability for repeated measurements.

As opposed to PET myocardial perfusion or viability imaging, semiquantitative analysis of cardiac inflammatory disease using PET deals with a high background activity as compared to the myocardium, which is less favorably displayed using activity polar maps. Metabolic substrate utilization switch and inhomogeneous myocardial uptake on repeated examinations also hamper the comparison of standard semiquantitative assessment using standardized polar maps. Along with visual qualitative interpretation of the static images, a number of image-derived PET metrics have been proposed in clinical oncology to achieve the common goal of objective and reproducible quantification of tracer uptake across vendors and over time that can also be applied to cardiac inflammatory PET studies:[14,15]

– Basic first-order metrics provide a semiquantitative value reflecting tracer uptake in the hottest voxel (SUV_{max})[16] or mean over a 1 mL spherical volume of interest (VOI) centered at the hottest voxel (SUV_{peak}).[14] The former metric is strongly affected by image noise and provides limited information about the extension of abnormal activity.

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- Second-order metrics (SUV$_{mean}$, MTV, TLG) add a refinement through definition of tumor volumes using either manual delineation (prone to large intra- and interobserver variability) or semi- or fully automated PET image segmentation techniques (usually provide better reproducibility of results).[10,17,18]
- Third-order metrics (textural features and radiomics) remain an active field of research aiming at capitalizing on the heterogeneity of tracer uptake and its textural features within the selected VOI to discriminate patterns of disease.[19,20]
- The most advanced quantification techniques rely on the use of parametric imaging derived from dynamic imaging and simplified or more complex compartmental modeling techniques in a way similar to coronary flow reserve quantification.[21,22]

The article of Manabe et al. in this issue of the Journal of Nuclear Cardiology is in line with the trend toward standardization of quantitative analysis.[23] The authors retrospectively analyzed 190 consecutive patients referred for general inflammatory or oncologic indications. A second-order metric, referred to as the volume of cardiac metabolic volume (CMV), derived from a PET activity threshold related to nearby background activity within a ROI defined in the liver, the left ventricle (LV), or the descending aorta (DA). Analysis was performed to determine the most suitable reference ROI characterized by less interdependency with CMV and with the extent of fasting which is an important quality parameter of cardiac inflammatory PET examinations. DA aroused as the ROI of choice with less CMV value dependency as compared to LV and no variation over time as opposed to the value of liver ROI, which significantly increased with prolonged fasting. Such contribution is of great importance since it provides us with a means to more reproducibly quantify abnormal cardiac metabolic volumes using a second-order metric that integrates information on the extent of the disease process, more robust than the mere SUV$_{max}$ routinely reported in most imaging centers. Adopting CMV and DA ROI could be easily implemented in the daily routine and have the advantage of keeping with the conventional throughput of patients injected with the radioactive tracer one hour before starting the acquisition.

In the meantime, several leaps forward in the concept of dynamic PET acquisition have occurred that increased the robustness of ^{18}F-FDG PET quantification during early post-injection phase. Improving quantification through early dynamic imaging and extrapolation of delayed regional activity from tissue tracer kinetics could obviate the need for conventional one-hour post-injection acquisition. Some of the technical advances that would enable such paradigm shift are extended axial field of view that would more reliably position the heart in the center of the field of view where count sensitivity is the highest, or continuous bed motion acquisition that would reduce axial sensitivity inhomogeneity and enable dynamic imaging on multiple bed positions.[24] The improved detector sensitivity and time-of-flight resolution implemented in the latest digital PET systems could also contribute to improved signal-to-noise ratio as suggested by preliminary results.[25]

Trends are evolving toward using the most relevant metrics available in PET quantification and evidence is gathering toward preferring dynamic imaging for this purpose. Yet, for diseases presenting with low incidence rates, such as cardiac inflammatory processes making the proof of an added clinical value of the more advanced quantification tools using dynamic imaging will take a tremendous amount of time. In this context, comparison of historical, contemporary, and future ^{18}F-FDG cardiac inflammatory PET studies using refined second-order metrics as emphasized by Manabe et al.[23] in this issue of the Journal of Nuclear Cardiology might provide a common reporting ground and enable pooling of data and experience over time.

Disclosure

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