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Reply: On Semiquantitative Methods for Assessing Vascular ^{18}F-FDG PET Activity in Large-Vessel Vasculitis

REPLY: We were pleased that discussion was brought forth by Laffon and Marthan because of our recent paper on quantitative and qualitative ^{18}F-FDG PET for large-vessel vasculitis (LVV) (*1*). Indeed, we agree it could be revealing to attempt a measurement strategy that involves the appreciation of the hottest N number of voxels (SUV_{max-N}) as proposed by the authors. If N is greater than the number of single SUV_{max} measurements from each region of interest drawn over the entire arterial tree, SUV_{max-N} could lead to an overall more reproducible value in addition to a potentially greater contribution of abnormal activity in regions of active vasculitis than in regions without inflammation.

Although specific methodology to quantify vascular inflammation will no doubt be tested and refined, we would like to emphasize our underlying thought process for the design of our quantitative methodology, with reference to how this and other strategies for quantitative PET might be used for LVV. We will organize our discussion around 3 questions: What can be deployed clinically? What is most useful in clinical trials? What are we trying to do with vascular imaging in LVV?

For clinical deployment (question 1), even with the recent advent of greater acceptance of ^{18}F-FDG PET in clinical evaluation of inflammatory disease (*2*), we acknowledge that large-vessel vasculitis is a rare disease that many interpreting physicians will not encounter frequently. Our experience is that extensive familiarity and care are necessary to rigorously apply a complex quantitative strategy that involves contouring of the arteries as applied in this study, which did not have the advantage of intravenous contrast medium for guidance. Regardless of how the specific voxels are aggregated mathematically, the contouring itself is likely to be beyond the abilities of the standard medical professional in routine clinical practice. Hence, our introduction of a qualitative metric such as PETVAS (*3*), which is similar, but not identical, to the emerging use of an ordinal scoring system in lymphoma (*4*). We showed that PETVAS is a reasonable clinically deployable alternative to what we felt was an inevitable question from the community, which is "why not use SUVs?" Another compelling reason to not yet favor the use of metrics such as SUV in the clinic for LVV relates to the common misapplication of quantitative metrics from the literature for sensitivity and specificity in image interpretation. The performance characteristics of a quantitative metric are appropriately applied if images can be reproduced in a uniform format, which must be standardized across vendors with identical imaging characteristics that harmonize important features such as resolution, noise, voxel size, and postreconstruction filtering. Despite recent meaningful attempts (*5*), such a level of uniform standardization will likely not soon be achievable in clinical practice.

For clinical trials (question 2), we see a role for complementary advanced quantitative strategies as we and others have proposed. Clinical trials more often involve multiple imaging time points of the same subject before and after a treatment or intervention, using the same imaging characteristics. Our project highlighted that both qualitative and quantitative methods are associated with clinical measures of disease activity, and both approaches could be used to facilitate discovery in research; however, qualitative approaches potentially offer more precision and reliability.

Regarding question 3, it may sound odd to ask "what are we actually trying to do?" As investigators conducting an ongoing, large prospective observational cohort study on LVV, we would like to emphasize that interpretation of ^{18}F-FDG PET findings should be considered in the context of disease activity assessment across other domains. ^{18}F-FDG PET is only 1 facet of the multidisciplinary approach needed to fully realize patient-specific treatment guidance. Comprehensive clinical, laboratory, and imaging assessment is often helpful to accurately assess disease activity and inform management decisions. The cumulative burden of vascular involvement does not always correlate with clinical outcomes. A small focal inflammatory lesion in a single artery may lead to severe vascular damage with disastrous consequences, whereas profound near pan-arterial intense inflammation may occur in an otherwise asymptomatic patient. To inform the details of a better qualitative or quantitative evaluation for individualized care with advanced methods proposed by our group or others, we must continue to define the complex associations between ^{18}F-FDG PET findings and clinical outcomes in LVV. Controlled environments, such as randomized clinical trials, will go further to answer questions related to the combinatory use of qualitative and quantitative PET, as well as specifics for the production of each.

DISCLOSURE

REFERENCES

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