FDG PET in infective endocarditis: There are still horizons to conquer

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Despite advances in PET/CT and PET/MR, the diagnosis of infective endocarditis (IE) remains a challenge. The European Society of Cardiology Guidelines (ESC) on the prevention, diagnosis, and treatment of IE from 2009[1] and 2015[2] reflect a clear shift in the role of radionuclide imaging. The recent guidelines indicate radionuclide imaging to be beneficial in unclear cases of prosthetic IE (PVE) more than 3 months after implantation and in detection of embolic foci in native valve IE (NVE). Of note, leukocyte scintigraphy was recognized in these guidelines as a substitute to PET.[3] The American Heart Association guidelines from 2015 acknowledged a potential role of PET but called for more evidence.[4]

The playing field of nuclear medicine in IE is growing, but there are still limitations. PET is not meant to substitute for clinical evaluation, echocardiography, and modified Duke Criteria (mDC). But incorporating the findings of radionuclide imaging into mDC can substantially increase their accuracy[5] and this principle was adopted by the aforementioned ESC guidelines.

In a meta-analysis by Kamani et al.[6] on pooled data from 351 episodes of NVE, the overall sensitivity was 36% and specificity 99% for PET. This low sensitivity was observed in the majority of previous studies[7–10] and therefore a negative PET scan should not lead to the exclusion of NVE.

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The suboptimal performance of PET in NVE diagnosis is explained by the small size of vegetations, higher mobility of the valve leaflets, lower inflammatory activity, antibiotic therapy, and insufficient physiological myocardial accumulation suppression of FDG.[11]

The study by Abikhzer et al.[12] however, showed a much better sensitivity of PET in NVE. This study in 54 subjects with suspected NVE (confirmed in 31 cases) showed the sensitivity of PET to be 68% and the specificity 100%. The inclusion of PET result as a major criterion in mDC increased their sensitivity from 48% to 77% and led to correct reclassification of 8/18 subjects from the category of possible IE to definitive, without impacting on the specificity.

In this issue of the Journal of Nuclear Cardiology, Primus et al. bring another piece into the mosaic of data describing the potential of PET in the diagnosis of IE.[13] They present a dual-center retrospective study assessing the value of FDG PET in a consecutive real-life cohort of patients examined for the suspicion of IE. The patient group was mixed comprising 32 patients with suspected NVE and 37 patients with suspected PVE. All but one patient had undergone transoesophageal echocardiography before PET imaging. Microbiological sampling was taken as a gold standard in patients treated by surgery. Multidisciplinary consensus in the Endocarditis Team (ET) reviewing complex follow-up data served as a reference for the patients treated medically. Dietary preparation combined with unfractionated heparin was used to suppress physiological accumulation of FDG in the myocardium; the cases with unsatisfactory suppression were excluded. Antibiotic therapy before PET was allowed in the patients (overall in 71% of patients, with median length of 21 days in cases of NVE and 17 days in PVE).

The evaluation of images was performed by 2 independent readers, and discrepancies were solved in consensus. The pattern of uptake was taken as interpretation criterion. The verdict was binary for each case,

stating the presence or absence of IE. Focal or heterogenous distribution of FDG was interpreted as IE.

The results of the study bring two main messages. Firstly, it supports the previous experience with FDG PET in PVE. The sensitivity and specificity for PVE were 87% and 86%, respectively. Incorporating PET result into mDC led to correct reclassification of 16/19 indeterminate cases with a gain in AUC and net reclassification index (NRI) of 0.90 indicating FDG PET/CT to be a beneficial test.

The second message is more surprising. In contrast to most of the previous literature, the authors showed a very promising potential of FDG PET/CT for the diagnosis of NVE. The sensitivity and specificity were 75% and 92%, respectively. As with PVE, the performance of mDC significantly improved if the PET data were included as major criteria. Ten of twelve equivocal cases were correctly reevaluated, the AUC improved from 0.775 to 0.883 and the reclassification index was 0.89.

Looking at the results of the study of Primus et al., we should search for the reasons for relatively substantial variance of the performance of PET in NVE when comparing with the previous studies. The authors highlight very rigorous use of transoesophageal echocardiography in their work-up which was repeated before PET to identify valve dysfunction. They have accomplished good level of myocardial suppression in their study cohort—the evaluation of valve uptake was possible in all included cases. They did not observe any relation of PET accuracy to the duration of antibiotic therapy nor CRP values. This has led them to suggest that a prolonged time before PET could allow the development of more intense inflammatory reaction and thus more intense FDG uptake.

The limitations of this study are the small sample size, the CT part of their PET/CT scans was unenhanced as the use of CT contrast could further improve accuracy of hybrid examination.[14] Then there is the issue of the interpretation criteria. It is not only the pattern but also a visual intensity of uptake that should be defined and some threshold should be provided. Conversely, in a recent study from Gazzili et al., only focal uptake exceeding the activity of healthy liver parenchyma was used as diagnostic criterion for IE in a retrospective series of FDG PET.[10] With this setting, high sensitivity and specificity was observed in the overall sample of 108 patients (93% and 91%) but low sensitivity of 23% was reached in a subset of patients with NVE. Interpretation of PET/CT in IE should probably include the visual evaluation assessing the intensity of uptake, its pattern, and also CT findings as it was previously proposed in the diagnosis of vascular graft infections.[15] Quantification did not bring any additional value in the present study.

FDG PET/CT is an established modality for the diagnosis of PVE, recognized in the guidelines issued in European territory.[2,16] It is gaining importance also in the USA, also becoming part of the relevant guidelines[17] and breaking some barriers in the reimbursement recently (https://www.snmmi.org/NewsPublications/NewsDetail.aspx?ItemNumber=37156). Its role beyond septic embolization detection in NVE and eventually in the diagnosis of cardiac implantable electronic devices infection require robust prospective studies. Overall performance of PET/CT in the diagnosis of IE could further improve in the future with the oncoming new generation large field of view cameras and eventually with more infection-specific radiopharmaceuticals. The future seems to be bright for PET in IE.

Disclosures

The author declares no potential conflicts of interest regarding the publication of this article.

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