Diagnostic performance and image interpretation of ^{18}F -FDG PET/CT in aortic graft infection: Two sides of the same coin

Giorgio Treglia, MD, MSc,^{a,b,c} Riemer H. J. A. Slart, MD, PhD,^{d,e} and Andor W. J. M. Glaudemans, MD, PhD^d

^a Clinic of Nuclear Medicine, Imaging Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Switzerland

^b Department of Nuclear Medicine and Molecular Imaging, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

^c Health Technology Assessment Unit, Academic Education, Research and Innovation Area, General Directorate, Ente Ospedaliero Cantonale, Bellinzona, Switzerland

^d Department of Nuclear Medicine & Molecular Imaging, Medical Imaging Center, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

^e Department of Biomedical Photonic Imaging, Faculty of Science and Technology, University of Twente, Enschede, The Netherlands

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Treatment of aortic diseases (aneurysms, stenosis) using aortic grafts has gained popularity over the past decades. Aortic graft infection (AGI) is fairly uncommon but the incidence of AGI is increasing due to a growing number of aortic graft procedures which will even increase more in the coming future as the easier “closed” aorta repair (EVAR/TVAR) has become available to repair aortic diseases also in elderly people.¹ AGI is one of the most devastating and challenging complications encountered by vascular surgeons as it is associated with significant morbidity and mortality; therefore, a prompt diagnosis is mandatory for a successful treatment.¹

Surgical, radiological and laboratory major criteria have been identified for the diagnosis of AGI.² Surgical major criteria include intraoperative identification of pus around a graft and situations where direct communication between the graft and a non-sterile site exists; radiological major criteria comprise increasing perigraft gas volume on serial computed tomography (CT) imaging or perigraft gas or fluid after the implantation; laboratory major criteria comprise isolation of microorganisms from percutaneous aspirates of perigraft fluid, explanted grafts, and other intraoperative specimens.² However, a perigraft abscess or fluid collection is not always present or accessible for biopsy in patients with AGI,² hampering a prompt diagnosis of AGI using standard diagnostic criteria.

Fluorine-18 fluorodeoxyglucose positron emission tomography/CT (^{18}F -FDG PET/CT) is emerging as a very useful imaging method for early detection of cardiovascular infectious and inflammatory diseases due to the increased uptake of ^{18}F -FDG in activated leukocytes and in other inflammatory cells such as lymphocytes, macrophages, and giant cells.^{3–5} The application of ^{18}F -FDG PET/CT in infectious and inflammatory diseases is provided in the EANM/SNMMI guideline published in 2013.⁶ Recent evidence-based articles have demonstrated the overall good diagnostic performance of ^{18}F -FDG PET or PET/CT for the diagnosis of vascular graft infection, including AGI (Table 1).^{7–9} All the published meta-analyses are concordant about the high sensitivity

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Reprint requests: Giorgio Treglia, MD, MSc, Health Technology Assessment Unit, Academic Education, Research and Innovation Area, General Directorate, Ente Ospedaliero Cantonale, Via Lugano 4F, 6500 Bellinzona, Switzerland; giorgiomednuc@libero.it

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Table 1. Published meta-analyses about the diagnostic performance of ¹⁸F-FDG PET or PET/CT in vascular graft infection

Authors	Year	Focus of the analysis	Articles included	Pooled sensitivity (95% CI)	Pooled specificity (95% CI)	Pooled positive likelihood ratio (95% CI)	Pooled negative likelihood ratio (95% CI)	Pooled diagnostic odds ratio (95% CI)
Kim et al ⁷	2019	PET and PET/CT	10	96% (89-98)	74% (67-81)	3.7 (2.9-4.9)	0.06 (0.02-0.15)	63 (23-173)
Rojas et al ⁸	2019	Graded ¹⁸ F-FDG uptake	6	89% (73-96)	61% (48-74)	2.32 (1.27-4.22)	0.17 (0.06-0.53)	13.2 (3.1-56.6)
		Focal ¹⁸ F-FDG uptake	7	93% (83-97)	78% (53-92)	4.3 (1.7-10.9)	0.89 (0.03-0.25)	48.7 (9.6-246)
		Semi-quantitative analysis	6	98% (42-99)	80% (70-88)	4.98 (3.12-7.94)	0.03 (0-1.54)	176.7 (3-10479)
Reinders	2018	PET only	4	94% (88-98)	70% (59-79)	NR	NR	28.4 (7.8-102.7)
Folmer et al ⁹		PET/CT	5	95% (87-99)	80% (69-89)	NR	NR	38 (8.5-170.4)

95% CI 95% confidence interval, NR not reported

and reasonable specificity of ¹⁸F-FDG PET or PET/CT in this setting, independently from the different image analysis (qualitative or quantitative) used for the diagnosis, but false positive and false negative results should be taken into account.⁷⁻⁹ In particular, reactive ¹⁸F-FDG uptake in inflammatory cells around the vascular graft can mimic infection and it is a well-known confounder of ¹⁸F-FDG PET image interpretation, in particular in cases of recent surgery.⁷⁻⁹ Interestingly, it has been demonstrated that the combination of ¹⁸F-FDG PET/CT reduces the false positive and false negative results compared to ¹⁸F-FDG PET only.⁹ The evidence-based articles available so far suggested that the diagnostic performance of ¹⁸F-FDG PET/CT for vascular graft infection should be examined in aortic and peripheral grafts separately, since it may vary significantly according to the graft location.⁷⁻⁹

To date, even if we have increasing evidence-based data about the diagnostic performance of ¹⁸F-FDG PET/CT in AGI, a major concern remains the lack of standardized and evidence-based interpretation criteria of ¹⁸F-FDG PET/CT images as there is a remarkable variability in the parameters used among the published studies to analyze the ¹⁸F-FDG PET images.⁷⁻⁹ The most commonly used parameters for ¹⁸F-FDG PET/CT image interpretation include the pattern of ¹⁸F-FDG uptake (focal/diffuse), the visual grading scale (VGS), the maximal standardized uptake value (SUV_{max}), the tissue to background ratio (TBR), or a combination of them.^{8,9} Furthermore, ¹⁸F-FDG PET/CT interpretation still depends on the expertise of the reader.⁷⁻⁹

The article of Einspieler et al recently published in the Journal of Nuclear Cardiology provides additional interesting findings about the diagnostic performance and image interpretation of ¹⁸F-FDG PET/CT in patients with suspicious AGI.¹⁰ In this retrospective single-center study, the authors compared different qualitative and quantitative ¹⁸F-FDG PET/CT parameters in a quite large patient population (n = 50) with suspicious AGI, of which eventually 28 had a proven infection. ¹⁸F-FDG PET/CT demonstrated a high (> 90%) diagnostic accuracy in patients with AGI considering SUV_{max} as quantitative measure and a modified five-point VGS as qualitative measure (taking into account both ¹⁸F-FDG uptake pattern around the graft and the ¹⁸F-FDG uptake in the liver as reference). Congruent and accurate findings were found by using SUV_{max} and VGS in about 87% of patients. Background and/or time corrected SUV were not superior to simple SUV_{max} measurements with respect to diagnosis of AGI.¹⁰

It should be underlined that, since quantitative ¹⁸F-FDG PET criteria have not proven to be powerful enough for the diagnosis of AGI, due to the high variability of the cut-off value of SUV_{max} or SUV_{max} ratio

against the background, visual assessment of ^{18}F -FDG PET/CT findings is still indispensable.^{7–9} Notably, the study of Einspieler et al. suggests that multiparametric assessment by means of qualitative and quantitative ^{18}F -FDG PET evaluation could overcome the limitations of single mode evaluation for the diagnosis of AGI but this should be confirmed by prospective and multicenter studies.

Beyond the diagnostic performance of ^{18}F -FDG PET/CT in AGI, it should be taken into account that this imaging method may detect additional infectious/inflammatory findings throughout the body in some patients with suspicious AGI as also confirmed by the study of Einspieler et al.¹⁰

As a commonly accepted opinion, false negative results of ^{18}F -FDG PET may occur because of the use of antibiotics prior to imaging, thus reducing the metabolic activity expected in infections and suppressing the ^{18}F -FDG uptake around the vascular graft.^{7–9} Surprisingly, however, Einspieler et al found that antibiotic treatment did not have a substantial impact on sensitivity of ^{18}F -FDG PET/CT with respect to AGI diagnosis.¹⁰ This controversial finding should be better elucidated in the future. Even type and location of aortic repair did not have a substantial impact on the diagnostic performance of ^{18}F -FDG PET/CT in patients with suspicious AGI.¹⁰

Interestingly, ^{18}F -FDG PET/CT has a significant impact on the clinical management in more than half of patients with a history of aortic repair and clinical suspicion of AGI;¹⁰ this information would suggest its use as initial imaging technique for diagnosis of AGI.¹⁰ Nevertheless, the standardization of ^{18}F -FDG PET/CT and a consensus about the parameters used for image interpretation are needed to use this technique as a valuable diagnostic imaging method in patients with suspicious AGI. In particular, multicenter studies on a large number of patients, including reliable gold standards, are warranted to further validate the diagnostic performance of ^{18}F -FDG PET/CT in this setting and the use of both qualitative and quantitative assessment as suggested by Einspieler et al. Furthermore, some other issues still have to be further investigated, e.g., if there are differences in the value of ^{18}F -FDG PET/CT between the classical “open” aorta repair and the nowadays more often used “closed” EVAR/TVAR procedures, or between central and peripheral aortic grafts. In the peripheral grafts, there might still be a role for white blood cell (WBC) scintigraphy, so also studies evaluating both ^{18}F -FDG PET/CT and WBC scans in patients with suspected peripheral graft infections are still necessary.⁹

Future perspectives should also include the use of textural analysis to characterize ^{18}F -FDG uptake

heterogeneity in patients with suspicious AGI. A retrospective study demonstrated that textural analysis of ^{18}F -FDG PET/CT images is feasible showing promising results in diagnosing AGI, but it requires additional external validation and refinement before it can be implemented in the clinical decision-making process.¹¹

Disclosures

The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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