FDG-PET for the detection of infection in left ventricle assist device: Is there light at the end of the tunnel?

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LEFT VENTRICULAR ASSIST DEVICES

Over the past decade, the use of continuous-flow left ventricular assist devices (LVAD) has increased at a rapid pace. In the United States, approximately 2400 LVAD are implanted annually[1] and more than 16,000 patients have already received a continuous-flow LVAD.[2] These devices are a life-saving option for advanced heart failure patients who are either not eligible for a heart transplant or too ill to safely wait for a transplant on medical therapy alone. LVAD constitute the following components: (1) an inflow cannula surgically implanted into the left ventricular apex that extracts the blood from the left ventricle (LV) into the pump; (2) a pump enclosure with an impeller that circulates blood; (3) an outflow graft that pulses back the blood from the pump into the ascending aorta; and (4) a surgically tunneled driveline that connects the pump to an external controller that operates and monitors the pump function. The external controller is connected by two power cables to a battery powered source or a power module. Survival rates of patients are continuously improving after implantation of LVAD, but the number of adverse events remains quite high. Approximately 80% of patients will have experienced a major adverse event in the first 2 years after LVAD implantation. The most frequent complications of LVAD are bleeding, infection, and arrhythmia.[3] LVAD infection starts usually at the entry point of the percutaneous driveline and extends from there progressively to the LVAD pump. In case of driveline infection, a new driveline can be implanted in another site and connected to the pump. In case of pump infection, replacing the LVAD pump is challenging because of the development of tight adhesions between the system and the heart. The only remaining option is to try to control the progression of pump infection with long-term systemic antibiotherapy and consider urgent cardiac transplant in eligible patients. The precise evaluation of the extent of infection in the LVAD system is, therefore, key to guide the clinical management of these patients.

NUCLEAR IMAGING FOR THE DETECTION OF LVAD INFECTION

White blood cell (WBC) SPECT and FDG-PET have both demonstrated their values for the detection of infection in cardiac implantable electronic devices and prosthesis[4] and might thus prove useful for the evaluation of LVAD. On the one hand, WBC SPECT was the first to be evaluated in this indication in a small study including eight patients with a suspicion of LVAD infection.[5] The accumulation of radiolabeled WBC was found highly specific for LVAD infection in this small cohort of patients and allowed for the identification of the extent of infection along the device. The logistics for WBC SPECT imaging are, however, quite demanding for Nuclear Medicine departments with the need to handle blood and radiolabeled cells in a hot lab under sterile conditions, and for patients who undergo two

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SPECT imaging sessions 4 and 24 hours after the injection of radiolabeled WBC. The late imaging sessions allow for the evaluation of WBC accumulation in the LVAD system with low residual blood signal and provide a higher specificity for the detection of infection than the earlier time point. Nevertheless, WBC SPECT can help to monitor over time the efficacy of antibiotherapy on the infective process. On the other hand, FDG-PET presents the advantages of short imaging session (less than 2 hours) and absence of blood handling. It also provides whole body imaging with high signal that can help to identify other causes of bacterial sepsis than the infection of the LVAD device in these fragile patients. FDG-PET has, however, some caveats for the evaluation of patients with LVAD. The distinction between infective and inflammatory processes can be difficult. In particular, the cardiac region surrounding the pump should be analyzed with caution, as inflammatory reactions might take place in the region where the cannula is inserted. In addition, physiologic myocardial FDG uptake may obscure signal from structures in close vicinity with the myocardium, in particular the regions where the graft is inserted into the myocardium. Preparation of patients with high-fat low-carbohydrate diet and 12 hours fasting should be considered to suppress FDG uptake in the myocardium and improve image quality. Furthermore, signal quantification might be affected by overcorrection of the PET signal caused by streaking artifacts around the pump on the low-dose CT or misregistration of drivelines between PET and CT acquisitions. A careful evaluation of the aspects of the low-dose CT and non-attenuation corrected PET acquisitions should thus be performed when interpreting FDG-PET images in this clinical situation. Until now, only a limited number of studies[6–9] have evaluated the diagnostic performance of FDG-PET imaging for the detection of LVAD infection. The study of Kanapinn et al.[10] published in this issue illustrated nicely how FDG-PET might find a role in the identification of LVAD infection.

DIAGNOSTIC CRITERIA FOR LVAD INFECTION USING FDG-PET IMAGING

Kanapinn et al.[10] identified retrospectively 30 patients imaged twice with FDG-PET among 211 patients implanted with LVAD in their institution. The first FDG-PET acquisition had been performed to exclude the presence of malignancy before registration on the list for cardiac transplantation. FDG-PET was repeated in patients with a suspicion of LVAD infection. They found based on receiver operating curves that the best threshold to identify LVAD infection was an increase of 3.9 in the max. SUV between the first and second FDG-PET acquisitions. One of the limitations of their approach is the need for a baseline FDG-PET imaging, which seems difficult to implement for all patients implanted with LVAD. Interestingly, the correlation between the increase in SUV max. between the two FDG-PET acquisitions and max. SUV measured on the second FDG-PET imaging was excellent. The identification of a threshold of max. SUV associated with high probability of LVAD infection might thus be achievable. In a similar work, Avramovic et al.[7] found that the quantification of global metabolic activity in the driveline on PET performed slightly better than max. SUV for the detection of infection. Interestingly, Dell'Aquila et al.[9] confirmed that the diagnostic performance of FDG-PET is excellent for the detection of driveline infection, but lower for pump infection. The results of these retrospective studies suggest that the probability of driveline infection is high in presence of intense FDG uptake (max. SUV $>$ 7-8) on PET, but these diagnostic criteria will need to be validated in multi-centric prospective studies with a larger number of patients. In the similar way as with patients with a suspicion of PVE,[11] WBC SPECT might be useful for patients with inconclusive FDG-PET, either in patients with borderline FDG uptake values or in the pump region where the precise analysis and quantification of FDG uptake is more difficult.

WHICH ROLE FOR FDG-PET IMAGING IN THE MANAGEMENT OF LVAD INFECTION?

This study also raises questions on the possible role of FDG-PET for the clinical management of patients with a suspicion of LVAD. Should patients with distal and proximal infection of the driveline be managed the same way? Is the intensity of FDG uptake and its extent in LVAD relevant to guide the choice between systemic antibiotherapy and the replacement of the driveline? Can FDG-PET help to monitor the efficacy of antibiotherapy in LVAD? In theory, the best way to test the clinical value of FDG-PET imaging in these clinical situations would be to set up prospective randomized studies that would compare patient outcome in two groups, one group of patients with access to FDG-PET imaging and the other group managed without. This kind of studies is, however, often difficult to run in critically ill patients, for whom the physicians in charge of the patient are often not ready to deny access to an already clinically approved imaging modality for making difficult clinical decisions. A more realistic and easier way could be to build multicentric registries of patients with LVAD imaged with FDG-PET. The close monitoring of the development

and progression of infection in these patients might help to identify the criteria on FDG-PET associated with the risk of progression of driveline infection to the pump and, hence, identify patients who are the most likely to benefit from driveline replacement. For example, it would have been interesting to know in the initial cohort of 211 patients implanted with LVAD and imaged at least once with FDG-PET from Kanapinn et al.[10] the infection rate and the average delay between the imaging session and the development of infection depending on the aspects observed on PET. Before these data become available, the integration of FDG-PET in diagnostic and therapeutic strategies of patients with LVAD should be done carefully and, in a similar way to the management of patients with infective endocarditis, discussed in a multi-disciplinary team.[11]

Disclosure

Fabien Hyafil, François Rouzet, and Khadija Benali have nothing to disclose in relation to this editorial.

References

1. Kirklin JK, Naftel DC, Pagani FD, et al. Seventh INTERMACS annual report: 15,000 patients and counting. J Heart Lung Transpl. 2015;34(12):1495–504.
2. Gordon RJ, Weinberg AD, Pagani FD, et al. Prospective, multicenter study of ventricular assist device infections. Circulation. 2013;127(6):691–702.
3. DeVore AD, Patel PA, Patel CB. Medical management of patients with a left ventricular assist device for the non-left ventricular assist device specialist. JACC Heart Fail. 2017;5(9):621–31.
4. Habib G, Lancellotti P, Antunes MJ, et al. Esc guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the european society of cardiology (ESC). endorsed by: European association for cardio-thoracic surgery (EACTS), the European association of nuclear medicine (EANM). Eur Heart J. 2015;36(44):3075–128.
5. Litzler PY, Manrique A, Etienne M, et al. leukocyte spect/ct for detecting infection of left-ventricular-assist devices: preliminary results. J Nucl Med. 2010;51(7):1044–8.
6. Kim J, Feller ED, Chen W, Dilsizian V. Fdg Pet/Ct imaging for lvad associated infections. JACC Cardiovasc Imaging. 2014;7(8):839–42.
7. Avramovic N, Dell'Aquila AM, Weckesser M, et al. Metabolic volume performs better than suvmax in the detection of left ventricular assist device driveline infection. Eur J Nucl Med Mol Imaging. 2017;44(11):1870–7.
8. Dell'Aquila AM, Mastrobuoni S, Alles S, et al. Contributory role of fluorine 18-fluorodeoxyglucose positron emission tomography/computed tomography in the diagnosis and clinical management of infections in patients supported with a continuous-flow left ventricular assist device. Ann Thorac Surg. 2016;101(1):87–94 **discussion 94**.
9. Dell'Aquila AM, Avramovic N, Mastrobuoni S, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography for improving diagnosis of infection in patients on cf-lvad: longing for more 'insights'. Eur Heart J Cardiovasc Imaging. 2017. https://doi.org/10.1093/ehjci/jex158.
10. Kanapinn P, Burchert W, Körperich H, Körfer J. ^{18}F-FDG PET/CT-imaging of left ventricular assist device infection: a retrospective quantitative intrapatient analysis. J Nucl Cardiol. 2018. https://doi.org/10.1007/s12350-017-1161-z.
11. Hyafil F, Rouzet F, Le Guludec D. nuclear imaging for patients with a suspicion of infective endocarditis: be part of the team! J Nucl Cardiol. 2017;24(1):207–11.