Contrast-enhanced ^{18}F-FDG PET/CT to differentiate primary cardiac lymphoma from primary cardiac angiosarcoma

Luca Camoni, MSc [a] and Domenico Albano, MD [a]

[a] Nuclear Medicine, University of Brescia, Brescia, Italy

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In this issue of Journal of Nuclear Cardiology, Liu et al.[1] compare the diagnostic performances of 18fluorine-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) and Contrast-Enhanced CT (CECT) in the study of 9 primary cardiac lymphoma (PCL) and 8 primary cardiac angiosarcoma (PCA).

PCLs had higher FDG uptake expressed as mean standardized uptake value (SUVmean), SUVmax, metabolic tumor volume, total lesion glycolysis, and tumor-to-liver ratio compared to PCA. Also, enhancement pattern and morphology of tumor were significantly different. Thus, they demonstrated that the combination of ^{18}F-FDG PET/CT and CECT might improve the diagnostic accuracy; moreover, the addition of semiquantitative parameter cut-off (based on SUVmean) could further improve the performance.

PCL is an extremely rare tumor accounting for 1% of all cardiac tumors,[2] while considering also the cardiac involvement by systemic lymphoma the rate increases. Diffuse large B-cell lymphomas (DLBCLs) are the most common PCL. Although most malignant cardiac tumors are associated with a poor outcome, patients with cardiac lymphoma, especially DLBCL, can be cured if they are treated early and appropriately. Usually, they have a good response after chemotherapy. However, fatal outcome is described especially due to lethal arrhythmia, representing only 1.3% of all cardiac tumors.[3] Thus, an early detection of PCL is fundamental and impacts the patient management. Considering the potential risks related to cardiac biopsy and sometimes the difficulties to obtain biopsy specimen, a non-invasive diagnosis is desirable and in this field imaging tools may play a role.

The usefulness of 18F-FDG PET/CT in the study of HL and DLBCL is already remonstrated with strong evidences present in literature.[4,5] However, only promising results based upon PCL and 18F-FD PET/CT are available[6-8] due to the low samples of patients included. DLBCL is for definition an FDG-avid lymphoma presenting a high FDG uptake.

In the study of the heart, the high physiological myocardial FDG-uptake, may interfere with the interpretations of the PET images. Indeed, for the study of cardiac diseases (such as sarcoidosis and infective endocarditis) the suppression of physiological myocardial uptake with a specific diet is requested. Different strategies have been proposed to reduce physiological myocardial FDG uptake, included 12- to 18-h pretest fasting, pretest administration of unfractionated heparin[9], and overnight high-fat, but specific diet based upon high-fat, high protein, and low-carbohydrate diet seems to reach better results.[10-12]

Several studies in the literature demonstrated that although fatty acids represent the preferred energy substrate by myocytes under aerobic conditions, glucose is an alternative energy substrate; in fact, the Randle cycle (fatty acid–glucose cycle) has established that fatty acid suppresses glucose metabolism and that glucose conversely suppresses fatty acid utilization by the myocytes. Glucose is most commonly used in postprandial states and fatty acids are mostly used in fasting.

Beyond the patient preparation with low-carbohydrate fat-allowed diet (as performed by Liu et al.[1]), another factor that could influence the sensitivity of 18F-FDG PET/CT in diagnosis of heart masses is the choice of the acquisition time. It could be hypothesized that higher sensitivity could be achieved with delayed PET/

Reprint requests: Luca Camoni, MSc, Nuclear Medicine, University of Brescia, Brescia, Italy; *camoni.luca@gmail.com*
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CT imaging compared to the standard PET acquisition, usually performed 1h after FDG injection. Delayed FDG PET/CT imaging could provide a better target-to-background contrast due to the clearance of the background activity, as demonstrated in several clinical settings.[13-15]

This physiological uptake is typical in the left ventriculus, while PCLs are often located in the fight-side, especially around the right atrioventricular groove because the thoracic duct drains lymph into the superior vena cava and subsequently into the RA and ventricle,[16] but the ventricular localization is possible.

The other fundamental point underlined by Liu et al.[1] is the integration of PET/CT and CECT. Of course, CECT is a useful tool for obtaining detailed anatomical information in this regard, even more in a district-like mediastinum. Several morphological factors (surrounding tissue infiltration, epicardial infiltration, necrosis, multiple chambers or vessel involvement, and extracardiac lesions) may be evaluated with CECT and help the diagnostic process.

Liu et al.[1] derived a SUVmean threshold of 5.17 to help the prediction of diagnosis. The idea to apply semiquantitative parameter with the aim to improve the diagnostic performance is interesting and shareable, particularly if the goal is to make this kind of analysis reproducible. However, some issues are present and it seems more premature to share this specific cut-off with international community, where SUV harmonization study is still ongoing.[17,18] Indeed, SUV is the most widely commonly and generally accepted metabolic feature in the current published literature for the assessment of disease activity in lymphoma and cancers, but it is intrinsically affected by many factors.[19] The main is the uptake time (time between the radiotracer injection and imaging acquisition), the size of the lesion, the risk of extravasation of administered radiotracer at the site of injection, the decay of the injected activity, the potential residual activity in the syringe or device used, the type of scanner used, and the acquisition and reconstruction protocols (time of flight, point spread function,...). Due to these limitations, there was a need to introduce new metabolic features more robust and efficient and less influenced by other factors. So, some features which take into account both the size as well as the metabolic activity were introduced: metabolic tumor volume (MTV) and total lesion glycolysis (TLG). MTV is defined as the measurement of the volume of FDG-avid disease, while TLG is defined as MTV x SUVmean within the lesion. However, despite positive evidences in other lymphomas for PCL the findings are too premature and need further evaluations.

The possible application of artificial intelligence and a machine learning approach in the diagnostic imaging field and particularity in the study of PCL may help the evaluation of heart and improve the diagnostic accuracy. Moreover, the introduction of new PET scanner (digital PET/CT) with higher accuracy and resolution or the application of PET integrate with magnetic resonance imaging (PET/MRI)[20] may further have an impact in this field.

References

1. Liu E, Huang J, Dong H, Chen Z, Liu C, Xie Q, et al. Diagnostic challenges in primary cardiac lymphoma, the opportunity of 18F-FDG PET/CT integrated with contrast-enhanced CT. J Nucl Cardiol 2021. https://doi.org/10.1007/s12350-021-02723-6
2. Burke A, Tavora F. The 2015 WHO Classification of Tumors of the Heart and Pericardium. J Thorac Oncol 2016;11(4):441-52.
3. Bonelli A, Paris S, Bisegna S, Milesi G, Gavazzi E, Giubbini R, et al. Cardiac lymphoma with early response to chemotherapy: A case report and review of the literature. J Nucl Cardiol 2021. https://doi.org/10.1007/s12350-021-02570-5
4. Barrington SF, Mikhaeel NG, Kostakoglu L, Meignan M, Hutchings M, Müeller SP, et al. Role of imaging in the staging and response assessment of lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group. J Clin Oncol 2014;32(27):3048-58.
5. Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. J Clin Oncol 2014;32(27):3059-68.
6. Qin C, Shao F, Hu F, Song W, Song Y, Guo J, et al. (18)F-FDG PET/CT in diagnostic and prognostic evaluation of patients with cardiac masses: a retrospective study. Eur J Nucl Med Mol Imaging 2020;47(5):1083-93.
7. Meng J, Zhao H, Liu Y, Chen D, Hacker M, Wei Y, et al. Assessment of cardiac tumors by (18)F-FDG PET/CT imaging: Histological correlation and clinical outcomes. J Nucl Cardiol 2020. https://doi.org/10.1007/s12350-019-02022-1
8. Kikuchi Y, Oyama-Manabe N, Manabe O, Naya M, Ito YM, Hatanaka KC, et al. Imaging characteristics of cardiac dominant diffuse large B-cell lymphoma demonstrated with MDCT and PET/CT. Eur J Nucl Med Mol Imaging 2013;40(9):1337-44.
9. Scholtens AM, van den Berk AM, van der Sluis NL, Esser JP, Lammers GK, de Klerk JMH, et al. Suppression of myocardial glucose metabolism in FDG PET/CT: Impact of dose variation in heparin bolus pre-administration. Eur J Nucl Med Mol Imaging 2020;47(11):2698-702.
10. Gazzilli M, Albano D, Durmo R, Cerudelli E, Mesquita Tinoco C, Bertagna F, et al. Improvement of diagnostic accuracy of 18fluorine-fluorodeoxyglucose PET/computed tomography in detection of infective endocarditis using a 72-h low carbs protocol. Nucl Med Commun 2020;41(8):753-8.
11. Treglia G, Bertagna F. Factors influencing the sensitivity of 18F-FDG PET/CT in the detection of infective endocarditis. Eur J Nucl Med Mol Imaging 2013;40(7):1112-3.
12. Lu Y, Grant C, Xie K, Sweiss NJ. Suppression of myocardial 18F-FDG uptake through prolonged high-fat, high-protein, and very-low-carbohydrate diet before FDG-PET/CT for evaluation of patients with suspected cardiac sarcoidosis. Clin Nucl Med 2017;42(2):88-94.
13. Houshmand S, Salavati A, Segtnan EA, Grupe P, Høilund-Carlsen PF, Alavi A. Dual-time-point imaging and delayed-time-point fluorodeoxyglucose-PET/computed tomography imaging in various clinical settings. PET Clin 2016;11(1):65-84.

14. Pietrzak AK, Marszalek A, Kazmierska J, Kunikowska J, Golusinski P, Suchorska WM, et al. Sequential delayed [18 F]FDG PET/CT examinations in the pharynx. Sci Rep 2020;10(1):2910.
15. Pietrzak AK, Kazmierska J, Marszalek A, Cholewinski W. Evaluation of physiologic and abnormal glucose uptake in palatine tonsils: Differential diagnostics with sequential dual-time-point 2-deoxy-2-[18F]FDG PET/CT. Q J Nucl Med Mol Imaging 2020;64(3):299-306.
16. Petrich A, Cho SI, Billett H. Primary cardiac lymphoma: An analysis of presentation, treatment, and outcome patterns. Cancer 2011;117(3):581-9.
17. Kaalep A, Sera T, Rijnsdorp S, Yaqub M, Talsma A, Lodge MA, et al. Feasibility of state of the art PET/CT systems performance harmonisation. Eur J Nucl Med Mol Imaging 2018;45(8):1344-61.
18. Tsutsui Y, Daisaki H, Akamatsu G, Umeda T, Ogawa M, Kajiwara H, et al. Multicentre analysis of PET SUV using vendor-neutral software: The Japanese Harmonization Technology (J-Hart) study. EJNMMI Res 2018;8(1):83.
19. Kostakoglu L, Chauvie S. Metabolic tumor volume metrics in lymphoma. Semin Nucl Med 2018;48(1):50-66.
20. Krumm P, Mangold S, Gatidis S, Nikolaou K, Nensa F, Bamberg F, et al. Clinical use of cardiac PET/MRI: current state-of-the-art and potential future applications. Jpn J Radiol 2018;36(5):313-23.