PET/CT and interstitial lung disease

Marcio Valente Yamada Sawamura[1], Ronaldo Adib Kairalla[2], Carlos Alberto Buchpigel[1]

The combination of PET with CT enabled the acquisition of functional anatomical images with high resolution. PET/CT requires the administration of a radiotracer, ^{18}F-FDG being the most commonly used nowadays. ^{18}F-FDG is a glucose analog capable of demonstrating metabolic activity in organs and lesions on PET/CT. The major clinical application of ^{18}F-FDG PET/CT is in oncology, especially in tumor detection, staging, and diagnosis of residual or recurrent cancer, but it can also be used in order to evaluate cardiovascular diseases, brain disorders, and systemic diseases, such as inflammatory, vascular, and infectious diseases.[1,2]

In the present issue of the *Jornal Brasileiro de Pneumologia*, Bastos et al.[3] investigated the correlation of ^{18}F-FDG PET/CT with HRCT and inflammatory serological markers in patients with systemic sclerosis-associated interstitial lung disease (ILD) in a cross-sectional study involving 23 patients. Although the authors were unable to demonstrate significant differences in metabolic activity between inflammatory and fibrotic areas in the lungs of these patients, they shed a light on the use of PET/CT in ILD. In their study, both ground-glass opacities (GGO) and honeycomb areas on HRCT had a remarkable metabolic activity on ^{18}F-FDG PET/CT.[3] GGO is a challenging finding on HRCT, because it can represent partial filling of airspaces, interstitial thickening (due to fluid, cells, and/or fibrosis), partial collapse of alveoli, increased capillary blood volume, or a combination of these.[4] In the context of ILDs, one of the big questions regarding imaging is whether GGO represents inflammatory (and potential reversible) changes or early interstitial fibrosis; this could be valuable information for the management of these patients. One interesting result is that Bastos et al.[3] found a correlation between GGO on HRCT and serum levels of CCL2, an inflammatory mediator, known to stimulate inflammation and collagen production, which results in fibroblast proliferation and fibrosis. This finding corroborates the fact that GGO may indicate early fibrotic activity in such cases. The drawbacks of the data obtained from Bastos et al.[3] are that all patients had advanced ILD and the majority (17 out of 23) were being treated with prednisone, azathioprine, or methotrexate, which could influence cytokine levels and ^{18}F-FDG uptake on PET/CT.

The results of Bastos et al.[3] agree with those of other authors that investigated the use of ^{18}F-FDG PET/CT in idiopathic pulmonary fibrosis (IPF),[5] in the differentiation of IPF from a non-IPF IPD,[6] and in other ILDs.[7] As suggested by these studies,[5-7] ^{18}F-FDG PET/CT could not differentiate inflammatory and fibrotic changes in lung parenchyma but may have a role in the prognosis and follow-up of these patients. In sarcoidosis, several studies demonstrated the usefulness of ^{18}F-FDG PET/CT in staging, evaluating disease activity, and monitoring treatment response.[8]

Currently, specific biomarkers for PET/CT are increasingly being developed. One of them, ^{68}gallium-fibroblast activation protein inhibitor (^{68}Ga-FAPI) binds to fibroblast activation protein alpha, which is present in active fibroblasts but is negligible or absent in resting fibroblasts.[9] Although ^{68}Ga-FAPI is still in an initial research phase, this radiotracer might be a promising imaging agent for the evaluation of ILD progression and treatment response on PET/CT.

REFERENCES

1. Jones T, Townsend D. History and future technical innovation in positron emission tomography. J Med Imaging (Bellingham). 2017;4(1):011013. https://doi.org/10.1117/1.JMI.4.1.011013
2. Townsend DW. Combined positron emission tomography-computed tomography: the historical perspective. Semin Ultrasound CT MR. 2008;29(4):232-235. https://doi.org/10.1053/j.sult.2008.05.006
3. Bastos AL, Ferreira GA, Mamede M, Mancuzo EV, Teixeira MM, Santos FPST, et al. PET/CT and inflammatory mediators in systemic sclerosis-associated interstitial lung disease. J Bras Pneumol. 2022;48(4):e20210329.
4. Hochhegger B, Marchiori E, Rodrigues R, Mançano A, Jasinowodolinski D, Chate RC, et al. Consensus statement on thoracic radiology terminology in Portuguese used in Brazil and in Portugal [published correction appears in J Bras Pneumol. 2022 Jan 10;47(6):e20200595errata]. J Bras Pneumol. 2021;47(5):e20200595. https://doi.org/10.36416/1806-3756/e20200587
5. Meissner HH, Soo Hoo GW, Khonsary SA, Mandelkern M, Brown CV, Santiago SM. Idiopathic pulmonary fibrosis: evaluation with positron emission tomography. Respiration. 2006;73(2):197-202. https://doi.org/10.1159/000088062
6. Nusair S, Rubinstein R, Freedman NM, Amir G, Bogot NR, Izhar U, et al. Positron emission tomography in interstitial lung disease. Respirology. 2007;12(6):843-847. https://doi.org/10.1111/j.1440-1843.2007.01143.x
7. Nabashi T, Kubo T, Nakamoto Y, Handa T, Koyasu S, Ishimori T, et al. 18F-FDG Uptake in Less Affected Lung Field Provides Prognostic Stratification in Patients with Interstitial Lung Disease. J Nucl Med. 2016;57(12):1899-1904. https://doi.org/10.2967/jnumed.116.174946
8. Treglia G, Annunziata S, Sobic-Saranovic D, Bertagna F, Caldarella C, Giovanella L. The role of 18F-FDG-PET and PET/CT in patients with sarcoidosis: an updated evidence-based review. Acad Radiol. 2014;21(5):675-684. https://doi.org/10.1016/j.acra.2014.01.008
9. Bergmann C, Distler JHW, Treutlein C, Tascilar K, Müller AT, Atzinger A, et al. 68Ga-FAPI-04 PET-CT for molecular assessment of fibroblast activation and risk evaluation in systemic sclerosis-associated interstitial lung disease: a single-centre, pilot study. Lancet Rheumat. 2021;3(3):E185-E194. https://doi.org/10.1016/S2665-9913(20)30421-5

1. Departamento de Radiologia e Oncologia, Faculdade de Medicina, Universidade de São Paulo, São Paulo (SP) Brasil.
2. Divisão de Pneumologia, Instituto do Coração, Faculdade de Medicina, Universidade de São Paulo, São Paulo (SP) Brasil.