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SPOTLIGHT

^{18}F-FDG or ^{68}Ga/^{18}F-PSMA PET/CT in recurrent renal cancer?

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Radiolabeled (either ^{68}Ga or ^{18}F) prostate-specific membrane antigen (PSMA) for positron emission tomography (PET) imaging has been extensively used in patients with prostate cancer for the evaluation of the disease recurrence [1]. However, its biological properties are also favorable for the evaluation of neovasculature in some solid tumors [2]. Recent evidence has demonstrated the utility of ^{68}Ga/^{18}F-PSMA also in patients affected by renal cell cancer (RCC), particularly in those with metastatic disease.

RCC is a potentially lethal cancer with aggressive behavior, and has a propensity for distant spread. The common sites of metastases from RCC include lungs (33–72%), intra-abdominal lymph nodes (3–35%) and brain (7–13%) [3]. Bone metastases are also a frequent complication in patients with RCC [3].

^{18}F-Fluorodeoxyglucose (^{18}F-FDG) PET/computed tomography (CT) has been used for the evaluation of recurrent and metastatic RCC patients, but with a variable diagnostic performance due to the biological characteristics of the tumor. Only few papers are now available about the comparison between ^{18}F-FDG and ^{68}Ga/^{18}F-PSMA PET/CT in patients with RCC. The majority report a single clinical case, while only one paper was based on a collection of more than one patient. The first case was published in 2014 (Demerci et al. [3]) and demonstrated the superiority of ^{68}Ga-PSMA for the detection of metastases, particularly in the bone, in a patient with RCC. Similarly, Rowe et al. [4] demonstrated the superiority of ^{18}F-DCFPyL for the identification of osteolytic lesions in RCC patients. The authors noted that the uptake of ^{18}F-DCFPyL, an analog of PSMA radiolabeled with ^{18}F, in the bone lesions was superior to the uptake of ^{18}F-FDG, as an indirect sign of the increased neovascularization.

Later, in 2016, Sasikumar et al. [5] reported a complementary role of ^{68}Ga-PSMA and ^{18}F-FDG PET/CT for the detection of metastatic RCC. The authors underlined that some metastases were visible at ^{68}Ga-PSMA PET/CT and some others at ^{18}F-FDG PET/CT. The authors showed that ^{68}Ga-PSMA detects bone, visceral and soft tissue metastases, while ^{18}F-FDG reveals mainly bone lesions. This latter concept highlighted the heterogeneity of aggressiveness for RCC. A further concept was introduced by the authors: the opportunity to use ^{68}Ga-PSMA in RCC patients as a guide to ^{177}Lu-PSMA therapy.

The only large experience, performed in only eight patients, was made by Siva et al. [2] who evaluated the impact of ^{68}Ga-PSMA PET/CT for the detection of oligometastatic RCC patients who can be treated with local therapies. The authors demonstrated that PSMA was able to better assess the presence of metastatic lesions in lungs, adrenal glands and bone, than ^{18}F-FDG PET/CT. Moreover, they found that PSMA was able to monitor the response to therapy, thus opening the opportunity to use this receptorial tracer for the evaluation of response to new cytostatic agents (i.e., immunotherapy).

The behavior of radiopharmaceutical agents in recurrent RCC, however, depends on histopathology [6]. In fact, while clear cell RCC has a low glucose metabolism, thus demonstrating a high ^{68}Ga-PSMA uptake, metastatic sarcomatoid RCC shows a high glucose metabolism (therefore, a high ^{18}F FDG uptake). Therefore, the choice between ^{68}Ga/^{18}F-PSMA and ^{18}F-FDG PET/CT is strongly correlated with the differentiation of the primary and metastatic lesions.

From these preliminary results, some considerations should be kept in mind:

1. ^{68}Ga/^{18}F-PSMA PET/CT represents a potential useful imaging technique in patients affected by recurrent RCC, being able to detect metastasis and to guide the choice of specific treatments;
2. ^{68}Ga/^{18}F-PSMA PET/CT could be used for the evaluation of response to new therapeutic agents (i.e., tyrosine-kinase inhibitors or immunotherapy);

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3. the presence of PSMA expression could be an indicator for ^{177}Lu-PSMA therapy, thus opening the way for an alternative therapeutic strategy in recurrent RCC patients.

However, the scarce evidence and the limited value of single-patient studies should be further confirmed by studies with a large number of patients. In our opinion, multicenter trials are warranted to confirm the above-mentioned assumptions.

Compliance with ethical standards

Conflict of interest The authors declared that they have no conflict of interests.

Research involving human participants and/or animals None.

Informed consent Informed consent was not necessary for the present study.

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