Time to reconsider FDG-PET/CT for local and distant staging of urological malignancies

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FDG-PET has been a cornerstone in the work-up of many cancers since the 1980s, and the introduction of PET/CT, a valuable technique that makes it possible to add morphological details to metabolic findings, greatly increased the global accuracy of FDG-PET.

However, for many years FDG-PET/CT was not considered particularly useful in the management of urological cancers and deemed “unsuitable” for the clinical needs of urologists. This view was based on its low sensitivity and specificity in this setting, attributable primarily to the intrinsic low uptake of FDG by cancers arising from the transitional epithelium of the bladder and ureters and from the cells of the kidneys and prostate, but also to the physiological urinary elimination of FDG.

Nevertheless, thanks to the fusion of PET and CT images and to increasing understanding of the metabolic behavior of these cancers this view is now being challenged [1].

In this setting, the results of both functional and morphological images, provided these derive from carefully standardized procedures (mainly with regard to the amount of FDG injected, the acquisition time, the use of diuretics, and the scan delay time), seem to be quite interesting, and in many conditions close to those obtained by FDG-PET/CT in other organs and systems. Moreover, FDG-PET/CT is superior to CT in identifying more aggressive cancers

(mainly within the prostate) that warrant closer diagnostic attention and more aggressive therapies.

It has been reported that renal cell carcinoma (RCC) can actively take up FDG, and this mainly occurs at high grades of malignancy. Unfortunately, the physiological concentration of FDG in the renal pelvis and calices makes it difficult to distinguish between uptake in cancer tissue and in the urinary tract; furthermore, as RCC can also show low or moderately low uptake of FDG, FDG-PET/CT is not currently used in this cancer. However, particular attention should be devoted to the evaluation of incidentally observed renal solid masses with low uptake or no uptake of FDG, as compared to the surrounding background, in order to identify patients requiring referral for further evaluations, using alternative and more accurate procedures. FDG-PET/CT seems to perform better in local lymph node staging and restaging when compared to standard procedures (ceCT and MRI), especially in cases of suspected distant spread. Moreover, in the era of molecular-targeted therapies, FDG uptake can play a role in predicting overall survival in RCC and is an excellent tool for the evaluation of responses to therapy with new drugs, such as tyrosine-kinase inhibitors [2]; the RCC response to tyrosine kinase inhibitors, evaluated using FDG-PET/CT to measure tumor size and FDG uptake after 1 month, can predict progression free survival and overall survival.

The use of FDG-PET/CT in the diagnosis of upper tract urinary carcinomas (UTUC) has grown slowly compared to its use in other cancer types, although the emergence of PET/CT as a standard procedure has boosted its role in this setting. FDG-PET/CT seems to be highly sensitive (84 % for cancer >pT2) with a 95 % positive predictive value. Unfortunately, since the uptake is positively correlated with tumor size, the negative predictive value is not so reliable, making it necessary to perform further confirmatory investigations. It

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should be noted that false positive results are normally related to inflammation and infections.

Moreover, the sensitivity of FDG-PET/CT for detecting lymph node involvement does not exceed 60 % and pathological lymph nodes smaller than 1.5 cm are unlikely to be discovered by FDG-PET/CT. However, as with RCC, FDG-PET/CT performs optimally in restaging after treatment.

Although ceCT remains the first choice diagnostic method in RCC as well as in UTUCs, it can underestimate the tumor burden. For this reason, FDG-PET/CT is a more accurate method for the assessment of spread and/or recurrence outside the urinary tract in patients with urothelial carcinoma, especially when bone lesions are suspected [3].

Bladder cancer (BC) is the fourth most common cancer in males. Muscle-invasive BC (MIBC), which has a 5-year cancer-specific survival of 50 %, has a poorer prognosis than non-MIBC. Although the cornerstone of diagnosis is urinary cytology followed by cystoscopy, in some circumstances (for example large bladder diverticula) these methods can lack sensitivity. For this reason, in cases of non-diagnostic cystoscopy, a ceCT should always be performed and the bladder should be carefully evaluated on FDG-PET/CT scans. Unusual findings, suspected to be cancer, can appear as areas of high uptake, or as a thickening of the epithelium characterized by low uptake.

In MIBC, accurate loco-regional staging is crucial, especially in potential candidates for surgical treatment. The National Comprehensive Cancer Network (NCCN) recommends ceCT or MRI for local staging plus ceCT (or radiography) of the chest, and bone scan in the event of an elevation of Alkaline Phosphatases or when symptoms are present. The role of FDG-PET/CT in local and distant staging of bladder cancer is still under debate. Several studies and meta-analyses on this topic have found a pooled sensitivity and specificity value approaching 90 %; additionally, they have shown the superiority of FDG-PET/CT in discovering pathologically confirmed, distant metastases. Nevertheless, neither the European Association of Urology Guidelines nor the NCCN include FDG-PET/CT in the management of these cancers and further studies are needed to better address this topic [4].

Prostate cancer diagnosis on FDG-PET/CT deserves special consideration. The high incidence of inflammatory processes within the prostate can affect the sensitivity and, particularly, the specificity of FDG-PET/CT in prostate cancer detection; consequently, FDG is not considered an “ideal” tracer for imaging of the prostate gland. Nevertheless, every incidental case of FDG uptake within the prostate should be reported for further evaluation, irrespective of the patient’s age, particularly when the uptake is focal or at the periphery of the gland, where prostate

cancer more frequently arises. In fact, prostate cancers, mainly those with a Gleason score higher than 7, can actively take up FDG. Although the incidence of prostate cancer in focal prostate uptake does not exceed 10 %, and invasive procedures are not justified on the sole basis of metabolic findings, the possible presence of high-grade prostatic carcinoma should be considered. Furthermore, with the progressively wide availability of other relatively more specific tracers for prostate cancer restaging and follow-up (choline and PMSA) [5], FDG-PET/CT in this setting is not recommended, while PET/MRI, seems promising [6].

Although FDG-PET/CT for staging, restaging and follow-up of urinary tract cancers is not routinely included in the standard work-up by the majority of widely used guidelines, it can offer some benefits, mainly in the evaluation of distant spread. In addition, it seems to be promising when it is integrated into specific diagnostic algorithms including ceCT and MRI.

Moreover, FDG-PET/CT may provide crucial information about the grade of the cancer and its response to therapies, an area where other methods are generally inadequate. Finally, when FDG-PET/CT scans are performed for reasons other than urological malignancies, and also in the presence of cancer of unknown primary site, careful attention should always be paid to possible morphological and functional findings in the urinary tract; in this way, any unusual findings can be evaluated and patients can be referred for further specific evaluation.

Compliance with ethical standards

Conflict of interest The authors here declare the absence of any conflict of interest. This study does not contain any study performed by any of the authors on humans and animals.

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