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EDITORIAL COMMENTARY

The rising PET: the increasing use of choline PET/CT in prostate cancer

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The paper by Castellucci et al. [1] which appears in this issue of the journal is the last contribution, just in terms of time, dealing with the use of choline PET in the evaluation of biochemical relapse from prostate cancer. The paper adds an important voice in the discussion on the management of prostate cancer patients after prostatectomy. In particular, the authors aimed at studying the clinical utility of ^{11}C-choline PET/CT in patients with a "mild" serum prostate-specific antigen (PSA) increase after radical prostatectomy. Although "mild" is not a numeric value, they set the PSA cutoff at less than 1.5 ng/ml. One hundred and two patients were enrolled with an increase of serum PSA during follow-up ranging from 0.2 to 1.5 ng/ml. Choline PET/CT was used as the first diagnostic procedure and results were compared to pathology or a 12-month follow-up. Data from PSA kinetics, such as doubling time and velocity, were also evaluated.

The study reports positive ^{11}C-choline PET/CT findings in 29% of patients, including those who had local relapse, positive locoregional nodes or bone metastasis. Notably, the paper also suggested that PSA doubling time and locoregional lymph node involvement at diagnosis were the only significant independent predictive factors for relapse in multivariate analyses. The authors concluded that ^{11}C-choline PET/CT is effective in determining the best treatment strategy in patients with early, or mild, PSA relapse, namely below 1.5 ng/ml.

This paper stresses again the rising importance of PET/CT in prostate cancer, a field in which ^{18}F-FDG is of negligible use, therefore underlining the importance of PET as a technique able to study different entities, using different, specific radiopharmaceuticals.

The increasing ageing of the population, particularly in more developed countries, has resulted in an increase of prostate cancer incidence and this disease is now one of the leading causes of death in men [2]. After radical prostatectomy or radical radiation treatment, prostate cancer recurs in 20–50% of patients, and PSA increase is detectable before the disease can be confirmed with any imaging modality. Of course, PSA is not able to distinguish between local relapse, involvement of locoregional nodes or distant metastases; this is why imaging comes into play. Literature data confirmed that, as often occurs, detection of anatomical changes with magnetic resonance (MR), computed tomography (CT) or transrectal ultrasound (TRUS) has limited accuracy for assessment of recurrent disease [3]. In order to tailor a patient's therapy to the status of the illness, there needs to be an imaging method capable of assessing the real tumour burden and to localize all, or almost all, localizations. Treatment strategies at relapse vary depending on disease extension, including surgery, radiation treatment, hormonal therapy and palliative care.

Molecular imaging with PET is able to detect the diffusion of cancer before morphological changes can be identified with other imaging methods, and this is true also for prostate cancer. Different radiopharmaceuticals have been proposed, both for PET and SPECT, as well as potential applications of PET/MR imaging, as summarized in a recent review [4].

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From a survey issued by the European Association of Nuclear Medicine (EANM) (still unpublished data) we realized that the radiopharmaceuticals most widely used in prostate cancer are ^{11}C and ^{18}F-labelled choline (or acetate) but, surprisingly, ^{18}F-FDG is still used in many centres that responded to the questionnaire. Literature data showed that ^{18}F-FDG PET is not accurate in staging and restaging prostate cancer, due to the low glucose consumption, which characterizes this slow-growing tumour. Some exceptions may occur in aggressive diseases, in which ^{18}F-FDG may be proposed in selected cases. The large amount of literature available, thanks to the many publications from several European centres, is related to more suitable radiopharmaceuticals used to study prostate cancer. At least four different radiopharmaceuticals are employed: ^{11}C-choline, ^{11}C-acetate, ^{18}F-ethylcholine and ^{18}F-methylcholine. Although there are intrinsic differences in these radiopharmaceuticals, at present we are not able to assess if there is any significant difference in the diagnostic accuracy when they are used in the clinical scenario. The future will most probably show an increased use of the ^{18}F-labelled compounds, but just because they can be distributed to PET centres without access to a medical cyclotron and a radiopharmacy. Besides logistical reasons, licensing will play a role in the choice of the radiopharmaceutical that will be used in the near future. However, we're not going to deal with these issues in this contribution.

Literature data also showed that choline (or acetate) PET/CT should not be recommended to detect and stage primary prostate cancer, mainly because of its relatively low spatial resolution; at least when compared to CT, it limits the evaluation of local extension of the disease and the identification of small metastatic lymph nodes. On the other hand, there is consensus, at least among the nuclear medicine community, that choline PET/CT is of use when evaluating patients with biochemical relapse or with suspected relapse on other imaging modalities [5]. In particular, there are data supporting the use of choline PET/CT in different clinical settings: in selecting patients who can benefit from salvage radiation therapy or lymphadenectomy, or in identifying those patients who have local relapse after radiation treatment, or those who can benefit from radiation treatment planning individualization using dose painting techniques.

The paper by Castellucci et al. confirms that PET/CT has a role in the management of prostate cancer, also in those patients with a mild increase in PSA value. Does this mean that the use of choline PET/CT should be suggested in all relapsing patients with a PSA value above 1 ng/ml? The answer is yes, but there is still much resistance to accepting this concept. First of all, many clinicians still have no access to PET tracers alternative to FDG. This is true in many European and non-European countries, but also in countries where there are centres which are considered referral centres for the choline PET/CT technique, like Germany or Italy. Cost and licensing are the issues to be faced. Cost should be, again, viewed in the global setting: expensive examinations like PET/CT, when used in the appropriate way, are able to reduce the total costs of treatment. Giving better care is always synonymous with giving cheaper care, in the long run. Licensing is slowly improving, since ^{18}F-choline is now commercially available in a few European countries and hopefully the number will increase over the next few years, allowing also PET centres without the capability of producing radiopharmaceuticals to use this technique. The clinical perception of choline PET/CT from the point of view of surgeons, radiation oncologists and oncologists is something which is still in our hands, as nuclear medicine physicians. We should focus on: (1) using this technique in the most appropriate manner, in order to get useful results in most patients; (2) developing and applying a standard for executing and reading examinations, in order to avoid misleading results due to suboptimal quality of the acquisitions; and (3) collaborating and sharing data between different centres, in order to create robust databases for comparative effectiveness analyses.

In all these settings, scientific societies, the EANM *in primis*, should give adequate support for standard assessment, networking and data sharing. Thanks to new communication technologies and infrastructures this support can be given at acceptable costs and will be the winning choice for the diffusion of effective techniques able to improve patient care.

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