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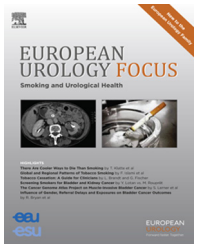

Prostate Cancer

Imaging for Prostate Cancer Recurrence

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Abstract

Context: Correct identification of metastatic sites in recurrent prostate cancer (PCa) is of crucial importance because it leads to further treatment decisions.
Objective: To provide an overview on current imaging procedures and their performance in recurrent PCa.
Evidence acquisition: Medline search via PubMed was performed with the keywords *imaging, recurrent*, and *prostate cancer* as well as more detailed searches including the keywords *bone scan, bone scintigraphy, computed tomography, magnetic resonance imaging, positron emission tomography, PET, choline, FDG, prostate-specific membrane antigen*, and *PSMA*, with emphasis on recent literature from 2010 to the present. Non-English published literature was excluded. Abstracts and full-text articles were reviewed and assessed for relevant content.
Evidence synthesis: In diagnostic imaging and particularly with newer technologies like positron emission tomography (PET), a profound lack of prospectively designed studies in recurrent PCa has to be noted. In most studies histologic validation has only been performed in a subset of patient cohorts. Heterogeneity of included patient cohorts, lack of standardized assessment, as well as diverging end points, hamper systematic comparison of different image modalities. Thus evidence for currently used imaging in recurrent PCa is only presented descriptively.
Conclusions: Computed tomography and magnetic resonance imaging (MRI) as well as bone scintigraphy still represent the standard imaging for recurrent PCa; however, particularly for detection of local recurrence, multiparametric MRI is a valuable imaging modality. PET using choline and particularly tracers against prostate-specific membrane antigen might improve visualization of metastatic lesions. These findings need to be validated in prospective trials.
Patient summary: Imaging of recurrent prostate cancer (PCa) is important to guide further treatment. Computed tomography, magnetic resonance imaging, and bone scintigraphy represent the current standard. Positron emission tomography, especially with cancer-specific tracers, might improve imaging of recurrent PCa in the future.

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1. Introduction

Between 27% and 53% of all patients undergoing radical prostatectomy (RP) or radiotherapy (RT) for primary treatment of prostate cancer (PCa) develop biochemical recurrence (BCR) [1]. However, among patients with BCR, heterogeneous progression risks exist [2,3]. Specifically, a better survival was recorded in patients with nodal recurrence compared with patients with bone or visceral metastasis after primary treatment [4]. The early addition of docetaxel to androgen-deprivation therapy alone recently emerged as an effective therapy in patients harboring a high burden of metastatic hormone-sensitive cancer [5,6]. Similarly, also in patients harboring hormone-insensitive castration-resistant cancer, a precise staging is necessary for the right timing and the selection of treatment regimen.

Tremendous advances in magnetic resonance imaging (MRI) techniques and the availability of functional/metabolic imaging allow earlier visualizing of PCa recurrence [7]. Further refinements of these techniques and the combined use of morphologic imaging with functional positron emission tomography (PET) imaging might enable the urologist to individualize treatment in patients with recurrent PCa.

Based on the increasing availability of novel sophisticated but expensive imaging modalities, it is mandatory for urologists to know the diagnostic accuracy of these techniques. We outlined the current different modalities for the imaging of recurrent PCa and their potential use as well as their limitations.

2. Evidence acquisition

In the preparation of this nonsystematic review, we performed a Medline search via PubMed with the keywords *imaging, recurrent*, and *prostate cancer*, as well as more detailed searches including the keywords *bone scan, bone scintigraphy, computed tomography, magnetic resonance imaging, positron emission tomography, PET, choline, FDG, prostate-specific membrane antigen*, and *PSMA*, with an emphasis on recent literature from 2010 to the present. Non-English published literature was excluded. Abstracts and full-text articles were reviewed and assessed for relevant content. The references of retrieved full-text articles were included for the consideration of relevant articles. In general, and particularly with newer technology like PET, a profound lack of prospectively designed studies in recurrent PCa has to be noted. The heterogeneity of included patient cohorts as well as end points also hampers systematic comparison of the different image modalities. In most studies, histologic validation (if any) was performed only in a subset of patient cohorts. In most of those histologically validated subsets of patients, little was reported on the pathologic work-up (eg, application of immunohistochemistry staining). This is especially important because series with a less diligent histologic work-up (eg, without immunostaining) automatically detect a biased high sensitivity of a method, potentially misleading urologists in their daily clinical practice. In PCa patients, however, up to 37% of tumor deposits are <2 mm and are often only detected after sophisticated histologic examination [8,9]. Consequently, the standardized definition and performance of pathologic examination as well as close collaboration of imaging specialists, urologists, and pathologists is mandatory within the interdisciplinary validation process. For all these reasons, interpretation and comparison of different imaging modalities must be performed with caution.

3. Evidence synthesis

3.1. Multiparametric magnetic resonance imaging

3.1.1. Detection of local recurrence after radical prostatectomy

Computed tomography (CT) is no longer recommended for depicting locoregional relapse of PCa after RP or RT owing to its poor contrast resolution. On the contrary, MRI, thanks to its inherent superior contrast and spatial resolution, is of great value to evaluate prostatic fossa after RP. Multiparametric MRI (mpMRI) is able to discriminate between locoregional relapse and a small amount of residual glandular healthy tissue or scarred, fibrotic, and granulation tissue (Fig. 1), and it may even be useful to assess the aggressiveness of nodule recurrence by means of apparent diffusion coefficient (ADC) values [10]. The presence on T2-weighted (T2w) images of a lobulated, semicircumferential, nodular- or plaque-like soft tissue thickening in the prostatectomy bed that appears slightly hyperintense compared with pelvic muscles should be considered suggestive of local recurrence [11,12]. When conventional T2w is not able to discriminate between local recurrence and postoperative changes, dynamic contrast-enhanced (DCE) sequences are of paramount importance for the differential diagnosis [13]. A recurrent tumor tends to enhance quickly and avidly in the arterial phase, which is followed by a plateau or washout on the signal intensity (SI) curve during the venous phase. Postoperative changes tend to show either no enhancement or mild enhancement in the venous phase [11].

Thus mpMRI can be currently considered the most reliable imaging biomarker to detect local PCa recurrence in patients with biochemical failure after RP that is crucial for the planning of salvage RT [14], particularly for those prostate-specific antigen (PSA) values at which PET/CT is not recommended (0.2–1 ng/ml) [15,16] (Table 1).

3.1.2. Detection of local recurrence after radiotherapy

In patients with local recurrence after RT, salvage therapies generally involve treatment of the entire prostate because the exact location of the recurrent tumor within the prostate is unknown [17]. At present, mpMRI is widely considered the state-of-the-art imaging modality. After RT, because of shrinkage and induced glandular atrophy and fibrosis, the peripheral, central, and transition zones appear less distinct from each other due to diffusely decreased SI on T2w imaging. T2w alone is of limited diagnostic accuracy because the recurrent tumor as well as normal surrounding parenchyma both appear hypointense. For instance, mpMRI

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