Incidental Prostate Cancer: A Real Need for Expansion in Guidelines?

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In this issue of European Urology Oncology, Capitano and colleagues [1] recommend that incidental prostate cancer (PCa), classified as T1a or T1b PCa, should be clearly discussed in international guidelines because it represents a different clinical situation compared to T1c PCa. Indeed, T1a/b PCa is mentioned only once in the recently updated European Association of Urology guidelines [2]. Is it really a major issue not to expand on this?

T1a/b PCa is unexpectedly discovered after prostate surgery for benign prostatic obstruction (BPO) in patients with a normal digital rectal examination. According to the most recent TNM classification [3], T1a is defined as an International Society of Urological Pathology (ISUP) grade 1 cancer visible in <5% of the resected tissue, while T1b corresponds to either ISUP grade 1 cancer present in >5% of the resected tissue or to any ISUP grade ≥2 cancer.

We agree with the authors that this 5% threshold is highly questionable, as no standardization is available on how to measure this 5% ratio (eg, percentage of positive chips or proportion of carcinoma area). In addition, its clinical value has not been confirmed [4]. By contrast, the classification that includes the ISUP grade group seems valid, provided the discrimination between ISUP grade 1 and ISUP grade ≥2 is reliable on a small amount of tissue often subject to cationization artifacts. Nonetheless, defining and grading PCa is the basis of pathology and does generally not require subchild psychiatry. The rules for ISUP classifications have been widely published and their reproducibility seems acceptable, at least for differentiating ISUP grade 1 from higher grades, even between general pathologists [5]. As for biopsies, if in doubt, requesting advice from a colleague pathologist is good practice.

Tissue obtained following BPO surgery mainly comes from the transition zone (TZ), leading to the question of the status of the remaining gland. In the active surveillance (AS) era, the question is whether the patient has pT0 cancer but to rule out any clinically significant PCa (csPCa) left in place, at least in patients with life expectancy of >10 yr.

Although the level of evidence is limited, the literature suggests that very low prostate-specific antigen (PSA) after BPO surgery (mainly <1 ng/ml), very low PSA density (PSAd) after BPO surgery (<0.03 ng/ml/cm³), and the absence of suspicious lesions on multiparametric magnetic resonance imaging (mpMRI) are predictors of the absence of residual tumor [6,7]. If not performed before BPO surgery, mpMRI might be useful for detection of residual suspicious lesions and trigger targeted biopsy to rule out residual csPCa [8]. Because of potential misleading postoperative inflammatory changes in the peripheral zone (PZ), mpMRI should not be obtained until at least 6–8 wk after surgery. Nonetheless, it must be stressed that patients with negative mpMRI findings may still have csPCa, especially if their PSAd is high [7].

In practice, several different clinical scenarios can be distinguished on the basis of preoperative and postoperative work-up and patient life expectancy.

Patients with favorable prognostic factors (initial PSA <10 ng/ml, low PSA and low PSAd after surgery) and only ISUP grade 1 cancer in the resected tissue can be considered at low risk [6]. AS or watchful waiting should be offered on the basis of the individual’s life expectancy. This treatment
plan is similar to that for patients with T1c carcinoma. According to available data, we do not see any rationale for suggesting special rules for patients with T1a/b cancers. These patients might even need less intense follow-up given the suggested better prognosis of T1a/b compared to PZ cancers [9], but solid data on this topic are lacking. It should be noted that the proposed active monitoring performed in the ProtecT trial [10] has not yet been proven to be less effective compared to a follow-up strategy including repeated biopsies and mpMRI [2]. This is true for AS in general and is not specific to T1a/b cancers.

In patients with initial PSA >10 ng/ml and only ISUP grade 1 in the resected tissue, the initial prostate volume and postoperative PSA and PSAd must be considered.

Patients with ISUP grade 2 cancer in the resected tissue should be considered at intermediate risk. Clarifying the potential risk of a remaining significant cancer is needed and additional work-up should include mpMRI and biopsy of the PZ and any suspicious lesion in the TZ. Available guidelines consider AS an acceptable option for selected intermediate-risk lesions defined according to either initial PSA >10 ng/ml or biopsy ISUP grade 2 [2]. For the few situations with a higher ISUP grade, AS is no longer a valid option. The real question is the need for rebiopsy.

In patients with lower life expectancy (for whom no preoperative PSA may have been ordered), the discovery of incidental PCa may have been ordered, the discovery of incidental PCa should not change the management strategy, unless the ISUP grade is high, which is unusual.

Therefore, even if a revision of the T1 substages might be of interest, we do not believe that these T1a/T1b cancers represent a distinct situation, once usual prognostic parameters (PSA level, PSAd, ISUP grade group) are taken into consideration. The key issue is to grade the lesion correctly and not to rush to any active treatment whatever the T1 stage. The individual’s life expectancy should be the main driver for further explorations.

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References