Prostate Cancer Diagnosis Without Histological Proof: Is Treating Images Reasonable?

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Magnetic resonance imaging (MRI) has become a pivotal examination in the diagnostic pathway for prostate cancer (PCa) and is recommended before almost any prostate biopsy. Recently, research groups have combined MRI and prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) in an attempt to improve the diagnosis of clinically significant PCa (csPCa) [1]. The cost-effectiveness and practicality of adding PSMA PET/CT to the MRI-based diagnostic pathway remains questionable given the cost of PSMA PET/CT and its lack of availability in some countries. Still, combining two sensitive tests has, at least in theory, one major advantage: patients with nonsuspicious findings on both examinations might be able to safely forego biopsy [1].

In the October 2022 issue of European Urology Open Science, Heetman et al. [2] raise a completely different and much more provocative idea: it may be possible to treat, without tissue confirmation, patients with highly positive findings on MRI (eg, Prostate Imaging-Data and Reporting System [PI-RADS] score of 4–5) and PSMA PET/CT (eg, maximum standardized uptake value [SUVmax] ≥8 mSv) [2].

Their conclusion is based on a retrospective assessment of 459 patients who underwent both MRI and PSMA PET/CT at their institution, either for staging purposes or in the context of a trial on active surveillance. In total, 185 patients (40.3%) had positive MRI (PI-RADS 4–5) and positive PSMA PET/CT (SUVmax ≥8 mSv) findings. Of these 185 patients, 181 (97.8%) had International Society of Urological Pathology grade group (GG) ≥2 cancer at biopsy. In addition, all 70 patients with a PI-RADS score of 4–5 on MRI and SUVmax ≥16 mSv on PSMA PET/CT had GG ≥2 cancer, and 62 (88.6%) had GG ≥3 cancer.

Although provocative, the idea of treating patients without histological proof of cancer is not new in medicine. As mentioned by the authors, most renal masses are surgically removed without prior biopsy [3]. In the setting of a cirrhotic liver, hepatocarcinoma can be diagnosed on the basis of typical imaging criteria, without the need for biopsy [4].

However, several factors call for caution before treating patients on the sole basis of concordant prostate MRI and PSMA PET/CT findings. First, the examples of renal masses and hepatocarcinoma are not valid comparisons. Liver biopsy in cirrhotic patients is associated with much higher morbidity than prostate biopsy, and the prevalence of hepatocarcinoma is extremely high for cirrhotic livers. Removing a suspicious small renal mass that proves to be benign is deemed acceptable because many benign renal masses will progress over time, and the morbidity of robot-assisted nephron-sparing surgery is low [5]. On the contrary, radical prostatectomy and prostate radiotherapy are associated with substantial morbidity [6]; submitting a patient without PCa to such therapies does not seem acceptable. Therefore, PCa treatment without histological proof can be considered only if the imaging diagnosis is nearly certain.

Is this really the case? Heetman et al. [2] report specificity of 96.6% (112/116) and sensitivity of 52.8% (181/343) for GG ≥2 cancer, which translates into a positive predictive value (PPV) of 97.8% (181/185). These results are good. But are they enough? Would the urological community accept to subjecting approximately two in 100 patients to unnecessary prostate surgery or radiotherapy simply to avoid biopsy? In addition, because all the patients in the series described by Heetman et al had known PCa, the prevalence of GG ≥2 cancer was high (74.7%, 343/459). This
is not representative of the cohorts of patients with suspected PCa, in which the prevalence of csPCa is usually in the range from 35% to 55% [7]. Unfortunately, PPV mathematically decreases with prevalence [8]. In a population with csPCa prevalence of 45%, considering sensitivity of 52.8% and specificity of 96.6%, the PPV for combined MRI and PSMA PET/CT would be 92.7%. This is still very good, but the proportion of patients unnecessarily treated would now become seven in 100.

And yet this is probably an optimistic prediction. We should also take into consideration the inter-reader reproducibility of prostate MRI, which is moderate at best [9], and that of PSMA PET/CT, which is good but not perfect [1]. Therefore, there is no guarantee that the excellent diagnostic specificity of combined MRI and PSMA PET/CT reported by experienced centers in recent studies will be reproduced in less experienced centers.

Finally, csPCa is not a homogeneous entity. GG 2 cancers with cribriform/intraductal architecture, GG 2 cancers without cribriform/intraductal architecture, and GG 5 cancers do not all have the same prognosis and may not need the exact same management. Even if prostate biopsy is not a perfect tool because of sampling errors, it can provide details on tumor aggressiveness that imaging is unlikely to show, at least in the near future. As mentioned by the authors, DNA testing will be increasingly used in the age of immunotherapy, and surgery is far from being the only treatment for PCa. In the absence of biopsy, no pathological data would be available after radiation or ablative therapies, which could be prejudicial in the event of metastatic evolution.

Reducing the number of unnecessary prostate biopsies is indeed a huge challenge facing the urological community. Modern imaging can and will help in selecting appropriate patients for biopsy. However, this will be achieved mainly by improving the selection of patients with very low risk of csPCa who can safely avoid biopsy. Should we also forego biopsy in patients with highly suspicious imaging findings? We believe that given the relatively safe profile of prostate biopsy [10], there is more to lose than to gain here. At a time when images invade our lives, it is probably also necessary to remember that medicine is about treating patients, not their scans.

Conflicts of interest: The authors have nothing to disclose.

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