available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Editorial

Referring to the article published on pp. 156–160 of this issue.

Radical Prostatectomy Without Biopsy: Audacious, Imprudent, or Innovative?

Parth K. Modi, Scott E. Eggener *

Section of Urology, Department of Surgery, University of Chicago, Chicago, IL, USA

> "All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident."
>
> Arthur Schopenhauer, German philosopher

In this issue of *European Urology*, Meissner and colleagues [1] present data for a series of 25 men who underwent radical prostatectomy without preoperative histologic confirmation of prostate cancer, instead relying on highly suspicious results from multiparametric magnetic resonance imaging (MRI; Prostate Imaging-Reporting and Data System score ≥4) and a prostate-specific membrane antigen (PSMA) positron emission tomography (PET) scan (≥4 on a 5-point Likert scale and maximum standardized uptake value ≥4). For many, the guttural response will understandably be shock and scorn. For us, the concept is discomfiting but provocative. After digestion of the data, the strategy has become more intriguing. While it remains surprising that any man would opt for prostatectomy to forego the potential morbidity of a biopsy, the authors affirm that the patients were counseled extensively and proceeded with appropriate informed consent.

Why do so many of us feel uncomfortable about the concept of radical treatment without histologic confirmation? Is it in principle a bad idea that should never become mainstream? Or is it simply not feasible given current diagnostic capabilities? One could make the argument that we should never proceed with radical surgery without tissue diagnosis. Moreover, obtaining tissue before surgery offers additional benefits in counseling patients regarding management options and important details for individualizing surgical or radiation treatment. This is particularly true with the emergence of novel prognostic and predictive biomarkers. However, insistence on tissue diagnosis is not consistent with current urologic practice, as there are many examples of standard-of-care surgery without prior biopsy, including orchiectomy, adrenalectomy, and nephrectomy. We do not feel that the idea of radical surgery without prior biopsy is, prima facie, unreasonable. It is not far-fetched to imagine a future in which noninvasive diagnostic modalities may make prostate biopsy superfluous.

However, there is a high bar to be met for such reliance on imaging. First, prostate MRI and PSMA PET scans must be of sufficient quality and reliability. While recent research has demonstrated the value of PSMA PET added to MRI in identifying clinically significant prostate cancer in the biopsy-naïve population [2], additional data are needed. Importantly, high-volume cohorts from experienced centers suggest that PSMA PET is imperfect in identifying clinically significant cancer within the prostate [3]. Second, the costs of such high-quality imaging tests may be prohibitive. In the study by Meissner et al, each imaging study was reviewed by two qualified radiologists, which may not be possible or cost-effective in many settings. Finally, even if high-quality imaging with near-perfect positive predictive value were available to confirm the presence of clinically significant prostate cancer, this might not be enough. A thorough discussion of management options for men with prostate cancer might include radiotherapy with or without hormone therapy, active surveillance, focal therapy, and clinical trial options. These decisions are informed by more precise information about cancer characteristics than even the best imaging tests alone can currently provide.

We must also consider the asymmetric risks and benefits faced by patients considering radical prostatectomy with-

DOI of original article: https://doi.org/10.1016/j.eururo.2021.11.019
* Corresponding author. Section of Urology, Department of Surgery, University of Chicago, Mail Code 6038, 5841 South Maryland, Chicago, IL 60637, USA. Tel. +1 773 702 5195; Fax: +1 773 702 1001.
E-mail address: seggener@gmail.com (S.E. Eggener).

https://doi.org/10.1016/j.eururo.2022.03.008

out prior biopsy. The maximum potential benefit one might gain is relatively minor: the avoidance of a prostate biopsy. In the modern era, this represents the avoidance of small risks of infection, hematuria, urinary retention, and some discomfort [4,5]. By contrast, the potential risks of proceeding with surgery include inadequate consideration of alternative management options, the risk of unnecessary surgery, and potential complications and side effects. Let us consider a counterexample of active surveillance for low-risk prostate cancer. In this setting, we routinely recommend that patients undergo numerous prostate biopsies and additional blood and imaging tests to avoid, or merely delay, radical treatment. Implicit in this recommendation is a value judgment that the downsides of one or several biopsies as part of a surveillance protocol are preferable to the downsides of potentially unnecessary upfront radical therapy for prostate cancer. It seems inconsistent to simultaneously advocate for patients to take on even a small risk of unnecessary surgery or have less than perfect information for treatment decision-making to simply avoid one prostate biopsy.

Finally, this study raises important and interesting ethical questions. How were these patients counseled? What risk of no cancer or low-grade cancer on final pathology were the patients led to expect? Should the surgeons simply have refused to perform surgery without a definitive diagnosis of prostate cancer? The authors appropriately obtained institutional review board approval to analyze and report this series. However, it is not clear if there was any oversight required or obtained before proceeding with surgery in these patients. While formal oversight by a regulatory body or within a trial protocol may not be a legal requirement before nonstandard surgery, we would regard it ethically and scientifically preferable. Absent regulatory review, surgical innovators can look to the IDEAL framework, which provides recommendations for a scientifically rigorous and transparent process [6].

The dustbin of urologic (and medical) history is overflowing with anachronistic, now laughable, paradigms that were once routine and unquestioned. As an example, bilateral adrenalectomies were common in the treatment of metastatic prostate cancer. Conversely, we must be careful about what we mock, as it might eventually evolve into a standard. Within the past generation, contentious ideas such as active surveillance, laparoscopic surgery, and prostate MRI have all been lambasted by smart and accomplished but closed-minded urologists. Ultimately, we recognize that the potential morbidity of prostatectomy is the exact reason why the paradigm discussed warrants pause, critical analysis, and extensive validation before implementation outside of a clinical trial. As we continue to work to improve the care for men with prostate cancer, we should remain open-minded about potential new advances but steadfast in demanding rigorous evaluation of these ideas before their widespread adoption.

Conflicts of interest: The authors have nothing to disclose.

References

[1] Meissner VH, Rauscher I, Schwamborn K, et al. Radical prostatectomy without prior biopsy following multiparametric magnetic resonance imaging and prostate-specific membrane antigen positron emission tomography. Eur Urol. 2022;82:156–60.
[2] Emmett L, Buteau J, Papa N, et al. The additive diagnostic value of prostate-specific membrane antigen positron emission tomography computed tomography to multiparametric magnetic resonance imaging triage in the diagnosis of prostate cancer (PRIMARY): a prospective multicentre study. Eur Urol 2021;80:682–9.
[3] Raveenthiran S, Yaxley WJ, Franklin T, et al. Findings in 1,123 men with preoperative ^{68}Ga-prostate-specific membrane antigen positron emission tomography/computerized tomography and multiparametric magnetic resonance imaging compared to totally embedded radical prostatectomy histopathology: implications for the diagnosis and management of prostate cancer. J Urol 2022;207:573–80.
[4] Shankar PR, Ellimoottil C, George AK, et al. Testing-related health impact of transrectal and transperineal prostate biopsy as assessed by health utilities. J Urol 2021;206:1403–10.
[5] Stefanova V, Buckley R, Flax S, et al. Transperineal prostate biopsies using local anesthesia: experience with 1,287 patients. Prostate cancer detection rate, complications and patient tolerability. J Urol 2019;201:1121–6.
[6] McCulloch P, Altman DG, Campbell WB, et al. No surgical innovation without evaluation: the IDEAL recommendations. Lancet 2009;374:1105–12.