EDITORIAL

Clinical

ExoDx test for prostate cancer: the future is liquid—Editorial Comment

Prostate Cancer and Prostatic Diseases (2023) 26:443–444; https://doi.org/10.1038/s41391-023-00707-w

"*Do as much as possible for the patient, and as little as possible to the patient*". Nobel Peace Prize pioneering cardiologist Dr. Bernard Lown' statement cannot be more appropriate to the never-ending issue about medicine's overtreatment. In fact, overdiagnosis and unnecessary treatments can profoundly impact a patient's quality of life and impose an unwarranted economic burden on both individuals and the healthcare system. More specifically, this holds true in the field of prostate cancer (PCa), as the introduction of PSA screening in the late 1980s had progressively led to earlier detection of aggressive tumor, hence reducing mortality for PCa, but at the same time increasing detection of indolent tumor [1]. In response to this dilemma, a growing interest in understanding the role of liquid biopsy or biomarkers in PCa disease, diagnostics, and risk stratification is rising, especially for the purpose of minimizing the need of biopsies among patients who are more likely to exhibit non-threatening disease. Several biomarkers' assays have been proposed to help improve PCa risk stratification. However, most of these are limited by a variety of factors and they remain under scrutiny [2, 3].

In 2016, McKiernan et al. proposed a novel urine exosome gene expression assay that does not require pre-collection digital rectal exam, named the ExoDx Prostate test (IntelliScore) (EPI, Exosome Diagnostics, Waltham, MA, USA) [4] and relies on an algorithm that is independent of clinical features. Recently, the impact of the EPI test on the biopsy decision-making process was validated across 3 independent prospective multicenter clinical trials, designing a cutoff risk assessment score of 15.6 that can distinguish between benign/low-grade (Grade Group, GG1) and high-grade (GG2+) PCa for men aged 50, within the PSA "gray zone" of 2–10 ng/mL. In doing so, it avoided 27% of biopsies with a negative predictive value of 91% for detection of Gleason score 7 and higher [5].

The same research group more recently reported the findings at 2.5 years of a prospective, blinded, randomized, multicenter clinical utility study, the Decision Impact Trial of the ExoDx Prostate (NCT03235687) [6]. Eight hundred and thirty-three patients with complete follow-up either by using the EPI test or the standard of care (SOC) were included in the analysis. An EPI test was submitted for all the patients, but only those in the EPI arm received results during biopsy decision process. Overall, the test held promise as a valuable tool for risk stratification and identification of patients at a higher risk of high-grade disease. Patients receiving EPI low-risk scores (<15.6) significantly deferred the time to first biopsy and remained at a very low pathologic risk by 2.5-years after the initial study. Patients with low-risk (<15.6) EPI scores in the EPI arm had a significantly lower biopsy rate than patients with high-risk EPI scores, while patients in the SOC arm deferred biopsies at almost identical rates in the low vs high risk EPI patients. Regarding pathological outcomes, after 2.5 years follow-up, patients with low-risk EPI scores had very low probability of a ≥ GG2 PCa, while patients with high-risk EPI scores had much higher probability of HG PCa diagnosis, regardless of study arm.

The most interesting finding of studies like this—looking into the "clinical utility" of a given test—is to see how that test can impact the decision-making process in current clinical practice. However, when looking at the impact on clinical outcome itself, one should consider potential source of bias. In this case, the lack of information regarding the type of biopsies performed, such as cognitive or fusion biopsy, as well as pre-biopsy MRI features can be regarded as a major limitation. Notably, the SOC arm in the study included an MRI in only 22% of cases, and this does not reflect current daily clinical practice. Moreover, in some cases, the SOC arm potentially included the use of other commercially available biomarker tests, which is also a confounding factor. In addition, a comprehensive and extensive analysis regarding the cost-effectiveness and accessibility of the ExoDx Prostate Test remains to be determined. Certainly, a wider implementation of the test may require assessing its economic impact and feasibility in different healthcare settings.

Notwithstanding these limitations, PCa management is likely to be moving towards new minimally invasive tools, such as ExoDx Prostate Test, and therefore it is important to stay tuned to the findings from studies like this. Soon, the role of transcriptomics, genomics and artificial intelligence-based approaches might grow [7]. As technology evolves, all these tools will assist in predicting disease aggressiveness, tailoring individualized treatment, and optimizing patient outcomes.

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Received: 3 July 2023 Revised: 13 July 2023 Accepted: 27 July 2023
Published online: 12 August 2023

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AUTHOR CONTRIBUTIONS

AF: writing-original draft preparation; RA review and editing.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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