

The Role of Liquid Biomarkers for Early Detection of Prostate Cancer



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Screening helps to determine whether a full histopathological examination of prostate biopsy should be performed to diagnose prostate cancer. Although blood-based prostate-specific antigen (PSA) tests help clinicians to determine the need for this invasive tissue testing, PSA tests can give false-positive results that can result in unnecessary testing, treatment, and treatment complications.¹⁻⁴ New liquid biomarker-based tests can provide additional information and help circumvent these unnecessary outcomes.

In this *UroView*TM program, 2 specialists discussed the need for risk assessment tools and the role of new liquid tests in early detection of prostate cancer: David Albala, MD, chief of urology at Crouse Hospital and medical director for Associated Medical Professionals in Syracuse, New York; and Judd W. Moul, MD, urological oncologist at the Duke Cancer Center in Durham, North Carolina. This article summarizes the key takeaways from that conversation.

US PREVALENCE OF PROSTATE CANCER AND PSA-TEST SCREENING

According to Moul, the US incidence of prostate cancer has dropped to about 200,000 cases per year compared with 330,000 cases annually over the past 15 to 20 years. Previously the US Preventive Services Task Force gave PSA-test screening a low rating, but Moul said that more primary care physicians are reembracing PSA-test screening.

Albala added that when PSA testing was first introduced, the US incidence of prostate cancer was about 1 in 6 or 7 men. “But we saw a drop in the [number of] patients [with metastatic disease] who we were seeing,” noted Albala. “I remember when I was at the [Veterans Health Administration], we’d see many of these [patients with metastatic disease] come in, and the PSA era really changed that.”

CONSIDERATIONS FOR PSA-TEST SCREENING

Although PSA-test screening does need to be refined, it should continue because it is an effective basic screening, Moul said, with secondary tests often used to “fine-tune” decisions before completing a biopsy. Albala added that urologists do recognize that the PSA test has limitations, as it is not cancer specific. The wide criticism of PSA-test screening may have been derived from how the medical field used the information generated by the test, Moul said. Indeed, PSA testing does not match the accuracy of

tissue-based biopsy testing and is not recommended for diagnosis.³ However, as high PSA levels may indicate metastatic disease, PSA screening can help catch metastatic prostate cancer. Albala echoed Moul’s advocacy of PSA testing as a significant contributor to detecting prostate cancer; it has been used in various ways, he said, in testing free-to-total PSA ratios, PSA velocity, and PSA density in patients.

“Back when I [was] in training, 1 in 5 men [who presented with prostate cancer] typically presented with metastatic disease. And then in the PSA era, that dropped to 2% or 3%, meaning that only 2% to 3% of guys presenting with prostate cancer had [metastases],” Moul explained.

USE OF NOVEL LIQUID BIOMARKER TESTS IN PROSTATE CANCER SCREENING

Numerous next-generation tests to screen for prostate cancer have become commercially available, said Albala, including blood-based (eg, Prostate Health Index [PHI], 4Kscore) and urine-based tests (eg, Exosome, SelectMDx, PCA3).

When doing an Exosome test, practitioners do not need to complete a rectal exam, Moul explained, whereas with a PCA3 test, an attentive digital rectal exam must be done before the urine test. In completing the Exosome test, patients void urine through a special device; previously, this would be done in house, but as tests by mail have become available, patients are now able to collect the urine sample at home, return it through the mail, and receive results within a week. Regarding blood testing, Moul said that he has more experience with the PHI than other tests; the PHI predicts the likelihood of cancer in 4 risk groups: low, low-intermediate, intermediate, and high. Crucially, however, the Exosome test does not predict cancer or no cancer but rather the probability of Gleason 7 or higher. Moul believes that PHI and Exosome are somewhat complementary to one another.

Albala said that when most patients arrive at his clinic, they need to leave a urine sample, and it is often difficult to produce a second sample during the same visit. He has been using the Exosome test because patients can complete their second sample at home, but the Exosome and SelectMDx urine tests are comparable, Albala believes. With the SelectMDx test, a rectal massage is not necessary. Because urine tests predict prostate cancer slightly more accurately than do blood tests, Albala’s institution has pivoted more toward urine testing.



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“When a new test comes out, I look at the efficacy, cost, [adverse] effect profile, the ease of doing the test, and then the durability. I always think of those 5 things—whether it’s a new drug, a new procedure, or whatever—in the back of my head to try to put these tests in perspective because when new tests come out, there’s a lot of hype, a lot of excitement...You want to [come] back down to earth” and use tests when they are truly appropriate, Albala said.

IMPACT OF COVID-19 ON SCREENING

With the COVID-19 pandemic, the use of telehealth skyrocketed, allowing patients who did not want to come into the office to still meet with their physicians. A benefit of this trend, said Moul, is that it has helped him to develop a good therapeutic relationship with new patients, especially those with an elevated PSA level who would otherwise have been physically visiting the cancer center and been very uncomfortable and nervous. With telehealth, some first-time visits have been more relaxed and open. Exosome testing by mail has been especially convenient during this time, Moul stated.

SELECTING SECONDARY TESTS IN PROSTATE CANCER SCREENING

After a standard PSA test indicates that PSA level is elevated, borderline, or in the “gray zone,” many patients request more data before they undergo an invasive tissue biopsy, Moul explained. Those data can be generated by various secondary tests. A blood test (such as PHI) can be used to measure a patient’s risk of prostate cancer. Benefits of a PHI include fewer potential biopsies and more accurate detection of prostate cancer, helping doctors not only see whether a more aggressive type of cancer is detected but also better target any necessary treatment. Urine tests can detect the overexpression of PCA3 and assess risk of prostate cancer.⁵ The PHI test is the first choice of secondary blood tests at Duke, said Moul, because it is done in house and can be performed right away. They have even begun to train primary care physicians to do this test.

When Moul first came to Duke, they were using the PCA3 urine test as a secondary test to standard PSA blood testing, but because it was a first-generation test, the data were not robust enough. Now, said Moul, they tend to use Exosome as their secondary urine test, and they

have been satisfied with it. The Exosome diagnostics and SelectMDx tests are both widely used, said Moul, and his advice to new urologists is to become comfortable with at least 1 secondary blood test and 1 urine test to best be able to work with their patients.

Moul completes a rectal exam during a patient work-up to contextualize the PSA level based on prostate size, he explained. “Rectal exams are not perfect, and it’s hard to teach a primary care physician to do them—[plus] many of them are not that interested. But as urologists and as urology educators, we need to make sure that all residents who we train know how to do a good rectal exam, [including assessing the] size of the prostate,” Moul said.

If a patient is borderline on a rectal exam and has a borderline PSA level family history, a PHI is usually the next test Moul will order. Albala said that his institution uses PSA as its primary test, and for secondary tests, they previously used a blood test with 4K score but have started pivoting more toward urine tests.

ROLE OF MRI IN PROSTATE CANCER SCREENING

Among the challenges presented by the use of MRI to screen for prostate cancer is that MRI quality can vary, depending on the institution.

“Sometimes patients will come in with an MRI [they’ve had done elsewhere], and they want a fusion biopsy based on that outside MRI. That’s problematic...because...we tell them, ‘Well, you have to repeat the MRI at our institution before we do a fusion,’” Moul said.

Also, said both Albala and Moul, insurance coverage presents another challenge. Moul said that in North Carolina, for instance, many insurance plans will not cover MRI in the setting of no previous biopsy, and the expensive out-of-pocket costs can run from \$800 to \$2500 at their institutions, Albala and Moul stated.

UNMET NEEDS

Several areas of unmet need exist in the prostate cancer screening space. Underserved populations is one, said Moul; many underserved patients who are at high risk for prostate cancer present with disease too late in the clinic. Also, patient adherence in following through with tests is less than ideal. Finally, both Moul and Albala emphasized the need for standardization in assessing the size of the prostate through rectal exam. Moul noted that if they

could quickly capture the estimated size of the prostate, they could then more effectively contextualize the PSA level.

Albala echoed the need for a standardized way of assessing the size of the prostate. “I remember the days when Merck would give us the little models of the prostate. There was 30 g, 40 g, 50 g, and I remember trying to feel those. There was a disconnect with what you felt on the rectal exam and in the models, but that was the best that we had 20, 30 years ago. We are [getting] better, I think.”

In the urology community, Moul opined, more education is needed to better understand the use of secondary tests, including how to determine whether to use PHI or 4K, how to use a urine test, and when to order an MRI. Algorithms have been put in place at Duke, but much individual variation still exists.

CLOSING THOUGHTS

“We’ve become more sophisticated. We’ve used these tools [and] put them together,” Albala concluded. “That’s the beauty of what we deal with [in] practice, that we’re assimilating different tests to try to decide. Because biopsy is a big commitment and complications [can happen—although] they’re relatively minor, they do exist for patients—and if we can be better clinicians, make diagnoses with [a higher] comfort level, I think that’s what our goal is.” ●

REFERENCES

1. Prostate cancer screening guidelines. Memorial Sloan Kettering Cancer Center. Accessed May 26, 2021. <https://www.mskcc.org/cancer-care/types/prostate/screening/screening-guidelines-prostate>
2. American Cancer Society recommendations for prostate cancer early detection. American Cancer Society. Updated April 23, 2021. Accessed May 26, 2021. <https://www.cancer.org/cancer/prostate-cancer/detection-diagnosis-staging/acs-recommendations.html>
3. US Preventive Services Task Force; Grossman DC, Curry SJ, Owens DK, et al. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *JAMA*. 2018;319(18):1901-1903. doi:10.1001/jama.2018.3710.
4. Boerrigter E, Groen LN, Van Erp NP, et al. Clinical utility of emerging biomarkers in prostate cancer liquid biopsies. *Expert Rev Mol Diagn*. 2020;20(2):219-230. doi: 10.1080/14737159.2019.1675515
5. Prostate cancer: advancements in screenings. Accessed June 11, 2021. <https://www.hopkinsmedicine.org/health/conditions-and-diseases/prostate-cancer/prostate-cancer-advancements-in-screenings>