After a High PSA Result: What Happens Next

Phillip Koo, MD [00:00:00] Hi, I'm Phillip Koo from the Prostate Cancer Foundation. And today we're going to have a very important discussion about what to do when you have an abnormal PSA. So, we've been talking a lot about the importance of prostate cancer screening, but now it's important to transition to this conversation about what you do when have an abnormal PSA and to lead us in that discussion, we have Dr. Jim Hu, who's a professor of urology at the Weill Cornell Medical Center. So, thank you very much for joining us today.

Jim Hu, MD, MPH [00:00:27] Thanks, Phil, delighted to be here.

Phillip Koo, MD [00:00:30] So, let's first start off by talking about what is abnormal.

Jim Hu, MD, MPH [00:00:34] Sure, so abnormal, the general threshold we use regardless of age is a cutoff of 4.0. However, there are age-specific cutoffs. For example, we know that as a man gets older, the prostate gets bigger, there's benign prostatic hyperplasia, which also produces more background PSA.

Phillip Koo, MD [00:00:51] Are there any other things that could potentially cause a spurious increase in the PSA level?

Jim Hu, MD, MPH [00:00:56] Absolutely, so there's the possibility that someone can have a urinary tract infection, there's inflammation, but most commonly it would be the potential of the BPH causing background PSA, or as we are screening for prostate cancer, of course.

Phillip Koo, MD [00:01:14] Alright. So, now that you have this abnormal PSA, oftentimes it's ordered by a primary care physician, then you get the referral and it says abnormal PSA. So, what do you do next?

Jim Hu, MD, MPH [00:01:23] Absolutely. So most often, I think the correct answer is just to repeat the PSA because we know that, for example, if you take two consecutive PSAs, they're not going to be the same. Also, I'd give it some time. That is the half-life of PSA, about five half-lives or so would be about two or three months. So, I wouldn't be testing this days apart. But the next thing, if it is a consistent signal, that is on two consecutive PSAs there's elevation, I personally would order a prostate MRI.

Phillip Koo, MD [00:01:52] So, the prostate MRI is ordered. Let's sort of go down two paths. Let's say one path there clearly is a lesion that looks suspicious. What do you do then?

Jim Hu, MD, MPH [00:02:02] Sure. So just very quickly, prostate MRI read by the radiologist is scored on a scale of 1 to 5. One and 2, there's high confidence that there's nothing suspicious for prostate cancer. A three is in the middle. It's equivocal. A 4 has about a 50% chance of finding clinically significant cancer. Five, about 70, 75% chance of finding cancer. So, if it's a 3, 4, 5, that's where we have a discussion about the pros and cons of doing a prostate biopsy.

Phillip Koo, MD [00:02:30] So, you know, those pros and cons, 3, 4, 5, tell us how you sort of weigh that and give your advice with regards to whether or not the patient should pursue a prostate biopsy.

Jim Hu, MD, MPH [00:02:41] Absolutely. So, what are the cons of a prostate biopsy? Of course, it's a medical procedure. There's a chance of complications, although I think it's relatively low. It's uncomfortable. Most prostate biopsies are done awake under local anesthesia. That being said, for example, with a 3, where it's equivocal, there is the possibility of giving other biomarkers to determine, is there a higher risk of cancer? Is it worth doing? Whereas of course with a 4 or 5, we're talking at least a 50% chance of finding cancer.

Phillip Koo, MD [00:03:11] So then let's sort of backtrack and go back to the prostate MRI and talk about those cases in which you have an elevated PSA, but a prostate MRI that comes back as negative as a 1 or 2, what do you do then?

Jim Hu, MD, MPH [00:03:23] Sure, so one of the other key pieces of information MRI will give us is the prostate volume. And so, you can take, we talked about the absolute cutoff [of PSA] of 4, but that can be then individualized to a man's prostate size. And so, for example, we know we use PSA density, that is the total PSA divided by the prostate volume. And there's two thresholds that have been shown, or associated, with an increased risk of significant cancer that is either 0.15 or 0.20. And so even if someone has a normal or a low PI-RADs, 1 or 2 MRI but their PSA density is high, or let's say greater than 0.2, then that would be another reason despite a normal non-suspicious prostate MRI to move forward with the biopsy based on PSA density.

Phillip Koo, MD [00:04:06] So we're gonna reserve a conversation about how prostate biopsies are done for a later time. But you did mention biomarkers. So how do biomarker come into play in this space before biopsy?

Jim Hu, MD, MPH [00:04:18] Absolutely. So, let's just say, for example, and you pointed out that a lot of times primary care doctors order the PSA. There's also primary care doctors for a PSA that's 4 to 10, right? In the abnormal range, they'll go ahead and order a percent free PSA, or now there's 4K, there's prostate health index. These are all blood-based biomarkers that look at, for example, in the case of 4K or prostate health index PHI, they're looking at different kallikreins or different proteases, which is what PSA is, right, in the bloodstream. And there's algorithms, there's predictive tools, nomograms that are backed with long-term outcomes of biobanks to determine what the percent chance of prostate cancer is.

Phillip Koo, MD [00:05:01] So if you look back, you know, obviously we've had a lot of discussions about PSA and some of the controversies about PSAs in other videos. How would you say we've developed in terms of all these other tools and how is it different today than it might have been 15, 20 years ago?

Jim Hu, MD, MPH [00:05:18] Absolutely. Well, I think just and not to retread old things, but certainly PSA, I think there's still a lot of confusion, right? Like there's a lot of primary care doctors, guidelines aren't terribly clear. So, we know that, for example, based on a large, randomized trial, that PSA has benefit in men aged 55 to 69 years. I think the challenge is that as men get older, of course, the likelihood of dying from other causes or competing risks increases, right. And so, I think a lot of patients are aware, for example, Joe Biden recently, where he stopped PSA testing at age 73. Then in the news, he's found to have aggressive prostate cancer, starts hormone therapy at age 83, 84. So in fact, in that case, the PCP or the primary care doctor followed the guidelines. They stopped PSA testing. And so, I think it's just important to realize that we're moving towards, I think, an

individualized test. The challenge is, is that your primary care doctors, when they're dealing with all these other health issues, high blood pressure, diabetes, obesity. They just don't have the time to go over the nuances of PSA testing.

Phillip Koo, MD [00:06:21] So I think one of the take home messages, and maybe just to summarize, patients should make sure they're getting the PSA tests appropriately. Four is a good cutoff, but once you have 4, obviously go see a urologist, and there's a whole slew of tests and whatnot to really make sure that biopsy can be performed appropriately. Does that sort of sum it up?

Jim Hu, MD, MPH [00:06:40] Absolutely, I think of it as sometimes, particularly when you have patients that come in with multiple tests, like you said a 4K, another even urine test biomarkers, MRI, it's kind of like thinking about making an investment, right? You're not going to make an investment based on one thing, so you're looking at the battery of biomarkers and trying to see, you know, are three things favoring suspicion for prostate cancer while one does not, and then making a decision based on that.

Phillip Koo, MD [00:07:05] Well, that's great. So, thank you so much for helping clarify, I think a question that exists with so many of us. We appreciate the time.

Jim Hu, MD, MPH [00:07:12] Sure, absolutely. Thank you.