

Phoenix5 To help men and their companions overcome the effects of prostate cancer



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What Happens if PSA Comes Back After Surgery?

The return of PSA is a possibility that strikes terror in the heart of every radical prostatectomy patient; in fact, for many men, the dreaded follow-up PSA tests after surgery are almost worse than having the operation itself. What will you do if your PSA is no longer undetectable? The good news is, *you may not need to do anything for years.*

Does the man have a local recurrence of cancer that would respond to radiation, or does this represent micrometastases to lymph nodes and bone? Until now, there has been no way to tell.

In a landmark paper -- the largest, most complete study of the return of PSA after radical prostatectomy -- Hopkins doctors have developed guidelines to help patients and doctors know what to do if PSA comes back. Their remarkable effort -- an elegantly simple chart that accurately predicts a man's risk of developing metastatic cancer -- is the post-operative equivalent of the "[Partin tables.](#)" developed by urologist Alan W. Partin, M.D., and urologist-in-chief Patrick C. Walsh, M.D. Like those now-indispensable tables, this chart has the potential to revolutionize the way doctors and patients make decisions about what to do next.

"PSA is very sensitive in detecting any recurrence of cancer. That's because only prostate cells make PSA -- so if it goes up after a radical prostatectomy, it means prostate cells are still present somewhere. For all intents and purposes, it means that a few cells escaped the prostate before it was removed, and now have grown to the point where they're producing enough PSA to be detected," explains Walsh.

"Fortunately, for most men with organ-confined cancer, this never happens. However, for men who had more advanced disease at the time of surgery, the return of PSA is extremely frightening." Walsh originated this study to fill what he describes as a "large knowledge gap" for patients and doctors.

- "The first thing many patients want to know is, how long are they going to live?"
- And the first thing many doctors want to know is, when should they begin treatment, and how should they treat these patients?
- Does the man have a local recurrence of cancer that would respond to radiation, or does this represent micrometastases to lymph nodes and bone?"

Until now, there has been no way to tell. The study, published in the Journal of the American Medical Association, is based on 10,000 patient-years of follow-up data. Between 1982 and 1997, nearly 2,000 men underwent a radical prostatectomy at Johns Hopkins. Of these, 315 men developed an elevated PSA (defined as being higher than 0.2 nanograms/milliliter). Eleven of these men opted for early hormone therapy, and were not included in the study. The remaining 304 men were followed carefully.

"We set out to ask a few questions," says Walsh: "Could we predict how long it would take for patients who had metastases to show them on a bone scan, and then once that happened, how long would they live? The news is actually quite good: Most patients do very well for a long period of time." On average, it took eight years from the time a man's PSA first went up until he developed metastatic disease -- which suggests, Walsh says, that "there is no need to panic" at the first sign of a rise in PSA. Even after developing metastatic cancer (detected by bone scans and other imaging techniques), men still lived an average of five years -- and if the metastases showed up more than seven years after surgery, men had a seventy percent chance of being alive seven years later.

On average, it took eight years from the time a man's PSA first went up until he developed metastatic disease -- which suggests that there is no need to panic at the first sign of a rise in PSA.

"When men see their PSA levels rise again, they think that means the cancer is back and they need to get treated right " says oncologist Mario Eisenberger, M.D., a co-author of the study. "But men often live for years without having the cancer spread. This information will better equip doctors and their patients to decide what treatment -- if any -- is most appropriate."

This interval between the reappearance of PSA and the first sign of advanced disease can be predicted, the Hopkins researchers found, using three pieces of information:

- The Gleason score of the pathologic specimen (the removed prostate, evaluated by a pathologist after surgery). Is it Gleason 7 or lower, or Gleason 8 or greater.
- The time it takes for PSA to come back. Is it less than two years after surgery, or greater? And,
- How rapidly is the PSA level doubling? Is it greater or less than 10 months?

Using these criteria, men and their doctors can pinpoint the likelihood of developing metastatic disease. For example: If a man has Gleason 7 disease, has his first PSA recurrence more than two years after surgery, and has a PSA doubling time longer than 10 months, his likelihood of being free of metastasis at seven years is 82

WHAT THE NUMBERS MEAN

If you have a Gleason score of 5-7 Your PSA increased more than two years after surgery AND your PSA doubling time was greater than 10 months:
Your chance of *not developing metastasis* (having a bone positive scan) in:

Three years: 95 percent
Five years: 86 percent
Seven years: 82 percent

OR your PSA doubling time was less than 10 months:
Your chance of *not developing metastasis* in:

Three years: 82 percent
Five years: 69 percent
Seven years: 60 percent

being free of metastasis at seven years is 62 percent. Conversely, if a man has Gleason 7 disease, but his PSA goes up within two years of surgery, and the time it takes PSA to double is less than 10 months, his likelihood of being metastasis-free at seven years is 15 percent.

"So the first thing these tables can do is reassure the many patients who are going to have a long-term, symptom-free, metastasis-free interval, that close observation is all that's really necessary," says Walsh. On the other hand, says urologist Alan W. Partin, M.D., Ph.D., co-author of the study: "If their chances of progressing rapidly are high, they may wish to start hormonal therapy earlier or get involved in an experimental trial" of more aggressive treatment. "These tables are going to help men who are at low risk and help men at high risk make a more educated decision. We hope it will also decrease the anxiety for some of them." The tables will also provide invaluable baseline data for future drug research, adds Partin. "Until now, it's been difficult to know if a drug was helping someone, because you couldn't be sure what the disease would have done on its own. Now, researchers can compare their treatment groups with our study group and tell if their treatment is improving."

OR your time to first PSA recurrence was less than two years:
AND your PSA doubling time was greater than 10 months:

Your chance of *not developing metastasis* in:

Three years: 79 percent
Five years: 76 percent
Seven years: 59 percent

OR your PSA doubling time was less than 10 months:

Your chance of *not developing metastasis* in:

Three years: 81 percent
Five years: 35 percent
Seven years: 15 percent

If you have a Gleason score of 8-10 AND your time to first PSA recurrence was greater than two years:

Your chance of *not developing metastasis* in:

Three years: 77 percent
Five years: 60 percent
Seven years: 47 percent

OR your time to first PSA recurrence was less than two years:

Your chance of *not developing metastasis* in:

Three years: 53 percent
Five years: 31 percent
Seven years: 21 percent

PSA Anxiety:

The Downside of Ultra- Sensitive Tests

You've had the radical prostatectomy, but deep down, you're terrified that it didn't work. So here you are, a grown man, living in fear of a simple blood test, scared to death that the PSA- an enzyme made only by prostate cells, but all of your prostate cells are supposed to be gone -- will come back. Six months ago, the number was 0.01. This time, it was 0.02.

You have PSA anxiety. You are not alone.

This is the bane of the hypersensitive PSA test: Sometimes, there is such a thing as too much information. Daniel W Chan, Ph.D. is professor of

pathology, oncology, urology and radiology, and Director of Clinical Chemistry at Hopkins. He is also an internationally recognized authority on biochemical tumor markers such as PSA, and on immunoassay tests such as the PSA test. This is some of what he has to say on the subject of PSA anxiety:

The only thing that really matters, he says, is: "At what PSA levels does the concentration indicate that the patient has had a recurrence of cancer?" For Chan, and the scientists and physicians at Hopkins, the number to take seriously is 0.2 nanograms/milliliter. "That's something we call biochemical recurrence. But even this doesn't mean that a man has symptoms yet. People need to understand that it might take months or even years before there is any clinical physical evidence."

On a technical level, in the laboratory, Chan trusts the sensitivity of assays down to 0.1, or slightly less than that. "You cannot reliably detect such a small amount as 0.01," he explains. "From day to day, the results could vary -- it could be 0.03, or maybe even 0.05" -- and these "analytical" variations may not mean a thing. "It's important that we don't assume anything or take action on a very low level of PSA. In routine practice, because of these analytical variations from day to day, if it's less than 0.1, we assume it's the same as nondetectable, or zero."

FURTHER READING

Pound, CP; Partin, AW; Einsenberger, MA; Chan, DW; Pearson, JD; and Walsh, PC. "[New Method to Assess Risk of Advanced Cancer After Prostate Removal.](#)" *Journal of the American Medical Association*, Vol.281, pp.1591-1597.

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