EDITORIAL

Reassessing PSA

The review article by Alan So and the Vancouver group on PSA is an excellent summary of the key performance characteristics of this important molecule. Indeed, the discovery of this marker has revolutionized clinical urology. The impact of PSA has altered our practice in three ways. It has completely changed the face of prostate cancer. This disease has become the commonest cancer in North American men. This would not have happened without the increase in case finding that occurred as a result of PSA screening. It has produced dramatic stage migration and transformed the identification of disease recurrence and hormone refractory disease.

Secondly, it is beginning to have an impact in the management of benign prostate disease. The findings of the recent MTOPS trial of BPH are that men with a PSA in the high normal range are at increased risk of urinary retention and other complications of BPH, and the PSA has a role in guiding therapy.[1]

Thirdly, PSA has dramatically increased the profile of our specialty. Genito urinary cancer now comprises 28% of all newly diagnosed cancers. Men are urged to 'get tested' and 'see your doctor'. This has increased our footprint on the health care landscape substantially.

However: the argument for the usefulness of PSA in early detection has received a serious challenge from the results of the Prostate Cancer Prevention Trial (PCPT) published last month in the NEJM.[2] This is required reading for all urologists. The study, which randomized 18 882 men between placebo and finasteride for 7 years, mandated a biopsy in all men at the end of the study. The primary finding, a 25% reduction in the risk of a positive biopsy, is enormously tantalizing. However, this reduction comprised a decrease from 24.4% to 18.4%. In other words, one in four men having a biopsy with a normal PSA were found to have prostate cancer.

This is the first sizeable cohort of men with a normal PSA subject to systematic biopsies. It is a cause for concern. This is only mildly less than the proportion of men with an elevated PSA found to have cancer (about 1 in 3). It suggests that the PSA test has provided an excuse to perform prostate biopsies, and that it has been the increase in biopsies that has been responsible for the increase in diagnosis and stage migration. This rate of positive biopsies is 10 times the mortality rate.

What does this mean for screening? Despite the clear benefits, there are significant costs that cannot be denied. Evidence of benefit includes the dramatic stage migration that has occurred in the last decade, the Swedish randomized study indicating that early radical treatment cuts mortality from prostate cancer by half,[3] and the fall in mortality in many constituencies. However, the PCPT data suggests that the risks of overtreatment are staggeringly high if most or all patients are treated radically. Supporting this, recent CaPSure data indicated that, in the US, 95% of diagnosed patients receive definitive therapy.[4]

There are several solutions. Discontinuing PSA testing would return us to the bad old days of men presenting with incurable locally advanced and metastatic disease. The approach that makes sense is to continue to screen, but to be far more selective about who is treated. Higher grade patients warrant radical intervention. However, we should accept that the majority of men with PSA driven positive biopsies are not destined to suffer from the disease. Patients with small amounts of Gleason 2-6 cancer should not, in most cases, be treated. We must strenuously resist the knee jerk surgical reaction that 'it's a cancer, and we'd better get rid of it'. This approach needs to be changed in two ways. The perspective should be, 'It's a cancer, and we MAY have to get rid of it'. Secondly, we have to alter our patients' understanding of what it means to live with untreated cancer. This is a formidable communications challenge that many urologists have not faced in the past.

Additionally, research which focuses on identifying molecular markers for biologically aggressive disease in good risk prostate cancer must be the highest priority. Existing markers, including PSA doubling time, should be further evaluated with respect to their ability to identify the 'bad actors' and provide a basis for definitive therapy in these highly prevalent patients. We owe our patients (some of whom will be ourselves) no less.

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Editor-in-Chief

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2. Thompson I et al. The influence of Finasteride on the development of prostate cancer. *NEJM* July2003;349(3):213.
3. Holmberg L et al. A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. *N Engl J Med* 2002 Sep 12;347(11):781-789.
4. Harlan S, Carroll P. Time trends in patients choice of watchful waiting from CapSure. *J Urol* Nov 2003;170:1804-1807.