

PSA TESTING UPDATE FOR GP'S

Dr Troy Gianduzzo

UPDATED UROLOGICAL SOCIETY OF AUSTRALIA AND NEW ZEALAND PSA GUIDELINES

Recently the Urological Society of Australia and New Zealand released a policy statement on PSA testing. In essence the policy states that a single initial PSA test combined with a DRE should be offered to all men from the age of 40 after an informed discussion of the risks and benefits of PSA testing. In men aged 75-80 years, screening should be considered on an individual basis. The USANZ policy along with a detailed analysis of the relevant literature can be accessed via my website www.troygianduzzo.com.au under the tab "Prostate News" located on the bottom right corner of the home page.

In essence, the aim of this policy is to risk stratify patients into high risk or low risk for the subsequent development of prostate cancer by comparing a patient's PSA to the median PSA for his age. An initial PSA test should be offered to all men at the age of 40 after an informed discussion of the pros and cons of PSA testing. Patients who have a PSA higher than the median for their age (PSA > 0.6 ng/mL, age 40-49 yrs; PSA > 0.7 ng/mL, age 50-59 yrs) are at a higher risk for the subsequent development of prostate cancer and should be followed more closely with annual PSA and DRE. Conversely patients with a PSA value less than the median could be followed less frequently. It is important to note that a PSA above the median does not mean that the patient necessarily needs a biopsy. Rather it is a risk stratification tool to identify patients who should be followed more closely.

Patients with a significant rise in PSA levels (>0.35/yr for values <4.0 and >0.75 /yr for values >4.0) should be considered for TRUS biopsy. In addition men with a low free: total PSA ratio should also be carefully considered. Men with a positive family history of prostate cancer should be offered annual screening with PSA and DRE irrespective of their PSA value. It is vitally important that PSA testing is combined with a DRE as a "normal" PSA value does not exclude prostate cancer. *A patient with an abnormal DRE should be referred for consideration of a TRUS biopsy irrespective of the PSA level.*

DOES PSA TESTING DECREASE PROSTATE CANCER MORTALITY?

Two trials published in the 26 March, 2009 edition of the New England Journal of Medicine addressed whether

PSA screening decreases prostate cancer mortality. Andriole et al published the first report on prostate cancer mortality from the PLCO (Prostate, Lung, Colorectal and Ovarian) Cancer screening Trial.¹ In this report, 76 693 men aged 55-74 years were randomly allocated to screening or usual care. The study concluded that there was no significant difference in prostate cancer mortality between the 2 groups with 50 deaths in the screening group at 7 years and 44 in the control group.

However this study has been criticised heavily because of significant contamination in the control group in which 52% of the controls had received PSA testing by the 6th year. In addition 44.1% of patients in the control group had at least 1 PSA test at baseline and 53.9% of controls had a prior DRE.

The European Randomised Study of Screening for Prostate Cancer (ERSPC) reported on 182 160 men aged 50-74 from seven European countries who were randomised to screening or no screening.² There were 214 cancer related deaths in the screening group and 326 deaths in the control group. After correction for non-compliance, there was a reduction in the detection of advanced disease and a 27% reduction in the risk of death from prostate cancer. In this report, the survival curves began to separate at 7 years suggesting that longer follow-up may show a more marked difference. The number needed to treat to save one life in this trial was 48 while the number needed to screen was 1410 indicating a potential overtreatment effect. However follow-up was relatively short with a median of 9 years and it is possible that the differences between the groups may become more marked over time.

In addition the number needed to screen in the ERSPC study is similar to that seen in breast cancer screening studies. In a recent meta-analysis of breast cancer screening for the U.S. Preventive Services Task Force the number needed to screen to prevent one breast cancer death was 1904 (95%CI: 929-6378) for women aged 39-49 years, 1339 (95% CI: 322-7545) for ages 50-59, and 377 (95%CI: 230-1050) for ages 60-69.³ It is also interesting to note that in Australia in 2006 there were 17,444 prostate cancers diagnosed and 2,952 deaths representing 29% and 13% of all non-cutaneous cancers in men respectively. The mortality to incidence ratio was 0.19. For breast cancer in that same year there were 12,614 diagnoses and 2,618 deaths representing 28% and 15% of all non-cutaneous cancers in women with a ratio of 0.20.⁴

Another notable study is The Tyrol Prostate Cancer Demonstration Project.⁵ This study evaluated the prostate cancer mortality rates in the state of Tyrol in Austria, where PSA testing is widely available free of charge, in comparison to the rest of Austria where PSA testing is not freely available. Thus it compared a screened population to an unscreened population in the same country. Prostate cancer deaths in Tyrol in 2005 were 54% lower than expected compared to a 29% reduction in the rest of Austria which represented a 25% improvement.

DOES PSA TESTING LEAD TO OVERTREATMENT?

These and other studies suggest that PSA testing and prostate cancer treatment do decrease the risk of prostate cancer mortality. However there is some concern regarding the overtreatment of clinically insignificant disease. In response to this, active surveillance is gaining acceptance as an alternative strategy in select patients.

Patients diagnosed with low volume, Gleason 6 disease may indeed have indolent disease and such patients may be candidates for an active surveillance protocol. The aim of this approach is to monitor a patient who appears to have an indolent cancer and then institute active primary treatment such as radical prostatectomy, radiotherapy or brachytherapy with curative intent if or when the cancer becomes clinically significant. This approach is distinctly different from “watchful waiting” in which delayed palliative hormonal manipulation is utilised in men with a limited life-expectancy because of age or co-morbidities. A number of active surveillance protocols have been proposed but in essence each approach involves regular PSA monitoring every 3-6 months, regular DRE every 6-12 months and interval TRUS prostate biopsies. Should the cancer be upstaged or upgraded the patient can then be offered active primary treatment at that point.

The advantage of active surveillance is that it avoids overtreatment of a potentially clinically insignificant tumour. In addition it may allow the patient to gain an extra few years in which their quality of life is maintained without incurring treatment side-effects before active treatment is required. Disadvantages of this strategy include possible understaging the initial tumour, potential missed opportunity for cure and the possible need for more aggressive treatment when it is required such as the need to perform a non-nerve-sparing prostatectomy when a nerve-sparing procedure could have been performed at the outset.⁶

WHEN TO REFER

Patients aged 40-75 with an abnormal PSA, an abnormal DRE, a normal but rapidly rising PSA or a low free:total PSA ratio should be referred for assessment. It is important to note that a ‘normal’ PSA does not necessarily exclude prostate cancer. Patients >75yo should be assessed individually in context of their co-morbidities and overall life expectancy.

WHEN TO REFER
Abnormal age-adjusted PSA
Rapid rise in PSA even though PSA may be “normal”. (rise in PSA > 0.35 / yr for total PSA values <4 and >0.75 /yr for values 4-10)
Low percentage free:total PSA <11%
Abnormal DRE

WESLEY ROBOT

Recently The Wesley Hospital was the first private hospital in Australia to acquire the new da Vinci “S” robotic unit. Compared to the standard da Vinci unit the da Vinci “S” system offers vastly improved vision with a 3D high definition system and has more refined ergonomics and instrumentation. I will soon be commencing robotic radical prostatectomy at The Wesley Hospital as a compliment to my laparoscopic radical prostatectomy program. In addition I will continue to offer low dose rate brachytherapy seed implants, high dose rate brachytherapy as well as active surveillance in select patients and thus provide a complete prostate cancer care service.

REFERENCES

1. Andriole, G. L., Crawford, E. D., Grubb, R. L., 3rd, Buys, S. S., Chia, D., Church, T. R. et al.: Mortality results from a randomized prostate-cancer screening trial. *N Engl J Med*, 360: 1310, 2009
2. Schroder, F. H., Hugosson, J., Roobol, M. J., Tammela, T. L., Ciatto, S., Nelen, V. et al.: Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med*, 360: 1320, 2009
3. Nelson, H. D., Tyne, K., Naik, A., Bougatsos, C., Chan, B. K., Humphrey, L.: Screening for breast cancer: an update for the U.S. Preventive Services Task Force. *Ann Intern Med*, 151: 727, 2009
4. (AIHW), A. I. o. H. a. W.: Australian Cancer Incidence and Mortality (ACIM) books.: AIHW, 2009
5. Bartsch, G., Horninger, W., Klocker, H., Pelzer, A., Bektic, J., Oberaigner, W. et al.: Tyrol Prostate Cancer Demonstration Project: early detection, treatment, outcome, incidence and mortality. *BJU Int*, 101: 809, 2008
6. Mohler, J., Bahnsen, R. R., Boston, B., Busby, J. E., D’Amico, A., Eastham, J. A. et al.: NCCN clinical practice guidelines in oncology: prostate cancer. *J Natl Compr Canc Netw*, 8: 162