Newsletter
Edition no. 1
October 2007

PATHCHAT

PATHCHATPATHCHATPATHCHATPATHCHATPATH

In this edition Read more about

The latest on....Prostate Cancer Screening

By: Dr Frank Kramer
MBChB (Pret) FFPath (SA)

The goal of early detection of prostate cancer has been the identification of those with clinically significant cancer. The development of PSA testing in the 1990s has been the most important advance that has been made in detecting prostate cancer at an early stage.

Recently, more sensitive and specific tests for screening for prostate cancer have been developed, which have improved the detection of both aggressive (faster growing) and non-aggressive (slow growing) prostate cancers. The natural history of prostate cancer is that it is progressive over time but over what period of time is uncertain. The challenge, therefore, is to identify the biology of the cancer, so that those cancers requiring treatment are detected early and treated effectively, which will significantly reduce the morbidity and mortality. Furthermore, unnecessary biopsies and over- treatment of cancers not requiring treatment, resulting in significantly reduced quality of life (e.g. urinary and erectile dysfunction) may be prevented.

Age of onset of screening

The age for starting PSA screening together with digital rectal examination (DRE) has traditionally been 50 years of age. However, high-risk groups such as men with a family history of prostate cancer and black African population groups, may benefit from screening at an earlier age. Furthermore, autopsy reports have shown histologic evidence of prostate cancer in ± 25% of men in the 4th decade of life, and cases have been reported in men in their 30's.Therefore it would be reasonable to obtain a baseline PSA measurement at age 40 to assess the risk for subsequent prostate cancer detection. Such a risk assessment may be useful in deciding on the appropriate surveillance strategy or whether a prostate biopsy should be performed. Current guidelines recommend that for men who choose to begin PSA screening, should do so at age 40.

PSA testing

Total PSA (tPSA) Total PSA was the only PSA-based test available before the discovery of the molecular forms of PSA. tPSA results are more reliable if the patient abstains from ejaculation 48 hours prior to collecting blood, preferably drawn before DRE, as these may result in elevated levels of serum PSA.

Traditionally, a PSA cut-off for prostate biopsy is taken as 4.0ng/ml. There are a number of issues regarding this threshold value:

- Only up to 30% of men biopsied are diagnosed with prostate cancer
- Those with benign prostate disease (BPH, prostatitis) also have elevated levels
- Diagnostic grey zone 4 - 10 ng/ml
- Lack of sensitivity: ± 25% of men biopsied have cancer below the PSA threshold of 4.0 ng/ml, therefore using this value will miss a significant number of potentially curable cancers.

Proposed solutions have been as follows:

- A tPSA level of 2.5ng/ml has been suggested as being more appropriate as a cut-off level.
- The sensitivity (cancer detection) and specificity (elimination of unnecessary biopsies) may be increased by using PSA velocity, the measurement of molecular forms of PSA such as complexed PSA (cPSA) and percent-free PSA (%fPSA), and using age-adjusted reference ranges.

The latest on….Prostate Cancer Screening (...continue)

PSA Velocity (PSAV)

PSA velocity (PSAV) is defined as the rate of change of PSA over time. PSAV is best used in younger men (in their 40s) when beginning an early detection program. These men have predominantly normal PSA levels but rises in PSA levels of > 0.2-0.4 ng/ml per year should raise the suspicion of prostate cancer.

More specifically: those with tPSA levels of < 4ng/ml that has a PSAV >0.5ng/ml/year; and in those with tPSA levels of 4-10ng/ml that has PSAV >0.75/year, a biopsy should be considered. Measurement should be made on at least 3 consecutive specimens drawn over at least 18-24 month intervals.

Percent-free PSA (%fPSA)

PSA circulates in the plasma in both free and complexed forms. Free PSA can be measured and expressed as a ratio with total PSA. Studies have shown that the % free PSA is significantly lower in men who have prostate cancer compared to men who do not. A low %fPSA is associated with cancer (<10%), while a high %fPSA (>25%) is indicative of BPH. It is typically not used to define cancer but to identify BPH patients to avoid biopsies. In a recent study, men who had total PSA levels between 4.0 and 10.0 ng/ml (the diagnostic "grey zone") had fPSA performed, and a 25% fPSA cut-off detected 95% of prostate cancers and 20% of unnecessary biopsies.

"Relax, Mr. Wilde,
it's just a simple prostate examination!"

Complexed PSA (cPSA)

Direct measurement of the complexed form of PSA is now available, and shows great promise. cPSA been shown to outperform tPSA over all PSA ranges and is being proposed to be used as a initial line test for prostate cancer detection, in addition to staging and monitoring. Levels of cPSA are higher in men with prostate cancer while healthy men and those with benign prostatic disease have higher levels of free PSA. Recent trials have shown that cPSA offers an advantage in terms of sensitivity and specificity compared to total PSA. A cPSA cut off value of 2.2 ng/ml (equivalent to tPSA cut off value of 2.5 ng/ml) decreases the number of unnecessary biopsies in the tPSA range of 2.5-6.0 ng/ml. Results are similar for cPSA and %fPSA, but the advantage of cPSA is that it is a single test, whereas %fPSA requires two laboratory tests. Finally, cPSA provides the best stability under normal sample handling conditions.

For further information:
contact local Ampath laboratory

CLYNICAL COMiNTS

Our laboratory has been requesting clinical information on our patient request forms for several years.

The assistance that this data gives us in helping to interpret results is very valuable and we encourage and appreciate it.

At times the coincidence of doctor's handwriting, patient's interpretation of their symptoms and data capturers' limited understanding of medical terminology produces results which are both baffling and amusing. Nevertheless, we usually manage to decipher them and appreciate the efforts of all concerned in assisting with clinical background to the reports that we sign out.

From time to time I shall publish a few of our more interesting examples. Here are some to start off with:

Irritable bruel syndrome
dronk in haar kop
chronic obstructive always disease
indigestive problems
complete male and female sex workout (!)

An all-time classic was: "Hederkina Linfoeus (2B) RI DT" which was meticulously transcribed from the clinical information and was eventually translated as:
Hodgkins Lymphoma 1977 (stage) 2B, on radiotherapy!