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## Low initial PSA levels links to lower risk of prostate cancer death

A landmark prostate cancer screening study of middle-aged and elderly men that included repeat visits showed that an initial prostate-specific antigen (PSA) level of 3.0 ng/ml appears to be an appropriate minimum cut-off level to determine the need for biopsy.

Few men in the study with low first-time prostate-specific antigen levels below 3.0 ng/ml developed prostate cancer and died from the disease.

Researchers also found that within this group of low-risk men, the higher the initial prostate-specific antigen level, the greater the risk of developing prostate cancer and more aggressive disease, and of dying from prostate cancer.

'Our results strengthen the justification of the use of prostate-specific antigen in risk stratification for screening purposes,' said lead author Dr Meelan Bul of the Department of Urology, Erasmus University Medical Centre, Rotterdam, The Netherlands.

'This means that we can possibly avoid unnecessary testing, diagnosis and treatment of less aggressive disease, with the accompanying side-effects, by focusing biopsies and other follow-up in men with higher initial prostate-specific antigens above 3.0[ng/ml],' Dr Bul added.

This investigation was part of the larger European Randomised Study of Screening for Prostate Cancer. Researchers analysed both incidence of and deaths from prostate cancer among 42 376 men between the ages of 55 and 74 years, randomized to either screening or a control arm.

They found 15 758 (79%) of the men had an initial prostate-specific antigen level under 3.0 ng/ml. Between 1993 and 2008, 915 of those men were diagnosed with prostate cancer – with a median follow up of 11 years – with only 23 deaths.

Of the 915 diagnosed, 182 were detected between screenings, often indicating a faster-moving disease, and overall 169 (1.1%) were determined to be aggressive prostate cancers.

Overall, prostate cancer incidence and deaths increased significantly with higher prostate-specific antigen levels. Only 129 men (1.8%) of 7126 men with prostate-specific antigen scores below 1.0 ng/ml were eventually diagnosed with prostate cancer, with just three deaths (0.04%). Of the 6156 men with prostate-specific antigen scores between 1.0 and 1.9 ng/ml, 415 (6.7%) developed prostate cancer, with 11 deaths (0.18%).

The researchers found 2476 men with prostate-specific antigen levels between 2.0 and 2.9 ng/ml, with 371 cases of prostate cancer (15.7%) and nine deaths (0.36%).

Dr Bul commented: 'The 3.0 score appears to be an appropriate threshold for the study because approximately 80% of the men aged 55 to 74 years had a prostate-specific antigen under 3.0, with few deaths from prostate cancer. At the same time, we still found a group of men with aggressive prostate cancer and we need improved methods of detecting aggressive disease.'

The investigators suggested that future research should focus on improving the detection of aggressive prostate cancers, including better risk stratification methods and new molecular and genetic markers.

**Stephen Pinn**

## Targeted therapy for metastatic renal cell cancer in older patients

Targeted therapy has become the mainstay of treatment for metastatic renal cell carcinoma, but the efficacy of this therapy within the older population is poorly understood.

Data from patients with metastatic renal cell carcinoma treated with first-line anti-vascular endothelial growth factor therapy were collected from 14 centres via the International mRCC Database Consortium (Khambati et al, 2011).

A total of 1381 patients were given targeted therapy as their first-line treatment. Of those, 144 (10%) were 75 years or older (median=78 years, range=75–89 years). Four per cent of these individuals were favourable risk, 69% intermediate risk, and 27% poor risk as per the prognostic factors determined by Heng et al (2009). There was no statistical difference in these prognostic groups between the older (≥75 years) and younger populations (<75 years) ($P$=0.1779).

The initial treatment for those ≥75 years was with sunitinib ($n$=98), sorafenib ($n$=35), bevacizumab ($n$=7), and AZD2171 ($n$=4). The older population had fewer nephrectomies (71% *vs* 80%, $P$=0.0133) and fewer brain metastases (3% *vs* 9%, $P$=0.0128). Only 23% of older patients went on to receive second-line therapy in comparison to 39% of the younger population ($P$<0.0001).

The overall response rate, median treatment duration and overall survival for the older *vs* younger group were 18% *vs* 25% ($P$=0.0975), 5.5 months *vs* 7.5 months ($P$=0.1388), and 16.8 months *vs* 19.7 months ($P$=0.3321) respectively.

When adjusted for known poor prognostic factors, age over 75 years was not found to be associated with poorer overall survival (hazard ratio=1.002, 95% confidence interval=0.781–1.285) or shorter treatment duration (hazard ratio=1.018, 95% confidence interval=0.827–1.252).

Overall response rates, treatment duration and overall survival rates were not different between the older and younger populations and age was not a prognostic factor. Thus the decision to use targeted therapy should not depend on age alone.

Heng DYC, Xie W, Regan MM et al (2009) Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor–targeted agents: results from a large, multicenter study. *J Clin Oncol* **27**: 5794–9

Khambati H, Choueiri TK, Kollmannsberger CK et al (2011) Efficacy of targeted drug therapy for metastatic renal cell carcinoma in the elderly patient population. *J Clin Oncol* **29** (suppl 7): abstr 318