Prostate Cancer: What are the Prospects and Guidelines for Screening and Prevention?

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Prostate specific antigen (PSA) is an exceptional biomarker for prostate cancer. While there has been a significant decrease in prostate cancer mortality since the introduction of PSA screening, the benefit of screening can be diminished by the loss of quality of life (QoL) stemming from both the diagnosis itself and the adverse effects of treatment. Harry J. de Koning, MD, PhD, Erasmus MC, Rotterdam, the Netherlands, quantified the effects of screening strategies on prostate cancer mortality and QoL.

According to Prof. de Koning, PSA screening can reduce prostate cancer mortality. The European Randomized Study of Screening for Prostate Cancer [ERSPC] trial was initiated in the early 1990s to evaluate the effect of screening with PSA testing on death rates from prostate cancer. In a 2009 publication, PSA-based screening was shown to reduce the rate of death from prostate cancer by 20% (95% CI, 0.65 to 0.98; p=0.04) [Schröder FH et al. *N Engl J Med* 2009]. After a median follow-up of 11 years in the core age group, the relative reduction in the risk of death from prostate cancer in the screening group was 21% (rate ratio, 0.79; 95% CI, 0.68 to 0.91; p=0.001) and 29% after adjustment for noncompliance [Schröder FH et al. *N Engl J Med* 2012].

Extremely early detection, however, can present its own set of problems. Screening has advanced the time of diagnosis by about 11 or 12 years. Up to 50% of the screen-detected tumors would never have been diagnosed in the absence of screening. However, over-diagnoses and over-treatment can lead to long-lasting treatment-induced side effects (such as incontinence and sexual dysfunction) that can negatively impact QoL. Indeed, simply receiving a diagnosis of prostate cancer has a negative effect on QoL [Korfage IJ. *Br J Cancer* 2006]. Recent data from the ERSPC study using a Microsimulation Screening Analysis indicated that PSA screening led to a gain of 8.4 life-years but of only 6.5 quality adjusted life years (QALYs) [Heijnsdijk EAM et al. *N Engl J Med* 2012].

Despite the findings that the benefits of PSA testing are diminished by about 20% when QoL is taken into account, Prof. de Koning believes that PSA testing can reduce advancement of disease and mortality. However, quantifying and informing both patients and physicians about the unfavorable side effects of PSA screening is crucial.

Prof. de Koning outlined his criteria to be taken into consideration when deciding to implement a screening program. It is important that claims of substantial positive health outcomes such as life-years gained, improvements in cognitive, motor and/or socioemotional development, and significant increases in management and treatment options be substantiated with certainty, preferably in randomized, controlled trials. The balance between adverse events and QALYs gained needs to be clarified prior to patient participation in any program. There needs to be a reasonable ratio between costs and benefits, and an understanding that implementation of the testing program will not lead to substantial unintended effects and that other developments do not change this ratio and effects in the short-run.

Longer follow-up data from both the ERSPC QoL and cost-effectiveness analyses are essential for making universal recommendations regarding screening, but it is possible that limited testing of middle-aged men at relatively long intervals is a cost-effective public health policy.

Peer-Reviewed
Highlights from the

EUROPEAN SOCIETY OF MEDICAL ONCOLOGY

2012 CONGRESS