

PSA at 60 may predict risk of death from prostate cancer

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THE DEBATE ON PSA SCREENING TO DETECT PROSTATE CANCER IS ONGOING. TWO LARGE studies published in 2009 gave an unclear message. The European ERSPC trial showed a significant reduction in prostate cancer mortality as a result of screening but with a significant risk of overtreatment in order to save lives (48 additional patients requiring treatment for each life saved). The American PLCO study showed no benefit from screening, but has been criticised for the large amount of PSA testing outside the study in the control arm, contaminating the results and potentially diluting any benefit.

A meta-analysis incorporating these two studies and four other randomised controlled trials (a total of 387,286 men), published in the *BMJ*, has examined the overall evidence for PSA screening.¹ It found that screening increased the probability of being diagnosed with prostate cancer, relative risk 1.46 (95% CI: 1.21-1.77, $p < 0.001$) but had no significant effect on mortality from prostate cancer RR 0.88 (95% CI: 0.71-1.09, $p = 0.25$) or overall mortality RR 0.99 (95% CI: 0.97-1.01, $p = 0.44$).

However, patients continue to ask their GPs for PSA tests, and many will ask to have their PSA monitored on a regular basis. A second study, in the *BMJ*, assessed the potential of another strategy to improve the efficacy of PSA screening.² It recognised that the key question in a prostate cancer screening programme is not whether a man has prostate cancer but whether that cancer is likely to cause symptoms or shorten his life.

The case control study looked at 1,167 men who had PSA tests in the early 1980s at the age of 60, and followed them up to the age of 85, with the aim of evaluating whether this early PSA result would be linked with subsequent prostate cancer mortality. Clearly, this would allow risk stratification at a young age, with the potential to target PSA screening or chemoprevention strategies at higher risk patients.

There were 43 cases of metastasis and 35 deaths from prostate cancer during the study. PSA at the age of 60 was strongly associated with subsequent risk of developing prostate cancer and also of dying from the disease. For men with PSA > 2 ng/ml the odds ratio of dying from prostate cancer was 26 (95% CI: 6.2-113). Around a quarter of the men had a PSA > 2 ng/ml at 60,

and while only a minority subsequently developed prostate cancer, 90% (95% CI: 78-100%) of deaths from prostate cancer occurred in these men.

Men with a PSA < 1 ng/ml, about half the population studied, had negligible rates of subsequent metastasis or death (0.5% risk of metastasis by age 85, and 0.2% risk of death from prostate cancer).

These findings offer a potential opportunity of predicting risk of death from prostate cancer at the age of 60, and targeting PSA screening or chemoprevention strategies for this higher risk group. However, this is a relatively small study of 1,167 men – the ERSPC looked at more than 160,000 men. Furthermore, the study involved a predominantly western European population, and it remains to be seen if these results can be reproduced in other ethnic groups, particularly high-risk groups such as Afro-Caribbeans.

If men request testing at the age of 60, it is important to remember that being in the higher risk group is not an inevitable harbinger of prostate cancer. While a PSA < 1.0 can almost rule out subsequent death from prostate cancer, even being on the 95th centile for PSA at age 60 (5.2 ng/ml) only predicts one in six men subsequently dying from prostate cancer. Higher PSA levels therefore only indicate an at-risk population who can be advised to undergo regular PSA testing.

The accompanying editorial concludes: 'For now, clinicians are best advised to individualise their approach to PSA based screening. Young men at high risk of prostate cancer, such as those with a strong family history and higher baseline PSA concentrations, should be followed closely and could also be considered for risk reduction approaches with 5-alpha reductase inhibitors or dietary and lifestyle modifications (or both). Conversely, elderly men and those with a low risk of disease could be tested less often, if at all. Approaches such as these will hopefully make the next 20 years of PSA based screening better than the first 20.'³

REFERENCES

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