Low testosterone levels linked to increased mortality

A recent study has attributed low testosterone levels to earlier death in elderly men. Declining levels of serum testosterone have been considered as a factor leading to the deterioration of health in older men; however, there have been few scientific reports to back up this theory. Laughlin *et al*. carried out a prospective study of 794 men aged 50–91 years from 1984 to 2004 in a Southern California community. The group's median total testosterone level was 300 ng/dl.

During the study, 538 deaths occurred. Men with total testosterone levels in the lowest quartile (<241 ng/dl) had a 40% higher risk of death over the following 20 years than men with normal testosterone levels. Other risk factors, such as age, pre-existing disease, obesity, and lifestyle choices, were examined, but did not explain the association of low testosterone with mortality. Low testosterone levels seemed to increase the risk of death attributable to cardiovascular and respiratory disease (hazard ratios 1.38 [95% CI 1.02–1.85] and 2.29 [95% CI 1.25–4.20], respectively).

Testosterone levels above the median for this group did not show any clear survival advantage; therefore, the authors suggest that randomized, placebo-controlled trials are needed to investigate the potential of physiologic testosterone replacement therapy to extend duration and quality of life for elderly men with testosterone insufficiency.

Original article Laughlin GA *et al*. (2007) Low serum testosterone and mortality in older men. *J Clin Endocrinol Metab* [doi:10.1210/jc.2007-1792]

Upgrading prostate cancer patients with a Gleason score of 7 and tertiary grade 5 is warranted

The Gleason score is a well-established indicator of prognostic significance in patients with prostate cancer, but there is still debate about how best to treat men with a Gleason score of 7 (3+4 or 4+3) and a tertiary pattern of 5. The US International Society of Urologic Pathology have recommended that men with this Gleason score and pattern should have their cancer reclassified as Gleason score 8 or 9.

Patel *et al*. investigated the prognostic importance of Gleason score 7 with tertiary grade 5 compared with other Gleason scores in 2,370 men with clinical tumor category 1c–3b, node-negative and nonmetastatic prostate cancer. Gleason scores were assigned and Cox regression analysis was used to judge whether there was a significant association between Gleason score and the rate of disease progression.

Men with a Gleason score 7 and tertiary grade 5 experienced PSA failure significantly more quickly than did men with Gleason score 7 without tertiary grade 5 (median time 5.0 years vs 6.7 years), and at a similar rate to men with Gleason score 8–10 (median time 5.1 years). Men with a Gleason score of 6 maintained low PSA levels for significantly longer (median time 15.4 years).

The authors conclude that it might be prudent to upgrade men with a Gleason score of 7 and a tertiary grade 5 to a higher level, and alter their treatment regimen accordingly.

Original article Patel AA *et al*. (2007) PSA failure following definitive treatment of prostate cancer having biopsy Gleason score 7 with tertiary Grade 5. *JAMA* **298:** 1533–1538

Reduced PSAV threshold is predictive of prostate cancer in men with serum PSA <4 ng/ml

Evaluations of the predictive utility of PSA velocity (PSAV) in prostate cancer have tended to focus on men with serum levels of PSA ≥4 ng/ml, in whom a PSAV >0.75 ng/ml/year indicates a need for prostate biopsy. Increasingly, men are being diagnosed as having prostate cancer with serum PSA levels <4 ng/ml. Recent research findings have suggested that a lower PSAV threshold is more appropriate for identifying a need for prostate biopsy in these individuals.

Loeb and co-workers have used data from a community-based screening study to investigate the relationship between PSAV and prostate cancer in 11,792 men aged >40 years (mean 66 years) with serum PSA levels <4 ng/ml. In total, 501 participants were diagnosed as having prostate cancer at a median of 68 months after enrollment. The authors identified a PSAV threshold of 0.4 ng/ml/year as the best predictor of prostate cancer (sensitivity 56%, specificity 83%, positive predictive value 12%, negative predictive value 98%);