EDITORIAL

Weighing up the risks and benefits of androgen deprivation therapy

AUTHOR
Dr Jonathan Rees
MD MRCS MRCGP
GPwSI Urology, Bristol

ANDROGEN DEPRIVATION THERAPY (ADT) IS COMMONLY PRESCRIBED FOR THE TREATMENT of prostate cancer, and many men remain on this therapy for several years after their cancer is diagnosed. ADT is known to be linked to increased insulin resistance, raised total cholesterol and triglycerides, increased body fat and decreased lean body mass. This suggests that this class of therapy may have a negative impact on cardiovascular and metabolic health.

In 2006, a large observational study showed that treatment with ADT (in the form of a gonadotrophin releasing hormone agonist) was associated with a 44% increase in rates of type 2 diabetes, a 16% increased risk of coronary heart disease, an 11% increased risk of myocardial infarction (MI) and a 16% increased risk of sudden cardiac death in men with prostate cancer.[1]

These increased risks, apart from diabetes, were not seen in those prostate cancer patients who had been treated by subcapsular orchidectomy. This suggests that it is ADT, rather than low testosterone levels, causing the increase in cardiovascular risk. However, findings since this initial publication have been inconsistent and the relationship between ADT and cardiovascular risk is far from established.

Two studies published in *European Urology* recently have provided further data. The first, using the Danish Cancer Registry, followed 31,571 patients with prostate cancer to look for the risk of MI and stroke.[2] A total of 9,204 patients (29%) received medical ADT and 2,060 (7%) were treated by orchidectomy. The median age of the patients was 71, and median follow-up was 3.3 years.

Patients receiving medical ADT had an increased risk for MI and stroke with hazard ratios of 1.31 (95% CI:1.16-1.49) and 1.19 (95% CI:1.06-1.35) respectively. No increased risks were seen for patients who were treated by orchidectomy.

The second study looked at the effect of ADT on diabetes control in patients with established type 2 diabetes.[3] Cohorts of 2,237 matched pairs of patients with both prostate cancer and diabetes who did and did not receive ADT were studied.

Mean HbA_{1c} at the outset of the study was 7.24 for both groups, but by one year had increased in the ADT group to 7.38 and decreased in the non-ADT group to 7.14 (P = 0.008), despite the ADT group being more likely to have been started on new medication for diabetes. The authors of this study concluded that: 'ADT is associated with worsening of diabetes control and increases in HbA_{1c} levels despite the use of additional diabetes medications.'

An accompanying editorial warns clinicians not to 'throw out the baby with the bathwater'.[4] It encourages clinicians to be mindful of the risks and to ensure that men receiving ADT are 'medically optimised' in terms of cardiovascular risk reduction. The risks (notwithstanding the side effects and costs) of ADT mean that a definite decision should be made regarding risk versus benefit for all men receiving this treatment.

'For men with high-risk prostate cancer the oncological benefits of ADT are likely to outweigh the cardiovascular risks'

For men with high-risk prostate cancer, however, the oncological benefits of ADT are likely to outweigh the cardiovascular risks.

GPs should take note of the above, and also bear in mind the possibility of intermittent ADT for patients with prostate cancer requiring hormonal therapy but who are either having side effects or are at significant cardiovascular risk. Further studies in the same issue of the journal, summarised in an accompanying editorial, demonstrate the effectiveness of exercise regimens in countering the side effects of long-term ADT therapy.[5] Clearly given the presence of increased cardiovascular risk in these men on ADT, advice from their GP on exercise and diet is essential.

REFERENCES
1 Keating NI, O'Malley AJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer. *J Clin Oncol* 2006;24:4448-56
2 Jespersen C, Norgaard M, Borre M et al. Androgen-deprivation therapy in treatment of prostate cancer and risk of myocardial infarction and stroke: A nationwide Danish population-based cohort study. *Eur Urol* 2014;65:704-709
3 Keating NI, Liu P-H, O'Malley AJ et al. Androgen-deprivation therapy and diabetes control among diabetic men with prostate cancer. *Eur Urol* 2014;65:816-824
4 Nguyen PL. Androgen-deprivation therapy and cardiovascular harm: Let's not throw out the baby with the bathwater. *Eur Urol* 2014;65:710-712
5 Harrison MR, Jones LW. Exercise as treatment for androgen deprivation therapy-associated physical dysfunction: Ready for prime time? *Eur Urol* 2014;65:873-874