EDITORIAL

Androgen deprivation therapy and cardiovascular risk

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TWO PAPERS PUBLISHED RECENTLY HIGHLIGHT THE POTENTIAL CARDIOVASCULAR RISK associated with androgen deprivation therapy (ADT) for prostate cancer.

ADT, using gonadotrophin releasing hormone agonists, is a mainstay of treatment for men with advanced prostate cancer. It reduces prostate cancer specific morbidities such as pathological fracture, spinal cord compression etc.

However, the benefits of ADT are countered by several potential adverse effects. Well known side effects include hot flushes, fatigue and loss of libido, but there is perhaps less awareness of the potential cardiovascular risk.

The first study, from the United States, looked at excess cardiac mortality associated with ADT use in a cohort of 5,077 men with prostate cancer, with a median age of 69.5 years, treated with brachytherapy.[1] In this group, 1,521 men (30%) also received neoadjuvant ADT for a median duration of four months.

At baseline, 2,653 men (52%) had no history of cardiovascular disease (CVD) and no risk factors, 2,168 men (43%) had one significant CVD risk factor (diabetes mellitus, hypercholesterolaemia or hypertension) and 256 men (5%) had established CVD e.g. previous myocardial infarction (MI) or known heart failure.

After a median follow-up of around five years, no association was seen between the use of ADT and cardiac mortality in the men with either no CVD or one CVD risk factor.

However, in the men with known CVD, ADT was associated with significantly increased cardiac mortality, with an adjusted hazard ratio of 3.28 (95% CI: 1.01-10.64; P = 0.048). The five-year cumulative incidence of cardiac mortality in this group was 7% in men treated with ADT versus 2% in those who had not received ADT.

The second study, from Hong Kong, looked specifically at the risk of acute MI in 452 Chinese men with prostate cancer, treated with radical prostatectomy or radiotherapy, with or without additional ADT.[2]

There were 252 patients, mean age 69.5 years, in the ADT group, mean duration of treatment 40 months, and 200 patients, mean age 68.2 years, in the group that did not receive ADT. Baseline characteristics of the two groups were similar, with respect to CVD risk factors; diabetes mellitus (13.1 vs 15.5%), hypertension (52 vs 58.5%), hyperlipidaemia (28.6 vs 26%), previous history of CVD (8.3 vs 8.5%) and Eastern Cooperative Oncology Group Performance Status (ECOG PS).

After a mean follow-up of 81 months, the incidence of new MI was 5.1% in the whole cohort. However, this risk was significantly higher in the ADT group (7.9%) compared with the group who had not received ADT (1.5%), P = 0.002.

Hyperlipidaemia and poor ECOG PS were also significant risk factors for developing acute MI.

Other pre-existing medical conditions (including diabetes mellitus, hypertension and history of stroke), age, and duration of ADT were not associated with increased risk.

'An awareness of CVD risk allows GPs to look proactively at modifiable risk factors in these men'

Clearly ADT continues to have a vital role in managing advanced prostate cancer, especially aggressive disease.

An awareness of CVD risk allows GPs to look proactively at modifiable risk factors in these men, to encourage smoking cessation, weight loss and increased exercise – all of which have been independently associated with improved prostate cancer outcomes in their own right – and to consider medical treatment for risk factors such as dyslipidaemia.

REFERENCES
1 Ziehr D, Chen M-H, Zhang D et al. Association of androgen-deprivation therapy with excess cardiac-specific mortality in men with prostate cancer. *BJU Int* 2015;116:358-65
2 Teoh J, Samson YS, Chan PKF et al. Risk of acute myocardial infarction after androgen-deprivation therapy for prostate cancer in a Chinese population. *BJU Int* 2015;116;382-87

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