PROSTATE CANCER

ADT use associated with acute kidney injury

Androgen deprivation therapy (ADT) is associated with an increased risk of acute kidney injury (AKI) in men with newly diagnosed nonmetastatic prostate cancer, according to data published in the *Journal of the American Medical Association*.

ADT is associated with a number of adverse renal outcomes caused by its induction of a hypogonadal state associated with dyslipidaemia and hyperglycaemia, both of which can thicken the renal interstitial membrane and disrupt glomerular function. ADT can also antagonize vasodilatory effects of testosterone on the renal vessels and result in oestrogen deficiency. All of these mechanisms could potentially result in injury to the kidneys. AKI is rare, but its associated mortality is as high as ~50%. Furthermore, “One case report has associated flutamide with acute kidney injury,” Dr Laurent Azoulay, who worked on the study, explained to *Nature Reviews Urology*. “Thus, we tested the hypothesis that the use of ADT may be associated with an increased risk of AKI in patients with prostate cancer.”

The team used a nested case–control analysis with information from the UK Clinical Practice Research Datalink (CPRD) linked to the Hospital Episodes Statistics Database to identify men diagnosed with nonmetastatic prostate cancer between 1997 and 2008, who were followed up until the end of 2009 from their diagnosis of prostate cancer to their first ever hospitalization for AKI. Up to 20

controls were selected from the risk set for each case and matched to the cases by age, year of cohort entry and follow-up duration.

For the primary analysis, the team investigated whether current or past use of ADT was associated with AKI risk compared with never use. Two secondary analyses estimated the odds ratio of AKI according to specific ADT regimens and duration of use. Overall, 10,250 men met the criteria for inclusion in the study, resulting in 42,070 person-years follow-up duration, in which 232 cases of AKI were identified.

“ADT is associated with a number of adverse renal outcomes...”

Compared with a complete lack of ADT use, current use of ADT was significantly associated with an increased risk of AKI (OR 2.48; 95% CI 1.61–3.82). Past use of ADT was also associated with a slight increase in AKI risk, which did not reach statistical significance (OR 1.25; 95% CI 0.68–2.29). The effect of specific ADT regimens was demonstrated in the secondary analyses, which showed that current use of combined androgen blockade was associated with an increased risk of AKI (OR 4.50; 95% CI 2.80–7.27), a finding also observed—to a lesser

degree—for other combination therapies (OR 4.04; 95% CI 1.88–8.69). ORs for use of oral antiandrogens and bilateral orchiectomy were not significant, though were above 1.

“Overall, we observed that the use of ADT was associated with an increased risk of AKI, and that the risk varied between different types of therapies. To our knowledge, this is the first population-based study on the topic, which will require replication in other settings,” concludes Azoulay.

“The take home message of our study is that AKI is a rare event and, therefore, there is no question that the benefits of ADT outweigh its risks in patients who clearly need it (such as those with metastatic disease). This is less certain in patients with less advanced forms of the disease.”

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