Androgen Deprivation Therapy and Risk of Acute Kidney Injury in Patients With Prostate Cancer

Francesco Lapi, PharmD, PhD; Laurent Azoulay, PhD; M. Tamim Niazi, MD; Hui Yin, MSc; Serge Benayoun, MD, MSc; Samy Suissa, PhD

IMPORTANCE The use of androgen deprivation therapy (ADT) in the treatment of advanced prostate cancer has been shown to delay the clinical progression of the disease. However, the testosterone suppression associated with this therapy may lead to a hypogonadal condition that can have detrimental effects on renal function, thus raising the hypothesis that ADT-induced hypogonadism could potentially lead to acute kidney injury (AKI).

OBJECTIVE To determine whether the use of ADT is associated with an increased risk of AKI in patients newly diagnosed with prostate cancer.

DESIGN AND SETTING A nested case-control analysis using medical information extracted from the UK Clinical Practice Research Datalink linked to the Hospital Episodes Statistics database.

PARTICIPANTS Men newly diagnosed with nonmetastatic prostate cancer between January 1, 1997, and December 31, 2008, were selected and followed up until December 31, 2009. Cases were patients with incident AKI during follow-up who were randomly matched with up to 20 controls on age, calendar year of prostate cancer diagnosis, and duration of follow-up.

MAIN OUTCOMES AND MEASURES Conditional logistic regression was used to estimate odds ratios (ORs) with 95% CIs of AKI associated with the use of ADT. ADT was categorized into 1 of 6 mutually exclusive groups: gonadotropin-releasing hormone agonists, oral antiandrogens, combined androgen blockade, bilateral orchiectomy, estrogens, and combination of the above.

RESULTS A total of 10 250 patients met the study inclusion criteria. During a mean follow-up of 4.1 (SD, 2.9) years, 232 incident cases of AKI were identified (rate, 5.5/1000 person-years). Overall, current use of any ADT was associated with an increased risk of AKI when compared with never use (OR, 2.48 [95% CI, 1.61-3.82]), generating a rate difference of 4.43/1000 persons per year (95% CI, 1.54-7.33). This association was mainly driven by a combined androgen blockade consisting of gonadotropin-releasing hormone agonists with oral antiandrogens (OR, 4.50 [95% CI, 2.61-7.78]), estrogens (OR, 4.00 [95% CI, 1.06-15.03]), other combination therapies (OR, 4.04 [95% CI, 1.88-8.69]), and gonadotropin-releasing hormone agonists (OR, 1.93 [95% CI, 1.20-3.10]).

CONCLUSIONS AND RELEVANCE In a cohort of patients with newly diagnosed nonmetastatic prostate cancer, the use of ADT was significantly associated with an increased risk of AKI. These findings require replication in other well-designed studies as well as further investigation of their clinical importance.