

Letters

COMMENT & RESPONSE

Androgen Deprivation Therapy and Subsequent Dementia

To the Editor To date, only a few reports in the literature provide clinical evidence for the role of androgen deprivation therapy (ADT) in the risk of dementia.¹⁻³ Among these 3 studies, only the study by Nead et al¹ reported a positive association between ADT and the risk of dementia. To explain the discrepancy in the hazard ratio (HR), a better understanding of the methodological differences among studies should be obtained.

First, unlike the other 2 studies,^{2,3} Nead et al¹ used a concrete definition for inclusion of prostate cancer and also for the definition of a dementia event using an electronic medical record review. Moreover, they considered important confounding factors for the adjusted HR. However, some cynical points could be raised about the nongeneralized population data and about adopting a different index date without considering time-dependent exposure for the 2 groups. For the latter issue, this could induce an immortal bias, which is well described in the study by Khosrow-Khavar et al.³ Khosrow-Khavar et al³ weighed the methodological diversity, including the determination of the latency period, which could explain the discrepancy in HR, which is related with protopathic bias.

However, unless the lag period is determined by scientific estimation, as in the study by Khosrow-Khavar et al,³ the lagging period itself could affect the result, which usually has a direction toward the null. The lagging period also increases the number of censored cases, which has an impact on the incidence of the event, especially in elderly cohorts. Besides the lagging period, misclassification bias could be another reason for the discrepancy. The definitions of cohort, exposure, and event should be more concrete and close to the real settings, as in the study by Nead et al.¹

Finally, the absolute percentage of patients in the ADT group is much higher than that of the control group in the other

2 studies.^{2,3} The situation is the exact reverse in the current study,¹ and this could have affected the result of the crude incidence rate of dementia directly and crude HR indirectly. Determination of the event without concreteness also could have affected the outcome. Considering the decreasing pattern of ADT treatment for localized prostate cancer and the increased proportion of localized prostate cancer compared with that of metastatic prostate cancer in the aged population,⁴ the current study is more likely to explain the possible link between ADT and the risk of dementia.

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