

A New Controversy over Prostate Cancer's Treatment



By *Chuck Dinerstein, MD, MBA* — July 3, 2019



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Prostate cancer is the most common cancer among men, excluding skin cancers. It is, as a generalization, a slow process, and treatment include surgery, radiation, and chemotherapies. Prostate treatment ads promoting radiation therapy over surgical intervention can be heard throughout the day on radio and television. The cancer is driven, in part, by testosterone so that androgen deprivation therapy (ADT) is often used in conjunction with surgery or radiation to slow cancer progression and mortality. A new study looks at one specific unintended consequence of ADT, dementia.

The study was a retrospective review of SEER, the Surveillance, Epidemiology, and End Results dataset of the National Cancer Institute, which covers about a quarter of our nations Medicare beneficiaries. The men, were over 66, with localized or advanced prostate cancer who were followed for ten years. The usual demographics were collected as well as specific information on the severity of prostate cancer. ADT is most frequently given as an injection every three months, and the number of doses was noted in the dataset. Finally, the outcomes were a diagnosis of Alzheimer's or dementia subsequent to the diagnosis of prostate cancer. Roughly 60,000 men had been given ADT, 90,000 had not. Men receiving ADT tended to have more aggressive forms of prostate cancer, were slightly older, with more co-morbidities and had undergone less surgical intervention.

- Patients receiving ADT had a greater incidence of both dementia and Alzheimers.
- The risk of developing Alzheimer's was 20% greater in those men receiving ADT
- The risk of developing dementia was 14% greater in that same cohort.
- There did appear to be a dose-dependency with the risk for both conditions rising to a peak at 4 to 8 cycles of ADT and then leveling off.

- Only men with no co-morbidities “showed an association between exposure to ADT and diagnosis of Alzheimer disease ... or dementia.”
- Patients undergoing synchronous surgery had a lower risk, while the risk increased for those patients undergoing radiation or chemotherapy.

The researchers concluded

“While our study suggests an association between ADT and subsequent dementia diagnosis, we were unable to further investigate possible biological mechanisms of this association. It is important to note that dementia may have a latency period of 1 decade or more prior to cognitive manifestations,... Hence, it is possible that ADT has a modifying or augmenting, rather than de novo, effect on development of dementia.”

No physician would prescribe this therapy “to be safe,” you can see that as the patients treated with ADT had more aggressive and advanced cancers, less amenable to surgery. But it demonstrates how “do no harm” is far more complicated than we had anticipated. For this cancer, as with nearly all diseases, there is no magic bullet, every treatment has a cost and benefit. For those that like numbers; on the risk side, the number of patients you must treat to cause harm (dementia or Alzheimers) in one individual is 18, on the benefit side, the number of patients you must treat to save one life at ten years is roughly 46. [1] Put in other terms, for every life you save, two others will develop Alzheimers or dementia. Tough call. While economists can calculate quality years of life, patients will have the choice between the cancer they have and the dementia they may get. My bet is that cancer in the here and now is a higher priority than possible dementia in the future.

[1] The numbers needed to treat or NNT for prostate cancer does not separate those treated with any specific modality, so at best is a very rough measure.

Source: [Association Between Androgen Deprivation Therapy Use and Diagnosis of Dementia in Men With Prostate Cancer](#) [2] JAMA Network Open DOI: 10.1001/jamanetworkopen.2019.6562

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