Editors' Pick

Does ADT benefit unfavourable intermediate-risk prostate-cancer patients treated with brachytherapy boost and external beam radiotherapy? A propensity-score matched analysis

Mendez LC., Martell K., Warner K., Tseng CL., Chung H., Loblaw A., Rodrigues GB., Morton G.

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What was your motivation for initiating this study?

Two strategies have been shown to improve clinical outcomes for intermediate-risk prostate-cancer patients who are treated with external beam radiotherapy (EBRT): dose escalation and short-term androgen deprivation therapy (ADT). Brachytherapy enables dose escalation beyond that achievable with external beam radiotherapy alone. The benefit of ADT has been definitively shown for patients who are treated with a modest dose of external beam. Whether or not ADT remains beneficial for those who are treated to a higher radiation dose is a matter of debate, particularly when brachytherapy is used as the method of dose escalation. The randomised trial RTOG 0815 may partly answer that question when the results mature, but pending that, we wished to explore this question using our institutional database of intermediate-risk patients who had been treated with high-dose-rate (HDR) brachytherapy boost. Although propensity score analyses are observational retrospective studies with potential caveats, this type of methodology enables the creation of an equivalent group by matching covariates (or known prognostic features) before treatment comparison. In this context, our group became interested in use of this type of methodology to investigate the role of ADT in unfavourable intermediate-risk (UIR) patients who had been treated with HDR brachytherapy boost.

What were the main challenges during the work?

This study analysed data that had been collected from patients who were treated with HDR brachytherapy boost plus EBRT between 2009 and 2016 in a single institution in Ontario, Canada. This is a reference institution for prostate brachytherapy in the province, where hundreds of men receive this treatment strategy every year. Although data were available for a total of 326 UIR patients who had been uniformly treated with 15Gy HDR brachytherapy boost followed by EBRT 37.5Gy in 15 fractions to the prostate and proximal seminal vesicles, we were only able to match 156 patients through the propensity-score analysis. This has potentially limited performance of a more robust analysis and was the main challenge of this work.

What are the most important findings of your study?

We believe that the long-term biochemical disease-free benefit that is seen with short-term ADT use in UIR patients is an important finding. It is unknown at this point how this benefit might translate into other meaningful clinical benefits, such as freedom from salvage treatments or development of metastases. The reduction in metastases-free survival at six years with the use of ADT did not reach statistical significance, but raises the hypothesis that there may be other meaningful long-term benefits to this strategy.

What are the implications of this research?

The decision whether or not to use short-term ADT in patients with UIR disease who receive a brachytherapy boost must weigh the potential gain in biochemical disease-free survival with the potential extra morbidity entailed. This should be discussed with the

patient. It may be that some patients with unfavourable risk disease have a greater probability of benefiting from ADT treatment than others - e.g. those with a predominance of Gleason pattern 4. However, such considerations require further study.

Lucas C. Mendez MD
Assistant professor
Department of Oncology
Western University
& radiation oncologist
London Health Science Centre
London, Ontario, Canada

Gerard C Morton MB FRCPC
Professor, Dept of Radiation Oncology
University of Toronto
Sunnybrook Odette Cancer Centre
Toronto, Ontario, Canada