Editors' pick

Prostate high-dose-rate brachytherapy as monotherapy for prostate cancer: late toxicity and patient-reported outcomes from a randomised phase II clinical trial

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What was your motivation for initiating this study?

High-dose-rate (HDR) brachytherapy has been shown to be a safe and effective treatment for localised prostate cancer when used as a boost that is combined with external beam radiotherapy [1,2], or when delivered over multiple fractions/implants as monotherapy [3]. We have previously published efficacy results from a randomised trial between 19Gy in a single-fraction and two-fractions of 13.5Gy. Five-year biochemical disease-free survival was only 73.5% in the single-fraction arm, compared with 95.0% in the two-fraction arm [4]. However, there is limited long-term prospective data on toxicity from two-fraction HDR monotherapy despite endorsement by National Comprehensive Cancer Network (NCCN) guidelines [5]. We sought to report long-term toxicity and patient-reported outcomes from the HDR monotherapy trial, specifically to identify whether the higher biological dose delivered in the two-fraction arm was associated with worse late toxicity and patient-reported outcomes.

What were the main challenges during the work?

The main challenge that we encountered was ensuring regular collection of patient-reported quality of life and toxicity outcomes during the study period. Frequent completion of quality-of-life questionnaires can be demanding on patients, and we were gratified to find such a high patient compliance.

What are the most important findings of your study?

For patients treated with two fractions of 13.5Gy, there was no evidence of increased toxicity when compared with a single fraction of 19Gy [6]. In fact, there was a strong trend towards a lower cumulative incidence of grade 2 or higher genitourinary (GU) toxicity in the two-fraction arm when compared with the single-fraction arm (five-year cumulative incidence of 47% versus 62%, $p = 0.051$). Grade 3 GU toxicity, which was rare, was only seen in the single-fraction arm, with a five-year cumulative incidence in this arm of only 2%. Gastrointestinal (GI) toxicity was low in both arms, with a five-year cumulative incidence of grade 2 toxicity of 12% and 9%, in the single and two-fraction arms respectively. No grade 3 GI toxicity occurred.

Patient-reported outcomes demonstrated an early decline in urinary quality of life six and 12 months after treatment in both treatment arms. However, beyond the first year, no significant differences compared with baseline were observed in the two-fraction arm. In contrast, a significant decline in urinary quality of life was seen four and five years after treatment in the single-fraction arm ($p = 0.0001$ and $p = 0.0077$, respectively). High bowel domain scores were maintained in the two-fraction arm, with no significant decrease from baseline at any time point. Bowel domain scores tended to be lower in the single-fraction arm. The slightly worse toxicity and quality of life outcomes with single-fraction treatment were also seen when the analysis was restricted to those without biochemical failure.

What are the implications of this research?

Two fractions of HDR brachytherapy as monotherapy for localised prostate cancer are both safe and effective. The higher efficacy did not come at a cost of higher toxicity. In addition to having superior biochemical control compared with single-fraction HDR brachytherapy, there was no evidence of worse GU/GI toxicity when compared with single-fraction HDR brachytherapy. In fact, our study found that two-fraction HDR brachytherapy appeared to have a more favourable side-effect profile than single-fraction HDR brachytherapy, with fewer late patient-reported declines in urinary quality of life compared with single-fraction HDR brachytherapy.

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