

Current prostate cancer treatment: Not what but when?

Peter A. Massaro, MD, MASc, FRCSC; Ilias Cagiannos, MD, FRCSC

Division of Urology, The Ottawa Hospital, Ottawa, ON, Canada

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In their paper, Taussky et al compare the rates of biochemical recurrence and salvage treatment between patients with low- and intermediate-risk prostate cancer treated with permanent seed prostate brachytherapy or radical prostatectomy from 2005–2011. The primary endpoint was biochemical recurrence or salvage therapy at 48 \pm 4 months after localized therapy. Younger patients, as well as those with higher-volume disease (higher initial prostate-specific antigen [PSA] and percentage of positive biopsies) were more likely to develop a biochemical recurrence. However, the central finding in this study was that there was no difference in the biochemical recurrence rate after radical prostatectomy or brachytherapy, which agrees with earlier publications. A recent systematic review by Wolff et al of limited, randomized data demonstrated no significant difference in biochemical progression-free survival in patients with low- to intermediate-risk prostate cancer treated with brachytherapy or radical prostatectomy.¹ Patients treated with brachytherapy, however, reported better preservation of sexual function, but worse short-term (<5 years) urinary function.

One of the challenges in comparing radical prostatectomy and radiotherapy for localized prostate cancer is identifying comparable endpoints when the underlying therapeutic mechanism for each modality differs substantially. Radical prostatectomy is an extirpative process, while radiotherapy results in prostate cancer cell death through a number of mechanisms, including cellular apoptosis, senescence, and mitotic catastrophe.² Consequently, different definitions for biochemical recurrence have been proposed over the years post-radical prostatectomy³ and radiotherapy.⁴⁻⁶ How best to define and compare biochemical recurrence rates after surgery and radiotherapy remains a matter of debate.^{3,7} As

highlighted in the discussion of the present study, the biochemical recurrence rate after radiotherapy can vary drastically depending on its definition. Additionally, without longer followup and a larger study population, it is possible that a difference in biochemical recurrence rates between radical prostatectomy and brachytherapy could be missed.

Endpoints, such as overall mortality or prostate cancer-specific mortality, provide more robust endpoints for comparison, but rely on substantially longer followup. A recent systematic review of observational data compared these endpoints for radical prostatectomy and radiotherapy.⁸ Overall and prostate cancer-specific mortality favoured radical prostatectomy, although the most common non-surgical modality was external beam radiotherapy. On subgroup analysis, however, both mortality outcomes favoured surgery over brachytherapy. Of note, patients who undergo radiotherapy tend to be older and have greater comorbidity. Further, as shown in the present study and supported by others,⁸ patients are more likely to receive salvage therapy after radical prostatectomy than radiotherapy and, when offered, salvage therapy after radiotherapy is typically in the form of androgen-deprivation therapy. With high-quality, randomized trials comparing surgery to radiotherapy unlikely to be available in the future,^{9,10} interpretation of available observational results, regardless of the endpoints evaluated, must be framed in the context of an individual patient.

It is important to note that patient selection in this study occurred between 2005 and 2011. Presently, the landscape continues to shift toward managing low- and select intermediate-risk prostate cancers with active surveillance and we have already seen increased use of this approach in Canada over a similar period of time,^{11,12} with evidence of its long-term safety¹³ and uptake in our national guidelines.¹⁴ Consequently, a reduction in radical prostatectomy and radiotherapy rates has been observed over a similar period of time for low-risk patients.¹¹ Therefore, perhaps the most valuable data from this study lies in the results for patients with intermediate-risk tumours, those most likely to benefit

from either localized therapy. From the data presented, it is unclear whether a difference in biochemical recurrence rate exists between radical prostatectomy and brachytherapy for the nearly one-third of patients with intermediate-risk disease. Compared to the brachytherapy group, patients who underwent radical prostatectomy had more Gleason 7 tumours, a higher percentage of positive biopsies, and a proportionally higher rate of intermediate risk disease. Further, none received adjuvant therapy despite 24% having pT3 disease, of which 50% were associated with a positive surgical margin. Since the radical prostatectomy group had higher-risk disease, one could speculate that with the addition of selective adjuvant radiotherapy, biochemical recurrence rates might favour this group; however, this would require further analysis and again depends on the definition of biochemical recurrence for each group.

In the absence of high-quality, randomized data, radical prostatectomy and primary radiotherapy, including brachytherapy, remain appropriate treatment options for men with low- and intermediate-risk localized prostate cancer.¹ Active surveillance with delayed curative intent is becoming a favoured approach and standard of care for appropriate men with low- and select intermediate-risk prostate cancers. Patients should continue to be counselled regarding accepted treatment options complete with cancer-related outcomes, potential adverse effects, and need for additional therapy in order to make an informed decision. Due to the retrospective nature of the current study, the proportion of patients who met with both an urologist and radiation oncologist could not be determined, but in general, consultation with both clinicians before undergoing treatment further supports the shared decision-making process with a patient. Nevertheless, in the current landscape of prostate cancer management, the first and more important discussion to have with patients is not the choice of therapeutic modality, but whether immediate therapy is required at all.

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Correspondence: Dr. Ilias Cagiannos, Division of Urology, The Ottawa Hospital, Ottawa, ON, Canada; icagiannos@toh.ca