RE: Mortality After Radical Prostatectomy or External Beam Radiotherapy for Localized Prostate Cancer

We read with concern the recently published article by Hoffman et al. stating that overall mortality and disease-specific mortality were statistically significantly improved by radical prostatectomy (RP) as compared with external beam radiotherapy (EBRT) in patients with localized prostate cancer (PC) (1). The authors conclude that possible explanations for this finding include residual selection bias or a true survival advantage. We believe the former is true and the following statements should be considered to prevent misleading conclusions by the readers:

The retrospective analysis was based on the population-based Prostate Cancer Outcomes Study (PCOS). Of the total patients initially sampled for the PCOS (n = 5672), only 3533 patients responded. It was previously acknowledged that responders differed statistically significantly from the nonresponders (eg, were much more likely to receive radical prostatectomy) and results from the PCOS might therefore not be applicable to the general population of PC patients (2).

The authors state at the end of their discussion: “our data provide the best estimate for the long-term comparative effectiveness of RP and EBRT” (1) We cannot understand why other large-scale retrospective comparisons with conflicting results are neither mentioned nor discussed (3,4). These articles provide more details on EBRT dose, duration of androgen deprivation therapy, and the rate of patients undergoing adjuvant or salvage EBRT after RP, all of which statistically significantly impact upon patients’ outcomes. The authors stated that propensity scores adjust for “potential treatment selection confounders” (1). However, we doubt that differences in patient characteristics, such as older age, higher comorbidities, and more frequent high-risk disease, can be fully compensated for by the propensity scores. We wonder about the authors’ definition of high-risk disease, including a prostate-specific antigen cutoff of greater than 10 ng/mL. We believe that if tumor classification would have been analyzed in more detail (proportion of patients ≥ cT3), including a prostate-specific antigen cutoff for high-risk disease of greater than 20 ng/mL, the confounding factors for treatment selection would have been even more pronounced in favor of RP. In this context, we wonder whether the biopsy Gleason score was used for both EBRT and RP patients. Otherwise the comparison would be further biased.

We believe that only a proper randomized comparison between the two modalities can ultimately judge which treatment might be superior. Meanwhile sufficient evidence indicates that dose escalation using modern image-guided intensity-modulated radiotherapy (IMRT) techniques provides an improved therapeutic ratio (5–7). In addition to the methodological caveats, this retrospective, population-based, observational database analysis derived from studies conducted in the mid-1990s does not take into account modern radiation delivery techniques such as IMRT and therefore cannot be considered as current “best estimate for long-term comparative effectiveness of RP versus EBRT” (1). The results of this article are therefore limited and cannot be extrapolated for contemporary treatment decisions.

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References

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