



Letter to the Editor

Reply to Amar U. Kishan, William Hall, and Daniel Spratt's Letter to the Editor re: Sebastian Berg, Alexander P. Cole, Marieke J. Krimphove, et al. Comparative Effectiveness of Radical Prostatectomy Versus External Beam Radiation Therapy Plus Brachytherapy in Patients with High-risk Localized Prostate Cancer. Eur Urol 2019;75:552–5 Comparing Apples to Oranges: A Self-fulfilling Prophecy?

We acknowledge the points made by Kishan, Hall, and Spratt on our article comparing radical prostatectomy versus external beam radiation therapy (EBRT) plus brachytherapy (BT) in patients with high-risk localized prostate cancer [1]. We agree that there are inherent limitations when using retrospective observational data to compare interventions as dissimilar as surgery and radiation therapy. While techniques such as propensity score weighting can mitigate some these limitations [2], patients who choose surgery over radiation differ in ways that can be difficult to capture in retrospective studies. Insofar as these differences are associated with overall survival, this can lead to unmeasured confounding.

While Kishan's own retrospective study using pooled institutional data examining cancer specific survival [3] may overcome some of these limitations, it introduces other problems. Men at 12 academic centers who received androgen deprivation therapy (ADT) + EBRT + BT in the era before ASCENDE-RT [4] were by definition receiving cutting edge care and may have had other advantages (eg, close follow up, other experimental treatments). Selection bias is also a factor: How many patients with Gleason 9–10 disease are fit enough and have a small enough prostate to receive these three treatments? In other words, it is apples and oranges all over again.

Perhaps the take-home message from their findings is that men with high-risk prostate cancer require multimodal therapy, as many experts have astutely pointed out. Nonetheless, once we acknowledge that many of these men will need a combination of treatments including radiation and ADT, why would radiating the prostate twice be better than removing it followed by radiation? [5]. One potential explanation is that many men who have surgery

in these retrospective studies had adverse pathology but never receive adjuvant EBRT + ADT, or they receive it too late [6].

Conceptually, our paper is not the end all of evidence, but was rather designed as a scientific counterpoint to two other recent high-profile studies by Kishan et al. [3] and another by Ennis et al. which showed no difference between EBRT + BT and surgery [7]. Taken together, these three retrospective studies (ours included) highlight the extent to which subtle differences in data sources, follow-up, and inclusion criteria can substantially impact results [8]. Until a prospective trial is performed, these remain “expert opinion”, and all remain couched in our own perspectives.

Conflicts of interest: Alexander P. Cole has nothing to disclose. Quoc-Dien Trinh has received personal fees from Astellas and Bayer, and research funding from Intuitive Surgical.

References

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