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Dose-escalation of radiation may improve outcomes of squamous cell carcinoma of bladder

Letter to the Editor

We read with interest the article "A propensity analysis comparing definitive chemo-radiotherapy for muscle-invasive squamous cell carcinoma of the bladder vs. urothelial carcinoma of the bladder using the National Cancer Database" by *Fischer-Valuck* et al. [1] which has addressed outcomes of squamous cell carcinoma (SCC) of bladder. Outcome of SCC bladder is poor as compared to urothelial cancer (UC) with the estimated 3- and 5-year OS for SCC being 27.5% and 20.5% compared to 43.8% and 29.5% for UC, respectively ($P < 0.0001$). However, there is limited data regarding the optimal treatment approach for SCC of bladder and most of the decisions are extrapolated from data of UC.

In order to improve outcomes of SCC of bladder, a number of strategies have been recommended in passing by the authors including intensification of treatment like addition of chemotherapy, immunotherapy and radiotherapy dose escalation.

The standard dose for UC of bladder is 60–64 Gy as received by patients in the reported cohort (median RT dose – 63 Gy). However, because SCC is less sensitive to radiation as compared to UC, this may be an inadequate dose and patients may benefit with an escalated radiation dose. Higher dose of radiation has shown a clear benefit in SCC of both head-neck [2] and cervix for improved outcomes, and the same may be extrapolated to the bladder. The main concern in bladder radiotherapy is delivery of an adequate dose due to the close proximity of bowel, which results in significant acute and late small bowel toxicity. However, with newer techniques like intensity modulated therapy (IMRT), image guided radiotherapy (IGRT) and adaptive radiotherapy (ART), adequate dose can be delivered to target while maintaining dose to small bowel within tolerance limits.

Data from our own institute by *V. Murthy* et al. [3] and from the UK by *Hafeez* et al. [4] has suggested that dose escalation with IGRT for transitional cell carcinoma (TCC) of bladder is feasible; with good oncological outcomes and acceptable acute and late toxicities. Appropriately selected patients received focused radiation to the tumor in the bladder to an effective dose of 68–70 Gy safely which is a well-established tumoricidal dose for SCC. Both studies had shown acceptable acute and late grade III or higher genitourinary and gastrointestinal toxicity.

Also, although *Fischer-Valuck* et al. have stated that patients had undergone TURBT and received definitive concurrent CTRT, it is not clear what proportion had undergone maximal TURBT or received concurrent chemotherapy, both of which can have significant influence on outcomes in patients undergoing bladder preservation. As age and comorbidities may prevent a significant proportion of patients from receiving chemotherapy, radiation dose escalation may assume an important role in improving outcomes, extrapolating data from HN SCC, that has shown concurrent chemotherapy accounts for approximately 10 Gy of radiation dose [5]. It is time to test the hypothesis of dose escalation in a prospective manner in SCC similar to the ongoing dose escalation trial in TCC of bladder (RAIDER-NCT02447549).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctro.2019.07.005.

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