COMMENTARY

Integrating systemic perioperative chemotherapy with radical nephroureterectomy

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Referring to the article published on pp. 9938-9944 in this issue

RAMAN JD. Integrating systemic perioperative chemotherapy with radical nephroureterectomy. *Can J Urol* 2019;26(5):9945.

Radical nephrourerectomy (RNU) alone for high risk upper-tract urothelial carcinoma (UTUC) (pT3/pT4 or LN+) is likely inadequate for long term cancer control. Data from the UTUC collaborative group highlights that the 5 year recurrence-free and cancer-specific survival is less than 40% for these aggressive tumors.[1] Integration of systemic multimodal therapy is therefore requisite to better ensure durable oncologic outcomes. Prior work examining the NCDB database highlights unfortunately a relative underutilization of systemic chemotherapy either in the adjuvant or neoadjuvant setting.[2] Clearly, improved collaboration between urologists and medical oncologists is essential for improved adoption of multimodal approaches for UTUC.

If one accepts the premise that perioperative chemotherapy is critical for high risk UTUC, the timing of administration remains a critical debate in hand. Adjuvant chemotherapy (AC) affords the opportunity to review RNU pathology and perhaps treat only those who are truly pathologically high risk. Furthermore, data from the POUT trial highlights improved 2 year disease-free survival (70% versus 51%) for high risk UTUC patients receiving AC versus surveillance following RNU.[3] Clearly, if a patient successfully receives AC (including the appropriate number of cycles and optimal agents), then the treatment is effective. Yet, this is not always the case. A previous multicenter study highlights that over two-third of high risk UTUC patients fail to receive AC even in the setting of positive LN.[4] The underlying cause of this is multifactorial but may be attributable in part to perioperative complications, reduction in renal function, or physician and patient preference.[5,6]

It is therefore my belief that when feasible chemotherapy should be administered in a neoadjuvant (NAC) setting. The preceding article[7] highlights this point through use of the NCDB database to demonstrate that NAC yields pathologic downstaging and superior survival outcomes compared to a control population undergoing RNU alone. These observations are similar to single center studies[8] and collectively encourage the completion of currently accruing prospective trials that can provide more evidence in this realm.

The final challenge in this regard is accurate patient selection. Who should get NAC and how do we overcome the shortcomings of UTUC staging? Clearly the potential for overtreatment exists. At present, nomograms incorporating clinical, laboratory, radiographic, and biopsy information yield the best current information to predict the likelihood of non-organ confined UTUC and therefore guide use of NAC.[9] Nonetheless, even the best nomograms have shortcomings and novel imaging techniques and integration of genomics likely will aid in this realm in the future. □

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