

Kidney-sparing management for high-risk upper tract urothelial carcinoma: Where do we stand?

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SUMMARY

A prospective cohort study by Chen *et al.* has been recently published in the European Urology Oncology, which compared the management of high-risk upper tract urothelial carcinoma (UTUC), stratified as per the European Association of Urology guidelines, by endoscopic cryoablation (ECA) versus radical nephroureterectomy (RNU).^[1] The study was conducted at the Department of Urology, Huashan Hospital, Shanghai, China, between March 2019 and December 2021. The patients with high-risk UTUC were explained about the treatment modalities (ECA and RNU), and the recruitment in both groups was done per patients' preference. Patients were followed up every 3 months up to 2 years and every 6 months thereafter. The primary outcome was overall survival (OS), and the secondary outcomes were progression-free survival (PFS), intravesical recurrence-free survival (IVRFS), change in renal function, and treatment-emergent adverse effects (TEAE). A total of 116 patients, 13 in the ECA group and 103 in the RNU group were enrolled. After propensity matching, 12 patients in the ECA group and 48 in the RNU group were considered for statistical analysis. The median follow-up was 28.2 months. The 2-year OS was 81.8% in the ECA group and 83.6% in the RNU group, and there was no statistically significant difference between the two (hazard ratio [HR] - 0.94, 95% CL (Confidence Limit) 0.20–4.37; $P = 0.94$). The difference between the 2-year PFS of the two groups was also not significant, which was 72.7% in the ECA group and 71.2% in the RNU group (HR - 1.04, 95% CL 0.34–3.15; $P = 0.95$). Moreover, there was no statistically significant difference in the 2-year IVRFS between the two groups ($P = 0.76$). The percentage change in glomerular filtration rate was significantly lower in the ECA group than in the RNU group ($P = 0.006$), but the progression to higher chronic kidney disease (CKD) stage was not significantly different in both the groups ($P = 0.24$). Five patients in the ECA group had 6 TEAEs such as hematuria, flank pain, and urinary tract infections, whereas 20 TEAEs were seen in 17 patients of the RNU group.

COMMENTS

This is the first study on the feasibility, functional outcomes, and oncologic outcomes of ECA for selected patients with high-risk UTUC. RNU with perioperative chemotherapy is the current gold standard for the management of high-risk UTUC.^[2] However, in certain situations, this extirpative surgery can be avoided with kidney-sparing approaches and comparable survival outcomes can still be achieved. Kidney-sparing techniques have been employed in a well-selected group of patients including single papillary tumors <2 cm in size, no carcinoma *in situ*, no hydronephrosis, and low-risk UTUC.^[2] They benefit patients with anatomically or functionally solitary kidneys or CKD. This study provides initial data on the safety of this novel kidney-sparing technique for the management of high-risk UTUCs. Prospective study design and propensity matching for balancing baseline patient and tumor characteristics are the strengths of this study. However, one could argue the actual need for propensity matching. As evident from in this study, before matching, both the groups were balanced for baseline characteristics except the preoperative CKD stage. Understandably, patients undergoing ECA had a higher CKD stage.

Although authors have tried to balance baseline characteristics, several other factors influencing outcomes between the two groups such as necrosis, carcinoma *in situ*, variant histology, clinical nodes, and tumor architecture were not considered.^[3] For instance, giving ECA to a patient with clinically suspicious lymph nodes would be counterproductive. Another major drawback of the present study is the lack of final histopathology details and surgical staging of patients who underwent RNU. This information would have helped in the assessment of the eligibility of the patients for adjuvant chemotherapy.

One critical piece of information missing from this study was whether patients in the ECA group received any adjuvant treatment. Similarly, for the RNU group, it is not clear whether perioperative chemotherapy was received or not. Perioperative chemotherapy has been shown to improve disease-free survival in a recent trial. The results of this trial (POUT trial) were available during the recruitment of patients during

this study.^[4] Therefore, high-risk or locally advanced UTUC patients not receiving perioperative chemotherapy cannot be considered the current standard of care.

One could argue the sample size for the ECA group in the present study. Was this sample size sufficient to justify the insignificance in the perioperative and oncological outcomes? Considering the prospective study design, the authors should have better addressed this issue. In the current format, we believe that the study results are difficult to interpret and prevent us from making any useful inferences.

Despite its limitations, the present study adds a modality to the armamentarium of surgeons for the management of UTUC. However, it is not clear which patient population will be best managed with this strategy. Important inferences that can be drawn from this study are that in a group of well-selected patients or patients with compromised renal function, ECA can be considered an alternative for patients with UTUC. Further studies with better methodology are needed to explore this modality.

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