Renal outcome after surgery for upper tract urothelial carcinoma

Accurate staging in patients with upper tract urothelial carcinoma (UTUC) is not easily achievable from preoperative work-up. Thus, the preferred treatment for UTUC is based on radical nephroureterectomy (RNU) with bladder-cuff excision for the vast majority of patients. However, recent evidence has shown that the loss of renal units by RNU is related to postoperative renal function decline. This greatly reduces the possibility of receiving adjuvant platinum-based chemotherapy if needed. Kaag et al. conducted a retrospective data review of 388 patients undergoing RNU from four US institutions; they found that the mean estimated glomerular filtration rate (eGFR) decreased by 24% after surgery. Using a cutoff of 60 mL/min/1.73 m², 49% of patients were eligible for chemotherapy before surgery, but only 19% of patients remained eligible postoperatively. Using a cutoff of 45 mL/min/1.73 m², 80% of patients were eligible for chemotherapy preoperatively, but only 55% remained eligible after surgery. In particular, patients of old age (≥70 years) are more likely to experience a decline in renal function after RNU. Based on this observation, they suggested neoadjuvant chemotherapy for patients with advanced stages of carcinoma. Similar observations were concluded by Lane et al. who found a 21% median relative reduction in renal function, and fewer than 50% of patients with sufficient renal function to receive platinum-based chemotherapy remain suitable postoperatively.

Although the rarity of UTUC makes it a difficult disease process to study, a large multi-institutional collaboration by the French Collaborative National Working-Group on UTUC and the UTUC collaboration recently addressed most of the issues based on a Western data pool. UTUC is reaching potentially epidemic proportions in the East, especially in Taiwan and China, because of exposure to carcinogenic herbal remedies. Data from China in the article by Xiong et al. using a 10-year study of a cohort of 785 cases attending Peking University First Hospital from 2002 to 2011 demonstrated a particularly high prevalence (58.6%) of chronic kidney disease (CKD) in Chinese patients with UTUC and presenting 70.8% in the group age 70 years and older. Moreover, the study results showed that it is reasonable not to use serum creatinine alone to evaluate renal function as it would overlook a large proportion of patients with Stage 3 CKD in UTUCs, especially in those older than 70 years (39.3% vs. 54.1%, p = 0.022). Due to the relatively higher prevalence of CKD in Taiwan and China, a lot of the recent epidemiologic information has pointed to aristolochic acid (AA). The molecular mechanisms of AA nephropathy and interrelated UTUC were summarized by Yang et al. in a recent article. AA-induced renal damage involves both tubular and interstitial injuries. In the acute phase, toxicity causes proximal tubule injury whereas in the chronic phase the apoptosis of the tubular epithelial cells, defective activation of antioxidative enzymes, mitochondrial damage, impaired regeneration of proximal tubular epithelial cells, and interstitial cell proliferation lead to tubular atrophy and interstitial fibrosis. The aristolactams activated and the resultant formation of the AL-DNA adducts in urothelial tissue lead to A:T to T:A transverse mutations in the TP53 tumor suppression gene that is an important factor in UTUC carcinogenesis. In addition to TP53 change, more and more data indicate the importance of other candidate genes implicated in this process; this information thus forms a fingerprint for the applicable diagnostic map to identify such patients with potential renal function deterioration and synchronous/metachronous UTUC formation.

Pang et al. in this issue of Urological Science report the Chang Gang Memorial Hospital data regarding the longitudinal change in renal function after RNU in patients with UTUC. They used a retrospective study that included 186 patients, 87 men and 99 women, with a mean age of 67.2 years, who underwent unilateral RNU between 1997 and 2001. Their cohort showed a preoperative mean eGFR of 41.97 mL/min/1.73 m². In total, 86.0% of the patients’ preoperative eGFR was less than 60 mL/min/1.73 m². The mean eGFR was 35.85 mL/min/1.73 m² at the end of the 5-year follow up. Of the 26 patients with normal preoperative renal function, 17 patients (65.4%) had new CKD. Ten patients (5.4%) required hemodialysis at the end of the study. The authors concluded that the average renal function of the patients with UTUC was not as good as that in the general population. More than half of the patients with normal renal function had new-onset CKD after surgery. They suggest that in order to prevent further deterioration of renal function, the feasibility of partial nephrectomy or segmental ureterectomy should be reexamined for selected patients with localized UTUC. In addition, neoadjuvant chemotherapy should be considered for those who are not good candidates for local treatment. Though the data were only reflected in a large tertiary center providing information in north Taiwan, they illustrate the entire picture of UTUC faced in Taiwan. That is, relatively younger age, female sex, predominant and more profound renal function diminished in the patients with UTUC we treated. Taking the data obtained from China and Taiwan, it is apparent that the UTUC population with renal function deterioration is a major public health issue amongst ethnic Chinese. The progressive loss of renal function post-RNU will lead to more patients with CKD and impede the chance for chemotherapeutic treatment when needed and also increase the number of end stage renal failure casualties. Perhaps it is time to rethink the most appropriate surgical procedure for these patients and not just burn down the house for every case with UTUC.
Kidney-sparing surgery (KSS) has the obvious advantage of enabling preservation of renal function, ideally while maintaining the oncological outcomes normally obtained after radical extirpative surgery. KSS is usually restricted to patients with imperative indications such as renal insufficiency, solitary kidney, or bilateral UTUC and patients who are medically unfit for RNU. However, the favorable outcomes achieved with segmental ureterectomy and endoscopic extirpation or fulguration ablation of the tumor have encouraged several authors to propose the use of these procedures in patients with UTUC who also have normal, functioning contralateral kidneys. The elective indications for use of KSS in a wider range of patients with UTUC have been defined in recent journals and warrants special attention.

Conflicts of interest

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