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REVIEW

Treatment of upper urinary tract urothelial carcinoma

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Abstract
Upper urinary tract urothelial carcinoma (UUTUC) is relatively rare, occurring in only 5% of all urothelial cancers. It has not been as extensively studied and reviewed as carcinoma of the bladder. UUTUC has a propensity for multifocality, local recurrence, and development of metastases, which argues for an aggressive treatment approach. Open radical nephroureterectomy (ORNU) with removal of an ipsilateral bladder cuff still remains the gold standard treatment for patients with UUTUC and a normal contralateral kidney, which, however, is being challenged by minimally invasive approaches, such as endoscopic and laparoscopic approaches. They are rapidly evolving as reasonable alternatives of care depending on grade and stage of disease. Adjuvant therapy seems to be safe, although its efficacy is debatable. Immunotherapy appears to be most effective in patients with upper-tract carcinoma in situ. Chemotherapy and radiotherapy also show some improvement in recurrence rates, but there have been no randomized, prospective trials. Gene and molecular-targeted therapy is expected. Several controversies remain in our management, including a selection of endoscopic versus laparoscopic approaches, management strategies on the distal ureter, the role of lymphadenectomy, and the value of immunotherapy, chemotherapy, radiotherapy and genetics and molecular markers in UUTUC. Aims of this paper are to critically review the treatment of UUTUC.

Contents

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Introduction

Urothelial carcinomas occur with varying frequency at different sites along the urothelial tract. Primary UUTUC is a rare urological disease. Approximately 5% of all urothelial carcinomas occur in the kidneys and ureters (upper urinary tract). The vast majority of upper urinary tract tumors arise in the kidney, comprising 4—15% of all primary kidney neoplasms in the United States, whereas ureteral tumors represent only 1% [1]. Urothelial carcinoma of the bladder has been examined to a greater extent than urothelial tumors elsewhere.

The gold standard treatment for patients with UUTUC and a normal contralateral kidney is ORNU with removal of a bladder cuff. It is important to complete the nephroureterectomy with a cuff of urinary bladder due to the high rate of ureteral stump recurrence, which has been reported to be between 30% and 75% [2].

Nevertheless, the gold standard of ORNU with resection of a bladder cuff is being challenged by minimally invasive approaches to the managing of upper urinary tract transitional cell carcinoma (UUTTCC). For UUTUC, laparoscopic nephroureterectomy (LNU) has been used as an alternative to an open procedure [2]. Ureteroscopic management remains the initial diagnostic and possibly therapeutic procedure of choice. Percutaneous management is used to treat bulky tumors or tumors that cannot be accessed ureteroscopically. Low-grade UUTUC in appropriately selected patients can be safely and effectively treated endoscopically. High-grade disease tends to fail, regardless of treatment modality, and warrants aggressive therapy. Adjuvant therapy seems to be safe, although its efficacy is debatable. Immunotherapy appears to be most effective in patients with upper urinary tract carcinoma in situ [3]. Studies in gene and molecular-targeted therapy are encouraging. This paper will cover the therapeutic approaches to UUTTCC, including ORNU, LNU, endoscopic approaches, genetics and molecular markers, management of distal ureter and bladder cuff, the role of lymphadenectomy, and the value of immunotherapy, chemotherapy and radiotherapy.

Surgical treatment

Open surgery

ORNU

For almost a century, ORNU has been the gold standard for treatment of UUTUC. Nephrectomy should include perinephric fat and Gerota's fascia just as for radical nephrectomy for renal cell carcinoma [4]. Open nephroureterectomy can be performed through a variety of