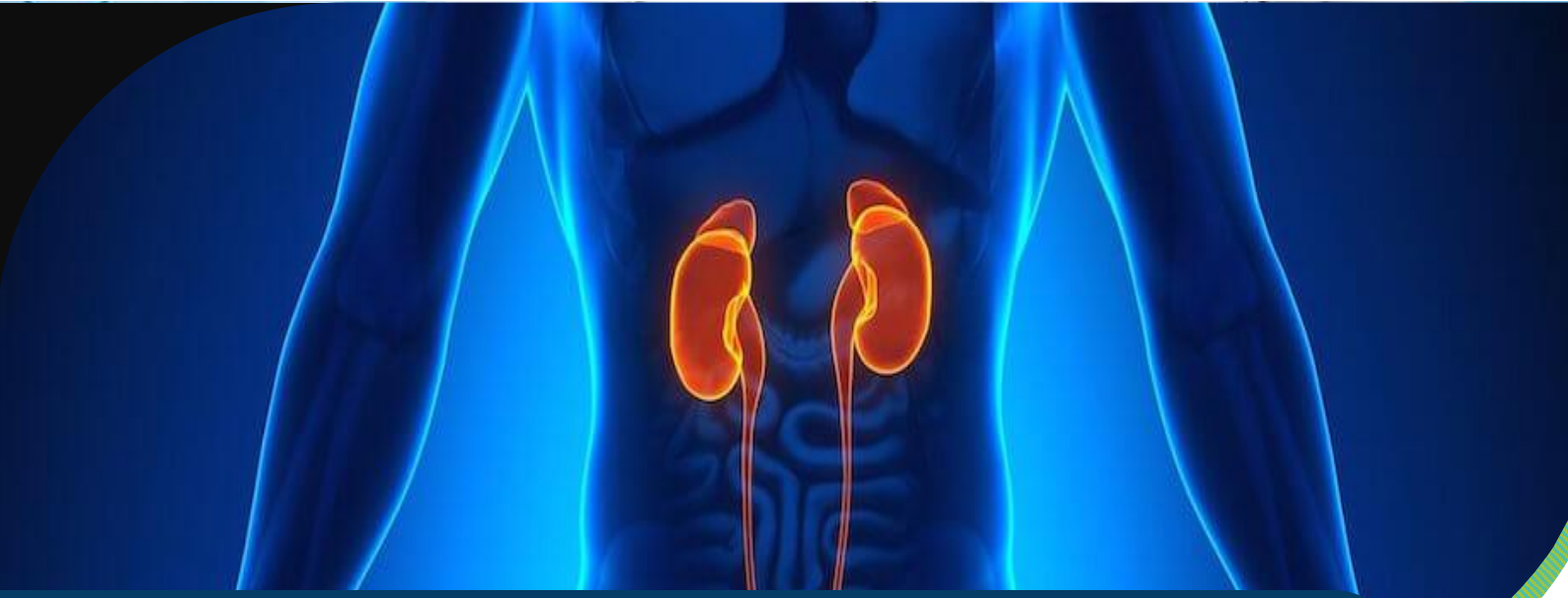

NU Rounds

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "**NU Rounds**" which contains latest and interesting news in the field of Urology.

Inside This Issue:

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

Rucaparib Approved for BRCA-Mutated metastatic castration-resistant prostate cancer

On May 15, Rucaparib, a PARP inhibitor, obtained expedited FDA clearance for use in men with metastatic castration-resistant prostate cancer (mCRPC) diagnosed with a deleterious BRCA mutation.

The approval is focused on results from TRITON2, an ongoing single-arm multicenter clinical trial involving 115 patients with BRCA-mutated mCRPC previously diagnosed with directed androgen-receptor therapy and taxane-dependent chemotherapy. Researchers assessed target response rate (ORR) and response duration (DOR) in 62 patients with measurable disease. The ORR reported was 44%. The mean DOR was not assessable, but the estimate was 1.7 to 24 months or more. Fifteen of the 27 patients (56 per cent) with reported objective responses had at least six months of DOR.

Fatigue, nausea, anaemia, increased ALT / AST, decreased appetite, rash, constipation, thrombocytopenia, vomiting, and diarrhea were the most common adverse reactions (in 20 per cent or more of patients) among all 115 patients with BRCA-mutated mCRPC, FDA said in a press release.

The prescribed dosage of rucaparib is 600 mg with or without medication, orally twice daily. Patients getting rucaparib for mCRPC would either undergo a related gonadotropin-releasing hormone at the same time, or would have undergone bilateral orchiectomy, the FDA states.

Source:

FDA press release. FDA grants accelerated approval to rucaparib for BRCA-mutated metastatic castration-resistant prostate cancer. https://www.fda.gov/drugs/fda-grants-accelerated-approval-rucaparib-brca-mutated-metastatic-castration-resistant-prostate

Role of Preoperative Chemotherapy in High Risk Upper Tract Urothelial Carcinoma

INTRODUCTION

Urothelial carcinoma is the fourth most common tumor form in developing nations. The upper urinary tract's urothelial carcinoma accounts for just 5 to 10 per cent of these events. Approximately 60 percent of UTUC patients present at presentation with muscle invasive disorder, 7 percent harboring observable metastases. Radical nephroureterectomy with excision of the bladder cuff is the preferred procedure for nonmetastatic UTUC and is high risk. Despite RNU, though, about a third of patients undergo recurrence of the disease within 3 years and ultimately die from the disease. Systemic preoperative chemotherapy has shown a safety benefit in

Lower urinary tract carcinoma urothelia. Two meta-analysis of limited longitudinal clinical trials of patients who obtained neoadjuvant chemotherapy before RNU reported promising findings. The use of NAC is however limited due to the lack of data from well-designed prospective trials. While the ECOG-ACRIN 8141 trial confirmed pathological responses using the NAC strategy, the study needs longer follow-up to assess the survival outcomes.

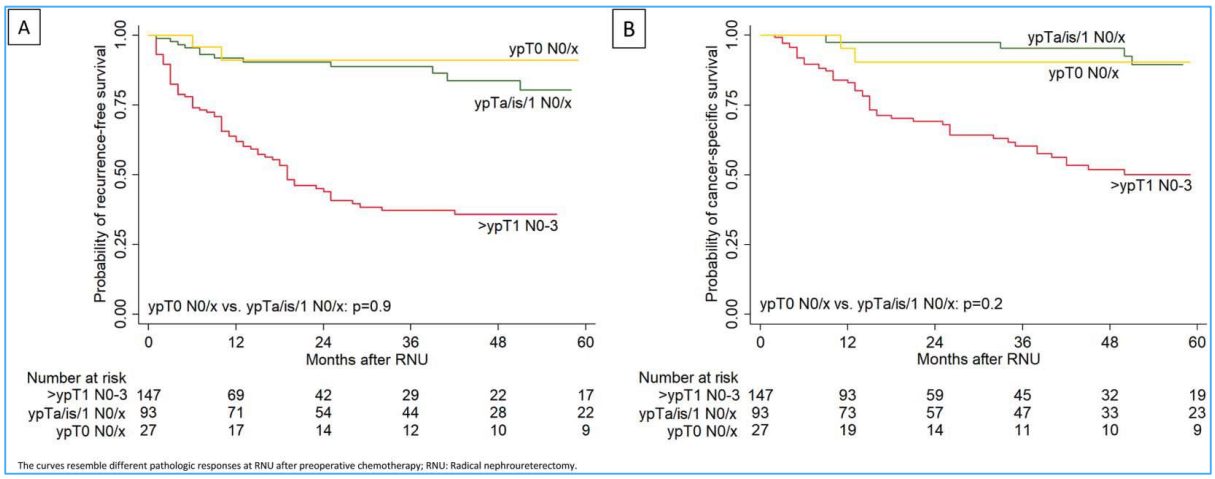
A large collaborative international retrospective study of high-risk UTUC patients who received various preoperative chemotherapy regimens was conducted while awaiting high level evidence. The primary aim of the study was to assess the rate of pathological downstaging (ypT1 N0/X or less) and pathological complete response (ypT0 N0/X) to PC at RNU. The secondary aims were to identify predictors of response and to investigate the impact of pathological response on recurrence and survival.

METHODS

This was an international observational study of patients who underwent preoperative chemotherapy and radical nephroureterectomy for high risk upper tract urothelial carcinoma between 2005 and 2017. Multiple imputation of chained equations was applied to account for missing values. Logistic regression analyses were performed to identify predictors of pathological response. Cox proportional hazard regression models were used to estimate recurrence-free survival, cancer specific survival and overall survival.

RESULTS

A total of 267 patients met our inclusion criteria. Among included patients 82 (31%) received methotrexate, vinblastine, doxorubicin and cisplatin; 123 (46%) gemcitabine and cisplatin; 25 (9%) gemcitabine and carboplatin; and 32 (12%) other regimens. The overall rates of pathological complete response and pathological downstaging were 10.1% and 44.9%, respectively. On multivariable analysis the use of gemcitabine and cisplatin, and gemcitabine and carboplatin was not statistically different from methotrexate, vinblastine, doxorubicin and cisplatin in achieving pathological complete response and pathological downstaging, respectively. The number of administered cycles did not appear to have an effect on pathological responses. Pathological downstaging was the strongest prognostic factor for recurrence-free survival (HR 0.2, p <0.001), cancer specific survival (HR 0.19, p <0.001) and overall survival (HR 0.40, p <0.001).



Kaplan-Meier estimates for recurrence-free (A) and cancer specific (B) survival

CONCLUSIONS

The most important prognostic factor at RNU is pathological downstage during preoperative chemotherapy and is consistent with enhanced RFS, CSS, and OS. Although there were no statistically meaningful variations in the pathological responses obtained between specific cisplatin-based regimens, our data indicate a non-statistically relevant tendency towards worse outcomes for GCb. The amount of cycles in chemotherapy didn't seem to be correlated with inflammatory responses. Overall, our findings support the beneficial function of preoperative chemotherapy focused on cisplatin in patients with high-risk UTUC, which may be used in medical care which recovery preparation. However, it takes findings from prospective clinical studies to adjust the UTUC management model.

REFERENCE

Foerster B, Abufaraj M, Petros F, et al. Efficacy of Preoperative Chemotherapy for High Risk Upper Tract Urothelial Carcinoma. J Urol. 2020;203(6):1101-1108.

3D reconstruction vs conventional CT angiography in patients undergoing zero-ischemia laparoscopic partial nephrectomy

INTRODUCTION

Laparoscopic partial nephrectomy (LPN) has become widely common as a viable alternative for minimally invasive nephron saving for clinical T1 renal tumours. The goal to enhance the clinical results of nephron-sparing surgery was to mitigate or even remove warm ischemic injury. Recent developments in surgical methodology now allow full removal of global ischemia during partial nephrectomy (PN), such as zeroischemia PN, unregulated "peak margin" PN, and clampless techniques. Zero-ischemia LPN is still a technologically difficult process. As such, a case-specific and detailed understanding of the particular renovascular anatomy is of considerable significance to surgical preparation and also orientation. In most facilities, renal angiography has been commonly used for preoperative assessment of patients with renal tumors. Though helical computerized tomography (CT) may still provide high-quality images of the renal tumor, vasculature, and collection method, three-dimensional (3D) reconstruction and printing technology has become increasingly common in the urological community. Such modalities of the picture is used for preoperative evaluation of patients with PN. Rare research, however, have documented the role of 3D reconstruction in zero-ischemia PN. The goal of the present study was to decide if 3D reconstruction may be the chosen radiological preoperative test, which can provide all the required details for surgical preparation and orientation.

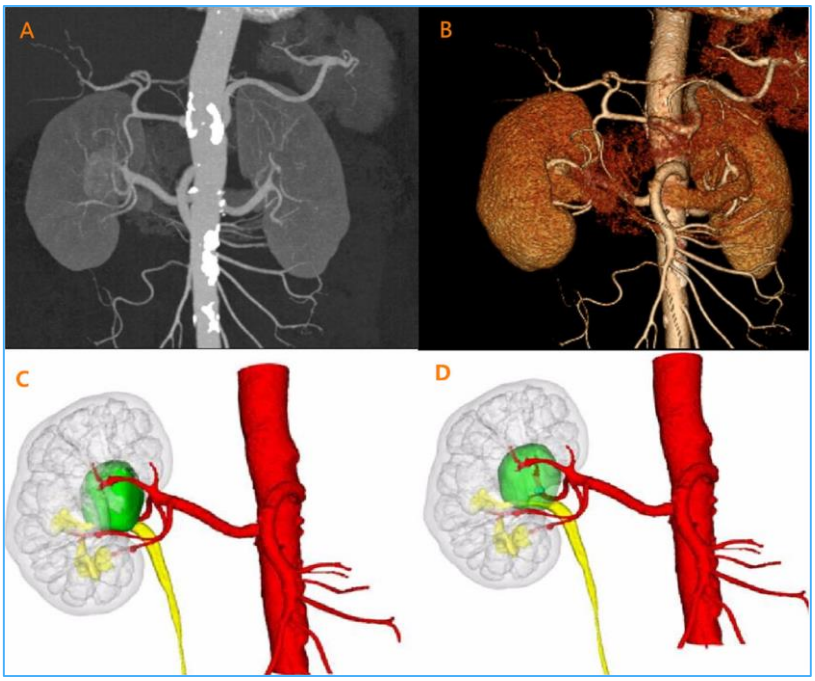
METHODS

A total of 60 consecutive patients undergoing zero-ischemia LPN between October 2017 and March 2018 who underwent CTA (CTA group including 30 patients) and 3D reconstruction (3D group including the remaining 30 patients) preoperatively were included. 3D reconstruction and CTA images were prepared which were used to demonstrate the number and spatial interrelationships of the location of renal tumors and tumor feeding arteries. These radiological findings were directly correlated with intraoperative surgical findings at laparoscopy. Baseline, perioperative variables and the rate of accurate tumor feeding artery orientation were compared between groups.

RESULTS

All LPNs were completed without conversion to renal hilar clamping or open surgery. Preoperative 3D reconstruction identified that 15 patients had only one tumor feeding artery, 12 had two, and another 3 had three, while the conventional CTA revealed that 22 patients had one tumor feeding artery, 8 had two ($P > 0.05$). The mean operation time was shorter and estimated blood loss was less in the 3D group ($P < 0.05$) and the rate of accurate tumor feeding artery dissection was higher in the 3D group

(91.7%) in comparison with the CTA group (84.2%). The baseline characteristics and renal function outcomes had no statistical differences between groups.



Conventional CTA and 3D reconstruction demonstrated a tumor located at the renal hilum. a Conventional CTA image could identify extrarenal arteries and the tumor, and sometimes the intrarenal artery branches, but failed to illustrate the relationship between tumor and its feeding arteries. b Conventional 3D reconstruction based on the CTA could reveal the relationship between kidney, tumor and extrarenal arteries, but it typically present kidney, tumor and renal vessels as opaque, which makes it impossible to visualize the intrarenal anatomy and tumor feeding arteries. c-d The 3D reconstruction images in our study included transparent kidney and 3D course of extra- and intrarenal tumor feeding arteries (c) and 3D surface rendered semitransparent renal tumor, which make it possible to show the target feeding arteries all around the tumor (d)

CONCLUSION

3D reconstruction provided detailed information for preoperative assessment and intraoperative alignment and dissection of tumor-specific feeding arteries, thus promoting zero-ischemia LPN, which is of considerable significance for optimizing the surgical result.

REFERENCE

Wu X, Jiang C, Wu G, et al. Comparison of three dimensional reconstruction and conventional computer tomography angiography in patients undergoing zero-ischemia laparoscopic partial nephrectomy. BMC Med Imaging. 2020;20(1):47.