

Original Article

Treatment of Distal Upper Tract Urothelial Cancer with Distal Ureterectomy Preserves Renal Function without Increasing Local Recurrence Rate Compared with Radical Nephroureterectomy

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ABSTRACT:

Introduction: Kidney sparing surgery like endoscopic resection and distal ureterectomy has been recently proposed as alternative surgical options to manage distal Upper Tract Urothelial Cancer. This study aims to compare the surgical, oncological and functional outcomes of distal ureterectomy and Radical Nephroureterectomy for distal Upper Tract Urothelial Carcinoma.

Methods and Material: Out of 57 patients with Upper Tract Urothelial Carcinoma treated surgically at a single institution between 2010 and 2016, nineteen patients had distal Upper Tract Urothelial Carcinoma. A retrospective review was performed on these 19 patients (11 Radical Nephroureterectomy and 8 distal ureterectomy). Radical Nephroureterectomy was performed using an open or laparoscopic approach (n= 4 and 7 respectively). All Distal Ureterectomy patients were performed via an open extra-peritoneal Gibson incision. Pelvic lymphadenectomy and Subsequent ureteroneocystostomy in the Distal Ureterectomy group was performed directly and was augmented by psoas hitch or using boari flap reconstruction. Demographic, clinical features and post-operative outcomes were compared between the Radical Nephroureterectomy and Distal Ureterectomy groups.

Results: There was a trend towards shorter mean duration of surgery (238 ± 34 vs. 286 ± 90 min) and length of hospital stay (LOS) (7.6 ± 2.8 vs. 17.3 ± 20.7 days) in the Distal Ureterectomy group compared to the Radical Nephroureterectomy group (P=NS). Peri-operative Complication of Clavien grade 1-2 was seen in 4(33.33%) Radical Nephroureterectomy and 3(37.5%) Distal Ureterectomy cases respectively. All patients had high grade Upper Tract Urothelial Carcinoma with equivalent pTNM staging in both groups with clear surgical margins. Immediate post-operative renal function improvement was statistically significant in the Distal Ureterectomy group (Radical Nephroureterectomy 2.27 ± 5.93 vs 10.86 ± 9.92 Distal Ureterectomy, $p=0.034$). Three out of 11 Radical Nephroureterectomy group patients required dialysis.

Conclusions: Local recurrences were similar after Distal Ureterectomy and Radical Nephroureterectomy with equivalent pathological outcomes in distal Upper Tract Urothelial Carcinoma. There was a clear trend towards shorter hospital stay and better renal function preservation in favor of Distal Ureterectomy with fewer patients requiring dialysis.

KeyWords: Distal ureterectomy, Local recurrence, Radical Nephroureterectomy, Upper tract urothelial carcinoma

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Introduction

Upper Tract Urothelial Carcinoma (UTUC) accounts for 5% of the urothelial malignancy. Radical Nephroureterectomy (RNU) with excision of cuff of bladder has been the gold standard treatment for UTUC.¹ Kidney sparing surgery like endoscopic resection and Distal Ureterectomy (DU) of the ureter has been proposed as alternative surgical options to manage distal UTUC. The proximity to the bladder makes distal ureteric tumors more amendable for local resection and anastomosis with the bladder. In fact with the loss of functional renal unit, RNU can result in progressive loss of renal function and can lead to CKD and the increased incidence of cardiovascular morbidity.^{2, 3, 4} This study aims to compare the surgical, oncological and functional outcomes of DU and RNU for distal UTUC.

Methods and Materials

Out of 57 patients with UTUC treated surgically at a single institution between 2010 and 2016, nineteen patients had distal UTUC. A retrospective review was performed on these 19 patients (11 RNU and 8 DU). None of the patient was treated endoscopically prior to either RNU or DU. RNU was performed using an open or laparoscopic approach (n= 4 and 7 respectively). The distal ureteric dissection in RNU was performed by open either lower midline or Gibson incision. All DUs were performed via an open extra peritoneal Gibson incision. The distal ureter was meticulously dissected around the distal ureter to avoid going into the tumor and the bladder cuff was distally obtained by removing 1cms of the bladder mucosa circumferentially around the ureteral orifice. The ureteroneocystostomy in DU group was performed directly when the length of the distal ureter was adequate or augmented by psoas hitch or reconstruction using boari flap depending upon the gap created after distal ureterectomy. Frozen section of the proximal ureteral margins was done in all patients. Pelvic lymphadenectomy was performed selectively in 41.67% RNU and 75% DUs. Patients in both groups followed the same surveillance regimen which includes cystoscopy urine cytology and CT urography for a minimum period of 5 years.

Demographic, clinical features and post-operative outcomes were compared between the RNU and DU groups.

Stata version 12 was used to analyze the data. Fisher exact and the chi square test were used to analyze the categorical variables and student t-test and Kolmogorov –Smirnov test for the numerical variables. The Kaplan Meier curve was used to estimate the recurrence free survival.

Results

Base line data: There was more aged patient in the DU than RNU although no statistical difference was observed between the two groups (RNU 71±9.46) vs. DU 77 ± 13.84. Male were affected more in both the group (RNU-63% vs. DU- 64%) and more common in the Chinese race (50% vs.87.5). The incidence of comorbidities in both the group was comparable. (Table 1)

Table 1: Clinical details of RNU and DU

Variables	RNU	DU	P value
Number	11	8	
Age	71	77	0.2307**
Side			0.463*
Right	6	3	
Left	5	5	
No of lymph nodes	10.00± 8.57	12.17± 5.98	0.6334**
Hospital stay	17.27±20.46	7.63±2.77	0.2061**
Duration of surgery	286.09±89.94	237.88±74.45	0.1697**
Creatinine change	-8.18±89.98	-15.86±13.73	0.8274**
Local Recurrence	3	3	0.960*
Lymph node dissection	5	6	0.198*
Dialysis	3	0	0.107*
Post op complications	4	2	0.599*
Distal margins	3	2	0.912*
Metastasis	3	4	0.330*
Death	3	4	0.346*

Operative outcome: There was a trend towards shorter mean duration of surgery (238±34 vs. 286 ±90 min) and length of hospital stay (LOS) (7.6±2.8 vs. 17.3±20.7 days) in the DU group compared to the RNU group (P=0.1697 and P=0.2061). Peri operative Complication of Clavien grade 1-2 was seen in 4(33.33%) RNU and 3 (37.5%) DU group) respectively with no 3-4 Clavien complications (p=0.599).

Pathological outcome: Oncologically, all patients had high grade UTUC with equivalent pTNM staging ($p=0.917$). Invasive UTUC dominated in both group. Lymph node dissection was carried out in 5 patient in RNU and 6 patient in DU group ($p=0.198$) with similar mean Lymph node count (12.2 ± 5.9 vs. 10 ± 8.6 , $p=0.63$) and positive Lymph nodes (2 in RNU and 1 in DU group ($p=0.62$). Proximal surgical margin was positive in 3 patients in RNU and 2 in DU group ($p=0.912$)

Table 2: Pathological Staging details

Variables	RNU	DU	P value*
pT stage			0.917
pTa	0	0	
PT1	2	2	
pT2	1	1	
PT3	6	4	
PT4	1	0	
LN stage			0.672
Positive	2	1	
Margins	3	2	0.912

Oncological outcome: During the median follow up 23.3 months local recurrence occurred in 7 patients 4 in RNU group and 3 in DU group ($p=0.96$). Metastasis seen in 3 in RNU group and 4 in DU group ($p=0.33$). Diseases specific mortality occurred in 3 in RNU group and 4 in DU group ($p=0.346$). There was no difference in KM survival estimates (log rank=NS). Although significant number of local recurrence, metastasis and even death seen in the table but same patient finding was noted in all. One of the recurrences in DU group underwent subsequent RNU and one planning or RNU whereas one patient with recurrence was too old and unfit for further surgery.

Renal functional outcome:Renal function was measured immediately before and 3-4 weeks after the surgery in all patient. The creatinine change was seen in RNU group and DU group were 8.18 ± 89.98 and -15.86 ± 13.73 ($p=0.8274$). The renal function was better preserved in the DU group as compared with the RNU group which was reflected by the change in eGFR improvement, 2.27 ± 5.93 in RNU group and 10.86 ± 9.92 in DU group ($p=0.034$). Three out

of 11 RNU group required dialysis because of preoperative compromised renal function rather than postoperative change.

Table 3: Details of eGFR

	RNU	DU	P value
Pre-operative eGFR	41.09 ± 28.39	51.00 ± 18.46	0.427
Post-operative eGFR	43.91 ± 25.36	61.86 ± 26.47	0.1691
Difference in eGFR	2.27 ± 5.93	10.86 ± 9.92	0.0344

Table 4: Comorbidities associated with UTUC

	RNU	DU	P value*
Diabetes Mellitus	4	5	0.260
Hypertension	7	6	0.662
Hyperlipidaemia	7	6	0.599
IHD	2	1	0.737
CKD	6	3	0.463

Discussion

The aggressive nature of the UTUC has established RNU as the standard of care for distal ureteric tumors.¹ However due to the direct impact on the overall renal function leading to the increased cardiovascular morbidity.^{2,3,4} Kidney Sparing Surgery has been considered the alternative option to treat selected cases of UTUC. The role of endoscopic surgery is limited to low grade and small sized tumors. Higher recurrence rate and the stringent follow up regime makes the endoscopic procedure less favorable than segmental resection.⁵ Systematic review and meta-analysis supports similar oncological outcomes between SU and RNU, with better preservation of renal function after SU.^{6, 7, 8} Although Initially KSS was indicated only for limited cases of severely impaired renal function, solitary kidney, bilateral synchronous tumors or the necessity of platinum based chemotherapy for future treatment; the indication has been extended to include low risk ureteral tumors and selected high risk cases.⁹ The long term cancer specific survival of SU is comparable with endoscopic and RNU group.¹⁰ The overall outcome of the Urothelial carcinoma (UC) depends upon tumor stage, tumor grade and the location within the ureter irrespective of the treatments. Tumors of distal ureter are more common and show relatively low stage and low

grade than the tumor of the other location.⁸ The anatomic proximity of the distal ureter with the bladder makes it more amendable to resection and reconstruction. With the favorable results of segmental ureterectomy, distal ureterectomy has been performed with encouraging outcomes in clinically localized UC of the distal ureter. There are no randomized and prospective studies comparing the results of DU with RNU but all available retrospective data recommends DU as the first line of treatment options for the distal ureteric UC in selected cases.^{9, 10, 11}

The present study includes patient with nonmuscles invasive and muscle invasive UTUC, In fact majority of patients in both group are muscle invasive UTUC. (72% in RNU and 62% in DU). There was no significant difference in disease recurrence and overall survival between the two groups in our study. Dalpiaz et al reported no difference in recurrence between nonmuscles invasive and muscle invasive UTUC for both types of surgery.¹¹ After reviewing all the database of 2044 patients, Jeldres concluded that there is no statistical difference between SU and RNU in terms of cancer specific mortality rates in patient with pT1-2 vs pT3-4.¹²

All the recurrence in RNU group and 2 out of 3 recurrences in DU group had pT3 stage. one patient in DU group with pT2 disease had local recurrence as well as bladder recurrence. Chemotherapy was offered to the entire muscle invasive patient but only few received it due to compromised health parameters and old age. So it seems that it is the stage and grades of the disease not the type of surgery that dictates the future recurrence, metastasis and overall cancer specific mortality of the patient.

Our present analysis showed a significant improvement in renal function after DU in comparison to RNU and this finding is very important to suggest DU even for muscle invasive high grade tumors as the preservation of the renal function which allows patient to undergo chemotherapy treatment.

As seen in our analysis the shorter operating time and hospital stay, although not statistically significant would help patient to recover faster and ready for the auxiliary treatment if needed.

Conclusions:

In this relatively rare condition of distal UTUC, local recurrences were similar after DU and RNU with equivalent pathological outcomes. Despite the small numbers, there was a clear trend towards shorter hospital Stay and better renal function preservation in favor of DU. Significantly, this translates in the longer term to fewer patients requiring dialysis and fitness for chemotherapy if needed.

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