Oncologic Outcomes Following Robot-Assisted Laparoscopic Nephroureterectomy with Bladder Cuff Excision for Upper Tract Urothelial Carcinoma

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Purpose: Robot-assisted laparoscopic nephroureterectomy with bladder cuff excision is a minimally invasive alternative to open surgery for managing upper tract urothelial carcinoma. We report oncologic outcomes following robot-assisted laparoscopic nephroureterectomy with bladder cuff excision.

Materials and Methods: The records of the initial 65 patients who underwent robot-assisted laparoscopic nephroureterectomy with bladder cuff excision for upper tract urothelial carcinoma between 2008 and 2014 were reviewed from our institutional review board approved, prospectively maintained database. All patients underwent surgery with the single docking technique. Baseline demographic features, pathological variables and perioperative data were analyzed. Kaplan-Meier methodology was used for survival analysis. Cox proportional hazards regression was applied to determine the prognostic effect of different variables on survival.

Results: Mean patient age was 69.1 years. Final pathological evaluation revealed pT2 stage or lower in 65% of patients, pT3 in 28.3% and pT4 in 6.7%. High grade pathological findings were present in 85% of patients, including 13.3% with concomitant carcinoma in situ and 30% with lymphovascular invasion. Median followup was 25.1 months (range 6 to 68.9). At 2 and 5 years overall survival was 86.9% and 62.6%, cancer specific survival was 92.9% and 69.5%, and recurrence-free survival was 65.3% and 57.1%, respectively. A total of 23 patients experienced disease recurrence. Bladder recurrence developed in 15 patients, 12 had isolated bladder recurrence and 8 had metastatic disease. On univariate analysis age greater than 70 years, preoperative hydronephrosis, nodal disease and concomitant carcinoma in situ were significantly associated with decreased recurrence-free survival ($p = 0.002$, 0.04, 0.006 and 0.001, respectively). However, none was statistically significant on multivariate analysis. On univariate analysis impaired preoperative renal function (creatinine greater than 2 mg/dl) and lymphovascular invasion were associated with reduced cancer specific survival ($p = 0.03$ and 0.01, respectively). However, only lymphovascular invasion was associated with decreased cancer specific survival on multivariate analysis ($p = 0.048$).

Conclusions: Our reported data on oncologic outcomes following robot-assisted laparoscopic nephroureterectomy with bladder cuff excision for upper tract urothelial carcinoma demonstrate satisfactory oncologic control at intermediate term followup. Long-term outcomes are required to assess true efficacy.

Key Words: urinary bladder, carcinoma, robotics, nephrectomy, mortality

Abbreviations and Acronyms

CIS = carcinoma in situ

CSS = cancer specific survival

GFR = glomerular filtration rate

LVI = lymphovascular invasion

MFS = metastasis-free survival

OS = overall survival

RFS = recurrence-free survival

RNUBCE = robotic nephroureterectomy with bladder cuff excision

UTUC = upper tract urothelial carcinoma

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UPPER tract urothelial carcinoma is an uncommon malignancy affecting the renal pelvicalyceal system and/or the ureter with an estimated incidence of 3% to 5% of all urothelial cancers.[1] Nephroureterectomy with bladder cuff excision is the gold standard management of high grade or bulky UTUC. Oncologic principles necessitate that the entire ureter along with a bladder cuff be excised during nephroureterectomy, besides lymphadenectomy in appropriate cases (high grade disease, bulky primary on preoperative imaging, and/or radiological evidence of lymph node involvement).[2] Oncologic outcomes following laparoscopic nephroureterectomy has been extensively reported as well as being compared to the open approach in multiple prior reports, with advantages of less postoperative pain, less blood loss and quicker recovery with laparoscopic technique.[3-5]

Pure laparoscopic bladder cuff excision with watertight closure of the cystotomy with free hand suturing is a daunting task even for experienced laparoscopic surgeons. Robotic assistance with improved dexterity, EndoWrist® instrumentation and 3-dimensional visualization with magnification helps perform nephroureterectomy with bladder cuff excision in minimally invasive fashion.

Multiple reports have been published documenting the perioperative feasibility and safety of the robotic approach as well as encouraging early oncologic outcomes.[6-8] Reporting on long-term oncologic outcomes after RNUBCE has been scarce.

We present our large, single center experience with intermediate term oncologic outcomes after pure RNUBCE to manage UTUC. To our knowledge this is the largest series of the oncologic efficacy of pure RNUBCE for UTUC.

MATERIALS AND METHODS

Patient Selection
The records of the initial 65 patients who underwent RNUBCE for UTUC from 2008 to 2014 were reviewed using our institutional review board approved, prospectively maintained database. Patients with a minimum followup of 6 months were included in final analysis. All patients underwent routine preoperative blood studies and imaging.

Surgical Technique
All patients were treated with surgery using our previously reported single docking RNUBCE technique.[6] We performed RNUBCE with single port placement and single docking of the robot without intraoperative patient repositioning or robot redocking. We initially used the da Vinci® S robotic platform, and subsequently the da Vinci Si and Xi platforms.

A bladder cuff was excised in all patients and cystotomy was closed initially in 2 layers with polyglactin suture. Since the introduction of the barbed V-Loc™ suture in 2010, we have used it for watertight closure of the bladder. In patients with bulky and/or T3 disease, or high grade tumors in the renal pelvis, or upper or mid ureter, we performed regional lymphadenectomy, including hilar, paracaval and retrocaval nodes for right tumors, and hilar and para-aortic lymph nodes for left tumors. In patients with distal ureteral tumors ipsilateral pelvic lymphadenectomy was done. Intravesical mitomycin following robotic nephroureterectomy was administered intermittently at our institution during the study period. Lymph node dissection was also performed if there was radiological evidence of nodal involvement regardless of stage or grade.

Followup
Followup in clinic was scheduled 3 months postoperatively for the first oncologic surveillance, including office flexible cystoscopy, followed by 6 to 12-month followup with cystoscopy and imaging surveillance. All patients with pT2-4 and/or nodal disease were referred to medical oncology for consideration of adjuvant chemotherapy.

Statistical Analysis
Baseline demographic features, pathological variables and perioperative data were analyzed. Patient characteristics are reported using the mean, median and SD for continuous variables, and the frequency and relative frequency for categorical variables. Surgical complications were reported and classified using the modified Dindo-Clavien grading system.[9]

OS, CSS, RFS and MFS were calculated with the standard Kaplan-Meier methodology. Kaplan-Meier curves and corresponding estimated 24 and 60-month survival rates are provided. A Cox proportional hazards regression model was used to determine the prognostic effect of different variables on survival. Statistical analysis was done with SAS®, version 9.2.

RESULTS

Patient Data
Of 65 patients 60 had sufficient data available and met the study inclusion criteria required for analysis. Mean ± SD age was 69.1 ± 11.1 years and mean body mass index was 27.3 ± 5.7 kg/m^2. ASA® score was 3 or greater in 68.3% of patients, 45% had ipsilateral hydronephrosis on preoperative imaging and 8 (13.3%) had a history of prior/concurrent nonmuscle invasive bladder cancer. None of the patients received neoadjuvant chemotherapy prior to surgery. Table 1 lists patient demographic and preoperative characteristics.

Pathological Data
Final pathological analysis showed pT2 stage or lower in 65% of patients, pT3 in 28.3% and pT4 in 6.7%. High grade pathological results were present in 85% of patients, 8 (13.3%) had concomitant CIS