

Comparison of Laparoscopic, Hand-Assisted, and Open Surgical Nephroureterectomy

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ABSTRACT

Background and Objectives: The aim of this study was to compare oncologic outcomes after laparoscopic nephroureterectomy, hand-assisted laparoscopic nephroureterectomy, and open nephroureterectomy for upper urinary tract urothelial cancer.

Methods: Between April 1995 and August 2010, 189 patients underwent laparoscopic nephroureterectomy, hand-assisted laparoscopic nephroureterectomy, or open nephroureterectomy for upper urinary tract urothelial cancer. Of these patients, 110 with no previous or concurrent bladder cancer or any metastatic disease were included in this study. Cancer-specific survival, recurrence-free survival, and intravesical recurrence-free survival rates were analyzed by the Kaplan-Meier method and compared with the log-rank test. The median follow-up period for the cohort was 70 months (range, 6–192 months).

Results: The 3 groups were well matched for tumor stage, grade, and the presence of lymphovascular invasion and concomitant carcinoma in situ. The estimated 5-year cancer-specific survival rates were 81.1%, 65.6%, and 65.2% for laparoscopic nephroureterectomy, hand-assisted laparoscopic nephroureterectomy, and open nephroureterectomy, respectively ($P = .4179$). The estimated 5-year recurrence-free survival rates were 33.8%, 10.0%, and 41.2% for laparoscopic nephroureterectomy, hand-assisted laparoscopic nephroureterectomy, and open nephroureterectomy, respectively ($P = .0245$). The estimated 5-year intravesical recurrence-free survival rates were 64.8%, 10.0%, and 76.2% for laparoscopic nephroureterectomy, hand-assisted laparoscopic nephroureterectomy, and open nephroureterectomy, respectively ($P < .0001$).

Conclusion: Although there was no significant difference in cancer-specific survival rate among the laparoscopic

nephroureterectomy, hand-assisted laparoscopic nephroureterectomy, and open nephroureterectomy groups, hand-assisted laparoscopic nephroureterectomy may be inferior to laparoscopic nephroureterectomy or open nephroureterectomy with regard to recurrence-free survival and intravesical recurrence-free survival rates.

Key Words: Nephroureterectomy, Laparoscopic, Hand-assisted laparoscopic.

INTRODUCTION

Upper urinary tract urothelial cancers (UUTUCs) are uncommon and account for only 5% to 10% of urothelial carcinomas.¹ Radical nephroureterectomy (RNU) with excision of the bladder cuff is the gold-standard treatment for UUTUCs, regardless of the location of the tumor in the upper urinary tract.¹

Surgery for nonmetastatic UUTUC has changed considerably during the past decade. It has been feared that tumor dissection during laparoscopic procedures may be associated with a higher risk of recurrence.² Although this remains a matter of controversy,³ one randomized controlled trial, comparing laparoscopic nephroureterectomy (LNU) with open nephroureterectomy (ONU), showed that oncologic outcomes were comparable for both groups.⁴ However, there has been no study of oncologic outcomes after LNU compared with hand-assisted laparoscopic nephroureterectomy (HALNU) and ONU for patients with UUTUC.⁵

To better understand the oncologic efficacy of less invasive surgery for nonmetastatic UUTUC, we conducted a critical retrospective review of patients with UUTUC who underwent RNU over a 15-year inclusion interval. The objective of this study was to compare the oncologic outcomes of UUTUC after LNU, HALNU, and ONU.

METHODS

We retrospectively analyzed the clinical and demographic information of 195 consecutive patients with histopathologically confirmed UUTUC treated by RNU between 1995

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and 2010 at our institute. Patients with T4 disease, node-positive disease, a history of bladder cancer, or concomitant bladder cancer were excluded. Finally, a total of 108 patients with Tis-T3N0M0 UUTUC were enrolled in this study. Clinical information and follow-up data for the patients were obtained from the UUTUC database after we received their informed consent. This study was approved by the institutional review board.

All the patients underwent ONU, HALNU, or LNU with extrafascial dissection of the kidney, as well as complete resection of the distal ureter and its orifice. ONU was performed through a flank incision combined with a lower quadrant incision or midline incision. HALNU was performed by the transperitoneal approach with a 6- to 8-cm hand incision on the right lower abdomen in right-sided HALNU and mid abdomen in left-sided HALNU and 2 trocars as previously described.⁶ The hand-assisted device (LAPDISC; Hakko Co, Ltd Chikuma, Japan) was applied to the wound, and the surgeon's nondominant hand was inserted into the abdomen. LNU was performed by the retroperitoneal or transperitoneal approach. The patient was placed in the lateral position. When the retroperitoneal approach was selected, a retroperitoneal working space was created with a PDB balloon (Covidien, Mansfield, Massachusetts). In both approaches, 4 trocars were inserted in the usual manner. In each procedure, the kidney, the ureter, and a bladder cuff were excised en bloc. Lymphadenectomy was performed at the surgeon's discretion. Until 1999, all patients underwent ONU. Since 2000, we have performed laparoscopic surgery in principle (HALNU in 2000–2002 and LNU in 2003 and thereafter) (Figure 1). If there was wariness about performing laparoscopic surgery (eg, because of a history of abdominal surgery or suspicion of incomplete resection of T3 upper or middle ureteral cancer), ONU was carried out. In

98 of the 108 patients (90.7%), distal ureterectomy was performed by bladder cuff excision. Endoscopic ureteral detachment (the pluck technique)^{6,7} was carried out in 6 of the 9 HALNUs (66.7%) and 2 of the 65 LNUs (3.1%) (Table 1).

Computed tomography (chest to pelvis), cystoscopy, and urinary cytology were performed every 3 months in the first 5 years after RNU and semiannually or annually thereafter in patients without evidence of recurrent disease. Additional radiographic and diagnostic tests were performed when clinically indicated. At the time of the retrospective analysis, the median follow-up time was 60 months (range, 6–192 months). Postoperative adverse events (AEs) were evaluated according to the Common Terminology Criteria for Adverse Events v4.0.

Cancer-specific survival (CSS), recurrence-free survival (RFS), and intravesical recurrence-free survival (ivRFS) rates were estimated by the Kaplan-Meier method and evaluated with the use of the log-rank test. Clinicopathologic factors in each group were compared by use of the χ^2 or Kruskal-Wallis test. Statistical significance was set at $P < .05$, and statistical tests were performed with JMP software, version 10.0.0 (SAS Institute, Cary, North Carolina).

RESULTS

The characteristics of the patients who underwent ONU, HALNU, and LNU are shown in Table 1. There was no significant difference in age, tumor site, pT stage, tumor grade, or lymphovascular invasion among the 3 groups. The pluck technique was more frequently selected in HALNU patients, followed by LNU patients in this order ($P < .0001$).

Table 2 shows perioperative data, including the operative time, blood loss, time to discharge, and postoperative AEs, for each surgical approach. There was no significant difference in operative time among the 3 groups. The amount of blood loss was significantly smaller in LNU and HALNU patients than in ONU patients ($P < .0001$). The patients who underwent LNU had a shorter hospital stay than those who underwent ONU or HALNU ($P < .0001$). There was no significant difference in the incidence of postoperative AEs among the groups. In the ONU group, 3 cases of wound dehiscence, 1 case of ileus, and 1 postoperative hemorrhage greater than grade 3 were observed. The AEs of grade 3 or greater in the HALNU group were 1 kidney infection and 1 case of hypotension. In the LNU group,

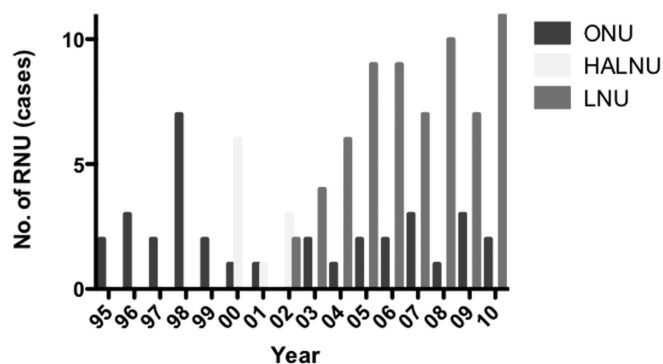


Figure 1. Trends for use of each procedure of RNU for stage I through stage III UUTUC.

Table 1.
Patient Characteristics

Characteristic	RNU			P Value
	ONU	HALNU	LNU	
No. of patients	34	9	65	
Median age (range) (y)	69 (32–88)	65 (53–71)	70 (50–88)	.1878
Conversion to ONU	—	1 (11%)	6 (9%)	.8566
Tumor site (main)				.6423
Renal pelvis	20 (59%)	4 (44%)	35 (54%)	
Upper ureter	3 (9%)	0 (0%)	6 (9%)	
Mid ureter	4 (12%)	1 (11%)	5 (8%)	
Lower ureter	4 (12%)	3 (33%)	17 (26%)	
Renal pelvis and ureter	3 (9%)	1 (11%)	2 (3%)	
pT stage				.5375
pTis	0 (0%)	0 (0%)	2 (3%)	
pTa	3 (9%)	0 (0%)	14 (22%)	
pT1	7 (21%)	2 (22%)	10 (15%)	
pT2	8 (24%)	3 (33%)	11 (17%)	
pT3	16 (47%)	4 (44%)	28 (43%)	
Grade (1973 WHO ^a classification)				.9203
1	1 (3%)	0 (0%)	2 (3%)	
2	14 (41%)	4 (44%)	33 (51%)	
3	19 (56%)	5 (56%)	30 (46%)	
Lymphovascular invasion				.1944
Positive	13 (38%)	2 (22%)	14 (22%)	
Negative	21 (62%)	7 (78%)	51 (78%)	
Management of distal ureter				<.0001
Bladder cuff	33 (97%)	3 (33%)	62 (95%)	
Pluck technique	0 (0%)	6 (67%)	2 (3%)	
Simple incision	1 (3%)	0 (0%)	1 (2%)	

^aWHO = World Health Organization.

5 patients had postoperative AEs of grade 3 or greater, including 3 cases of wound dehiscence, 1 postoperative hemorrhage, 1 kidney infection, 1 lung infection, and 1 increase in creatinine level.

Figures 2, 3, and 4 present Kaplan-Meier estimates of CSS, RFS, and ivRFS, respectively, in each group. The 5-year CSS rates of patients who underwent ONU, HALNU, and LNU were 74.2%, 72.9%, and 87.4%, respectively ($P = .5611$). The 5-year RFS rates were 57.1% in the ONU group, 12.5% in the HALNU group, and 69.2% in the LNU group ($P = .0416$). The 5-year ivRFS

rates of patients who underwent ONU, HALNU, and LNU were 71.1%, 12.5%, and 69.2%, respectively ($P = .0017$). Multivariate Cox regression analysis showed that the operative technique (HALNU) and tumor grade (grade 3) were independent factors for intravesical recurrence (**Table 3**).

DISCUSSION

In this study there was no significant difference in CSS, RFS, and ivRFS rates between LNU and ONU. To date,

Table 2.
Perioperative Data

Variable	RNU			P Value
	ONU (n = 34)	HALNU (n = 9)	LNU (n = 65)	
Median operative time (range) (min)	286 (130–577)	325 (237–390)	327 (168–601)	.4450
Median blood loss (range) (mL)	475 (100–3670)	250 (50–880)	220 (0–2500)	<.0001
Median time to discharge (range) (d)	14.5 (5–36)	17 (9–24)	10 (4–62)	<.0001
Postoperative AEs of grade 3 or greater				.5908
Yes	5 (15%)	2 (22%)	7 (11%)	
No	29 (85%)	7 (78%)	58 (89%)	

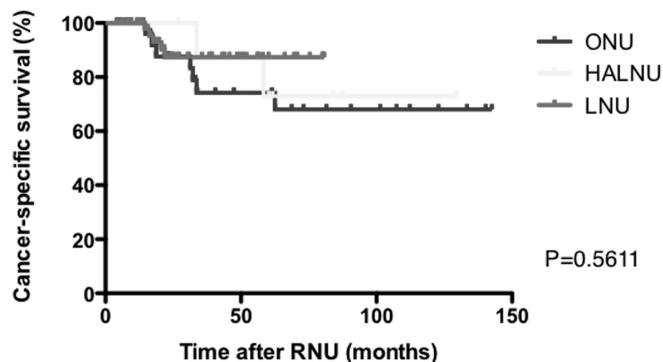


Figure 2. Kaplan-Meier estimates of CSS.

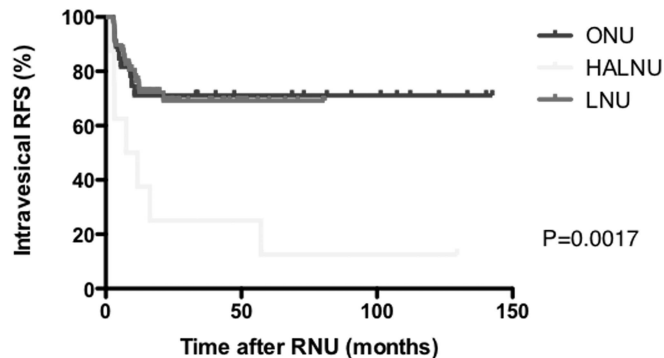


Figure 4. Kaplan-Meier estimates of ivRFS.

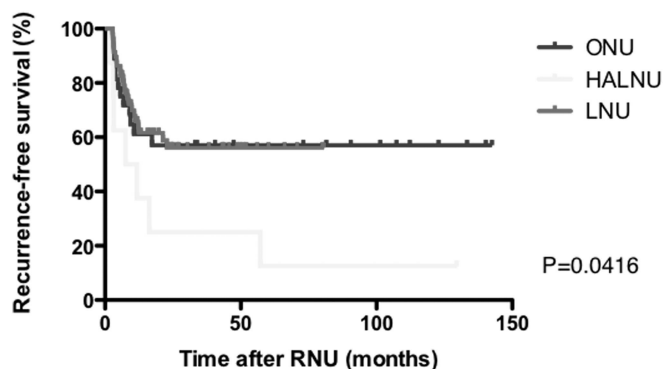


Figure 3. Kaplan-Meier estimates of RFS.

many studies have reported that LNU is comparable with ONU with regard to oncologic outcomes.^{2,8–14} A recent cumulative analysis including 21 studies showed that LNU offered oncologic efficacy and reliable perioperative safety comparable with ONU, although most of the included studies were retrospective.¹⁵ The Cochrane Collaboration’s review using comprehensive searches concluded that oncologic outcomes of organ-confined disease were comparable for LNU and ONU.⁵ Only one prospective

randomized study showed that LNU was superior to ONU in terms of the perioperative outcomes and comparable with ONU for oncologic outcomes in patients with organ-confined disease.⁴ On the basis of these reports, the European Association of Urology Guideline Group considers that ONU and LNU are equivalent in terms of efficacy in a grade B recommendation.¹

Meanwhile, we found that HALNU was comparable with ONU and LNU with regard to CSS but was inferior to ONU and LNU for RFS and ivRFS. There are studies reporting benefits of HALNU such as less intraoperative blood loss and a shorter hospital stay with an equivalent intermediate-term oncologic outcome compared with ONU.^{16,17} In a meta-analysis of studies comparing HALNU with LNU, there were no significant differences in the operative time, the length of stay, or the risks of perioperative transfusion or complications, but HALNU was associated with significantly less operative blood loss and risk of open conversion than LNU.¹⁸ Another study with a small series and a short-term follow-up period showed no difference in oncologic outcomes between LNU and HALNU.¹⁹ Thus most studies reported the equivalence or superiority of HALNU

Table 3.

Univariate and Multivariate Cox Regression Analyses for Prediction of Intravesical Recurrence After Radical Nephroureterectomy

	Univariate			Multivariate		
	HR ^a	95% CI ^a	P Value	HR	95% CI	P Value
Age	1.00	0.97–1.04	.9078			
Sex	1.42	0.68–3.37	.3639			
Operative technique						
ONU	1.00	Reference		1.00	Reference	
HALNU	4.72	1.77–12.4	.0026	5.52	2.05–14.6	.0011
LNU	1.08	0.49–2.52	.8582	1.10	0.50–2.57	.8207
Architecture	1.51	0.76–3.13	.2401			
Multiplicity	1.29	0.62–2.54	.4853			
Tumor size	1.35	0.69–2.64	.3726			
Grade (3 vs 1 or 2)	2.12	1.08–4.36	.0292	2.41	1.21–5.02	.0118
pT stage						
Ta/Tis	1.00	Reference				
T1	1.36	0.43–4.59	.5991			
T2	1.43	0.49–4.67	.5134			
T3	1.04	0.40–3.23	.9342			
Lymphovascular invasion	0.77	0.32–1.62	.5060			

^aCI = confidence interval; HR = hazard ratio.

compared with ONU or LNU. However, a large multicenter study showed that HALNU was an independent risk factor for intravesical recurrence compared with LNU,²⁰ like this study.

In our study the difference in ivRFS among the 3 surgical techniques was larger than that for all RFS because the first recurrence site was the bladder in all patients who underwent HALNU and had a recurrence during follow-up. We excluded patients with unresectable or metastatic tumors because minimally invasive surgery is not recommended for advanced UUTUC.³ To avoid contamination causing recurrence of bladder cancer itself other than intravesical recurrence of UUTUC, we also excluded patients with a history of bladder cancer or concomitant bladder cancer. In these circumstances, the HALNU technique was associated with a high risk of intravesical recurrence. Because early ligation of the ureter⁷ was not performed during RNU in our series, even in ONU and LNU patients, we think that the hand manipulation during HALNU might release cancer cells into the urinary tract and those cells might be seeded in the bladder mucosa. As shown in **Figure 1**, we performed HALNU before introducing LNU. This may mean that inexperience in using laparoscopic

procedures was associated with a higher incidence of intravesical recurrence. We suggest that HALNU should not be performed during training for unskilled laparoscopic surgeons.

There were several limitations to this study. First, this was a retrospective study with selection biases and a small number of patients, especially in the HALNU group, at a single institute. To determine the differences in the incidences of intravesical recurrence among ONU, HALNU, and LNU patients, a prospective randomized trial is needed. Second, RNU was performed by various surgeons over a long period. Finally, early ligation of the ureter was not performed during RNU.

We found that there was no significant difference in CSS among ONU, HALNU, and LNU patients but that RFS and ivRFS in HALNU patients were inferior to those in ONU and LNU patients. LNU and HALNU were associated with diminished blood loss, which is compatible with the results of previous studies. Patients who underwent LNU had a shorter hospital stay than those undergoing ONU or HALNU. Thus, we suggest that LNU is the most appropriate technique, with a balance between lesser invasiveness

and favorable oncologic outcomes for patients with organ-confined disease and without a history of bladder cancer.

CONCLUSION

Although there was no significant difference in CSS among LNU, HALNU, and ONU patients, HALNU may be inferior to LNU or ONU in terms of RFS and ivRFS. LNU is a less invasive procedure with comparable long-term oncologic outcomes in comparison with ONU.

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