Surgical outcome predictor analysis following hand-assisted or pure laparoscopic transperitoneal nephroureterectomy using the Taiwan upper urinary tract urothelial carcinoma database

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Purpose: Taiwan has a high incidence of upper tract urothelial carcinoma (UTUC). This study aimed to compare the surgical outcomes following transperitoneal hand-assisted laparoscopic nephroureterectomy (TP-HALNU)
and transperitoneal pure laparoscopic nephroureterectomy (TP-LNU) from the Taiwan nationwide UTUC collaboration database using different parameters, including surgical volumes.

**Materials and methods:** The nationwide UTUC collaboration database includes 14 hospitals in Taiwan from the Taiwan Cancer Registry. We retrospectively reviewed the records of 622 patients who underwent laparoscopic nephroureterectomy between July 1988 and September 2020. In total, 322 patients who received TP-LNU or TP-HALNU were included in the final analysis. Clinical and pathological data and oncological outcomes were compared.

**Results:** Of the 322 patients, 181 and 141 received TP-LNU and TP-HALNU, respectively. There were no differences in clinical and histopathological data between the two groups. No differences were observed in perioperative and postoperative complications. There were no significant differences in oncological outcomes between the two surgical approaches. In the multivariate analysis, the cohort showed that age ≥70 years, positive pathological lymph node metastasis, tumors located in the upper ureter, and male sex were predictive factors associated with an increased risk of adverse oncological outcomes. A surgical volume of ≥20 cases showed a trend toward favorable outcomes on cancer-specific survival [hazard ratio (HR) 0.154, \( p = 0.052 \)] and marginal benefit for overall survival (HR 0.326, \( p = 0.019 \)) in the multivariate analysis.

**Conclusion:** Although different approaches to transperitoneal laparoscopic nephroureterectomy showed no significant differences in surgical outcomes, age, sex, lymph node metastasis, and tumor in the upper ureter in the following period were predictive factors for oncological outcomes. Higher surgical volume did not impact disease-free survival and bladder recurrence-free survival but was associated with improved overall survival and cancer-specific survival. Exploration of unknown influencing factors is warranted.

**KEYWORDS**
urothelial carcinoma, upper urinary tract urothelial carcinoma, laparoscopic nephroureterectomy, hand-assisted laparoscopic nephroureterectomy, oncological outcome, surgical volume

**Introduction**

Urothelial carcinoma (UC) is the fourth most common malignancy worldwide, with upper tract UC (UTUC) accounting for 5%–10% of these cases (1, 2). The gold standard for UTUC management is radical nephroureterectomy (NU), with the removal of the ipsilateral bladder cuff (2, 3). This procedure has historically been performed via an open approach [open NU (ONU)]; however, concerns regarding associated perioperative morbidity have led to the widespread adoption of minimally invasive surgery, laparoscopic NU (LNU), and robot-assisted NU (4–7).

LNU was first reported in 1991 (8). Its widespread adoption was initially limited by technical challenges and concerns about tumor cell dissemination via pneumoperitoneum (9), and it was later demonstrated that there was no difference in the risk of local recurrence between ONU and LNU (10). Minimally invasive NU results in shorter hospital stays, less blood loss, fewer complications, decreased use of postoperative pain medications, and superior patient satisfaction (5, 6, 9, 11–13). Most importantly, several multicenter retrospective studies, randomized trials, and systematic reviews have evaluated the oncological outcomes of ONU vs. LNU and have demonstrated equivalent oncological outcomes (4–7, 11, 13–16). It is not surprising, therefore, that for the exclusion of invasive tumors, larger tumors, or metastatic tumors, the use of LNU has increased in recent years (17).

However, the increased operation time, steep learning curve, and need for highly experienced laparoscopic surgeons have limited its widespread use. Hand-assisted laparoscopy (HAL) has provided a new minimally invasive alternative for patients with UTUC (18). HAL uses a unique approach that combines the finest aspects of open and laparoscopic surgery and en bloc specimen retrieval, thus maintaining the oncological principles used in open surgery (19).

LNU and hand-assisted LNU (HALNU) had comparable oncological and better perioperative and postoperative outcomes than ONU, but HALNU may be inferior to LNU or ONU in terms of recurrence-free survival and intravesical
recurrence-free survival rates (20, 21). However, these studies are heterogeneous as they encompassed transperitoneal or retroperitoneal approaches. Some studies showed different oncological results with either approach (22). Considering the limited number of laparoscopic retroperitoneal nephroureterectomy cases in Taiwan, we conducted a study focusing on the surgical outcomes following transperitoneal HALNU (TP-HALNU) or transperitoneal pure LNU (TP-LNU) using the Taiwan Nationwide UTUC collaboration database.

In Taiwan, the training of urology residents includes laparoscopic surgery in individual secondary or tertiary referral hospitals. Residents must pass their own training programs through direct observation of procedural skills. However, hands-on laparoscopic procedures have not been tested in the national licensure examination. Laparoscopic procedures are not restricted to subspecialists. Surgical volumes and methods of individualized centers may considerably vary. Several studies have revealed that the learning curve may vary among individual surgeons, and a consensus should be reached for the minimum number of cases to achieve proficiency (23). Surgical volumes also affect outcomes (24). The learning thresholds with fewer intraoperative and perioperative complications varied in the literature (25, 26). A recent study found longer operation time and a trend toward more complications with <20 cases (27). In addition, a higher surgical volume (≥20 cases) of laparoscopic hysterectomy was inversely related to the conversion rate to laparotomy (28). Although the length of the learning curve has individual differences, low surgical volumes may impact surgical outcomes. Hence, the surgical volume (≥20 cases or not) was taken into evaluation in this Taiwan UTUC collaboration study.

Materials and methods

The Taiwan Cancer Registry (TCR), a population-based cancer registry, is a nationwide cancer registry. Hospitals with >50-bed capacity that provide outpatient and hospitalized cancer care were recruited to participate in reporting all newly diagnosed malignant neoplasms to the registry. The TCR was queried for registered patients with malignant neoplasms of the renal pelvis and ureter between July 1988 and October 2020. The involved hospitals are listed in Supplementary Table S1.

All patients with a primary diagnosis of renal pelvic or ureteral neoplasm who underwent NU were identified using the International Classification of Diseases Ninth Revision diagnostic and procedure codes. Exclusion criteria included patients who did not undergo NU, who did not receive laparoscopic or HAL surgery, who had previous or synchronous bladder UC, who received neoadjuvant or adjuvant chemotherapy, and who underwent retroperitoneal laparoscopic surgery, as well as histological type other than UC, bilateral neoplasm, or graft neoplasm.

We retrospectively reviewed patient records from the Urology Research Study Group database of 14 participating Taiwanese hospitals. The database included patients with UTUC recorded between July 1988 and September 2020, of whom 322 patients who underwent LNU between June 2002 and August 2019 were selected for this study. This study was approved by the institutional review boards of our hospitals (CTH107-3-5-035 and 06-X34-105).

The demographic data included age and sex. The distribution of patients between the two surgical approaches was recorded. Tumor characteristics, including tumor size, tumor location, laterality, multiplicity, histological characteristics, surgical margin, and pathological staging, were recorded. Outcome assessments included complications, mortality, and a disease-free period. Complications included surgical complications recorded according to the Clavien–Dindo classification and postoperative complications, including ileus and ventral hernia. We also divided patients by the surgical volume of hospitals, with the higher volume group comprising all patients from hospitals with ≥20 nephroureterectomy cases and the lower volume group comprising patients from hospitals with <20 cases. Survival outcome parameters were defined as all-cause death, cancer-specific survival (CSS) as death due to UTUC, disease-free survival (DFS) as cancer recurrence or metastasis, and bladder recurrence-free survival (BRFS) as UC recurrence in the bladder.

Statistical analyses were performed using SPSS Statistics (IBM, Armonk, NY, USA, version 24). The Cox proportional hazard model was selected to assess the effect of the surgical approach on prognostic outcomes, alone and after adjusting for potential confounders. All parameters were analyzed using univariate analysis, and those of specific interest were included in the multivariate analysis. All statistical assessments were two-tailed and considered statistically significant at p < 0.05.

Results

In total, 663 patients who underwent LNU were included in this study. The patients were divided into four different surgical approach groups: TP-LNU, TP-HALNU, retroperitoneal LNU, and retroperitoneal HALNU, with 181, 141, 41, and 300 patients in each group, respectively (Figure 1). The transperitoneal group was enrolled, and 322 patients were enrolled in the final analyses.

Patient demographic and disease-specific characteristics are shown in Table 1. No significant difference in age was noted between these two groups, and the hand-assisted
group had more male patients. There were no significant differences in tumor size, laterality, or multiplicity. We noted no significant difference in perioperative complications according to the Clavien–Dindo classification and postoperative complications of ileus and ventral herniation. TP-HALNU showed a higher overall mortality rate (44.7% vs. 26%) in the TP-LNU group but not in surgery-related mortality. Patients with TP-HALNU had a higher percentage of bladder UC cases after NU. The follow-up period for each approach was 30.26 months for TP-LNU and 62.06 months for TP-HALNU.

Detailed tumor characteristics were also recorded, which showed no significant differences in tumor location, surgical margin status, or pathological staging (Table 2). TP-HALNU had more cases of high-grade tumors, less pathologically positive lymph nodes, and more bladder UC after NU.

In the univariate survival analysis, surgical approach, histologic grade, tumor size, tumor laterality, and tumor location in the renal pelvis, middle ureter, lower ureter, and bladder cuff were independent predictors of survival outcomes (Table 3). The female sex was associated with shorter BRFS, with a hazard ratio (HR) of 0.478 (p = 0.001), but was not associated with other survival parameters. Age >70 years was independently associated with poor overall survival (OS), CSS, and DFS [HR 3.324 (p = 0.001), 6.290 (p = 0.017), and 3.029 (p = 0.005), respectively]. Advanced pathological T staging and positive pathological N staging were associated with survival outcomes, with pT3 staging showing HR of 10.911 (p = 0.027) and 3.098 (p = 0.029) for CSS and DFS, and pN+ staging showing HR of 17.279 (p = 0.011) and 10.961 (p = 0.031) for OS and DFS, respectively. Tumor multiplicity was associated with DFS and BRFS, with HR of 3.446 (p < 0.001) and 1.784 (p = 0.014), respectively. Analysis of tumor location showed that only tumors located in the upper ureter were associated with DFS (HR 2.054, p = 0.047). Higher surgical volume (>20 cases) was associated with OS, with an HR of 0.425 (p = 0.046).

In the multivariate survival analysis, surgical approach, pathological T staging, tumor multiplicity, and tumor location in the renal pelvis, middle ureter, lower ureter, or bladder cuff showed no association with survival outcomes (Table 4). The female sex was associated with BRFS, with an HR of 0.421 (p < 0.001), but was not associated with other survival parameters. Age >70 years was associated with all four parameters except BRFS, with HR values of 4.146 (p = 0.001), 20.310 (p = 0.008), and 3.349 (p = 0.005), respectively. Positive pathological N staging was associated with OS and DFS, with HR values of 88.379 (p < 0.001) and 34.717 (p = 0.005), respectively. Analysis of tumor location showed that only tumors in the upper ureter were associated with BRFS, with an HR of 2.537 (p = 0.034). Higher surgical volume showed a trend toward better CSS (p = 0.052) and was associated with OS (HR 0.326, p = 0.019).

Discussion

The present study aimed to compare the surgical outcomes following TP-HALNU and TP-LNU from the Taiwan nationwide UTUC collaboration database for different parameters, including surgical volumes. We compared surgical outcomes, including OS, CSS, DFS, and BRFS, between the two surgical approaches in a nationwide database. Our study showed that the choice of surgical approach varies among urology departments or surgeon preferences, which shows a significant divergence between hospitals.
We noticed a significant difference in mortality between the two surgical approaches, with the TP-HALNU approach having an overall mortality rate of 44.7% compared to 26% in TP-LNU. This significant difference in overall mortality might be caused by the different follow-up periods (62 vs. 30 months). Although the two approaches showed significant differences in overall mortality, after the univariate and multivariate analyses for oncological outcomes, TP-LNU and TP-HALNU were not oncological predictors. Surgery-related mortality showed no difference, with a mortality rate of 0.7% vs. 0.6% between the two groups. The most common cause of death was listed as not UTUC-related. However, this was a cross-sectional, large-scale, retrospective cohort study using the UTUC collaboration database of the Taiwan Urology Association. Despite the presence of limitations, the results represent real-world data and demonstrate that either TP-LNU or TP-HALNU is feasible in the current setting in Taiwan. In addition, perioperative complications, according to the Clavien–Dindo classification, showed no significant difference between the two approaches.

Several previous studies comparing HALNU with LNU or ONU showed comparable oncological outcomes and better

### Table 1: Demographic data of UTUC patients.

| Variables          | TP-LNU (N = 181) | TP-HALNU (N = 141) | p-value |
|--------------------|------------------|--------------------|---------|
| N                  | %                | N                  | %       |
| Sex                |                  |                    |         |
| Male               | 58 (32.0)        | 57 (40.4)          | 0.019   |
| Female             | 123 (68.0)       | 84 (59.6)          |         |
| Age (mean ± SD)    | 69.46 ± 10.8     | 69.62 ± 9.77       |         |
| Tumor size         |                  |                    |         |
| <1 cm              | 15 (8.5)         | 9 (6.4)            | 0.416   |
| ≥1 and <2 cm       | 53 (30.1)        | 39 (27.7)          |         |
| ≥2 and <3 cm       | 44 (25.0)        | 29 (20.6)          |         |
| ≥3 cm              | 63 (35.8)        | 61 (43.3)          |         |
| Laterality         |                  |                    |         |
| Left               | 91 (50.3)        | 63 (44.7)          | 0.319   |
| Right              | 90 (49.7)        | 78 (55.3)          |         |
| Multiplicity       |                  |                    |         |
| No                 | 148 (85.1)       | 95 (67.4)          | <0.001  |
| Yes                | 26 (14.9)        | 46 (32.6)          |         |
| Clavien–Dindo classification | | | |
| No                 | 123 (68.7)       | 105 (75.5)         | 0.131   |
| Grade I            | 26 (14.5)        | 7 (5.0)            |         |
| Grade II           | 21 (11.7)        | 20 (14.4)          |         |
| Grade III          | 5 (2.8)          | 5 (3.6)            |         |
| Grade IV           | 3 (1.7)          | 1 (0.7)            |         |
| Grade V            | 1 (0.6)          | 2 (0.7)            |         |
| Post-OP complication |                |                    |         |
| Ileus              | 2 (1.1)          | 1 (0.7)            | 0.731   |
| Ventral hernia     | 3 (1.7)          | 2 (1.5)            | 0.887   |
| Mortality          |                  |                    |         |
| No                 | 134 (74.0)       | 78 (55.3)          | 0.008   |
| UTUC related       | 3 (1.7)          | 8 (5.7)            |         |
| Non-UTUC related   | 11 (6.1)         | 12 (8.5)           |         |
| Unknown            | 32 (17.7)        | 42 (29.8)          |         |
| Surgery related    | 1 (0.6)          | 1 (0.7)            |         |
| Follow-up (months) median | 30.26          | 62.06              |         |

### Table 2: Tumor characteristics of UTUC patients.

| Variables          | TP-LNU (N = 181) | TP-HALNU (N = 141) | p-value |
|--------------------|------------------|--------------------|---------|
| N                  | %                | N                  | %       |
| Tumor location     |                  |                    |         |
| Renal pelvis       | 111 (61.3)       | 99 (70.2)          | 0.097   |
| Upper ureter       | 38 (21.0)        | 31 (22.0)          | 0.830   |
| Middle ureter      | 19 (10.5)        | 16 (11.3)          | 0.880   |
| Lower ureter       | 29 (16.0)        | 25 (17.7)          | 0.684   |
| Bladder cuff       | 1 (0.6)          | 2 (1.4)            | 0.422   |
| NU histology       |                  |                    |         |
| Low grade          | 39 (22.0)        | 28 (20.0)          | 0.003   |
| High grade         | 138 (78.0)       | 112 (80.0)         |         |
| Surgical margin    |                  |                    |         |
| Free               | 178 (98.3)       | 137 (97.9)         | 0.750   |
| Positive           | 3 (1.7)          | 3 (2.1)            |         |
| Pathological stage T |                |                    |         |
| pTis               | 3 (1.7)          | 5 (3.6)            | 0.601   |
| pTa                | 52 (28.7)        | 32 (22.9)          |         |
| pT0                | 3 (1.7)          | 1 (0.7)            |         |
| pT1                | 49 (27.1)        | 46 (32.9)          |         |
| pT2                | 35 (19.3)        | 30 (21.4)          |         |
| pT3                | 36 (19.9)        | 25 (17.9)          |         |
| pT4                | 3 (1.7)          | 1 (0.7)            |         |
| Pathological stage N |                |                    |         |
| pN0                | 64 (35.4)        | 13 (9.3)           | <0.001  |
| pN+                | 3 (1.7)          | 1 (0.7)            |         |
| pNx                | 114 (63.0)       | 126 (90.0)         |         |
| Bladder UC after NU|                  |                    |         |
| No                 | 135 (77.1)       | 95 (67.9)          | 0.045   |
| Yes                | 40 (22.9)        | 45 (32.1)          |         |

UTUC, upper tract urothelial carcinoma; NU, nephroureterectomy; TP-LNU, transperitoneal laparoscopic NU; TP-HALNU, transperitoneal hand-assisted laparoscopic NU; pNx, regional lymph nodes cannot be assessed; UC, urothelial carcinoma.
perioperative and postoperative outcomes (20, 21, 29–32). However, HALNU may be inferior to LNU or ONU with respect to RFS and BRFS rates (20, 33) and may be associated with higher intravesical recurrence (32). The current study demonstrated no oncological outcome difference between TP-LNU and TP-HALNU in both univariate and multivariate analyses.

In this study, we concluded that age was an independent predictor of survival outcomes. The multivariate analysis showed an association between age and OS, CSS, and DFS, with an increased risk in patients aged ≥70 years. Another independent predictor was sex, which was a lower risk factor in female patients with BRFS. This finding is consistent with previous reports illustrating that male sex was strongly associated with intravesical recurrence in patients with UTUC who received radical NU (34–36). Other than BRFS, no significant association was noted between sex and survival outcomes. Another obvious independent predictor associated

### TABLE 3 Comparative univariate survival analysis of UTUC patients.

| Univariate analysis | OS HR (95% CI) | p-value | CSS HR (95% CI) | p-value | DFS HR (95% CI) | p-value | BRFS HR (95% CI) | p-value |
|---------------------|----------------|---------|----------------|---------|----------------|---------|----------------|---------|
| Approach            |                |         |                |         |                |         |                |         |
| TP-LNU              | 1              |         |                |         |                |         |                |         |
| TP-HALNU            | 0.854 (0.423, 1.724) | 0.659   |                  |         |                |         |                |         |
| Sex                 |                |         |                |         |                |         |                |         |
| Male                |                |         |                |         |                |         |                |         |
| Female              | 0.897 (0.460, 1.749) | 0.750   |                  |         |                |         |                |         |
| Age                 |                |         |                |         |                |         |                |         |
| <70                 |                |         |                |         |                |         |                |         |
| ≥70                 | 3.324 (1.597, 6.919) | 0.001   | 6.290 (1.389, 28.477) | 0.017 | 3.029 (1.405, 6.529) | 0.005 | 1.518 (0.988, 2.331) | 0.057 |
| NU histology        |                |         |                |         |                |         |                |         |
| Low grade           |                |         |                |         |                |         |                |         |
| High grade          | 1.062 (0.497, 2.272) | 0.876   | 1.843 (0.408, 8.321) | 0.427 | 1.861 (0.716, 4.835) | 0.203 | 0.829 (0.507, 1.356) | 0.455 |
| pT stage            |                |         |                |         |                |         |                |         |
| pTis/pTa/pT0        |                |         |                |         |                |         |                |         |
| pT1                 | 0.628 (0.268, 1.471) | 0.285   | 1.886 (0.171, 20.818) | 0.604 | 1.103 (0.370, 3.287) | 0.860 | 0.932 (0.523, 1.663) | 0.813 |
| pT2                 | 0.576 (0.205, 1.617) | 0.295   | 5.954 (0.665, 53.284) | 0.111 | 2.491 (0.905, 6.857) | 0.077 | 1.310 (0.717, 2.391) | 0.380 |
| pT3                 | 1.328 (0.566, 3.117) | 0.314   | 10.911 (1.312, 90.732) | 0.027 | 3.098 (1.125, 8.531) | 0.029 | 1.770 (0.976, 3.289) | 0.060 |
| pT4                 |                |         |                |         |                |         |                |         |
| pN stage            |                |         |                |         |                |         |                |         |
| pN0                 |                |         |                |         |                |         |                |         |
| pN+                 | 17.279 (1.896, 157.5) | 0.011   |                  |         |                |         |                |         |
| Tumor size          |                |         |                |         |                |         |                |         |
| <1 cm               |                |         |                |         |                |         |                |         |
| ≥1 and <2 cm        | 1.313 (0.291, 5.933) | 0.724   |                  |         |                |         |                |         |
| ≥2 and <3 cm        | 0.867 (0.173, 4.330) | 0.861   |                  |         |                |         |                |         |
| ≥3 cm               | 1.380 (0.314, 6.067) | 0.670   |                  |         |                |         |                |         |
| Multiplicity         |                |         |                |         |                |         |                |         |
| No                  |                |         |                |         |                |         |                |         |
| Yes                 | 1.770 (0.883, 3.549) | 0.108   | 1.509 (0.465, 4.902) | 0.493 | 3.446 (1.741, 6.822) | <0.001 | 1.784 (1.124, 2.832) | 0.014 |
| Laterality          |                |         |                |         |                |         |                |         |
| Left                |                |         |                |         |                |         |                |         |
| Right               | 1.969 (0.984, 3.941) | 0.056   | 1.114 (0.374, 3.318) | 0.846 | 0.875 (0.442, 1.732) | 0.701 | 0.744 (0.485, 1.141) | 0.175 |
| Renal pelvis        |                |         |                |         |                |         |                |         |
| No                  |                |         |                |         |                |         |                |         |
| Yes                 | 0.922 (0.466, 1.822) | 0.815   | 2.882 (0.638, 13.020) | 0.169 | 1.678 (0.756, 3.722) | 0.203 | 1.451 (0.905, 2.328) | 0.122 |
| Upper ureter        |                |         |                |         |                |         |                |         |
| No                  |                |         |                |         |                |         |                |         |
| Yes                 | 1.358 (0.654, 2.821) | 0.411   | 1.557 (0.479, 5.060) | 0.461 | 2.054 (1.010, 4.176) | 0.047 | 1.515 (0.939, 2.446) | 0.089 |
| Middle ureter       |                |         |                |         |                |         |                |         |
| No                  |                |         |                |         |                |         |                |         |
| Yes                 | 1.510 (0.586, 3.895) | 0.394   | 0.042 (0.000, -)  | 0.431 | 0.554 (0.133, 2.318) | 0.419 | 0.470 (0.190, 1.161) | 0.102 |
| Lower ureter        |                |         |                |         |                |         |                |         |
| No                  |                |         |                |         |                |         |                |         |
| Yes                 | 1.133 (0.496, 2.589) | 0.766   | 0.903 (0.200, 4.075) | 0.894 | 1.130 (0.466, 2.739) | 0.786 | 1.151 (0.659, 2.011) | 0.622 |
| Bladder cuff        |                |         |                |         |                |         |                |         |
| No                  |                |         |                |         |                |         |                |         |
| Yes                 | 0.049 0.803 | 0.049   | 0.849 4.973 (0.668, 37.009) | 0.117 | 3.313 (0.812, 13.518) | 0.095 |
| Surgical volume     |                |         |                |         |                |         |                |         |
| Lower (<20)         | 0.425 (0.183, 0.985) | 0.046   | 0.366 (0.080, 1.679) | 0.196 | 1.042 (0.502, 2.163) | 0.912 | 1.146 (0.727, 1.806) | 0.556 |
| Higher (≥20)        |                |         |                |         |                |         |                |         |

UTUC, upper tract urothelial carcinoma; OS, overall survival; CSS, cancer-specific survival; DFS, disease-free survival; BRFS, bladder recurrence-free survival; HR, hazard ratio; CI, confidence interval; TP-LNU, transperitoneal laparoscopic nephroureterectomy; TP-HALNU, transperitoneal hand-assisted laparoscopic nephroureterectomy; UTUC, upper tract urothelial carcinoma; OS, overall survival; CSS, cancer-specific survival; DFS, disease-free survival; BRFS, bladder recurrence-free survival; HR, hazard ratio; CI, confidence interval.
with oncological outcomes was positive pathological lymph node metastasis, which is an obvious risk factor associated with worse outcomes.

NU with bladder cuff excision is the gold standard treatment for UTUC (37–39), so tumors located at the bladder cuff present challenges for radical resection. There are several approaches to bladder cuff excision, including the open technique, transurethral incision of the ureteral orifice, intussusception technique, transvesical laparoscopic detachment, and laparoscopic stapling (40, 41). In our study, tumor location at the bladder cuff was not associated with oncological outcomes. However, this database did not provide detailed records of the bladder cuff excision methods or the margin status of the bladder cuff. This could be a possible confounding factor, although one large patient cohort in Taiwan concluded that the method by which the bladder cuff is removed does not affect cancer-specific outcomes (42).

Retroperitoneoscopic NU (RPNU), with or without hand assistance, is also a widely accepted treatment option for UTUC. Previous studies have shown that RPNU had comparable oncological outcomes compared with ONU (43), LNU (44), or HALNU (45), and may have better perioperative and postoperative outcomes than LNU (44). However, intestinal retraction is considerably easier with the transperitoneal approach. Besides, peritoneal tear during RPNU occurred in certain cases, even with experienced surgeons (46). The impact of peritoneal tear includes conversion to the transperitoneal approach, but the limited number of retroperitoneal LNU cases in the Taiwan UTUC database may confound the analysis. Thus, in this study, we compared TP-HALNU and TP-LNU and observed comparable outcomes. We suggest that either approach is safe and feasible, depending on surgeons’ preferences and experiences.

For surgical volume, we observed that higher surgical volume did not impact DFS or BRFS but was associated with a trend toward favorable CSS (HR 0.326, p = 0.019). Several previous studies have reported fewer intraoperative and
perioperative complications associated with the surgical learning curve, reporting different learning thresholds at 50 or 100 cases at a single center (25, 26). In the current study, lower surgical volume (<20 cases) did not significantly influence DFS or BRFS. However, higher surgical volume was associated with a trend toward improved CSS ($p = 0.052$). Although this result implies that surgical volume matters in oncological outcomes, it is difficult to conclude that lower surgical volume impacts OS by influencing the quality of oncological control in the results. A poor correlation between PFS and OS may occur when considering different tumor characteristics, recurrence patterns, subsequent heterogeneous treatment, and quality of care, which were not shown in this study (47).

From this study, we suggest that either method is safe and feasible, depending on the surgeon’s preferences and experiences. Larger-scale and prospective studies are required, considering the surgical volume and learning curve.

**Limitations**

The current study had several limitations. First, the original database included retrospectively reviewed patients with a lack of detailed records on several parameters, including bladder cuff resection method, margin status of the bladder cuff, the extent of lymph node dissection, perioperative intravesical chemotherapy, and behavioral adjustments such as smoking discontinuation. All mortality data were retrieved from the National Cancer Registry, and patients without an assigned code for cause of death were grouped into “Unknown” in the mortality parameter. This could have caused a statistical bias for CCS. The current study enrolled 14 hospitals in which patients were not randomized for the two surgical approaches. The choice of approach, the extent of lymph node dissection, and the follow-up protocol were mainly decided by each surgeon’s or urology department’s preference, which may cause bias in comparing outcomes between different approaches.

**Conclusion**

No significant differences in oncological outcomes and postoperative complication rates were observed between the TP-LNU and TP-HALNU groups. Age, sex, and lymph node metastasis were independent predictors of oncological outcomes. Higher surgical volume did not impact DFS and BRFS but was associated with improved OS and CSS. Exploration of unknown influencing factors is warranted.

**Data availability statement**

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

**Ethics statement**

The studies involving human participants were reviewed and approved by IRB of Cardinal Tien hospital (CH1107-3-5-035) and IRB of Taipei Tzu Chi General Hospital (06-X34-105). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

**Author contributions**

C-CK and B-JC contributed to the conception and design of the study. B-JC, and C-CK organized the database and performed the statistical analysis. C-CK wrote the first draft of the manuscript. H-SC and B-JC contributed to the manuscript revision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

Reviewers H-YK and F-JH declared a shared affiliation with the authors C-YH and C-HC to the handling editor at the time of review. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2022.934355/full#supplementary-material.
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