Trends in utilisation, perioperative outcomes, and costs of nephroureterectomies in the management of upper tract urothelial carcinoma: a 10-year population-based analysis

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I.T and F. G.-H. equal contribution.

Objective
To perform a population-based study to evaluate contemporary utilisation trends, morbidity, and costs associated with nephroureterectomies (NUs), as contemporary data for NUs are largely derived from single academic institution series describing the experience of high-volume surgeons and it is unclear if the same favourable results occur at a national level.

Patients and Methods
Using the Premier Hospital Database, we captured patients undergoing a NU with diagnoses of renal pelvis or ureteric neoplasms from 2004 to 2013. We fitted regression models, adjusting for clustering by hospitals and survey weighting to evaluate 90-day postoperative complications, operating-room time (OT), prolonged length of stay (pLOS), and direct hospital costs among open (ONU), laparoscopic (LNU) and robotic (RNU) approaches.

Results
After applying sampling and propensity weights, we derived a final study cohort of 17,254 ONUs, 13,317 LNUs and 3,774 RNUs for upper tract urothelial carcinoma (UTUC) in the USA between 2004 and 2013. During that period, minimally invasive NU (miNU) increased from 36% to 54%, while the total number of NUs decreased by nearly 20%. No differences were noted in perioperative outcomes between the three surgical approaches, including when the analysis was restricted to the highest-volume hospitals and highest-volume surgeons. The OT was longer for LNU and RNU (P < 0.001), while the pLOS rates were decreased (P < 0.001). Adjusted 90-day median direct hospital costs were higher for LNU and RNU (P < 0.001), which disappeared when adjusting for the highest-volume groups, except for RNUs performed by high-volume surgeons.

Conclusions
During this contemporary 10-year study, miNU has been replacing ONU for UTUC with a recent surge in RNU, along with a concurrent reduction in total NUs performed. Despite not being associated with a clinically significant improvement in perioperative outcomes, the costs for miNUs were consistently higher. However, higher hospital volumes suggest a potential cost containment strategy when performing miNUs.

Keywords
nephroureterectomy, upper urinary tract carcinoma, trend, utilisation, outcome

Introduction
Urothelial carcinoma (UC) is the fourth most common malignancy worldwide, with upper tract UCs (UTUCs) accounting for 5–10% of these cases [1]. The ‘gold standard’ for the management of UTUC is radical nephroureterectomy (NU) with removal of the ipsilateral bladder cuff [1]. This procedure has historically been performed via an open approach (i.e., open NU [ONU]) but with the advent of minimally invasive surgery (MIS), laparoscopic NU (LNU) and more recently robotic NU (RNU) have gained in popularity [2–5]. The approaches for the minimally invasive
NU (miNU) have been reported to have potentially shorter hospital stays, decreased use of postoperative pain medications, superior patient satisfaction [2,3,6], and most importantly, equivalent oncological outcomes, irrespective of surgical approach [2–8].

Contemporary data for NU are largely derived from single-institution series describing the experience of high-volume surgeons and teaching hospitals. It is unclear if the same favourable results occur at a national level. In the present study, we performed a population-based assessment of the contemporary utilisation trends, perioperative outcomes, and costs for ONU, LNU and RNU among a wide range of hospitals and surgeons in the USA.

**Patients and Methods**

**Data Source**

The Premier Hospital Database (PHD; Premier, Inc., Charlotte, NC, USA) is a Health Insurance Portability and Accountability Act (HIPAA) compliant patient-level information system developed for comparative analysis research. There are ≈600 participating hospital capturing >84 million unique patients and 335 million hospitalisations, translating into 20% of annual discharges in the USA. A unique identifier key exists for each patient, thereby permitting longitudinal data analyses. This study was exempt from Institutional Review Board approval at the involved institutions given the de-identified nature of the data.

**Study Population**

The study population was identified by review of the administrative data. Using International Classification of Diseases, 9th Revision, Clinical Modification (ICD9) codes, we captured patients with a procedure code for NU (55.51) as the primary indication for the admission coupled with a diagnosis of a renal pelvis (189.1) or ureteric (189.2) neoplasms between 2004 and 2013. To minimise the possibility of capturing patients at a higher risk for perioperative morbidity, we excluded any patients who underwent a major surgical procedure within 3 months prior to the index procedure and limited our analysis to patients undergoing elective surgery, determined by administrative data, as well as surgery on the day of or after admission.

To identify patients undergoing RNU, we conducted an exhaustive review of the charge-master for each patient matching terms specific to robotic surgery based on a review of the Intuitive Surgical® catalogue (e.g. ‘ROBOTIC’ or ‘DA VINCI’ or ‘ENDOWRIST’), as has been previously described [9]; beginning in the final quarter of 2008, we added ICD9 codes (17.4×) and Current Procedural Terminology (CPT) codes (S2900) to our search algorithm. Similarly, LNU was flagged with billing and ICD9 codes (54.21). Procedures without robotic or laparoscopic supplies were categorised as ONU.

**Patient and Hospital Characteristics**

Relevant patient, hospital, and surgical characteristics were examined. Patient characteristics included: age, gender, race, marital status, health insurance type, and Charlson Co-morbidity Index (CCI) [10]. Hospital characteristics included: hospital size, teaching status, location, and geographic region. Surgical characteristics included: year of procedure, as well as annual surgeon and hospital volumes, which were calculated based on the number of NUs performed by surgeons and hospitals in a given year, and divided into tertiles [11].

**Outcomes**

Perioperative outcomes included: postoperative complications, operating-room time (OT), and prolonged length of stay (pLOS). We identified 90-day postoperative complications using ICD9 codes, which were further classified using the Clavien–Dindo system and subdivided into minor (Grades I–II), and major non-fatal (Grades III–IV) complications [12,13]. Mortality (Grade V) was determined by disposition codes. Because we used a hospital discharge database, we captured only complications managed within the hospital setting during the index admission or a readmission within 90 days; evaluation and management in the outpatient setting, therefore, was not included in our analysis. OT was estimated based on billing data and represented the total minutes in the operating room. pLOS was defined as >75th percentile of LOS, which was calculated based on the number of days between admission and discharge dates. Subpopulation analysis of the highest-volume hospitals and surgeons was performed to assess the impact of surgical volume on outcomes.

**Costs**

To estimate resource utilisation, we tabulated 90-day direct hospital costs associated with the index hospitalisation for the NU, as well as subsequent readmissions to capture the economic impact of postoperative complications. Of note, the PHD includes both costs and charges for each billable item. The total costs equalled the summation of costs for all individual billing items and were further categorised into costs associated with the operating room, supplies, room and board, and other (including laboratory, radiology, pharmacy, and miscellaneous uncategorisable items). The proportion of overall cost attributable to each category was calculated. Sunk and fixed costs associated with the robotic platform, including capital costs and annual maintenance respectively, were excluded because these costs are not available in the database.
All costs were adjusted to 2013 American dollars using the medical component of the Consumer Price Index.

**Statistical Analysis**
Patient, hospital, and surgical characteristics were summarised with descriptive statistics. Frequencies and proportions were calculated for categorical variables and compared using the chi-square test. Medians and interquartile ranges were used to describe continuous variables, given the normal distributions. To assess utilisation and perioperative outcomes, we generated adjusted logistic and median regression models for categorical and continuous outcomes, respectively. To minimise bias among the patients undergoing different surgical approaches, we applied inverse probability of treatment weight with propensity weighting, all characteristics were comparable over-year until 2009, after which time there has been a relative plateau at ≥1500 cases annually in the USA. In contrast, the proportion of miNU has steadily increased from 2% to >30% over the study period (P < 0.001).

During the 10-year study period, the annual total number of NUs decreased by ≈20%, from 3706 in 2004 to 2970 in 2013 (Fig. 1). The number of ONUs progressively decreased year-over-year until 2009, after which time there has been a relative plateau at ≥1500 cases annually in the USA. In contrast, the proportion of miNU has steadily increased from 36% to 54% (P < 0.001), with RNU primarily driving this trend beginning in 2010 (Fig. 1). In addition, the number of unhealthy patients (CCI ≥2) undergoing RNU increased substantially from 2% to >30% over the study period (P < 0.001).

**Outcomes**
There were no significant differences in the odds of overall 90-day mortality, any complications, and major non-fatal complications of LNU and RNU vs ONU (Table 2). RNU had a higher odds of minor complications than ONU [adjusted odds ratio (AOR) 1.33, 95% CI 1.03–1.72; P < 0.001]. Compared with ONU, pLOS was decreased for LNU (AOR 0.7, 95% CI 0.57–0.85; P < 0.001) and RNU (AOR 0.5, 95% CI 0.36–0.68; P < 0.001). The total OT was 9 and 55 min longer for LNU and RNU, respectively (both P < 0.001). The adjusted 90-day median direct hospital costs were $1142 and $3326 higher for LNU and RNU than for ONU (both P < 0.001). The differences were mostly driven by the increased costs of supplies (LNU: +$1661, RNU: +$2387; P < 0.001), and operating room costs (LNU: +$409, RNU: +$1875; P < 0.001) (Fig. 2).

When we restricted our analysis to the highest-volume hospitals (≥7 cases/year) or highest-volume surgeons (≥3 cases/year), there was no difference in the odds of any, minor, non-fatal major complication, or mortality. Within the highest-volume hospitals, pLOS was lower for LNU (AOR 0.75, 95% CI 0.45–1.26; P = 0.27) and RNU (AOR 0.48, 95% CI 0.28–0.84; P < 0.05). This was more pronounced for the highest-volume surgeons, where the odds of a pLOS was even lower for LNU (AOR 0.64, 95% CI 0.39–1.03; P = 0.07) and RNU (AOR 0.38, 95% CI 0.19–0.78; P < 0.05) compared with ONU. More importantly miNUs were no longer significantly more costly than ONUs for the highest-volume hospitals (LNU: +$86; P = 0.84; RNU: +$1590; P = 0.05), or LNU for the highest-volume surgeons (+$333; P = 0.67). Nevertheless, this difference persisted for the RNUs performed by the highest-volume surgeons (+$1959; P < 0.05) (Table 3).

**Discussion**
The present contemporary study reveals several important trends about the surgical management of UTUC over the past decade in the USA. We found a progressive decrease in the annual number of NUs in the management of UTUC. Over the same period, miNU has played an increasingly common role, with RNU replacing LNU as the most common form of miNU by the end of the study. Compared with ONU, miNU was not associated with a clinically significant reduction in the overall morbidity and mortality, although the costs for miNU, particularly RNU, were consistently higher.

The present study shows that there has been a persistent downward trend in the annual number of NUs performed in the USA (Fig. 1), irrespective of hospital location or teaching status (data not shown). This finding is surprising because the incidence of UTUC from 2000 to 2012 has remained stable at ≈1.5 cases/100 000 population, based on data from the Surveillance, Epidemiology, and End Results Program [14].
This apparent discrepancy in the incidence of UTUC and the use of NU raises the possibility that an increasing number of renal-sparing options (e.g. segmental ureterectomy, ureteroscopic ablation, and percutaneous resection) are being used, especially for low-risk disease [15] possibly driven by the concerns about post-nephrectomy chronic kidney disease [16]. While the assessment of renal-sparing procedures is beyond the scope of the present study, it certainly warrants additional investigation because it would represent an important contemporary shift in the management of UTUC. 

We found an increase in the miNU utilisation, particularly during the final years of the study (Fig. 1), which has also been noted in a prior population-based study using the Nationwide Inpatient Sample [17]. This trend parallels the widespread dissemination of MIS for the management of...
many urological malignancies including RCC [18], prostate cancer [19], and bladder cancer [20]. Compared with ONU and LNU, RNU has the potential benefit of a less technically challenging resection of the distal ureter and bladder cuff given the ease of accessing the retrotrigonal region and additional degrees of articulation afforded by EndoWrist® instruments for closing the cystotomy [21]. The progressive familiarity with the robotics platform by the urological community may explain why we observed a trend for less healthy patients (CCI ≥2) to undergo RNU, essentially paralleling the popularity of this approach. Unlike prior studies that associate MIS with cost savings stemming from a reduced LOS [22], we found in our present cohort that miNU was consistently more costly than ONU despite lower rates of pLOS (Table 2). A detailed itemisation of the medical expenditures in our present cohort showed that the cost savings for miNU, attributed to reduced room and board expenditures, was far outweighed by the increased operating room and supply expenditures, as well as longer OTs (Fig. 2). We speculate that supply costs may be higher for miNU because of the unique complexity in managing the distal ureter and bladder cuff. There are a multitude of well-described techniques for resecting distal ureter and bladder cuff including: open resection, transurethral resection of the ureteric orifice (‘Pluck Technique’), endoscopic ureteric intussusception (‘Stripping Technique’), as well as techniques that are completely laparoscopic (‘Pure Laparoscopic’) [23].

With the exception of the pure laparoscopic approach, all other techniques require additional open or cystoscopic equipment, which unquestionably increases the costs beyond what is typical for a standard robotic procedure. A strength of the present study is that we applied the standardised and well-accepted Clavien–Dindo Classification system to our population-based, contemporary cohort to characterise the morbidity and mortality of NU [13]. Despite the differences in the extent and number of incisions for these competing surgical approaches, our present analysis revealed generally comparable 90-day postoperative complications, although the rate of minor complications was higher for RNU (Table 2). Our present findings are consistent with a recent meta-analysis of 21 studies, pooling the collective experience of centres across the world, which also found no significant differences between LNU and ONU in terms of complications and mortality [24]. The absence of any meaningful improvement in surgical morbidity with miNU reveals that surgical approach is not the primary driver for postoperative complications after NU. We think that performance status probably plays a more important role, as previous investigations across a wide range of surgical populations have identified frailty as an independent risk factor for surgical morbidity and mortality, particularly among elderly patients [25]. Therefore, the comparable CCI distribution among patients undergoing the three surgical approaches may explain the similar morbidity and mortality outcomes in the present study.  

**Fig. 1** The distribution of NUs performed yearly in the USA according to surgical approach. LNU, laparoscopic nephroureterectomy; ONU, open nephroureterectomy; RNU, robotic nephroureterectomy.

**Table 2** Perioperative outcomes and direct hospital costs associated with each approach.

<table>
<thead>
<tr>
<th>Categorical outcomes</th>
<th>ONU</th>
<th>LNU</th>
<th>RNU</th>
<th>LNU AOR (95% CI)</th>
<th>RNU AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-day complications, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any (Clavien–Dindo &gt; 0)</td>
<td>37.5</td>
<td>35.4</td>
<td>41.5</td>
<td>0.91 (0.78–1.07)</td>
<td>1.24 (0.98–1.57)</td>
</tr>
<tr>
<td>Minor (Clavien–Dindo 1–2)</td>
<td>27.3</td>
<td>26.8</td>
<td>32.9</td>
<td>0.97 (0.82–1.14)</td>
<td>1.33 (1.03–1.72) *</td>
</tr>
<tr>
<td>Major (Clavien–Dindo 3–4)</td>
<td>10.2</td>
<td>8.6</td>
<td>8.6</td>
<td>0.84 (0.64–1.11)</td>
<td>0.91 (0.63–1.30)</td>
</tr>
<tr>
<td>Mortality (Clavien–Dindo 5)</td>
<td>2.3</td>
<td>1.9</td>
<td>1.5</td>
<td>0.84 (0.46–1.52)</td>
<td>0.59 (0.26–1.33)</td>
</tr>
<tr>
<td>pLOS, %</td>
<td>26.4</td>
<td>18.7</td>
<td>14.5</td>
<td>0.70 (0.57–0.85) *</td>
<td>0.50 (0.36–0.68) *</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Continuous outcomes</th>
<th>Unadjusted median (IQR)</th>
<th>Adjusted difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OT, min</td>
<td>236 (121)</td>
<td>240 (133)</td>
</tr>
<tr>
<td>Direct costs, $b</td>
<td>17708 (9106)</td>
<td>14590 (8303)</td>
</tr>
</tbody>
</table>

*P < 0.001. *Propensity-weighted regression analysis adjusted for hospital clustering, using ONU as the reference group. *Costs were adjusted to 2013 American dollars. IQR, interquartile range.
Based on the trend for centralisation of complex surgical procedures in the USA [26], we assessed outcomes for the highest-volume providers and indeed observed improved outcomes for miNU in relation to ONU. In this subgroup analysis, miNU was associated with fewer minor complications and hospital costs were no longer higher compared with ONU. The one exception was RNU performed by high-volume surgeons, which remained more costly than ONU, although the difference was almost half of what it was in the analysis of the total cohort ($1959 vs $3534; Table 3). These findings imply an opportunity for a reduction in costs and improvement in patient outcomes by centralising NU, particularly miNU, to high-volume centres and surgeons.

A limitation of our present study is the possible misclassification and selection bias inherent in using administrative data. We attempted to minimise this effect by capitalising on the granularity of the available billing data, cross-referencing diagnosis and procedure codes. While our billing data are granular, it is possible that even our analysis of costs is not sufficiently detailed to elucidate the underlying cost disparities among the surgical approaches. In addition, we lack information about patient positioning, surgical incision, and technique used for handling of the bladder cuff, thus limiting our ability to analyse the potential impact associated with each of these different configurations. Our database also lacks clinical stage and grade, pathological oncological information, and chemotherapy status, all of which can potentially impact the risk for complications differentially between ONU and miNU. Also, complications were limited to inpatient complications, although we included 90-day data to capture complications that led to hospital readmission; outpatient complications were excluded due to the inability to reliably capture these in the data set.

In conclusion, from 2004 to 2013, miNU was increasingly used for managing UTUC and by the end of the study accounted for about half of all NUs performed in the USA. More recently, LNUs plateaued, while RNUs continue increasing, along with a reduction in the total number of NUs. Whether this reduction is related to a concurrent increase in renal-sparing methods needs to be elucidated. Comparable perioperative outcomes suggest that the morbidity profile may be driven primarily by patient-specific characteristics as opposed to surgical approach. Long-term oncological and functional outcomes particularly of RNU remain to be seen.

![Fig. 2](https://example.com/fig2.png)

**Table 3** Adjusted perioperative outcomes and direct hospital costs within the highest-volume hospitals and surgeons.

<table>
<thead>
<tr>
<th>Categorical outcomes</th>
<th>Highest-volume hospitals</th>
<th>AOR (95% CI)*</th>
<th>Highest-volume surgeons</th>
<th>AOR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-day complications, %</td>
<td>LNU</td>
<td>RNU</td>
<td>LNU</td>
<td>RNU</td>
</tr>
<tr>
<td>Any (Clavien–Dindo &gt; 0)</td>
<td>0.88 (0.56 to 1.38)</td>
<td>0.85 (0.53 to 1.36)</td>
<td>0.89 (0.65 to 1.23)</td>
<td>0.81 (0.51 to 1.3)</td>
</tr>
<tr>
<td>Minor (Clavien–Dindo 1–2)</td>
<td>0.83 (0.55 to 1.27)</td>
<td>0.67 (0.37 to 1.22)</td>
<td>0.73 (0.52 to 1.02)</td>
<td>0.74 (0.41 to 1.33)</td>
</tr>
<tr>
<td>Major (Clavien–Dindo 3–4)</td>
<td>1.04 (0.52 to 2.11)</td>
<td>1.4 (0.6 to 3.28)</td>
<td>1.54 (0.85 to 2.77)</td>
<td>1.16 (0.52 to 2.59)</td>
</tr>
<tr>
<td>Mortality (Clavien–Dindo 5)</td>
<td>0.39 (0.08 to 1.86)</td>
<td>1.01 (0.18 to 5.7)</td>
<td>2.19 (0.54 to 8.89)</td>
<td>1.77 (0.31 to 10.24)</td>
</tr>
<tr>
<td>pLOS, %</td>
<td>0.75 (0.45 to 1.26)</td>
<td>0.48 (0.28 to 0.84)*</td>
<td>0.64 (0.39 to 1.03)</td>
<td>0.38 (0.19 to 0.78)*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Continuous outcomes</th>
<th>LNU</th>
<th>RNU</th>
<th>LNU</th>
<th>RNU</th>
</tr>
</thead>
<tbody>
<tr>
<td>OT, min</td>
<td>16.2 (12.3 to 34.7)</td>
<td>76.2 (55.3 to 97.1)*</td>
<td>15 (12.1 to 32.1)</td>
<td>54 (26 to 82)*</td>
</tr>
<tr>
<td>Direct costs, $</td>
<td>86 (763 to 934)</td>
<td>1590 (636 to 3102)</td>
<td>333 (763 to 934)</td>
<td>1959 (128 to 3291)*</td>
</tr>
</tbody>
</table>

*P < 0.05, †P < 0.001. *Propensity-weighted regression analysis adjusted for hospital clustering, using ONU as the reference group. †Costs were adjusted to 2013 American dollars.
Acknowledgements
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Conflicts of Interest
Ilker Tinay reports grants from ‘Turkiye Kanserle Savas Vakfi’ scholarship programme, and Steven L. Chang grants from Kidney Cancer SPORE Career Development Award (5P50CA101942-09), during the conduct of the study. All other authors have nothing to disclose.

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Abbreviations: AOR, adjusted odds ratio; CCI, Charlson Comorbidity Index; ICD9, International Classification of Diseases, 9th Revision, Clinical Modification codes; (p)LOS, prolonged length of stay; MIS, minimally invasive surgery; (L) (mi)(O)(R)N(U), (laparoscopic) (minimally invasive) (open) (robotic) nephroureterectomy; OT, operating-room time; PHD, Premier Hospital Database; (UT)UC, (upper tract) urothelial carcinoma.
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