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Oncological outcomes after laparoscopic and open radical nephroureterectomy: results from an international cohort

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What's known on the subject? and What does the study add?
Despite widespread adoption of laparoscopic nephroureterectomy (LNU) for upper tract urothelial cancer (UTUC), few studies have confirmed that it shares equivalent oncological outcomes with conventional open nephroureterectomy.

This second large multicentre study confirms oncological equivalence for ONU and LNU in cohorts of both low *and* high risk patients.

OBJECTIVE

- To compare oncological outcomes in patients undergoing open radical nephroureterectomy (ONU) with those in patients undergoing laparoscopic radical nephroureterectomy (LNU).

PATIENTS AND METHODS

- A total of 773 patients underwent radical nephroureterectomy at nine centres worldwide; 703 patients underwent ONU and 70 underwent LNU.
- Demographic, perioperative and oncological outcome data were collected retrospectively.
- Statistical analysis of data was performed using chi-squared, Mann–Whitney *U*- and log-rank tests, and Cox regression analyses.
- The median (interquartile range) follow-up for the cohort was 34 (15–65) months.

RESULTS

- The two groups were well matched for tumour stage, presence of lymphovascular invasion (LVI) and concomitant carcinoma *in situ* (CIS).
- There were more high-grade tumours (77.1% vs. 56.3%; $P < 0.001$) but fewer lymph node positive patients (2.9% vs. 6.8%; $P = 0.041$) in the LNU group.
- Estimated 5-year recurrence-free survival (RFS) was 73.7% and 63.4% for the ONU and LNU groups, respectively ($P = 0.124$) and estimated 5-year cancer-specific survival (CSS) was 75.4% and 75.2% for the ONU and LNU groups, respectively ($P = 0.897$).
- On multivariable analyses, which included age, gender, race, previous endoscopic treatment for bladder cancer, technique for distal ureter management, tumour location, pathological stage, grade, lymph node status, LVI and concomitant CIS, the procedure type (LNU vs. ONU) was not predictive of RFS (Hazard ratio [HR] 0.80; $P = 0.534$) or CSS (HR 0.96; $P = 0.907$).

CONCLUSION

- The present study is the second large, independent, multicentre cohort to show oncological equivalence between ONU and LNU for well selected patients with upper urinary tract urothelial cancer, and the first to suggest parity for the techniques in patients with unfavourable disease.

KEYWORDS

laparoscopic radical nephroureterectomy, prognosis, urinary tract cancer, transitional cell carcinoma, recurrence, survival

INTRODUCTION

Open radical nephroureterectomy (ONU) with excision of an ipsilateral bladder cuff has long been considered the standard management for upper urinary tract urothelial cancer (UTUC) [1]. However laparoscopic radical nephroureterectomy (LNU), first performed by Clayman in 1991 [2], has rapidly achieved acceptance as an alternative method for extirpation of UTUC, despite a relative lack of data to support its oncological validity. This absence of data is largely attributable to the relative infrequency of UTUC which accounts for only 5% of urothelial malignancies [1]. Most centres therefore have too few numbers to generate adequate prospective randomized data for analysis. Until recently, reports comparing outcomes after ONU and LNU comprised eight retrospective series [3–10] and one prospective series [11]. All of the studies were single centre and all contained fewer than 70 patients undergoing LNU. None of the studies to date have shown a significant difference between the techniques for either recurrence-free survival (RFS) or cancer-specific survival (CSS). No multicentre prospective randomized trial comparing outcomes of ONU and LNU has been performed to date and, given the widespread acceptance of LNU by patients and physicians, it is unlikely that such a study will ever take place. It is therefore probable that decision making in UTUC will rely on large multicentre retrospective series.

Recently, Capitanio et al [12] reported the results of a large retrospective multicentre study comprising 1249 patients from 13 centres worldwide, of whom 270 patients underwent LNU. None received adjuvant chemotherapy and, in over half of the patients, no form of bladder cuff excision was performed. Overall, there was no significant difference between the groups for either RFS or CSS. The two groups differed significantly, however, with ONU patients having statistically significantly higher T-stage, more lymph-node positivity and higher rates of lymphovascular invasion (LVI), which are all factors typically associated with unfavourable outcomes [13]. The authors therefore concluded that oncological equivalence for the techniques could only be assumed for favourable-risk patients. In the present series, we report our findings of a similar, smaller, multicentre study comparing the oncological efficacy of ONU and LNU, in which the groups were better matched for unfavourable risk factors.

PATIENTS AND METHODS

This was a multicentre retrospective study using data collected at nine centres worldwide. Before data transfer all participating sites provided the necessary data-sharing agreements. Data transfer was performed electronically using anonymized institutional data sets. A computerized database was constructed which was analysed to assess data inconsistencies. Resolution of identified anomalies was achieved via regular communication with individual sites, following which the database was frozen and the final data set produced for the current analysis.

The primary database comprised 785 patients who underwent radical nephroureterectomy between 1987 and 2008, of which all the LNUs were performed after 2000. Twelve patients who received neoadjuvant chemotherapy were excluded from the current analysis, leaving 773 patients. Specifically, 27 (3.5%) patients were treated in Bolzano, Italy; 155 (20.1%) in Kitasato, Japan; 51 (6.6%) in Madrid, Spain; 98 (11.7%) in Montreal (McGill University Health Centre), Canada; 138 (17.9%) in four hospitals in the Trent Region of the United Kingdom [14], 58 (7.5%) in Munich, Germany; 98 (12.9%) in Padua, Italy; 87 (11.23) in Regensburg, Germany; and 61 (7.9%) in Verona, Italy. Surgery was performed at each site according to surgeon preference. Regional lymphadenectomy was generally performed if lymph nodes were abnormal on preoperative computed tomography (CT) or if palpable intra-operatively. Extended lymphadenectomy was not routinely performed. The distal ureter was managed in one of two ways: either endoscopically, typically using the Abercrombie technique [15]; or by bladder cuff excision, using an open or laparoscopic approach. Sixty-six patients (10.4%) underwent adjuvant chemotherapy, predominantly with cisplatin combination therapy.

PATHOLOGICAL EVALUATION

All surgical specimens were processed in accordance with standard pathological procedures at each institution. Tumours were staged according to the American Joint Committee on Cancer–Union Internationale Contre le Cancer TNM classification [16]. In view of the retrospective nature of the study, with almost half of the cases performed before 1998, tumour grading was assessed according to the 1973 WHO grading classification [17]. LVI was defined as the presence of tumour cells within an endothelium-lined space without underlying muscular walls.

FOLLOW-UP REGIMEN

Patients were followed up in accordance with individual site surveillance protocols. In general, however, a majority of patients were observed every 3 to 4 months for the first year after nephroureterectomy, every 6 months from the second to fifth years, and annually thereafter. Follow-up typically consisted of a history, physical examination, routine full blood count, serum chemistry studies, urinary cytology and cystoscopic evaluation of the urinary bladder. Regular chest x-ray and radiographical evaluation of the contralateral upper urinary tract were less frequently performed. Elective bone scan, chest and abdominal CT, and MRI were performed where clinically indicated. Disease recurrence was defined as local failure at the operative site, regional lymph node spread, or distant metastasis. Bladder recurrences were not considered as recurrence in the analysis of RFS. Cause of death was determined in one of three ways: either by the treating physicians at the time of death; by chart review corroborated by death certificates; or by death certificates alone. Most patients who were identified as having died from recurrent UTUC had progressive, widely disseminated metastases at the time of death. Patients who died in the perioperative period (i.e. death within 30 days of surgery) were censored at time of death for CSS analyses.

STATISTICAL ANALYSIS

The Fisher's exact test and the chi-square test were used to evaluate the association between categorical variables. Differences in variables with a continuous distribution across dichotomous categories were assessed using the Mann–Whitney *U*-test. The Kaplan–Meier method was used to calculate survival functions, and differences were assessed with the log-rank statistic. Univariable and multivariable Cox regression models addressed time to recurrence and cancer-specific mortality after nephroureterectomy for UTUC. Statistical significance in this study

TABLE 1 Clinical and pathological characteristics of 773 patients treated with either ONU or LNU for UTUC

Clinical or pathological characteristic	Total cases ($n = 773$)	ONU ($n = 703$)	LNU ($n = 70$)	*P*-value
Median (IQR) age,	68 (61–75)	68 (61–75)	70 (60–75)	0.625
Gender, *n* (%)				0.893
Male	533 (69.0)	484 (68.8)	49 (70.0)	
Female	240 (31.0)	219 (31.2)	21 (30.0)	
Race, *n* (%)				**<0.001**
Caucasian	617 (79.8)	578 (82.2)	39 (55.7)	
Other	156 (20.2)	125 (17.8)	31 (44.3)	
History of previous bladder tumour, *n* (%)				**0.019**
No	559 (72.3)	500 (71.1)	59 (72.3)	
Yes	214 (27.7)	203 (28.9)	11 (15.7)	
Management of the distal ureter, *n* (%)				**<0.001**
Open or laparoscopic bladder cuff	683 (88.4)	613 (87.2)	70 (100.0)	
Endoscopic ureteric detachment	90 (11.6)	90 (12.8)	0 (0.0)	
Tumour location, *n* (%)				**0.016**
Renal pelvis	409 (53.1)	366 (52.3)	43 (61.4)	
Ureter	235 (30.5)	221 (31.6)	14 (20.0)	
Both renal pelvis and ureter	48 (6.2)	47 (6.7)	1 (1.4)	
Missing	78 (10.1)	66 (9.4)	12 (17.1)	
Pathological stage, *n* (%)				0.720
pTis	9 (1.0)	8 (1.0)	1 (1.4)	
pTa	163 (21.1)	145 (20.6)	18 (25.7)	
pT1	195 (25.2)	175 (24.9)	20 (26.8)	
pT2	147 (19.0)	139 (19.8)	8 (11.4)	
pT3	215 (27.8)	196 (27.9)	19 (27.1)	
pT4	44 (5.7)	40 (5.7)	4 (5.7)	
Grade, *n* (%)				**<0.001**
G1	99 (12.7)	88 (12.4)	11 (15.7)	
G2	224 (29.0)	219 (31.2)	5 (7.1)	
G3	450 (58.2)	396 (56.3)	54 (77.1)	
LVI, *n* (%)				0.709
Absent	614 (79.4)	561 (79.8)	53 (75.7)	
Present	148 (19.1)	132 (18.8)	16 (22.9)	
Missing	11 (1.4)	10 (1.4)	1 (1.4)	
Concomitant CIS, *n* (%)				0.132
No	683 (88.4)	625 (88.9)	58 (82.9)	
Yes	90 (11.6)	78 (11.1)	12 (17.1)	
Lymphadenectomy performed, *n* (%)				0.212
No	588 (76.1)	539 (76.7)	49 (70.0)	
Yes	185 (23.9)	164 (23.3)	21 (30.0)	
Lymph node status, *n* (%)				**0.041**
Not performed	590 (76.3)	541 (77.0)	49 (70.0)	
Negative	133 (17.2)	114 (16.2)	19 (27.1)	
Positive	50 (6.5)	48 (6.8)	2 (2.9)	
Median (IQR) follow-up duration, months	34 (15–65)	36 (16–68)	17 (8–35)	**<0.001**
Adjuvant chemotherapy, *n* (%)				**0.007**
No	707 (91.5)	649 (92.3)	58 (82.9)	
Yes	66 (8.5)	54 (7.7)	12 (17.1)	
Tumour recurrence analysis (non-bladder)				
Number of recurrences (%)	182 (23.5)	165 (23.5)	17 (24.3)	
Median (IQR) time to recurrence, months	30 (12–65)	34 (14–67)	14 (7–30)	
Estimated 5-year RFS, % (SE)	73 (1.8)	73.7 (1.9)	63.4 (8.1)	0.124
Overall and cancer-specific mortality analysis				
Total number of deaths from any cause (%)	257 (33.2)	246 (35.0)	11 (15.7)	
Number of deaths from recurrent tumour (%)	155 (20.1)	146 (20.8)	9 (12.9)	
Median (IQR) time to cancer-specific death, months	34 (15–65)	36 (16–68)	17 (8–36)	
Estimated 5-year CSS, % (SE)	75.4 (1.8)	75.4 (1.9)	75.2 (8.5)	0.897

P-values less than 0.05 are shown in bold type.

FIG. 1. Recurrence-free survival rates in 773 patients treated with either ONU (n = 703) or LNU (n = 70) for UTUC.

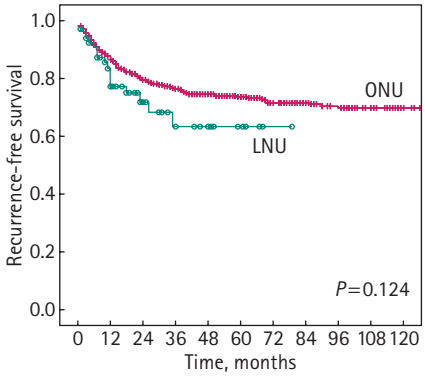
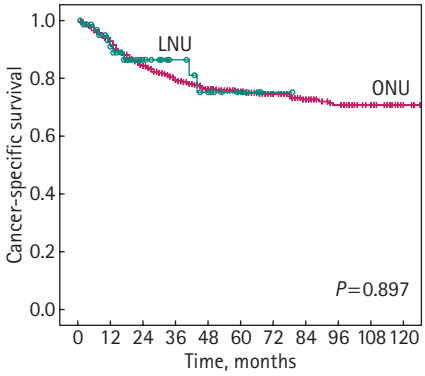


FIG. 2. Cancer-specific survival rates in 773 patients treated with either ONU (n = 703) or LNU (n = 70) for UTUC.



was set as $P \leq 0.05$. All reported P values are two-sided. Analyses were performed with Statistical Package for Social Sciences software, v. 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Of 773 evaluable patients, 70 (9%) underwent LNU and 703 (91%) underwent ONU. The clinical and pathological correlates for each of the groups are presented in Table 1. The two subgroups of patients were significantly different in a number of respects: patients in the LNU group were more likely to have a renal pelvis tumour ($P = 0.016$), and to have received adjuvant chemotherapy ($P = 0.007$); they were less likely to be Caucasian ($P < 0.001$), to have undergone endoscopic ureteric detachment ($P < 0.001$), or to have received previous treatment for a bladder tumour ($P = 0.019$). When histopathological variables were analysed the groups were similar for pathological T-stage, LVI, and the presence of concomitant cancer *in situ* (CIS). Patients in the LNU group had a higher proportion of high-grade tumours ($P < 0.001$), but less frequently demonstrated lymph node metastases ($P = 0.041$).

The median (interquartile range [IQR]) duration of follow-up for the entire study group was 34 (15–65) months. There was a significant difference in follow-up duration between the ONU group (36 months; IQR 16–68 months) and the LNU group (17 months; IQR 8–35 months; $P < 0.001$). At last follow-up there were 182 (23.5%) recurrences, including 165 (23.5%) in the ONU group and 17 (24.3%) in the LNU group. Five-year RFS estimates for the ONU and LNU groups were 73.7% and 63.4% respectively, which was nonsignificant using log-rank testing ($P = 0.124$; Fig. 1). In all, 257 patients (33.2%) patients died during the study period, including 155 (20.1%) patients with progressive UTUC. Estimated 5-year CSS estimates for ONU and LNU groups were 75.4% and 75.2% respectively, which was nonsignificant ($P = 0.897$; Fig. 2).

Univariable and multivariable Cox regression analyses were performed to assess the impact of a number of variables on RFS and CSS respectively (Table 2). Multivariable analyses comprised age, gender, race, previous treatment for bladder cancer, procedure type, technique for distal ureter management, tumour location, pathological stage, grade, lymph node status, LVI and concomitant CIS. A history of previous bladder tumour, non-Caucasian race, endoscopic ureteric detachment, tumour location, muscle invasion, lymph node positivity, LVI and concomitant CIS were all independently predictive of non-bladder tumour recurrence. However, only race, tumour multifocality, tumour stage, lymph node positivity, LVI and CIS were predictive on both univariable and multivariable analyses. For CSS age, multifocality, pathological stage, LVI and CIS were predictive of death from progressive UTUC on both univariable and multivariable analyses.

The type of procedure, either ONU or LNU, was not predictive of RFS or CSS on either univariable or multivariable analyses. To further explore the association of type of surgery with RFS and CSS, we performed subgroup analyses stratifying the cohort according to pathological tumour stage (<pT2 vs. ≥ pT2 and <pT3 vs. ≥ pT3), history of adjuvant chemotherapy, and lymph node status. The type of surgery was not associated with RFS or CSS, regardless of pathological tumour stage, chemotherapy exposure or lymph node status (Table 3).

DISCUSSION

In this study we set out to compare outcomes after LNU and ONU for UTUC in our cohort of patients. The results corroborate recent evidence suggesting equivalence for ONU and LNU in terms of RFS and CSS. The findings also concur with earlier studies reporting the prognostic significance of tumour multifocality [18], LVI [12,13,19,20], and lymph node metastases [12,13,21], and the absence of a difference in outcome when renal pelvis tumours are directly compared with solitary ureteric tumours [22,23].

In consideration of the aforementioned findings it should be appreciated that this study had a retrospective design and, therefore, is subject to all of the inherent bias associated with such analyses. Furthermore, a relatively small proportion of patients underwent LNU as compared with ONU, increasing the susceptibility of the study to error. There are a number of other limitations. Firstly, performance scores were not available for a majority of patients, and were therefore not included. Whilst poor performance score has consistently been associated with an adverse outcome following nephrectomy for clear-cell RCC [24,25], and was reported to predict adverse outcomes after radical nephroureterectomy in a recent study [12], its value as a prognostication tool after extirpative surgery for UTUC has not yet been established. Its omission from this study is therefore regrettable, but we do not believe it necessarily invalidates the data presented herein. Secondly, the absence of lymphadenectomy data for a majority of patients (76.1%) suggests possible understaging of the cohort. However, whilst there are proponents of an extended lymph node dissection on oncological grounds [26], there remains no convincing published data that routine lymphadenectomy favourably influences either RFS or CSS [27] . Moreover, in this study multivariable analyses stratified for lymph node status demonstrated no significant benefit for lymphadenectomy in terms of RFS and CSS. Finally, the lack of

TABLE 2 Univariable and multivariable Cox regression analyses predicting RFS and CSS in 773 patients after radical nephroureterectomy for UTUC

	Risk of tumour recurrence				Risk of cancer-specific death			
	Univariable analyses		Multivariable analysis		Univariable analyses		Multivariable analysis	
Variable	Hazard ratio (HR [95% CI])	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age (continuous)	1.02 (1.00–1.03)	**0.025**	1.02 (1.00–1.04)	0.098	1.02 (1.00–1.04)	**0.010**	1.02 (1.00–1.04)	**0.044**
Gender								
Female vs. male	0.92 (0.67–1.27)	0.622	0.82 (0.56–1.20)	0.311	0.82 (0.57–1.17)	0.268	0.73 (0.48–1.12)	0.149
Race								
Other vs. Caucasian	1.42 (1.02–1.97)	**0.040**	1.89 (1.12–3.01)	**0.007**	1.23 (0.84–1.78)	0.287	1.39 (0.84–2.31)	0.199
History of bladder tumour								
Positive vs. negative	1.32 (0.97–1.80)	0.083	1.71 (1.15–2.55)	**0.008**	1.33 (0.95–1.86)	0.099	1.69 (1.11–2.59)	**0.015**
Type of procedure								
LNU vs. ONU	1.48 (0.89–2.44)	0.129	0.80 (0.40–1.61)	0.534	0.96 (0.49–1.88)	0.897	0.96 (0.44–2.06)	0.907
Management of distal ureter								
Endoscopic vs. bladder cuff	0.61 (0.37–1.02)	0.059	2.29 (1.21–4.35)	**0.011**	0.70 (0.42–1.18)	0.181	2.26 (1.18–4.27)	**0.014**
Tumour location		**0.019**		**0.004**		**0.049**		**0.037**
Ureteric vs. renal pelvis	1.18 (0.83–1.68)	0.352	1.57 (1.06–2.33)	0.025	1.07 (0.73–1.56)	0.735	1.40 (0.91–2.14)	0.123
Multifocal vs. renal pelvis	2.13 (1.26–3.60)	0.005	2.53 (1.38–4.64)	0.003	2.00 (1.15–3.50)	0.015	2.23 (1.16–4.27)	0.016
Grade		**<0.001**		0.091		**<0.001**		0.218
G2 vs. G1	2.52 (0.98–6.50)	0.055	1.90 (0.63–5.76)	0.258	1.97 (0.75–5.17)	0.168	1.66 (0.54–5.12)	0.381
G3 vs. G1	7.92 (3.25–19.31)	<0.001	2.80 (0.96–8.15)	0.059	6.69 (2.74–16.36)	<0.001	2.31 (0.77–6.93)	0.134
Tumour stage		**<0.001**		**<0.001**		**<0.001**		**<0.001**
T1 vs. Ta/Tis	1.42 (0.71–2.84)	0.316	0.83 (0.35–1.95)	0.662	1.54 (0.68–3.49)	0.300	0.90 (0.36–2.31)	0.834
T2 vs. Ta/Tis	3.58 (1.89–6.79)	<0.001	2.53 (1.21–5.31)	0.014	4.08 (1.92–8.69)	<0.001	2.43 (1.06–5.59)	0.037
T3 vs. Ta/Tis	6.69 (3.72–12.03)	<0.001	4.65 (2.29–9.48)	<0.001	9.00 (4.50–18.03)	<0.001	5.44 (2.46–12.00)	<0.001
T4 vs. Ta/Tis	40.31 (20.95–77.60)	<0.001	13.75 (5.56–33.99)	<0.001	55.47 (25.99–118.4)	<0.001	15.01 (5.57–40.42)	<0.001
Lymph node status								
Positive vs. negative	6.35 (4.36–9.24)	**<0.001**	2.40 (1.46–3.94)	**0.001**	6.73 (4.49–10.07)	**<0.001**	2.34 (1.38–3.98)	**0.002**
LVI								
Present vs. absent	3.81 (2.80–5.17)	**<0.001**	1.81 (1.24–2.64)	**0.002**	4.57 (3.30–6.34)	**<0.001**	2.07 (1.40–3.08)	**<0.001**
Concomitant CIS								
Present vs. absent	1.94 (1.33–2.83)	**0.001**	1.79 (1.11–2.87)	**0.017**	1.81 (1.20–2.74)	**0.005**	1.66 (1.00–2.76)	**0.050**

P-values less than 0.05 are shown in bold type.

TABLE 3 Multivariable Cox regression analyses comparing recurrence-free survival and cancer specific survival according to surgery type (ONU vs. LNU), stratified for tumour stage (T-stage), nodal stage (N-stage) and chemotherapy status

	Risk of tumour recurrence (ONU vs. LNU)		Risk of cancer-specific death (ONU vs. LNU)	
Strata	HR (95% CI)	*P*	HR (95% CI)	*P*
T-stage				
<pT2	3.66 (1.33–10.1)	0.012	1.65 (0.35–7.90)	0.531
≥pT2	1.21 (0.64–2.31)	0.555	0.98 (0.44–2.17)	0.962
Stratified	1.55 (0.91–2.63)	0.108	1.06 (0.52–2.14)	0.872
T-stage				
<pT3	2.84 (1.28–6.32)	0.010	1.51 (0.44–5.18)	0.513
≥pT3	0.91 (0.44–1.88)	0.795	0.77 (0.32–1.83)	0.547
Stratified	1.38 (0.81–2.37)	0.238	0.91 (0.45–1.85)	0.798
N-stage				
Nx	1.28 (0.66–2.46)	0.231	0.73 (0.30–1.76)	0.483
N0	3.05 (0.84–11.0)	0.089	1.31 (0.22–7.96)	0.771
N1	0.21 (0.03–1.81)	0.156	0.36 (0.04–3.00)	0.346
Stratified	1.41 (0.81–2.43)	0.224	0.91 (0.44–1.87)	0.911
Adjuvant chemotherapy				
No	1.65 (0.80–3.34)	0.173	0.46 (0.11–1.93)	0.290
Yes	0.78 (0.32–1.90)	0.589	1.20 (0.49–2.91)	0.690
Stratified	1.07 (0.61–1.88)	0.811	0.79 (0.38–1.64)	0.535

a standardized cross-sectional follow-up regimen means that the values for tumour recurrence may represent an underestimation of the true degree of residual or metastatic disease. However, as indicated in Fig. 1, a majority of recurrences occurred within the first 3 years of surgery, and it is therefore probable that most recurrences would have been detected clinically within the study period. Ultimately, however, the absence of curative treatment for metastasis means that CSS remains the true endpoint following non-bladder tumour recurrence and, as indicated by similar 5-year estimates for RFS and CSS, CSS does not appear to have been adversely affected.

The present study represents the second large international multicentre study to report on outcomes of ONU and LNU in UTUC. It differs from that of Capitanio *et al.* [12] in a number of ways. Firstly and most pertinently, our patients were better matched for unfavourable risk factors. Pathological T-stage and rates of LVI and concomitant CIS were similar among the groups. Whilst there was a disproportionately higher rate of lymph node metastases in the ONU group (6.8% vs. 2.9%; $P = 0.041$), there was a higher rate of high-grade disease in the LNU group (77.1% vs. 56.3%; $P < 0.001$). Although high-grade disease was not found to be predictive of RFS or CSS on multivariable analyses in the present study, previous larger studies have reported a prognostic role for tumour grade [13]. In addition subgroup analyses have shown no significant difference in oncological endpoints when patients were stratified for lymph node status, although it should be appreciated that because of low numbers of patients with lymph node positivity in the LNU arm, the results do not have adequate statistical power to definitively conclude biological equivalence. Nevertheless, given these considerations we believe that the two groups are at least comparable in terms of risk status. Secondly, in contrast to Capitanio et al, we included patients who received adjuvant chemotherapy, typically for the finding of lymph node metastasis. Whilst the authors acknowledge that there remain a lack of data to support the use of adjuvant chemotherapy after radical nephroureterectomy for UTUC, it is undoubtedly a fact that many centres offer such treatment, and we therefore believe that inclusion of these cases in the current analysis at least reflects real-life practice. The administration of adjuvant chemotherapy for unfavourable features after radical nephroureterectomy is a relatively recent phenomenon, and as a result more patients in the LNU arm received post-operative chemotherapy than did in the ONU arm (17.1% vs. 7.7%; $P = 0.007$). It is thus conceivable that a favourable response to adjuvant chemotherapy may have masked a poorer postoperative outcome in the LNU group. However, in our study subgroup analyses stratified for chemotherapy status failed to demonstrate a difference between the groups for either RFS or CSS. Finally, in our study 88.4% of patients underwent formal bladder cuff excision, compared with only 56.9% of patients in the study by Capitanio *et al.* The reasons for this discrepancy are not clear but, as partial ureterectomy has long been associated with unacceptable rates of distal ureteric recurrence [1,28] and consequently is not widely performed, the discrepancy may rather relate to a historical vogue for endoscopic ureteric detachment as a prelude to ONU in the latter study. Certainly in the past, questions have been raised regarding the oncological validity of endoscopic ureteric detachment [29–31]. However, there appears to be no detrimental effect on either RFS or CSS when the studies are directly compared. This with a recent study by Walton *et al.* [14], that showed oncological equivalence for endoscopic ureteric detachment, when compared with open bladder cuff excision in patients undergoing open nephroureterectomy for UTUC.

In conclusion, allowing for the caveats outlined above, this study represents the second large, multicentre trial to report oncological equivalence for ONU and LNU in UTUC, and the first to suggest parity for the techniques in patients with unfavourable disease.

CONFLICT OF INTEREST

None declared.

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Abbreviations: **ONU**, open radical nephroureterectomy; **LNU**, laparoscopic radical nephroureterectomy; **RFS**, recurrence-free survival; **CSS**, cancer-specific survival; **LVI**, lymphovascular invasion; **CIS**, cancer *in situ*; **UTUC**, upper urinary tract urothelial cancer.