Open Nephroureterectomy Compared to Laparoscopic in Upper Urinary Tract Urothelial Carcinoma: A Meta-Analysis

Guihong Liu1, Zeqin Yao1, Guoqiang Chen1, Yalang Li2 and Bing Liang1*

1 Department of Urology, Sanya Central Hospital (Hainan Third People’s Hospital), Sanya, China, 2 Department of Urology, Yuzhou People’s Hospital, Xuchang, China

Background: In this meta-analysis, we will focus on evaluating the effects of open nephroureterectomy compared with laparoscopic nephroureterectomy on postoperative results in upper urinary tract urothelial carcinoma subjects.

Methods: A systematic literature search up to January 2021 was performed, and 36 studies included 23,013 subjects with upper urinary tract urothelial carcinoma at the start of the study; of them, 8,178 were laparoscopic nephroureterectomy, and 14,835 of them were open nephroureterectomy. They were reporting relationships between the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma. We calculated the odds ratio (OR) or the mean difference (MD) with 95% CIs to evaluate the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma using the dichotomous or continuous method with a random or fixed-effect model.

Results: Laparoscopic nephroureterectomy in subjects with upper urinary tract urothelial carcinoma was significantly related to longer operation time (MD, 43.90; 95% CI, 20.91–66.90, p < 0.001), shorter hospital stay (MD, −1.71; 95% CI, −2.42 to −1.00, p < 0.001), lower blood loss (MD, −133.82; 95% CI, −220.92 to −46.73, p = 0.003), lower transfusion need (OR, 0.56; 95% CI, 0.47–0.67, p < 0.001), and lower overall complication (OR, 0.79; 95% CI, 0.70–0.90, p < 0.001) compared with open nephroureterectomy. However, no significant difference was found between laparoscopic nephroureterectomy and open nephroureterectomy in subjects with upper urinary tract urothelial carcinoma in 2–5 years recurrence-free survival (OR, 0.90; 95% CI, 0.69–1.18, p = 0.46), 2–5 years cancer-specific survival (OR, 0.94; 95% CI, 0.69–1.28, p = 0.68), and 2–5 years overall survival (OR, 1.31; 95% CI, 0.91–1.87, p = 0.15).
Background

Urothelial carcinoma of the upper urinary tract is a rare type of malignancy with 1–5% of all urological cancers (1). Because synchronous or metachronous tumors are an inherited behavior of urothelial cancer, radical nephroureterectomy, the bladder cuff excision is considered the standard management for urothelial carcinoma of the upper urinary tract, particularly for muscle-invasive and/or high-grade carcinoma (2). Of present, open nephroureterectomy is the most frequently used procedure for urothelial carcinoma of the upper urinary tract with high risk. Though open nephroureterectomy has been shown to produce long-term local control and improve survival, it may be related to significant morbidity (2). Meanwhile, the first laparoscopic nephroureterectomy was executed in 1993 (3). Minimally invasive methods have rapidly advanced, and laparoscopic surgery of the upper urinary tract has turned into an accepted method by urological surgeons (4). Laparoscopic nephroureterectomy is similarly in effect as open nephroureterectomy surgery for urothelial carcinoma of the upper urinary tract, though causing less perioperative morbidity; as urothelial carcinoma of the upper urinary tract is an aggressive malignancy with a high possibility for disease reappearance and mortality. It is hypothesized that cancer cell dissemination and high-pressure pneumoperitoneum throughout laparoscopic nephroureterectomy could be related to a higher risk of bladder cancer, local recurrence, and port-site metastasis (5). So, the oncologic efficiency of laparoscopic nephroureterectomy compared with open nephroureterectomy remains conflicting. Several studies have compared the results of laparoscopic nephroureterectomy and open nephroureterectomy for urothelial carcinoma of the upper urinary tract. Yet, the role of laparoscopic nephroureterectomy is not recognized (6). The surgical practice and experience have developed much since the first laparoscopic nephroureterectomy procedure (3). So, we performed this meta-analysis study to assess the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma.

Methods

The present study followed the meta-analysis of studies in the epidemiology statement (7), which was performed following an established protocol.

Conclusion: Laparoscopic nephroureterectomy in subjects with upper urinary tract urothelial carcinoma may have a longer operation time, shorter hospital stay, and lower blood loss, transfusion need, and overall complication compared to open nephroureterectomy. Further studies are required to validate these findings.

Keywords: open nephroureterectomy, laparoscopic, upper urinary tract urothelial carcinoma, complications, perioperative results, survival

Study Selection

Studies included were those with statistical measures of association (odds ratio (OR), mean difference (MD), frequency rate ratio, or relative risk, with 95% CIs) between the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma.

Human studies only in the English language were considered. Inclusion was not restricted by size or type of study. Publications excluded were review articles and commentary and studies that did not supply a degree of relationship. Figure 1 shows the whole study process.

The articles were integrated into the meta-analysis when the following inclusion criteria were met:

1. The study was a randomized controlled trial or retrospective study.
2. The target population is subjects with upper urinary tract urothelial carcinoma.
3. The intervention program was the open nephroureterectomy and laparoscopic nephroureterectomy.
4. The study included comparisons between the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma.

The exclusion criteria were the following:

1. Studies that did not compare open nephroureterectomy to laparoscopic nephroureterectomy.
2. Studies with surgery other than upper urinary tract urothelial carcinoma.
3. Studies did not concentrate on the effect on postoperative results.

Identification

A search protocol strategy was organized according to the PICOS principle (8), and we defined it as follow: P (population): subjects with upper urinary tract urothelial carcinoma; I (intervention/exposure): open nephroureterectomy and laparoscopic nephroureterectomy; C (comparison): efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma; O (outcome): perioperative, and postoperative results; S (study design): no restriction (9). First, we conducted a systematic search of Embase, PubMed, Cochrane Library, OVID, and Google scholar till January 2021, by a blend of keywords and related words for open nephroureterectomy, laparoscopic, upper urinary tract urothelial carcinoma, complications, perioperative results,
and survival as shown in Table 1. All selected studies were gathered in an EndNote file, duplicates were removed, and the title and abstracts were revised to eliminate studies that did not report the relationship between the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma. The remaining studies were examined for related information.

**Screening**

Data were abbreviated based on the following: study associated and subject associated features onto a homogeneous form. We extracted the following data separately: the last name of the primary author, study period, publication year, country, the studies region, and design of the study; type of the population, the total number and subjects number, demographic data, and clinical and treatment features; the evaluation period associated with measurement, quantitative method and qualitative method of assessment, source of information, and assessment of outcomes; and statistical analysis MD or relative risk, with 95% CI of the relationship between efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma (10). If a study fit for inclusion based upon the above-mentioned principles, data were extracted individually by two authors. In case of discrepancy, the corresponding author gave a final choice. When there were diverse data from a study, the data were extracted separately. In case of bias risk in the studies, each study was assessed using two authors who individually evaluated the methodological quality of the selected studies. We used the “risk of bias tool” from the RoB 2: a revised Cochrane risk-of-bias tool for randomized trials to evaluate methodological quality (11). In terms of the evaluation criteria, each study was valued and allocated to one of the next three risks of bias: low: if all quality criteria were met; unclear or moderate: if one or more of the quality criteria were partly met or unclear; high: if one or more of the criteria were not met, or not
included. Any discrepancies were addressed by a reassessment of the original article.

**Eligibility**
The main result concentrated on the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma. An assessment of the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma was extracted forming a summary.

**Inclusion**
Sensitivity analyses were limited only to studies reporting the relationship between the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma. For subcategory and sensitivity analysis, we compared the effect of open nephroureterectomy compared with laparoscopic nephroureterectomy.

**Statistical Analysis**
The dichotomous or continuous method with random-effect or fixed-effect models was used to calculate the OR or MD and 95% CI. We used the Chi-squared test to perform biological heterogeneity analyses between different studies. We calculated the I² index and the I² index is from 0 to 100%. Values of about 0%, 25%, 50%, and 75% indicate no, low, moderate, and high heterogeneity, respectively (8). When I² was higher than 50%, we chose the random effect model; when it was lower than 50%, we used the fixed-effect model. A subgroup analysis was performed by stratifying the original evaluation per liver cancer and different outcomes of chemotherapy as described before. In this analysis, a p-value for differences between subgroups of <0.05 was considered statistically significant. Publication bias was evaluated quantitatively using the Egger regression test (publication bias considered present if p ≥ 0.05), and qualitatively, by visual examination of funnel plots of the logarithm of ORs or MDs vs. their SE (10). All p-values were two-tailed. All calculations and graphs were performed using Reviewer manager version 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark).

**RESULTS**
A total of 2,534 unique studies were identified, of which 36 studies (between 2007 and 2020) fulfilled the inclusion criteria and were included in the study (12–47).

The 36 studies included 23,013 subjects with upper urinary tract urothelial carcinoma at the start of the study; 8,178 of them were laparoscopic nephroureterectomy, and 14,835 of them were open nephroureterectomy. All studies evaluated the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma.

Study size ranged from 26 to 3,984 subjects with upper urinary tract urothelial carcinoma at the start of the study. The details of the 36 studies are shown in Table 2. About 16 studies reported data stratified to operation time, 13 studies stratified to the hospital stay, 10 studies stratified to the blood loss, 5 studies stratified to transfusion need, 10 studies stratified to the overall complication, 25 studies stratified to the 2–5 years recurrence-free survival, 28 studies reported data stratified to studies stratified to 2–5 years cancer-specific survival, and 20 studies reported data stratified to 2–5 years overall survival.

Laparoscopic nephroureterectomy in subjects with upper urinary tract urothelial carcinoma was significantly related to longer operation time (MD, 43.90; 95% CI, 20.91–66.90, p < 0.001) with high heterogeneity (I² = 98%), shorter hospital stay (MD, −1.71; 95% CI, −2.42 to −1.00, p < 0.001) with high heterogeneity (I² = 98%), lower blood loss (MD, −133.82; 95% CI, −220.92 to −46.73, p = 0.003) with high heterogeneity (I² = 96%), lower transfusion need (OR, 0.56; 95% CI, 0.47–0.67, p < 0.001) with low heterogeneity (I² = 42%), and lower overall complication (OR, 0.79; 95% CI, 0.70–0.90, p < 0.001) with low heterogeneity (I² = 28%) compared with open nephroureterectomy as shown in Figures 2–6.

However, no significant difference was found between laparoscopic nephroureterectomy and open nephroureterectomy in subjects with upper urinary tract urothelial carcinoma in 2–5 years recurrence-free survival (OR, 0.90; 95% CI, 0.69–1.18, p = 0.46) with high heterogeneity (I² = 89%), 2–5 years cancer-specific survival (OR, 0.94; 95% CI, 0.69–1.28, p = 0.68) with high heterogeneity (I² = 89%), and 2–5 years overall survival (OR, 1.31; 95% CI, 0.91–1.87, p = 0.15) with high heterogeneity (I² = 91%) as shown in Figures 7–9.

Selected studies stratified analysis that did and did not adjust for age, ethnicity, and the effect of different laparoscopic nephroureterectomy procedures between the two groups was not performed since no studies reported or adjusted for these factors.

Based on the visual examination of the funnel plot as well as on qualitative measurement by the Egger regression test, there was no indication of publication bias (p = 0.85). Though, most of the comprised studies were evaluated to be of a low methodological quality. All studies did not have selective reporting bias, and no articles had incomplete result data and selective reporting.

**DISCUSSION**
This meta-analysis study based on 36 studies included 23,013 subjects with upper urinary tract urothelial carcinoma at the start of the study; 8,178 of them were laparoscopic nephroureterectomy, and 14,835 of them were open nephroureterectomy (12–47). Laparoscopic nephroureterectomy in subjects with upper urinary tract urothelial carcinoma may have a longer operation time, shorter hospital stay, and lower blood loss, transfusion need, and overall complication compared with open nephroureterectomy; however, no significant difference was found between laparoscopic nephroureterectomy and open nephroureterectomy in subjects with upper urinary tract urothelial carcinoma in 2–5 years recurrence-free survival, 2–5 years cancer-specific survival, and 2–5 years overall survival (12–47). Though the analysis of outcomes should be done
with caution because of the low number of subjects in some of the studies evaluating each parameter in this meta-analysis, suggesting more studies relating the type of operation method, and postoperative results in subjects with upper urinary tract urothelial carcinoma to validate these findings. The need for more studies is very obvious in the results of 2–5 years overall survival with their low p-values (p = 0.15), showing the need for further research possibly to significantly influence confidence in the effect evaluation.

From the time of the first study comparing open nephroureterectomy with laparoscopic nephroureterectomy in 1993 (3), many studies have tried to show laparoscopic nephroureterectomy as a possible substitute of open nephroureterectomy for urothelial carcinoma of the upper urinary tract, however, there was no comprehensive comparison found. This present meta-analysis with its high-level results establishes a role of laparoscopic nephroureterectomy in the surgical management of urothelial carcinoma of the upper urinary tract. The procedure of laparoscopic nephroureterectomy involves nephrectomy and distal ureterectomy, with the same ontological value as open nephroureterectomy. Laparoscopic access could be done through

| Study                         | Country          | Total | Laparoscopic nephroureterectomy | Open nephroureterectomy |
|-------------------------------|------------------|-------|---------------------------------|--------------------------|
| Koda et al. (12)              | Japan            | 106   | 79                              | 27                       |
| Manabe et al. (13)            | Japan            | 224   | 58                              | 166                      |
| Rouprêt et al. (14)           | France           | 46    | 20                              | 26                       |
| Hemai et al. (15)             | USA              | 48    | 21                              | 27                       |
| Taweemonkongsap et al. (16)   | Thailand         | 60    | 31                              | 29                       |
| Terakawa et al. (17)          | Japan            | 240   | 120                             | 120                      |
| Capitainio et al. (18)        | Multicenter      | 1,249 | 270                             | 979                      |
| Greco et al. (19)             | Germany          | 140   | 70                              | 70                       |
| Simone et al. (20)            | Italy            | 80    | 40                              | 40                       |
| Waldert et al. (21)           | Austria          | 102   | 43                              | 59                       |
| Favaretto et al. (22)         | USA              | 162   | 53                              | 109                      |
| Stewart et al. (23)           | UK               | 62    | 23                              | 39                       |
| Walton et al. (24)            | Multicenter      | 773   | 70                              | 703                      |
| Ariane et al. (25)            | France           | 609   | 150                             | 459                      |
| Metcafe et al. (26)           | USA              | 849   | 446                             | 403                      |
| Fairey et al. (27)            | Canada           | 849   | 446                             | 403                      |
| Xylinas et al. (28)           | France           | 482   | 132                             | 350                      |
| Fradet et al. (29)            | Canada           | 612   | 345                             | 267                      |
| Kitamura et al. (30)          | Japan            | 99    | 65                              | 34                       |
| Zou et al. (31)               | China            | 122   | 21                              | 101                      |
| Blackmur et al. (32)          | UK               | 26    | 13                              | 13                       |
| Hanske et al. (33)            | Germany          | 896   | 599                             | 297                      |
| Kim et al. (34)               | Korea            | 372   | 100                             | 272                      |
| Miyazaki et al. (35)          | Japan            | 849   | 222                             | 627                      |
| Liu et al. (36)               | China            | 265   | 52                              | 213                      |
| Abe et al. (37)               | Japan            | 214   | 114                             | 100                      |
| Kido et al. (38)              | Japan            | 426   | 75                              | 351                      |
| Kim et al. (39)               | Korea            | 1,521 | 615                             | 906                      |
| Lee et al. (40)               | Korea            | 298   | 137                             | 161                      |
| Kim et al. (41)               | Korea            | 1,693 | 715                             | 978                      |
| Nazzani et al. (42)           | Multicenter      | 3,897 | 1,093                           | 2,804                    |
| Shigeta et al. (43)           | Japan            | 176   | 72                              | 104                      |
| Alotman et al. (44)           | Saudi Arabia     | 50    | 24                              | 26                       |
| Ye et al. (45)                | China            | 48    | 24                              | 24                       |
| Azawi et al. (46)             | Denmark          | 1,384 | 1,063                           | 321                      |
| Moschini et al. (47)          | Multicenter      | 3,984 | 757                             | 3,227                    |
| **Total**                     |                  | 23,013| 8,178                           | 14,835                   |
transperitoneal or retroperitoneal spaces. Transperitoneal access gives more working space and easier handling, while retroperitoneal access avoids disturbance of the intraperitoneal organs and the risk of intraperitoneal corruption by malignant cells (48); however, the process of laparoscopic nephroureterectomy has not been standardized yet, particularly

| Study or Subgroup | Laparoscopic nephroureterectomy | Open nephroureterectomy | Odds Ratio M.H. Random, 95% CI | Year |
|--------------------|---------------------------------|-------------------------|-------------------------------|------|
| Roupert, 2007      | 18                              | 20                      | 26                            | 2.6% | 2007 |
| Matsubay, 2007     | 49                              | 58                      | 139                            | 166  | 4.9% | 1.06 [0.47, 2.41] | 2007 |
| Terakawa, 2008     | 27                              | 31                      | 24                            | 29   | 3.2% | 1.41 [0.34, 5.85] | 2008 |
| Hoc, 2008          | 108                             | 120                     | 107                           | 120  | 4.9% | 1.09 [0.48, 2.50] | 2008 |
| Hemal, 2008        | 18                              | 21                      | 23                            | 27   | 2.9% | 1.04 [0.21, 5.27] | 2008 |
| Farhat, 2010       | 38                              | 53                      | 73                            | 109  | 5.2% | 1.25 [0.61, 2.56] | 2010 |
| Stewart, 2011      | 14                              | 23                      | 25                            | 39   | 4.2% | 0.87 [0.36, 2.22] | 2011 |
| Metcalfe, 2012     | 365                             | 446                     | 265                           | 403  | 6.3% | 2.34 [1.02, 4.92] | 2012 |
| Fanney, 2013       | 303                             | 446                     | 270                           | 403  | 6.3% | 1.04 [0.69, 1.59] | 2013 |
| Blackmur, 2015     | 7                               | 13                      | 13                            | 13   | 2.8% | 0.02 [0.03, 5.36] | 2015 |
| Miyazaki, 2016     | 161                             | 222                     | 366                           | 627  | 6.2% | 1.88 [0.35, 1.06] | 2016 |
| Liu, 2017          | 39                              | 52                      | 129                           | 213  | 5.3% | 1.95 [0.56, 6.89] | 2017 |
| Abe, 2018          | 98                              | 114                     | 72                            | 100  | 5.3% | 2.38 [1.26, 4.53] | 2018 |
| Kido, 2018         | 61                              | 75                      | 207                           | 351  | 4.8% | 0.00 [0.38, 1.82] | 2018 |
| Kim, 2019a         | 439                             | 615                     | 667                           | 906  | 6.4% | 0.80 [0.63, 1.00] | 2019 |
| Lee, 2019          | 88                              | 137                     | 109                           | 161  | 5.9% | 0.86 [0.53, 1.39] | 2019 |
| Kim, 2019b         | 593                             | 715                     | 765                           | 978  | 6.4% | 1.35 [0.66, 2.74] | 2019 |
| Moschini, 2020     | 103                             | 757                     | 1105                          | 3227 | 6.4% | 0.30 [0.14, 0.66] | 2020 |
| Azpel, 2020        | 388                             | 1063                    | 71                            | 321  | 6.3% | 2.02 [1.51, 2.71] | 2020 |
| Alothman, 2020     | 16                              | 24                      | 18                            | 26   | 3.8% | 0.68 [0.27, 2.89] | 2020 |

Total (95% CI) 5005 8245 100.0% 1.31 [0.91, 1.87] 2020

Heterogeneity: Tau² = 0.51; Chi² = 221.98, df = 19 (P = 0.00001); I² = 91%
Test for overall effect: Z = 1.45 (P = 0.15)

**FIGURE 2** | Forest plot of the effect of open nephroureterectomy compared with laparoscopic nephroureterectomy on operation time in subjects with upper urinary tract urothelial carcinoma.

**FIGURE 3** | Forest plot of the effect of open nephroureterectomy compared with laparoscopic nephroureterectomy on hospital stay in subjects with upper urinary tract urothelial carcinoma.
management of the distal ureter. Numerous disposal methods have been designated in the clinical trials, e.g., open surgery (14, 21), the Pluck technique (24, 25), and the LigaSure Atlas system (20). Open surgery is still the most prevalent for bladder cuff excision; however, no significant difference in oncological results was shown between different methods (49).

As a mini-invasive technique, laparoscopic nephroureterectomy has been accepted over the world as a promising alternative, with some advantages over open nephroureterectomy as shown in this meta-analysis, e.g., less blood loss, less requirement of transfusion, less overall complication, and shorter hospital stay (50–52). This may...
FIGURE 7 | Forest plot of the effect of open nephroureterectomy compared with laparoscopic nephroureterectomy on 2–5 years recurrence-free survival in subjects with upper urinary tract urothelial carcinoma.

FIGURE 8 | Forest plot of the effect of open nephroureterectomy compared with laparoscopic nephroureterectomy on 2–5 years cancer-specific survival in subjects with upper urinary tract urothelial carcinoma.

FIGURE 9 | Forest plot of the effect of open nephroureterectomy compared with laparoscopic nephroureterectomy on blood loss in subjects with upper urinary tract urothelial carcinoma.
Liu et al. Urinary Tract Urothelial Carcinoma

be due to the large cuts necessary even in laparoscopic nephroureterectomy for the removal of separated samples as well as bladder cuff. Formerly, it was proven that in invasive or large tumors, surgeons should avoid laparoscopic nephroureterectomy (2). With the improvement in methodology and experience of surgeons, the criteria of laparoscopic nephroureterectomy have been intensely expanded. Subjects with high stages (T3/T4) and high grades (G3) experienced laparoscopic nephroureterectomy with similar oncological results as open nephroureterectomy (50–52). Even though different methodology, the oncological values of surgical management of urothelial carcinoma of the upper urinary tract were similar (50–52), and the high risk of regional recurrence and port-site metastasis in laparoscopic nephroureterectomy is still high. Kondo et al. (53) showed that template-based lymphadenectomy decreases the risk of regional lymph node recurrence between subjects with upper/middle ureteral tumor, though templated lymphadenectomy is hard for laparoscopic methodology (54). Xylinas et al. (55) also showed that laparoscopic methodology was an independent risk factor of intravesical recurrence, due to the high pressure that may activate cancer spread (53). Ariane et al. (25) showed a significant number of port-side metastasis with the laparoscopic nephroureterectomy (25); however, other studies showed that surgical methods did not affect postoperative recurrence or survival (55–57). Several meta-analyses have compared laparoscopic nephroureterectomy with open nephroureterectomy, and laparoscopic nephroureterectomy revealed improvement in cancer-specific survival and extravesical recurrence-free survival (6, 50–52); However, either the 5-year survival or the 2-year survival variables did not differ much between laparoscopic nephroureterectomy and open nephroureterectomy.

This meta-analysis reported the relationship between the type of different surgical techniques and postoperative results in subjects with upper urinary tract urothelial carcinoma. Though, additional studies are required to confirm these possible relationships. Similarly, additional studies are required to deliver a clinically meaningful difference in perioperative and postoperative results in subjects with upper urinary tract urothelial carcinoma. These studies must include larger homogeneous samples. This was also recommended in earlier similar meta-analysis studies which showed a similar result of laparoscopic nephroureterectomy and open nephroureterectomy on perioperative and postoperative results in subjects with upper urinary tract urothelial carcinoma (50, 51). Well-conducted studies are also needed to assess these factors and the combination of different ages, ethnicity, and the effect of different laparoscopic nephroureterectomy procedures between the two groups, because this meta-analysis study could not answer whether they are related to the outcomes.

In summary, the data recommend that laparoscopic nephroureterectomy in subjects with upper urinary tract urothelial carcinoma may decrease the risk of hospital stay, blood loss, transfusion need, and overall complication and prolong the operation time compared with open nephroureterectomy in subjects with upper urinary tract urothelial carcinoma. Further studies are needed to validate these findings.

Limitations

There may be selection bias in this study because many studies found were omitted from the meta-analysis. The studies omitted did not fulfill the inclusion criteria of this meta-analysis. Also, we could not respond whether the outcomes are related to age, ethnicity, and the effect of different laparoscopic nephroureterectomy procedures between the two groups or not. The study designed to evaluate the association between the efficacy and safety of open nephroureterectomy compared with laparoscopic nephroureterectomy in the treatment of upper urinary tract urothelial carcinoma was based on data from previous studies, which might cause bias induced by incomplete details. The meta-analysis was based on 36 studies; 9 studies were small, ≤100. Variables including age, ethnicity, and nutritional status of subjects were also the possible bias-inducing factors. Some unpublished articles and missing data may cause a bias in the pooled effect. Also, the criteria of surgical treatment choice were not fully explained. Subjects were using different treatment schedules, the dosage of the anesthesia, sedation use, and health care systems. Also, the varying definition of recurrence-free survival, cancer-specific survival, and overall survival might cause biases. In addition, the pathological variables, the length of follow-up, the operation procedures, and the experience of the surgeons were not the same in the selected studies.

CONCLUSION

Laparoscopic nephroureterectomy in subjects with upper urinary tract urothelial carcinoma may have a longer operation time, shorter hospital stay, and lower blood loss, transfusion need, and overall complication compared with open nephroureterectomy, however, no significant difference was found between laparoscopic nephroureterectomy and open nephroureterectomy in subjects with upper urinary tract urothelial carcinoma in 2–5 years recurrence-free survival, 2–5 years cancer-specific survival, and 2–5 years overall survival. Though the analysis of the results should be done with caution due to the lower number of subjects in some of the studies evaluating each parameter in this meta-analysis, suggesting more studies relating the type of operation method, and postoperative results in subjects with upper urinary tract urothelial carcinoma to validate these findings.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

BL: conception and design. GL, ZY, GC, YL, and BL: administrative support, provision of study materials or subjects, data analysis and interpretation, manuscript writing, and final approval of manuscript. GL, ZY, GC, and YL: collection and assembly of data. All authors contributed to the article and approved the submitted version.
open radical nephroureterectomy in patients with locally advanced upper tract urothelial carcinoma. World J Urol. (2016) 34:859–69. doi: 10.1007/s00345-015-1712-3

35. Miyazaki J, Nishiyama H, Fujimoto H, Ohyama C, Koie T, Hinotsu S, et al. Laparoscopic versus open laparoscopic nephroureterectomy in muscle-invasive upper tract urothelial carcinoma: subanalysis of the multi-institutional laparoscopic database of the Japanese urological association. J Endourol. (2016) 30:520–5. doi: 10.1089/end.2015.0757

36. Liu, J.-Y., Dai Y-B, Zhou F-J, Long Z, Li Y-H, Xie D, et al. Laparo scopic versus retroperitoneal radical nephroureterectomy: a population-based analysis. World J Urol. (2017) 25:726–33. doi: 10.1007/s00345-016-1248-9

37. Kido K, Hatakeyama S, Fujita N, Yamamoto H, Tobisawa Y, Yoneyama T, et al. Laparoscopic versus open nephroureterectomy for the treatment of upper tract urothelial carcinoma: a Korean multicenter collaborative study. Cancer Res Treat. (2019) 51:240. doi: 10.4143/crt.2018.118

38. Lee H, Kim HJ, Lee SE, Hong SK, Byun S-S. Comparison of oncological outcomes from a multicenter study. BMC Surg. (2017) 17:1–10. doi: 10.1186/s12893-016-0202-x

39. Abe T, Kondo T, Harabayashi T, Takada N, Matsumoto R, Osawa T, et al. Comparative study of lymph node dissection, and oncological outcomes of laparoscopic and open radical nephroureterectomy for patients with urothelial carcinoma of the upper urinary tract undergoing regional lymph node dissection. Jpn J Clin Oncol. (2018) 48:1001–11. doi: 10.1093/jjco/hyy128

40. Shigeta K, Hatakeyama S, Fujita N, Yamamoto H, Tobisawa Y, Yoneyama T, et al. Oncologic outcomes for open and laparoscopic radical nephroureterectomy in patients with upper tract urothelial carcinoma. Int J Clin Oncol. (2018) 23:726–33. doi: 10.1007/s10147-018-1248-9

41. Kim TH, Hong B, Seo HK, Kang SH, Ku JH, Jeong BC. The comparison of oncologic outcomes between open and laparoscopic radical nephroureterectomy for the treatment of upper tract urothelial carcinoma: a Korean multicenter collaborative study. Cancer Res Treat. (2019) 51:240. doi: 10.4143/crt.2017.417

42. Lee H, Kim HI, Lee SE, Hong SK, Byun SS. Comparison of oncological and perioperative outcomes of open, laparoscopic, and robotic nephroureterectomy approaches in patients with non-metastatic upper-tract urothelial carcinoma. PLoS ONE. (2019) 14:e0210401. doi: 10.1371/journal.pone.0210401

43. Kim SH, Song MK, Kim JK, Hong B, Kang SH, Ku JH, et al. Laparoscopy versus open nephroureterectomy in prognostic outcome of patients with advanced upper tract urothelial cancer: a retrospective, multicenter, propensity-score matching analysis. Cancer Res Treat. (2019) 51:963. doi: 10.4143/crt.2018.465

44. Nazzani S, Bazinet A, Preisser F, Mazzone E, Tian Z, Mistretta FA, et al. Comparative study of lymph node dissection, and oncological outcomes of laparoscopic versus open radical nephroureterectomy in patients with upper urinary tract urothelial carcinoma. Int J Clin Oncol. (2017) 22:145–52. doi: 10.1007/s10147-016-1024-7

45. Meraney AM, Gill IS. Financial analysis of open versus laparoscopic radical nephrectomy and nephroureterectomy. J Urol. (2002) 167:1757–62. doi: 10.1016/S0022-5347(05)65194-4

46. Xylinas E, Kluth L, Passoni N, Trinh Q-D, Rieken M, Lee RK, et al. Prediction of intravesical recurrence after radical nephroureterectomy: development of a clinical decision-making tool. Eur Urol. (2014) 65:650–8. doi: 10.1016/j.eururo.2013.09.003

47. Ploussard G, Xylinas E, Lotan Y, Novara G, Margulis V, Rouprêt M, et al. Conditional survival after radical nephroureterectomy for upper tract carcinoma. J Urol. (2015) 67:803–12. doi: 10.1016/j.juro.2014.08.003

48. Kobayashi Y, Saika T, Miyai Y, Saequisa M, Arata R, Akebi N, et al. Preoperative positive urine cytology is a risk factor for subsequent development of bladder cancer after nephroureterectomy in patients with upper urinary tract urothelial carcinoma. World J Urol. (2012) 30:271–5. doi: 10.1007/s00345-011-0731-y

Conflict of Interest: The 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.

Publisher’s Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2021 Liu, Yao, Chen, Li and Liang. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.