Laparoscopic or Open Nephroureterectomy: Which Is the More Efficient Way to Go?

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Upper urinary tract transitional cell carcinoma (UTCC) is a rare disease but is associated with high recurrence rates and significant risk of progression. Open radical nephroureterectomy (ONU) has been the standard treatment for several decades. Because the performance of the open procedure requires either two incisions or an extended flank incision, the laparoscopic nephroureterectomy (LNU) is an appealing option. LNU is associated with less intraoperative blood loss, decreased postoperative pain, and decreased hospital stay [1,2]. Although there is always a standing question about the oncologic efficacy of newer laparoscopic approaches, the low incidence of urothelial carcinoma of the upper urinary tract represents a problem for the evaluation of the LNU outcome regardless of the follow-up period. Several single-institution studies with limited experience have been published, and the majority of these investigators have concluded that LNU should be performed in patients with favorable tumor characteristics, while ONU should take place in the advanced tumor cases [1–6].

A large multi-institutional noncomparative study including 1363 patients who underwent ONU (n = 1050) or LNU (n = 313) was reported recently [7]. Complete resection of the distal ureter was performed in all cases, while lymphadenectomy took place in 46.8% and 31.6% of the ONUs and LNUs, respectively. The extent of the lymphadenectomy varied widely among the institutions. A limited portion of the studied population was managed by neoadjuvant (3%) and/or adjuvant chemotherapy (13%), respectively. The median follow-up period of the study was 37.2 mo (range: 1.2–250 mo). High-grade tumors, lymphovascular invasion, sessile tumor architecture, tumor necrosis, and concomitant carcinoma in situ were associated with positive lymph nodes and tumor recurrence. The 5-yr recurrence-free survival and 5-yr cancerspecific survival rates were 69% and 73%, respectively. These results should be carefully considered, since the majority of the tumors addressed were invasive high grade (61%). Local recurrence was observed in 3% of the patients. Patients with noninvasive disease (<pT1) had 95% 5-yr recurrence-free survival and 96% 5-yr cancerspecific survival rates. Positive lymph nodes were detected in 23% of the patients who underwent lymphadenectomy. The study was not comparative in nature but revealed interesting information on the oncologic efficacy of nephroureterectomy in a large population regardless of the approach used.

Recently, a significant effort has been made to elucidate the outcome of LNU by performing large multi-institutional studies. Kamihira et al provided a large multi-institutional study that evaluated the outcome of LNU and proposed several risk factors that influence the recurrence of the tumor and overall survival [8]. In total, 959 out of 1003 patients were treated with LNU, and the remaining cases were converted to open procedure. Bladder cuff was removed along with the specimen in the majority of cases (972 cases in total). Lymphadenectomy was performed in 979 patients. Intraoperative and postoperative complications were observed in 9.3% and 7.4% of the cases, respectively. Tumor stage, lymph node metastasis, male sex, tumor multifocality, existence of previous or coexistent bladder tumor, hand-assisted approach, and adjuvant chemotherapy were factors influencing the oncologic results. Intravesical, extravesical, and local recurrences
were detected in 264, 134, and 56 patients, respectively, and port-site recurrence was detected in 1 patient. Overall survival and recurrence-free survival rates were 70% and 42%, respectively, at 5 yr. LNU proved to be oncologically efficient, but the comparison with the established ONU technique remained the main issue to be resolved in order to determine the indications of the procedure.

The current study by Capitanio et al takes one step forward by providing a large multi-institutional comparative assessment of ONU and LNU [9]. A total of 1249 patients was included. The results of the study showed that patients with more favorable disease were treated by LNU. The latter observation reflects the aforementioned conclusion of several studies to manage advanced disease using ONU [3,10]. In fact, LNU patients had more favorable pathological stages, more frequent papillary architecture, less lymphovascular invasion, and less frequent primary tumor location in the ureter versus the renal pelvis. These observations reflect factors that have been previously associated with lower disease recurrence rates [7]. Cancer-specific survival estimates at 5 yr were higher and recurrence estimates were lower in the case of LNU. Nevertheless, the ONU group had addressed tumors of poorer prognosis. The statistical analysis revealed that both techniques had similar 5-yr oncologic efficacy in earlier cancer stages. Thus, the oncologic outcome of LNU in the latter cases could be considered as equal to ONU. The oncologic efficacy of LNU in advanced disease cases remained questionable.

The retrospective multi-institutional nature of the study introduced several biases in data collection such as local and bladder recurrence data, port-site metastasis, comorbidities of the patients, and body mass index. Especially the absence of local recurrence data represents a problem for the confirmation of cancer control. Bladder recurrence is a significant problem of the disease and has been reported to range between 10% and 55% in series with at least midterm follow-up [2]. In fact, rupture of the renal pelvis has been reported to result in dissemination of the disease [6]. Moreover, retroperitoneal local recurrence has been observed in 5.4% of patients after LNU or ONU [2]. The excision of a bladder cuff around the ureteral orifices has been proposed in an attempt to minimize bladder recurrence and to provide better oncologic results. Several techniques have been introduced. Yet, it remains unclear which technique provides the best outcome [2,11]. Additionally, the technique used for bladder cuff excision could be related to local recurrence, especially with the pluck technique, during which the ureter was not occluded [2]. Distal ureter clipping has been proposed to prevent tumor dissemination to the bladder or retroperitoneum, and the cytostomy after the excision of the cuff should always be closed [2,12]. The current study failed to address the above issue due to the absence of appropriate data. Because some of the institutions participating in the study did not perform bladder cuff excision, it would have been very interesting to compare the oncologic outcome in terms of local and bladder recurrence with or without bladder cuff excision and in respect to the approach used.

Additionally, lymphadenectomy had not been performed in high number of patients, and the staging of the tumors was probably not accurate. In fact, 57.6% and 75.6% of the ONU and LNU patients, respectively, did not undergo lymphadenectomy. A statistically significant difference between the two populations was also observed, raising questions regarding the challenging nature of laparoscopic lymphadenectomy. The mean number of acquired lymph nodes was low (5.5 and 4.7) and probably not adequate for staging. The above limitations of the current study reflect the two major problems with the management of upper urinary tract urothelial carcinoma: the absence of clear indications and a standard template for the performance of regional lymph node dissection. Kondo et al noted an improved cancer-specific survival in patients of advanced stage (pT3 or higher), while lymphadenectomy did not prove to be beneficial when the whole population was taken in to consideration. The same investigators proposed a relatively wide template for lymph node dissection, especially on the right side, that included paracaval, retrocaval, and interaortocaval nodes [13]. The acquisition of lymph nodes has been observed to be lower with the laparoscopic approach in comparison to ONU, but large series with both ONU and LNU have also revealed low lymph node acquisition [5,7]. As a result, the debate on the influence of lymphadenectomy in the survival of the UTCC patients is still open.

Another limitation of the current study is the absence of data regarding the port-site metastasis. Port-site metastasis has been reported in a total of eight cases and probably occurs in <1–2% of LNU cases [2]. The current large series would have been excellent in investigating the incidence of this oncologic issue.

Generally, the present study provides valuable comparative data based on a large experience. Nevertheless, several oncologic aspects that are questionable were not elucidated. Randomized prospective multi-institutional studies are probably the key to addressing the above unclarified issues.

Conflicts of interest: The authors have nothing to disclose.

References

The outcomes of upper urinary tract urothelial carcinoma (UTUC) are relatively poorly explored. Three types of databases may be used to better elucidate the effect of risk factors and the impact of various therapeutic modalities: randomized controlled trials (RCTs), multi-institutional case series [1–4], and population-based registries [5].

RCTs are ideal for assessing therapeutic alternatives. Unfortunately, RCTs are virtually nonexistent for UTUC; therefore, it is doubtful that multi-institutional, randomized trials will provide information regarding most bias-free relative efficacy of available treatment options for UTUC within a short or intermediate time frame. Moreover, the applicability of the findings from RCTs may not be ideal in the general population. The findings of an RCT comparing open nephroureterectomy (OUN) and laparoscopic nephroureterectomy (LNU) at high-volume tertiary-care referral centers, for example, may not be applicable in the community or even in lower volume, less specialized institutions.

To circumvent this limitation, several investigators, including the Upper Tract Urothelial Carcinoma Collaboration, relied on multi-institutional databases [1–4]. The current study by Capitano et al [2], which specifically addressed the efficacy of ONU versus LNU, represents an example of a large-scale database. Despite an excellent confidence level regarding the lack of the presence of outcome differences, such databases are limited by selection criteria. Patients who are treated at tertiary-care centers that maintain clinical records and that participate in multi-institutional studies may be different from those treated in the community or even at less prestigious referral centers. Moreover, the investigation, treatment, and follow-up at such tertiary-care centers may differ from other institutions. Consequently, results derived from tertiary-care centers need to be validated in the community to ensure generalizability in that setting.

Population-based data sets, such as the Surveillance, Epidemiology, and End Results (SEER) registry, may circumvent the tertiary-care selection biases [6–9]. The amount of detail that may derived from such databases, however, cannot parallel that of either RCTs or well-designed institutional databases. Therefore, limited specificity is the price of generalizability in population-based databases. Moreover, population-based registries are rare. The SEER database allows the study of urologic tumors in the United States; however, except for the Scandinavian countries, no equivalent is yet available in Europe, Asia, or Africa. Efforts should be made to develop population-based tumor registries in other countries and on other continents. Moreover, efforts should be made to increase the amount of information available for each individual patient within the existing population-based databases.

In summary, as highlighted by Liatsikos and Kallidonis [10], Capitano et al’s study [2] suffers from several limitations for which the authors cannot control. Unfortunately, there are no alternatives for completely circumventing various selection biases that undermine the validity and the generalizability of all databases. Consequently, it is necessary to use both types of databases to estimate the generalizability of clinical research in the field of UTUC.