Research Article

Dong Wang, Zejun Xiao*, Jianzhong Shou, Changling Li, Nianzeng Xing

Comparison of laparoscopy and open radical nephrectomy of renal cell cancer

https://doi.org/10.1515/med-2019-0040
received February 12, 2019; accepted April 17, 2019

Abstract: Objective: The aim of this study was to summarize the current evidence to evaluate the effects of laparoscopic radical nephrectomy (LRN) and open radical nephrectomy (ORN) in the treatment of renal cell carcinoma. Methods: A comprehensive literature search was performed using PubMed, Embase and Google Scholar to identify all relevant studies. 8 published studies were included in this meta-analysis. We pooled the odds ratios (OR), standardised mean difference (SMD) and conducted heterogeneity, and quality assessment. Results: The outcome of treatment effects included surgical blood loss, surgical time, postoperative complications, and post-operative length of hospital stay. Comparing open radical nephrectomy for kidney cancer patients, the pooled SMD of surgical time was 0.47, (95% confidential index CI = [0.09, 0.85]), the pooled SMD of operative blood loss was -68.98, (95% CI = [-99.63, -38.34]), the pooled SMD of post-operative length of hospital stay was -4.32, (95% CI = [-4.62, -4.03]), and the pooled OR of postoperative complications was 0.52, (95% CI = [0.30, 0.91]). Conclusion: LRN was found to significantly decrease patients' blood loss. In addition, LRN offers less post-operative length of hospital stay.

Keywords: Laparoscopic radical nephrectomy; Open radical nephrectomy; Meta-analysis

1 Introduction

Renal cell carcinoma (RCC) is a malignant tumor originating from renal tubular epithelial cells and accounts for roughly 90% of all malignant kidney cancer [1]. Kidney cancers account for 2% to 3% of all malignant tumors, with an incidence of 5.8/100000 [2]. According to reports, in the past 20 years, the incidence of kidney cancer is annually growing at a rate of 2% all the world [3]. RCC is not sensitive to chemotherapy and radiotherapy, and surgical resection, of which radical nephrectomy is recognized as a possible cure for kidney cancer [4]. In 1968, Roson et al first reported the use of open radical nephrectomy (ORN) for the treatment of renal cancer, which was to release the kidney outside the perirenal fascia, and then the perirenal fascia, perirenal fat, kidney and tumor, ipsilateral adrenal gland were all resected [5]. Parallel regional lymph node dissection was performed, including the abdominal aorta or the inferior vena cava lymph node from the diaphragm angle to the abdominal aorta bifurcation. The method described by Roson for the next few decades is recognized as the standard method for surgical treatment of kidney cancer. Regardless of the intraperitoneal route ORN or the lumbar route ORN, due to the huge incision in the operation area, postoperative patients recover slowly, and can have potential complications such as incisional hernia, wound infection, and liquefaction [6]. In 1991, Clayman et al first reported successful laparoscopic nephrectomy by intraperitoneal route. Subsequently, Guar invented a simple and practical balloon dilator to establish a retroperitoneal space technique, which enabled retroperitoneal laparoscopic renal surgery [7]. It is generally believed that the indication for laparoscopic radical nephrectomy (LRN) is that the renal tumor is confined to the renal capsule, and there is no peripheral tissue invasion and no local lymph node metastasis and venous tumor thrombus.

Meta-analysis is a powerful comprehensive method, which can perform systematic analysis and determination of multiple independent research results with the same research purposes. When individual experiments cannot be made clear, and the results or multiple results of the same purpose are contradictory, meta-analysis can be

***Corresponding author: Zejun Xiao,** Department of Urology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China, E-mail address: xiaozejunvol@163.com
Dong Wang, Jianzhong Shou, Changling Li, Nianzeng Xing, Department of Urology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

Open Access. © 2019 Dong Wang et al., published by De Gruyter. BY-NC-ND This work is licensed under the Creative Commons Attribution 4.0 License.

used to synthesize multiple identical experiments. Therefore, meta-analysis is especially suitable for multiple research results that are contradictory or different. This study aims to systematically review and analysize randomized controlled trials of LRN and ORN. Comparing the operation time of the two operations, the amount of intraoperative blood loss, the post-operative length of hospital stay, and the postoperative complications, can provide a basis for the choice of clinical surgical methods.

2 Methods

2.1 Searching method

We conducted a search of PubMed, Embase, Ovid, Splinger and Google Scholar databases that were published between 1993 and 2018. We limited the search to studies published in English. The medical subject heading terms and keywords used included "renal cell carcinoma", "RCC", "Laparoscopic", "open", "radical nephrectomy". Duplicate articles and unpublished studies from international meetings were excluded.

2.2 Inclusion criteria

Studies were selected carefully on the basis of following criteria: Compared studies of the effects of LRN with ORN in the treatment of renal cell carcinoma prospective and retrospective controlled studies; patients with renal cell carcinoma; information collected including surgical blood loss, surgical time, postoperative complications, postoperative hospital stay.

2.3 Excluding standard

Non-clinical controlled trials; non-kidney cancer research; other surgical treatment; data description is not clear.

2.4 Data extraction

Subjects and abstracts of the literature were independently collected by two authors, and if they were considered to be inconsistent with the inclusion criteria, they would be considered as unqualified studies. For all possible related trials, the full report was obtained as much as possible. Once the full text was obtained, the two authors independently extracted the following data: the author of the literature, the age of the publication, the type of design, the basic data of the patient, the operation time, the amount of blood loss, postoperative hospital stay, postoperative follow-up, etc. The independently extracted data were then compared. If there was any disagreement on any data extraction details, it was resolved through discussion and indicated on the data collection form.

2.5 Statistical analysis

We used RevMan (version 5.3) to perform all the statistical analyses. To obtain the pooled odds ratios (ORs), SMD with 95% confidence intervals (CIs), a random effects model was applied. The heterogeneity between and within trials was evaluated using chi-square test p value < 0.1 or an I^2 measure > 50%, based on a statement from the Cochrane Handbook.

3 Results

3.1 Literature searches and characteristics of eligible studies

Figure 1 shows the flow diagram of study selection process. After screening, we obtained 8 studies. The detailed characteristics for the 8 eligible studies are summarized in Table 1.

3.2 Meta-analysis of the operating time of LRN and ORN

The operating time is reported in four studies (Figure 2). The pooled SMD from these 4 studies was -0.60 (95% CI, [-1.96, 0.76], P=0.39). We performed a sensitivity analysis for included studies where we sequentially excluded each study from our meta-analysis. Using this approach, we found that heterogeneity was mainly caused by the studies of Vasdev 2011. Subsequently, the I^2 estimate of the variance between the studies is 63% and P= 0.06, which showed moderate heterogeneity. According to our analysis, the operating time of between LRN and ORN was significant (P = 0.01) and the operating time of LRN was less than ORN.

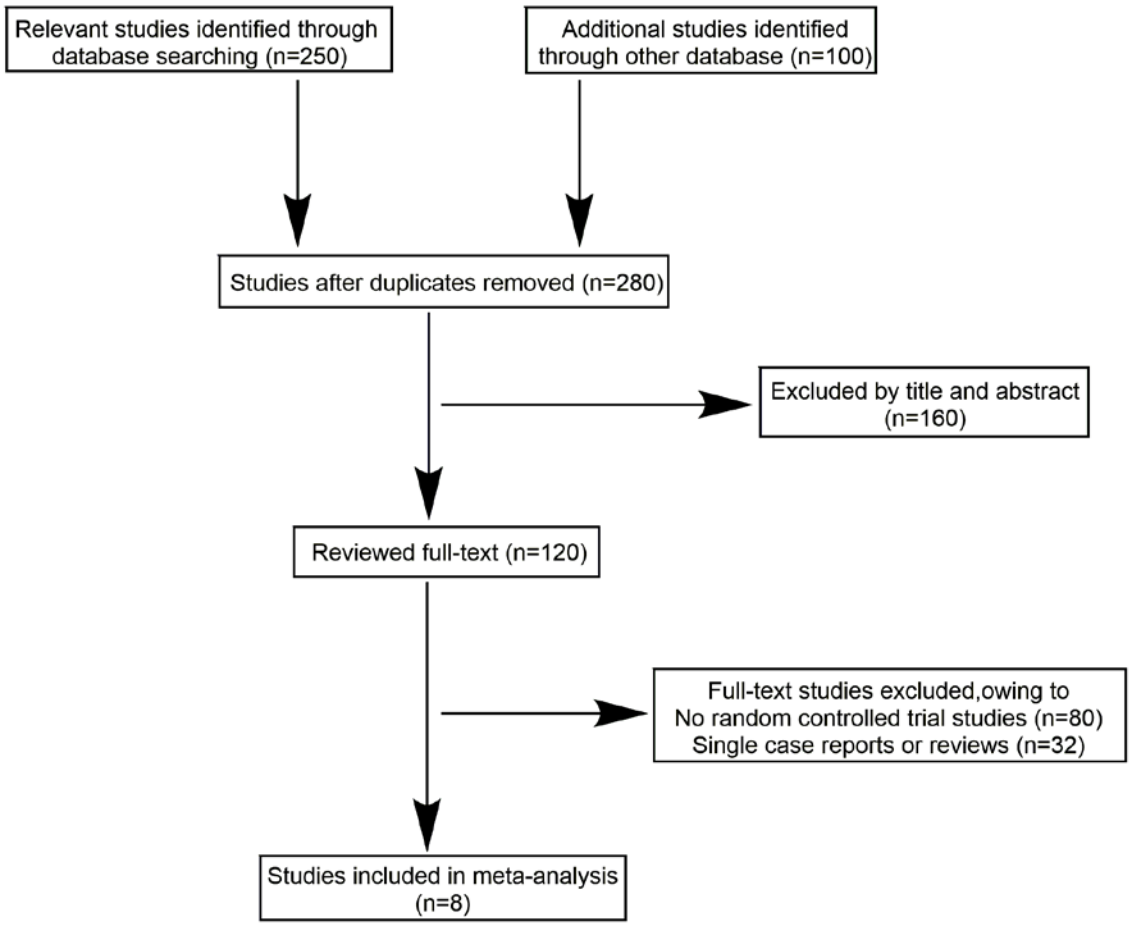

Figure 1: The study selection process

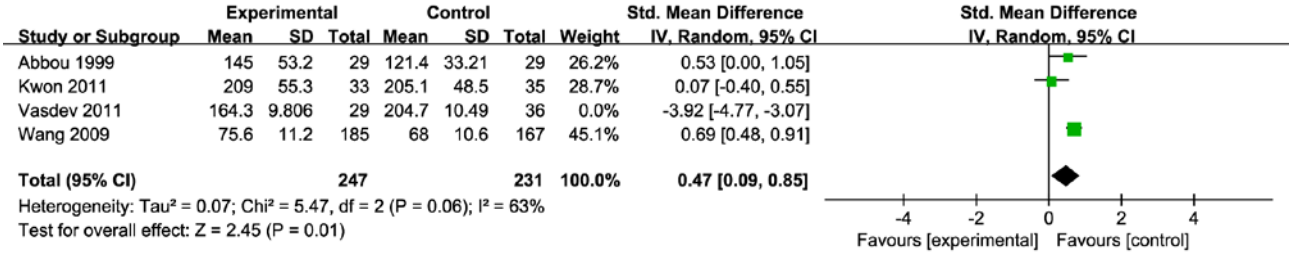

Figure 2: The forest plot for the operating time between LRN and ORN group

3.3 Meta-analysis of the operative blood loss of LRN and ORN

The operative blood loss is reported in four studies (Figure 3). Compared with ORN, LRN was associated with a 68.98ml reduction in blood loss (95% CI, [-99.63, -38.34]. The heterogeneity of the data was moderate (P = 0.03) while the I^2 estimate of the variance between the studies was 67%. According to our analysis, the difference between LH and OH was significant (P < 0.00001). LRN significantly decreases patients' blood loss.

3.4 Meta-analysis of the post-operative length of hospital stay of LRN and ORN

The post-operative length of hospital stay is reported in three studies (Figure 4). Data from these 3 studies was

Table 1: Baseline characeristics of included studies

References	country	Group	NO. of patients	Age (years)	Male/female
Abbou 1999 (13)	France	LRN	29	63.0	17/12
		ORN	29	58.8	16/13
Bensalah 2009 (14)	France	LRN	44	65±13	28/16
		ORN	135	63±11	86/49
Jeon 2011 (15)	Korea	LRN	88	57.8±12.4	58/30
		ORN	167	55.1±13.2	104/63
Kwon 2011 (16)	Korea	LRN	33	56.1±11.9	24/9
		ORN	35	55.0±10.8	22/13
Laird 2015 (17)	UK	LRN	25	66.7 (60.6-73.2)	16/9
		ORN	25	65.6 (58.0-74.8)	16/9
Vasdev 2011 (18)	UK	LRN	29	81.8±0.5	16/13
		ORN	36	82.6±0.4	20/16
Wang 2009 (19)	China	LRN	185	60.4±17.5	102/83
		ORN	167	63.1±18.3	89/78
Xu 2014 (20)	China	LRN	88	56.5±13.3	55/33
		ORN	526	57.32±12.4	341/185

Age is exhibited as the mean ± standard deviation (SD) or median (range)

analyzed in a random-effects model and the pooled OR was -3.55 (95% CI, [-5.62, -1.47]). The I^2 estimate of the variance between the studies was 97% and $P < 0.00001$, which showed high heterogeneity. We performed a sensitivity analysis for included studies where we sequentially excluded each study from our meta-analysis. Using this approach, we found that heterogeneity was mainly caused by the studies of Xu 2014. Subsequently, the I^2 estimate of the variance between the studies is 0% and $P = 0.44$, which showed low heterogeneity. According to our analysis, the operating time of between LRN and ORN was significant ($P < 0.00001$) and the post-operative length of hospital stay of LRN was less than ORN.

3.5 Meta-analysis of the postoperative complications of LRN and ORN

The postoperative complications are reported in four studies (Figure 5). Random-effects meta-analysis demonstrated that patients with LRN had higher postoperative complications compared with ORN (OR=0.52; 95% CI, [0.30, 0.91]). The I^2 estimate of the variance between these studies was 27% and P = 0.25, which showed no significant heterogeneity. According to our analysis, the perioperative mortality of LRN was higher than ORN ($P = 0.02$).

4 Discussion

Open radical nephrectomy has a clear clinical effect and simple operation features. At the same time, it is accompanied by radical nephrectomy, which can easily damage blood vessels, cause massive hemorrhage, damage the pleura, cause postoperative infection and other complications. There are many layers of muscles that need to be cut off during surgery, and the wounds are long. Besides, every muscle layer needs stitches so that the recovery time is long. Compared with open radical nephrectomy, laparoscopic radical nephrectomy has a very obvious advantage. The therapeutic effect of laparoscopic radical nephrectomy is similar to that of open radical nephrectomy, which avoids damage to blood vessels during surgery.

This study systematically analyzed the clinical effects of LRN and ORN. The operative time, operative blood loss, post-operative length of hospital stays and postoperative complications were selected in the laparoscopic radical nephrectomy group and the open radical nephrectomy group. Studies have shown that after surgery with LRN, the operation time, intraoperative blood loss, hospital stay were better than ORN ($P < 0.05$). In summary, LRN can safely and effectively remove renal tumors, which can achieve the same clinical effects as ORN.

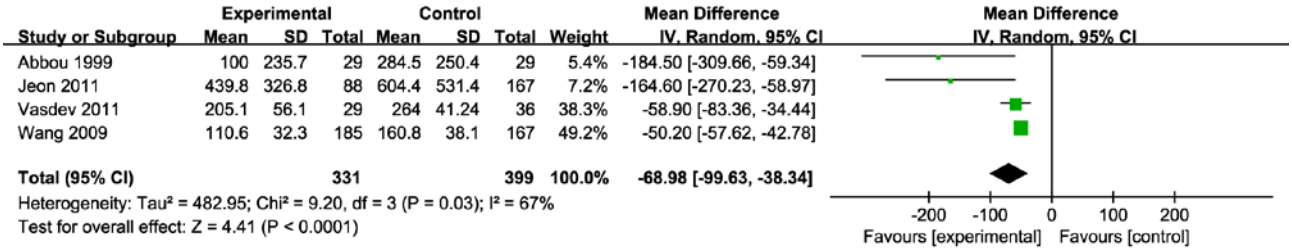

Figure 3: The forest plot for the operative blood loss between LRN and ORN group

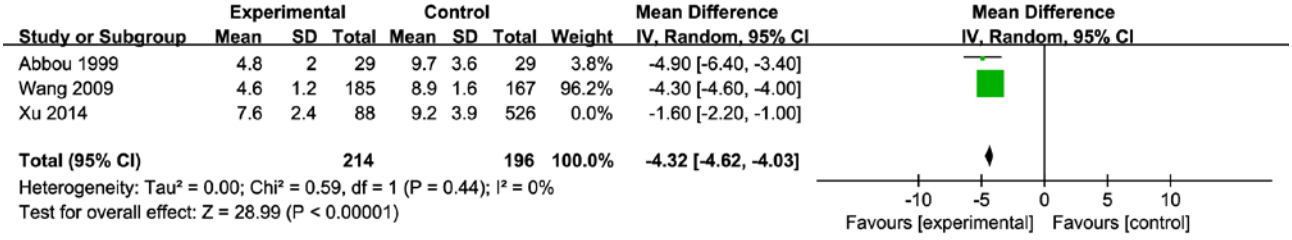

Figure 4: The forest plot for the post-operative length of hospital stay between LRN and ORN group

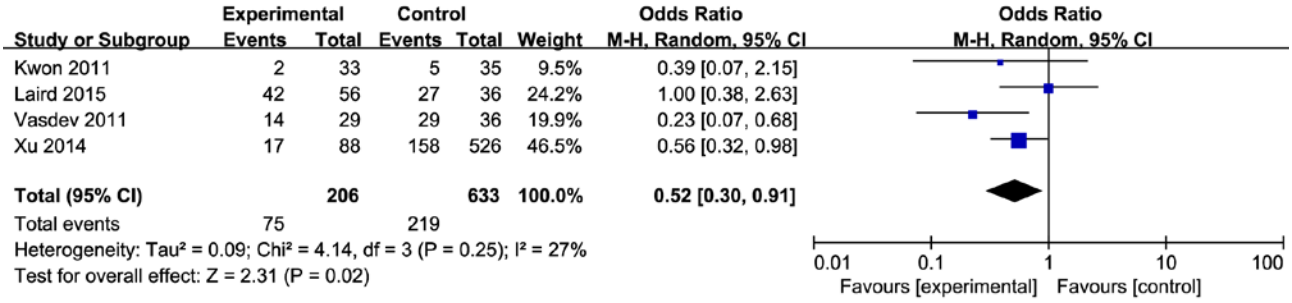

Figure 5: The forest plot for the postoperative complications between LRN and ORN group

Due to the development of partial nephrectomy, ablation and cryoablation, LRN is becoming less in the application of small renal cancer and small renal cell carcinoma [8]. With the continuous development of laparoscopic technology, the application range of LRN is expanding. For large size renal tumor, technical problems have also been raised for the application of LRN [9]. An increase in tumor volume will reduce the space for surgery, causing the corresponding lymph nodes to enlarge. The possibility of cancer rupture and the possibility of surgery to cause tumors to invade other organs are enhanced [10]. For these reasons, open radical nephrectomy is a technical challenge for larger tumor treatments. However, LRN has the advantages of sufficient operation space, clear anatomical landmark position and mature technology. In theory, the treatment of larger tumors is a more sensible choice. There should be a clear range for the size of the tumor to which the LRN is applied. Dunn et al reported that LRN can be selected for tumor size range <10 cm [11]. Hemal et al reported a tumor size range of 7 to 10 cm [12]. However, the extent of tumor size is not a factor in determining LRN use. Advances in laparoscopic techniques and increasing surgeon experience have helped to improve the adverse effects of LRN on larger kidney cancers.

Meta-analysis is based on existing literature for analysis, belonging to the second analysis, so the quality of the literature will affect the accuracy and objective of the analysis. This meta-analysis has the some shortcomings. Renal cancer surgery is a surgical procedure taken in view of the patient's basic condition. There is no randomized and double-blind approach. However, the baseline level between the two groups is not statistically significant, and

the level of surgery performed by the doctor at the same time will cause certain quality bias. The length of the study varies, especially in studies without long-term survival, some of which affect the accuracy of the analysis, and the data is a retrospective analysis. The length of the study varies, especially in studies without long-term survival, some of which affect the accuracy of the analysis. This meta-analysis cannot be further stratified from other possible confounding factors. The conclusions of this study need to be confirmed by more detailed data. Meta-analysis is not an experimental study, and publication bias may occur during the study, which is an inherent limitation of meta-analysis. Therefore, in order to obtain more scientific experimental results, large-sample, high-quality randomized controlled double-blind experiments are still needed to obtain high-quality evidence-based medical evidence.

Funding: This work was supported by The National Science and Technology Major Project of the Ministry of Science and Technology of China (2017ZX09304015).

Conflicts of interest: The authors have no conflicts of interest to declare.

References

[1] Haque I, Subramanian A, Huang CH, Godwin AK, Van Veldhuizen PJ, Banerjee S, et al. The Role of Compounds Derived from Natural Supplement as Anticancer Agents in Renal Cell Carcinoma: A Review. International Journal of Molecular Sciences 2018;19(1):107

[2] Arabsalmani M, Mohammadian-Hafshejani A, Ghoncheh M, Hadadian F, Towhidi F, Vafaee K, et al. Incidence and mortality of kidney cancers, and human development index in Asia; a matter of concern. J Nephropathol 2017;6(1):30-42

[3] Mohammadian M, Pakzad R, Towhidi F, Makhsosi BR, Ahmadi A, Salehiniya H. Incidence and mortality of kidney cancer and its relationship with HDI (Human Development Index) in the world in 2012. Clujul Medical 2017;90(3):286-293

[4] Sandhu SS, Symes A, A'Hern R, Sohaib SA, Eisen T, Gore M, et al. Surgical excision of isolated renal-bed recurrence after radical nephrectomy for renal cell carcinoma. British Journal of Urology International 2015;95(4):522-525

[5] Laird A, Choy KCC, Delaney H, Cutress ML, O'Connor KM, Tolley DA, et al. Matched pair analysis of laparoscopic versus open radical nephrectomy for the treatment of T3 renal cell carcinoma. World Journal of Urology 2015;33(1):25-32

[6] Alberto B, Antonio F, Gunter J, Francesco P, Francesco M. Complications of laparoscopic surgery for renal masses: prevention, management, and comparison with the open experience. European Urology 2009;55(4):836-850

[7] Benoit T, Peyronnet B, Roumiguié M, Verhoest G, Beauval JB, Delreux A, et al. Laparoscopic nephrectomy for polycystic kidney: comparison of the transperitoneal and retroperitoneal approaches. World Journal of Urology 2016;34(7):901

[8] Lee C, You D, Yoo S, Song C, Hong B, Hong JH, et al. Oncological outcomes of patients with incidental pathological T3a stage small renal cell carcinoma after partial nephrectomy. Journal of Cancer Research & Clinical Oncology 2016;142(7):1651-1657

[9] Bolton EM, Hennessy D, Lonergan PE, Darcy FT, Manecksha RP, Lynch TH. Evaluating the perioperative safety of laparoscopic radical nephrectomy for large, non-metastatic renal tumours: a comparative analysis of T1-T2 with T3a tumours. Irish Journal of Medical Science (1971 -) 2017(5):1-6

[10] Fenn NJ, Gill IS. The expanding indications for laparoscopic radical nephrectomy. Bju International 2004;94(6):761-765

[11] Dunn MD, Portis AJ, Shalhav AL, Elbahnasy AM, Heidorn C,., Mcdougall EM, et al. Laparoscopic versus open radical nephrectomy: a 9-year experience. Journal of Urology 2000;164(4):1153-1159

[12] Hemal AK, Kumar A, Kumar R, Wadhwa P, Seth A, Gupta NP. Laparoscopic versus open radical nephrectomy for large renal tumors: a long-term prospective comparison. J Urol 2007;177(3):862-866

[13] Abbou CC, Cicco A, Gasman D, Hoznek A, Antiphon P, Chopin DK, et al. Retroperitoneal laparoscopic versus open radical nephrectomy. J Urol 1999;161(6):1776-1780

[14] Bensalah K, Salomon L, Lang H, Zini L, Jacqmin D, Manunta A, et al. Survival of patients with nonmetastatic pT3 renal tumours: a matched comparison of laparoscopic vs open radical nephrectomy. BJU Int 2009;104(11):1714-1717

[15] Jeon SH, Kwon TG, Rha KH, Sung GT, Lee W, Lim JS, et al. Comparison of laparoscopic versus open radical nephrectomy for large renal tumors: a retrospective analysis of multi-center results. BJU Int 2011;107(5):817-821

[16] Kwon SY, Jung JW, Kim BS, Kim TH, Yoo ES, Kwon TG. Laparoscopic versus Open Radical Nephrectomy in T2 Renal Cell Carcinoma: Long-Term Oncologic Outcomes. Korean J Urol 2011;52(7):474-478

[17] Laird A, Choy KC, Delaney H, Cutress ML, O'Connor KM, Tolley DA, et al. Matched pair analysis of laparoscopic versus open radical nephrectomy for the treatment of T3 renal cell carcinoma. World J Urol 2015;33(1):25-32

[18] Vasdev N, Hussein HK, Davidson A, Wood H, O'Riordan A, Soomro NA. Radical renal surgery (laparoscopic and open) in octogenarians. Surgeon 2011;9(3):135-141

[19] Wang L, Wang L, Yang Q, Xiao C, Sun Y. Retroperitoneal laparoscopic and open radical nephrectomy for T1 renal cell carcinoma. J Endourol 2009;23(9):1509-1512

[20] Xu H, Ding Q, Jiang HW. Fewer complications after laparoscopic nephrectomy as compared to the open procedure with the modified Clavien classification system--a retrospective analysis from southern China. World J Surg Oncol 2014;12:242