RETROPERITONEAL LAPAROSCOPIC NEPHRECTOMY FOR RENAL TUBERCULOSIS: A META-ANALYSIS AND SYSTEMATIC REVIEW

***Zaky Ariandy, Firman Nugroho.**

RSU Santo Yoseph Labuan Bajo, Manggarai Barat, Nusa Tenggara Timur, Indonesia.

ABSTRACT

Introduction: *Renal tuberculosis is one of the most common form of urogenital tuberculosis.* ***Objective:*** *This study aims to compare the outcomes of retroperitoneal laparoscopic nephrectomy (RLN) compared to other surgical approaches for treating renal tuberculosis.* ***Material &Methods:*** *A comprehensive search of the scientific literature was conducted using databases such as PubMed, Scopus, ScienceDirect, and Cochrane to identify randomized controlled trials (RCTs) as well as prospective and retrospective studies comparing the effectiveness of RLN with other treatments (transperitoneal laparoscopic nephrectomy and open surgery) in the management of renal tuberculosis. Data from the included studies were pooled and analyzed.* ***Results:*** *A total of 6 cohort studies were incorporated into this meta-analysis. The overall RLN was associated with a significantly shorter length of stay (WMD: −1.92; 95% CI: −3.22, - 0.62; p = 0.004). The terms of operative duration (p = 0.56), blood loss (p = 0.59), and overall complications (p = 0.76) did not show any differences. The present meta-analysis has limitations that need to be considered. The limited number of research studies may have impacted the statistical findings, and all the studies included were observational, which may have resulted in bias. Blinding was not implemented, and there was high heterogeneity in some outcomes, which may have affected the accuracy of the results. Recalculating the mean and standard deviation could have introduced bias.* ***Conclusion:*** *RLN shows a potential advantage regarding the lower length of stay.*

Keywords: *Urogenital tuberculosis, nephrectomy, laparoscopy.*

ABSTRAK

Pendahuluan: *Tuberkulosis renal merupakan salah satu bentuk tuberkulosis urogenital yang paling umum.* ***Tujuan:*** *Penelitian ini bertujuan untuk membandingkan hasil NefrektomiLaparoskopi Retroperitoneal (NLR) dengan metode pembedahan lain dalam menangani tuberkulosis renal.* ***Bahan & Cara:*** *Dilakukan pencarian literatur pada beberapa database seperti PubMed, Scopus, ScienceDirect, dan Cochrane seperti randomized controlled trials (RCTs) serta penelitian prospektif dan retrospektif yang membandingkan hasil NLR dengan metode lain (nefrektomi laparoskopi transperitoneal dan operasi terbuka) dalam menangani tuberkulosis renal. Data dari penelitian yang diinklusi kemudian digabungkan dan dianalisis.* ***Hasil:*** *Sebanyak enam penelitian diinklusi dalam meta-analisis ini. RLN ditemukan memiliki waktu rawat inap yang lebih singkat (WMD: −1.92; 95% CI: −3.22, - 0.62; p = 0.004). Tidak ditemukan perbedaan yang signifikan pada aspek durasi operasi (p = 0.56), kehilangan darah (p = 0.59), dan komplikasi secara keseluruhan (p = 0.76). Meta analisis ini memiliki beberapa keterbatasan. Jumlah penelitian yang terbatas mungkin dapat berdampak pada hasil analisis. Selain itu, semua penelitian yang diinklusi bersifat observasionalsehingga dapat menyebabkan bias. Blinding tidak dilakukan dan terdapat tingkat heterogenitas yang tinggi sehingga dapat mempengaruhi hasil. Bias juga dapat disebabkan oleh perhitungan ulang rata-rata dan standar deviasi.* ***Simpulan:*** *NLR menunjukkan keuntungan pada aspek durasi rawat inap yang lebih rendah.*

Kata kunci: *Tuberkulosis urogenital, nefrektomi, laparoskopi.*

Correspondence: Zaky Ariandy; c/o: RSU Santo Yoseph Labuan Bajo. JL. Sunter Hijau 1 Blok B4 No. 2, Sunter Jaya, Tanjung Priok, Jakarta Utara 14350, Indonesia. Email: zakyariandy@gmail.com.

INTRODUCTION

Renal tuberculosis is the most common type of urogenital tuberculosis. Antituberculosis chemotherapy for six months is the mainstay treatment of urogenital tuberculosis, but even so, surgical treatment is still warranted in cases with nonfunctioning organs, complications, and extensive spread.[1]

Retroperitoneallaparoscopic nephrectomy (RLN) is a minimally invasive procedure that has been increasingly used in treating kidney diseases,

especially squamous cell carcinoma. The retroperitoneal approach involves dissecting the kidney from the posterior aspect.[2] This technique has shown better outcomes than open nephrectomy (ON) by reducing the length of stay and yielded similar or better results to transperitoneal laparoscopic nephrectomy (TLN).[3,4]

However, the efficacy and safety of retroperitoneal laparoscopic nephrectomy compared to other treatments in renal tuberculosis have conflicting results in the literature. A systematic review and meta-analysis were conducted to synthesize the available data on retroperitoneal laparoscopic nephrectomy for treating renal tuberculosis, focusing on outcomes such as disease control, complication rates, length of hospital stay, and overall patient outcomes. This information may thus help decision-making and improve the overall outcome of the patients.

OBJECTIVE

This study aims to compare the outcomes of retroperitoneal laparoscopic nephrectomy (RLN) compared to other surgical approaches for treating renal tuberculosis.

MATERIAL & METHODS

This study adhered to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) 2020 guideline.

The literature search for this systematic review was conducted independently by two reviewers (AZ and FN) in relevant electronic databases, including PubMed, Scopus, ScienceDirect, and Cochrane. The search was limited to articles published up to April 1st, 2023. The combined search phrases used in creating the search string were: ("renal tuberculosis" OR "tuberculous nephritis" OR "tuberculous pyelonephritis" OR "renal TB") AND ("nephrectomy" OR "kidney removal" OR "renal surgery") AND ("retroperitoneal" OR "retroperitoneal approach") AND ("outcome" OR "results" OR "prognosis" OR "complications" OR "mortality"). Truncation, wildcards, and Boolean operators were used to refine the search. Articles were included if they were written in English or Bahasa Indonesia. The reference lists of included articles were cross-checked to ensure the relevant information was included. Any disagreements between the reviewers were resolved through discussion, and a third reviewer (DG) was consulted for a final decision when consensus could not be reached. The search strategy adhered to the PRISMA guideline for systematic reviews and meta-analyses.

The selection of relevant literature for this meta-analysis followed the PICOS principles. The population (P) included patients diagnosed with renal tuberculosis. The intervention (I) of interest was retroperitoneal laparoscopic nephrectomy, while the comparison (C) group included other surgical interventions or medical treatments for renal tuberculosis. The outcomes (O) of interest were treatment efficacy regarding operative duration, blood loss, length of hospital stay, and overall complications. Studies (S) eligible for inclusion were randomized controlled trials (RCTs) and prospective or retrospective observational studies. Exclusion criteria were single-arm studies that did not compare retroperitoneal laparoscopic nephrectomy to other interventions, conference abstracts, reviews, case reports, and unpublished studies. Additionally, studies with incomplete or unavailable data were excluded from the analysis.

The data collection process involved independent extraction of data by two reviewers (ZA and FN) using a standardized data extraction form created on Microsoft Excel. The data items collected included: (1) study characteristics such as author, year of publication, study design, sample size, and country of origin; (2) patient characteristics such as age, gender, and BMI; (3) intervention details including the type of retroperitoneal laparoscopic nephrectomy performed; (4) comparison group details such as type of surgical intervention or medical treatment for renal tuberculosis used in the studies; and (5) outcomes of interest, including treatment efficacy in terms of duration of surgery, length of hospital stay, blood loss, blood transfusion, and overall complications.

The quality assessment of the studies included in the meta-analysis was performed using the Newcastle-Ottawa Scale (NOS) for cohort studies. Additionally, each study's evidence level was assessed using the Oxford Evidence-Based Medicine Center criteria. Any disagreements between the reviewers regarding the inclusion of studies or the quality assessment were resolved through discussion or with the assistance of a third reviewer when necessary.

This meta-analysis was conducted using Review Manager Version 5.0 (The Cochrane

Collaboration, Oxford, London, UK) and SPSS Version 25 for Mac (IBM Corp., Armonk, NY). Dichotomous and continuous variables were expressed using odds ratios (ORs) and weighted mean differences (WMDs), respectively. Data from studies reporting only medians, quartiles, or extreme ranges were converted to means and standard deviations (SDs).[5] All outcomes were reported with 95% CIs. Statistical heterogeneity between studies was tested using the chi-square test and inconsistency (I2). The pooled effect size results are expressed by the Z test and are statistically significant at $p < 0.05$. Random effects are applied when I2> 50%. If not, a fixed effects model is employed. Sensitivity analysis was performed to assess the robustness between studies through an exclusion-by-exclusion method. In addition, confounding factors such as year of publication, region, and study design between studies were assessed by meta-regression tests.

When the number of studies included was ten or more, funnel plot and Egger's regression test are considered reliable in detecting potential bias in the literature. As the included studies were only six, funnel plots and Egger's regression tests were not applicable for assessing publication bias. However, we still performed a visual inspection of the forest plots to detect any asymmetry, which may indicate the presence of publication bias.

RESULTS

A total of 263 publications were initially identified through the search strategy. After removing duplicates and screening the titles, abstracts, and full texts, 6 cohort studies were included in this meta-analysis.[6-11] Four other articles seemed to meet the inclusion criteria but were ultimately excluded because they do not have any comparison to other treatments [12-14] and one article compares treatment with other non-tuberculous diseases.[15] These studies were conducted between 2000 and 2019 and were carried out in China (4 studies), India (1 study), and South Korea (1 study).

Figure 1 shows the PRISMA flow chart. In total, 481 patients were included in the meta-analysis, with 273 undergoing RLN and 204 undergoing other types of nephrectomy (ON and TLN).Summarizes the relevant features and variables of the study. There were no significant differences between the two groups in terms of male gender (p=0.31), BMI (p=0.26), and age (p=0.36)

One of the cohorts was of good quality, while the quality of the studies overall was mostly moderate or poor.A total of six studies were included in the analysis for operating time (OT), with a total of 477 patients, 273 of whom underwent RLN and 204 who underwent other treatments. Pooled results revealed that RLN had a longer operating time,

Table 1. .Overview of included studies.

Reference	Study Design	Approach	Patient(s)	Comparability	Quality score	Level of evidence
Li (2019) [6]	Cohort	RLN	158	1, 3	5	3
		Open	100			
Chen (2018) [9]	Cohort	RLN	11	1, 2, 3	5	3
		TLN	13			
Zhang (2016) [11]	Cohort	RLN	69	1, 2, 3	4	3
		Open	51			
Zhang (2005) [7]	Cohort	RLN	22	1, 2	6	3
		Open	22			
Kim (2000) [10]	Cohort	RLN	4	-	5	2
		TLN	9			
Hemal (2000) [8]	Cohort	RLN	9	1, 2	5	3
		Open	9			

Comparability: 1 = gender (M/F); 2 = age (years); 3 = body mass index

although this was not statistically significant (p=0.56). The studies also assessed estimated blood loss (EBL), and the pooled results suggested that RLN resulted in lower EBL than other treatments, but this was statistically insignificant (p = 0.59). The studies also analyzed hospital stay (LOS), and the pooled results showed that RLN had a significantly shorter LOS than other treatments (WMD: −1.92; 95% CI: −3.22, - 0.62; p = 0.004). However, regarding overall complications, there was no statistically significant difference between surgical approaches (odds ratio [OR]: 0.92; 95% CI: 0.55, 1.55; p=0.76). The rate of overall complications in RLN was 15.38%, with 42 out of 273 cases experiencing complications, while the rate in other approaches was 19.12%, with 39 out of 204 cases experiencing complications.

The results of our study indicated a high degree of heterogeneity in the outcomes of interest, which included operative time (OT), estimated blood loss (EBL), and length of stay (LOS) among the studies we analyzed. Although most of the studies were of moderate or low quality, we attempted to minimize potential sources of bias through a meta-regression analysis that considered factors such as region, year of publication, and study design. However, our analysis did not identify any significant sources of heterogeneity (p > 0.05). Nevertheless, it is crucial to recognize that studies with small sample sizes may introduce some degree of bias that cannot be entirely eliminated. We also assessed for potential publication bias using funnel plot evaluations and observed no indication of bias for OT, EBL, and LOS outcomes..

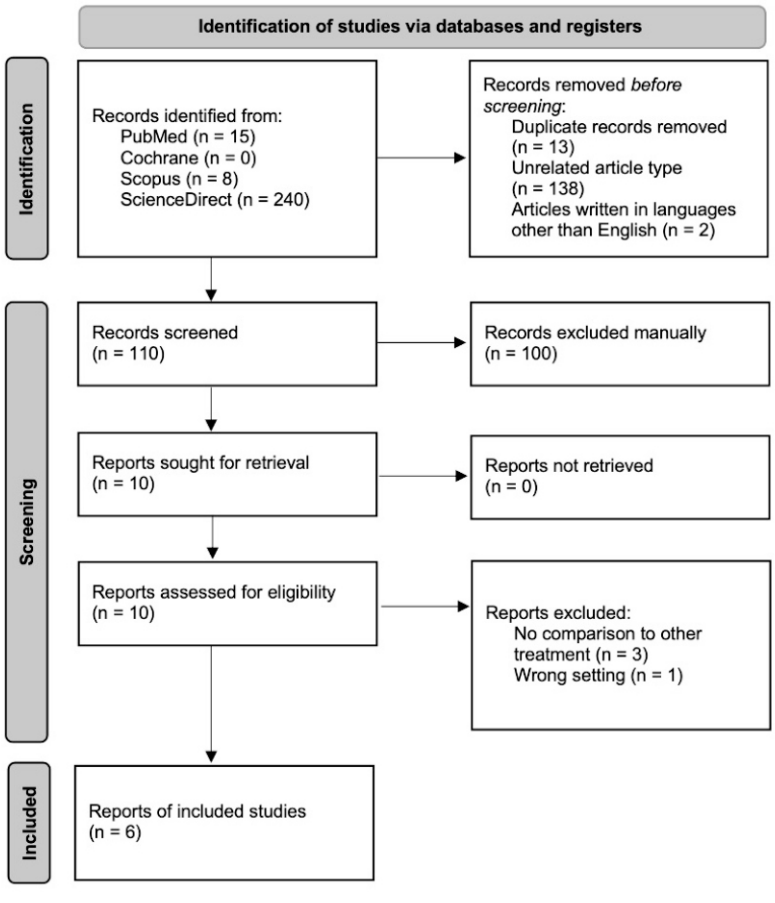

Figure 1.PRISMA Flow Chart.

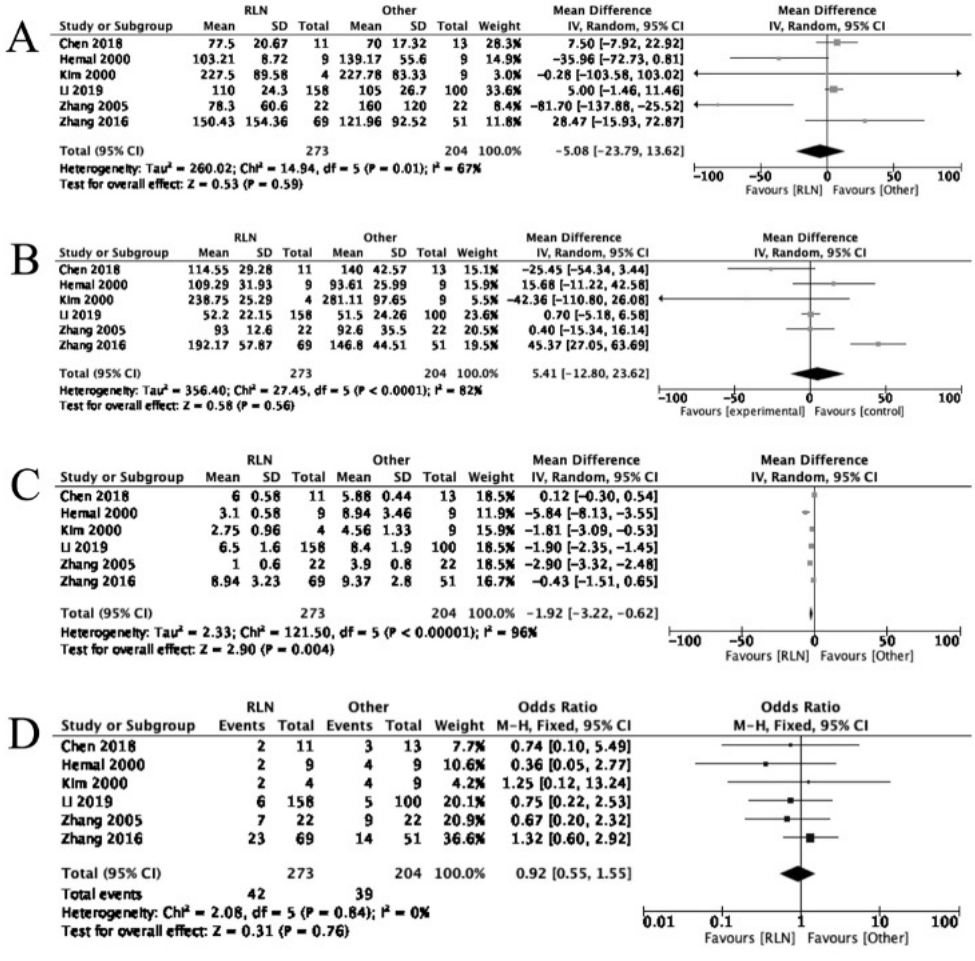

Figure 2. Forest plot of outcomes: A Blood loss (ml); B Operative duration (min); C Length of stay (day); D Overall complications

DISCUSSION

Although we did not find significant differences in operative duration between RLN and other approaches, it is essential to note that the surgeon's skill and familiarity with a specific approach can play a role. Chen (2018) found that operative duration was similar between transperitoneal and retroperitoneal approaches because of the surgeon's familiarity with the former.9 However, it is worth considering that RLN has a smaller operation space and a higher risk of losing direction, which may contribute to a longer operative duration as surgeons require time to become oriented to the view presented by retroperitoneoscopy.[8,16] Additionally, Li (2019) reported that enlargement of pyonephrosis may narrow the retroperitoneal space, making it challenging to use surgical instruments and perform single-port surgical procedures.[6]

Our analysis did not reveal significant differences in estimated blood loss between RLN and other approaches. However, previous studies have highlighted certain challenges associated with retroperitoneal laparoscopic procedures that may contribute to increased blood loss. Pyonephrosis enlargement and swollen lymph nodes at the renal hilus may make it challenging to identify the renal vessels and lead to bleeding. At the same time, it is also noted that renal tuberculosis can cause severe perinephritis and widespread adhesion of the perirenal and renal hilum, making it challenging to separate adhesion tissues with laparoscopy. Despite these potential challenges, it is found that blocking the renal artery near the abdominal artery before freeing the kidney can decrease hemorrhage and

facilitate specimen removal. It is also worth noting that, although we did not observe any significant differences, RLN has the disadvantages of limited working space, difficulty in identifying the anatomical structure, and a longer learning curve compared to the transperitoneal approach, which may lead to increased blood loss.[12] Further research is needed to fully elucidate the impact of these factors on operative duration and blood loss during RLN and other approaches. The lack of significant differences in operative duration and estimated blood loss may suggest that RLN is a safe and feasible option for patients with renal tuberculosis and that it can be performed with similar efficiency as other approaches.

Our meta-analysis shows no significant difference in complications between RLN and other surgical approaches, including TLN and open surgery. However, our analysis indicates that RLN has a lower overall complication rate. The most common complications reported in the studies were the leakage of caseous material and subcutaneous emphysema, but they were treated promptly without any long-term effects. The studies also reported other complications like fever, abdominal tuberculosis, pneumonia, wound infection, hematoma in retroperitoneum, renal vein injury, and lumbar vein injury.[12,14,15] It's worth noting that the TLN approach risks disseminating tuberculosis into the abdominal cavity. However, antituberculosis chemotherapy administered for two weeks before surgery can help control active TB and reduce the risk of dissemination, adhesion, and other complications. Moreover, studies have shown that kidneys with large lesions correlate with higher complication rates, which should be considered when deciding on the most appropriate surgical approach.[17,18]

One of the significant advantages of RLN over other surgical approaches is its significantly lower LOS, which we found in our meta-analysis. There are a few possible reasons for this. Firstly, RLN has been associated with lower complication rates, which may reduce the length of stay required to treat these complications. Secondly, compared to TLN and open surgery, RLN is less likely to interfere with bowel activity. This may result in a faster resumption of oral intake and a shorter LOS. In contrast, TLN and open surgery often require bowel mobilization, which can cause damage to gastrointestinal function and delay the resumption of oral intake. This delay in the resumption of oral intake and bowel activity may result in a longer LOS, as patients cannot tolerate solid food and thus cannot be discharged. [19,20] It is also possible that other factors, such as patient characteristics or postoperative care, may contribute to the differences in LOS observed between RLN and other surgical approaches. However, our meta-regression analysis did not identify any significant sources of heterogeneity that could explain these differences. Additional research is needed to fully understand the factors contributing to LOS in patients undergoing RLN and other surgical approaches. Nonetheless, the evidence suggests that RLN may be a favorable surgical option for reducing LOS in patients with renal tumors.

LIMITATION

The present meta-analysis has several limitations that should be considered when interpreting the results. Firstly, the study included a limited number of research studies, which may have affected the reliability of statistical findings. Secondly, all included studies were retrospective cohort studies, which may have resulted in bias compared to randomized controlled trials. Additionally, blinding was not implemented in the studies, which may have affected the accuracy of the results. Furthermore, there was high heterogeneity in some of the outcomes despite our efforts to minimize potential sources of bias through meta-regression analysis. It is also worth noting that some of the included studies reported median and interquartile ranges, which required recalculating the mean and standard deviation, potentially introducing bias. Lastly, all of the approaches were conducted by different surgeons with varying levels of experience and expertise, which may have impacted the accuracy of our comparison. Despite these limitations, our findings contribute to the current literature on operative duration, blood loss, length of stay, and overall complication for RLN compared to other surgical approaches. Further studies, particularly randomized controlled trials, are needed to confirm our findings and address the limitations of this meta-analysis.

CONCLUSION

Our analysis suggests that RLN may have a potential advantage regarding the lower length of stay. However, RLN shows similar outcomes in

other aspects when compared to TLN and open surgery. Because of the high heterogeneity among studies, additional evidence is required, preferably from randomized controlled trials.

ACKNOWLEDGEMENT

We would like to express our gratitude for the support and guidance provided throughout this meta-analysis and systematic review.

REFERENCES

1. Çek M, Lenk S, Naber KG, Bishop MC, Bjerklund Johansen TE, Botto H, et al. EAU guidelines for the management of genitourinary tuberculosis. Eur Urol. 2005;48(3):353-62.
2. Ren T, Liu Y, Zhao X, Ni S, Zhang C, Guo C, et al. Transperitoneal Approach versus Retroperitoneal Approach: A Meta-Analysis of Laparoscopic Partial Nephrectomy for Renal Cell Carcinoma. PLoS ONE. 2014 Mar 21;9(3):e91978.
3. Fu J, Ye S, Ye H jian. Retroperitoneal Versus Transperitoneal Laparoscopic Partial Nephrectomy: A Systematic Review and Meta-analysis. Chin Med Sci J Chung-Kuo Hsueh Ko Hsueh Tsa Chih. 2015 Dec;30(4):239-44.
4. Garg M, Singh V, Sinha RJ, Sharma P. Prospective randomized comparison of transperitoneal vs retroperitoneal laparoscopic simple nephrectomy. Urology. 2014 Aug;84(2):335-9.
5. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005 Apr 20;5(1):13.
6. Li X, Liu ZJ, Liu JW, Cai M, Chen S, Yu T, et al. A clinical comparative analysis of retroperitoneal laparoscopic tuberculous nephrectomy and open tuberculous nephrectomy. J Laparoendosc Adv Surg Tech A. 2019 Jul;29(7):909-13.
7. Zhang XU, Zheng T, Ma X, Li HZ, Li LC, Wang SG, et al. Comparison Of Retroperitoneoscopic Nephrectomy Versus Open Approaches To Nonfunctioning Tuberculous Kidneys: A Report Of 44 Cases. J Urol. 2005 May;173(5):1586-9.
8. Hemal AK, Gupta NP, Kumar R. Comparison of retroperitoneoscopic nephrectomy with open surgery for tuberculous nonfunctioning kidneys. J Urol. 2000 Jul;164(1):32-5.
9. Chen Y, Zheng H, Liang G, Wang D, Qiu J, Fang Y. Comparison of transperitoneal and retroperitoneal laparoscopic nephrectomy for nonfunctional tuberculous kidneys: A single-center experience. J Laparoendosc Adv Surg Tech A. 2018 Mar;28(3):325-9.
10. Kim HH, Lee KS, Park K, Ahn H. Laparoscopic nephrectomy for nonfunctioning tuberculous kidney. J Endourol. 2000 Jun;14(5):433-7.
11. Zhang S, Luo Y, Wang C, Xiong H, Fu SJ, Yang L. Open surgery versus retroperitoneal laparoscopic nephrectomy for renal tuberculosis: A retrospective study of 120 patients. PeerJ. 2016;2016(11).
12. Tian X, Wang M, Niu Y, Zhang J, Song L, Xing N. Retroperitoneal laparoscopic nephroureterectomy for tuberculous nonfunctioning kidneys: A single-center experience. Int Braz J Urol. 2015;41(2):296-303.
13. Li C, Yang Y, Xu L, Qiu M. Retroperitoneal laparoscopic nephroureterectomy with distal and intramural ureter resection for a tuberculous non - functional kidney. Int Braz J Urol. 2018;44(6):1174-81.
14. Xu B, Hu J, Chen A, Hao Y, Liu G, Wang C, et al. Risk Factors Related with Retroperitoneal Laparoscopic Converted to Open Nephrectomy for Nonfunctioning Renal Tuberculosis. J Endourol. 2017;31(6):588-92.
15. Chibber PJ, Shah HN, Jain P. Laparoscopic nephroureterectomy for tuberculous nonfunctioning kidneys compared with laparoscopic nephroureterectomy for other diseases. J Laparoendosc Adv Surg Tech A. 2005 Jun;15(3): 308-11.
16. M M, Sb B, A O, W J, Sb M, K V, et al. Vena caval transection during retroperitoneoscopic nephrectomy: report of the complication and review of the literature. J Urol. 2004:8;172(1).
17. Manohar T, Desai M, Desai M. Laparoscopic Nephrectomy for Benign and Inflammatory Conditions. J Endourol. 2007 Nov;21(11):1323-8.
18. Yan MB, Lu J, Li XF, Guo ZY. Clinical analysis of retroperitoneoscopic nephroureterectomy for renal tuberculosis. Chronic Dis Transl Med. 2015 Dec 1;1(4):217-20.
19. T O, H N, S H, K N, E H. Comparison of transperitoneal and retroperitoneal laparoscopic nephrectomy for renal cell carcinoma: a single-center experience of 100 cases. Int J Urol Off J Jpn Urol Assoc. 2008:8;15(11).
20. L W, Q Y, C X, Y S. Retroperitoneal laparoscopic and open radical nephrectomy for T1 renal cell carcinoma. J Endourol. 2009 Sep: 8;23(9).