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Transperitoneal versus extraperitoneal approach in laparoscopic radical prostatectomy

A meta-analysis

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Abstract

Background: To compare the transperitoneal approach with extraperitoneal approach in laparoscopic radical prostatectomy (LRP) (including pure and robotic-assisted LRP) using meta-analytic techniques.

Methods: Medline (PubMed), Embase, Ovid, CMB, and Cochrane databases were searched for studies that compared the transperitoneal and extraperitoneal approaches in LRP from January 2000 to January 2017. Outcomes included were operative time, operative bloods joss (milliliters), rate of transfusion, rate of open conversion, rate of intraoperative complications, rate of postoperative complications, and time of postoperative catheterization.

Results: Thirteen studies including 1674 patients were selected for the meta-analysis. 850 (50.8%) cases had undergone transperitoneal LRP (TLRP) and 824 (49.2%) cases had undergone the extraperitoneal LRP (ELRP). Comparison of operative time between the TLRP group and the ELRP group showed no significant differences (weighted mean difference [WMD] = 21.21,95% CI = –1.16–43.57, *P* = .06). No significant differences were observed in blood loss (WMD = −6.04, 95%CI = −43.38–31.29, *P* = .75) and the rate of transfusion (odds ratio [OR] = 1.03, 95%CI = 0.55–1.96, *P* = .92) between the 2 groups. No significant differences were observed for the rate of intraoperative complications (OR = 1.25, 95%CI = 0.57–2.21, *P* = .75) and the rate of open conversion (OR = 1.12, 95%CI = 0.32–4.97, *P* = .75). Significant differences were observed in the TLRP group compared with the ELRP group (OR = 1.69, 95%CI: 1.23–2.32, *P* = .001) regarding the rate of postoperative complications.

Conclusions: Our meta-analysis findings revealed that the TLRP group showed no significant differences in most important indicators compared with ELRP. Moreover, TLRP showed higher rate of postoperative complications compared with ELRP.

Abbreviations: ELRP = extraperitoneal laparoscopic radical prostatectomy, LC = learning curve, LRP = laparoscopic radical prostatectomy, RP = radical prostatectomy, SD = standard deviations.

Keywords: extraperitoneal approach, laparoscopic radical prostatectomy, meta-analysis, robotic-assisted, transperitoneal approach

1. Introduction

Prostate cancer is one of the most common tumors of the male reproductive system. Radical prostatectomy (RP) is the most effective treatment for localized prostate cancer.[1] Two main operation methods have been used for localized prostate cancer, namely the open radical prostatectomy and the laparoscopic radical prostatectomy (LRP). Open radical prostatectomy has been the standard treatment until the introduction of LRP by Schuessler et al in 1997.[2] Since then, LRP has increasingly gained popularity among the patients as well as surgeons because of its inherent advantages over open surgery.[3,4] In recent years, robotic-assisted LRP was widely carried out.[5] While few studies[6,7] revealed no significant differences in the surgical effects between robotic-assisted and pure LRP. However, the debate related to the surgical approach for performing LRP, mainly during the learning curve (LC), still remained controversial. The transperitoneal approach is favored by most surgeons due to greater working space and familiar landmarks of the pelvis and its contents, but others prefer the extraperitoneal approach due to lack of contact with the intraperitoneal organs.[8–11] Hence, the present study aimed to evaluate the available published literature that compared the transperitoneal approach with extraperitoneal approach in LRP (including pure and robotic-assisted LRP). Meta-analytic techniques were applied to assess the potential advantages of each approach.

2. Methods

According to the Author Instruction, our meta-analysis does not contain identifiable individual patient characteristics or data such as eyes, date of birth, initials, birthmarks, etc. So the Informed consent is not obtained in the manuscript.

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KW and QZ have contributed equally to this work.

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All authors declare that they have no any conflict of interests.

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2.1. Study selection

A Medline (PubMed), Embase, Ovid, CBM, and Cochrane database were used to perform the search for studies that compared the transperitoneal with extraperitoneal approach in LRP (including pure and robotic-assisted LRP) between 2000 and 2017. MeSH search headings used were: "laparoscopic," "radical prostatectomy," "robotic-assisted," "extraperitoneal," and "transperitoneal" and their combinations were also searched. The function of "related articles" was applied to enlarge the search. The references of each included study were also seriously reviewed. To ensure that any relevant studies were not missed, many scholars in the field of endourological surgery were consulted. This analysis included only comparative clinical full-text studies, and the final articles included in the study were agreed upon by all authors in this manuscript.

2.2. Data extraction

The following data were independently extracted by 2 reviewers (ZQF and WK) from each study: year of publication, first author, characteristics of targeted population, research design, interventions, and outcomes of interest. To avoid missing of the related study data, the 2 reviewers made great efforts to contact the authors of the original study where information was lacking or unclear. Any conflicts regarding the outcomes of interest between the investigators were subsequently reviewed and an agreement was reached on the final interpretation of the data.

2.3. Inclusion criteria

The studies that we included in our meta-analysis met the following criteria: comparison of the transperitoneal approach with extraperitoneal approach in LRP (including pure and robotic-assisted LRP); human studies; inclusion of at least 3 outcome measures; documentation of the operative technique as "pure laparoscopic," or "robotic-assisted laparoscopic"; multiple studies were from the same institute and/or authors, where the higher quality study or the more recent publication was included in the analysis; English and Chinese language articles published in the peer-reviewed journals; retrospective observational studies.

2.4. Exclusion criteria

The exclusions were as follows: abstracts, editorials, expert opinions, case reports, reviews, and studies lacking control groups; studies reporting 3D LRP; studies comparing laparoscopic and open radical prostatectomy; repeated reports between the authors, centers, and patient community.

2.5. Outcomes of interest and definitions

The following outcomes were used to compare the TLRP with ELRP:

1. Intraoperative parameters included were operative time (minutes), operative blood loss (milliliters), the rate of transfusion, the rate of open conversion, and the rate of intraoperative complications.
2. Postoperative parameters included were the rate of postoperative complications, and the time of postoperative catheterization (days).

2.6. Statistical analysis

This meta-analysis was performed according to the recommendations from Cochrane Collaboration and the Quality of Reporting of Meta-analyses guidelines.[12,13] Review Manager Version 5.1 software and Stata Manager V4.1 software (Copenhagen, Denmark, TX) were used in this meta-analysis. Statistical analysis of dichotomous variables was carried out by using odds ratios (ORs) as the summary estimate, continuous variables were analyzed using the weighted mean difference (WMD),[14] and few studies reported using 95% confidence intervals (CIs). ORs represented the odds of an adverse event that occurred in the TLRP group compared with ELRP group, whereas WMD summarized the difference between the 2 groups with respect to continuous variables, accounting for sample size. If the P value was $<.05$ and the 95% CI did not include the value 1, then the OR and WMD were considered statistically significant. When continuous data were presented as ranges and means, we used statistical algorithms and "bootstrap" resampling techniques to calculate and verify the standard deviations (SD).[15]

The quality of the studies was assessed using the Newcastle-Ottawa Scale with some modifications to match the requirements of this study.[15] The quality of the studies was evaluated according to 3 factors: patient selection, similarity between the study groups, and assessment of outcome. A score of 0 to 9 (as stars) was allocated to each study. The maximum number of stars in the selection, comparability, and outcome categories was 3, 4, and 2, respectively. Studies achieving ≥5 stars were considered to be of high quality.[16]

Heterogeneity was evaluated using the Higgins chi-square test. The P value and I^2 value were used for evaluating statistical heterogeneity. If $I^2 < 50\%$ and $P > .1$, then it is considered as nonsignificant heterogeneity between the included studies, and data were pooled by the fixed-effects model. The random effects model was used in the condition where the heterogeneity was significant ($I^2 > 50\%$, $P < .1$). Subgroup analyses were performed according to the specific laparoscopic means. The influence of low-quality studies on the overall effect was detected by sensitivity analysis. Begg funnel plot and Egger test were used to assess the publication bias of literatures in all comparison models.

3. Results

3.1. Eligible studies

We identified many studies published between 2000 and 2017 that met the selection criteria. Search strategy generated 102 relevant clinical studies. Among these, 17 full-text articles were identified for further investigation. Of these 17, 4 studies were excluded for various reasons, which were as follows: the data of 2 studies were incomplete, which contained only averages, 1 study did not contain the control group, and data of another study was unclear. Finally, 13 retrospective non-randomized comparative studies were identified for inclusion (Fig. 1).

3.2. Study characteristics

The characteristics of 13 studies that fulfilled the inclusion criteria are summarized in Table 1. Analysis of 1674 patients was performed. Of these, 850 (50.8%) patients had undergone TLRP and 824 (49.2%) had undergone ELRP. Ten studies recorded the purely LRP, which included 1164 patients. Three studies recorded the robotic-assisted LRP, which included 510 patients.

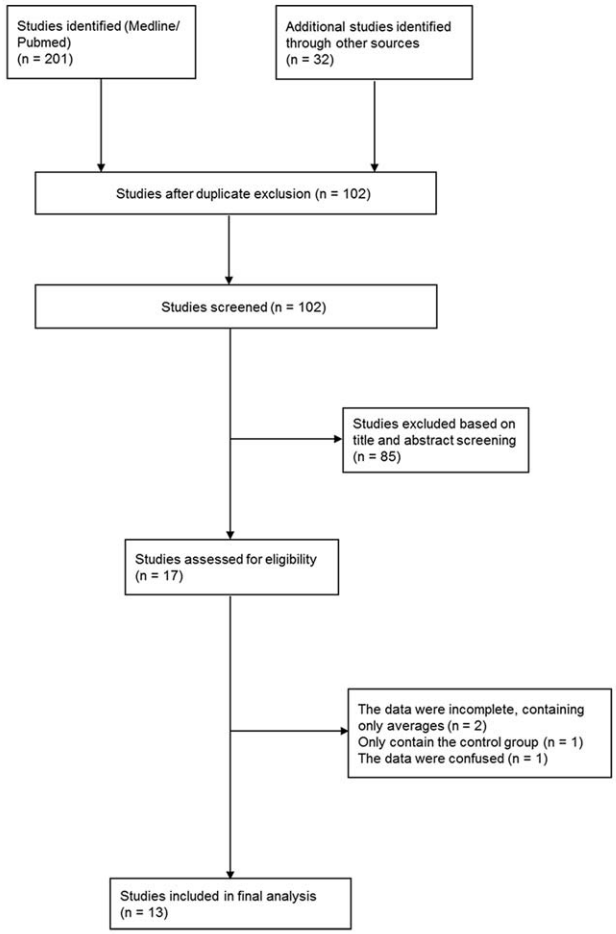

Figure 1. Flow diagram outlining the study selection process according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Conversion to open surgery was reported in 6 (0.6%) cases among 7 studies. Thirty nine (4.3%) cases needed donor blood transfusion among 6 studies. Intraoperative complications occurred in 19 (2.7%) cases in the TLRP group and 14 (1.9%) cases in the ELRP group. Postoperative complications occurred in 127 (14.9%) cases in the TLRP group and 77 (9.3%) cases in the ELRP group. In this meta-analysis, all included studies were non-randomized, and data collected was all retrospective.

3.3. Meta-analysis of TLRP versus ELRP groups.

3.3.1. Intraoperative parameters. Comparison of operative time between the TLRP group and the ELRP group showed no significant difference (95%CI = −1.16–43.57, *P* = .06). No significant difference in the blood loss (WMD = 21.21, 95% CI = −43.38–31.29, *P* = .75) and the rate of transfusion (OR = 1.03, 95%CI = 0.55–1.96, *P* = .92) were observed between the 2 groups. The intraoperative complications included rectal injury, vascular injury, bladder injury, epigastric injury, and ureteral injury. No significant differences were obtained in the rate of intraoperative complications (OR = 1.25, 95% CI = 0.57–2.21, *P* = .75) and the rate of open conversion (OR = 1.12, 95% CI = 0.32–4.97, *P* = .75) between the 2 groups. Overall, meta-analysis of the related data regarding intraoperative parameters demonstrated no significant differences in the TLRP group when compared with the ELRP group (Table 2 and Fig. 2).

3.3.2. Postoperative parameters. A pooled analysis of 13 studies indicated significant difference in the TLRP group compared with the ELRP group (OR = 1.69, 95%CI: 1.23–2.32, *P* = .001) regarding the rate of postoperative complications, such as ureteric leak, ureteric stricture, urinary incontinence, and bladder neck stenosis. The TLRP group showed higher rate of postoperative complications than the ELRP group. Analysis of 10 studies suggested that the TLRP group showed no significant difference compared with the ELRP group regarding the time of postoperative catheterization (WMD = 0.50, 95% CI: −0.16–1.17, *P* = .14).

3.4. Subgroup analysis

3.4.1. The transperitoneal approach versus extraperitoneal approach in purely laparoscopic radical prostatectomy. There were no significant differences observed in the results for all outcomes from the original analysis. In contrast to the latter, the rate of postoperative complications remained consistent (the TLRP group 15.1%, the ELRP group 10.4%, OR = 1.13, 95%CI: 1.06–2.24, *P* = .02) between the 2 groups.

3.4.2. The transperitoneal approach versus extraperitoneal approach in robotic-assisted laparoscopic radical prostatectomy. This comparison revealed similar results as the outcomes of the original analysis. The analytic outcomes in the rate of postoperative complications were consistent with the overall analysis (the TLRP group 14.6%, the ELRP group 7.4%, OR = 1.08, 95%CI: 1.19–3.79, *P* = .01).

3.5. Sensitivity analysis

Sensitivity analysis included 7 high-quality studies with a score of ≥5 “stars” on the modified Newcastle-Ottawa Scale. Sensitivity analysis of the above studies showed no significant differences regarding the outcomes. These data were presented in Fig. 3.

3.6. Publication bias

The funnel plots based on the outcomes are shown in Fig. 4. Because all studies laid inside the 95% CI limits, no evidence of publication bias was noted. Egger test was performed to provide statistical evidence regarding funnel plot symmetry. Results still did not reveal any evidence of publication bias in operative time (*P* = .112), blood loss (*P* = .603), rate of transfusion (*P* = .384), rate of open conversion (*P* = .185), rate of intraoperative complications (*P* = .182), rate of postoperative complications (*P* = .515), and rate of postoperative catheterization (*P* = .152).

4. Discussion

Till date there is a considerable and ongoing debate about the merits of TLRP versus ELRP has been going on. Issues regarding surgical effects and patient-related outcomes still remained unclear. Meta-analysis of the related clinical trials presented statistical comparisons of the surgical effects and postoperative outcomes.

Some studies revealed that TLRP had bigger operative space and shorter operative time than ELRP.[17,18] However, our analysis indicated that no significant differences were revealed between the TLRP and ELRP groups in the operative time. Thus, we deduced that there was no inevitable connection between the operative space and operative time.

Table 1

The basic characteristic of included studies.

Study	Study design	Country	Group	Patients	Operative time, mL	Blood loss, mL	The time of postoperative catheterization, d	Outcomes measures	Study quality (stars rating)
Gao ZL	RCG	China	TLRP	12	262.0,11.3	270.6,15.4	7.4,2.3	1,2,3,4,6,7	☆☆☆☆☆
2006			ELRP	19	196.5,9.7	261.0,12.5	7.2,1.6		
Siqueira TM Jr	RCG	Brazil	TLRP	40	175.0,48.4	177.5,148.5	NA	1,2,4,5,6	☆☆☆☆☆
2010			ELRP	40	267.6,70.57	292.4,173.7	NA		
Hoznek A	RCG	France	TLRP	20	224.2,37.5	NA	5.3,6.75	1,3,6,7	☆☆☆☆☆
2002			ELRP	20	169.6,31.25	NA	4.2,3.5		
Brown JA	RCG	USA	TLRP	122	NA	NA	NA	3,4,6	☆☆☆☆☆☆☆
2004			ELRP	34	NA	NA	NA		
Porpiglia F	RCG	Italy	TLRP	80	179.4,54.6	562.5,209	7.53,4.36	1,2,3,5,6,7	☆☆☆☆☆
2006			ELRP	80	133.7,27	595.34,310.11	7.21,1.93		
Ruiz L	RCG	France	TLRP	165	248,58.2	678,520	5.1,4.5	1,2,3,5,6,7	☆☆☆☆
2004			ELRP	165	220,48	803,520	6.6,7.5		
Eden CG	RCG	UK	TLRP	100	238.9,75.8	310.5,208.3	11.3,3.3	1,2,3,4,5,6,7	☆☆☆☆
2004			ELRP	100	190.6,35.8	201.5,131.6	10.1,4.2		
Remzi M	RCG	Austria	TLRP	39	279,70	290,254	7.2,4.25	1,2,4,5,6,7	☆☆☆☆
2005			ELRP	41	217,51	189,140	6.1,5		
Chung JS	RCG	Korea	TLRP	105	162.1,31.5	361.7,150.4	7.3,2.6	1,2,4,5,6,7	☆☆☆☆☆☆
2011			ELRP	155	150.3,47.7	350.8,165.5	7.7,2.3		
Wang ZR	RCG	China	TLRP	39	256,45	335,296	14.2,2.7	1,2,5,6,7	☆☆☆
2010			ELRP	15	263,62	352,314	11.2,3.3		
Wang S	RCG	China	TLRP	21	299,4	618,44	14.6,3.8	1,2,5,6,7	☆☆☆☆
2008			ELRP	12	309,4	677,46	12.3,2.9		
Atug F	RCG	China	TLRP	40	236.23,62.25	NA	NA	1,5,6	☆☆☆☆
2006			ELRP	40	229.15,59.75	NA	NA		
Horstmann M	RCG	Switzerland	TLRP	67	224,52.6	281,204.1	6.5,2.5	1,2,4,5,6,7	☆☆☆☆☆
2011			ELRP	103	192,49.0	276,190	6.2,1.0		

Continuous variables are presented as means, SD; Blood loss = intraoperative blood loss, ELRP = extraperitoneal LRP, NA = not available, RCG = retrospective control group, TLRP = transperitoneal LRP.

1 = operative time; 2 = intraoperative blood loss; 3 = the rate of transfusion; 4 = the rate of open conversion; 5 = the rate of intraoperative complications; 6 = the rate of postoperative complications; 7 = the time of postoperative catheterization.

Table 2

Meta-analysis of the TLRP versus ELRP.

Outcome of interest	No.studies	No.patients	OR/WMD	95%CI	*P*-value	Heterogeneity *P* value	I^2
Operative time	12	1518	21.21	−1.16,43.57	.06	<.00001	98%
Intraoperative blood loss	10	1398	−6.04	−43.38,31.29	.75	<.00001	84%
The rate of transfusion	6	917	1.03	0.55,1.96	.92	.24	26%
The rate of open conversion	7	977	1.25	0.32,4.97	.75	.74	0%
The rate of intraperative complications	10	1447	1.12	0.57,2.21	.75	.93	0%
The rate of postoperative complications	13	1674	1.69	1.23,2.32	.001	0.79	0%
The time of postoperative catheterization	10	1358	0.50	−0.16,1.17	.14	.002	66%

The point estimate of the OR and WMD was considered statistically significant at the level of $P<.05$ if the 95% CI did not include the value one.
If an I^2 value is <50% and *P* value is >.1, it may be considered to indicate nonsignificant heterogeneity.
CI=confidence interval, OR=odds ratio, ELRP=extraperitoneal LRP, TLRP=transperitoneal LRP; WMD=weighted mean difference.

The prostate tissue consists of venous plexuses surrounding the prostate. The lateral venous plexuses of the prostate communicate with the vesical plexuses presented on the lower part of the bladder and pudendal venous plexus. As the prostate had abundant venous supply and complicated venous communications with the pelvic venous plexuses, bleeding remains difficult to be controlled during prostatectomy when the veins were injured. Several detailed anatomic studies[19,20] were performed in adult cadavers, which provided important insights into the periprostatic anatomy, especially regarding the periprostatic vein complex. These observations provided a more anatomic approach to radical prostatectomy with a consequent reduction in the operative bleeding. Laparoscopic amplification could help the operator identify the periprostatic venous plexuses more clearly and decrease the blood loss more significantly than the open radical prostatectomy. However, no significant differences regarding the operative blood loss between the 2 approaches of the LRP were found. In clinical operation, the rate of blood transfusion was basically consistent with the rate of blood loss.[21] Our study revealed no significant differences with the rate of blood transfusion between the 2 groups.

A lot of intraoperative complications, such as vascular injury, bladder injury, intestinal injury, and ureteral injury might occur during the LRP. TLRP was performed in the abdominal cavity, and theoretical possibility showed that the transperitoneal approach might increase the rate of intraoperative injury.

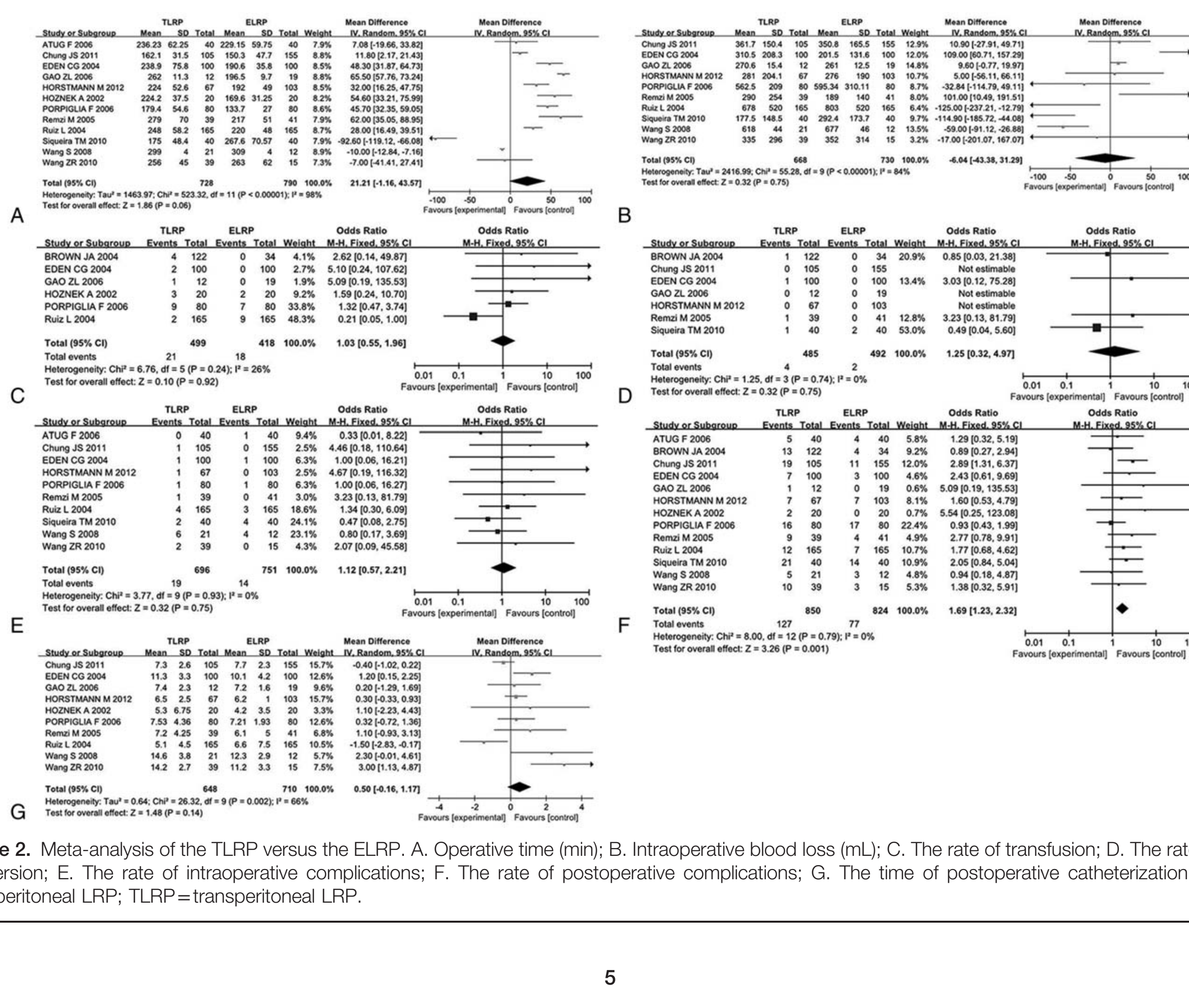

Figure 2. Meta-analysis of the TLRP versus the ELRP. A. Operative time (min); B. Intraoperative blood loss (mL); C. The rate of transfusion; D. The rate of open conversion; E. The rate of intraoperative complications; F. The rate of postoperative complications; G. The time of postoperative catheterization. ELRP=extraperitoneal LRP; TLRP=transperitoneal LRP.

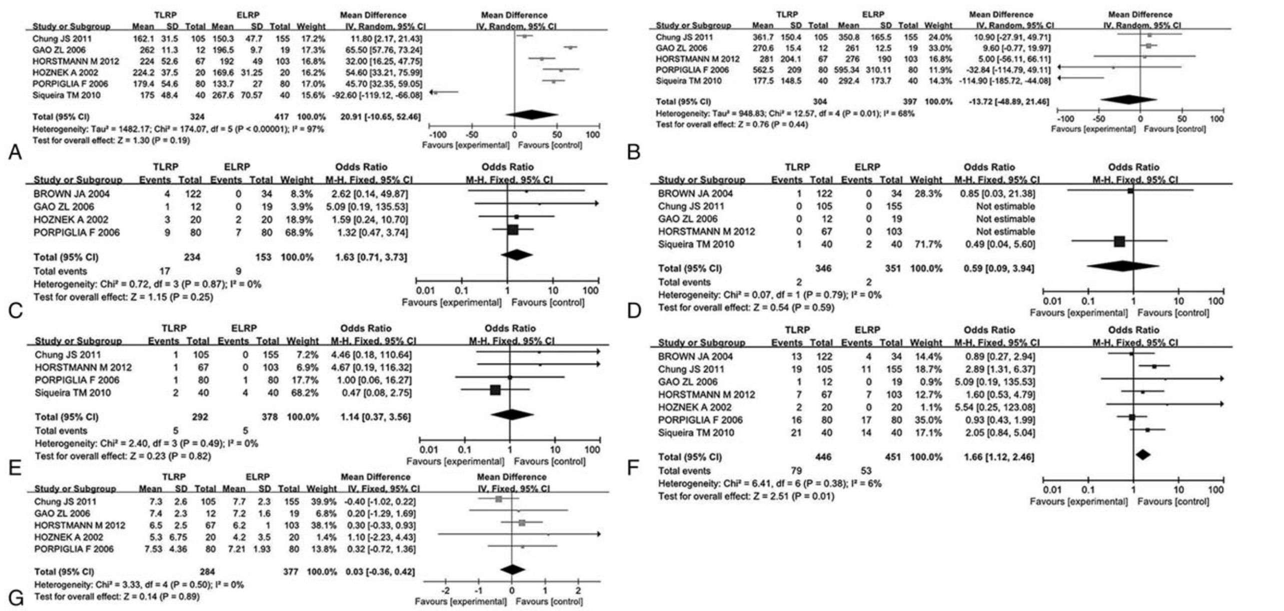

Figure 3. Sensitivity analysis. A. Operative time (minute); B. intraoperative blood loss (mL); C. the rate of transfusion; D. the rate of open conversion; E. the rate of intraoperative complications; F. the rate of postoperative complications; G. the time of postoperative catheterization.

However, our study revealed no significant differences regarding the rate of intraoperative complications. The bigger operative space of practical surgery in TLRP was considered, eliminating the theoretical possibility of intraoperative organs and vascular injury. Intraoperative complications were the chief causes that led to the conversion to open radical prostatectomy, and there were no differences regarding the rate of open conversion in our analysis.

Postoperative complications included urinary incontinence, urinary retention, fecal incontinence, urethral bleeding, urinary

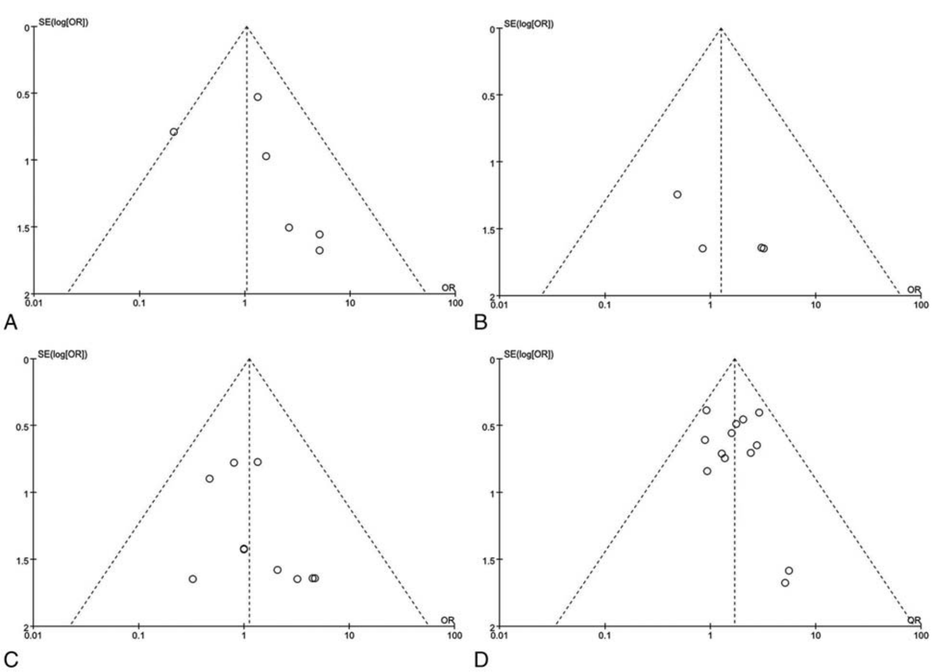

Figure 4. The funnel plots based on the outcomes. A. The rate of transfusion, (funnel plots illustrating meta-analysis of transfusion rate. OR indicates odds ratio. SE [effect estimate] versus effect estimate for each study under the outcome. Studies are marked by a dot and 95% CI by lines.); B. the rate of open conversion (funnel plots illustrating meta-analysis of open-conversion rate. OR indicates odds ratio. SE [effect estimate] versus effect estimate for each study under the outcome. Studies are marked by a dot and 95% CI by lines.); C. the rate of intraoperative complications, (funnel plots illustrating meta-analysis of intraoperative-complications rate. OR indicates odds ratio. SE (effect estimate) versus effect estimate for each study under the outcome. Studies are marked by a dot and 95% CI by lines.); D. the rate of postoperative complications, (funnel plots illustrating meta-analysis of postoperative-complications rate. OR indicates odds ratio. SE [effect estimate] versus effect estimate for each study under the outcome. Studies are marked by a dot and 95% CI by lines.).

leakage, pulmonitis, ileus, and erectile dysfunction. Of these, urinary incontinence and erectile dysfunction remained the most concerned for urologists. In the LRP, the operator could more clearly observe the anatomical structure of the neurovascular bundles that control the urethral sphincter and corpus cavernosum.[22,23] Before the anastomosis of bladder neck and posterior ureteral, posterior lip of the bladder neck was formed as a tennis-racket to strengthen the posterior wall. The above two laparoscopic techniques could effectively decrease the possibility of urinary incontinence and erectile dysfunction. Our analysis demonstrated an interesting finding that a higher rate of overall postoperative complications in the TLRP group than the ELRP group, but showed no significant difference between the 2 groups regarding the rate of urinary incontinence ($P=.26$, $I^2=0\%$) and erectile dysfunction ($P=.76$, $I^2=0\%$). We considered more adverse postoperative influences on celiac organs due to some factors related to the entering of peritoneal cavity (such as the intraperitoneal insufflation of CO_2),[11] which might in turn lead to higher rate of overall postoperative complications in the TLRP group.

The aim of postoperative catheterization was to prevent urine extravasation before healing of the anastomosed stoma.[24] Catheterization could be removed when angiography demonstrated no extravasation in urethrography. Regarding the catheterization time, our study revealed no significant differences. Hereby, we deduced that there were no significant differences regarding the healing time of anastomosed stoma between the 2 groups.

Sensitivity analysis was conducted by excluding the low-quality trials from the included studies. Then we analyzed the effect on the overall results. These removed studies did not alter the results obtained from the overall analysis. No significant differences were revealed regarding any of the outcomes from the overall results. This increased the credibility of our overall analysis results.

This meta-analysis study, which included several non-randomized studies, has 1 limitation that must be considered. Some critics doubt that the meta-analytic techniques described in our setting would lead to a bias. However, Deeks et al[25] have provided a rigorous scientific method to estimated non-randomized interventional studies. By using resampling techniques, they found that the "results of randomized and non-randomized studies sometimes. But do not always differ and both similarities and differences may often be explicable by other confounding factors." Therefore, if randomization could not be conducted due to some factors, non-randomized studies can be included as well as to guide clinical research. Although randomized controlled trials (RCTs) are difficult to be conducted in LRP, further larger RCTs with a rigorous methodology are required for a more comprehensive comparison of the 2 approaches.

In several studies, ranges were recorded rather than standard deviations, and doubt remained that this might lead to publication bias. However, a recent study by Stela Pudar Hozo,[26] provided scientific as well as rigorous method to estimate the standard deviation. The article reported that using these formulas we can "use clinical trials when not all the information is available and/or reported". In addition, funnel plot and Egger test in all comparison models revealed no significant publication biases.

However, our study has some limitations. Firstly, our study included trials with small sample sizes. Secondly, the heterogeneity was significant when pooling the data of operative time, time of postoperative catheterization, and intraoperative blood loss. This cannot be readily interpreted, and hence the pooled results' value may be limited.

In conclusion, bigger operative space did not represent better operative effects in the TLRP. Our meta-analysis revealed that TLRP demonstrated no significant differences with most of the important indicators compared with ELRP. Moreover, the TLRP had a significantly higher rate of postoperative complications compared with ELRP.

Author contributions

Conceptualization: Kun Wang, Qianfeng Zhuang.
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