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Original Article

Postoperative outcomes of laparoscopy vesus open nephrectomy in polycystic kidney disease

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Abstract: Background: Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary nephropathy characterized by continuous enlargement of kidney cysts. Kidney volume control is one of the most important treatments of ADPKD. Clinical outcomes of laparoscopic nephrectomy (LN) and traditional open nephrectomy (TN) are still inconclusive. Methods: We searched Embase, Medline, and Cochrane library (up to June 2015) for relevant studies. Meta-analysis was used. The primary outcome was the overall risk of operative complications. Quality assessment was evaluated by the Newcastle-Ottawa scale for cohort studies. Results: Seven retrospective cohort studies were included. Compared with TN, LN was not associated with fewer risk of postoperative complications (OR = 0.53, 95% CI 0.23 to 1.19, P = 0.12). The number needed to treat was 567 according to trial sequential analysis. The risks of arteriovenous fistula thrombosis, wound dehiscence/incision hernia, prolonged ileus, wound hematoma, infections and tear of visceral organ between LN and TN were not significant. Subgroup analysis by hand-assisted laparoscopy (HAL) found the risk of complications decreased significantly in the non-HAL group (OR = 0.36, 95% CI 0.16 to 0.81, P = 0.01) compared with TN, but not in the HAL group (OR = 0.37, 95% CI 0.04 to 3.30, P = 0.37). Conclusions: LN was not associated with decreased risk of complications compared with TN in adult patients with ADPKD. More randomized controlled trials will be needed to demonstrate this in the future.

Keywords: Polycystic kidney disease, autosomal dominant, meta-analysis, nephrectomy, laparoscopy

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disorder with the prevalence of 1/400 to 1/1000. End stage renal disease (ESRD) will be present in half of the patients by the age of 60 years old due to the progressive enlarging cysts [1]. Nephrectomy is required when enlarged polycystic kidneys have the following intractable symptoms: abdominal pain with a prevalence of 85%, recurrent infection with a prevalence of 10-98%, cyst hemorrhage or rupture with a prevalence of 50%, stones with a prevalence of 25%, or malignancy with a prevalence of 1.5% [2]. About 20% of ADPKD patients with extremely large kidneys need native nephrectomy before or after renal transplantation. High risk of urinary tract infection post-transplant is some other important indication for nephrectomy in ADPKD [3].

Traditional open nephrectomy (TN) is the empirical surgical treatment of ADPKD. Since the first report of laparoscopic nephrectomy (LN) in ADPKD in 1996 [4], LN has become more popular compared with TN in recent years. LN showed benefits in reduced hospital days, decreased blood loss or transfusion, and fewer postoperative pain compared with TN [5]. However, LN spent more operative time than TN, and had more cyst rupture or organ injury when compared with TN [6]. However, there was little evidence in the postoperative outcomes between TN and LN of ADPKD. This meta-analysis was performed to testify the associations in the postoperative outcomes between LN and TN in ADPKD.

Materials and methods

Information sources and search

Databases of Medline, Embase, Ovid, and Cochrane library (published up to June, 2015) were searched for eligible studies. The electronic search included the following terms: “nephrectomy or nephrectomize or SNX or STNx

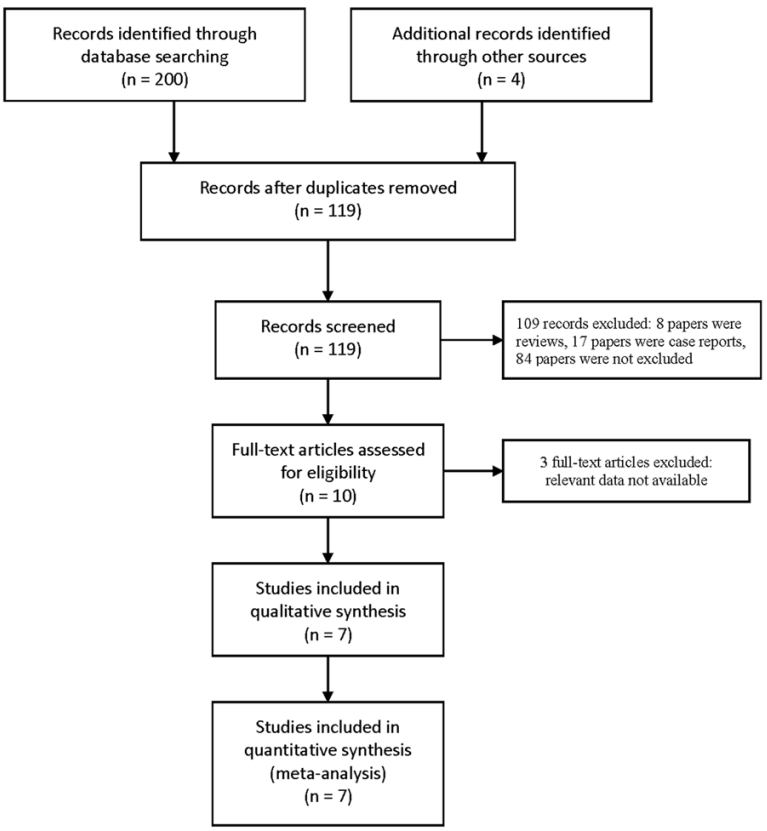

Figure 1. Flow of study identification, inclusion, and exclusion (PRISMA 2009).

or kidney resection or kidney removal", "autosomal dominant polycystic kidney disease or polycystic kidney disease or ADPKD or PKD", "laparoscopic nephrectomy or laparoscopy or open nephrectomy or traditional nephrectomy". Google Scholar and clinical trials website were checked to find relevant studies.

Inclusion and exclusion criteria

We included studies according to the PICOS criteria: (1) studies in adult patients with ADPKD; (2) evaluation of nephrectomy in ADPKD; (3) comparing the laparoscopic nephrectomy with the open nephrectomy; (4) odds ratio (OR) and 95% confidence interval (CI) from the operation related indexes should be available. Articles were excluded with the following criteria: (1) renal cyst, cancer or autosomal recessive polycystic kidney disease; (2) cyst puncture decompression or partial nephrectomy; (3) repeated publications; (4) data was not available after we contacted the authors. There were not any restrictions in language, country, ethnicity and course of disease.

Data extraction and methodological quality assessment

Z. C. and X. C. checked the included studies independently to extract the relevant data. D. B. checked the accuracy of the data. When discrepancy happened, we discussed and checked the relevant studies. We used the Newcastle-Ottawa scale (NOS) for cohort studies to evaluate the methodological qualities of the studies [7]. The primary outcome was the risk of overall postoperative complications. The secondary outcomes were the risk of arteriovenous fistula thrombosis, the risk of wound dehiscence/incision hernia, the risk of prolonged ileus, the risk of wound hematoma, the risk of infections and the risk of tearing of visceral organ.

Statistical analysis

Results in two or more studies will be performed by meta-analysis. $P < 0.05$ was considered as statistically significant. Heterogeneity was assessed through Q test and I^2 statistics [8]. $I^2 < 25\%$ was considered as low and $I^2 > 75\%$ as high. We estimated the OR with 95% CI for the count data in the random effects model. Z test was used to detect the statistical significance. Subgroup analyses were performed by hand-assisted laparoscopy (HAL) and Clavien classification of the complications [9]. Sensitivity analysis was performed by the influence analysis which excluded each study one by one to check the stability of the results. Publication bias was detected by the Begg's funnel plot and Egger's test [10]. Trial Sequential Analysis (TSA) was used to check the stability of the primary outcome. Softwares used were the Revman 5.4 (Cochrane group) and TSA 0.9.

Results

Study characteristics

204 studies were found in the initial search. The selection process was shown in **Figure 1**.

Table 1. Characteristics of the included trials

Studies	Country	Settings	Number of patients	Groups	Bilateral/ unilateral	Approach	Conversion to TN	Age (years)	Matching	Outcomes
Mary 2013	USA	Retrospective	58	LN	UL/BL	HAL TP	2	51.4±8.0	1, 2, 3, 6	①②③④⑥⑦
		Single center	18	TN	UL/BL	TP		49.3±8.3		
Verhoest 2012	France	Retrospective	21	LN	NA	TP	0	53±10.1	1, 2, 3, 4, 5, 6	①②③④⑤⑥
		Single center	19	TN	NA	TP		53±10.6		
Mahesh 2007	India	Retrospective	13	LN	UL/BL	TP/RP	2	49.1±6.2	1, 3	①②④⑦
		Single center	14	TN	NA	NA		NA		
Seshadri 2001	Canada	Retrospective	10	LN	NA	TP	1	47±10.2	1, 2, 3, 6	①②⑤⑥
		Single center	10	TN	NA	NA		51±10.3		
Gill 2001	USA	Retrospective	10	LN	BL	RP	0	51±11.3	1, 2, 3, 5, 6	①③④⑤⑦
		Single center	10	TN	NA	TP		49±9.7		
Patel 2011	UK	Retrospective	5	LN	BL/UL	HAL	0	NA	1, 3	①
		Single center	26	TN	NA	TP		NA		
Saleh 2006	Canada	Retrospective	6	LN	UL	TP	0	52±8	1, 2, 3, 4, 5	①
		Two centers	6	TN	UL	TP		52±9		

LN, laparoscopic nephrectomy; TN, open nephrectomy; BL, bilateral; UL, unilateral; RP, retroperitoneal; TP, transperitoneal; HAL, hand-assisted laparoscopy; N, number; Matching: 1 = age, 2 = sex, 3 = diagnosis, 4 = American Society of Anesthesiologists (ASA) score, 5 = body mass index (BMI), 6 = surgical indication: Outcomes: ① the risk of overall postoperative complications; ② the risk of arteriovenous fistula thrombosis; ③ the risk of wound dehiscence/incision hernia; ④ the risk of prolonged ileus; ⑤ the risk of wound hematoma; ⑥ the risk of infections; ⑦ the risk of tear of visceral organ. NA, not available.

Table 2. Assessment of the quality of the studies according to NOS

Studies	Selection				Comparability	Outcome assessment			NOS score
	①	②	③	④	⑤	⑥	⑦	⑧	
Mary 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	7
Verhoest 2012	Yes	Yes	Yes	Yes	Yes	Yes	No	No	6
Mahesh 2007	Yes	Yes	Yes	Yes	Yes	Yes	No	No	6
Seshadri 2001	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	7
Gill 2001	Yes	Yes	Yes	Yes	Yes	Yes	No	No	6
Patel 2011	Yes	No	Yes	No	Yes	Yes	No	No	4
Saleh 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8

① Representativeness of the exposed cohort; ② selection of the non-exposed cohort; ③ ascertainment of exposure; ④ demonstration that outcome of interest was not present at start of study; ⑤ comparability of cohorts on the basis of the design or analysis; ⑥ assessment of outcome; ⑦ was follow-up long enough for outcomes to occur; ⑧ adequacy of follow up of cohorts.

Seven retrospective cohort studies with 234 participants were included [3, 6, 11-15]. The characteristics of the included articles were listed in **Table 1**. Half of the patients got the LN, and the other half got the TN. Five patients in LN converted to TN in total [6, 12, 13]. One patient succumbed to overwhelming sepsis after TN [3]. Two studies came from the Europe [3, 14], four studies came from North America [6, 11, 12, 15], and one came from Asia [13]. Most of the studies were in Caucasians except for one study in East Asians [13]. All the studies were performed at a single center. Large size, cyst hemorrhage, pain, and renal transplantation were the most common indications for nephrectomy. All the studies reported the surgical approach. HAL was used in two studies [3, 6]. Five studies demonstrated whether the operations were before or after transplantation [3, 11, 12, 14, 15].

The quality assessment was shown in **Table 2**. Selection and comparability were sufficient in most studies. Follow-up of the outcome assessment was unclear in five studies. Follow-up was reported in two studies.

Quantitative data synthesis

There were no significant differences in the risk of overall postoperative complications between LN and TN (seven studies, 234 participants, **Figure 2**): OR = 0.53, 95% CI 0.23 to 1.19, P = 0.12.

There were no significant differences between LN and TN in the following secondary outcomes: the risk of arteriovenous fistula thrombosis (four studies, 171 participants, OR = 0.98; 95% CI 0.30 to 3.22, P = 0.98, **Figure 3**); the risk of wound dehiscence/incision hernia (three studies, 136 participants, OR = 0.69, 95% CI 0.16 to 3.02, P = 0.63, **Figure 4**); the risk of prolonged ileus (four studies, 171 participants, OR = 0.48, 95% CI 0.11 to 2.17, P = 0.34, **Figure**

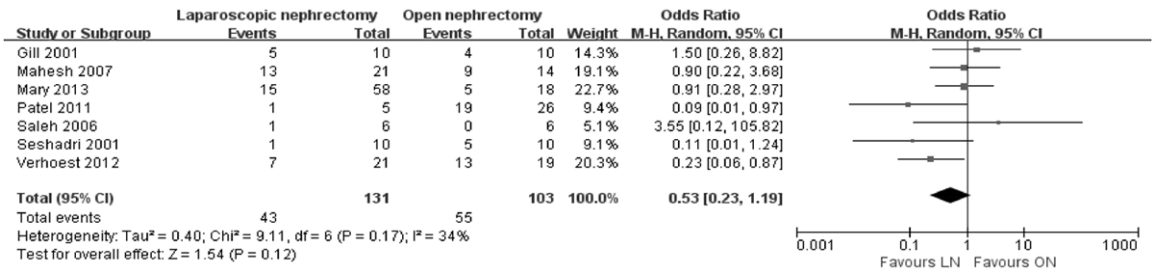

Figure 2. Meta-analysis of the risk of overall postoperative complications between LN and TN in ADPKD.

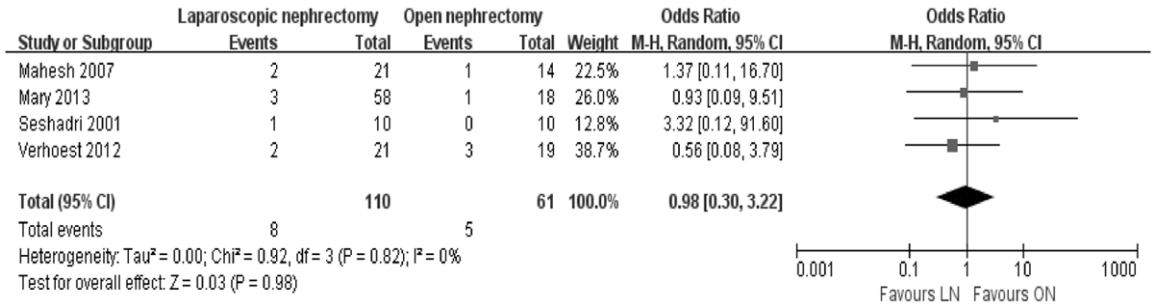

Figure 3. Meta-analysis of the risk of arteriovenous fistula thrombosis between LN and TN in ADPKD.

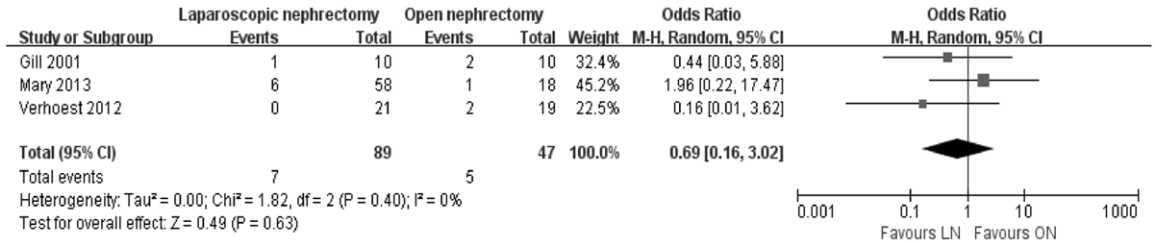

Figure 4. Meta-analysis of the risk of wound dehiscence/incision hernia between LN and TN in ADPKD.

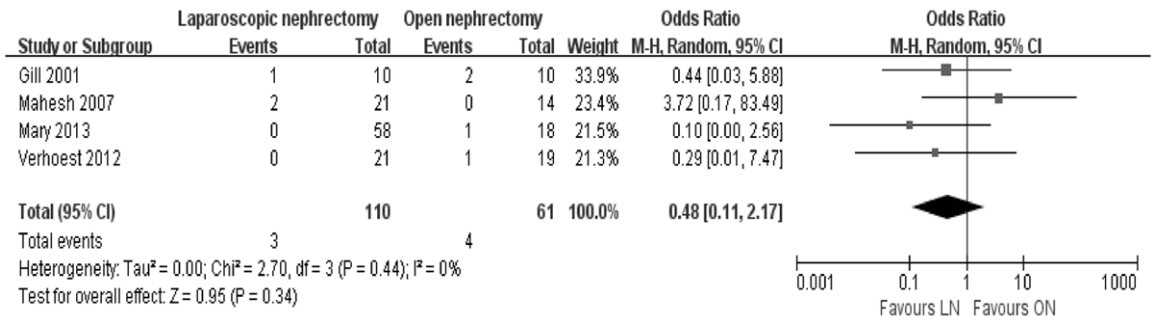

Figure 5. Meta-analysis of the risk of prolonged ileus between LN and TN in ADPKD.

5); the risk of wound hematoma (three studies, 80 participants, OR = 1.83, 95% CI 0.28 to 11.90, *P* = 0.53, **Figure 6**); the risk of infections (three studies, 136 participants, OR = 0.51, 95% CI 0.09 to 2.98, *P* = 0.46, **Figure 7**); the risk of tear of visceral organ (four studies, 171 participants, OR = 0.37, 95% CI 0.11 to 1.27, *P* = 0.11, **Figure 8**).

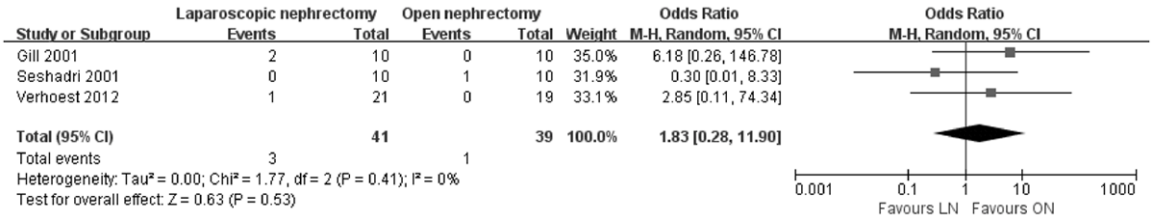

Figure 6. Meta-analysis of the risk of wound hematoma between LN and TN in ADPKD.

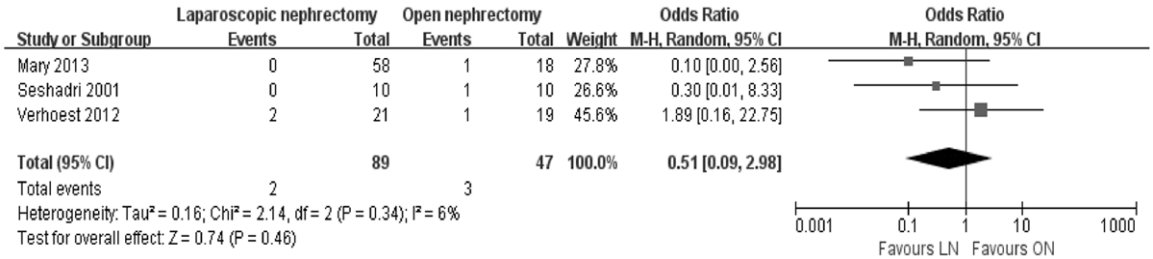

Figure 7. Meta-analysis of the risk of infections between LN and TN in ADPKD.

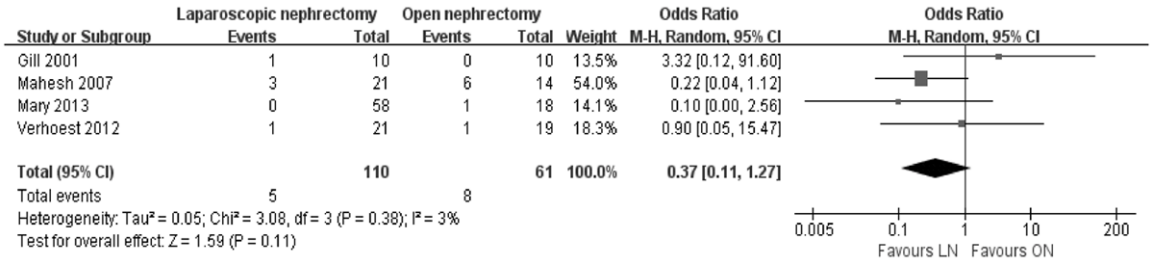

Figure 8. Meta-analysis of the risk of tear of visceral organ between LN and TN in ADPKD.

Subgroup analysis by Clavien classification found the difference of complications in Clavien 1-2 was similar between LN and TN (five studies, 191 participants, OR = 0.46; 95% CI 0.14, 1.47, P = 0.19, **Figure 9**). The result was also not significant in Clavien 3-4 complications (five studies, 191 participants, OR = 0.63; 95% CI 0.20, 1.97, P = 0.43). In subgroup analysis by HAL, the risk of complications declined significantly in the non-HAL group (four studies, 115 participants, OR = 0.36; 95% CI 0.16, 0.81, P = 0.01) compared with TN (**Figure 9**). However, the difference was not significant in the HAL group compared with TN (two studies, 107 participants, OR = 0.37; 95% CI 0.04, 3.30, P = 0.37).

Sensitivity analyses

To check the stability of the result in the overall complications, TSA used a priori assumptions of 23% OR reduction, 59% TN group complication rate (type I error, two sided $\alpha = 0.05$, power $1-\beta = 0.80$, **Figure 10**). The cumulative Z-score curve neither crossed the traditional significant boundary, nor crossed the monitoring boundary. The number needed to treat was 567. Therefore, the primary outcome still needed more studies to test. Sensitivity analysis after exclusion of each solitary study did not find substantial change in the results. **Figure 11** showed the influence analysis for the primary outcome. Heterogeneity in all the comparisons was not significant.

Publication bias

Begg's funnel plot (**Figure 12**) and Egger's test for the overall complications did not find significant publication bias (P = 0.548 and P = 0.433, respectively).

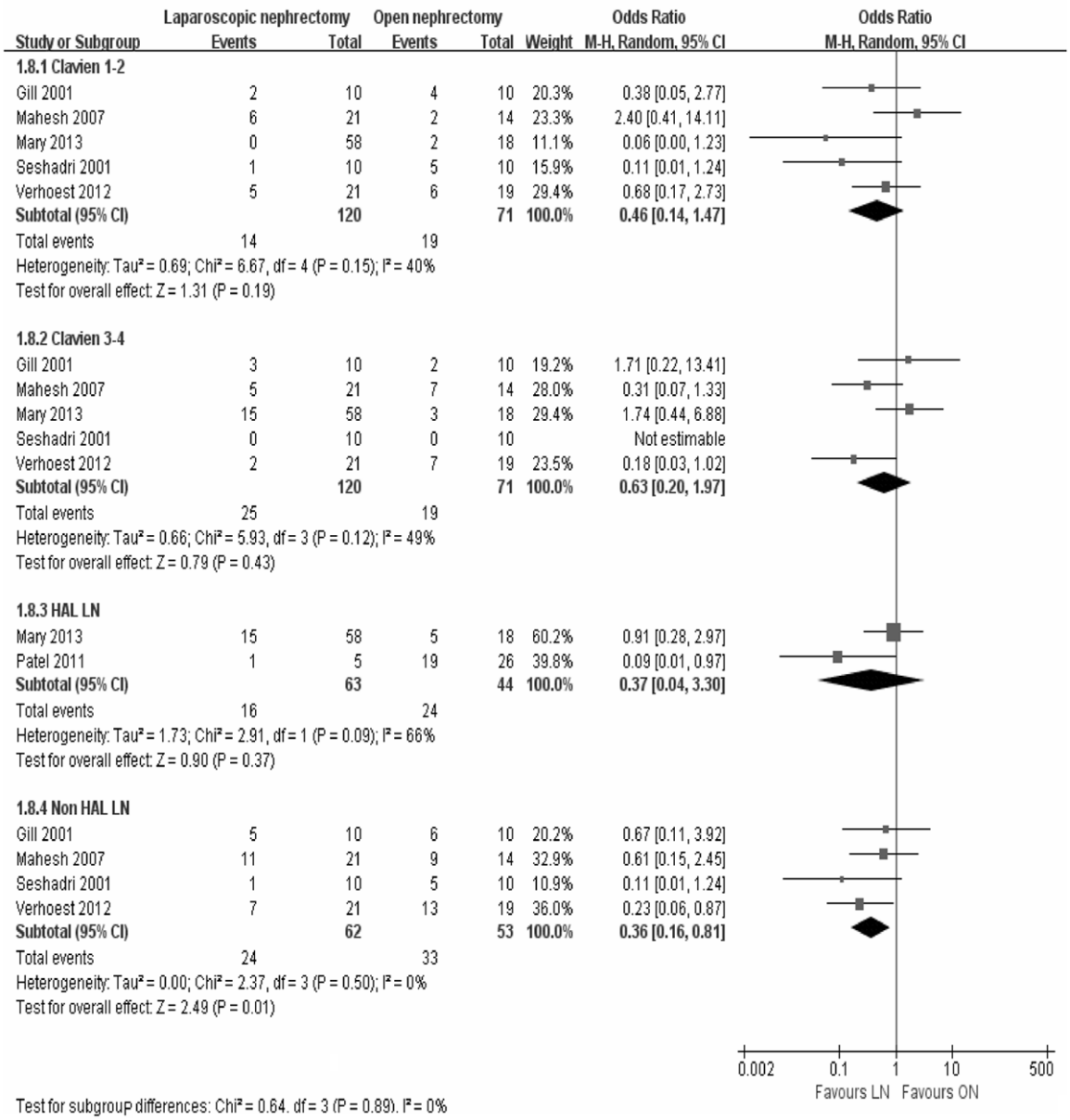

Figure 9. Subgroup analyses for the risk of overall postoperative complications between LN and TN in ADPKD.

Discussion

TN is considered as the gold standard in nephrectomy of ADPKD. Complication morbidity was an important indicator to evaluate the operation. Complication risk was 40 to 60% with a 3% rate of mortality in TN [16]. TN needed a large incision, and led to a higher mortality rate and morbidity rate when compared with LN [5, 17]. The complication rate of LN was less according to some previously published studies [18]. However, our results revealed that the risk of postoperative complications was similar between LN and TN in ADPKD. TSA indicated at least 567 patients were needed to prove this association.

The arteriovenous fistula formed thrombosis may be related to transient ischemia or arm position in the operation [6], and the risk of thrombosis was similar between LN and TN. The ileus happened after the nephrectomy partly because noxious fluid from the ruptured cysts [11]. In addition, cyst aspiration and kidney extraction in the nephrectomy could confuse the colon mesentery which was thin and

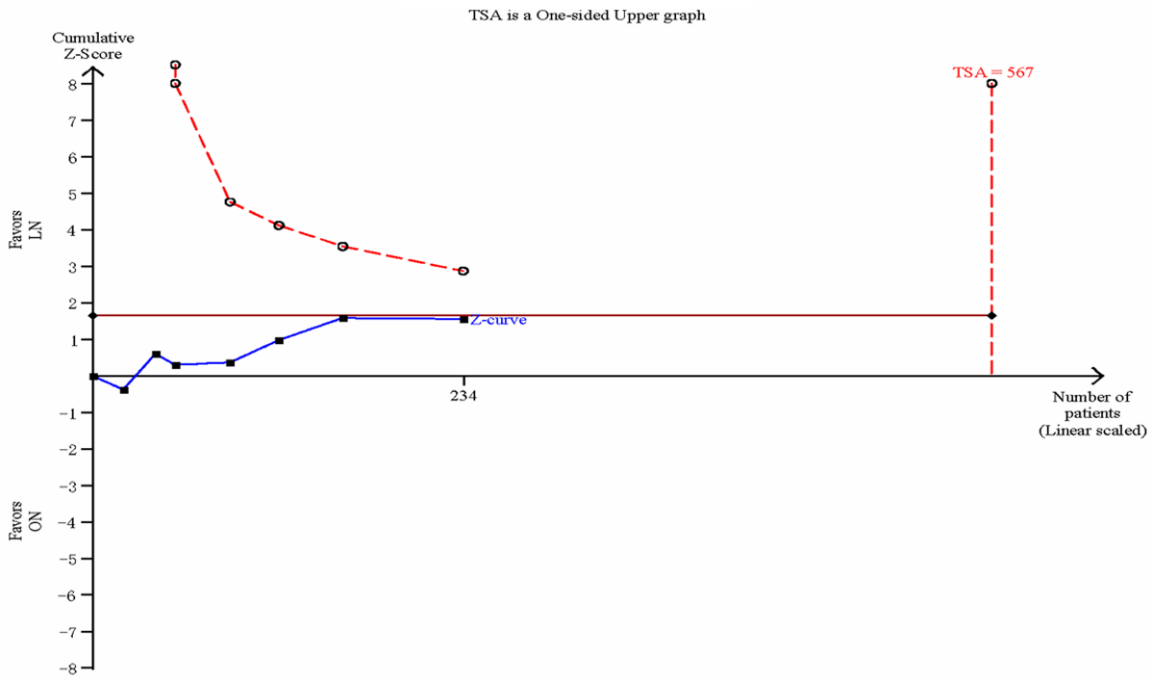

Figure 10. TSA for the risk of overall postoperative complications. Conventional test boundary was 0.05. Z-curve was the cumulative Z value of the studies by the publication year.

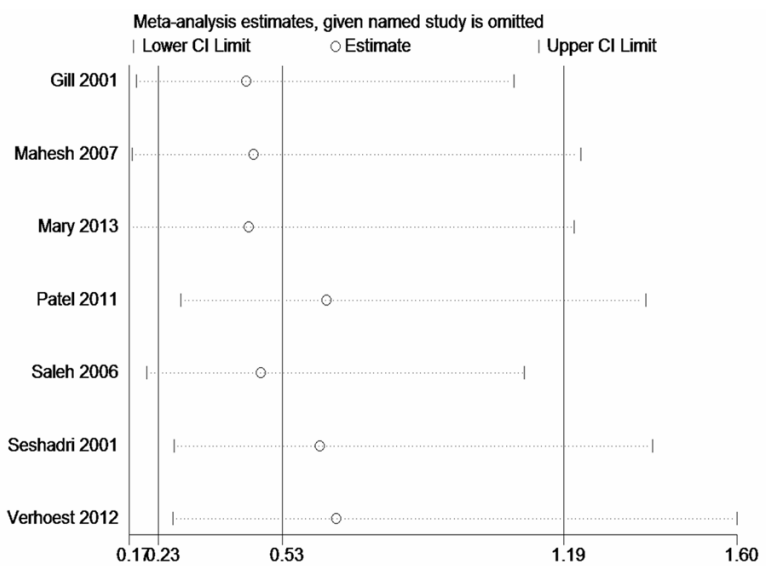

Figure 11. Influence analysis for the risk of overall postoperative complications.

stretched around the large polycystic kidney. One thing to be noted was the trocar insertion in the LN. Because of the huge size of the kidney, inserting open visual trocar first and preoperative computed tomography assessment were recommended to avoid intestinal tract injury [12]. Wound dehiscence/incision hernia, wound hematoma, and tear of visceral organ appeared to be less in LN compared with TN, but the result was not significant.

We found LN decreased the risk of complications in the non-HAL group. Nearly half of the complications were wound injury. LN has its superiority mainly in slight wound injury compared with TN [19]. Although LN needs pneumoperitoneum which may lead to some additional adverse events, the incidence was far less than the wound injury [3, 6]. HAL did not decrease the risk of complications significantly when compared with TN. HAL always needed an additional incision to take out an enlarged kidney of ADPKD [6]. Moreover, HAL could lead to hand fatigue, blunt hand feeling, enteroplegia risk and relatively long recovery time. However, HAL had allegedly short operative time and tactile sensation when compared with the total laparoscopy [20]. Complications in wound com-

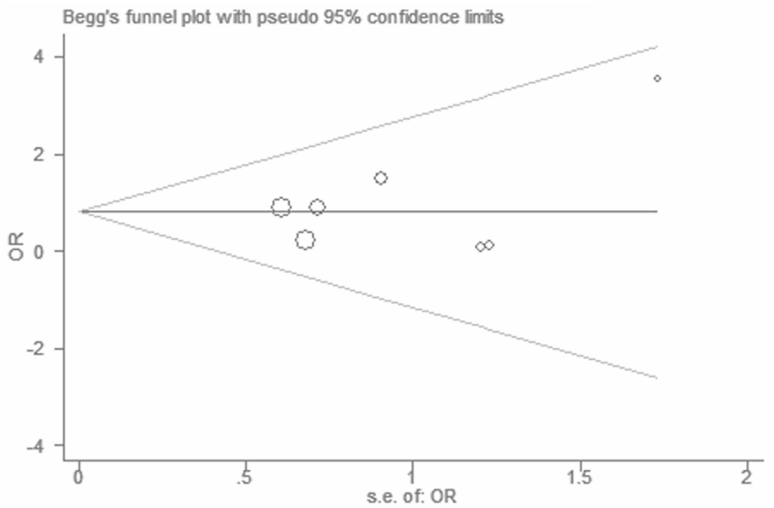

Figure 12. Funnel plot for the risk of overall postoperative complications.

plications (Clavien 1-2) and organ injury (Clavien 3-4) did not differentiate between the two groups. The results still were not clear, and needed more studies to prove.

Two-thirds of the included studies used exclusively the transperitoneal approach for the LN [6, 12-14], while the other two used the retroperitoneal approach and mixed approaches [3, 11]. There was no difference in complications between the retroperitoneal and the transperitoneal approaches. Nevertheless, in consideration of large kidney volume in ADPKD, the transperitoneal way provided larger space and more convenience for the surgeon. Patients with intra-abdominal adhesions better chose retroperitoneal approach to avoid violating the peritoneal cavity [14].

There was minimal heterogeneity in most of our results. However, this meta-analysis had several limitations: first, the sample size was scant. More large-scaled randomized controlled trials (RCTs) are needed to testify outcomes. Secondly, there was insufficient data for meta-analysis between pre-transplant and post-transplant patients. Severe complications (Clavien 3-4) happened more frequently in post-transplant patients compared with pre-transplant patients [3]. Third, unilateral or bilateral operations were only separately compared by Mary et al.'s study [6]. There was not enough evidence to detect difference between unilateral nephrectomy and bilateral nephrectomy. Last, prognosis of the ADPKD patients after the nephrectomy was not available in most of the studies. Seshadi et al. [12] reported that nobody had recurrent pain, infection or hemorrhage at one year after surgery.

In conclusion, LN was not associated with reduced risk of postoperative complications compared with TN in adult patients with ADPKD. More RCTs will be needed to demonstrate this in the future.

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Disclosure of conflict of interest

None.

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