



# Laparoscopic radical hysterectomy has higher risk of perioperative urologic complication than abdominal radical hysterectomy: a meta-analysis of 38 studies

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## Abstract

**Objective** A meta-analysis was performed to assess risks of intraoperative and postoperative urologic complications in laparoscopic radical hysterectomy (LRH) and abdominal radical hysterectomy (ARH).

**Methods** We searched Pubmed, EMBASE, and Cochrane library for studies published up to December, 2018. Manual searches of related articles and relevant bibliographies of published studies were also performed. Two researchers independently performed data extraction. Inclusion criteria of studies were: (1) had information of perioperative complications, and (2) had at least ten patients per group.

**Results** A total of 38 eligible clinical trials were collected. Intraoperative and postoperative urologic complications were reported by 34 studies and 35 studies, respectively. When all studies were pooled, odd ratios (OR) of LRH for the risk of intraoperative urologic complications compared to abdominal radical hysterectomy (ARH) was 1.40 [95% confidence interval (CI) 1.05–1.87]. The OR of LRH for postoperative complication risk compared to ARH was 1.35 [95% CI 1.01–1.80]. However, significant adverse effects of intraoperative urologic complications in LRH were not observed among articles published after 2012 (OR 1.12, 95% CI 0.77–1.62) in cumulative meta-analysis or subgroup analysis. The incidence of bladder injury was statistically higher than that of ureter injury ( $p=0.001$ ). In subgroup analysis, obesity and laparoscopic type (laparoscopic assisted vaginal radical hysterectomy) were associated with intraoperative urologic complications.

**Conclusion** LRH is associated with significantly higher risk of intraoperative and postoperative urologic complications than abdominal radical hysterectomy.

**Keywords** Intraoperative urologic complication · Postoperative urologic complication · Laparoscopic radical hysterectomy · Abdominal radical hysterectomy · Meta-analysis

Radical hysterectomy with bilateral pelvic lymph node dissection is the standard treatment for early uterine cervical cancer. Most of urologic complications that developed during surgery were associated with gynecologic field. The incidence of perioperative urologic complication is relatively higher in radical hysterectomy than that in other gynecologic surgeries. Intraoperative injuries of the bladder and the ureter as well as vesicovaginal and ureterovaginal fistulas in the postoperative period are important complications of radical

hysterectomy [1]. Bladder injuries can occur during bladder dissection to obtain adequate vaginal resection margin. Bladder injuries are frequent urologic complications in radical hysterectomy. Incidence of bladder injuries during radical hysterectomy ranges from 0.4 to 3.7% [2]. Clinically, ureter injury is more important because of its general tendency to be unrecognized. On the other hand, bladder injuries can be easily recognized and repaired immediately. Ureter injuries occur between uterine arteries and bladder. Changes in surgical techniques that limit extreme dissection of ureter injury have reduced ureteral injuries for many years. However, ureteral injury is still a major complication of radical hysterectomy.

Radical hysterectomy can be performed using laparoscopic radical hysterectomy (LRH) or abdominal radical hysterectomy (ARH). LRH is an alternative to ARH because

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laparoscopic surgery is associated with less postoperative pain, shorter length of hospital stay, better cosmetic outcome, and faster recovery of bowel function compared to open surgery [3]. Although LRS has many advantages, it has not been widely used by gynecologic oncologists due to technical difficulties, long learning curve, and concerns of surgical complications.

Many studies have compared perioperative complications including urologic complications of patients treated by LRH with those of patients treated by ARH. Most of these studies have reported that there is no statistical significance in surgical complications including urologic complications between the two groups. Several studies have reported that LRH is associated with a low rate of perioperative complications [4–7]. However, the population examined was usually too small to definitively evaluate perioperative complications. A few meta-analysis [8, 9] have evaluated oncologic safety and effectiveness of LRH compared to those of ARH. However, they did not focus on urologic complications. The important step of technical skill in radical hysterectomy is unroofing of ureteral tunnel and wide dissection of periureteral tissue and bladder which is associated with perioperative urologic complication.

Thus, the objective of this study was to determine the risk of intraoperative and postoperative urologic complications in LRH compared to that in ARH through a meta-analysis.

## Methods

### Literature search

A comprehensive, systemic search for published studies was conducted using Pubmed, EMBASE, and Cochrane library up to December 2018. Predefined keywords used for the search were ‘laparoscopic radical hysterectomy’, ‘abdominal radical hysterectomy’ in combination with ‘urologic complication’, and ‘uterine cervical cancer or carcinoma’. We also scanned bibliographies of relevant articles to locate additional publications. Only articles written in English were included.

### Selection criteria

We included comparative studies designed to assess intraoperative and postoperative complications of LRH and ARH in uterine cervical cancer. We also included laparoscopic radical parametrectomy [10] and laparoscopic radical trachelectomy [11] in addition to LRH. Robotic radical laparoscopy (RRH) was excluded. Review, editorials, letters, and meeting abstracts were excluded. Publications including fewer than 10 patients were also excluded. Three randomized controlled studies have been reported. Two of them were

excluded since their patient numbers were less than ten. We excluded those studies without available data for perioperative complications. If data were duplicated, the larger study was selected in meta-analysis.

### Data extraction

Two researchers independently evaluated the eligibility of all studies retrieved from the database based on predetermined criteria. Disagreements between evaluators were resolved by discussion. Of articles found in the three databases, duplicate articles and those that did not meet the selection criteria were excluded. We extracted the following data from the remaining studies: first author, journal name, year of publication, year enrolled, country where research was conducted, study design, study population, operation type, body mass index, and intraoperative and postoperative urologic complications. Intraoperative urologic complications included bladder injury, ureteral injury while postoperative urologic complications included ureterovaginal fistula, vesicovaginal fistula, ureteral stenosis, and urinary tract infection. Postoperative urinary retention and urinary incontinence were excluded.

### Main and subgroup analyses

We investigated the association between laparoscopic radical hysterectomy and risk of urologic complication as a main analysis. We also performed subgroup analyses for published year, quality of study design, body mass index (BMI, kg/m<sup>2</sup>), country, and operation method [laparoscopic assisted radical vaginal hysterectomy (LARVH) vs. total laparoscopic radical hysterectomy (TLRH)]. Published years of articles were divided into two groups: before 2012 and after 2012. Matched, prospective cohort studies were categorized as high quality while retrospective studies were categorized as low quality in the current meta-analysis. We considered BMI > 24 as obese group and BMI < 24 as standard group. Countries were categorized as Asia, America, and Europe. LARVH involved opening the paravesical and pararectal space, resecting a vaginal cuff, ligating the cardinal ligament and the uterosacral ligament, and unroofing of the ureter.

### Statistical analyses

Data for dichotomous variables were analyzed using odds ratio (OR). To compute pooled odds ratio with 95% CI, we used adjusted OR and 95% CI reported in each article whenever possible. We also carried out subgroup meta-regression analysis to assess the effect of subgroups and covariates such as published year, quality of study methodology, BMI, country, and operation method. We evaluated the possible heterogeneity in results across studies using Higgins I [12]

to measure the percentage of total variation across studies. We considered an  $I^2$  value  $> 30\%$  as indicative of substantial heterogeneity. We estimated a pooled OR with 95% CI using both fixed-effects [13] and random-effects models [14]. Fixed-effects model was utilized in the absence of significant heterogeneity while a random-effect model was used in the presence of significant heterogeneity. We evaluated publication bias of studies included in the final analysis using Begg's funnel plot and Egger's test. Meta-analyses were conducted using Stata MP version 15.0 software package (StatCorp, College Station, TX, USA).

## Results

### Literature search

We identified a total of 38 relevant studies published between 2001 and 2018 in the final analysis. Figure 1 shows a flow diagram of the process used to identify relevant studies. A total of 2705 articles were searched. We identified 322 articles from the three databases and bibliographies of relevant articles. After exclusion of 132 duplicate articles, the remaining 190 articles were screened by review according to their titles, abstracts, and publication types. Of these articles, 111 articles that did not meet the selection criteria were excluded. After reviewing the full text for the remaining 79 articles, we included 38 articles in the final analysis. The main reason for excluding 41 studies from the final review was due to no available data for urologic complication ( $N=27$ ). Other reasons included less than 10 patients ( $N=4$ ), comparison between robotic radical hysterectomy (RRH) vs. LRH or comparison between RRH and ARH ( $N=5$ ). Five articles were published in the same institution ( $N=5$ ). The largest study was selected for meta-analysis.

Intraoperative and postoperative complications were not described in four [6, 7, 11, 15] and three articles [4, 16, 17], respectively. Intraoperative and postoperative urologic complications were analyzed in 34 studies and 35 studies, respectively. We excluded one article in postoperative urinary complication due to publication bias and heterogeneity ( $I^2=35.9\%$ ,  $p=0.02$ ) during meta-analysis.

### Characteristics of the 38 studies included in the final analysis

Table 1 shows main characteristics of the 38 studies [4–7, 10, 11, 15–46] included in the final analysis. Their study design types were retrospective study ( $n=25$ ), matched case–control study ( $n=10$ ), prospective cohort study ( $n=2$ ), and RCT ( $n=1$ ). Locations of these studies were America ( $n=9$ ), Europe ( $n=12$ ), and Asia ( $n=13$ ). The enrollment

period (year) of participants across studies ranged from 1991 to 2016.

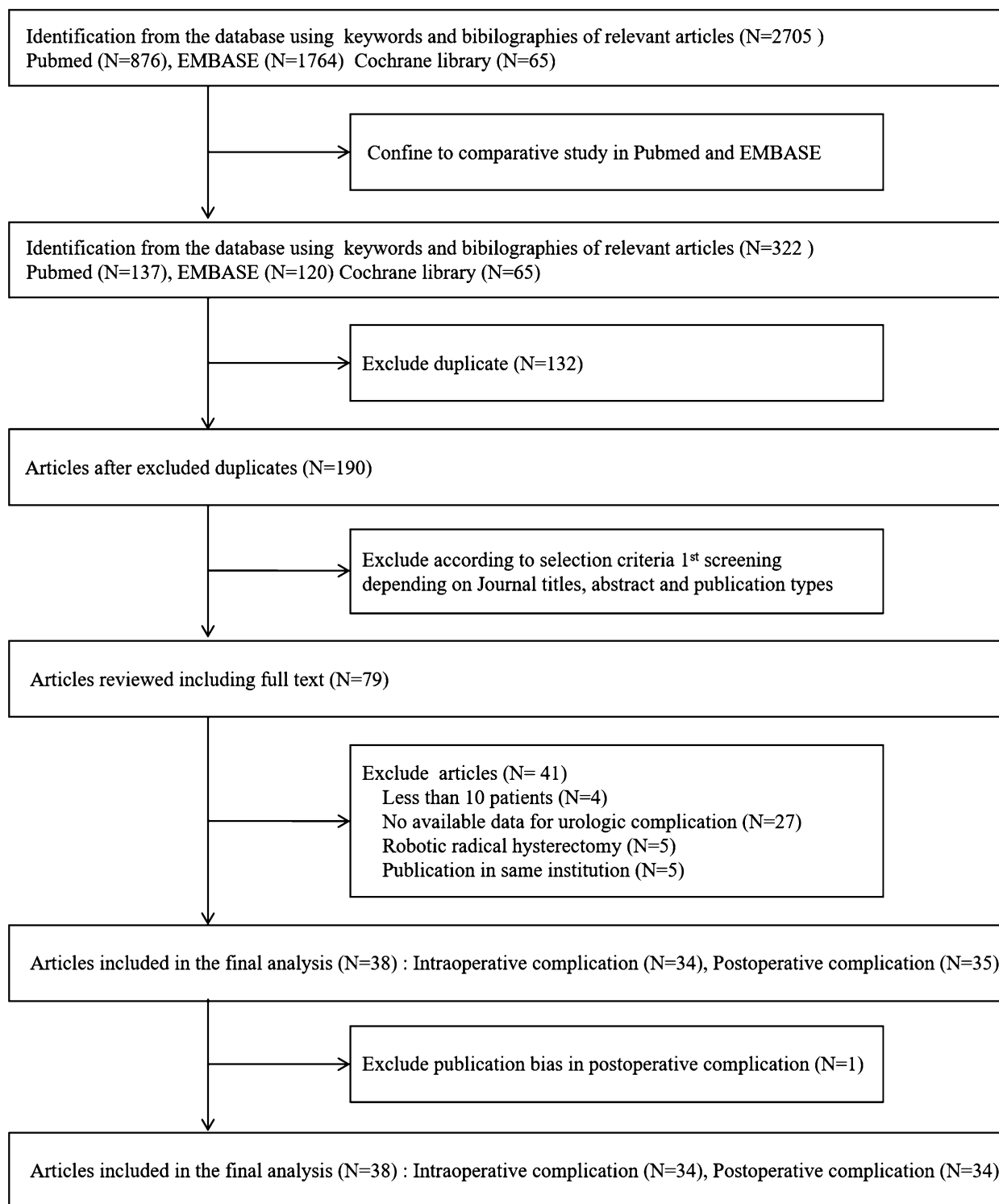
We identified 2720 patients in LRH and 4084 patients in ARH (2582 patients in LRH vs. 3989 patients in ARH in intraoperative analysis, 2398 patients in LRH vs. 2367 patients in ARH in postoperative analysis). LARVH and TLRH were performed in 7 and 26 studies, respectively. Median or mean BMI was described in 24 studies. If BMD was greater than 24, the group was classified as obese ( $n=10$ ). If BMD was less than 24, then the group was classified as standard ( $n=10$ ). BMI was reported in 14 studies.

### LRH and risk of urologic complications

Figures 2 and 3 show the effect of LRH on the risk of intraoperative and postoperative urologic complications in meta-analysis of 34 studies, respectively. Intraoperative complications were detected in 98 of 2,582 patients (bladder injury,  $n=65$ ; ureter injury,  $n=33$ ) who underwent LRH. The incidence of bladder injury was significantly higher than that of ureter injury ( $p=0.001$ ). In a fixed-effects meta-analysis of 34 studies including intraoperative urologic complications, the overall risk was increased in the laparoscopic group (OR 1.40; 95% CI 1.05–1.87,  $p=0.022$ ). In a fixed-effects meta-analysis of 34 studies including postoperative urologic complications, overall risk was increased (OR: 1.35; 95% CI 1.01–1.80,  $p=0.039$ ). There was no heterogeneity among studies of intraoperative urologic complications ( $I^2=0.0\%$ ,  $p=0.850$ ) or among studies of postoperative complications ( $I^2=0.0\%$ ,  $p=0.763$ ). No publication bias was observed in these selected studies. Results of assessment of publication bias showed symmetric distribution. All scattered hollow round points were symmetrical on both sides, indicating that the bias of data applied in this study was small (Fig. 4). Cumulative meta-analysis for intraoperative urologic complication of laparoscopic radical hysterectomy was performed. As shown in the cumulative meta-analysis plot (Fig. 5), the summary estimate for intraoperative complications began to be significantly higher in the laparoscopy group than that in the laparotomy group after inclusion of the study (2001) reported by Malur et al. [18]. The OR remained significantly higher in the laparoscopy group up to the study reported by Van De Lande et al. [33] in 2012. As time went on, the OR tended to decrease. The OR remained statistically insignificant after the study reported by Wright et al. [17] in 2012. The meta-regression showed a strong evidence of an association between published year and intraoperative urologic complication ( $p=0.036$ , coefficient:  $-0.084$ ).

### Subgroup meta-analysis

Table 2 shows the effect of laparoscopy on intraoperative urologic complication in subgroup meta-analyses



**Fig. 1** Flow diagram of the identification of relevant studies for meta-analysis of this study

by published year, quality of study, BMI, country, and laparoscopic type. Significant harmful effects of intraoperative urologic complications in LRH were observed among articles published before 2012 (OR 2.0, 95% CI

1.24–3.23), but not in articles published after 2012 (OR 1.12, 95% CI 0.77–1.62) (Fig. 6). There was no significant association between postoperative urologic complications and published year (articles before 2012: OR 1.35; 95%

**Table 1** Characteristics of 38 studies included in the current meta-analysis

Authors [Reference]	Year	Journal	Year enrolled	Country	Study design	Population (N)		Op type	BMI <sup>b</sup> (kg/m <sup>2</sup> )
						Laparoscopy	open		
Malur et al. [18]	2001	Surg Endosc	1991–1994	Germany	Matched	70	70	LARVH	25
Lee et al. [19]	2002	JAAGL	Unknown	Taiwan	Prospective cohort	30	30	TLRH	UK
Abu-Rustum et al. [20]	2003	Gynecol Oncol	2000–2002	USA	Retrospective	19	195	TLRH	23
Steed et al. [21]	2004	Gynecol Oncol	1996–2003	Canada	Retrospective	71	205	LARVH	25
Jackson et al. [22]	2004	Gynecol Oncol	1996–2003	UK	Matched	50	50	LARVH	24.8
Sharma et al. [6]	2006	Int J Gynecol Cancer	1999–2005	England	Retrospective	35	32	LARVH	28.1
Zakashansky et al. [23]	2007	Int J Gynecol Cancer	2000–2006	USA	Matched	30	30	TLRH	UK
Uccella [24]	2007	Gynecol Oncol	2004–2007	Italy	Retrospective	50	48	TLRH	23
Li et al. [25]	2007	Gynecol Oncol	1998–2005	China	Retrospective	90	35	TLRH	UK
Ghezzi et al. [26]	2007	Gynecol Oncol	2004–2007	Italy	Retrospective	50	48	TLRH	23
Frumovitz et al. [27]	2007	Obstetrics & Gynecology	2004–2006	USA	Retrospective	35	54	TLRH	28.1
Sobiczewski et al. [16]	2009	Int J Gynecol Cancer	2001–2004	Poland	Retrospective	22	58	TLRH	UK
Malzoni et al. [28]	2009	Ann Surg Oncol	1995–2007	Italy	Retrospective	65	62	TLRH	26
Estape et al. [29]	2009	Gynecol Oncol	2006–2008	USA	Retrospective	17	14	TLRH	UK
Papacharalabous et al. [30]	2009	Gynecol Surg	2003–2006	UK	Retrospective	14	12	LARVH	UK
Pahisa J et al. [4]	2010	Int J Gynecol Cancer	1997–2007	Spain	Retrospective	67	23	LARVH	27.2
Darai et al. [7]	2010	Surg Endosc	2001–2008	France	Retrospective	16	13	TLRH <sup>a</sup>	24.5
Soliman et al. [31]	2011	Gynecol Oncol	2007–2010	USA	Retrospective	31	30	TLRH	29.5
Lee et al. [5]	2011	Eur J Obstet Gynecol	1994–2001	ROK	Matched	24	48	TLRH	23.4
Nam et al. [32]	2012	Annal of Oncology	1997–2008	ROK	Matched cohort	263	263	LARVH	UK
Van De Lande et al. [33]	2012	Int J Gynecol Cancer	1998–2005	Netherland	Retrospective	63	93	TLRH	UK
Wright et al. [17]	2012	Gynecol Oncol	2006–2010	USA	Retrospective cohort	217	1610	TLRH	UK
Campos et al. [34]	2013	Trials	1999–2004	Brazil	RCT	16	14	TLRH	UK
Jiang et al. [10]	2013	JLS	2006–2011	China	Retrospective	18	22	LRP	UK
Bogani et al. [15]	2014	J Surg Oncol	2004–2013	Italy	Matched	45	45	TLRH	23.2
Kong et al. [44]	2014	Int J Gynecol Cancer	2006–2013	ROK	Retrospective	40	48	TLRH	22.3
Ditto et al. [35]	2015	Eur J Surg Oncol	2002–2013	Italy	Matched	60	60	TLRH	24.3
Laterza et al. [36]	2015	Eur J of OG Reprod Biol	2002–2007	Italy	Matched	27	27	TLRH	23.8
Lu et al. [37]	2015	J Minim Invasive Gynecol	2003–2014	China	Prospective	108	98	TLRH	UK
Suh et al. [38]	2015	PLoS One	2003–2011	ROK	Matched	55	55	TLRH	UK
Vieira et al. [11]	2015	Gynecol Oncol	2002–2013	USA	Retrospective	42	58	LRT	23.4
Cai et al. [39]	2016	Int J of Gynaecol Obstet	2007–2013	China	Retrospective	99	30	TLRH	UK
Wang et al. [45]	2016	Int J Gynecol Cancer	2002–2012	China	Matched cohort	203	203	TLRH	23.9
Mendivil et al. [40]	2016	Surg Oncol	2009–2013	USA	Retrospective	49	39	TLRH	27.9
Zhang et al. [41]	2017	Medicine (Baltimore)	2008–2012	China	Retrospective	35	42	LARVH	22.7

**Table 1** (continued)

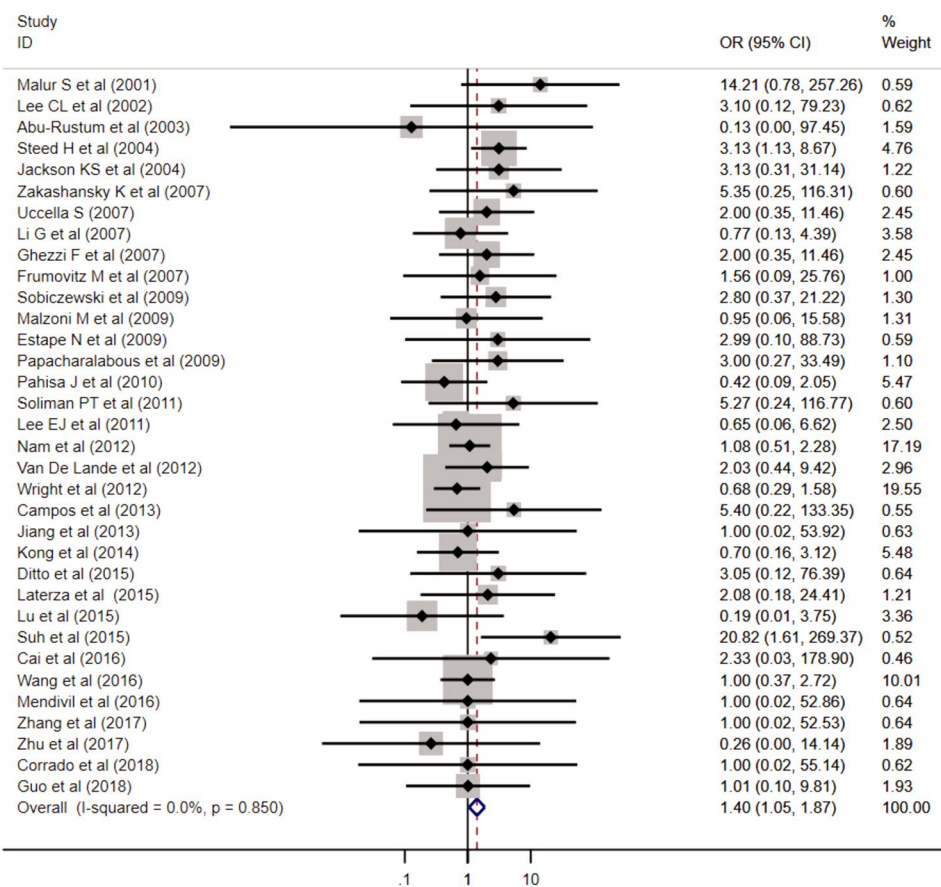
Authors [Reference]	Year	Journal	Year enrolled	Country	Study design	Population (N)		Op type	BMI <sup>b</sup> (kg/m <sup>2</sup> )
						Laparoscopy	open		
Zhu et al. [46]	2017	Int J Gynecol Cancer	2011–2014	China	Retrospective cohort	30	80	TLRH	24.8
Corrado et al. [42]	2018	In J Gynecol Cancer	2001–2016	Italy	Retrospective	152	101	TLRH	23.5
Guo et al. [43]	2018	Onco Targets Ther	2000–2013	China	Retrospective	412	139	TLRH	22.8

OR odd ratio, CI confidence interval, ROK Republic of Korea, TLRH total laparoscopic radical hysterectomy, LARVH laparoscopic assisted radical vaginal hysterectomy, LRP laparoscopic radical parametrectomy, LRT laparoscopic radical trachelectomy, BMI Body Mass Index, Cx urologic complication, JAAGL J Am Assoc Gynecol Laparosc, Eur J of OG Reprod Biol Eur J of Obstet Gynecol Reprod Biol, UK unknown

<sup>a</sup>TLRH with colorectal resection

<sup>b</sup>Mean or median

**Fig. 2** Intraoperative urologic complications of laparoscopic radical hysterectomy compared to abdominal radical hysterectomy in a fixed effect model of case–control studies. Forest plot showed intraoperative complication in 34 studies. No significant between-study heterogeneity was detected ( $I^2=0\%$ ,  $p=0.850$ ) (OR 1.40; 95% CI 1.05–1.87,  $p=0.022$ )

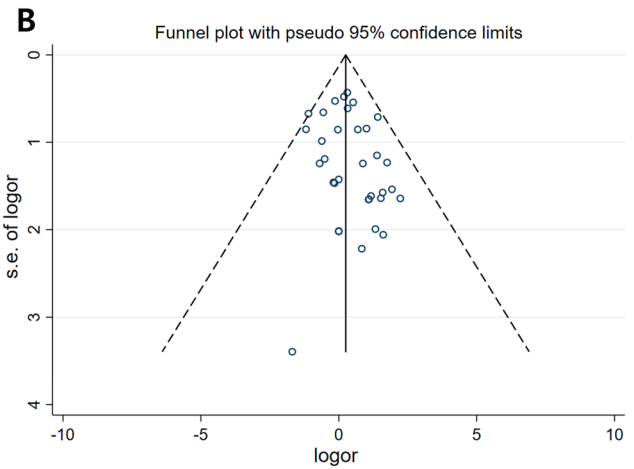
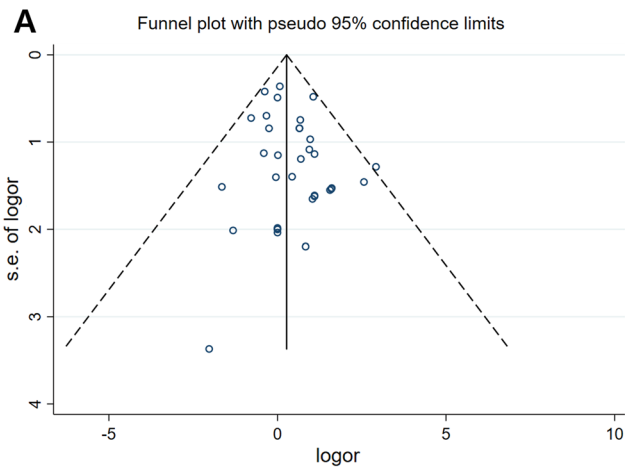
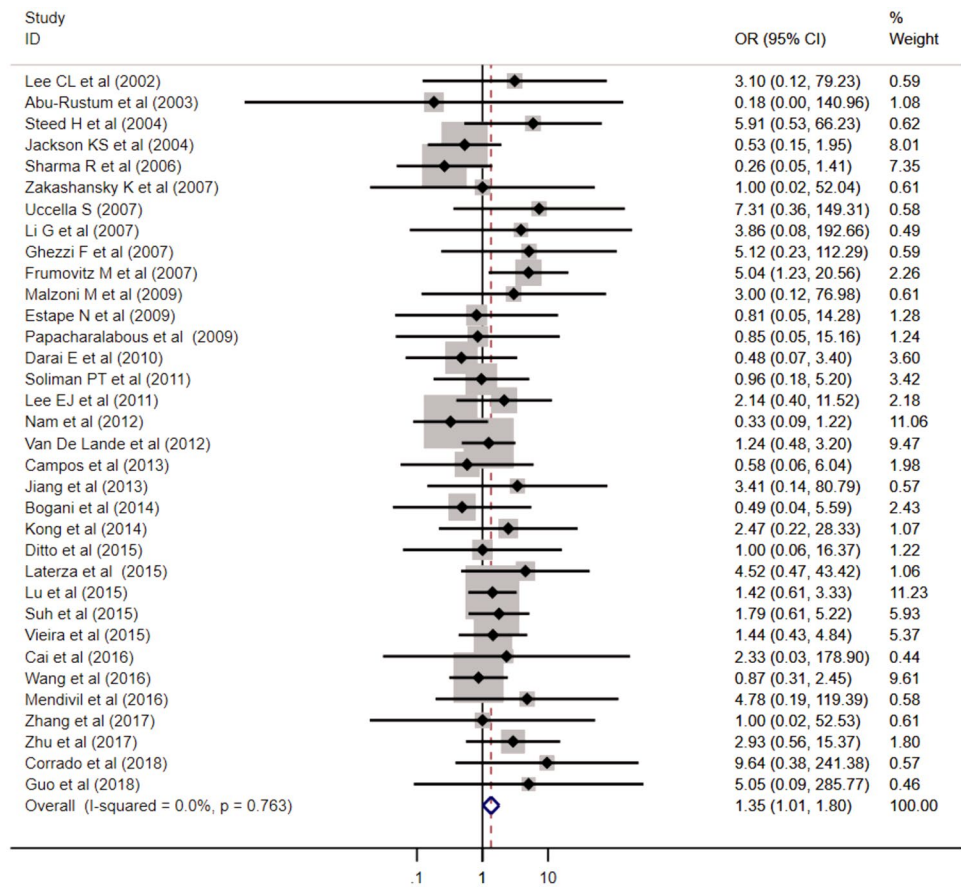


CI 0.829–1.352; articles after 2012: OR 1.352; 95% CI 0.948–1.928).

There was no evidence for an association between the quality of study design and intraoperative urologic complications. Intraoperative urologic complications in LRH showed significant association with obese patients (OR 2.12, 95% CI 1.14–3.96), but not with patients having standard BMI (OR 1.08, 95% CI 0.61–1.92). In a fixed-effects meta-analysis of 26 studies including TLRH, the

overall risk of intraoperative urologic complications was not increased (OR 1.28, 95% CI 0.90–1.83). However, the overall risk of intraoperative urologic complications was increased in 7 studies including LARVH (OR 1.67, 95% CI 1.01–2.77). Subgroup meta-analysis of 13 Asian studies (OR 1.12, 95% CI 0.72–1.74) and 9 American studies (OR 1.39, 95% CI 0.83–2.33) showed that the overall risk of intraoperative urologic complications was not increased. However, the overall risk of intraoperative urologic

**Fig. 3** Postoperative urologic complications of laparoscopic radical hysterectomy compared to abdominal radical hysterectomy in a fixed effect model of case–control studies. Forest plot showed intraoperative complication in 34 studies. No significant between-study heterogeneity was detected ( $I^2=0\%$ ,  $p=0.763$ ) (OR 1.35; 95% CI 1.01–1.80,  $p=0.039$ )



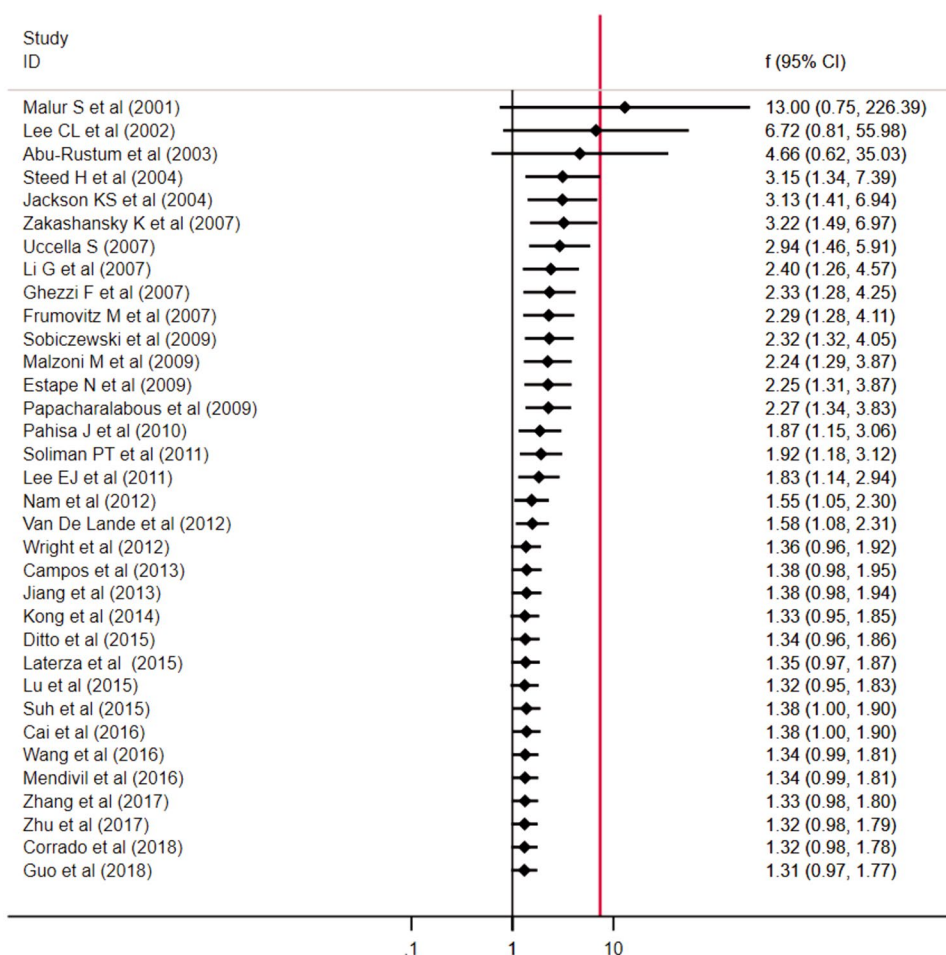
**Fig. 4** Funnel plots of intraoperative (A) and postoperative (B) urologic complications of laparoscopic radical hysterectomy compared to abdominal radical hysterectomy

complications was increased in a subgroup meta-analysis of 12 European studies (OR 2.05, 95% CI 1.13–3.69). No significant association was observed for study quality, BMI, country, or laparoscopic type in a meta-regression analysis.

**Discussion**

LRH is thought to be associated with better recovery, smaller scar, and faster back to normal life than ARH [3].

**Fig. 5** Cumulative meta-analysis intraoperative urologic complications of laparoscopic radical hysterectomy compared to open radical hysterectomy

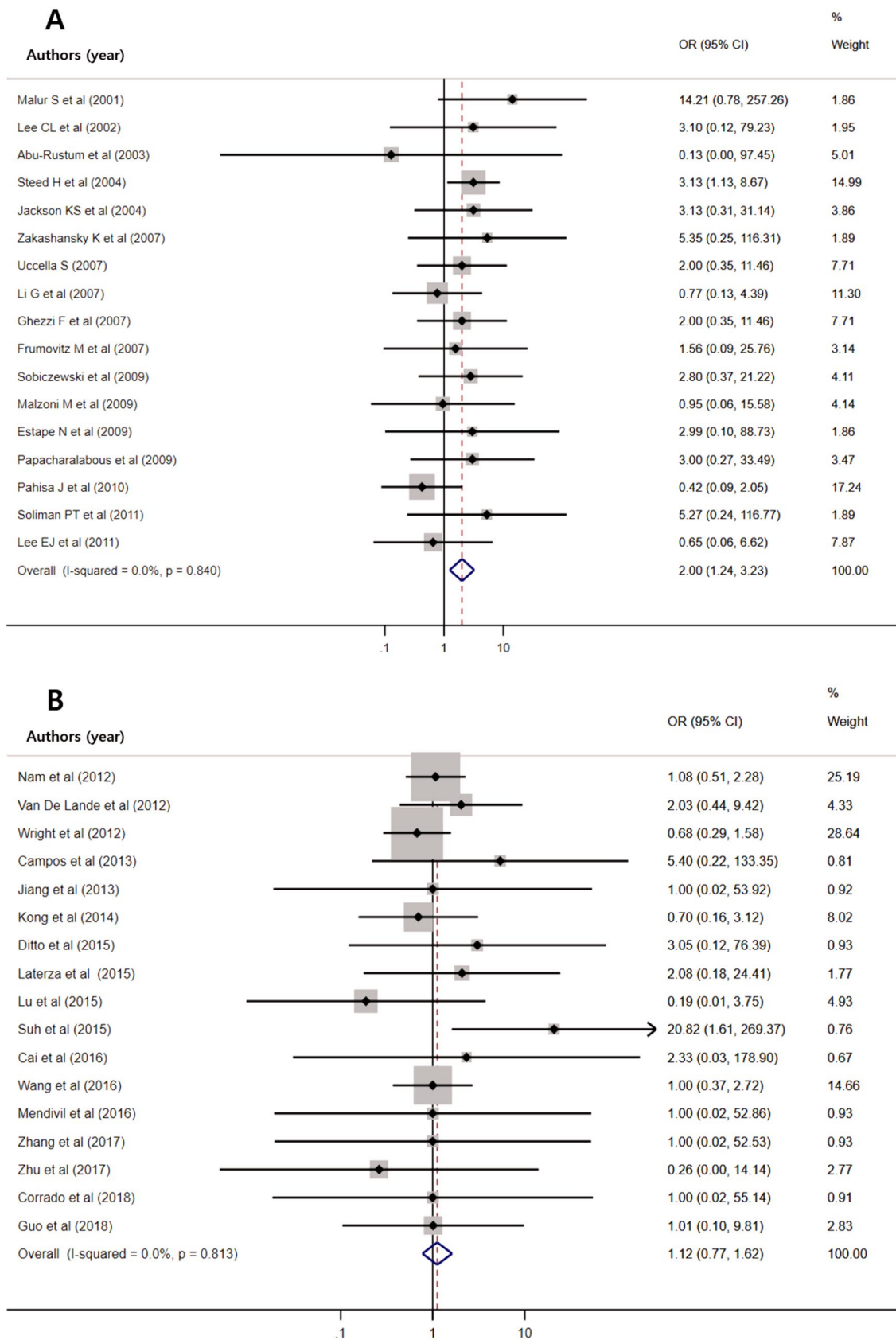


**Table 2** Association between laparoscopic radical hysterectomy and intraoperative urologic complication in subgroup analysis by published year, quality of study methodology, body mass index, country and laparoscopic type (N=34)

Category	No of studies	Summary OR (95% CI)	p	Heterogeneity, I <sup>2</sup> (%)	Model used
All	34	1.40 (1.05–1.87)	0.022	0.0	Fixed effect
Published year					
Before 2012	17	2.0 (1.24–3.23)	0.004	0.0	Fixed effect
After 2012	17	1.12 (0.77–1.62)	0.549	0.0	Fixed effect
Quality of study methodology					
High quality	14	1.32 (0.91–1.93)	0.142	15.5	Fixed effect
Low quality	20	1.52 (0.96–2.39)	0.073	0.0	Fixed effect
Body mass index (kg/m <sup>2</sup> )					
Standard (< 24)	10	1.08 (0.61–1.92)	0.794	0.0	Fixed effect
Obese (> 24)	10	2.12 (1.14–3.96)	0.018	0.0	Fixed effect
Country					
Asia	13	1.12 (0.72–1.74)	0.603	0.0	Fixed effect
America	9	1.39 (0.83–2.33)	0.207	0.0	Fixed effect
Europe	12	2.05 (1.13–3.69)	0.017	0.0	Fixed effect
Operation method					
TLRH	26	1.28 (0.90–1.83)	0.174	0.0	Fixed effect
LARVH	7	1.67(1.01–2.77)	0.045	28.2	Fixed effect

OR odd ratio, CI confidence interval, TLRH total laparoscopic radical hysterectomy, LARVH laparoscopic assisted radical vaginal hysterectomy; BMI, body mass index





**Fig. 6** Intraoperative urologic complications of laparoscopic radical hysterectomy compared to abdominal radical hysterectomy in a fixed effect model of case–control. Subgroup meta-analysis results for articles published before 2012 (A) and articles published after 2012 (B) are shown

Many comparative studies have reported that survival outcome and perioperative complications after LRH are comparable to those after ARH in patients with uterine cervical cancer. Most of these studies comparing LRH with ARH were retrospective studies or small sized RCT with limited data. Recently published large-scale RCT (LACC trial) [47] showed that minimally invasive radical hysterectomy including LRH was associated with lower rates of overall survival and disease-free survival compared to ARH. Unfortunately, perioperative complications were not described in LACC trial. The incidence of urologic complications during LRH is thought to be higher than that of any other gynecologic surgical procedure due to wide dissection of periureteral tissue and bladder, unroofing the ureter in the cardinal ligament, and the distorted pelvic anatomy caused by mass such as cervical cancer. Most of previous comparative studies revealed no statistical significance in urologic complications between LRH and ARH.

In 2012, we performed a meta-analysis of perioperative urologic complications related to LRH and reported that the risk of intraoperative urologic complications was higher in LRH group than that in ARH group based on data released through 2011 [48]. Although the incidence of intraoperative urologic complications was significantly higher in LRH, studies analyzed were performed at different time. The risk of intraoperative urologic complications in LRH had a tendency to decrease as time went by in cumulative meta-analysis. Laparoscopy continue to evolve. It could reduce complications due to technical changes and the development of instruments. The learning curve over time could also affect complication rate. The accumulation of surgical experience, the improvement of surgical skill, and the development of laparoscopic instruments such as advanced bipolar devices, Endo-GIA staplers, and Endo-Clips could reduce complications, thus affecting surgical outcomes as time went by. Thus, we performed meta-analysis again by including data released between 2012 and 2017. Our results showed that there was still an association between LRH and risk for intraoperative urologic complications. However, subgroup analysis showed that LRH among published articles after 2012 (OR 1.12, 95% CI 0.77–1.62) was not associated with a significant increased risk of intraoperative complications. There was a strong evidence for an association between published year and intraoperative urologic complications in meta-regression. Postoperative urologic complications were also higher in the LRH group, inconsistent with our previous study [48]. In subgroup analysis by published year, articles published after 2012 or before 2012 were not associated with high incidence of postoperative urologic complication in LRH. Difference became evident as the number of studies and patients included in the meta-analysis became larger.

There were two large comparative studies [49, 50] of perioperative complications about LRH versus ARH. Uppal

et al. [49] reported perioperative complications of LRH and robotic radical hysterectomy (RRH) compared with ARH for 7180 cases of uterine cervical cancer from 2012 to 2015 using the National Inpatient Sample (NIS) from the Healthcare Cost and Utilization Project in USA. Perioperative complications were significantly lower for LRH and RRH. However, intraoperative urologic complication including ureter and bladder injury was higher in LRH and RRH than that in ARH ( $p=0.027$ ). Ratios of LRH and RRH in all study groups were 17.2% and 82.2%, respectively. They did not distinguish LRH from RRH. Thus, we excluded that study from the meta-analysis. Kim et al. [50] have reported that intraoperative complications of LRH have lower (OR 0.73; 95% CI 0.63–0.86) than ARH for 6,335 cases of uterine cervical cancer from 2011 to 2014 using the Korea Health Insurance Review and Assessment Service database. Intraoperative complications included vascular and intestinal injury in addition to ureter and bladder injury. Unfortunately, accurate assessment of urologic complications was difficult because the article [50] did not describe urinary complications that could be distinguished from other intraoperative complications.

Risks of bladder injuries are statistically higher than those of ureter injuries. In radical hysterectomy, ureter injuries usually occur during dissection of periureteral tissue to confirm ureter passage and find the uterine artery. The process of unroofing the ureter in the cardinal ligament, an important step in radical hysterectomy, plays a crucial role in inducing ureteral injury.

In the subgroup meta-analysis by country, results of European studies showed that the risk of urinary complications during surgery was significantly higher, although there was no significant difference between results of Asian and American studies. It is not easy to predict basic laparoscopic surgery technique. The habit of using chopsticks for Asian people and different surgical education systems in different countries might affect the outcome [51]. With regard to surgical approach, the incidence of intraoperative urologic complication rate was increased during LARVH. Vaginal route allows a precise dissection of vaginal cuff. In LARVH, after the uterine ligament was cut, the bladder and ureter are seen by traction of the uterus through vaginal route. This provides a theoretical background in which complications may be different due to differences in surgical methods. Obesity is a predisposing factor of perioperative urinary track complications in patients undergoing cancer surgery through laparoscopy [52, 53]. The current meta-analysis showed that intraoperative urologic complications were higher in patients who were relative overweight with LARVH, consistent with our previous study [48]. Our meta-analysis has several limitations. First, most studies involved were retrospective. They failed to provide the highest level of evidence. As a result,

selective deflection and missing data could degrade the quality of study. A randomized clinical trial comparing LRH with ARH in patients with early stage uterine cervical cancer is needed. Results of such study will help determine the risk of perioperative urologic complications in LRH. Recently, RRH has been replacing LRH. One meta-analysis showed that RRH was superior to LRH in perioperative complication [54]. However, it focused on all intraoperative and postoperative complications related to surgery, not urologic complications. In the future, a study is needed to assess the risk of perioperative urologic complications of RRH and LRH. Second, we included only English language articles which might be a bias of our study. Exclusion of studies written in language other than English might have affected our outcomes. However, there have been few studies on this topic written in non-English languages. Third, we did not classify the incidence of urologic complications according to the type of radical hysterectomy. Although most patients underwent type III radical hysterectomy, some patients underwent type II radical hysterectomy. The incidence of urologic complications might be higher in advanced uterine cervical cancer and type III radical hysterectomy. Bladder dysfunction and urinary incontinence were excluded from the analysis of postoperative complication because many articles did not describe them as it was uncommon to evaluate these complications objectively in postoperative care. This might have led to biased results in analysis of postoperative urologic complications. Stage of the disease and diabetes that could act as a predisposing factor of the urinary track injury during radical hysterectomy [55] was not evaluated either.

Despite these limitations, our meta-analysis demonstrated that there was an association between LRH and risk for intraoperative and postoperative urologic complications. We also confirmed that intraoperative urologic complication decreased after 2012 in subgroup analysis and meta-regression. Of the 38 studies included in this meta-analysis, two studies [21, 38] reported that intraoperative urologic complications were significantly higher in the LRH group. Thus, publication bias is minimal. It was confirmed by funnel plot. Although this meta-analysis was based on results of retrospective studies, it included more than 4,000 patients with a comprehensive review of the available literature. Our findings should be verified by large-scale prospective cohort studies or randomized controlled trials in the future.

### Compliance with ethical standards

**Disclosures** Jong Ha Hwang and Bo Wook Kim have no conflicts of interest or financial ties to disclose.

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