Urologic complication in laparoscopic radical hysterectomy: Meta-analysis of 20 studies

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1. Introduction

Cervical cancer remains the second most frequent cancer among women worldwide. The current standard treatment for early cervical cancer is radical hysterectomy and lymph node dissection. However, several surgeons gained experience to replace a laparotomy with a laparoscopy. Laparoscopic radical hysterectomy (LRH) and pelvic lymphadenectomy have been developed for treatment of gynaecologic cancers, and have gradually become accepted as important in the management of early cervical cancer with operative and oncologic safety. Laparoscopic surgery is associated with less postoperative pain, shorter hospitalisation, better cosmetic results, fast recovery and return.
of bowel function in comparison with open surgery. However, despite these many advantages of laparoscopic surgery, LRH has not been widely used by gynaecologic oncologists because of its technical complexity, long learning curve, and concerns of surgical morbidity. Among the complications, urinary tract injuries can have major personal, financial and social costs.

Many studies have compared the total complications including urologic complications of patients treated by LRH with those of patients treated by abdominal radical hysterectomy (ARH). Most of these studies found no statistical significance between two groups and the results of several studies indicated that LRH is associated with a low rate of intraoperative or postoperative complications. However, the population examined was usually too small to definitively evaluate urologic complications and there has been no clear assessment of urologic complications in LRH.

The aim of this study was to assess the risk of intraoperative and postoperative urologic complications of LRH and lymph node dissection vs. ARH and lymph node dissection by conducting a meta-analysis.

2. Methods

2.1. Literature search

A comprehensive, systemic search for published studies was conducted using Pubmed, EMBASE and Cochrane library through December 2011. The predefined keywords used for the search were ‘laparoscopic radical hysterectomy’, ‘urologic complication’ and ‘cervical cancer’. We also scanned the bibliographies of relevant articles to locate additional publications. Only articles written in English were included.

2.2. Selection criteria

We included case-control studies and cohort studies designed to assess intraoperative and postoperative complications of laparoscopic and open radical hysterectomy. We rejected review, editorial, letters, or meeting abstracts. Publications including fewer than 10 patients were excluded. Only one randomised controlled trial has been reported; it was excluded since there were fewer than 10 patients. We excluded those studies with no available data for outcome measures. If data were duplicated, the first published study was included in the analysis.

2.3. Data extraction

Two researchers independently evaluated the eligibility of all studies retrieved from the database based on the predetermined criteria. Disagreements between evaluators were resolved by discussion. Of the 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, year of publication, journal name, country, study design, years enrolled, characteristics, study population, odds ratio (OR) with 95% confidence interval (CI), and intraoperative and postoperative urologic complications. Intraoperative urologic complications included bladder injury and ureteral injury. Postoperative urologic complications included ureterovaginal fistula, vesicovaginal fistula, ureteral stenosis and urinary tract infection. Postoperative urinary retention and urinary incontinence were excluded.

2.4. Main and subgroup analyses

We investigated the association between laparoscopic radical hysterectomy and risk of urologic complication as the main analysis. We also performed subgroup analyses by the type of LRH analyses by quality of study design (comparative study vs. matched case-control studies, classifying one cohort study and four matched case-control studies as high quality studies in the current meta-analysis), body mass index (BMI, kg/m²; standard; ≥18.5 & <25 vs. obese; ≥25 & <30), and operation type [laparoscopic assisted radical vaginal hysterectomy (LARVH) vs. total laparoscopic radical hysterectomy (TLRH)]. LAVRH was performed vaginally and involved opening the pararectal space, resecting a vaginal cuff, ligating the cardinal ligament and inferior half of the uterosacral ligament, and dissecting the ureter out of the uterosacral ligament. All procedures were performed laparoscopically, except the vaginal cuff incision and closure in one study, which we regarded it as TLRH in the subgroup analysis.

2.5. Statistical analyses

To compute pooled odds ratio with 95% CI, we used the 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 study characteristics such as study design, BMI and type of LRH. We examined the heterogeneity in results across studies using Higgins $\hat{I}^2$, which measures the percentage of total variation across studies. We considered an $\hat{I}^2$ value >50% as indicative of substantial heterogeneity. We estimated a pooled OR with 95% CI on the basis of both fixed-effects and random-effects models. When substantial heterogeneity was not found, the pooled estimate calculated based on the fixed effects model was represented. We evaluated the publication bias of the studies included in the final analysis using Begg’s funnel plot and Egger’s test. Data were analysed using Stata SE version 10.0 software package (StatCorp, College Station, TX).
3. Results

3.1. Literature search

In total, 20 studies published between 2001 and 2011 were included in the final analysis. Fig. 1 shows a flow diagram of the process used to identify relevant studies. We identified 304 articles from the two databases and the bibliographies of relevant articles. After the exclusion of 58 duplicate articles, the remaining 246 articles were screened by review according to their titles and abstracts. Of these articles, 218 articles that did not meet the selection criteria were excluded. After reviewing the full text for the remaining 28 articles, we included 20 articles in the final analysis. The main reasons for excluding the final eight studies from the final review were <10 patients (n = 3), comparison between robotic radical hysterectomy (RRH) vs. LRH (n = 2), and comparison between RRH and ARH (n = 3). Intraoperative and postoperative urologic complications were analysed in 18 studies and 16 studies, respectively.

3.2. Characteristics of the 20 studies included in the final analysis

Table 1 shows the main characteristics of the 20 studies included in the final analysis. The study design types were comparative study (n = 15), matched case-control study (n = 4), and prospective cohort study (n = 1). The locations of the studies were North America (n = 6), Europe (n = 10), and Asia (n = 4). The enrolment period participants across studies ranged from 1991 to 2010.

We identified 870 patients in LRH and 1199 patients in ARH (819 patients in LRH vs. 1154 patients in ARH in intraoperative analysis, 781 patients in LRH vs. 1118 patients in ARH in postoperative analysis). LARVH and TLRH were performed in seven studies and 13 studies, respectively. Median BMI was used in six studies and mean BMI was used in eight studies. BMI was unknown in six studies. BMI was obese (P25 & <30) in seven studies and standard (P18.6 & <25) in seven studies.

3.3. LRH and risk of urologic complications

Fig. 2 shows the effect of LRH on risk of intraoperative and postoperative urologic complications in the meta-analysis of 18 and 16 studies, respectively. Intraoperative complications were detected in 48 of 804 patients (bladder injury, n = 37; ureter injury, n = 11) who underwent LRH. The incidence of bladder injury was statistically higher than that of ureter injury (p < 0.001). In a fixed effects meta-analysis of 18 studies including intraoperative urologic complications, the...
Table 1
Characteristics of the 20 studies included in the meta-analysis.

<table>
<thead>
<tr>
<th>Authors [reference]</th>
<th>Year</th>
<th>Journal</th>
<th>Year enrolled</th>
<th>Country</th>
<th>Study design</th>
<th>Population (N)</th>
<th>Laparoscopy BMIb (kg/m²)</th>
<th>Laparoscopic type</th>
<th>Intraoperative cx, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al.</td>
<td>2002</td>
<td>JAAGL</td>
<td>Unknown</td>
<td>Taiwan</td>
<td>Prospective</td>
<td>30</td>
<td>14.1 (0.78–257.26)</td>
<td>LARVH</td>
<td>3.20 (0.13–81.78)</td>
</tr>
<tr>
<td>Abu-Rustum et al.</td>
<td>2003</td>
<td>Gynecol Oncol</td>
<td>2000–2002</td>
<td>USA</td>
<td>Comparative</td>
<td>19</td>
<td>14.1 (0.78–257.26)</td>
<td>TLRH</td>
<td>0.75 (0.04–13.78)</td>
</tr>
<tr>
<td>Nam et al.</td>
<td>2004</td>
<td>Gynecol Oncol</td>
<td>1997–2002</td>
<td>ROK</td>
<td>Comparative</td>
<td>84</td>
<td>25</td>
<td>LARVH</td>
<td>0.84 (0.08–9.44)</td>
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<tr>
<td>Zakashansky et al.</td>
<td>2007</td>
<td>Int J Gynecol Cancer</td>
<td>2000–2006</td>
<td>USA</td>
<td>Matched</td>
<td>30</td>
<td>3.13 (1.13–8.67)</td>
<td>LARVH</td>
<td>5.35 (0.25–116.31)</td>
</tr>
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<td>Uccella et al.</td>
<td>2007</td>
<td>Gynecol Oncol</td>
<td>2004–2007</td>
<td>Italy</td>
<td>Comparative</td>
<td>50</td>
<td>25</td>
<td>LARVH</td>
<td>2.00 (0.35–11.46)</td>
</tr>
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<td>Li et al.</td>
<td>2007</td>
<td>Gynecol Oncol</td>
<td>1998–2005</td>
<td>China</td>
<td>Comparative</td>
<td>90</td>
<td>25</td>
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<td>0.77 (0.13–4.39)</td>
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<td>Ghezzi et al.</td>
<td>2007</td>
<td>Gynecol Oncol</td>
<td>2004–2007</td>
<td>Italy</td>
<td>Comparative</td>
<td>50</td>
<td>25</td>
<td>LARVH</td>
<td>2.00 (0.35–11.46)</td>
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<tr>
<td>Frumovitz et al.</td>
<td>2007</td>
<td>Obstetrics &amp; Gynecology</td>
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<td>USA</td>
<td>Comparative</td>
<td>35</td>
<td>25</td>
<td>LARVH</td>
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<td>Int J Gynecol Cancer</td>
<td>2001–2004</td>
<td>Poland</td>
<td>Comparative</td>
<td>22</td>
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<td>LARVH</td>
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<td>Malzoni et al.</td>
<td>2009</td>
<td>Ann Surg Oncol</td>
<td>1995–2007</td>
<td>Italy</td>
<td>Comparative</td>
<td>65</td>
<td>25</td>
<td>LARVH</td>
<td>0.95 (0.06–15.58)</td>
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<td>Estape et al.</td>
<td>2009</td>
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<td>USA</td>
<td>Comparative</td>
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<td>25</td>
<td>LARVH</td>
<td>2.64 (0.10–69.88)</td>
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<tr>
<td>Papacharalabous et al</td>
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<td>Gynecol Surg</td>
<td>2003–2006</td>
<td>UK</td>
<td>Comparative</td>
<td>14</td>
<td>25</td>
<td>LARVH</td>
<td>3.00 (0.27–33.49)</td>
</tr>
<tr>
<td>Pahisa et al.</td>
<td>2010</td>
<td>Int J Gynecol Cancer</td>
<td>1997–2007</td>
<td>Spain</td>
<td>Comparative</td>
<td>67</td>
<td>25</td>
<td>LARVH</td>
<td>27.2</td>
</tr>
<tr>
<td>Darai et al.</td>
<td>2010</td>
<td>Surg Endosc</td>
<td>2001–2008</td>
<td>France</td>
<td>Comparative</td>
<td>16</td>
<td>25</td>
<td>LARVH</td>
<td>5.17 (0.24–112.28)</td>
</tr>
<tr>
<td>Soliman et al.</td>
<td>2011</td>
<td>Gynecol Oncol</td>
<td>2007–2010</td>
<td>USA</td>
<td>Comparative</td>
<td>31</td>
<td>25</td>
<td>LARVH</td>
<td>29.5</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; CI, confidence interval; ROK, Republic of Korea; TLRH, total laparoscopic radical hysterectomy; LARVH, laparoscopic assisted radical vaginal hysterectomy; BMI, body mass index; Cx, urologic complication; JAAGL, J Am Assoc Gynecol Laparosc.

* TLRH with colorectal resection.

b Mean or median.
overall risk was increased in the laparoscopic group (OR, 1.97; 95% CI 1.23–3.13). In a fixed effects meta-analysis of 16 studies including postoperative urologic complications, overall risk was not significant (OR, 1.35; 95% CI 0.84–2.16). There was no heterogeneity among studies of intraoperative urologic complications ($p = 0.640$) or among studies of postoperative complications ($p = 0.910$). No publication bias was observed in the selected studies (Begg’s funnel plot was symmetric; Egger’s test, $p$ for bias = 0.07; Fig. 3). Cumulative meta-analysis for intraoperative urologic complication of laparoscopic radical hysterectomy was performed (Fig. 4). As shown in the cumulative meta-analysis plot, the summary estimate for intraoperative complications began to be significantly higher in the laparoscopy than in the laparotomy group after 2004 with inclusion of the study by Steed et al. After that, the OR remained significant higher in the laparoscopy group up to the most recent study. However, as time went on, the OR tended to decrease.
3.4. Subgroup meta-analysis

Table 2 shows the effect of laparoscopic effects on intraoperative urologic complication in subgroup meta-analyses by quality of study, BMI, country and laparoscopic type. Significant harmful effects of intraoperative urologic complications in LRH were observed among the high-quality studies (OR 3.45, 95% CI 1.21–9.98), but not in the low-quality studies (OR, 1.68, 95% CI 0.99–2.83). There was significant association between intraoperative urologic complications in LRH and obese patients (OR, 2.16, 95% CI 1.04–4.49), but not patients with standard BMI (OR, 1.67, 95% CI 0.77–3.64). In a fixed effects meta-analysis of 13 studies including TLRH (OR, 1.63, 95% CI 0.88–3.04), the overall risk of intraoperative urologic complications was not increased. However, the overall risk of intraoperative urologic complications was increased in 5 studies including laparoscopy assisted radical vaginal hysterectomy (LARVH) (OR, 2.49, 95% CI 1.22–5.08). The meta-analysis of four Asian studies (OR, 0.92, 95% CI 0.31–2.77) showed the overall risk of intraoperative urologic complications was not increased, whereas the overall risk of intraoperative urologic complications was increased in a meta-analysis of five North American studies and nine European studies. No significant association was observed for study design, BMI, laparoscopic type in a meta-regression analysis.

4. Discussion

The incidence of urologic complications during LRH is thought to be higher than any other gynecologic surgical procedure because of wide dissection of periure-
thral tissue and bladder and the distortion of the normal pelvic anatomy by a mass such as cervical cancer. However, previous comparative studies revealed no statistical significance in urologic complications between LRH and ARH. In the 20 studies that were studied in this meta-analysis, only one study reported that intraoperative urologic complications were significantly higher in the laparoscopic group.

The finding from this meta-analysis indicated that LRH is associated with the risk of intraoperative urologic complications. Our results show that the risks of bladder injuries are statistically higher than that of ureter injuries. In radical hysterectomy, extensive dissection of ureteral adventitial tissue to confirm ureter passage and find the uterine artery was required. Ureter injuries usually in the dissection of the distal portion of the ureter near its entrance in the bladder, which is the trickiest step in radical hysterectomy. Bladder injuries occur during bladder dissection to obtain sufficient vaginal resection margin, which might be a more risky procedure to induce intraoperative urologic complications.

In the subgroup meta-analyses by study design, low-quality studies showed no significant increased risk for intraoperative urologic complication, while high-quality studies showed a significant increased risk for intraoperative urologic complications. These inconsistent findings between two groups can be explained by the quality of the study methodologies. In the subgroup meta-analysis by country, North America and Europe showed significant increased risk for intraoperative urologic complications, whereas the Asian patients showed no significant difference. One study reported that the use of chopsticks was associated with statistically significant better mean time in placing a piece of bowel on a retrieval bag and measuring a piece of bowel. Fine motor movement is needed for use of chopsticks, which may translate into better laparoscopic skill. However, it is difficult to predict baseline laparoscopic skill. Although Asian people are accustomed to using chopsticks, there is no sufficient evidence whether chopstick use aids in learning laparoscopic surgery. Concerning the method for surgical approach, the intraoperative urologic complication rate increased when LAVRH was performed. Vaginal route allows a precise incision to the vaginal cuff. In LAVRH, the bladder base and ureters are brought to view by traction on the uterus via the vaginal route after the ligaments of the uterus have been divided. Therefore, there is a theoretical possibility that urologic complications are different between TLRH and LAVRH. Our observations showed LAVRH is vulnerable to intraoperative urologic complications. The most common laparoscopic procedure associated with bladder injury is laparoscopic assisted vaginal hysterectomy in laparoscopic surgery.

Overweight or obese patients were associated with poor surgical outcomes such as laparotomy conversion in laparoscopic surgery. Overweight or obese patients were associated with poor surgical outcomes such as laparotomy conversion in laparoscopic surgery. However, the results were inconsistent. Obesity does not increase the risk of intraoperative and postoperative complications in benign gynaecologic surgery and endometrial cancer as it does in total laparoscopic hysterectomy. The current meta-analysis revealed that intraoperative urologic complications are higher in overweight patients.

The studies that were analysed were conducted at different times. As time went by, the risk for intraoperative urologic complications in laparoscopic radical hysterectomy and bladder and the distortion of the normal pelvic anatomy by a mass such as cervical cancer. However, previous comparative studies revealed no statistical significance in urologic complications between LRH and ARH. In the 20 studies that were studied in this meta-analysis, only one study reported that intraoperative urologic complications were significantly higher in the laparoscopic group.

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tomy had a tendency to decrease. Laparoscopy is continually evolving, and the effects of technical changes and development of instruments might lessen complications. The learning curve over time also might have influenced complication rate. With the improvement in surgical skill and instruments over time, the incidence of intraoperative complications might be decreased further.

Our meta-analysis has several limitations. First, it does not provide the highest level of evidence because all studies except one were retrospective. Therefore, selection bias and missing data might reduce the quality. A phase III randomised clinical trial comparing laparoscopic radical hysterectomy with abdominal radical hysterectomy in patients with early stage cervical cancer is ongoing, the outcome of which will be helpful to determine the risk of intraoperative urologic complications in LRH. Second, the exclusion of non-English language articles might bias our findings. However, there have been few studies on this topic written in languages other than English. Upon reviewing the English abstracts of these non-English articles, none met our main eligibility criteria. Therefore, their exclusion would not likely have substantially altered our results. Third, the accumulation of surgical experience and development of laparoscopic instruments such as advanced bipolar devices (LigaSure, Harmonic scalpel and Enseal), Endo-GIA staplers, and Endo-Clips could affect the surgical outcomes as time went by. Fourth, we did not categories the incidence of urologic complications according to the stage. The incidence of urologic complications might increase in more advanced stages. Although most of the patients underwent type III radical hysterectomy, patients with type II radical hysterectomy were also included in our analysis, which could affect the results. We did not include bladder dysfunction and urinary incontinence in the postoperative analysis due to insufficient data and difficulty of objective evaluation, which can be a bias to assess postoperative urologic complications.

Despite these limitations, our meta-analysis demonstrates that there is an association between LRH and risk for intraoperative urologic complications. In subgroup analysis, the intraoperative urologic complication rate of patients who underwent LAVRH was higher compared with TLRRH. Emphasis should be placed on prevention of urologic complications by meticulous surgical technique and on management of urologic complications in LRH. To our knowledge, this is the first meta-analysis of urologic complications in LRH. This study of more than 2000 patients represents the largest and most comprehensive review of the available literature in this topic. Our findings from retrospective studies should be confirmed in large-scale prospective cohort studies or randomised controlled trials providing the highest level of evidence in the future research.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

References


