Surgical and Oncological Outcome of Total Laparoscopic Radical Hysterectomy versus Radical Abdominal Hysterectomy in Early Cervical Cancer in Singapore

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Abstract

Introduction: The Wertheim’s radical abdominal hysterectomy (RAH) has been the traditional surgical approach for operable Stage IB cervical cancer in Singapore whereas total laparoscopic radical hysterectomy (TLRH) was introduced only in 2009. In this study, we aimed to compare the long-term surgical outcome between the two routes of surgery in our center.

Methods: This is a prospective study performed in a single large tertiary institution in Singapore. Inclusion criteria included surgically fit patients with early cervical cancer and no radiological evidence of regional or distant metastases.

Results: From November 2009 to December 2014, 51 TLRHs and 85 RAHs were performed. Median blood loss in the TLRH group was significantly lower than in the RAH group (300 vs. 500 mL; P = 0.002) as was median hospital stay (5 vs. 6 days; P = 0.001). Operative time was significantly higher in the TLRH group (262 vs. 228 min; P < 0.001). There was no significant difference in bladder recovery. Intraoperative complications were encountered in 2 (3.9%) TLRH patients and 1 (1.2%) RAH patient. Postoperative complications occurred in 3 (5.9%) TLRH patients and 8 (9.4%) RAH patients. With a median follow-up of 117 (range 1.6–314.6) weeks in the TLRH group and 143.3 (range 0.4–304.7) weeks in the RAH group, 9 (17.6%) TLRH patients and 7 (8.2%) RAH patients had recurrence. There was no significant difference in the overall 3-year survival between the TLRH group and the RAH group for tumor size ≤2 cm (100.0% vs. 97.0%; P = 0.37). However, there was a trend toward lower survival for the TLRH group for tumor size >2 cm (61.9% vs. 85.4%; P = 0.06).

Conclusion: The results of our study suggest that with appropriate patient selection, TLRH can be a safe and effective procedure for the management of early cervical cancer in Singapore, especially in women with small tumors ≤2 cm but should be used with caution in women with larger tumors.

Keywords: Cervical cancer, laparoscopic surgery, radical hysterectomy, surgical outcomes

INTRODUCTION

Cervical cancer is the fourth most common cancer and one of the leading causes of death in women worldwide.1 In Singapore, as a result of cervical cancer screening, the incidence has declined over the last three decades, and it is currently the 10th most common cancer in women, affecting 3.2% of the local female population.2 Abdominal radical hysterectomy (RAH) is the de facto standard of surgical management of Stage IA2 to Stage IIA cervical cancer in Singapore for many years. However, with the advancement in minimally invasive (MIS) techniques as well as emerging evidence from many established cancer centers, there is a growing trend towards MIS for the management of early cervical cancer. The study by Roussey et al.3 showed that total laparoscopic radical hysterectomy (TLRH) has similar oncologic outcomes to the open approach, with shorter hospital stay and faster recovery. Since 2009, TLRH has been the surgeon of choice for early cervical cancer at our center. Since then, there have been many studies comparing surgical outcomes between TLRH and RAH, and our study aims to compare the long-term surgical outcome between TLRH and RAH in our center.

Methods: This is a prospective study performed in a single large tertiary institution in Singapore. Inclusion criteria included surgically fit patients with early cervical cancer and no radiological evidence of regional or distant metastases.

Results: From November 2009 to December 2014, 51 TLRHs and 85 RAHs were performed. Median blood loss in the TLRH group was significantly lower than in the RAH group (300 vs. 500 mL; P = 0.002) as was median hospital stay (5 vs. 6 days; P = 0.001). Operative time was significantly higher in the TLRH group (262 vs. 228 min; P < 0.001). There was no significant difference in bladder recovery. Intraoperative complications were encountered in 2 (3.9%) TLRH patients and 1 (1.2%) RAH patient. Postoperative complications occurred in 3 (5.9%) TLRH patients and 8 (9.4%) RAH patients. With a median follow-up of 117 (range 1.6–314.6) weeks in the TLRH group and 143.3 (range 0.4–304.7) weeks in the RAH group, 9 (17.6%) TLRH patients and 7 (8.2%) RAH patients had recurrence. There was no significant difference in the overall 3-year survival between the TLRH group and the RAH group for tumor size ≤2 cm (100.0% vs. 97.0%; P = 0.37). However, there was a trend toward lower survival for the TLRH group for tumor size >2 cm (61.9% vs. 85.4%; P = 0.06).

Conclusion: The results of our study suggest that with appropriate patient selection, TLRH can be a safe and effective procedure for the management of early cervical cancer in Singapore, especially in women with small tumors ≤2 cm but should be used with caution in women with larger tumors.
centers worldwide showing total laparoscopic radical hysterectomy (TLRH) to be a safe and feasible alternative to the conventional radical hysterectomy, TLRH was thus introduced as an alternative approach in the management of early cervical cancer in Singapore in 2009.[3-15] A prospective pilot study was published in 2013, comparing TLRH with RAH by the Department of Gynaecologic Oncology, KK Women’s and Children’s Hospital, and the results established the safety and feasibility of TLRH in our study population.[16] However, the recently published prospective randomized trial Laparoscopic Approach to Cervical Cancer (LACC) showed that TLRH had a lower 3-year overall survival compared to RAH (93.8% vs. 99%), and this has impacted the practice of TLRH worldwide.[17] In this study, we aimed to compare the long-term surgical and oncological outcomes between the two routes of surgery in our center.

**METHODS**

This is a prospective study performed by the Department of Gynaecologic Oncology, KK Women’s and Children’s Hospital (KKH), Singapore, between November 2009 and December 2014.

The inclusion criteria were – (a) early cervical cancer, defined as FIGO (2009)[18] Stage IA–IIA cervical cancer and (b) clinical and radiological absence of lymph node and distant metastases. The exclusion criteria were (a) an age of more than 70 years; (b) a uterus that was more than 12 weeks in size; (c) pregnancy; and (d) previous midline laparotomies. Patients who were medically unfit and/or had preexisting medical conditions, for which pneumoperitoneum is contraindicated, were also excluded from the study.

Demographic factors, characteristics of the tumor, intraoperative and postoperative surgical outcomes, histological risk factors, recurrence, and overall survival were recorded prospectively.

The method of surgery is as described in the pilot study published in 2013.[16] In summary, the TLRH was carried out through four-port laparoscopy, and the uterine manipulator was used in most cases in this study. For the colpotomy, the manipulator was removed, and intracorporeal colpotomy was carried out with the aid of the LiNA colpotomy tube (LiNA Medical, Devon, UK) to ensure adequate surgical margins. The vaginal cuff was sutured either laparoscopically or transvaginally.

Patients with high-risk features or had lymph node metastases received adjuvant treatment. All patients were followed up every 3 months in the first 2 years, followed by 6 monthly checkups for the subsequent 3 years, in accordance with the KKH Gynaecological Cancer Centre’s protocol. Systemic examination, including pelvic examination and vaginal vault smear, was performed at each visit. If there was any suspicion of a recurrence, radiological imaging and tissue biopsy were performed.

The Mann–Whitney U test and Chi-square test were used for statistical analysis. The Kaplan–Meier and log-rank test were used for survival analysis. Categorical variables were reported as proportion, while continuous variables were reported as median and range values. All analyses were performed in relation to treatment modality, using the Statistical Package for the Social Sciences version 22 (SPSS Inc., Chicago, IL, USA). All statistical tests were two-sided with exact significance reported. \( P < 0.05 \) was considered as statistically significant.

**RESULTS**

From November 2009 to December 2014, a total of 51 TLRHs and 85 RAHs were performed. There was no statistical difference between the age, parity, BMI, ethnicity, FIGO stage, or histology between the two groups. Although there was a trend toward a larger median tumor size in the open surgery group (2 cm vs. 3 cm), it did not reach statistical significance (Table 1).

The surgical outcomes for both groups are shown in Table 2. The median operative time for the TLRH group (262 min) was longer than that of the RAH group (262 vs. 228 min; \( P < 0.0001 \)). Compared to the RAH group, the TLRH group had significantly lower blood loss (300 vs. 500 mL; \( P = 0.002 \)) and shorter hospital stay (5 vs. 6 days; \( P = 0.001 \)).

Intraoperative complications were encountered in 2 (3.9%) patients in the TLRH group and 1 (1.2%) patient in the RAH group. In the TLRH group, the complications included one intraoperative bowel injury and one case of hemorrhage from the parametrial vessels requiring conversion to laparotomy. In the RAH group, one intraoperative ureteric injury was observed. No intraoperative bladder complications were observed in the two groups.

Postoperative complications occurred in 3 (5.9%) TLRH patients, namely, one patient with a long-term voiding disorder requiring intermittent catheterization and two with vault dehiscence which were repaired. There were no wound infections in TLRH group. There were 8 (9.4%) postoperative complications in the RAH group, including one having a long-term voiding disorder, one with vault dehiscence, one with a ureterovaginal fistula, and five having wound infections.

There were no statistically significant differences in the histological risk factors, or adjuvant treatment received between the two groups, as shown in Table 3. In comparing the surgical outcomes for the TLRH group in 2009–2011 to
that of the TLRH group in 2011–2014, there was a significantly lower rate of close or positive vaginal margin involvement in 2011–2014 at 1 case (3.0%) compared to 2009–2011, in which there were 5 (27.8%) cases ($P = 0.02$). There were no significant differences for positive lymph node metastases, positive parametrial involvement, and adjuvant treatment between the two time frames.

With a median follow-up of 29.2 (range 0.4–78.7) months in the TLRH group, 9 (17.6%) patients were found to have recurrences. The sites of recurrence included vaginal vault, peritoneum, lung, retroperitoneum, adnexa, liver, and iliac bone. In the RAH group, the median follow-up was 35.8 (range 0.1–76.2) months, with recurrence in 7 (8.2%) patients in the vaginal vault, upper abdomen, iliac fossa, kidney, lung, and bone.

Eight patients (15.7%) from the TLRH group were deceased, of which seven had identified recurrence. In the RAH group, seven patients (8.2%) were deceased, of which four patients had recurrence.

Kaplan–Meier analysis [Figure 1] showed the mean survival for the TLRH and RAH groups were 267 and 280 weeks, respectively. The overall 3-year survival for the TLRH group is 86.4% and that for the RAH group is 95.0%. However, the log-rank analysis showed no statistically significant difference in the overall survival between the two groups ($P = 0.175$). This is likely due to the limited sample size and the short follow-up time of <3 years, which limits determination of 5-year survival.

From another perspective, for tumor sizes ≤2 cm, overall survival is 100% and 97% ($P = 0.37$) for the TLRH and RAH groups, respectively [Figure 2]. For tumor sizes >2 cm, the overall survival is 61.9% in the TLRH group and 85.4% in the RAH group ($P = 0.06$) [Figure 3]. This is consistent with recommendations for the use of TLRH for smaller tumors and open abdominal surgery for larger tumors, hence the importance of proper patient selection for TLRH to be chosen as a surgical method over RAH.

### Discussion

Radical hysterectomy is the conventional treatment for patients with early cervical cancer and can be associated...
with serious intraoperative and postoperative morbidity. A substantial number of studies comparing MIS radical hysterectomy to traditional abdominal radical hysterectomy appear to have superior surgical outcomes compared to the abdominal route.\textsuperscript{[3-15]}

Diver \textit{et al.} studied a total of 383 women with cervical cancer undergoing either MIS techniques (laparoscopic and robotic) for radical hysterectomy compared to the traditional laparotomy approach and found that MIS approach does not compromise patient outcomes, including overall survival, rate of recurrence, and the frequency of pelvic lymph node dissection or positivity. Morbidity was decreased in the MIS group, including decreased estimated blood loss (50 vs. 500 mL; \(P < 0.001\)), fewer blood transfusions (3.0\% vs. 26.2\%; \(P < 0.001\)), and shorter hospital stay (1.9 vs. 4.9 days; \(P < −0.001\)).\textsuperscript{[19]} In a recent systematic review and meta-analysis of 4205 patients comparing intraoperative and postoperative outcomes of laparoscopic versus abdominal radical hysterectomy, it was shown that TLRH was associated with lower estimated blood loss, shorter hospital stay, quicker return to normal bowel activity, and shorter duration of bladder catheterization than RAH. TLRH also demonstrated lower odds of transfusion and ileus than RAH.\textsuperscript{[20]} However, TLRH was associated with longer operation time and fewer retrieved lymph nodes compared with RAH. Another systematic review and meta-analysis of 4013 women who had undergone radical hysterectomy through robotic, laparoscopic, or abdominal route of surgery found that robotic radical hysterectomy (RRH) was associated with less estimated blood loss and shorter hospital stay than RAH.\textsuperscript{[21]} RRH was also associated with lower odds of febrile morbidity, blood transfusion, and wound-related complications compared to RAH. However, RRH was comparable to TLRH in all intra- and post-operative outcomes.\textsuperscript{[21]} Similarly, the results of our study show improved surgical outcomes in the TLRH group compared to the RAH group, namely, significantly lower blood loss and hospital stay though the median operative time was longer.

Table 3: Histological risk factors and the adjuvant therapy

| Variable                              | TLRH \((n=51), n (%)\) | RAH \((n=85), n (%)\) | \(P^a\) |
|---------------------------------------|------------------------|------------------------|--------|
| LVSI present                          | 17 (33.3)              | 35 (41.2)              | 0.52   |
| Positive lymph node metastases        | 7 (13.7)               | 12 (14.1)              | 0.39   |
| Positive parametrial involvement      | 4 (7.8)                | 15 (17.6)              | 0.14   |
| Close/positive vaginal margin involvement | 6 (11.8)              | 5 (5.9)                | 0.36   |
| Adjuvant treatment                    |                        |                        |        |
| None                                  | 29 (56.9)              | 38 (44.7)              | 0.38   |
| Radiotherapy                          | 9 (17.6)               | 23 (27.1)              |        |
| Chemotherapy                          | 0 (0.0)                | 2 (2.4)                |        |
| Concurrent chemoradiotherapy          | 13 (25.5)              | 22 (25.9)              |        |

\(^a\)Chi-square test, LVSI: Lymphovascular space invasion, RAH: Wertheim’s radical abdominal hysterectomy, TLRH: Total laparoscopic Wertheim’s radical hysterectomy

Figure 1: Kaplan–Meier analysis for overall survival

Figure 2: Kaplan–Meier analysis of survival for cervical tumor \(\leq 2\) cm
In this study, there was a trend toward a higher relapse rate of 17.6% in the TLRH group compared to RAH (93.8% vs. 90.5%; 95% CI, 1.63–8.58), and the 3-year overall survival for MIS radical hysterectomy was lower compared to RAH (91.2% vs. 97.1%; hazard ratio for disease recurrence or death from any cause, 0.80; 95% CI, 0.49–1.32) group.

Similarly, in our series, 43.1% of TLRH patients needed adjuvant treatment compared to 55.3% of RAH patients. The higher close/positive vaginal margin involvement seen in the TLRH group in our study can potentially be addressed by performing vaginal cuff incision and closure through the vaginal route, that is, a laparoscopic-vaginal radical hysterectomy, as described by Nam et al.

Regarding oncological outcomes, there were no statistically significant differences between LVSI, positive lymph node metastases, parametrial involvement, vaginal margin involvement, and adjuvant treatment between the two groups in our study. Nam et al. reported a higher proportion of patients who do not require adjuvant therapy in the TLRH group compared to the RAH group (56.9% vs. 78.7%).

In our series, the 3-year overall survival in the TLRH group was similar compared to the RAH group (100.0% vs. 97.0%; P = 0.06). In a comparative study between laparoscopic-vaginal radical hysterectomy and abdominal radical hysterectomy in patients with early cervical cancer between 1997 and 2002, Nam et al. found that in the laparoscopic group, patients with large tumor volume (>4.2 cm³) or tumor diameter >2 cm had significantly higher recurrence rate of 42.9% (3/7) than those with small volume (1/40) (P = 0.0021). The 3-year progression-free survivals were 97.1% in laparoscopic group (<4.2 cm³) and 98.9% in abdominal group. Based on these findings, it was recommended that laparoscopic surgery should be limited to patients with small-volume disease (tumor diameter ≤2 cm or tumor volume <4.2 cm³). In the study by Kim et al., it was also shown that MIS radical hysterectomy was not a poor prognostic factor for those with cervical tumor size ≤2 cm on preoperative MRI as well (adjusted HR 1.146; 95% CI, 1.039–4.986; P = 0.0021). The 3-year progression-free survivals were 97.1% in laparoscopic group (<4.2 cm³) and 98.9% in abdominal group. Based on these findings, it was recommended that laparoscopic surgery should be limited to patients with small-volume disease (tumor diameter ≤2 cm or tumor volume <4.2 cm³).

In contrast, a follow-up cohort study over 14 years looking at long-term survival outcomes between laparoscopic and open radical hysterectomy, Nam et al. found that survival outcomes did not differ between the two groups. The laparoscopic and open groups had 5-year recurrence-free survival rates of 92.8% and 94.4%, respectively (P = 0.499); 5-year overall survival rates of 95.2% and 96.4%, respectively (P = 0.451); and 5-year disease-specific survival rates of 95.2% and 96.4%, respectively (P = 0.387).
**Conclusion**

The results of our study suggest that with appropriate patient selection, TLRH can be a safe and effective procedure for the management of early cervical cancer in Singapore, especially in women with small tumors ≤2 cm, with benefits including less blood loss, shorter recovery time, less pain, lower rates of wound infection, and improved cosmesis. Although the 3-year overall survival of the TLRH group is comparable to the RAH group for patients with tumor size ≤2 cm, it should be used with caution with larger tumors.

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**Conflicts of interest**

There are no conflicts of interest.

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