Outcomes of Total Laparoscopic Radical Hysterectomy and Bilateral Pelvic Lymphadenectomy in Early Stage Cervical Cancer at King Chulalongkorn Memorial Hospital

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Objective: To study clinical characteristics and gynecologic oncology outcomes of total laparoscopic radical hysterectomy (TLRH) in early stage cervical cancer.

Material and Method: A retrospective study of early stage cervical cancer patients treated by TLRH and bilateral pelvic lymphadenectomy, between January 2010 and February 2013, was done.

Results: *TLRH* is an option of treatment for early stage cervical cancer. We performed 23 cases of TLRH, between January 2010 and February 2013. Mean operative time and estimated blood loss were 182 minutes (120 to 300), and 308.7 ml (50 to 1,200), respectively. Mean pelvic lymph nodes retrieval of left, 9.6 (4 to 25) and right, 8.5 (4 to 21) pelvic nodes. The vaginal length was anterior, 2.2 cm (1.0 to 4.0), and posterior, 2.4 cm (1.0 to 4.0), respectively. The right and left parametrium was 2.3 cm (1.5 to 3.0) and 2.4 cm (1.0 to 4.0), respectively. Three cases had post-operative radiation, one with deep stromal invasion and the others with positive pelvic nodes. No abdominal conversion is required. No recurrence was detected. The mean progression free survival was 63.7 months.

Conclusion: TLRH with pelvic lymphadenectomy is safe and effective in the treatment of early stage cervical cancer.

Keywords: Total laparoscopic radical hysterectomy, Cervical cancer, Progression free survival

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Cervical cancer is the most common gynecologic cancer in developing countries. It is also considered to be the second most common cancer in women worldwide⁽¹⁾. Although the incidence of cervical cancer is decreasing in the developed countries because of good screening programs, the incidence of cervical cancer in developing countries is not changing⁽¹⁾.

Radical hysterectomy with pelvic lymphadenectomy is still a cornerstone of the treatment for early stage cervical cancer⁽¹⁾. Previously, the abdominal approach by exploratory laparotomy for radical hysterectomy with pelvic lymphadenectomy was considered the standard treatment^(2,3). The abdominal radical hysterectomy that is currently used for treating early stage cervical cancer is classified as class III in Piver Rutledge classification⁽⁴⁾. Moreover, Abu-Rustum et al has also classified radical hysterectomy into

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various types⁽²⁾. Abdominal radical hysterectomy has been used as an important tool for treating early stage cervical cancer (FIGO 1a2-IIa) for a long time^(3,5). Nowadays, the exploratory laparotomy approach is still the most common route for radical hysterectomy in Thailand. Starting last decade, laparoscopic radical hysterectomy with pelvic lymphadenectomy increased in popularity. Several studies confirm the safety and feasibility of the procedure⁽⁶⁻¹⁰⁾. Moreover, the laparoscopic approach has many advantages over the abdominal approach. For example, laparoscopic approach has less blood loss, shorter hospital stays, and rapid returns to work without compromising the oncologic outcome. However, the laparoscopic approach still has limitations such as being time consuming, the use of expensive instrumentation, and the high surgical skill required. The requirement of such extremely high levels of surgical skill is considered as a major obstacle to initiate the laparoscopic approach in many institutions. Moreover, oncologic outcomes of laparoscopic radical hysterectomy with pelvic lymphadenectomy depend on the level of surgical skill of the operators, parametrium adequacy, lymph node number, and resection margin.

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In Thailand, cervical cancer is the second most common cancer in women. The most common approach for radical hysterectomy in Thailand is exploratory laparotomy. For our institution, laparoscopic hysterectomy was started last decade. We summarized the data, clinical characteristics, and oncologic outcomes of the laparoscopic radical hysterectomy in our institution that were done between January 2010 and February 2013.

Material and Method

The present study was retrospectively conducted after the protocol was approved by the Ethical Committee of the Faculty of Medicine, Chulalongkorn University. All the cervical cancer cases treated in King Chulalongkorn Memorial Hospital between January 2010 and February 2013 were reviewed.

Number of cases were calculated by the formula, $n = Z_{\alpha}^{2}pq/d^{2}$. The reference *p*-value was the positive surgical margin rate, $0.014^{(11)}$. The q-value was 1-p, 0.986. The d-value was an allowable error, 0.05. The calculated number was 21 cases.

The data of those patients treated with laparoscopic radical hysterectomy were extracted. The data were extracted from the medical records, outpatient department (OPD) cards, inpatient department (IPD) data, and operative records. All the baseline characteristics of the patients such as age, parity, underlying disease, previous surgical procedure, and menopausal status were collected. The details of the disease and operative findings such as stage, cell type, tumor size, operator, operative time, blood loss, margin, number of lymph nodes, and complications were collected. Details of the other aspects such as adjuvant treatment and recurrence were also collected. The disease-free interval was calculated from the date of treatment to the last follow-up date.

The procedure, total laparoscopic radical hysterectomy, is described below. Preoperative cepharosporin was given 15 minutes before skin incision. The sequential compression device was applied. All patients were in the lower lithotomy position with arms parallel to body. One 10 mm camera port was at the umbilicus. Three 5 mm instrumental ports were at lower abdomen, one was at center, and two were lateral to rectus muscles. Harmonic scalpel and bipolar coagulator were used for hemostasis. A Rubin uterine manipulator and a tenaculum were used as a uterine manipulator. The operation started with transection of the round ligament to open the retroperitoneum. Bilateral pelvic lymphadenectomy

was performed starting from external iliac, internal iliac, obturator, to common iliac groups. A radical hysterectomy (Piver type 2 or 3) with or without bilateral salpigo-oophorectomy was performed. The uterine arteries were secured and divided at the level of their origins. The parametria and the uterosacral ligaments were dissected. The vagina was circumcised. A sufficient surgical margin was aimed for. All specimens were removed and the vaginal vault was transvaginally closed.

After collecting all the data, statistical analysis was conducted. Baseline characteristics were presented as percentages, mean, mode, or median. Parametric data, non-parametric data, and survival data were calculated with the appropriate statistical analysis, unpaired t-test, and Mann-Withney U test by SPSS version 17.

Results

After review of all the data, we found 23 cases of laparoscopic radical hysterectomy. The mean age of the patients was 49.5 years old (SD 11.51). Half of the patients were post-menopausal (12 from 23 patients). Eight patients had underlying diseases such as hypertension or diabetes and those underlying diseases were controlled before surgical intervention was conducted. Some of the patients had previous surgery such as cesarean section, salpingo-oophorectomy, or tubal resection. Mean body mass index (BMI) of the patents was 24.92 kg/m² (SD 5.58).

According to the operative data, the mean operative time was 182 minutes and the mean blood loss was 308.7 ml. There were two cases that operative blood loss was more than 500 ml. Three patients received blood transfusion. In eight of the 23 patient cases we were unable to identify gross lesions from the specimen. The mean diameter of the lesion was 1 cm (ranging from 0 to 3 cm). Eighteen patients (78%) were stage IB1. Seventeen cases (73.9%) were squamous cell carcinoma, 12 of them (52.2%) are non-keratinizing squamous cell carcinoma. The mean hospital stay was 3.52 days. Comparing mean operative time, estimated blood loss, and hospital stays between the first ten cases and the others, found that operative time and hospital stays were statistically significant shorter in the last 13 cases, (208 vs. 162 minutes, and 4.5 vs. 2.8 days, respectively). There was not a statistically significant difference in estimated blood loss (200 vs. 300 ml) (Table 1). Details of the general characteristics and disease characteristics were shown in Table 2 and 3 For specimen evaluation, we also recorded the details of the specimens. The mean number of left pelvic nodes was 9.65 nodes, which was similar to right side (8.48 nodes). Out of the 23 cases, two cases had nodal metastasis discovered from the pathological reports. The mean length of the anterior and posterior vaginal walls was 2.23 and 2.39 cm, respectively. The mean width of the right and left parametrium were 2.30 and 2.39 cm, respectively. Three cases had post-operative radiation, one case due to deep stromal invasion and the others due to positive pelvic nodes. Conversion rate in our institution for laparoscopic radical hysterectomy was 0%. Details of the specimen evaluations are also shown in Table 2 and 3. As of the date of data collection (September 2016), all of the patients in the present series were free of disease. The recurrence rate in our series is 0% and the survival rate is 100%. The mean disease-free survival is 63 7 months

Discussion

Laparoscopic radical hysterectomy with bilateral pelvic node dissection is now becoming a standard option for early stage cervical cancer treatment. The various benefits of the laparoscopic approach when compared with the exploratory approach include lower operative blood loss, shorter hospital stays, and less pain. However, the laparoscopic approach requires better surgical skill and a steeper learning curve than the exploratory laparotomy approach^(11,12). Therefore, the popularity of laparoscopic radical hysterectomy amongst surgeons is limited in Thailand.

In our study, the mean age of the patients was 49.5 years old, which is within the most common age group range for cervical cancer. The youngest patient in our series was only 31 years old. The most common cell type was squamous cell, which is comparable with previous studies. The most common stage of cervical cancer in the present study was IB1, which was the most common stage for a radical hysterectomy to be performed. Lymph node metastasis was found in two cases out of the 23 cases (8.7%), which correlated with the rate of nodal metastasis in the previous study. Our mean operative time is 182 minutes and that is comparable to other series⁽¹³⁻¹⁵⁾. The mean blood loss in our series was 308.7 ml, which is comparable to the report findings of several other studies^(15,16). However, those studies were published several years ago. As such, some surgical techniques and instrumentation may be different. With the advance laparoscopic camera, system, and vascular sealing instrumentation, nowadays laparoscopic surgery is much more convenient than in the past. For those reasons, operative time,

 Table 1. Mean operative time, estimated blood loss, and hospital stay grouping in order of cases

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	The first	The 11 th cases	<i>p</i> -value
	ten cases	to 23rd cases	
	(n = 10)	(n = 13)	
Operative time (minutes)	208	162	0.015*
Estimated blood loss (ml)	200	300	0.34#
Hospital stay (days)	4.5	2.8	0.001*

* *p*-value derived from unpaired t-test

[#] p-value derived from Mann-Whitney U test

Table 2. Characteristics of the patients and diseases

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Variable	Total $n = 23$ mean \pm SD	Range		
Age (years)	49.5±11.5	31 to 74		
BMI (kg/m ²)	24.9±5.6	17.6 to 38.2		
Parity	2.1±1.1	0 to 5		
Operative time (minutes)	182.4±46.7	120 to 300		
Estimated blood loss (ml)	308.7±276.6	50 to 1,200		
Hospital stay (days)	3.5±1.3	2 to 7		
Lymph node (L)	9.7±5.0	4 to 25		
Lymph node (R)	8.5±4.0	4 to 21		
Anterior vagina (cm)	2.3±0.7	1 to 4		
Posterior vagina (cm)	2.4±0.7	1 to 4		
Parametrium (L)	2.4±0.8	1 to 4		
Paramentrium (R)	2.3±0.5	1.5 to 3		

BMI = body mass index; L = left; R = right

Table 3.	Stage and	cell types	of cervical	cancer
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	Total n = 23, n (%)
Stage	
Ia1	2 (8.7)
Ia2	1 (4.3)
Ib1	18 (78.3)
IIa	2 (8.7)
Cell type	
Squamous cell (total)	17 (73.9)
- NKSCCA	12 (52.2)
- Poorly differentiate SCCA	2 (8.7)
- Papillary SCCA	1 (4.3)
- Unclassified SCCA	2 (8.7)
Adenocarcinoma (total)	6 (26.1)
- Poorly differentiated	5 (21.7)
- Unclassified adenocarcinoma	1 (4.3)

NKSCCA = non-keratinizing squamous cell carcinoma; SCCA = squamous cell carcinoma

operative blood loss, and operative complications seems to be reducing in recent studies.

According to specimen adequacy, the margins of the specimen including vaginal length and parametrial width were approximately 2.3 cm on average which has been considered as acceptable for specimen adequacy in several studies⁽⁹⁾. Our conversion rate was 0%. Up until the time of writing (September 2016), all the patients in our series are currently free of disease. The shortest duration of follow-up calculated from the last patient in the series is 41 months. The mean disease-free survival is 63.7 months. However, there might be a selective bias in this study, such as small tumor size, early stage, multiparity, and low BMI. Further study should be conducted to collect more cases and quality of life after surgery, such as post-operative bladder function and sexual life.

In conclusion, laparoscopic radical hysterectomy is now considered an option of a surgical treatment for early stage cervical cancer patients. The treatment outcome is comparable to the exploratory laparotomy approach. The limitation of laparoscopic radical hysterectomy is that it is skill dependent, and therefore, achieving a successful laparoscopic radical hysterectomy requires practice and skillful operators.

What is already known on this topic?

Cervical cancer is the most common gynecologic cancer in Thailand. The standard treatment for early stage cervical cancer is radical hysterectomy or radiation treatment. Currently, laparoscopic surgery is playing important role in this surgical procedure. Although it is not a standard treatment for early stage cervical cancer, it has been proved to be a choice of treatment that is safe and effectiveness.

What this study adds?

This study is confirming that laparoscopic radical hysterectomy is safe and effective with favorable oncological outcomes, a five years disease free survival rate of 100%.

Potential conflicts of interest

None.

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ผลการรักษามะเร็งปากมดลูกระยะเริ่มต้นด้วยการผ่าตัดมดลูกผ่านกล้องแบบ radical และการเลาะต่อมน้ำเหลือง อุ้งเชิงกรานที่โรงพยาบาลจุฬาลงกรณ์

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วัตถุประสงค์: เพื่อศึกษาลักษณะทางคลินิกและผลการรักษาทางมะเร็งวิทยานรีเวช ของการผ่าตัดมดลูกผ่านกล้องแบบ radical ในผู้ป่วยมะเร็งปากมดลูกระยะเริ่มต้น

วัสดุและวิธีการ: เป็นการศึกษาแบบ retrospective ในผู้ป่วยมะเร็งปากมดถูกระยะเริ่มด้น ที่ได้รับการรักษาด้วยการผ่าตัดมดถูก ผ่านกล้องแบบ radical ในระหว่างเดือนมกราคม พ.ศ. 2553 ถึง กุมภาพันธ์ พ.ศ. 2556

ผลการศึกษา: ในระยะเวลาที่ศึกษา มีผู้ป่วยมะเร็งปากมดลูกระยะเริ่มต้น 23 ราย ที่ได้รับการรักษาด้วยวิธีผ่าตัดมดลูกผ่านกล้อง แบบ radical ระยะเวลาเฉลี่ยของการผ่าตัดคือ 182 นาที (120-300 นาที) ปริมาณเลือดที่เสียจากการผ่าตัดเฉลี่ย 308.7 มิลลิลิตร (50-1,200 มิลลิลิตร) จำนวนต่อมน้ำเหลืองอุ้งเชิงกรานข้างซ้ายและข้างขวาเฉลี่ยคือ 9.6 (4-25) และ 8.5 (4-21) ตามลำดับ ความ ยาวของช่องคลอดทางด้านหน้า และด้านหลังคือ 2.2 เซนติเมตร (1.0-4.0 เซนติเมตร) และ 2.4 เซนติเมตร (1.0-4.0 เซนติเมตร) ตามลำดับ เนื้อเยื่อ parametrium ข้างขวาและข้างซ้าย คือ 2.3 เซนติเมตร (1.5-3.0 เซนติเมตร) และ 2.4 เซนติเมตร (1.0-4.0 เซนติเมตร) ตามลำดับ มีผู้ป่วย 3 ราย ได้รับการรักษาเพิ่มเติมด้วยรังสีรักษาหลังการผ่าตัด เนื่องจากมี deep stromal invasion 1 ราย และมะเร็งลุกลามไปต่อมน้ำเหลือง 2 ราย ในการศึกษานี้ไม่พบการเปลี่ยนจากการผ่าตัดผ่านกล้องเป็นผ่าตัดทาง หน้าท้อง ไม่พบการกลับเป็นซ้ำของมะเร็ง ระยะเวลาที่ผู้ป่วยปลอดมะเร็งเฉลี่ย 63.7 เดือน

สรุป: การผ่าตัดมดลูกผ่านกล้องแบบ radical มีความปลอดภัย และมีประสิทธิภาพ ในการรักษามะเร็งปากมดลูกระยะเริ่มต้น