Original Article

Surgical Management of Early-stage Cervical Cancer: Survey of Practice among Thai Gynecologic Oncologists

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Objective: To acquire a comprehensive picture of the current surgical management of early-stage cervical cancer by conducting an on-line digital survey among practicing Thai gynecologic oncologists.

Materials and Methods: Thai gynecologic oncologists who had been practicing in the field for at least one year were invited to complete an on-line self-administered questionnaire. This study represents a part of the main study that addressed early-stage cervical cancer management.

Results: One hundred seventy gynecologic oncologists responded to the survey questionnaires. Approximately half of the respondents would abort the radical hysterectomy procedure if preoperative imaging reveals node enlargement suspected of cancer metastasis. If pelvic/para-aortic lymph node metastasis was found during operation, more respondents would abandon the procedure especially for the finding of pelvic node metastasis (65.3%). Thirty-nine respondents (22.9%) reported that they perform laparoscopic surgery for early-stage cervical cancer. This number had dropped significantly after 2018. Criteria used by the respondents for consideration of ovarian preservation at the time of radical hysterectomy varied. Approximately half of the respondents indicated that the combination of criterion including large tumor size, deep stromal invasion, and lymph-vascular space invasion must be met for any patients to be considered as having intermediate-risk for recurrence.

Conclusion: There are large disparity in the current management of early-stage cervical cancer among practicing Thai gynecologic oncologists.

Keywords: Cervical cancer, Gynecologic oncologist, Practice pattern

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Cervical cancer is one of the most common gynecologic cancer worldwide, with an age-standardized incidence rate of 13.1 per 100,000 and an age-standardized mortality rate of 6.9 per 100,000[(1)]. In medium to low resource region, in particular, the incidence and mortality rate are even higher. Fortunately, the incidence of cervical cancer has expected to dramatically decline due to rapid development of screening tool and human papillomavirus vaccine.

Surgical treatment is a fundamental method in managing women with early-stage cervical cancer. Currently, management of cervical cancer appears more varied compared to that of endometrial or ovarian cancers mostly due to local tradition and regional variation. Each institution employs certain treatment modality or combination of treatments, such as radical surgery, adjuvant radiotherapy (RT), and neoadjuvant chemotherapy (NACT) based on their resources and experience. The aim of this survey was to acquire a comprehensive picture of the current surgical management of early-stage cervical cancer by conducting an on-line digital survey among practicing Thai gynecologic oncologists, the data would be helpful for determining the current practice and identifying the areas that need further improvement in our setting.

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Materials and Methods

Thai Gynecologic Cancer Society (TGCS) initiated a cross-sectional survey study in 2018 to obtain and evaluate information regarding practice pattern of Thai gynecologic oncologists who are members of TGCS. Inclusion criteria were Thai gynecologic oncologists who had been practicing in the field for at least one year. Individuals not having clinical practice in the country at the time of this survey and those who were the registered member but performed only benign

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gynecologic conditions were not eligible. A list of practicing gynecologic oncologists was retrieved from TGCS membership registry. Eligible potential participants were invited to complete an on-line self-administered questionnaire, which was opened for response from August to October, 2019. The questionnaires were accessible through the website: https://forms.gle/e1WsBLcX5jVsXVgG8.

The survey encompassed general aspect and organ-specific aspect of cares including work status and work-related problems, management of cervical cancer, endometrial cancer, and ovarian cancer. This study represents a part of the main study that addressed surgical management of early-stage cervical cancer. Pattern of care, current working situation, obstacles, and impact of fellowship training were taken into account. Human Research Ethics Committee of each collaborating institution independently approved this study (Phramongkutklao Hospital: IRBRTA216/2563, Rajavithi Hospital: 104/2562, Faculty of Medicine, Chiang Mai University: OBG-2562-06506).

Data were analyzed using SPSS statistical software, version 22 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were used to analyze demographic data, which were expressed as numbers with percentage. Chi-square or Fisher exact tests, as deemed appropriate, were used for hypothesis testing of categorical data comparing two groups. The *p*-value <0.05 was considered significant.

Results

Of 250 eligible practicing Thai gynecologic oncologists invited to participate, 170 gynecologic oncologists (68.0%) responded to the survey questionnaires. Median age of the respondents was 39 years (30 to 74 years) and approximately two-thirds of them (63.5%) were female. Length of their career as a gynecologic oncologist ranged from one year to 42 years with a median of five years. Ninety-nine respondents (58.2%) had practiced for five years or longer. Most respondents worked mainly at tertiary care hospitals (83.5%) in public setting (89.4%). Eighty-six respondents (50.6%) worked in institutions that had fellowship training program.

Table 1 shows number of respondents who would call off radical hysterectomy based on information about status of retroperitoneal lymph node obtained through preoperative imaging (computerized tomography/magnetic resonance imaging) and intraoperative finding. Approximately half of the respondents would abort the radical hysterectomy procedure if preoperative imaging reveals node enlargement suspected of cancer metastasis. If pelvic/para-aortic lymph node metastasis or suspicious enlargement was found during operation, more respondents would abandon the procedure especially for the finding of pelvic node metastasis.

Table 2 demonstrates number of respondents who perform laparoscopic surgery as a primary treatment for early-stage cervical cancer with consideration given to the effect of hospital setting (public vs. private), hospital level

Table 1. Number of respondents who would abandon radical hysterectomy based on retroperitoneal lymph node status

Status of retroperitoneal lymph node	n (%)
Preoperative imaging	
Pelvic node enlargement (suspicious node)	87 (51.2)
Para-aortic node enlargement (suspicious node)	97 (57.1)
Intraoperative finding	
Pelvic node positive/enlargement	111 (65.3)
Para-aortic node positive/enlargement	101 (59.4)

Table 2. Number of respondents who perform laparoscopic surgery for cervical cancer according to practice characteristics

Practice characteristics	Performing laparoscopic surgery (n = 170)		*p*-value
	No (n = 131)	Yes (n = 39)	
Hospital setting			0.60
Public, n = 152	117 (77.0)	35 (23.0)	
Private, n = 18	14 (77.8)	4 (22.2)	
Hospital level			0.78
Secondary, n = 28	21 (75.0)	7 (25.0)	
Tertiary, n = 142	110 (77.5)	32 (22.5)	
Practice type			0.02*
Service and training, n = 86	60 (69.8)	26 (30.2)	
Service only, n = 84	71 (84.5)	13 (15.5)	
Practice duration			<0.001*
<5 years, n = 71	65 (91.5)	6 (8.5)	
≥5 years, n = 99	66 (66.7)	33 (33.3)	

* Statistically significant

(secondary vs. tertiary), practice type (service with training vs. service only), and gynecologic oncology career duration (<5 years vs. ≥5 years). Thirty-nine respondents (22.9%) reported that they perform laparoscopic surgery for early-stage cervical cancer. The proportion of respondents who perform laparoscopic surgery remained unchanged regardless of hospital setting and hospital level. However, significantly higher proportion of respondents who worked in the centers with combined service & training and those who had five-year or longer working experience perform laparoscopic surgery.

Of the 39 respondents who performed laparoscopic surgery, 11 (28.2%) stated that, before 2018, they would perform laparoscopic radical hysterectomy in all early-stage cervical cancer cases, in whom the procedure was indicated and 24 (61.5%) reported that they would do it only for patients with tumor size smaller than 2 cm. Three respondents (7.7%) who perform laparoscopic surgery for early-stage cervical cancer did not employ it for radical hysterectomy in any cases. After 2018, however, the proportion of respondents who would do laparoscopic radical hysterectomy dropped significantly. Five respondents (12.8%) would perform the procedure in all eligible cases and 21 (53.8%) would do it in patients with tumor smaller than 2 cm. Of note, 11 respondents (28.2%) would not perform laparoscopic radical hysterectomy in any cervical cancer patients. This pattern of interval change was independent of hospital setting, hospital level, practice type, and practice duration.

Table 3 displays criteria used by the respondents for consideration of ovarian preservation at the time of radical hysterectomy. Of the five criteria listed in the survey questionnaires, the number of criteria required to be met before proceeding with the procedure were: all five in 29 respondents (17.1%), four in 31 respondents (18.2%), three in 38 respondents (22.4%), two in 49 respondents (28.8%), and any criterion in 23 respondents (13.5%) including young age in 21, early-stage disease in one, and high potential for postoperative radiation in one.

Table 4 demonstrates various histological criteria employed by the respondents to allocate patients after radical surgery into intermediate-risk group, which would benefit from adjuvant pelvic radiotherapy with or without concurrent chemotherapy. Approximately half of the respondents indicated that all three criteria including large tumor size, deep stromal invasion, and lymph-vascular space invasion must be met for any patients to be considered as having intermediate-risk for recurrence.

Table 3. Criteria for ovarian preservation at the time of radical hysterectomy

Criteria	n (%)
Young age	166 (97.6)
Early-stage disease	103 (60.6)
High potential for postoperative radiation	94 (55.3)
Cell type	91 (53.5)
Small tumor size	50 (29.4)
Others*	3 (1.8)

* Others included no gross ovarian pathology, young age with risk factors, and microinvasive cancer

Table 4. Histopathological criteria for intermediate-risk grouping

Criteria	n (%)
One feature	
Large tumor size	4 (2.4)
Deep stromal invasion	5 (2.9)
LVSI*	2 (1.2)
Two features	
Large tumor size & deep stromal invasion	7 (4.1)
Deep stromal invasion & LVSI*	6 (3.5)
Large tumor size & LVSI*	2 (1.2)
All three features	80 (47.1)
Others	64 (37.6)

* LVSI = lymph-vascular space invasion

Discussion

This survey presents opinion of practicing gynecologic oncologists on the issues related to surgical management of early-stage cervical cancer. The study cohort represents a young-to-middle generation gynecologic oncologists mostly working at tertiary care hospital in public setting. The decision to abort radical hysterectomy procedure based on the preoperative imaging finding suspicious for nodal metastasis was equally divided. However, intraoperative finding of nodal metastasis (suspected/confirmed) had more weight on their decision to abandon the procedure. Of note, at least one-third of the respondents would proceed with radical hysterectomy despite the intraoperative finding suggestive for nodal metastasis. Approximately one-fourth of the respondents had laparoscopy as part of their surgical armamentarium especially middle generation oncologists who worked in academic setting. However, the number of oncologists who performed laparoscopic surgery for early-stage cervical cancer had dropped significantly after 2018. Regarding ovarian transposition during radical hysterectomy, the criteria employed by the respondents varied. Approximately half of the respondents specified that the combination of large tumor size, deep stromal invasion, and lymph-vascular space invasion are required for a patient to be classified as having intermediate-risk disease.

Effectiveness of primary surgical management including radical hysterectomy with pelvic and/or para-aortic lymphadenectomy for early-stage (stage IA2, IB1-2, IIA1) is well recognized and the radical surgery is particularly suitable for younger patients with potential benefits of ovarian and vaginal function preservation[2,3]. However, the procedure could be associated with significant long-term morbidities

with regard to bladder, bowel, and sexual function, resulting from damage to pelvic autonomic nerves[4-7]. In addition, for patients who had pelvic/para-aortic lymph node metastasis, parametrial metastasis, or involved vaginal margins confirmed by histopathological examination, adjuvant postoperative pelvic radiation with concurrent chemotherapy is usually indicated in an attempt to reduce the risk of recurrence[8]. For these women, the rate of treatment-related morbidities are potentially much higher compared to those who have either radical surgery or concurrent chemoradiation without appreciable survival benefit[9]. Therefore, some surgeons choose to abort the radical hysterectomy procedure in patients with preoperative or intraoperative findings suspicious for nodal metastasis in order to minimize complication from combined treatment modalities. However, this practice remains debatable[10]. Our data emphasized the disparity in practice on this issue.

Laparoscopic approaches have been pursued to improve recovery times and maintain surgical and oncologic outcomes with minimizing the morbidity of surgery. In the past two decades with rapid improvement in laparoscopic surgical techniques, laparoscopic surgery has become a reality in the treatment of cervical cancer. In 1989, Dargent et al[11] describe an endoscopic surgical technique to remove pelvic lymph node in patients with early-stage cervical cancer. They were capable of removing pelvic lymph node to the level of the bifurcation of the common iliac artery. Subsequently, Nezhat et al[12] described one of the first successful laparoscopic radical hysterectomy. Also, Puntambekar et al[13] reported the results of performing laparoscopic radical hysterectomy and pelvic lymphadenectomy in 248 stage IA2-IB1 cervical cancer patients. They observed small amount of blood loss (median 165 mL), short operative time (median 92 minutes), adequate number of resected lymph node (median 18 nodes), manageable complications, and short hospital stay (median 3 days). After a median follow-up of 36 months, seven patients recurred (2.8%). With continued improvement in techniques and equipment, total laparoscopic radical hysterectomy has gained popularity while multiple subsequent reports confirmed its safety and feasibility. Spirtos and et al[14] had treated stage IA2 to IB cervical cancer patients with laparoscopic radical hysterectomy and lymphadenectomy. The recurrence rate was 5.1% after 3 years. Li et al[15] compared laparoscopic (90 patients) and abdominal (35 patients) radical hysterectomy and lymphadenectomy for stage IB to IIA cervical cancer in a non-randomized study from August 1998 to December 2005. For the laparoscopy group, the author observed a significant increase in operating time (263 minute vs. 217 minute) and a significant decrease in the bowel function recovery time (1.96 days vs. 2.40 days). Of note, operative blood loss, number of resected pelvic lymph nodes, bladder function recovery time, postoperative hospital stay, recurrence rate, and mortality rate were not different between the two approaches. In 2018, however, Ramirez et al[16] published a multicenter phase 3 randomized trial of laparoscopic or robotic radical hysterectomy (319 patients) versus abdominal radical hysterectomy (312 patients) for early-stage cervical cancer (92% stage IB1) -the LACC trial- of which the findings created a profound concern regarding the adequacy of the minimally invasive approach. They found that patients treated with minimally invasive surgery had poorer disease-free survival (hazard ratio [HR] for recurrence or death from cervical cancer 3.74) and worse overall survival (HR for death from any cause 6.00) compared to those treated with conventional open abdominal radical hysterectomy. In Thailand, laparoscopic radical hysterectomy had been popular among many gynecologic oncologists until 2018. In this survey, we could observe a substantial impact of the LACC trial -after the release of its findings in 2018- on the decision of Thai gynecologic oncologists to adopt the laparoscopic approach for radical hysterectomy.

It is observed that approximately 40% of women diagnosed with early-stage cervical cancer are younger than 40 years[1]. Therefore, the consideration on preservation of ovarian function is frequently an important issue during surgical planning. McCall et al[17] were the first to describe ovarian preservation in premenopausal women with early-stage cervical cancer. Currently, the ovarian transposition procedure has been proposed to relocate at least one ovary away from the pelvis in patients who are potential candidates for postoperative pelvic radiation. However, the safety and appropriateness of ovarian transposition in early-stage cervical cancer remains controversial due to the concern of occult ovarian metastasis. Therefore, certain clinico-pathological criteria are usually applied to avoid performing the procedure in patients whose risk for occult ovarian metastasis is too high. In our study, although young age was clearly a prerequisite for ovarian transposition, other additional criteria adopted by the respondents varied widely. These findings represent the lack of universally accepted evidence-based guideline for this particular issue leading to the discrepancy in practice.

Conclusion

Our survey has confirmed large disparity in the current surgical management of early-stage cervical cancer among practicing Thai gynecologic oncologists with regard to criteria for abandoned radical hysterectomy based on retroperitoneal lymph node status, laparoscopic surgery for early-stage cervical cancer before and after the LACC trial, and criteria for ovarian transposition procedure. Major limitation was the cross-sectional descriptive nature of the study. Therefore, this study should be considered exploratory and serve as a foundation for future in-depth study aiming to assess certain issues.

What is already known on this topic?

1) Usually, radical surgery is suitable for younger patients with early-stage cervical cancer. Most guidelines suggest that the procedure be abandoned in case of suspected or confirmed lymph node involvement.

2) Popularity of laparoscopic hysterectomy with

pelvic lymph node dissection dropped significantly around the world after the release of the LACC trial's results.

3) Ovarian preservation by performing ovarian transposition procedure has been proven to increase quality of life in younger patient with cervical cancer. However, occult ovarian metastasis remains a concern.

What this study adds?

This study shows discrepancies in practice among Thai gynecologic oncologists in certain issues. These include cancellation of radical hysterectomy based on lymph node status, number of Thai gynecologic oncologists who continue to do laparoscopic hysterectomy after LACC trial, and ovarian preservation criteria. However, the causes of these discrepancies could not be further illustrated from the available data from this survey.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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การรักษามะเร็งปากมดลูกระยะเริ่มแรกด้วยการผ่าตัด: การสำรวจแนวปฏิบัติของแพทย์มะเร็งนรีเวชไทย

กษิติ เที่ยงธรรม, ณัฐพงษ์ เสริมสุขเจริญชัย, กฤษณมน ฤทธิภาชัย, ศรัญญา ชาญพานิชกิจโชติ, จิตติ หาญประเสริฐพงษ์, กิตติภัต เจริญขวัญ, สมาคมมะเร็งนรีเวชไทย

วัตถุประสงค์: เพื่อศึกษาภาพรวมของการรักษามะเร็งปากมดลูกระยะเริ่มแรกด้วยการผ่าตัด โดยการสำรวจความเห็นของแพทย์ทางมะเร็งนรีเวชที่ปฏิบัติงานในประเทศไทย

วัสดุและวิธีการ: แพทย์ทางมะเร็งนรีเวชที่ปฏิบัติงานในประเทศไทยมาเป็นเวลาอย่างน้อย 1 ปี ได้รับการเชิญเข้าร่วมโครงการวิจัย โดยตอบแบบสอบถามออนไลน์ด้วยตนเอง การศึกษานี้เป็นส่วนย่อยซึ่งรายงานในส่วนที่เกี่ยวข้องกับการผ่าตัดรักษามะเร็งปากมดลูกระยะเริ่มแรก

ผลการศึกษา: แพทย์ทางมะเร็งนรีเวช 170 คน ร่วมตอบแบบสอบถาม ผู้ตอบแบบสอบถามประมาณกึ่งหนึ่ง จะยกเลิกการผ่าตัดตัดมดลูกแบบกว้าง หากพบว่าผลการตรวจภาพถ่ายทางรังสีก่อนผ่าตัดสงสัยการแพร่กระจายของมะเร็งไปที่ต่อมน้ำเหลือง แต่หากตรวจพบหรือสงสัยการแพร่กระจายไปยังต่อมน้ำเหลืองในขณะที่ทำการผ่าตัด ผู้ตอบแบบสอบถามถึงร้อยละ 65 จะยุติการผ่าตัด ประมาณ 1 ใน 4 ของผู้ตอบแบบสอบถามเลือกใช้การผ่าตัดผ่านกล้องในการรักษาผู้ป่วยกลุ่มนี้ อย่างไรก็ตามหลังจากปี พ.ศ. 2561 จำนวนแพทย์ที่รักษาโดยการผ่าตัดผ่านกล้องลดลงอย่างมีนัยสำคัญ เกณฑ์ที่ใช้ในการพิจารณาอนุรักษ์รังไข่ระหว่างการผ่าตัดมดลูกเพื่อการรักษาผู้ป่วยกลุ่มนี้มีความหลากหลาย ประมาณกึ่งหนึ่งของผู้ตอบแบบสอบถามอาศัยเกณฑ์ที่ประกอบด้วยขนาดของก้อนมะเร็ง ความลึกของการลุกลามและการลุกลามเข้าสู่หลอดเลือดหลอดน้ำเหลืองในการพิจารณาจัดผู้ป่วยให้อยู่ในกลุ่มที่มีความเสี่ยงปานกลาง ซึ่งอาจได้ประโยชน์จากการให้รังสีรักษาหลังผ่าตัด

สรุป: การรักษามะเร็งปากมดลูกระยะเริ่มแรก โดยแพทย์ทางมะเร็งนรีเวชไทย มีความหลากหลายในบางประเด็นที่ยังมิได้มีแนวทางมาตรฐานในการรักษา