
SPECIAL ARTICLE

What We Have Learned from Over 1400 Radical Hysterectomy Operations in Chiang Mai University Hospital

Jatupol Srisomboon MD,
Prapaporn Suprasert MD,
Chailert Phongnarisorn MD,
Kittipat Charoenkwan MD,
Chalong Cheewakriangkrai MD,
Sithicha Siriaree MD,
Charuwan Sae-Teng MD,
Chumnan Kietpeerakool MD.

Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand

Introduction

Standard treatment for patients with stage IA2-IIA cervical cancer is either radical surgery or radiation therapy. Radical hysterectomy and pelvic lymphadenectomy (RHPL) is a major gynecologic operation requiring advanced surgical skills and experience, and is carefully selected for patients who are candidates for surgical treatment. During the period 1997-2007, 1419 radical hysterectomy operations have been carried out at the Department of Obstetrics and Gynecology, Chiang Mai University Hospital (CMUH). The surgical techniques are modified from the Tokyo method performed by Professor Shoichi Sakamoto of Tokyo University who came to Chiang Mai to demonstrate his surgical techniques in 2000. Basically, there are 20 steps of the RHPL operation which are systematic and simple to teach the fellows and beginners in gynecologic cancer operations⁽¹⁾.

Are retroperitoneal drainage and peritonization necessary after RHPL?

Traditionally, retroperitoneal drainage and closure of pelvic peritoneum are carried out after RHPL for invasive cervical cancer. In the past, routine drainage is performed to remove the lymphatic fluid and blood that may accumulate in the retroperitoneal space and cause infection, lymphocyst and ureteric fistula. However, various studies on the RHPL-related morbidity show that infectious morbidity can be significantly reduced by perioperative antibiotic prophylaxis, pelvic lymphocyst cannot be virtually prevented by retroperitoneal drainage, and ureteric complications are mainly attributed to the surgical technique not the result of drainage⁽²⁾.

A prospective randomized study was conducted in CMUH between July 1999 and May 2000 to evaluate the postoperative morbidity in patients with early-stage cervical cancer undergoing

RHPL with no drainage and no peritonization (48 cases) compared with retroperitoneal drainage and peritonization (52 cases). No significant difference was noted in the 2 groups regarding operative time, blood loss, intraoperative complications, hospital stay, and postoperative morbidities including febrile infections, pelvic lymphocyst, and ureteric fistula⁽³⁾. Therefore, routine retroperitoneal drainage and peritonization can be safely omitted after RHPL for invasive cervical cancer.

What is the appropriate management for bladder dysfunction after RHPL ?

Bladder dysfunction is the most common complication associated with RHPL due to pelvic autonomic nerve damage during parametrial resection. Prolonged bladder catheterization is suggested to resolve hypotonic bladder dysfunction either via suprapubic catheterization (SPC) or transurethral catheterization. Intermittent self-catheterization (ISC) is an acceptable technique for urinary drainage to avoid long-term retention of catheter.

A prospective randomized study was undertaken in CMUH between September 1998 and June 1999 to compare the voiding time and complications between ISC (38 cases) and SPC (33 cases) in patients with invasive cervical cancer undergoing RHPL. ISC every 4 hours after voiding was initiated on day 7 postoperatively in the ISC group, whereas in the SPC group, the catheter was clamped on day 7 after the operation. The duration for clamping in the SPC group was 4 hours and was released after self voiding to check the residual urine. Both ISC and SPC were discontinued when postvoiding residual urine volume was less than 75 ml for 2 consecutive voids. No difference was noted in both groups in respect of perioperative morbidity and the frequency of urinary tract infection. Mean voiding time in the ISC group was significantly less than that in the SPC group (13 days versus 17 days, respectively, $P = 0.02$)⁽⁴⁾. Consequently, patients performing ISC after RHPL appear to resume earlier bladder function than those

undergoing SPC without significant difference in the frequency of urinary tract infection and perioperative morbidity.

What is the role of extraperitoneal pelvic lymphadenectomy (EPL) in management of cervical cancer ?

Lymph node metastasis is the most important prognostic factor of early-stage cervical cancer after treatment with RHPL. The 5-year survival for patients with negative lymph nodes is 85-95% compared with 40-60% of patients with positive lymph nodes. Surgical evaluation of pelvic lymph nodes prior to radical surgery could be performed via either transperitoneal or extraperitoneal approach. However, if the patients receive adjuvant radiation after transperitoneal lymphadenectomy, bowel complications are significantly higher than those receiving radiation after EPL. In cases with grossly nodal metastases, radical hysterectomy can be abandoned to minimize serious morbidity occurring after combined treatment with radiation.

EPL can be performed via either midline or Maylard incision. The roles of EPL in management of cervical cancer are as follows:⁽⁵⁻⁷⁾

1. Stage IA2 cervical cancer patient undergoing inadvertent simple hysterectomy. Since the incidence of lymph node metastases is 5-7% while the parametrial involvement is only 0.5%. Such patient can be treated with EPL for surgical evaluation of the pelvic lymph nodes.

2. Stage IB cervical cancer patients undergoing inadvertent simple hysterectomy. Since the incidence of lymph node metastases is 15-25% and the risk of parametrial involvement is high up to 10-15%. These patients can be treated with initial EPL to evaluate the nodal status. If no nodal metastases is detected, the operation will be followed by radical parametrectomy and upper vaginectomy^(8,9). However, if there is nodal metastases, the subsequent radical operation should be abandoned to decrease the complications caused by combined treatment with radiation.

3. Stage IB-IIA cervical cancer patients

with planned RHPL. If nodal metastases are found during EPL, radical hysterectomy can be abandoned and proceeds the patients to radiation therapy. Surgical evaluation of pelvic lymph nodes with EPL prior to radical hysterectomy was performed in 30 patients with stage IA2-IIA cervical cancer with uneventful consequences in CMUH between April 2002 and June 2002. Radical hysterectomy was abandoned and the treatment plan was switched to radiation therapy in 20% of cases by using this protocol⁽⁷⁾.

4. Surgical staging of patients with cervical cancer prior to radiation therapy. If lymph node metastases are detected above the common iliac vessel, extended-field radiation should be instituted in addition to pelvic radiation.

In summary, EPL could be safely performed to surgically evaluate the lymph node status in cervical cancer patients prior to radical hysterectomy, radical parametrectomy and radiation.

Should radical hysterectomy be abandoned or continued if positive lymph nodes are detected during the operation ?

There is still controversy when pelvic node metastases are detected during the operation either to continue or abandon radical hysterectomy. Some gynecologic oncologists omitted hysterectomy to avoid the morbidity of combined treatment. Some surgeons still performed radical hysterectomy and proceeded to radiation for better pelvic control and survival. For positive nodes, some performed only biopsy while others removed grossly positive nodes or completed pelvic lymphadenectomy.

In CMUH, radical hysterectomy (RH) is abandoned if grossly positive nodes are identified during the operation. Complete pelvic lymphadenectomy is carried out to remove all grossly positive nodes and proceeds the patients to radiation therapy. A study was undertaken in CMUH between January 2001 and January 2003 to evaluate the outcomes of patients with stage IB-IIA cervical cancer whose radical hysterectomy was abandoned

for grossly positive nodes (23 cases) and compared with patients whose positive nodes were pathologically identified after the operation (35 cases). Both groups were subsequently treated with concurrent cisplatin-based chemoradiation⁽¹⁰⁾.

There were significant differences in terms of number of positive nodes and number of patients receiving extended-field radiation. Complications in both groups were not significantly different, but the 2-year disease-free survival was significantly lower in the abandoned RH group compared to that in the RHPL group (58.5% vs 93.5%, respectively, $P = 0.01$). This was because the abandoned RH group had worse prognostic factors⁽¹⁰⁾. Since the complications are not significantly different, a prospective randomized study is ongoing in CMUH to evaluate the outcomes in patients found to have grossly positive nodes intraoperatively by comparing between the abandoned RH group and the continued RH group.

What is the prognosis of invasive cervical cancer patients with high-risk pathologic factors ?

After RHPL, patients who have either lymph node metastases, parametrial involvement or positive surgical margins are considered high risk to recur and fare worse survival. Adjuvant radiation is recommended to decrease recurrence and improve survival. Between January 1998 to January 2003, there were 156 patients with stage IA2-IIA cervical cancer in CMUH found to have at least 1 high-risk pathologic factor after RHPL. With a median follow-up of 26 months, the projected 5-year progression-free survival and overall survival were 80% and 93%, respectively. Tumor recurrence occurred in 12 patients (7.7%) in which 8 of these had lymph node metastases, the remaining had parametrial invasion⁽¹¹⁾.

The incidence of lymph node metastases among 251 patients with stage IB1 cervical cancer undergoing RHPL in CMUH between January 2000 and December 2002 was 24%. Histologic grade, depth of stromal invasion (DSI), lymphovascular

space invasion (LVSI), parametrial invasion, and uterine corpus invasion were significantly correlated with pelvic node metastases. The strongest predicting factor of pelvic node metastases was LVSI⁽¹²⁾. The incidences of lymph node metastases in patients with stage IB2 and stage IIA cervical cancer appear to be higher than that of stage IB1 but the parametrial involvement was not significantly different as shown in Table 1⁽¹³⁾. In

Table 1. Comparison of stage IB1, IB2, and IIA cervical cancer in CMUH : 2000-2005⁽¹³⁾

Outcomes	Stages of cervical cancer (number)		
	IB1 (358)	IB2 (61)	IIA (46)
Positive nodes	25%	10%	38%
Parametrial involvement	12%	39%	11%

The incidence of pelvic node metastases also depends on the extent of LVSI in the cervical tumor. Among the 397 patients with stage IB1 cervical cancer undergoing RHPL in CMUH between January 1998 and December 2002, 146 (36.8%) had tumor with LVSI in which 82 (21%) and 64 (16%) had minimal (< 10 LVSI / cervical specimen) and

general, the incidence of parametrial invasion depend on the tumor size, gross appearance of the tumor, tumor grade, depth of stromal invasion, LVSI, radicality of parametrial resection and thoroughness of pathologic examination. Among the patients with clinical parametrial involvement, i.e., stage IIB cervical cancer, the parametrial invasion was pathologically confirmed in only 21-55%⁽¹⁴⁾.

Table 2. The extent of LVSI and the incidence of lymph node metastases⁽¹⁵⁾

LVSI	Number	Lymph node metastases
Negative	251	15 (6%)
Positive	146	44 (30%)
Minimal	82	18 (22%)
Extensive	64	26 (41%)

Should adjuvant radiation be instituted for stage IA2-IIA cervical cancer with deep stromal invasion (DSI) and/or LVSI but without lymph node metastases ?

In general, after RHPL for cervical cancer, adjuvant radiation is recommended for patients who are high risk of recurrence, i.e., lymph node metastases, parametrial involvement, and positive surgical margins. However, approximately half of the

extensive (≥ 10 LVSI / cervical specimen) LVSI, respectively. Fifty nine (15%) patients had pelvic node metastases. The extent of LVSI either minimal or extensive appeared to significantly associate with the risk of lymph node metastases in stage IB1 cervical cancer as shown in Table 2⁽¹⁵⁾.

recurrences in patients with early-stage cervical cancer occur in those with negative nodes. The independent risk factors in these patients are large tumor size, DSI, and LVSI. A decrease in recurrence and improvement of survival were noted in patients with these intermediate -risk factors who received adjuvant radiation.

The outcomes of 150 patients with node-negative stage IA2-IIA cervical cancer who had DSI

and/or LVS1 after RHPL in CMUH between 1999 and 2004 were evaluated. Eighty-eight (58.4%) patients were treated with RHPL alone while the remaining 62 (41.6%) patients received adjuvant radiation with or without chemotherapy. Overall 11 (7.3%) patients developed recurrence. The estimated 5-year disease-free survival of the patients was high at 91%. Adjuvant treatment did not significantly affect the survival rate. Conclusively, node-negative cervical cancer patients with DSI and/or LVS1 have excellent survival outcome⁽¹⁶⁾. Adjuvant radiation may not be necessary in such cases. Small-field radiation may be considered to decrease local recurrence and avoid morbidity of combined treatment. However, the prognosis of node-negative cervical cancer patients with DSI and/or LVS1 also depends on the radicality of parametrial resection and the completeness of pelvic node dissection.

Does Pap smear from vaginal stump benefit in early detection of recurrent cervical cancer after RHPL ?

Approximately 10-15% of patients develop recurrence after RHPL for early-stage cervical cancer. The important goal of postoperative follow-up is to early detect and treat tumor recurrence to improve survival. The surveillance program usually consists of history taking, physical exam, vaginal cytology and radiological studies. The value of vaginal cytology in detecting recurrence is still controversial in routine follow-up practice.

A study was conducted to evaluate the value of vaginal cytology in detecting recurrent cervical cancer after RHPL in 565 patients with staging IB-IIA cervical cancer between January 2000 and May 2006 in CMUH. With the median follow-up of 35 months, 23 (4%) patients developed recurrence. Of the total 4,376 vaginal smears, 5 (0.1%) showed abnormal cytology but only 1 had recurrence. The sensitivity of vaginal cytology for detection of recurrence was only 4.3%. Vaginal cytology appears to have limited value in detecting recurrence after RHPL for early-stage cervical cancer⁽¹⁷⁾.

What are the advantages of nerve-sparing radical hysterectomy ?

Conventional RHPL has been accepted as a standard treatment for stage IB-IIA cervical cancer with 5-year survival rate of over 80% depending on the substage and the pathologic risk factors. However, the operation is associated with significant postoperative complications including bladder dysfunction, colorectal motility disorder, and sexual dysfunction. These morbidities result from injury to the pelvic autonomic nerves during dissection of the parametrium.

Nerve-sparing surgical approach has been advocated to avoid pelvic nerve disruption during radical hysterectomy. A prospective study was conducted in CMUH from January to August 2005 to assess the feasibility and safety of the procedures as well as its impact on urinary voiding function in 21 patients with stage IB-IIA cervical cancer and 1 patient with clinical stage II endometrial cancer. The nerve-sparing procedure could be performed successfully and safely in all of the patients. On day 14 postoperatively, 77% of the patients had postvoiding residual urine less than 50 ml⁽¹⁸⁾.

Earlier resumption of bladder function was noted when compared with those in the historical control. However, a larger comparative study with long-term follow-up is needed to evaluate the advantage of this procedure on the reduction of postoperative bladder, colorectal, and sexual dysfunctions. Furthermore, the recurrence and survival must be determined to reassure that such procedure does not compromise the radicality of parametrial resection.

Alternative approaches for RHPL

Other than the midline abdominal and Maylard approaches for RHPL, such procedure can be carried out via laparoscope and minilaparotomy. Laparoscopic approach appears to have lower blood loss, longer operating times, and either shorter hospital stay or earlier return of bowel function. The safety and feasibility of the operation has clearly

been established with equivalency in specimen size and parametrial width. Most critiques credit this operation to a “learning curve” and describe that increased experience will result in a decrease in the operating time. Since 2003, over 60 operations of total laparoscopic radical hysterectomy (TLRH) have been performed with satisfactory outcomes in CMUH. The operative time and complications significantly decreased after passing the learning curve of the operation⁽¹⁹⁾. Type 3 RHPL via a small transverse abdominal incision (6-10 cm), the so-called minilaparotomy is also an attractive and challenging procedure. Using the rotating-retractors technique, such procedure is feasible, safe, adequate, and could be associated with benefits on recovery for selected patients with small early-stage cervical cancer⁽²⁰⁾.

Conclusion

From the experience of over 1400 RHPL operations for patients with early-stage cervical cancer in CMUH between 1997 and 2007, we have learned that retroperitoneal drainage and peritonization can be safely abandoned after the operation. Intermittent self-catheterization can resume bladder function earlier than the suprapubic cystostomy. Extraperitoneal pelvic lymphadenectomy has various roles in managing patients with inadvertent simple hysterectomy of invasive cervical cancer and surgical staging of cervical cancer. Radical hysterectomy may be safely performed in patients found to have positive nodes during the operation without significant increase in the complication rate after adjuvant radiation. The strongest predicting factor of pelvic node metastases in early-stage cervical cancer is the presence of LVSI. The risk of nodal metastases is highly associated with the severity or the extent of LVSI. Patients with stage IB2 and IIA cervical cancer have much higher incidence of lymph node metastases than those with stage IB1. Adjuvant radiation may not be necessary in patients with node-negative stage IA2-IIA cervical cancer who have intermediate-risk factors which are the intracervical factors, i.e.,

deep stromal invasion and/or LVSI in the cervical specimens after RHPL. Pap smear from the vaginal stump appears to have limited value in detecting recurrence after RHPL for early-stage cervical cancer. Nerve-sparing RHPL aiming at preserving pelvic autonomic nerves will play an important role in the future to minimize bladder, colorectal, and sexual dysfunctions after the operation. Alternatively, RHPL can be carried out via the laparoscopic and the minilaparotomy approaches.

References

1. Srisomboon J. Cervical cancer: diagnosis and treatment. Bangkok : PB Foreign Book Center; 2004:140-50.
2. Srisomboon J, Suprasert P, Phongnarisorn C. Experience with radical hysterectomy and pelvic lymphadenectomy with no peritonization and no retroperitoneal drainage for cervical cancer. *Thai J Obstet Gynaecol* 1999;11(Suppl.1):69-74.
3. Srisomboon J, Phongnarisorn C, Suprasert P, Cheewakriangkrai C, Siriaree S, Charoenkwan K. A prospective randomized study comparing retroperitoneal drainage with no drainage and no peritonization following radical hysterectomy and pelvic lymphadenectomy for invasive cervical cancer. *J Obstet Gynaecol Res* 2002;28:149-53.
4. Suprasert P, Srisomboon J, Phongnarisorn C. A prospective randomized study comparing voiding time between suprapubic catheterization and intermittent self-catheterization following radical hysterectomy and pelvic lymphadenectomy for cervical cancer. *Thai J Obstet Gynaecol* 2002;14:73-9.
5. Srisomboon J, Phongnarisorn C, Suprasert P, Charoenkwan K, Cheewakriangkrai C, Siriaree S, Porapakham P, et al. The role of extraperitoneal pelvic lymphadenectomy in management of early stage cervical cancer. 7th Annual Scientific Meeting of The Thai Gynecologic Oncology Group, Montien Pattaya Hotel, Cholburi, Thailand, Augrust 10-12, 2002.
6. Srisomboon J, Phongnarisorn C, Suprasert P, Charoenkwan K, Cheewakriangkrai C, Siriaree S, et al. Technique and application of extraperitoneal pelvic lymphadenectomy in cervical cancer. 17th Annual Scientific Meeting of The Royal Thai College of Obstetricians and Gynecologists, Lee Garden Hotel, Hat-Yai, Songkhla, Thailand, October 16-18, 2002.
7. Srisomboon J, Porapakham P, Phongnarisorn C, Suprasert P, Cheewakriangkrai C, Charoenkwan K, Siriaree S, et al. Surgical evaluation of pelvic lymphnodes by extraperitoneal pelvic lymphadenectomy before radical hysterectomy for early stage cervical cancer. 17th Annual Scientific

Meeting of The Royal Thai College of Obstetricians and Gynecologists, Lee Garden Hotel, Hat-Yai, Songkhla, Thailand, October 16-18,2002.

8. Srisomboon J, Phongnarisorn C, Suprasert P. Radical parametrectomy, upper vaginectomy and pelvic lymphadenectomy of invasive cervical cancer following simple hysterectomy. *Thai J Obstet Gynaecol* 2000;12(2):141-4.
9. Phongnarisorn C, Srisomboon J. Total laparoscopic radical parametrectomy and upper vaginectomy after inadvertent simple hysterectomy of early stage cervical cancer. International Symposium on Radical Hysterectomy Dedicated to Hidekazu Okabayashi., Kyoto, Japan, February 7-10,2007.
10. Suprasert P, Srisomboon J, Charoenkwan K, Siriaunkul S, Khunamornpong S, Siriaree S, et al. Outcomes of abandoned radical hysterectomy in patients with stage IB – IIA cervical cancer found to have positive nodes during the operation. *Int J Gynecol Cancer* 2005;15:498-502.
11. Siriwaranya T, Suprasert P, Siriaunkul S, Khunamornpong S, Srisomboon J, Charoenkwan K, et al. Outcome of high – risk early stage cervical cancer treated with radical hysterectomy and pelvic lymphadenectomy. *Thai J Obstet Gynaecol* 2003;15:93-9.
12. Udomwan P, Charoenkwan K, Siriaunkul S, Srisomboon J, Khunamornpong S, Suprasert P. Prevalence and predicting factors for pelvic lymph node metastasis in stage IB1 cervical carcinoma. *Thai J Obstet Gynaecol* 2003;15:161-7.
13. Srisomboon J, Charoenkwan K, Siriaunkul S, Khunamornpong S, Suprasert P, Phongnarisorn C, et al. Survival and prognostic factors for patient with early – stage cervical cancer treated with radical surgery :stage IB1 vs IB2. The 57th Annual Congress of the Japan Society of Obstetrics and Gynecology, Kyoto, Japan, April 2-5,2005.
14. Suprasert P, Srisomboon J. Radical hysterectomy for stage IIB cervical cancer : a review. *Int J Gynecol Cancer* 2005;15:995-1001.
15. Chandacham A, Charoenkwan K, Siriaunkul S, Srisomboon J, Suprasert P, Phongnarisorn C, et al. Extent of lymphovascular space invasion and risk of pelvic lymph node metastases in stage IB1 cervical cancer. *J Med Assoc Thai* 2005;88(suppl.2):S31-36.
16. Suprasert P, Srisomboon J, Siriaunkul S, Khunamornpong S, Phongnarisorn C, Siriaree S, et al. Clinical outcomes and prognostic factors of node – negative cervical cancer patients with deep stromal invasion or lymphovascular space involvement following radical hysterectomy. *J Med Assoc Thai* 2006;89:1368-75.
17. Injumpa N, Suprasert P, Srisomboon J, Nimmanahaeminda K, Phongnarisorn C, Siriaree S, et al, Limited value of vaginal cytology in detecting recurrent disease after radical hysterectomy for early stage cervical carcinoma. *Asian Pac J Cancer Prev*. 2006;7(4):656-68.
18. Charoenkwan K, Srisomboon J, Suprasert P, Tantipalakorn C, Kietpeerakool C. Nerve-sparing class III radical hysterectomy: a modified technique to spare the pelvic autonomic nerves without compromising radicality. *Int J Gynecol Cancer* 2006; 16:1705-12.
19. Phongnarisorn C. Total laparoscopic nerve-sparing radical hysterectomy and pelvic lymphadenectomy in early stage cervical cancer : a surgical technique. In Srisomboon J, Suprasert P, editors. *Cervical cancer prevention and treatment*. Chiang Mai : Jaras Publishing; 2008:133-54.
20. Charoenkwan K, Siriaree S, Cheewakriangkrai C, Srisomboon J. Minilaparotomy for type 3 radical hysterectomy and pelvic lymphadenectomy in early-stage cervical cancer. *Am J Obstet Gynecol* 2008 (in press).