The Prospective Study of the Value of Extraperitoneal Pelvic Lymph Node Dissection for Patients with Stage IB2-IIB Cervical Cancer

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ABSTRACT

Objective: To evaluate the value of extraperitoneal pelvic node dissection as a new diagnostic tool for evaluation of retroperitoneal pelvic node status in cervical cancer stage IB2-IIB patients after neoadjuvant chemotherapy. Complications of the procedure were also evaluated.

Methods: Patients with cervical cancer stage IB2-IIB received neoadjuvant chemotherapy for 3 cycles. After that the patients underwent extraperitoneal pelvic node dissection and the nodes were sent for frozen section. If the frozen section was negative for metastases, radical hysterectomy was performed. If the frozen section was positive, radical hysterectomy was abandoned and the patients were treated by radiation. The value of extraperitoneal pelvic node dissection as a diagnostic tool for evaluating the extent of the disease was compared to that of transperitoneal pelvic node dissection as historical control.

Results: Twenty-three patients were included in the study. Nineteen patients (83%) underwent radical hysterectomy after extraperitoneal node dissection; however, the procedure was abandoned in 3 patients (13%) due to positive frozen section of the lymph nodes. The frozen section lymph node yielded a false negative result in one patient (4%). The operative time, lymph node yield and the incidence of postoperative complications were not statistically different between extraperitoneal approach and transperitoneal approach.

Conclusion: Extraperitoneal pelvic node dissection seems more suitable than transperitoneal pelvic node dissection for the evaluation of retroperitoneal pelvic node status in cervical cancer patients.

Keywords: Cervical cancer; extraperitoneal node dissection

Cervical cancer is the most common cancer in Thailand with an incidence of 6,192 new cases in 2001. At Siriraj Hospital, the incidence of new cases of cervical cancer is 479 cases in 2005. The management of invasive cervical cancer depends on FIGO stage which is achieved by clinical evaluation. Early carcinoma (FIGO IA, IB1) is usually managed by surgery whereas advanced stage disease (FIGO IB2-IV) requires primary treatment with chemoradiation therapy. As for locally advanced stage cervical cancer, there have been data showing benefit from neoadjuvant chemotherapy followed by radical hysterectomy with pelvic node dissection (RHND). The data from an Italian multicenter randomized study showed a survival benefit for cervical cancer stage IB2 - IIB patients treated with neoadjuvant chemotherapy followed by RHND.

RHND for early stage has potential benefit for preservation of ovarian function, improved coital function and the ability to identify surgical pathologic risk factors such as lymph node involvement. In a randomized trial, comparing radical surgery with radiotherapy for stage IB- IIA cervical cancer including 343 patients, the authors found identical 5-year overall and disease free survival rates in both groups after a median follow up of 87 months. It is of note that in this study the combination of surgery and adjuvant radiotherapy had the worst morbidity.

The presence of lymph node metastases is the most important adverse predictor of survival in early stage cervical cancer. It had been reported that pelvic lymph node metastasis was 15.4% in stage IB and 28.6% in stage II. Several methods have been used to assess pelvic and para-aortic lymph node including computed tomography, magnetic resonance imaging and lymphangiography. Unfortunately, the identification of lymph node metastases prior to surgery in these patients with cervical cancer is unsatisfactory. Novel modalities to identify patients with lymph node metastases such as positron emission tomography or sentinel lymph node mapping are still under research.

Discrepancies between clinical FIGO staging system and surgical/histopathological findings occur in about 25-30% of patients with cervical cancer. Therefore, following radical hysterectomy (RH), a subset of patients with histologically documented risk factors, such as lymph node metastases, have a clear benefit from adjuvant pelvic
radiation. Serious bowel complications have been reported in patients with cervical cancer who have had operative evaluation through a transperitoneal approach followed by radiation therapy. Pre-treatment surgical staging by extraperitoneal approach appears to be associated with less long-term radiation morbidity compared with the transperitoneal approach probably due to the less postoperative intra-abdominal adhesion.

Some investigators abandoned radical surgical procedure in case of lymph node involvement in order to reduce the high morbidity of the complication of combined radical surgery and radiotherapy. The authors also report a similar sensitivity in detecting nodal status for extraperitoneal lymph node dissection as compared with the transperitoneal approach.

The aim of our prospective study was to evaluate the value of the extraperitoneal pelvic node dissection as a new diagnostic tool for the evaluation of retroperitoneal node status in patients with cervical cancer stage IB2-IIB after neoadjuvant chemotherapy. The complication of the procedure was also evaluated.

MATERIALS AND METHODS

Patients aged less than 70 years with stage IB2-IIB squamous cell carcinoma of the uterine cervix were eligible. Exclusion criteria were GOG performance status greater than 2, severe systemic disease, other malignancy (except for adequately treated basal cell carcinoma), inadequate bone marrow reserve (WBC < 3,000/mm³ and/or absolute neutrophil count < 1,500/mm³ and/or platelet count < 100,000/mm³), abnormal liver function (serum bilirubin > 1.5 mg/dL), and abnormal renal function (creatinine clearance < 60 mL/min). The clinical staging procedure was performed according to the system adopted by FIGO. Whole abdominal computed tomography (CT) was also included in the pretreatment evaluation. If whole abdominal CT showed liver metastases or paraaortic node involvement, the patient would be excluded from the study. The study was examined and approved by the Ethics Committee of Siriraj Hospital.

Treatment plan

All the patients received neoadjuvant chemotherapy. Chemotherapy consisted of cisplatin 70 mg/m² and paclitaxel 175 mg/m² every 3 weeks for 3 cycles. After neoadjuvant chemotherapy, the patients were clinically reassessed and classified either as suitable or unsuitable for surgery. The latter were treated by radiation therapy. If the patient was suitable for surgery, extraperitoneal pelvic node dissection was performed. All lymph nodes were sent for frozen section. If the frozen section showed lymph node metastases, RH would be abandoned. If the frozen section of lymph node was negative for malignancy, the patient would undergo RH. Postoperative radiation therapy was given to patients who had positive surgical resected margin and/or lymph node metastases and/or parametral involvement. Those who were in the intermediate risk group according to GOG protocol also received adjuvant radiation therapy.

Operative technique

A vertical midline incision is initially made from just inferior to the umbilicus to the symphysis pubis. The retroperitoneum was exposed by rolling the peritoneum sac medially. Inferior epigastric vessels were identified, ligated and cut, and then a round ligament was ligated and cut. The peritoneum was further rolled medially until the bifurcation of the iliac vessels, and psoas muscle were visualized. Pelvic lymph nodes, including the external iliac, internal iliac and obturator lymph nodes (Fig 1 and 2), were resected. The pelvic lymph node dissection was performed in the same way as on the other side.

Statistical analysis

To compare with our study group, we used patients with squamous cell carcinoma of cervix stage IB1 who underwent transperitoneal pelvic lymph node dissection and RH that was performed at the same period as historical controls. The difference of lymph node yield, operative time for pelvic lymph node dissection between extraperitoneal node dissection group and transperitoneal node dissection group were compared. As for comparison of post operative complication, we did not include the cases that RH was abandoned in the extraperitoneal group. The incidence of operative complication such as wound infection and lymphocyst was compared between extraperitoneal node dissection with RH group and transperitoneal node dissection with RH group.

The difference of lymph node yield was compared by Mann-Whitney U test, while that of operative time was compared by unpaired t-test. The difference of incidence of wound infection and lymphocyst was compared by Fisher’s exact test. Statistical significance was determined by P < 0.05.
TABLE 1. Comparisons of relevant variables between EPND and TPND (historical control).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EPND</th>
<th>TPND</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>Lymph node yield *</td>
<td>Median 23</td>
<td>21 (19 - 32)</td>
<td>0.35</td>
</tr>
<tr>
<td>Operative time (min)*</td>
<td>Mean 70</td>
<td>63 (55 - 102)</td>
<td>0.25</td>
</tr>
<tr>
<td>Wound infection</td>
<td>0/20 (0%)</td>
<td>2/23 (8%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Lymphocyst</td>
<td>1/20 (5%)</td>
<td>0/23 (0%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Gut obstruction</td>
<td>0/20 (0%)</td>
<td>0/23 (0%)</td>
<td></td>
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</tbody>
</table>

EPND = extraperitoneal node dissection  
TPND = transperitoneal node dissection  
*For lymph node yield and operative time for node dissection comparison, n = 23

RESULTS

Between December 2004 and July 2006, 23 patients were included in the study. The mean age of the patients was 44.4 years (range 28-35). Before neoadjuvant chemotherapy was given, 3 patients (13%) were in stage IB2, 5 (22%) in stage IIA, and 15 (65%) in stage IIB.

Nineteen patients (83%) underwent RH after extraperitoneal node dissection. The procedure was abandoned in 3 patients (13%) after extraperitoneal node dissection due to the histologically confirmed lymph node involvement by frozen section. One patient (4%) had lymph node involvement but RH was performed due to the false negative result of frozen section.

The difference of lymph node yield and operative time for pelvic lymph node dissection between the extraperitoneal lymph node dissection group and the transperitoneal lymph node dissection group (historical control) was not statistically different (Table 1).

Regarding post-operative complications, the incidence of wound infection, lymphocyst and gut obstruction was not statistically different between the extraperitoneal pelvic node dissection with RH group and the transperitoneal pelvic node dissection with RH group (historical control). However, there was no gut obstruction in both groups.

DISCUSSION

According to the FIGO classification, cervical cancer is clinically staged. However, with recent advances in identifying histopathological risk factors, this clinical staging is controversially discussed. Different risk factors assessable by surgical staging have been identified, which influence therapeutic treatment and prognosis. The information obtained from surgical staging allows the individualization of therapy, which may result in better clinical outcome.

We introduced the extraperitoneal lymph node dissection in patients with cervical cancer as the new diagnostic tool at the Division of Gynaecological Oncology, Department of Obstetrics and Gynaecology, Siriraj Hospital. We found that this approach provided nodal status evaluation that benefited for the plan of treatment. Gynaecological oncology group study showed that extraperitoneal approach made less bowel morbidity if adjuvant radiation was required. In our experience, however, an extraperitoneal approach resulted in easy removal of pelvic nodes because the intact peritoneum could be used as a pack. So we created the prospective study to prove the value of the extraperitoneal pelvic lymph node dissection in patients with cervical cancer.

In this study we used extraperitoneal approach to evaluate lymph node status before we decided whether radical hysterectomy would be performed or not. We included patients with cervical cancer stage IB2-IIIB because they might have more lymph node involvement compared to patients with stage IB1, although they were pre-treated with neoadjuvant chemotherapy.

According to our result, the RH was abandoned in 3 of 23 patients (13%). This treatment modification by surgical staging in 13% of patients with cervical cancer corresponds to 18% of previously published data.

The median number of lymph node yield and mean operative time for lymph node dissection in extraperitoneal approach group were comparable with transperitoneal approach group (historical control). According to operative complication, the incidence of wound infection, lymphocyst and gut obstruction were not statistically different between 2 groups. However, previously published data showed that extraperitoneal node dissection gave a slightly higher rate of lymphocyst compared to transperitoneal approach.

From the result of our study it seems that extraperitoneal pelvic node dissection is more suitable in terms of diagnostic tool than transperitoneal approach in patients with cervical cancer.

Comparing the established clinical staging by the FIGO classification with the surgical staging by extraperitoneal lymph node dissection, lymph node involvement had a significantly higher predictive value for survival than the FIGO stage. Therefore the lymph node involvement might be a better diagnostic tool to distinguish “low risk” from “high risk” patients than the FIGO stage. Furthermore, surgical evaluation allows a better individualization of the therapy and may result in better outcome.

In summary, extraperitoneal pelvic node dissection gave a comparable lymph node yield and operative complication to intraperitoneal pelvic node dissection. In accordance with previous studies on higher adjuvant radiation complication after transperitoneal lymph node dissection, we concluded that extraperitoneal pelvic node dissection might be more suitable as diagnostic tool than transperitoneal pelvic node dissection.

REFERENCES
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บทคัดย่อ
การศึกษาแบบไปซ้ำหน้าของคุณค่าของการะดับความหนาหรือแบบไม่ซ้ำของมันในผู้ป่วยมะเร็งปากกคลุม

มีอยู่ใน 1203

ถ้าเป็นนักการอย่างนั้น

วัตถุประสงค์: เพื่อประเมินคุณค่าของการะดับความหนาหรือแบบไม่ซ้ำของมันในสูดวิริย์หรือเพื่อประเมินสภาพคล่องของนักศึกษาในผู้ป่วยมะเร็งปากกคลุม

วิธีการ: ผู้ป่วยได้ถูกแบ่งตามเป็น 3 กลุ่ม หลังจากนั้นจะได้รับการตรวจโดยนักศึกษาในผู้ป่วยชอง และส่งผลต่อการตรวจแบบบางครั้ง ถ้าผลการตรวจไม่สม่ำเสมอในแต่ละช่อง ผู้ป่วยจะได้รับการตรวจแบบหลายช่องโดยที่ห้อง แต่การตรวจจะไม่เป็นช่องที่ผู้ป่วยจะได้รับการตรวจแบบที่เป็นช่องที่ผู้ป่วยที่ได้รับการตรวจแบบในผู้ป่วยที่มีเกิดใหม่

ผลการศึกษา: นักศึกษาได้ศึกษาจำนวน 23 ราย ผู้ป่วย 19 ใน 23 ราย (83%) ได้รับการตรวจแบบหลายช่องโดยรวมกับการตรวจแบบไม่ซ้ำของมันในนักศึกษา ผู้ป่วย 3 ใน 23 ราย (13%) ได้รับการตรวจแบบหลายช่อง และส่งผลต่อการตรวจแบบไม่ซ้ำของมันอย่างต่อเนื่อง จากการผลการตรวจแบบหลายช่อง ผู้ป่วย 1 ใน 23 ราย (4%) ได้รับการตรวจแบบหลายช่องโดยรวมกับการตรวจแบบไม่ซ้ำของมัน ผู้ป่วย 1 ใน 23 ราย (4%) ได้รับการตรวจแบบหลายช่องโดยรวมกับการตรวจแบบไม่ซ้ำของมัน

ข้อมูล: การตรวจแบบไม่ซ้ำของมันสามารถแบ่งตามประเภทที่ใช้ในการศึกษาแบบหลายช่องในผู้ป่วยมะเร็งปากกคลุม บางวิธีการตรวจแบบไม่ซ้ำของมัน