

Accuracy of Intraoperative Clinical Evaluation of Lymph Nodes in Women with Gynecologic Cancer

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Objective : To determine the accuracy of intraoperative clinical evaluation of lymph node metastasis in gynecologic cancer women.

Method : From May 2003 to April 2004, the characteristics of lymph node metastasis in women who underwent lymphadenectomy, lymph node sampling, or lymph node biopsy for surgical procedure of gynecologic malignancies were evaluated in 124 cases. The operation was performed by gynecologic oncologists. The overall clinical impression and lymph node characteristics (lymph node enlargement, consistency, shape, and adherence) were correlated with histologic diagnosis.

Results : The mean age was 51 years. The type of cancer were cervical cancer (48%), endometrial cancer (33%), ovarian cancer (17%), and vulvar cancer (2%). Overall, intraoperative clinical evaluation for lymph node metastasis had a high sensitivity, specificity, and accuracy(81%, 91%, and 90%, respectively), but had a high false-negative rate (19%). The positive and negative predictive values of intraoperative lymph node evaluation were 65% and 96%, respectively. Lymph node enlargement (size ≥ 2 cm) had a highest sensitivity(94%) and round shape of lymph nodes had highest specificity and accuracy (97% and 94%, respectively).

Conclusion : Intraoperative lymph nodes clinical evaluation for detecting lymph node metastasis in gynecologic malignancy had a high accuracy (when performed by experience surgeon) and may be useful in situation that complete lymphadenectomy is not feasible.

Keywords : Gynecologic cancer, Lymphadenectomy, Clinical evaluation

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Gynecologic malignancies tend to metastasize to regional lymph nodes, and determining lymph node status is important for appropriate staging and treatment. Indications for lymph node dissection in management of patients with gynecologic cancer include staging and removal of gross and microscopic disease.

Because of their anatomic location, most lymph nodes especially those in the pelvis of women with gynecologic cancers can not be palpated before surgery. Most gynecologic cancers are currently staged on the basis of surgicopathologic findings, i.e. ovarian cancer, endometrial cancer and vulvar cancer which include the histopathologic examination of lymph nodes removed at the time of surgery.

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Clinical evaluation of lymph node metastasis intraoperatively is important because it may affect further operative procedure whether to continue or abandon the operation. In case of cervical cancer, if lymph node metastasis is detected during the operation, the radical hysterectomy is usually omitted. Whilst in case of endometrial cancer or ovarian cancer, lymph node dissection is essential in proper surgical staging and debulking of metastatic tumor. Lymphadenectomy if performed by experienced surgeons is usually safe and cost-effective⁽¹⁻³⁾.

Intraoperative evaluation of lymph node metastasis by clinical method have been advocated by some authors to determine the need for performing lymph node dissection^(13,14). But some authors noted that clinical evaluation of lymph nodes is not accurate in identifying metastasis⁽⁴⁻⁶⁾. Accordingly, this study was carried out to investigate the accuracy of systema-

tic clinical evaluation of lymph node metastasis in gynecologic cancer patients receiving surgical treatment.

Material and Method

This was a prospective study that included all women with histologically proven gynecologic cancer who underwent lymphadenectomy, lymph node sampling, or lymph node biopsy as part of surgical procedure. The study was conducted at Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, between May 2003 and April 2004. All of the operations were performed by experienced gynecologic oncologists.

In women with cervical, endometrial, or ovarian cancers, lymph nodes were evaluated after opening the retroperitoneal spaces in the pelvis and the peritoneum over the lower vena cava and aorta and identifying the major blood vessels. In women with vulvar cancer, inguinal lymph nodes were evaluated after dissection of the subcutaneous fascia and identification of the cribriform fascia, the inguinal ligament, the saphenous vein, and the femoral vessels. A retroperitoneal lymphadenectomy was defined as complete removal of all lymph node-bearing tissue with skeletonization of pelvic and periaortic vessels to the level of the inferior mesenteric artery. The extent of dissection in the pelvis were the deep circumflex iliac veins distally, the obturator nerves inferiorly, the internal iliac arteries medially, and the aortic bifurcation proximally. The extent of para-aortic dissection were bifurcation of the aorta distally and the inferior mesenteric artery proximally.

In all cases, the characteristics of lymph node metastasis that were evaluated included: size, consistency, shape, and adherence to surrounding

structures. Lymph node enlargement was defined as maximum diameter of ≥ 2 cm. Consistency of lymph nodes was judged by palpation of the individual lymph nodes with the tips of the fingers and was classified as hard or soft consistency. Shape of lymph nodes was defined into flat and round shape. Judgement of lymph node adherence was determined by rolling the lymph nodes over the underlying structures. Consistency, shape, and adherence of lymph nodes were judged by individual surgeon. In addition, the overall impression on the basis of these 4 characteristics as to whether the lymph nodes were involved and final clinical impression for lymph node metastasis were recorded.

For each patient, the following data were recorded: age, parity, menopausal status, type of cancer, type of operation, blood loss, operative time, intraoperative complications, number of lymph node removed, the characteristics of the lymph nodes (size, consistency, shape, and adherence), and the overall intraoperative clinical impression of lymph node involvement. Final histopathologic diagnosis was certainly the gold standard for evaluation of the accuracy of lymph node characteristics and the final clinical impression. Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were calculated.

This study has been approved by ethical committee of the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University.

Results

One hundred twenty-four women entered in this study. Demographic characteristics according to type of cancer are presented in Table 1.

Table 1. Demographic characteristics according to type of cancer

| | Type of cancers | | | | Total |
|--|-----------------|----------------|---------------|----------------|-----------------|
| | CervixN | CorpusN | OvaryN | VulvaN | |
| Mean age \pm SD (years) | 46.0 \pm 9.2 | 56.0 \pm 9.5 | 51 \pm 14.4 | 67.0 \pm 3.0 | 51.0 \pm 11.3 |
| Parity (no. of cases) | | | | | |
| 0 | 4 (19%) | 6 (29%) | 11 (52%) | 0 (0%) | 21 (17%) |
| 1 | 8 (57%) | 6 (43%) | 0 (0%) | 0 (0%) | 14 (11%) |
| ≥ 2 | 47 (53%) | 29 (33%) | 11 (12%) | 2 (2%) | 89 (72%) |
| Median blood loss(ml) | 600 | 250 | 300 | 225 | 400 |
| Median operative time(minutes) | 210 | 180 | 180 | 165 | 186 |
| Mean number of lymph nodes/case \pm SD | 15.9 \pm 10.2 | 12.2 \pm 8.6 | 6.8 \pm 4.6 | 11.5 \pm 3.5 | 13.0 \pm 9.4 |
| Total lymph nodes | 936 | 501 | 149 | 23 | 1609 |

The mean patients age was 51 ± 11.3 years. The type of cancer were cervical, 59 (48%); endometrial, 41 (33%); ovarian, 22 (17%); and vulvar, 2 (2%). Mean number of lymph nodes per case was 13.0 ± 9.4 nodes.

Total clinical impression by surgeons compared with pathologic diagnosis are presented in Table 2.

Twenty one of 124 cases had lymph node metastasis (16.9%). Four of these 21 cases (19.0%) were missed for positive lymph nodes. The false positive and false negative rate were 9% and 19% respectively. For the characteristics of lymph node, the mean size of lymph node enlargement in positive and negative pathologic diagnosis was 3.0 and 1.7 cm respectively. The diagnostic values for clinical signs of lymph node metastasis are presented in Table 3.

Sensitivity and specificity of overall impression were 81% and 91%, respectively. Positive and negative predictive values of lymph node palpation were 65% and 96%, respectively. Overall accuracy of clinical impression was 90%. When characteristics of lymph nodes were considered separately, sensitivity of lymph node enlargement (size ≥ 2 cm) was the highest (94%) and round shape of lymph nodes demonstrated the highest specificity and accuracy (97% and 94%, respectively).

Table 2. Comparison of clinical impression with pathologic diagnosis

| Clinical impression | Pathologic diagnosis | | Total |
|---------------------|----------------------|----------|-------|
| | positive | negative | |
| positive | 17 | 9 | 26 |
| negative | 4 | 94 | 98 |
| Total | 21 | 103 | 124 |

Table 3. Diagnostic values for clinical signs of lymph node metastasis

| | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|---------------------------------|-----------------|-----------------|---------|---------|--------------|
| Overall clinical impression | 81 | 91 | 65 | 96 | 90 |
| Enlargement (size ≥ 2 cm) | 94 | 78 | 79 | 93 | 85 |
| Hard consistency | 71 | 91 | 62 | 94 | 88 |
| Round shape | 76 | 97 | 84 | 95 | 94 |
| Adherence to adjacent structure | 29 | 94 | 50 | 87 | 83 |

Discussion

Pelvic and aortic lymph nodes are common sites of metastasis for gynecologic malignancies, and there is no question that evaluation of lymph node status provides important prognostic information. Unfortunately, nuclear magnetic resonance, computerized tomography, and lymphangiography have low accuracy in the evaluation of lymph nodes and can not detect lymph node metastases measuring < 10 mm^(7,8). In addition, these techniques do not provide information about the pathologic features of the lymph node metastases, such as the number of lymph nodes involved, the size of the metastasis, and the presence of capsular invasion. Therefore, lymphadenectomy is the only procedure that facilitates an accurate and thorough evaluation of lymph node status. Nonetheless, the therapeutic role of lymphadenectomy in patients with gynecologic malignancies is still under debate, and the role of systematic lymphadenectomy in the treatment of gynecologic cancer patients is an even more controversial issue.

Assessment of the lymph nodes is an integral part of the treatment of gynecologic cancers. Histopathologic examination provides the most accurate method of ascertaining metastatic spread to lymph nodes, but lymphadenectomy is associated with significant operative risk in some cases⁽⁹⁾. On the other hand, some authors⁽¹⁰⁾ have reported excellent survival among women with early-stage endometrial cancer who did not undergo systematic lymphadenectomy and in whom the lymph nodes were evaluated by intraoperative palpation.

Several reports have cast doubt on the accuracy of clinical evaluation of lymph nodes among women with endometrial cancer and founded the basis for the surgical staging system adopted in 1988. Creasman et al⁽¹¹⁾ stated in their study that the surgeon should not determine the need for lymphadenectomy on the basis of intraoperative palpation of the nodal area, because $< 10\%$ of positive lymph nodes are grossly enlarged. Giardi et al⁽¹²⁾ used step serial sectioning of lymph nodes retrieved from 76 patients with endometrial cancer at risk for lymphatic spread and reported that 37% of lymph node metastases were < 2 mm in diameter and therefore could not be palpated. They speculated that mere sampling of lymph nodes directed especially toward enlarged nodes might not show the true frequency of nodal involvement.

In 2000, Arango et al⁽¹³⁾ reported of 36% false-negative rate, 3% false-positive rate, 72% sensitivity, and 56% positive predictive value for intraoperative

palpation by experienced gynecologic oncologists in the detection of lymph node metastasis in 126 women with gynecologic cancers. These authors noted that intraoperative palpation had low sensitivity and positive predictive value even when performed by experienced surgeons. Recently, Eltabbakh's study⁽¹⁴⁾ concluded that systematic intraoperative clinical evaluation of lymph nodes by a trained surgeon had high overall accuracy and correlated well with the final histopathologic diagnosis, but it had a high false-negative rate and cannot substitute histopathologic examination.

From our study, we found that clinical evaluation for lymph node metastasis had the high sensitivity, specificity, and accuracy (81%, 91%, and 90% respectively), but had a high false negative rate (4/21 cases, 19%). In false negative group, 2 cases were cervical cancer, one case was endometrial cancer, and one case was ovarian cancer.

The results were similar to other studies. Eltabbakh reported that overall clinical impression had a high accuracy but had a high false negative rate (25.8%)⁽¹⁴⁾. So, although this study show the high accuracy, sensitivity, specificity of clinical lymph node palpation, we do not recommend routine replacement of complete lymphadenectomy with selective lymphadenectomy on the basis of clinical evaluation. But it maybe useful in some situation such as in some women who are not surgical candidates because of poor medical condition or body habitus or in emergency operation that is not suitable for complete lymphadenectomy.

Conclusion

Intraoperative clinical evaluation of lymph nodes for detecting lymph node metastasis in gynecologic malignancy had a high sensitivity, specificity, and accuracy when performed by experienced gynecologic oncologist. But a relatively high false negative rate was observed. So, routine replacement of complete lymphadenectomy with selective lymphadenectomy on the basis of clinical evaluation especially by the inexperienced surgeons is not recommended.

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2. morbidity of complete lymphadenectomy in endometrial cancer. *Int J Gynecol Cancer* 1998; 8: 270-3.
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ความแม่นยำของการประเมินสภาพต่อมน้ำเหลืองในห้อยผ่าตัด ด้วยวิธีทางคลินิกในผู้ป่วยมะเร็ง อวัยวะสืบพันธุ์สตรี

จักรพันธ์ ขุนณรงค์, พีรพงศ์ อินทศร, ติฐิกานต์ บริบูรณ์หิรัญสาร

วัตถุประสงค์ : เพื่อศึกษาความแม่นยำในการประเมินการกระจายของมะเร็งไปที่ต่อมน้ำเหลือง ในผู้ป่วยมะเร็งอวัยวะสืบพันธุ์สตรี โดยวิธีทางคลินิกในห้อยผ่าตัด เปรียบเทียบกับผลการตรวจทางพยาธิวิทยา

วิธีการวิจัย : ระหว่างเดือนพฤษภาคม 2546 ถึง เดือนเมษายน 2547 มีผู้ป่วยสตรีเป็นมะเร็งอวัยวะสืบพันธุ์ จำนวน 124 คน ที่ได้รับการผ่าตัดเลาะต่อมน้ำเหลือง แพทย์ผู้ผ่าตัดเป็นผู้ประเมินสภาพต่อมน้ำเหลือง โดยมีเกณฑ์ในการประเมินคือ ขนาดต่อมน้ำเหลือง ความแข็ง รูปร่าง การยึดติดกับอวัยวะข้าง และความเห็นสุดท้ายของแพทย์ผู้ผ่าตัด โดยเปรียบเทียบเกณฑ์การประเมินกับผลทางพยาธิวิทยา และคำนวณทางสถิติต่อไป

ผลการวิจัย : ในกลุ่มผู้ป่วยที่เข้าร่วมการวิจัย มีอายุเฉลี่ย 51 ปี ชนิดของมะเร็งที่ทำการผ่าตัด คือ มะเร็งปากมดลูก 48% มะเร็งเยื่อบุโพรงมดลูก 33% มะเร็งรังไข่ 17% และมะเร็งปากช่องคลอด 2 % การประเมินทางคลินิกในขณะผ่าตัด มีความไว, ความจำเพาะ และความแม่นยำสูง (81%, 91% และ 90% ตามลำดับ) แต่มีผลลบสูง (19%) คุณค่าในการทำนายผลบวก และคุณค่าในการทำนายผลลบ มีค่า 65% และ 96%ตามลำดับ ขนาดต่อมน้ำเหลืองที่โตตั้งแต่ 2 เซนติเมตร มีความไวสูงสุด (94%) เมื่อเปรียบเทียบกับเกณฑ์การประเมินอื่น ๆ ขณะที่ลักษณะต่อมน้ำเหลืองที่กลม มีความจำเพาะและความแม่นยำสูงที่สุด (97% และ 94% ตามลำดับ)

สรุป : การประเมินสภาพต่อมน้ำเหลืองในห้อยผ่าตัด ด้วยวิธีทางคลินิก ในผู้ป่วยมะเร็ง อวัยวะสืบพันธุ์สตรี มีความน่าเชื่อถือและความแม่นยำสูง ในการตรวจการแพร่กระจายของมะเร็ง และอาจมีประโยชน์ในกรณีที่ไม่สามารถผ่าตัดต่อมน้ำเหลืองได้ทั้งหมด
