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# Pattern of distribution and metastasis of deep obturator and parametrial lymph nodes in early stage cervical cancer patients

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**Summary**

Pelvic lymphadenectomy has been widely performed as an essential part of the surgical treatment of early stage (IB-IIA) cervical cancer. In this study, the authors reviewed 128 patients who underwent this type of dissection to investigate the pattern of distribution and metastasis of deep obturator lymph node (DOLN) and parametrial lymph node (PLN), and the clinical hitstological factors that associated with detection of and metastasis to DOLN and PLN. The authors found the detection of DOLN and PLN significantly less common and more frequently unilateral compared with other groups of pelvic nodes. Tumor size and squamous cell carcinoma (SCC) antigen may help to identify patients suitable for individualized dissection of PLN.

*Key words:* Cervical cancer; Deep obturator lymph node; Parametrial lymph node; Distribution; Metastasis.

## Introduction

The early spread of cervical cancer is through the lymphatic tissue draining the uterine cervix and the upper vagina, therefore pelvic lymphadenectomy has been widely performed as an essential part of the surgical treatment of early stage (IB-IIA) cervical cancer, as well as of Stage IIB disease, in some European [1] and Asian countries [2], for the last several decades. Traditionally the extent of pelvic lymphadenectomy includes the common iliac, external iliac, internal iliac (hypogastric or interiliac), and obturator nodes, while some authors include deep inguinal, parametrial and presacral nodes [2], and others do not [3, 4]. In the 1990s of last century, some European authors advocated removal of the lymph nodes beneath the obturator nerve, known as the deep obturator lymph nodes (DOLN) [1,5]. However through review of the literature thereafter, the present authors did not find others that have further addressed the clinical significance of dissection of DOLN and most authors did not clarify whether this group of nodes was dissected or not in their studies [3, 4, 6]. Parametrial lymph node (PLN) refers to the lymph-fatty tissue surrounding the vessels connecting the uterine cervix and the internal iliac vascular system. Unlike stripping the lymph-fatty tissue from the vessel walls when performing dissection of nodes surrounding the great vessels such as common iliac or external iliac, PLNs were usually excised together with the parametria and examined for metastasis by microscopic evaluation of the paraffin embedded sections of the removed tissue [1, 7-9]. Hence, the chance of detection of PLNs may be affected by the extent of excision of parametria.

In 2007, the authors began to perform dissection of DOLNs and PLNs by skeletonizing vessels beneath the obturator nerve and among the parametria in the operations of cervical cancer patients. Here they present a retrospective analysis of 128 patients. The purpose was to determine the distribution, incidence, and pattern of metastasis of DOLNs and PLNs, investigate the clinico-pathological characteristics correlative of the distribution and metastasis of DOLN and PLN, and to clarify the impact of dissection of these two groups of nodes on the thoroughness of pelvic lymphadenectomy.

## Materials and Methods

One hundred and twenty-eight consecutive patients who underwent radical hysterectomy and bilateral systemic pelvic lymphadenectomy from July 2007 to June 2011 at Department of Gynecology, Sun Yat-sen University Cancer Center were included in this retrospective study. The median age of patients was 45 years (range 29–67). According the International Federation of Gynecology and Obstetrics (FIGO) staging criteria, 73 patients were Stage IB1 and 55 patients were Stage IIA (tumor size ≤ four cm). All the patients received no treatment prior to surgery. The clinical and histological characteristics are shown in Table 1.

Abdominal bilateral systematic pelvic lymphadenectomy was carried out prior to Okabayashi's radical hysterectomy using a high-frequency electronic knife. Lymph-fatty tissue was divided into seven groups on each side of the pelvis: starting from two cm above the bifurcation of external and internal iliac artery. Fatty tissue on the wall of common iliac vessel was designated as the common iliac group; those along the external iliac vessels as external iliac group; at the bifurcation of internal and external iliac

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Table 1. — *Clinical and histological characteristic in relation to detection of and metastasis to deep obturator lymph node and parametrial lymph node.*

| | | | N | DOLN | *p* value | PLN | *p* value | MPLN | *p* value |
|---|---|---|---|---|---|---|---|---|---|
| Age | ≤ median (45 years) | | 67 | 47 | 0.966 | 40 | 0.379 | 4 | 0.623 |
| | > median | | 61 | 43 | | 41 | | 5 | |
| FIGO Stage | IB1 | | 94 | 65 | 0.632 | 55 | 0.063 | 4 | 0.041 |
| | IIA | | 34 | 25 | | 26 | | 5 | |
| Tumor size | ≤ 2cm | | 40 | 26 | 0.694 | 18 | 0.004 | 0 | 0.030 |
| | > 2cm | | 88 | 54 | | 63 | | 9 | |
| SCC antigen | ≤ 1.5 μg/L | | 93 | 66 | 0.791 | 53 | 0.016 | 2 | 0.002 |
| | > 1.5 μg/L | | 35 | 24 | | 28 | | 7 | |
| Gross type | Exophytic | | 91 | 63 | 0.674 | 54 | 0.117 | 2 | 0.003 |
| | Endophytic | | 37 | 27 | | 27 | | 7 | |
| Histology | Squamous | | 115 | 83 | 0.170 | 75 | 0.177 | 9 | 0.591 |
| | Adeno/adenosquamous | | 13 | 7 | | 6 | | 0 | |
| Involvement of cervical canal | | Absent | 20 | 9 | 0.007 | 9 | 0.065 | 0 | 0.353 |
| | | Present | 108 | 81 | | 72 | | 9 | |
| Deep cervical stromal invasion | | Absent | 51 | 33 | 0.259 | 27 | 0.048 | 1 | 0.068 |
| | | Present | 77 | 57 | | 54 | | 8 | |
| LVSI[4] | Absent | | 115 | 82 | 0.465 | 73 | 0.891 | 8 | 0.922 |
| | Present | | 13 | 8 | | 8 | | 1 | |

DOLN: deep obturator lymph node; PLN: parametrial lymph node; MPLN: metastasis to parametrial lymph node; LVSI: lymphovascular space invasion.
Metastasis to deep obturator node was not analyzed as there was only one such case.

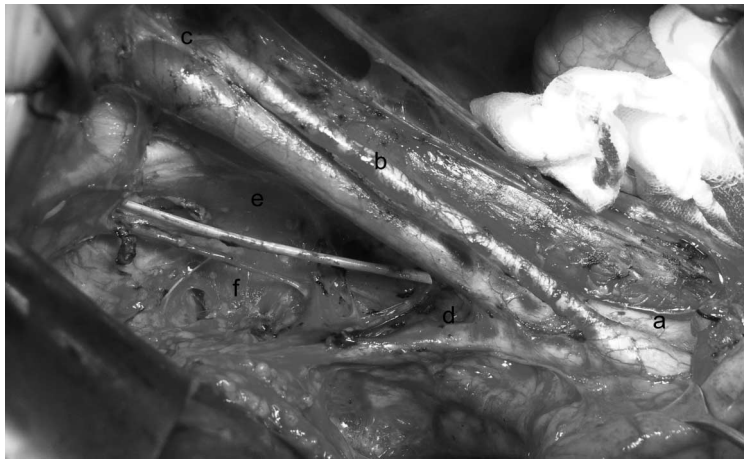


Figure 1. — Pelvic lymph node grouping in this study:a) common iliac group, b) external iliac group, c) distal external iliac group, d) internal iliac group, e) superficial obturator group, and f) deep obturator group.

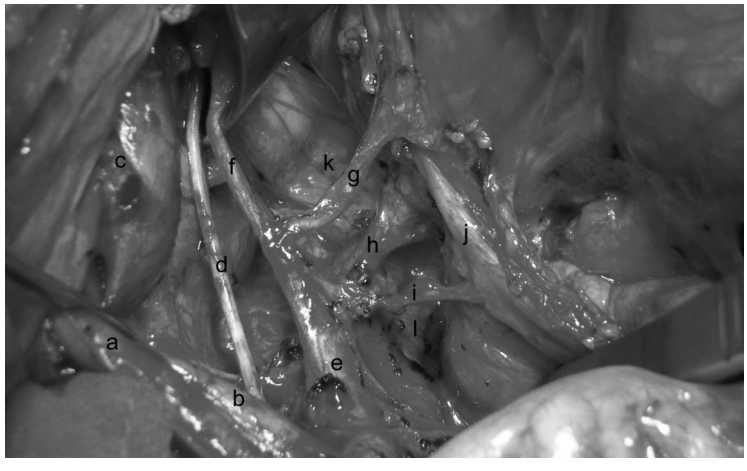


Figure 2. — Sructures of left pelvic side wall after lymphadenectomy: a) external iliac artery, b) exteanal iliac vein, c) deep iliac circumflex vein, d) obturator nerve, e) internal iliac artery, f) lateral umbilical ligament, g) uterine artery, h) deep uterine vein, i) small atery connecting the internal artery and ureter, j) ureter, k) paravesical space, and l) pararectal space.

Table 2. — *Distribution of patients according to side of pelvis and location of detected lymph node(s).*

| | Number of patients | | | |
|---|---|---|---|---|
| | Left side | Right side | Both sides | Without detected |
| Common iliac | 4 | 17 | 104 | 3 |
| External iliac | 8 | 5 | 113 | 2 |
| Internal iliac | 17 | 8 | 98 | 5 |
| Superficial obturator | 4 | 12 | 107 | 5 |
| Distal external iliac | 7 | 10 | 105 | 6 |
| Deep obturator | 19 | 23 | 48 | 38 |
| Parametrial | 31 | 18 | 32 | 47 |

Table 3. — *Total number and mean ± SD of pelvic lymph nodes in relation to nodal groups per patients in whom lymph nodes were detected in the specific site.*

| Nodal groups | Number of nodes (%) | Mean±SD (Range) |
|---|---|---|
| Left common iliac | 257 (7.6) | 2.38 ± 1.464 (1–8) |
| Right common iliac | 281 (8.4) | 2.32 ± 1.368 (1–8) |
| Left external iliac | 350 (10.4) | 2.89 ± 1.745 (1–9) |
| Right external iliac | 364 (10.8) | 3.08 ± 2.028 (1–10) |
| Left internal iliac | 273 (8.1) | 2.37 ± 1.442 (1–6) |
| Right internal iliac | 232 (6.9) | 2.19 ± 1.395 (1–9) |
| Left superficial obturator | 285 (8.5) | 2.57 ± 1.366 (1–7) |
| Right superficial obturator | 294 (8.7) | 2.47 ± 1.556 (1–11) |
| Left distal external iliac | 260 (7.7) | 2.39 ± 1.556 (1–7) |
| Right distal external iliac | 248 (7.4) | 1.92 ± 1.025 (1–8) |
| Left deep obturator | 160 (4.8) | 2.32 ± 1.239 (1–8) |
| Right deep obturator | 136 (4.0) | 2.16 ± 1.254 (1–5) |
| Left parametrial | 113 (3.4) | 1.79 ± 1.095 (1–6) |
| Right parametrial | 110 (3.3) | 2.20 ± 1.178 (1–5) |

vessels as internal iliac group; on the surface of deep iliac circumflex vein and inguinal ligament as distal external iliac group; on the surface of obturator nerve as superficial obturator group; beneath the obturator nerve and surrounding the obturator vessels as deep obturator group; surrounding the uterine vessels and the two to three cm distal part of ureter entering the "tunnel" and if present, on the surface of internal pudendal vein as parametrial group. Figure 1 shows the pelvic lymph node grouping in this study. A surgical suction apparatus [10] was used to facilitate dissection of deep obturator and parametrial nodes. Figure 2 shows the structures of the left pelvic side wall after the clearance of superficial, deep obturator, and parametrial nodes. All the fatty tissue was dissected and placed in separate specimen bottles according to their locations and sent for pathological evaluation.

The excised fatty tissue was palpated to detect lymph nodes. Palpable nodes were fixed, embedded in paraffin, processed, and cut into six-μm sections. When nodes were not palpable, fatty tissue was fixed *en bloc* and embedded. The nodes were counted and examined microscopically for metastatic involvement.

All surgical procedures were performed by the same surgeon (Y. Xiong), and pathologic assessment was performed by the same team.

*Statistical analysis*

Descriptive analysis was used to analyze the distribution of pelvic lymph nodes and pattern of node metastasis. Enumeration data was presented as rate and analyzed using chi-square test or Fisher's exact test. Logistic regression was employed to perform multivariate analysis. Statistical significance was assigned at a level of $p < 0.05$. All statistical analyses were performed with SPSS 13.0.

## Results

The distribution of pelvic lymph node is shown in Table 2. Pathological evaluation revealed that not all the fatty tissue removed contained lymph nodes. DOLN and PLN were detected in 70.3% (90/128) and 63.3% (81/128) of patients, respectively. In contrast, the frequencies of detection of lymph nodes around the great vessels (common iliac, external iliac, internal iliac, distal external iliac group) and above the obturator nerve (superficial obturator group) ranged from 95.3% (122/128) to 98.4% (126/128). The frequencies of detection of DOLN and PLN were significantly lower that those of other nodal groups (all, $p < 0.001$). The frequencies of unilateral detection of DOLN and PLN were 46.7% (42/90) and 60.5% (49/81), while those of other nodal groups ranged from10.3% (13/126) to 20.3% (25/123); the differences were statistically significant (all, $p < 0.001$).

The total and mean numbers of lymph nodes per patient in whom lymph nodes were detected in the specific site are shown in Table 3. The mean number of DOLN and PLN per patients in whom DOLN and PLN were detected was 2.16–2.32 and 1.79–2.20, respectively. The total number of pelvic lymph nodes of 128 patients was 3.363 (mean 26.35 ± 8.823, range 6–53). The DOLN and PLN occupied 8.8% (296/3363) and 6.7% (223/3363) of the total number of detected nodes.

As shown in Table 1, univariate analysis showed that involvement of cervical canal was associated with detection of DOLN ($p = 0.007$), tumor size ($p = 0.004$), squamous cell carcinoma (SCC) antigen ($p = 0.016$), and deep cervical stromal invasion ($p = 0.048$) were associated with detection of PLN. Logistic regression revealed that tumor size was the only independent factor that associated with detection of PLN ($p = 0.028$).

Nodal metastasis was found in 26.6% (34/128) of patients. The distribution of patients according to side of pelvis and location of detected positive lymph node(s) is shown in Table 4. Metastasis was most frequently seen in external iliac nodes (16/128), followed by internal iliac (14/128), parametrial (9/128), common iliac (8/128) and superficial obturator (8/128), distal external iliac (5/128), and deep obturator nodes (1/128). The only patient who had metastasis to DOLN also had metastasis to internal iliac and superficial obturator node of both sides and left common iliac node.

Solitary metastasis was found in 50.0% (17/34) of the node-positive patients; the other patients had at least two

Table 4. — *Distribution of patients according to side of pelvis and location of detected positive lymph node(s).*

| | Left pelvis | Right pelvis | Left and right pelvis | Sum[1] |
|---|---|---|---|---|
| Common iliac | 2 | 4 | 2 | 8 |
| External iliac | 6 | 8 | 2 | 16 |
| Internal iliac | 2 | 8 | 4 | 14 |
| Superficial obturator | 3 | 3 | 2 | 8 |
| Distal external iliac | 1 | 3 | 1 | 5 |
| Deep obturator | 0 | 1 | 0 | 1 |
| Parametrial | 4 | 5 | 0 | 9 |

[1] The number of patients sums to more than 34, since one patient may have more than one site involving positive lymph nodes.

Table 5. — *Distribution of solitary node metastasis.*

| Solitary lymph node metastasis | Number of patients |
|---|---|
| External iliac | 5 |
| Parametrial | 4 |
| Superficial obturator | 3 |
| Internal iliac | 3 |
| Distal external iliac | 1 |
| Common iliac | 1 |

metastatic nodes. As shown in Table 5, solitary metastasis was most frequently seen in the external iliac [5], followed by the parametrial [4], superficial obturator [3] and internal iliac [3], common iliac [1], and distal external iliac [1] node.

As shown in Table 1, univariate analysis showed that FIGO Stage ($p = 0.041$), tumor size ($p = 0.030$), gross type ($p = 0.003$), and SCC antigen ($p = 0.002$) were associated with metastasis of PLN. Logistic regression revealed that SCC antigen was the only independent factor that associated with metastasis of PLN ($p = 0.028$). No analysis of association between clinical and histological characteristics and metastasis of PLN was performed as metastasis of DOLN was only seen in one patient in this study.

## Discussion

As already mentioned above, dissection of DOLN was rarely emphasized in previous studies and the conventional resection of PLN was integrated with parametrectomy. In order to gain better understanding of the distribution and metastatic involvement of these two groups of lymph nodes, DOLN and PLN were dissected separately in a vessel-skeletonizing style in the present study. A surgical suction apparatus was used during the dissection. Through gentle blunt division of loose fatty tissue on the surface of vessel walls using the tip of the surgical suction, vessels were visualized and then fatty tissue was removed using an electronic knife until the anterior trunk of internal iliac vein, obturator artery and vein, any anastomosis to the pelvic side wall if present, uterine artery, superficial, and deep uterine veins were skeletonized. The present authors have found this technique convenient and safe for node dissection of areas with complexity of blood vessel anatomy. A similar surgical technique was reported by Hockel *et al.* for nerve-sparing extended radical hysterectomy [11].

The present study showed that lymph nodes are unevenly distributed in pelvis: the presence of node(s) around the smaller vessels, such as obturator vessels (DOLN) and uterine vessels (PLN), are less than that around the great vessels. European authors have reported the metastasis rate of deep obturator nodes, but the frequency of detection was not determined [1, 5]. The present authors found that DOLN could be detected in about 70% of patients and unilateral detection was significantly more common. The frequency of detection of PLN varies among studies. Some have reported lymph nodes present in 59%-93% of parametria using giant section techniques [1, 7, 8], while others report 7.1% in parametrial specimens of transvaginal trachelectomy [12]. In the present study, PLN was found in 63.3% of patients and unilateral detection was also significantly more common. The present authors believe that the pattern of distribution of DOLN and PLN observed in this study may serve as an important reference for interpretation of the quality control of pelvic lymphadenectomy. Interestingly, they found tumor size was significantly associated with detection of PLN; if this result is further confirmed by future studies, a tumor size-adapted individualized dissection of PLN may be feasible for surgeons who are less familiar with detailed anatomy of parametrium. They also found involvement of cervical canal was associated with detection of DOLN, but due to the lesser statistical power of univariate analysis, this should be further investigated in larger samples.

The incidence of pelvic lymph node metastasis was 26.6%; PLN ranked the third among nodal groups involved by metastasis and the second among those involved by solitary metastases in the present study. Since sentinel lymph node (SLN) is defined as the node that preferentially collects lymph flow and is the first to harbor metastasis, the present authors can conclude that parametrial area is one of the ‘hot spots’ to detect SLNs based on the present results. In the last decade, the use of SLN mapping procedure in cervical cancer has been studied by multiple groups and the external iliac, internal iliac, and obturator are the three main areas where SLNs were detected [13]. In literature, detection of SLNs in the parametrium is infrequent and likely because: (1) nodes may not be present in the parametrium (as demonstrated in the present study); (2) nodes are difficult to identify due to contamination with injected dye; and (3) nodes

were removed as part of the parametria. The present authors believe the high frequency of solitary metastasis to PLN in this study was related to its separate and thorough clearance and suggests parametrial region's importance with regards to detecting SLNs. Another clinical significance of distribution of solitary node metastasis is that it may help the clinician to understand and design the necessary extent of pelvic lymphadenectomy. From the results of the present study, dissection including common, external, distal external, internal iliac, superficial obturator, and parametrial node will identify all node-positive patients.

The present study showed the incidence of metastasis to DOLN was only 0.8%. The previously reported incidence of metastasis to DOLN was 1.5% [1], which is comparable to the present result. Furthermore, the patients who developed metastasis to DOLN had simultaneous metastasis to multiple nodal groups, which suggests that metastasis to DOLN is likely to occur secondarily. As node-positive patients will be given concurrent chemoradiation postoperatively according to present practice guidelines, one may thus argue that the routine dissection of DOLN in all patients is unnecessary. However, it should be taken into account that the incidence of metastasis defined by histology may be lower than the true number because of the limited number of sections evaluated during routine histological examination [10]. Furthermore, although the metastasis rate is as low as 0.8% in early-stage patients, given the fact that there are more than 100,000 new cases of cervical cancer in China every year [14], omitting the dissection of DOLN may result in a considerable large number of patients that will suffer from residual nodal metastasis. Hence, the present authors suggest routine removal of DOLN if lymphadenectomy is performed with a curative intent.

Risk factors of parametrial involvement (including PLN metastasis) have been studied by many authors. The known risk factors include tumor size, depth of invasion, lymphovascular space invasion, pelvic lymph metastasis and SLN [15-18]. In this study, the authors found FIGO Stage and gross type may also associate with PLN metastasis, and the SCC antigen was the only independent factor determined by multivariate analysis. As it can precisely measured before surgery, SCC antigen may also serve as a meaningful indicator for grouping patients suitable for individualized dissection of PLN.

## Conclusions

In summary, the present study demonstrated the pattern of distribution of and metastasis to DOLN and PLN in FIGO Stages IB1 and IIA (tumor size ≤ four cm) cervical cancer patients. Dissection of DOLN and PLN may affect the thoroughness of pelvic lymphadenectomy in at least 60% of patients. Tumor size and SCC antigen may help to identify patients with higher possibility of detection of and metastasis to PLN and suitable for individualized dissection. The present authors believe that this knowledge may be helpful for understanding the necessary extent of pelvic lymphadenectomy and identification of patients suitable for individualized node dissection.

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