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Analysis of A Single Para-Aortic Lymph Node Metastasis in Endometrial Cancer

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Abstract

Objective: To determine the indication for lymph node dissection in patients with endometrial cancer, we investigated the incidence and distribution of single metastatic lymph nodes in patients who underwent systematic pelvic and para-aortic lymph node dissection.

Methods: This study involved 910 patients with endometrial cancer who were treated at the Cancer Institute Hospital, Japan, between January 1994 and December 2015. All patients underwent an open hysterectomy with bilateral salpingo-oophorectomy and pelvic and para-aortic lymph nodes dissection.

Results: Lymph node metastasis was observed in 199 patients (21.9%), 45 (5%) of whom had single lymph node metastasis. Single lymph node metastasis accounted for 22.6% of all metastatic cases. Myometrial invasion >50% was observed in 30 patients, whereas 15 patients had <50% myometrial invasion. When mapping single lymph node metastatic sites, the para-aortic area had a frequency of 31.1% (14 cases). The distribution of single metastatic lymph nodes spanned a wide area between the pelvic and para-aortic regions. Considering single metastatic nodes and myometrial invasion, 8 patients (53.3%) who had myometrial invasion <50% had a single metastatic node in the para-aortic region. Four of 9 patients (45%) considered low-risk (endometrioid Grade 1-2, invasion depth <50%, no lymphovascular space invasion) showed metastasis to the para-aortic areas.

Conclusion: Single metastatic lymph nodes were widely distributed between the pelvic and para-aortic regions, suggesting that detection of a sentinel lymph node in patients with endometrial cancer could be problematic.

Keywords: Endometrial cancer; Single para-aortic metastasis; Sentinel lymph node

Introduction

In Japan, amongst gynecological malignancies, the incidence of endometrial cancer is increasing at the fastest rate. The possible causes of this rapid increase include lifestyle changes among Japanese women such as changes in diet, increased obesity rates, hormonal milieu, and the age at pregnancy [1]. Based on our institutional experience, the majority of patients with endometrial cancer are diagnosed with early-stage disease (International Federation of Gynecology and Obstetrics (FIGO) I and II) without clinical evidence of extrauterine spread, and most had excellent 5-year survival rates (stage I, 97.5%; stage II, 93.9%). By contrast, patients with FIGO stage III endometrial cancer, who accounted for 10–15% patients, had inferior 5-year survival rates (82.9%). Therefore, lymph node metastasis is an important prognosticator in patients with endometrial cancer, and detection of lymph node transitions requires systematic dissection, including pelvic and para-aortic lymph nodes. However, routine lymph node dissection of pelvic and para-aortic lymph nodes varies widely between institutions and surgeons, especially for tumors presumed to be low-grade. The sentinel lymph node (SLN) procedure might reduce the risks of complications associated with lymphadenectomy. For patients with endometrial cancer, although the SLN procedure has been evaluated recently its acceptance remains controversial [2,3]. SLN patterns in patients with endometrial cancer are influenced by injection site; therefore, there are a variety of SLN mapping results.

To determine the indication for systemic lymph node dissection in patients with endometrial cancer, we investigated the incidence and distribution of single nodal metastasis in patients who underwent systematic dissection of the pelvic and para-aortic lymph nodes.

Materials and Methods

Patients

Systematic pelvic and para-aortic lymph node dissection was performed in 910 patients with endometrial cancer at the Cancer Institute Hospital, Japan, between January 1994 and December 2015. Using the retrospectively maintained endometrial cancer database at the Cancer Institute Hospital, all available patient data were reviewed to identify the distribution of metastasis. In patients who had a single para-aortic metastatic node, the distribution of metastatic nodes was evaluated.

Surgical procedures

All patients underwent an open hysterectomy with bilateral salpingo-oophorectomy and pelvic and para-aortic lymph node dissection. For para-aortic lymph node dissection, nodal tissue on the right side was removed between the aorta medially and the right ureter laterally, extending from the right common iliac artery to the level of insertion of the right ovarian vein into the vena cava. On the

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left side, nodal tissue was removed between aorta medially and the left ureter laterally, extending from the common iliac artery to the level of insertion of the left ovarian vein into the left renal vein.

Results

Among the 910 patients, lymph node metastasis was observed in 199 patients (21.9%). Of the 199 patients who had positive lymph nodes, a single metastatic node was observed in 45 patients (5.0%), 2 metastatic nodes were seen in 24 patients, 3 metastatic nodes were noted in 19 patients, and ≥ 4 metastatic nodes were found in 111 patients. The clinical characteristics of the 45 patients with a single metastatic node are shown in Table 1. Among these, 27 (60%) had low-risk histology such as grade 1-2 endometrioid adenocarcinoma.

When mapping single lymph node metastatic sites, the majority of patients had a metastatic lymph node in the obturator areas, limited to the pelvic cavity (Figure 1). Fourteen patients (31.1%) had a single metastatic lymph node in the para-aortic region. The nodal frequencies in each para-aortic site were 3 cases in right b1, 4 cases in left b1, 3 cases in right b2, and 4 cases in left b2. Figure 2 shows the lymph node distribution in the 45 patients with a single metastatic node, according to the degree of myometrial invasion. Eight patients (53.3%) with <50% myometrial invasion had lymph nodes in the para-aortic region. Although 9 patients were considered low-risk (endometrioid Grade 1–2, invasion depth <50%, no lymphovascular space invasion), 4 (45%) showed transition to the para-aortic area (Figure 3). One patient with no myometrial invasion and grade 1 endometrioid adenocarcinoma has a single metastatic para-aortic lymph node. When mapping according to the presence or absence of cervical invasion, only 1 patient with cervical invasion had a single para-aortic node metastasis (Figure 4), and most patients with cervical invasion had metastatic lymph nodes in the obturator area. If the tumor was located in the body or fundus of the uterus, lymph node metastasis distribution was wide, ranging from the pelvic to the para-aortic regions.

Factor		N
FIGO stage	3c1	31
	3c2	14
Histological type	Endometrioid G1	12
	Endometrioid G2	15
	Endometrioid G3	5
	Mixed	11
	Serous	1
	Clear	1
Myometrial invasion	>50%	30
	<50%	15

Table 1: Clinical characteristics of the patients with a single metastatic node.

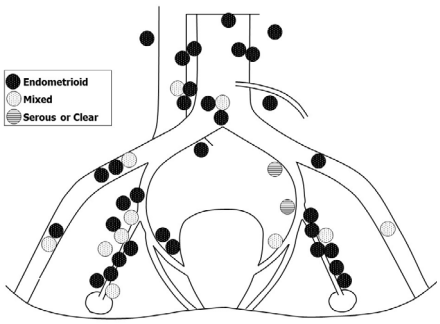

Figure 1: Lymph node distribution in 45 patients with a single metastatic node, according to histological type. The most frequently affected sites were the obturator area, followed by the para-aortic region.

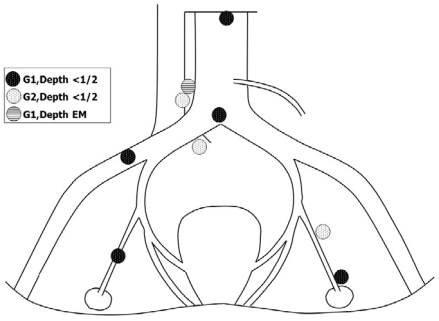

Figure 2: Lymph node distribution in the 45 patients with a single metastatic node, according to the degree of myometrial invasion. Among the patients who had <50% myometrial invasion, 8 (53.3%) had a single metastatic node in the para-aortic area.

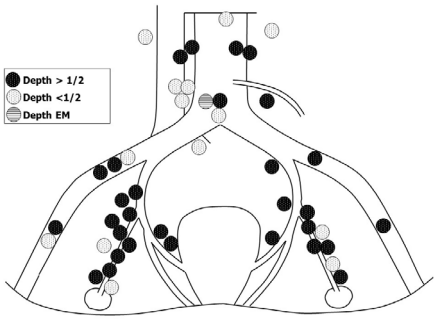

Figure 3: Distribution of low-risk patients who had a single metastatic node. Although there were 9 patients with a low preoperative risk (endometrioid Grade 1–2, invasion depth <50%, no lymphovascular space invasion), 45% of them showed metastasis to the para-aortic areas.

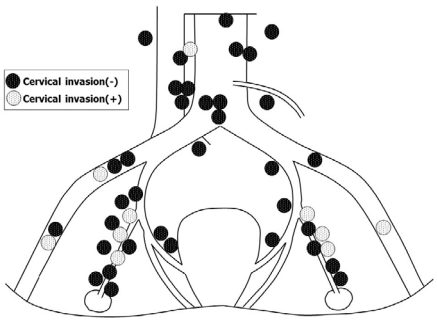

Figure 4: Distribution of 45 patients who had a single metastatic node according to cervical invasion status. If the primary tumor invaded the cervix, most patients had metastatic lymph nodes in the obturator areas. There was a single case of positive para-aortic nodal metastasis in a patient with cervical invasion.

Discussion

Although lymphatic spreading directly to the para-aortic lymph nodes via the infundibulopelvic ligament has been proposed in several anatomical studies, para-aortic metastases via the pelvic lymph node have been described recently [4-6]. The distribution of a single metastatic lymph node ranged widely across the pelvic and para-aortic regions. In the present study, a single para-aortic metastatic node was seen in 1.5% of patients with endometrial cancer who underwent systematic pelvic and para-aortic lymph node dissection. These findings suggested that

the detection of the sentinel lymph node could be problematic in these patients. In addition, single metastasis to the para-aortic lymph node was seen in patients who were considered low-risk preoperatively. Isolated para-aortic lymph metastasis has been reported in <5% of patients with endometrial cancer and has been associated with an increased risk of lymph metastasis [7]. Altay et al. [8] reported that the rate of isolated para-aortic metastasis was 4% among 173 patients with endometrial cancer and that the low precaval region had the highest frequency of single metastatic node distribution. They also reported 1 cases of single lymph node metastasis above the inferior mesenteric artery. Sautua et al. [9] reported that the rate of isolated para-aortic metastasis was 6.6% among 90 patients with endometrial cancer and that myometrial invasion was >50% in all cases. They pointed out that if they had performed para-aortic lymphadenectomy according to the intraoperative evaluation of positive pelvic nodes, they would have missed lymph metastasis in 46% of patients with para-aortic metastasis. The present study might be the first large-scale report of single lymph node metastasis in patients with endometrial cancer. Here, more than half the patients with a single metastatic para-aortic lymph node had <50% myometrial invasion. Moreover, a patient without myometrial invasion with grade 1 endometrioid adenocarcinoma had a single metastatic para-aortic lymph node. Although it is possible to avoid lymphadenectomy in cases that are considered low-risk preoperatively, these findings suggest that such a procedure should be considered even in those with low-risk. The routes of lymphatic spread of endometrial cancer are not clear. Some studies have suggested that para-aortic node metastasis spreads via the common iliac chain when the cervix is invaded, but via routes shared by the obturator and external iliac region when the primary tumor is located in the corpus alone [10,11]. Yokoyama et al. [12] suggested that most para-aortic metastasis occurs via a direct lymphatic route from the uterine body along the ovarian vessels, although some para-aortic metastasis resulted from pelvic lymph node metastasis. It has also been suggested that the obturator area is the most frequently affected site of metastasis in patients with endometrial cancer. This is concordant with the findings of the present study, which found that the most frequently affected site was the obturator area. In addition, in the present study, the isolated involvement of the para-aortic lymph nodes was relatively rare if the primary tumor was confined to the lower uterine segment. In patients with endometrial cancer, the SLN procedure could be an attractive solution for the debate on the need for lymphadenectomy; however, the acceptance of SLN is debatable [2,3]. Although the present study examined cases of single lymph node metastasis alone, because the lymph node metastasis was distributed over a wide area, we consider that it would be necessary to search a wide area to detect any lymph node metastases. It has been reported that cancer cells may transition through lymph nodes easily [13]; therefore, there is potential for metastases to distant lymph nodes via the SLN. It is important to search for high potential metastatic lymph nodes and to avoid possible non-detection of lymph node metastasis. If dissection can be avoided, SLN navigation surgery is minimally invasive, which is clinically beneficial for the patient. However, to avoid any effect on disease curability, in clinical practice, it is necessary to exercise caution.

Conclusion

The findings of the present study suggested that SLN detection in patients with endometrial cancer might be problematic because of the wide distribution of metastatic lymph nodes. Therefore, there is a need for further study to reveal the patterns of metastatic spread, including the SLN. Further studies are warranted to determine the role of routine systematic pelvic and para-aortic lymph node dissection in patients considered to have a low preoperative risk of recurrence.

Declaration of Interest

The authors have no conflicts of interest.

References

1. Matsuura M, Suzuki T, Morishita M, Tanaka R, Ito E (2009) Chemotherapy (CT) with radiotherapy versus CT alone for FIGO stage3c endometrial cancer. Eur J Gynaec Oncol 30: 40-44.
2. Cormier B, Rozenholc AT, Gotlieb W, Plante M, Giede C, et al. (2015) Sentinel lymph node procedure in endometrial cancer: A systematic review and proposal for standardization of future research. Gynecol Oncol 138: 478-485.
3. Kim CH, Collado FK, Barber EL, Soslow RA, Makker V, et al. (2013) Sentinel lymph node mapping with pathologic ultrastaging: A valuable tool for assessing nodal metastasis in low-grade endometrial cancer with superficial myoinvasion. Gynecol Oncol 131: 714-719.
4. Chiang AJ, Yu KJ, Chao KC, Teng NNH (2011) The incidence of isolated para-aortic nodal metastasis in completely staged endometrial cancer patients. Gynecol Oncol 121: 122-125.
5. Henriksen E (1949) The lymphatic spread of carcinoma of the cervix and of the body of the uterus. Am J Obstet Gynecol 58: 924-942.
6. Henriksen E (1975) The lymphatic dissemination in endometrial carcinoma. A study of 188 necropsies. Am J Obstet Gynecol 123: 570-576.
7. Kumar S, Podratz KC, Bakkum-Gamez JN, Dowdy SC, Weaver AL, et al. (2014) Prospective assessment of the prevalence of pelvic, paraaortic and high paraaortic lymph node metastasis in endometrial cancer. Gynecol Oncol 132: 38-43.
8. Altay A, Toptas T, Dogan S, Simsek T, Pestereli E (2015) Analysis of metastatic regional lymph node location and predictors of para-aortic lymph node involvement in endometrial cancer patients at risk for lymphatic dissemination. Int J Gynecol Cancer 25: 657-664.
9. Sautua RR, Goiri K, Calle MA, Marin IJ, Artola AL (2015) Incidence of nodal metastasis and isolated aortic metastases in patients with surgically staged endometrioid endometrial cancer. Int J Gynecol Cancer 25: 875-878.
10. Abu-Rustum NR, Gomez JD, Alektiar KM, Soslow RA, Hensley ML, et al. (2009) The incidence of isolated paraaortic nodal metastasis in surgically staged endometrial cancer patients with negative pelvic lymph nodes. Gynecol Oncol 115: 236-238.
11. Mariani A, Webb MJ, Keeney GL, Podratz KC (2001) Routes of lymphatic spread: A study of 112 consecutive patients with endometrial cancer. Gynecol Oncol 81: 100-104.
12. Yokoyama Y, Maruyama H, Sato S, Saito Y (1997) Indispensablity of pelvic and paraaortic lymphadenectomy in endometrial cancers. Gynecol Oncol 64: 411-417.
13. Fisher B (1985) The revolution in breast cancer surgery: Science or anecdotalism? World J Surg 9: 655-666.