A Questionnaire Survey on Current Surgical Procedures for Endometrial Cancer in Japan

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KONNO, R., SATO S. and YAJIMA, A. *A Questionnaire Survey on Current Surgical Procedures for Endometrial Cancer in Japan.* Tohoku J. Exp. Med., 2000, **190** (3), 193-203 — The current standards for surgical procedures and lymph node dissection of endometrial cancer in Japan were investigated using a questionnaire survey. The estimated clinical stages used in the questionnaire were predicted from preoperative diagnostic imaging, histopathology of endometrial biopsies and intraoperative findings using a new classification, Federation Internationale de Gynecologie et d'Obstetrique (FIGO) in 1988. Questionnaires were mailed to 235 institutions, and 212 institutions (90.2%) responded. As a standard surgery for endometrial cancer, institutions performed simple total hysterectomy or semi-radical hysterectomy and bilateral adnexectomy, which accounted for 86% of all respondents. For stage I carcinoma, simple (44%) or semi-radical (47%) hysterectomy was carried out in 91% of institutions, while radical hysterectomy was selected in 84% of institutions when stage II carcinoma was diagnosed clinically. The consensus of this survey was that dissection of both the para-aortic and pelvic lymph nodes can be omitted in G1 cases showing lesions confined to the endometrium, and that pelvic lymph nodes should be dissected, but para-aortic lymph node dissection could be omitted in G1 or G2 cases demonstrating myometrial invasion of 1/2 or less. Moreover, findings from this survey suggest that biopsy or dissection of the para-aortic lymph nodes was required in G3 cases, or in those patients diagnosed with myometrial invasion more than 1/2. ——— endometrial cancer; pelvic lymph node; para-aortic lymph node; surgical treatment; questionnaire survey © 2000 Tohoku University Medical Press

Endometrial carcinoma is one of the most common malignancies of the female genital tract. In Japan, the incidence of endometrial carcinoma has been increasing in recent years. In 1988, the Federation Internationale de Gynecologie et d'Obstetrique (FIGO) adopted a surgical staging system, which includes assessment of pelvic and para-aortic lymph node metastases (Creasman 1990). It is also reported that the degree of histological differentiation and myometrial invasion is evidently correlated with extrauterine progression of the lesion and pelvic or para-aortic lymph node metastasis (Boronow et al. 1984; Creasman et al. 1987;

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Morrow et al. 1991). In 1995, the Japan Society of Obstetrics and Gynecology (JSOG) abandoned the previous clinical staging system in favor of the surgical staging system adapted by FIGO (Japan Society of Obstetrics and Gynecology, The Japan Society of Pathology, Japan Radiological Society 1996).

We conducted a multicentric questionnaire survey to clarify the current standards for surgical treatment of endometrial cancer and the implications of pelvic and para-aortic lymph node dissection in Japan.

SUBJECTS AND METHODS

Written questionnaires were mailed to all 235 institutions belonging to the Japanese Gynecologic Oncology Group (JGOG). The clinical stages described in the questionnaire and in this paper were based on a new classification system, FIGO in 1988 (Creasman 1990), JSOG in 1995 (Japan Society of Obstetrics and Gynecology, The Japan Society of Pathology, Japan Radiological Society 1996). The new classification is based on surgical staging, however, in our questionnaire we used the classification of the stages estimated preoperatively by means of physical examination, diagnostic imaging, histopathology of endometrial biopsies and intraoperative findings.

Although the number of complete answers varied question by question, the results of the survey are described using the occupancy rate (%) of the number of valid answers. In this questionnaire, for instance, treatment of the lymph nodes was categorized into "dissection" and "biopsy." "Dissection" was defined as "surgery aiming at optimal resection" and "biopsy" as "surgery (sampling) to examine the presence or absence of metastasis." When it was difficult to distinguish between "dissection" and "biopsy," "dissection or biopsy" was therefore a possible answer.

RESULTS

Of the 235 institutions in which questionnaires were mailed, 212 (90.2%) responded.

Basic surgical techniques and treatment of lymph nodes

The majority of institutions performed simple total hysterectomy or semi-radical hysterectomy and bilateral adnexectomy as the standard surgical procedure for endometrial cancer, which accounted for 86% of all respondents (Fig. 1a). However, when cancers were divided into stage I and stage II, simple or semi-radical hysterectomy was carried out for stage I in 91% of institutions (Fig. 1b), while radical hysterectomy was selected in 84% of institutions when stage II cancer was suspected (Fig. 1c).

Institutions where the pelvic lymph nodes were generally dissected accounted for 72% of the total, and reached 99% when institutions selected either dissection or biopsy, when each case was included (Fig. 2). For the para-aortic lymph nodes

Fig. 1. (a) Basic surgery for endometrial carcinoma. (b) Basic surgery for stage I endometrial carcinoma. (c) Basic surgery for stage II endometrial carcinoma. TAH, simple total abdominal hysterectomy; BSO, bilateral salpingo-oophorectomy. RH, radical hysterectomy.

Fig. 2. Surgical treatment for pelvic lymph nodes.

Fig. 3. Surgical treatment for para-aortic lymph nodes.

(Fig. 3), either dissection or biopsy was selected depending on the individual case in 43% of institutions. Twenty % of institutions generally performed dissection, 19% of institutions performed inspection and palpation only and 12% of institutions performed biopsy, showing a large variation in diagnosis and treatment. The extent of the para-aortic lymph nodes treated by dissection and biopsy was from the lower part of the inferior margin of the left renal veins (326, b1) in 77% and 62% of institutions, respectively.

Peritoneal cytology was carried out in 87% of institutions.

Preoperative diagnostic imaging of lymph node metastasis

For preoperative diagnostic imaging of lymph node metastasis (more than one answer), CT was used in 201 institutions, while MRI was used in 143. Ultrasonography, lymphangiography and scintigraphy were used in 55, 20, and 17 institutions, respectively.

Relationship of the degree of histological differentiation and the depth of myometrial invasion to treatment of lymph nodes

Pelvic and para-aortic lymph nodes in cases of G1 tumors. In cases with G1 as the degree of histological differentiation and lesions confined to the endometrium, pelvic lymph node dissection was performed in 51% of institutions. For cases suspicious of myometrial invasion of 1/2 or less, pelvic lymph node dissection was performed in 80% of the institutions (Table 1). The para-aortic lymph nodes were not treated in cases in which lesions were confined to the endometrium (66%) or in myometrial invasion of 1/2 or less (44%), while in cases demonstrating myometrial invasion of more than 1/2, biopsy or dissection was

TABLE 1. *Relationship between the treatment of pelvic lymph nodes, histological grade and myometrial invasion*

Histological grade	Myometrial invasion	Treatment of pelvic lymph nodes (% of institutions)		
		Dissection	Biopsy	None
G1	Endometrium only	51	19	30
	≤ 1/2	80	11	9
	> 1/2	93	4	3
G2	Endometrium only	64	16	20
	≤ 1/2	83	10	7
	> 1/2	94	4	2
G3	Endometrium only	78	9	13
	≤ 1/2	89	6	5
	> 1/2	96	2	2

TABLE 2. *Relationship between the treatment of para-aortic lymph nodes, histological grade and myometrial invasion*

Histological grade	Myometrial invasion	Treatment of para-aortic lymph nodes (% of institutions)		
		Dissection	Biopsy	None
G1	Endometrium only	12	21	66
	≤ 1/2	22	34	44
	> 1/2	45	31	24
G2	Endometrium only	19	30	51
	≥ 1/2	30	36	34
	> 1/2	48	32	20
G3	Endometrium only	31	32	37
	≤ 1/2	41	34	25
	> 1/2	56	27	17

carried out in 76% of institutions (Table 2).

Pelvic and para-aortic lymph nodes in cases of G2 tumors. For G2 tumors, even though the lesion was limited to the endometrium, pelvic lymph node dissection was performed in 64% of institutions. As myometrial invasion proceeded, the frequency of lymph node dissection increased (Table 1). Concerning para-aortic lymph nodes, neither biopsy nor dissection was carried out for tumors confined to the endometrium in 51% of institutions, while tumors that were predicted to invade more than 1/2 of the myometrium, biopsy or dissection was performed in 80% of institutions (Table 2).

Pelvic and para-aortic lymph nodes in cases of G3 tumors. For G3 tumors, pelvic lymph node dissection was performed regardless of the depth of myometrial invasion in more than 78% of institutions (Table 1). With respect to para-aortic lymph nodes, even if the lesion was limited to the endometrium, 63% of institutions performed biopsy or dissection, and the frequency increased up to 83% in cases showing myometrial invasion more than 1/2 (Table 2).

Cases demonstrating cervical invasion or adnexal metastasis suggested by preoperative and intraoperative findings

In cases suspected of cervical invasion (stage II), 98% of institutions replied that pelvic lymph node dissection was performed and 82% of institutions answered that biopsy or dissection of the para-aortic lymph nodes was required. When adnexal metastasis was macroscopically detected, pelvic lymph node dissection was performed in 96% of institutions and dissection or biopsy of the para-aortic lymph nodes was carried out in 86% of institutions.

Cases demonstrating lymph node swelling suggestive of metastasis preoperatively or intraoperatively

In cases showing pelvic lymph node swelling, dissection or biopsy of the para-aortic lymph nodes was performed in 89% of institutions. In cases demonstrating para-aortic lymph node swelling, 92% of institutions performed pelvic lymph node dissection and 94% of institutions carried out dissection or biopsy of the para-aortic lymph nodes.

In cases showing a string of numerous para-aortic lymph node swellings, suggestive of obvious metastases, subsequent surgery involving the lymph nodes was discontinued in 10% of institutions. Biopsies of the lymph nodes were taken for pathological diagnosis to clarify lymph node metastasis in 46% of institutions, whereas optimal resection was performed as radical surgery in 43% of institutions.

Aggression and complications due to dissection and biopsy of the para-aortic lymph nodes

Seventy % of institutions responded that blood loss was increased by means of para-aortic lymph node dissection, but 72% of institutions answered that blood

loss did not change by the addition of biopsy. The frequency of blood transfusion was elevated in 46% of institutions, and not altered in 44% of institutions by the addition of biopsy. However, blood transfusion was elevated in 47% and unchanged in 50% of institutions by the addition of dissection. The operative time was increased by the addition of dissection in 97%, or biopsy in 72% of institutions, respectively. Two institutes reported deaths during surgery or immediately after surgery which involved dissection or biopsy of the para-aortic lymph nodes. Deaths were caused due to multiple organ failure related to massive bleeding.

Adjuvant treatment in cases showing para-aortic lymph node metastasis

When para-aortic lymph node metastasis was pathologically detected, chemotherapy (185 institutions) was selected more frequently than irradiation therapy in the pelvic (5 institutions) and para-aortic (98 institutions) areas. Hormone therapy and immunotherapy were used in 82 and 15 institutions, respectively.

Assessment of surgical treatment (dissection or biopsy) of the para-aortic lymph nodes

Thirty percent of institutions believed that the surgical risk remained unchanged, while 64% of institutions thought that the risk was increased by the addition of biopsy or dissection. The overall prognosis with dissection or biopsy, which was performed in order to make evidence for the alteration of adjuvant therapy, was considered to be improved in 31%, unchanged in 32% or unknown in 37% of institutions (Fig. 4).

The last question on the survey asked the significance of para-aortic lymph node dissection or biopsy. Seventy-three percent of institutions answered that dissection or biopsy should be determined according to each individual case, while 16% of institutions considered it necessary in all cases.

Fig. 4. An estimate of prognosis by the addition of para-aortic lymph node dissection or biopsy.

DISCUSSION

The findings of this questionnaire survey are discussed in comparison with domestic and foreign literature. Our findings have demonstrated that simple or semi-radical hysterectomy was carried out for stage I, while radical hysterectomy was frequently (84%) selected for stage II endometrial cancer. A similar questionnaire survey conducted by us (Yajima 1982) also showed a similar tendency, suggesting that stage II, FIGO in 1982, JSOG in 1983 (Japan Society of Obstetrics and Gynecology, The Japan Society of Pathology, Japan Radiological Society 1996) cancer of the endometrium being an indication for radical hysterectomy, this has remained unchanged in Japan. However, is radical hysterectomy mandatory for stage II patients? The 5-year survival rates, by clinical stage, according to the previous classification, FIGO in 1982, JSOG in 1983, in 223 patients who were treated at our department in the 21 years between 1970 and 1991 (Sato et al. 1992) are as follows: stage I, 95%; II, 86%; III, 54%; and IV, 9%; respectively. Basic surgery was simple total hysterectomy in most cases, but the 5-year survival rate did not differ from those in other reports. Many domestic and foreign studies have demonstrated that the survival rate does not vary between simple total hysterectomy and radical hysterectomy, and thus the type of hysterectomy is not a dependent prognostic factor (Creasman et al. 1987; Tamura et al. 1991; Haenggi et al. 1995; Leminen et al. 1995; Hareyama et al. 1997), indicating that there are no reasons that radical hysterectomy must necessarily be selected. In Western countries where more patients with this disease are encountered than in Japan, few institutions perform radical hysterectomy. These circumstances are also reflected in the recent FIGO classification in 1988 (FIGO 1989) which does not include evaluation of the parametrium evaluated as stage IIIc as an issue requiring attention according to the new staging system by JSOG in 1995. On the other hand, it has been reported that radical hysterectomy should be considered when gross cervical involvement is encountered (Boente et al. 1995; Elia et al. 1995). Since MRI has been reported to be useful, with regard to cervical invasion, as a preoperative diagnostic imaging modality for endometrial cancer (Toki et al. 1998), we should be very careful to select radical hysterectomy without clearly defined reasons.

There were three groups with views regarding treatment of the para-aortic lymph nodes in the results of this survey (Fig. 4). Group A (31%) believed that dissecting the para-aortic lymph nodes is necessary as a rule and improving prognosis, while group B (32%) did not need to perform direct surgery on the para-aortic lymph nodes, but rather diagnosed metastasis based on preoperative diagnostic imaging, curettage, intraoperative inspection, or palpation. Moreover, group C (37%) believed that they could not recognize the improvement in prognosis by means of treatment of the para-aortic lymph nodes and expected the establishment of standards to devise individualized treatment plans. Group B

	Histological grade		
Myometrial invasion	G1	G2	G3
Endometrium only
$\leq 1/2$
$> 1/2$

Fig. 5. Individualized surgery based on histological grade and myometrial invasion for endometrial cancer.

, Low risk group: omitted or dissection of the pelvic lymph nodes;

, Moderate risk group: dissection of the pelvic lymph nodes;

, High risk group: biopsy or dissection of the para-aortic lymph nodes.

based the rationale for the prudence on technical problems, slight benefits and uncertainty estimated from a balance that included limited time for consultation and surgery, as well as the risks during surgery involving the para-aortic lymph nodes. At the moment, we cannot determine whether treatment of the para-aortic lymph node can improve the prognosis of endometrial cancer, but the registration of patients with endometrial cancer has been carried out according to the new classification, FIGO in 1988, JSOG in 1995. Long-term follow-up will make it possible to determine the evaluation of para-aortic node dissection or biopsy.

Para-aortic lymph node metastasis has been demonstrated to greatly influence prognosis (Creasman et al. 1987). The frequency of para-aortic lymph node metastasis is reported to be about 5% for stage I and about 10% overall (Creasman et al. 1987; Nishiya et al. 1991; Hirabatake et al. 1997). The presence of para-aortic lymph node metastasis implies advanced disease in which the lesion has already spread throughout the entire body. Therefore, even though this metastatic lymph node is resected as thoroughly as possible, an improved prognosis cannot be expected by means of surgery only. Hence, it should be considered that the importance of biopsy or dissection of the para-aortic lymph nodes is mainly in achieving an accurate understanding of the progression and expansion of the lesions as an index for selecting an appropriate adjuvant therapy. Post-operative management includes radiotherapy and chemotherapy, but the most effective therapy may be controversial. JGOG is presently investigating the comparison of the efficacy and usefulness of adjuvant therapy between radiotherapy and chemotherapy.

Based on the questionnaire survey reported here, Fig. 5 summarizes the current situation of individualized surgical techniques based on the grade of histological differentiation and the depth of myometrial invasion. The consensus is that dissection of both the para-aortic and pelvic lymph nodes can be omitted in G1 cases showing lesions confined to the endometrium, and that pelvic lymph

nodes should be dissected, but para-aortic lymph node dissection can be omitted in G1 or G2 cases demonstrating myometrial invasion of 1/2 or less. In addition, biopsy or dissection of the para-aortic lymph nodes is necessary in G3 cases or those demonstrating myometrial invasion more than 1/2. These are important findings indicating the present status of lymph node management in treating uterine corpus cancer in Japan.

Since the new classification, FIGO in 1988, JSOG in 1995 involves surgical staging determined postoperatively, it cannot be used as an index for selecting the surgical technique. However, in endometrial cancer, it is crucial to preoperatively evaluate prognostic factors such as the histologic type, grade of differentiation and myometrial invasion as precisely as possible to determine the surgical technique including lymph node dissection. Further evaluation of an appropriate surgical procedure and adjuvant therapy for individuals diagnosed with endometrial cancer will most likely contribute to improvements in the quality of life and prognosis.

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