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Should all endometrioid uterine cancer patients undergo systemic lymphadenectomy?

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Abstract

Objective: To evaluate the potential benefits of systemic pelvic and para-aortic lymphadenectomy in endometrioid uterine cancer patients.
Methods: We conducted a retrospective study on 244 cases of endometrioid uterine cancer that involved surgery in the Center of Gynecologic Oncology, Peking University People's Hospital, Beijing, from January 2000 to May 2008. We conducted staging for each case to ensure accordance with FIGO 2009 surgical staging criteria. Clinical data, including histology, age at diagnosis, surgical procedure, adjuvant therapy, date of death or last follow-up, and date and sites of recurrence were collected for each patient.
Results: Among 244 endometrioid uterine cancer patients, 207 cases (84.8%) underwent systemic pelvic lymphadenectomy. Among these cases, pelvic lymph nodes in 17 cases (8.2%) exhibited tumor metastasis. Systemic aortic lymphadenectomy was performed in 127 cases (52.0%) among 244 total patients. Five cases (3.9%) exhibited positive aortic lymph nodes, of which four exhibited positive pelvic lymph nodes. We investigated the impact of positive retroperitoneal lymph nodes on staging: 4 (4/161, 2.5%), 6 (6/29, 20.7%), 6 (6/35, 17.1%), 1 (1/8) and 1 (1/6) case changed to stage IIIc from stage Ia, Ib, II, IIIa, and IIIb, respectively. Tumor-free and overall survival did not differ between patients who underwent pelvic lymphadenectomy or not ($P > 0.05$). Tumor-free survival improved in stage Ib pelvic lymphadenectomy patients ($P = 0.040$); para-aortic lymphadenectomy did not improve patient survival in all stages ($P > 0.05$).
Conclusion: Systemic lymphadenectomy is not warranted in stage Ia endometrioid uterine cancer.

Keywords: Uterine cancer; Endometrioid carcinoma; Lymphadenectomy; Staging; Prognosis

Introduction

Cervical carcinoma was determined to be the most common female genital tract malignancy worldwide.[1] However, due to the availability of cervical cytology screening, morbidity and mortality have decreased in developed countries. Uterine cancer, which is currently the most common malignancy of the female genital tract in the United States in 2010.[2] With the rapid development of the global economy, the incidence rate of uterine cancer also increased in recent years in China, particularly in prosperous regions.

Because lesions are located in the uterine cavity, patients with endometrial hyperplasia and carcinogenesis always exhibit irregular vaginal bleeding. Upon diagnosis, the disease is generally confined to the corpus; thus, the majority of uterine cancer patients who receive therapy in the hospital are early stage cases. The most important pattern of metastasis of uterine cancer is the spread to the lymphatic system. The tumor cells are transferred to the pelvic and aortic lymph nodes initially, and then to distant lymph nodes. Thus, surgical procedures indicated include not only hysterectomy and bilateral salpingo-oophorectomy, but also pelvic and para-aortic lymphadenectomy.

By performing lymphadenectomy during the primary surgical management of uterine cancer, potential metastasis in lymph nodes is avoided. Moreover, a systemic lymphadenectomy as part of a comprehensive staging surgical procedure could help to determine the FIGO stage of the tumor. Once the disease stage is confirmed, an appropriate adjuvant therapy could be chosen. Some physicians insist that systemic lymphadenectomy be performed for the reasons given above, whereas others argue that the occurrence of lymph node metastasis in low risk patients is very low.

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Moreover, routine lymphadenectomy is associated with a longer operation time and increased intraoperative complications. After this surgical procedure, lymph edema/lymph cyst formation, thrombosis and even pulmonary embolism are potentially seen in these patients.

The aim of this study is to evaluate the potential benefit of lymphadenectomy for endometrioid uterine cancer patients, particularly early stage patients.

Materials and methods

We retrospectively analyzed a total of 267 uterine cancer patients who underwent a surgical procedure, including hysterectomy, at Peking University People's Hospital in Beijing, China, from Jan. 2000 to May 2008. All histological samples were reviewed and confirmed by pathologists. The clinical data were collected for each patient. We conducted staging for each case to ensure accordance with FIGO 2009 surgical staging criteria.[3] Among the 267 cases, there were two cases with ovarian carcinoma, 15 cases of serous carcinoma, and six cases of clear cell carcinoma which were excluded from the study; retrospective analysis was conducted on the remaining 244 endometrioid uterine cancer patients.

Treatment for each patient included a surgical procedure followed by radiotherapy, chemotherapy regimens that differed according to the patient age, tumor grade, histological type, health status, and consent. Pelvic radiotherapy or tumor-directed radiotherapy was conducted in patients with high risk of recurrence or with lymph node metastasis. Some patients with high risk of recurrence also underwent chemotherapy with two or four courses of a CAP regimen (cyclophosphamide, doxorubicin, and cisplatin) or CP (cyclophosphamide and cisplatin).

Periodic surveillance, including general and pelvic examinations, vaginal top smear, abdominal-pelvic ultrasonography, and assessment of serous CA125, salivary acid (SA) was conducted every one to two months for the first year after surgery or confirmed diagnosis, every three to six months for the next three years, and yearly thereafter. Chest X-ray was performed every six months for the first two years, and every year for the next three years. If recurrence was suspected, a thorough evaluation was performed using CT, MRI or PET scan of the chest, abdomen and pelvis.

Data analysis was conducted using SPSS statistical software (version 10.0). The relationships between various qualitative clinical and pathological parameters were compared using the Pearson χ^2 test or Fisher's exact test. Comparisons of two or more than two groups of quantitative parameters were performed with the Student's *t*-test and one way ANOVA, respectively. Survival time was calculated from the date of diagnosis to the date of death or last follow-up. Survival curves were plotted using the Kaplan–Meier method, and the log-rank test was used for comparison. Multivariable analysis was conducted using Cox proportional hazards regression. A P value of less than 0.05 was considered to represent a statistically significant result.

Results

Lymph node metastasis in uterine cancer patients

Two hundred seven cases (84.8%) underwent systemic pelvic lymphadenectomy among the 244 evaluable uterine cancer patients. Among these patients, there were 17 cases (8.2%) in which pelvic lymph nodes exhibited tumor metastasis. There were six uterine cancer patients with single group positive pelvic lymph nodes and eight cases exhibiting multiple groups with a total of 25 positive groups, whereas no pelvic lymph node grouping data were available in the other three cases. The external iliac lymph node was the most common localization exhibiting lymph node metastasis. Nine groups of external iliac lymph nodes were identified, with metastasis observed in eight cases of 14 cases, giving a total of 25 positive pelvic lymph node groups. Obturator lymph nodes were the second most common site exhibiting metastasis, with seven cases and eight groups in the 14 patients.

The mean age of the patients with positive and negative pelvic lymph nodes was 56.2 ± 6.1 years old and 54.1 ± 10.0 years old, respectively, with a statistically insignificant difference ($t = 1.306$,$P = 0.204$). The relationships between pelvic lymph node metastases and the other clinical pathological characteristics are shown in Table 1.

Multivariable analysis was conducted that incorporated the following potential prognostic factors: cervical invasion, deep myometrium invasion, tumor grade, and estrogen receptor condition. The results indicated that deep myometrial invasion exhibited an odds ratios (OR) of 3.036 for pelvic lymph node metastasis.

Systemic aortic lymphadenectomy was performed on 127 cases (52.0%). Among these cases, five (3.9%) demonstrated positive aortic lymph nodes, and four of these cases

Table 1
Relationship between pelvic lymph node metastases and the other clinical pathological characteristics.

		Positive pelvic LN	Negative pelvic LN	X^2	P
Cervical	Invasion	7	33		
	Intact	10	157	4.249	0.039
Adnexa	Invasion	2	4		
	Intact	15	186	2.310	0.129
Myometrium	<1/2	7	157		
Invasion	≥1/2	10	33	13.872	< 0.001
Grade	G1	1	71		
	G2	12	94		
	G3	4	25	7.004	0.030
Estrogen	Positive	8	126		
Receptor	Negative	7	27	5.442	0.020
Progesterone	Positive	10	130		
Receptor	Negative	5	23	2.108	0.147