Expert Opinion

J Gynecol Oncol Vol. 25, No. 4:279-281
http://dx.doi.org/10.3802/jgo.2014.25.4.279
pISSN 2005-0380 · eISSN 2005-0399

Journal of Gynecologic Oncology
jgo

Role of lymphadenectomy for ovarian cancer

Mikio Mikami
Department of Obstetrics and Gynecology, Tokai University School of Medicine, Isehara, Japan

Japan Society of Gynecologic Oncology (JSGO) recently revised its *Ovarian Cancer Treatment Guidelines* and the 4th edition will be released next year. This Guidelines state that lymphadenectomy is essential to allow accurate assessment of the clinical stage in early ovarian cancer, but there is no randomized controlled trial that shows any therapeutic efficacy of lymphadenectomy. In patients with advanced stage tumors, lymphadenectomy should be considered if optimal debulking has been performed. I fully agree with this recommendation of the JSGO and I would like to discuss the role of lymphadenectomy in the management of ovarian cancer.

Keywords: Lymphadenectomy, Ovarian cancer

LYMPHADENECTOMY FOR EARLY OVARIAN CANCER

In 1988, the International Federation of Gynecology and Obstetrics (FIGO) published a surgical staging scheme for ovarian cancer that included pelvic and para-aortic lymph node sampling or lymphadenectomy. However, few studies have shown any benefit of lymphadenectomy in patients with early stage disease. Systematic lymphadenectomy may increase surgical morbidity, although it is necessary for accurate staging and has diagnostic value. Recently, Chan et al. [1] conducted a large-scale, retrospective study to assess the impact of lymphadenectomy on survival in patients with clinical stage I ovarian cancer and suggested that lymphadenectomy significantly improved the survival of such patients. In addition, a randomized study was conducted to investigate the effect of systematic lymphadenectomy in patients with pT1 and pT2 ovarian cancer [2], which showed that systematic lymphadenectomy had no influence on either progression-free survival or overall survival. Tumor involvement of pelvic lymph nodes has been reported to occur in 5%–14% of patients with pT1 disease and the para-aortic nodes are involved in 4%–12% (**Table 1**) [3-9]. Lymphatic spread of early stage ovarian cancer upstages the patient to FIGO stage III, making them appropriate candidates for adjuvant chemotherapy after surgery. The accurate assessment of lymph node metastasis and, therefore, accurate staging of the tumor may be the main value of systematic lymphadenectomy. Also, when the initial surgical staging is correct, patients with low-risk disease may be spared from undergoing cytotoxic chemotherapy.

According to the data from the Japan Society of Obstetrics and Gynecology tumor registry (2012), pelvic and para-aortic node dissection are currently performed only for about 40% of patients with early stage ovarian cancer in Japan. Surgical treatment of ovarian cancer, including systematic lymphadenectomy, should be performed only at gynecologic oncology specialized institutions in order to ensure accurate staging of the tumor. I think that lymphadenectomy is essential to allow accurate assessment of the tumor stage in all patients even with clinically early stage ovarian cancer.

LYMPHADENECTOMY FOR ADVANCED STAGE OVARIAN CANCER: COMPLETE DISSECTION VERSUS RESECTION OF BULKY NODES

Primary cytoreductive surgery (i.e., removal of as much of the tumor as possible at the initial operation along with resection of the bulky lymph nodes) has been an integral part of the treatment of advanced stage ovarian cancer since it

Received Sep 14, 2014, **Accepted** Sep 16, 2014

Correspondence to Mikio Mikami
Department of Obstetrics and Gynecology, Tokai University School of Medicine, Shimokasuya 143, Isehara, Kanagawa 259-1193, Japan. E-mail: mmikami@is.icc.u-tokai.ac.jp

Table 1. Frequency of lymph node metastasis in pT1 disease according to the stage and site

Author (year)	No. of patients	Positive rate (%)	Stage (%)			Positive rate (%)	
			Ia	Ib	Ic	PLN	PAN
Sakuragi et al. (2000) [3]	78	5.1	3.2	NA	6.4	0	5.1
Suzuki et al. (2000) [4]	47	10.6	5.6	NA	13.8	8.5	4.3
Cass et al. (2001) [5]	96	14.5	–	NA	NA	9.4	7.3
Takeshima et al. (2005) [6]	156	12.8	9.3	33.3	15.4	7.1	9.6
Harter et al. (2007) [7]	48	6.2	0	25.0	8.0	NA	NA
Fournier et al. (2009) [8]	54	9.3	3.8	0	17.4	NA	NA
Nomura et al. (2010) [9]	60	13.3	28.0	0	9.1	8.3	11.7
Mikami (Tokai Univ.) (2014)	89	12.3	4	50	17.6	10.1	6.7

PAN, para-aortic Lymph node; PLN, pelvic lymph node.

was reported that the size of postoperative residual tumor is a significant prognostic factor. However, it is still unclear whether systematic lymphadenectomy should be part of maximal cytoreductive surgery and the therapeutic value of systematic lymphadenectomy in women with advanced stage ovarian cancer remains controversial. Retrospective studies [10] have suggested that there is a clinically significant improvement of survival after systematic lymphadenectomy in patients undergoing cytoreductive surgery for advanced stage disease, but no prospective studies have been reported. Panici et al. [11] performed the first multicenter randomized clinical trial, which showed that systematic lymphadenectomy was associated with significant improvement of progression-free survival, although overall survival was similar in the systematic lymphadenectomy arm and the bulky nodes resection arm. In addition, a larger number of patients had lymph node metastasis in the systematic lymphadenectomy arm than in the bulky nodes arm and it was confirmed that lymph node metastasis is a statistically significant prognostic factor for survival. Furthermore, du Bois et al. [12] reported that the data from three prospective randomized trials of platinum/taxane-based chemotherapy for advanced stage ovarian cancer revealed that lymphadenectomy might mainly benefit patients who underwent complete intraperitoneal debulking to treat advanced stage disease. However, this report needs to be confirmed by the results of a prospective randomized trial. In these three trials, 24.8% of patients without suspected intraoperative lymph node involvement who underwent pelvic and para-aortic lymphadenectomy were shown to have histologically positive nodes, whereas the rate was 17.1% in patients who received incomplete retroperitoneal lymphadenectomy. Almost one third of positive nodes are not clinically detectable and may be missed by partial lymphadenectomy. A prospective randomized trial in patients with advanced stage ovarian cancer that compares complete intraperitoneal tumor resection with or without removal of suspicious lymph nodes (Lion trial) has been started, and the results will probably shed new light on this important question. In our series, patients with small residual tumor (<1 cm) who underwent complete pelvic and para-aortic node dissection showed better overall survival than those who underwent only pelvic node dissection or those who did not undergo lymph node resection (p<0.001) (**Fig. 1**).

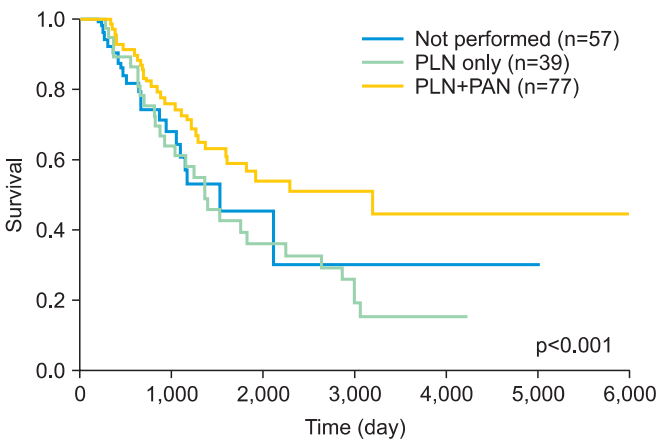

Fig. 1. Overall survival of patients with FIGO stage III–IV with residual tumor <1 cm according to the performance of lymphadenectomy.

I recommend that systematic pelvic and para-aortic lymphadenectomy should be performed in all the patients who are likely to achieve optimal cytoreduction.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

http://dx.doi.org/10.3802/jgo.2014.25.4.279

REFERENCES

1. Chan JK, Munro EG, Cheung MK, Husain A, Teng NN, Berek JS, et al. Association of lymphadenectomy and survival in stage I ovarian cancer patients. Obstet Gynecol 2007;109:12-9.
2. Maggioni A, Benedetti Panici P, Dell'Anna T, Landoni F, Lissoni A, Pellegrino A, et al. Randomised study of systematic lymphadenectomy in patients with epithelial ovarian cancer macroscopically confined to the pelvis. Br J Cancer 2006;95:699-704.
3. Sakuragi N, Yamada H, Oikawa M, Okuyama K, Fujino T, Sagawa T, et al. Ptrognostic significance of lymph node metastasis and clear cell histology in ovarian carcinoma limited to the pelvis (pT1M0 and pT2M0). Gynecol Oncol 2000;79:251-5.
4. Suzuki M, Ohwada M, Yamada T, Kohno T, Sekiguchi I, Sato I. Lymph node metastasis in stage I epithelial ovarian cancer. Gynecol Oncol 2000;79:305-8.
5. Cass I, Li AJ, Runowicz CD, Fields AL, Goldberg GL, Leuchter RS, et al. Pattern of lymph node metastases in clinically unilateral stage I invasive epithelial ovarian carcinomas. Gynecol Oncol 2001;80:56-61.
6. Takeshima N, Hirai Y, Umayahara K, Fujiwara K, Takizawa K, Hasumi K. Lymph node metastasis in ovarian cancer: difference between serous and non-serous primary tumors. Gynecol Oncol 2005;99:427-31.
7. Harter P, Gnauert K, Hils R, Lehmann TG, Fisseler-Eckhoff A, Traut A, du Bois A. Pattern and clinical predictors of lymph node metastases in epithelial ovarian cancer. Int J Gynecol Cancer 2007;17:1238-44.
8. Fournier M, Stoeckle E, Guyon F, Brouste V, Thomas L, MacGrogan G, et al. Lymph node involvement in epithelial ovarian cancer: sites and risk factors in a series of 355 patients. Int J Gynecol Cancer 2009;19:1307-13.
9. Nomura H, Tsuda H, Susumu N, Fujii T, Banno K, Kataoka F, et al. Lymph node metastasis in grossly apparent stages I and II epithelial ovarian cancer. Int J Gynecol Cancer 2010;20:341-5.
10. Chan JK, Urban R, Hu JM, Shin JY, Husain A, Teng NN, et al. The potential therapeutic role of lymph node resection in epithelial ovarian cancer: a study of 13918 patients. Br J Cancer 2007;96:1817-22.
11. Panici PB, Maggioni A, Hacker N, Landoni F, Ackermann S, Campagnutta E, et al. Systematic aortic and pelvic lymphadenectomy versus resection of bulky nodes only in optimally debulked advanced ovarian cancer: a randomized clinical trial. J Natl Cancer Inst 2005;97:560-6.
12. du Bois A, Reuss A, Harter P, Pujade-Lauraine E, Ray-Coquard I, Pfisterer J, et al. Potential role of lymphadenectomy in advanced ovarian cancer: a combined exploratory analysis of three prospectively randomized phase III multicenter trials. J Clin Oncol 2010;28:1733-9.