

The Effect of Para Aortic Lymph Node Dissection in Staging and Complete Cytoreductive Surgery of Ovarian Cancer

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Abstract

Objective: Lymphatic spread is a common feature of ovarian cancer both in early and advanced stages of the disease. There is also a controversial problem of the impact of para-aortic lymph node dissection between gynecologist oncologist experts. The aim of this study is evaluating the effect of Para aortic Lymph node dissection in ovarian cancer patients.

Methods: This descriptive cross-sectional study was performed on 100 ovarian cancer patients admitted in department of gynecology oncology of Ghaem hospital, Mashhad University of Medical Sciences, Iran, from November 2013 - 2014. All patients underwent surgical staging surgery and optimal debulking surgery as possible. In addition, concurrent systematic pelvic and para-aortic lymphadenectomy up to the level of inferior mesenteric artery was performed.

Results: A total of 100 patients were studied. The mean age was 47 years (SD = 13). In 73 patients optimal cytoreductive surgery was done with para aortic lymphadenectomy. 53 cases (72.6%) were in primary cytoreductive surgery and 20 cases (27.3%) in interval debulking surgery groups. Positive paraaortic lymph node in the first group was 6 cases (11.3) and in the second group was 2 cases (10%). 27 patients were in apparent stage I and 46 patients were in stage II-III-IV of disease. We found positive paraaortic lymph node in 11% of total patients. We found positive paraaortic lymph node without positive pelvic lymph node in two patients.

Conclusions: Lymph node dissection will produce a significant benefit in accurate and complete surgical staging; it will reduce residual disease and then progression-free survival.

Keywords: Lymphadenectomy, Ovarian Cancer, Para Aortic Lymph Node

1. Introduction

Intra peritoneal dissemination in ovarian cancer is a main manner, but retroperitoneal metastases and lymphatic spread are also common features in all stages of ovarian cancer both in early- and advanced-stage disease (1). According to the guidelines for surgical staging of ovarian cancer, systematic pelvic and para-aortic lymph node dissection is effective and suitable approach in these patients. In addition, in patients with positive lymph node, lymphadenectomy has a therapeutic and prognostic effect (2). Because of the level of lymph node dissection in early ovarian cancer determined accurate surgical staging; therefore, it has a significant prognostic effect and is correlated with survival of these patients. This method should be considered when dealing with this controversial problem in gynecologist oncologist (3). Generally, for over 100 years, lymphadenectomy has been accepted worldwide, but because of morbidity and mortality in this type of

surgery, it is less advocated by gynecologists. Maggioni and coworkers performed the first randomized trial entitled the value of systematic lymphadenectomy in comparison with sampling pelvic and para aortic lymph node in ovarian cancer. They concluded that risks for progress of disease and death of patients were not statistically different, but five-year and progression-free survival had slightly improved in the systematic lymph node dissection group. According to the study of lymph node dissection in early ovarian cancer in the research of Ivanov et al. it is reported that extension of the lymph node dissection was correlated with better survival rates in these patients (4). In a cohort study of 88 cases with stage I or II ovarian cancer, pelvic lymph node metastases was found in 14 cases (15.9%), and in 10 cases (11.4%) para-aortic metastases were detected (5). One of the important factors in the management of ovarian cancer is maximal surgical cytoreduction with the primary goal of maximum tumor resection. It has been established that improvements in surgical procedures and ade-

quate surgical staging (pelvic and paraaortic lymph node dissection) lead to higher survival rates and a reduction of morbidity in patients with early and advanced ovarian cancer (6). To evaluate therapeutic and prognostic effects of para aortic lymph node dissection in ovarian cancer, ignoring this procedure in most experienced surgeons, and lack of such procedure in our country, this study was performed to study the effect of para aortic lymph node dissection in ovarian cancer patients.

2. Methods

This descriptive cross-sectional prospective study was performed on all 100 patients with ovarian cancer admitted in department of gynecology oncology at Ghaem hospital, Mashhad University of Medical Sciences, Iran from November 2013 - 2014 with ethical code number MUMS.FM.REC.1394.626. According to the study of Case et al. with reporting 40% positive para-aortic lymph node and relative accuracy of 30%, sample size of 90 cases was examined.

The inclusion criteria were all patients with ovarian cancer who underwent surgical staging or cytoreductive surgery. In advanced stages, cytoreductive surgery was performed. Also, the patients who were candidate for neoadjuvant chemotherapy underwent cytoreductive surgery after 3 - 6 courses of chemotherapy. All histological types of epithelial ovarian cancer, sex cord and germ cell tumors were candidates for this study. Exclusion criteria included: 1. inability of frozen section for report intraoperative malignancy, 2. elderly patients (> 80 years old), 3. pregnancy, 4. suboptimal cytoreductive surgery, 5. pathological type of ovarian cancer without need to lymphadenectomy, and 6. unsuitable condition of patient under anesthesia. Lymphadenectomy procedure included complete removal of all tissues lying between arterial and venous vessels. After laparotomy and incision in the peritoneum overlying the iliac artery in the pelvic and identified left and right iliac artery, lymph nodes were properly dissected. The dissection was continued to be applied for nodal tissues surrounding the aorta, inferior vena cava until visualization of inferior mesenteric artery which was cut of level lymphadenectomy. Systematic para-aortic lymph node dissection included the removal of all lymph node tissues surrounding these structures. In addition, we assessed other parameters such as operation time. We estimated blood loss, associated mortality and morbidity, vascular injuries, lymph cysts, wound complication, and postoperative ileus. This study was approved by the ethics committee of the research council of Mashhad University of Medical Sciences. Informed consents were obtained from participants prior to participation.

2.1. Statistical Analysis

Statistical analysis was performed with the log-rank and χ^2 tests to compare univariate prognosis factors. The Cox proportional hazard regression model was used to determine the independent contributions of the prognostic variables in a multivariate analysis. Differences were considered statistically significant at $P \leq 0.005$. STATA 10 statistical software (Stata Corporation, College Station, Texas, USA) was used for the analysis

3. Results

A total of 100 patients who underwent cytoreductive surgery were included. Mean age of the patients was 47 years (SD = 13). Totally, 73 patients had optimal cytoreductive surgery with Para-aortic lymphadenectomy (Table 1). However, primary cytoreductive surgery was performed for 53 cases (72.6%), and interval debulking surgery along with Para-aortic lymph node dissection for 20 (27.3%). Positive Para-aortic lymph node was detected in 8 from 73 cases (11%) totally, and 6 from 53 (11.3%) patients of the first group and 2 from 20 (10%) patients of the second group. Based on adherence to FIGO staging, 27 patients were apparently in stage I and 46 patients in stage II-III-IV of disease. PALN was positive in only one of 27 patients in stage I (3.7%), and 7 of 46 (15.2%) patients in stage > I. Wholly, among 73 patients who underwent cytoreductive surgery with Para-aortic lymphadenectomy, 8 cases (11%) had positive para-aortic lymph node and 65 (89%) showed negative result. We found positive para-aortic lymph node without positive pelvic lymph node in 2 patients. The average number of removed para-aortic lymph node was 7 (5 - 15), and removed pelvic lymph nodes were 9 (5 - 11). In adherence to omental involvement, we observed invasion in 6 from 8 patients (75%) with positive para-aortic lymph node. In addition, lymph node involvement was significantly correlated with FIGO staging, grading tumor and histology of tumor with use of exact test ($P < 0.005$) and there is a significant correlation between lymphovascular involvement and paraaortic lymph node positive, and use of exact Fisher test (Tables 2 - 4).

Vascular injury occurred in one patient (common iliac) which was successfully repaired. Furthermore, this technique leads to increased time of operation about 20 minutes and the estimated blood loss higher rate about 60 cc. The rate of postoperative ileus was 30% and the rate of wound complication was 7%. The mortality and morbidity, lympho cysts formation, wound complication were not different between para-aortic lymph node dissection group and the other group.

Table 1. Paraaortic Positive Lymph Node in Patients with Optimal Cytoreductive Surgery Primary or Interval Surgery

	Number	PALN+ ^a
Optimal cytoreductive surgery	73	8 (11)
Primary	53	6 (11.3)
Interval	20	2 (10)

^aValues are expressed as No. (%).**Table 2.** Paraaortic Positive Lymph Node in Early or Late Stage of Ovarian Cancer

	Number	PALN+ ^a
Optimal cytoreductive surgery	73	8 (11)
Early Stage (I)	27	1 (3.7)
Late Stage (> I)	46	7 (15.2)

^aValues are expressed as No. (%).**Table 3.** Demographic and Clinic Pathologic Characteristic in 73 Patients of Ovarian Cancer with Optimal Cytoreductive Surgery and Paraaortic and Pelvic Lymphadenectomy^a

	Number	PLN+	PLN-	P Value	PALN+	PALN-	P Value
Age	47 ± 13						
Histology				0.9			0.59
Papillary serous	38 (52)	5 (6.8)	33 (45.2)		6 (8.2)	32 (43.8)	
Mucinous	7 (9.6)	1 (1.3)	6 (8.2)		1 (1.3)	6 (8.2)	
Endometrioid	4 (5.4)	0	4 (5.4)		0	4 (5.4)	
Clear cell tumor	5 (6.8)	0	5 (6.8)		0	5 (6.8)	
Poorly Differentiated	1 (1.3)	0	1 (1.3)		1 (1.3)	0	
Transitional cell	2 (2.6)	0	2 (2.6)		0	2 (2.6)	
Granulosa	10 (13.7)	0	10 (13.7)		0	10 (13.7)	
Disgerminoma	3 (4.1)	0	3 (4.1)		0	3 (4.1)	
Immature Teratoma	3 (4.1)	0	3 (4.1)		0	3 (4.1)	
Stage				0.4			0.24
Stage I	27 (37)	1 (1.3)	26 (35.6)		1 (1.3)	26 (35.6)	
Stage > I	46 (63)	5 (6.8)	41 (74.4)		7 (9.6)	39 (53.4)	
Lymphovascular Invasion				0.06			0.008
Yes	5 (6.8)	3 (4.1)	2 (2.6)		3 (4.1)	2 (2.6)	
No	68 (93.2)	3 (4.1)	65 (89)		5 (6.8)	63 (86.3)	
Omental Invasion				0.41			0.14
Yes	35 (47.9)	4 (5.2)	31 (42.5)		6 (7.8)	29 (39.7)	
No	38 (52.1)	2 (2.6)	36 (49.3)		2 (2.6)	36 (49.3)	
High grade (2, 3) tumor							
Yes	51 (70)	5 (6.8)	46 (63)	0.6	7 (9.6)	44 (60)	0.4
No	22 (30)	1 (1.3)	21 (37)		1 (1.3)	21 (29)	
Positive Ascitis				0.03			0.005
Yes	29 (39.7)	5 (6.8)	24 (32.9)		7 (9.6)	22 (30.1)	
No	44 (60.3)	1 (1.3)	43 (58.9)		1 (1.3)	43 (59)	
Total = 73	73						

^aValues are expressed as mean ± SD or No. (%).

4. Discussion

Early-stage ovarian cancer confined to the ovary may be upstaged by the extend of the lymphadenectomy and

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identification of micro metastasis. Obviously this procedure is important for determination of adequate adjuvant

Table 4. Demographic and Clinic Pathologic Characteristic 73 Patients of Ovarian Cancer with Optimal Cytoreductive Surgery and Para-Aortic Lymphadenectomy

Surgery	Stage	LVI	Omentum	Acitis	Type pathol- ogy	Grade	PLN	PALN	Age	No
Primary	3	-	+	+	PS	3	+	+	50	12
Primar	3	+	+	+	PS	2	+	+	60	13
Interval	4	-	+	+	M	3	+	+	28	22
Primar	3	-	+	+	Undiff	3	-	+	73	28
Interval	3	+	-	+	PS	2	+	+	54	61
Primar	3	+	+	+	PS	3	+	+	62	76
Primary	1	-	-	-	BS	1	+	+	26	79
Primar	3	-	+	+	PS	3	-	+	35	83

systemic chemotherapy. In addition, in advanced ovarian cancer case decision for accurate standard treatment surgery without any residual disease is a correct approach. Based on the present study results, Para-aortic lymph node dissection lead to changing the stage of the disease from 1 to 3; however, except in one case. So the patient were treated with chemotherapy. Unexpectedly we found positive Para-aortic lymph node in two case despite the report of negative pelvic lymph node. Undoubtedly procedure systematic pelvic and Para-aortic lymph node dissection leads to increased survival of these patients.

Lymph node involvement depends on several factors, including: ascites, stage of disease, high grade histology and pathological subtype of tumor (7). In our study, 75% of patients with omental involvement were positive Para-aortic lymph nodes. Due to establishing retroperitoneal metastases in all stage of ovarian cancer, the strategy systematic pelvic and para-aortic lymph node dissection must be applied in management of all cases of this disease. The presence or absence of gross enlarged lymph node is not sufficient for indication of systematic pelvic and para-aortic lymph node dissection (8, 9). In a study, two authors who evaluated all prospective or retrospective cohort studies of MEDLINE and EMBASE supplemented established that every patient with clinical early stage ovarian cancer needs to undergo complete pelvic and Para-aortic lymphadenectomy as a part of a staging laparotomy. The rate of lymph node metastases in all stages of this study was 14.2% and they had 2.9% positive lymph node only in the Para-aortic region (10). In current study, we found it in 11% and 3.7% respectively.

There is a meaningful correlation between para aortic lymphatic invasion and variables: 1-histologic type of tumor, 2-lymphovascular invasion, 3-positive ascites with use of exact test and we did not any find relation among paraaortic lymph node positive and variables such as 1-omental invasion 2- grade of tumor, and 3-stage of disease (P value 0.005).

Fortunately, according to experience of gynecologist oncologists, mortality and morbidity, wound complication was not significant in procedure of para-aortic lymph node dissection. Because of insignificant results of the current research we recommended further research with larger samples.

In conclusion, we must consider that ovarian cancer is highly aggressive. Omitting a systematic pelvic and para-aortic lymphadenectomy irrespective of the presence or absence of enlarged lymph nodes might play a potential role in unfavorable prognosis.

Footnotes

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