

# The Investigation of The Factors Affecting Retroperitoneal Lymph Node Metastasis In Epithelial Ovarian Cancer

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Araştırma

## Epitelyal Over Kanserinde Retroperitoneal Lenf Nodu Metastazı Etkileyen Faktörlerin Araştırılması

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### ÖZET

**Amaç:** Bu çalışmada, epitelyal over kanserli hastalarda lenf nodu tutulumu ile ilişkili faktörleri araştırıldı. Over kanserinin önemli yayılım yollarından biri lenfatik yayılımdır. Bu tip yayılım sıklıkla ileri evrelerde görülür. Bu nedenle, over kanserinde lenf nodu tutulumunu etkileyen faktörlerin belirlenmesi ve bu faktörlere yönelik yeni tedavi yöntemlerinin geliştirilmesi için elzemdir.

**Gereç ve Yöntem:** Çalışmamızda, son 10 yıl içerisinde Bakırköy Jinekoloji ve Pediatri eğitimi araştırma hastanesine başvuran ve opere edilen over kanseri olgularını değerlendirildi ve tek merkezli ve homojen bir hasta grubunda klinik ve patolojik faktörler olası lenf nodu tutulumu açısından araştırıldı.

**Bulgular:** Buna göre, preoperatif CA-125 protein seviyesi lenf nodu negatif olan hastalarda ( $469 \pm 954$ ), pozitif olanlara göre ( $1307 \pm 2937$ ) anlamlı olarak daha düşük bulundu ( $p=0,004 < 0,05$ ). Ayrıca, CA-125 değeri ile hastalığın cerrahi evresi arasında istatistiksel olarak anlamlı bir ilişki saptandı ve CA-125 düzeyi artışı ile lenf nodu tutulumunun arttığı tespit edildi ( $p < 0,04$ ). Bunun yanında, preoperatif CA-125 yüksekliği ve omentum tutulumu ile lenf nodu tutulumu arasında pozitif ilişki tespit edildi, ancak tümör histolojisi ve grade ile lenf nodu tutulumu arasında herhangi bir ilişki bulunmadı.

**Sonuçlar:** Çalışmadan elde edilen bulgular ışığında; Epitelyal over kanserinde lenfatik tutulum varlığı 5 yıllık sağ kalım açısından önemli olduğu ve evre artışı ile lenfatik tutulum arasında pozitif korelasyon olduğu tespit edildi. Bu konuda yürütülecek tüm risk faktörlerinin bir arada değerlendirildiği geniş serili çalışmalarla lenf nodu tutulumuna etki eden faktörlerin histopatolojik ve moleküler etkileri aydınlatılabilir.

**Anahtar sözcükler:** Over kanseri, lenf nodları, metastaz

### ABSTRACT

**Objective:** In this study, the factors associated with lymph node involvement in patients with epithelial ovarian cancer were investigated. One of the major spreading ways of ovarian cancer is lymphatic spread. This type of spread is often seen in advanced stages. Therefore, it is essential to determine the factors affecting lymph node involvement in ovarian cancer and to develop new treatment methods for these factors.

**Material and Method:** In our study, the ovarian cancer cases who were admitted to Bakırköy Gynecology and Pediatrics Education Research Hospital and operated in the last 10 years were evaluated and clinical and pathological factors in terms of possible lymph node involvement in a single-centered and homogeneous patient group were investigated.

**Results:** Accordingly, pre-operative CA-125 protein levels were significantly determined lower in patients with negative lymph node ( $469 \pm 954$ ) than those with positive lymph node ( $1307 \pm 2937$ ) ( $p = 0,004 < 0,05$ ). In addition, a statistically significant relationship was detected between CA-125 value and the surgical stage of the disease and lymph node involvement was determined to be increased with the increase in CA-125 level ( $p < 0,04$ ). Besides, a positive relationship was determined between high preoperative CA-125 levels and omentum involvement and lymph node involvement, but no relationship was found between tumor histology and grade and lymph node involvement.

**Conclusion:** In the light of the findings obtained from the study; it was detected that the presence of lymphatic involvement in epithelial ovarian cancer was important for 5-year survival and that there was a positive correlation between the stage increase and lymphatic involvement. The histopathological and molecular effects of factors affecting lymph node involvement can be enlightened by a large series of studies in which all risk factors in this regard are evaluated together.

**Keywords:** Ovarian cancer, Lymph node, Metastasis

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## Introduction

Epithelial ovarian cancers continue to be the most important cause of mortality among gynecological cancers in developed and developing countries. Ovarian cancer ranks fifth among female cancers, and second among gynecological cancers [1]. Ovarian cancer, on the other hand, ranks first among gynecological cancers causing death in the world. More than 225,000 women get diagnosed with ovarian cancer every year worldwide, and 140,000 of these patients die [2]. Malignant ovarian tumors develop from germ cells, sex cord-stromal cells or epithelial cells. Epithelial ovarian cancers constitute 90-95% of these cases [3]. Their symptoms are also seen in other benign gynecological diseases, so the majority of patients are diagnosed at late stage [1]. In the case that epithelial ovarian cancers (EOCs) are organ-confined and diagnosed at an early stage, 5-year survival exceeds 90%. Unfortunately, only 20% of ovarian malignancies are diagnosed at this stage and most cases are detected in late stages where 5-year survival is less than 20% [4]. Endometrioid ovarian cancer (ENOC) constitutes approximately 15-20% of EOCs and are the second most common histologic type. Clear cell ovarian cancer (CCOC) constitutes 5-10% of EOCs. They often exhibit a unilateral localization [5]. Both ENOC and CCOC are known to be associated with endometriosis and endometrial pathologies [6]. The mean age for clear cell carcinomas is known to be 52-56 [7]. The mean age of onset of endometrioid ovarian cancer is 56 years [8]. There are studies indicating that 5-year survival is lower in CCOC patients than in ENOC patients for all stages [9].

The parameters such as histological grade, stage, lymph node metastasis are the most commonly used to determine prognosis in ovarian cancers. Whether some biological factors (proto-oncogen, oncogen, regulatory factors, tumor suppressor genes) play a role in determining prognosis are also being investigated.

Recently, newly diagnosed ovarian cancer cases have increased by 30% and deaths due to ovarian cancer have increased by 18% [10]. In ovarian cancer, it is rarely possible for patients to receive early diagnosis because of the insidious appearance of the clinic. A large part of the patients are diagnosed in advanced stages. When the disease is detected, the treatment approach is to stage all patients surgically and, if necessary, to perform the cytoreductive surgical procedures at the same time. The fact that combined chemotherapy is performed after surgery in patients in advanced stages is currently accepted as a standard treatment approach.

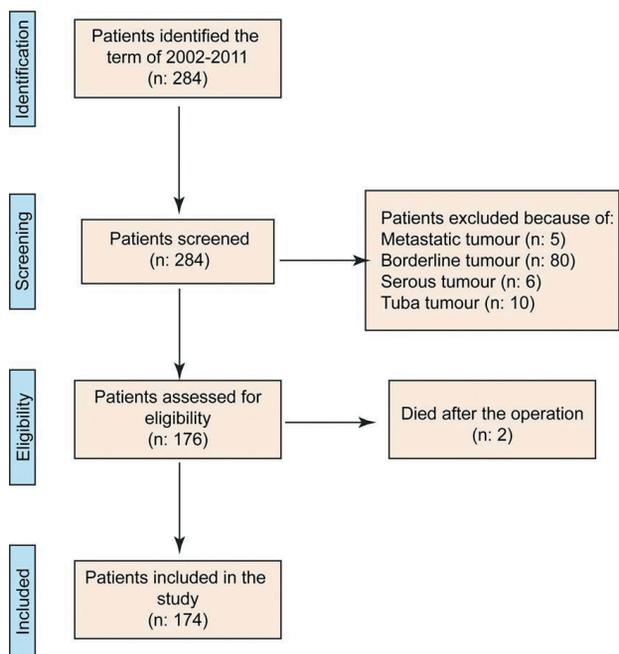
Among the patients who applied to our clinic between 2002 and 2011, 284 patients selected

according to the criteria determined before the study were included to this study. In this study conducted retrospectively, the relationship between epithelial ovarian cancer and lymph node involvement was investigated.

## Material and Methods

### The selection of patients

284 participants who were operated in our hospital between January 2002 and December 2011 were included to the study. Of these, 171 were primary epithelial ovarian cancer cases and were evaluated throughout our study. However, 5 patients with metastatic tumors, 80 patients with borderline tumors, 6 patients with serous cancer of the peritoneal surfaces, and concomitantly, 10 patients with endometrium and tuba cancer were excluded from the analysis. In addition, patients who had undergone chemotherapy or inadequate surgery before applying to our hospital were excluded from our study (20 patients). Patients who died due to reasons other than primary ovarian cancer or in the early postoperative period (2 patients) were excluded from the research group (Figure 1). This study which we carried out retrospectively was initiated with the approval of the Ethics Committee dated 10.08.2011 and numbered 2011-83 received from the Ethics Committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital.



**Figure 1.** Patient selection chart.

**Tablo 1** • Relationship between lymph node positivity and grade, surgical stage.

		Negative (n/%)		Positive (n/%)		
	Good	38	27,5 %	3	9,4 %	0,057
	Mid	55	39,9 %	13	40,6 %	
	Bad	45	32,6 %	16	50,0 %	
	Grades	Stage 1	59	42,8 %	0	
<b>Surgical stage</b>	<b>Stage 2-3-4</b>	Stage 2	6	4,3 %	2	6,3 %
	Stage 3	64	46,4 %	29	90,6 %	0,000
	Stage 4	9	6,5 %	1	3,1 %	

### The treatment of the patients included in the study

All patients underwent staging surgery and also cytoreductive surgery in appropriate cases in accordance with the International federation of gynecology and obstetrics (FIGO) guidelines due to primary ovarian cancer. Following midline incision, cytological samples were obtained from ascites fluid. In patients without ascites, abdominal washing fluid was sampled for cytological evaluation. All peritoneal surfaces were evaluated by inspection and palpation and biopsies were taken from suspicious points. Subsequently, all patients underwent infra-gastric (total) omentectomy. According to antegrade or operative findings, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed in retrograde fashion. Both pelvic (iliac and obturator) and para-aortic regions were reached by transperitoneal route and lymph tissues around the large vessels were excised to renal artery levels in aortic region (systemic lymphadenectomy). Routine appendectomy was performed in all cases who had not previously undergone appendectomy. Optimal cytoreduction was taken as  $\leq 1$ cm. Postoperative staging was carried out in accordance with pathological results and FIGO guidelines.

### The collection and analysis of data

All patient data included in the study were retrospectively collected by using the following resources: Hospital files; Special follow-up forms of gynaecological oncology; Council forms of gynecological oncology; Automation system of our hospital laboratories; Postoperative reports in the pathology department of our hospital.

In the analysis of the data collected during the study, the normality distribution was carried out with the Kolmogorov-Smirnov test. While analyzing the parametric data T-test was used, Mann-Whitney U test

in the analysis of non-parametric data. In the analysis of proportional data, on the other hand, chi-square test was used. The Fischer test was used when the chi-square test conditions could not be achieved. All analyses were carried out using SPSS 20.0.

### Results

The mean age ( $51.2 \pm 12.1$ ) of patients with lymph node-negative was significantly higher than patients with lymph node-positive ( $44.7 \pm 8.3$ ) ( $p = 0.000 < 0.001$ ). The mean number of cigarettes per day ( $19.4 \pm 11.7$ ) of patients with lymph node-negative was significantly higher than patients with lymph node-positive ( $11.2 \pm 11.7$ ) ( $p = 0.000 < 0.001$ ). The grades of patients with lymph node negative and positive did not indicate a significant difference ( $p > 0.05$ ). In patients with lymph node-positive, the stages were significantly higher than patients with lymph node-negative ( $p = 0.000 < 0.001$ ) (Figure 2a).

The presence of gravida, number of gravida, presence of parity, number of parity, duration of menopause, having infertility treatment or not did not differ significantly ( $p > 0,05$ ) in patients with lymph node positive or negative. The menopausal age (15.6 %) in patients with lymph node-positive was significantly lower ( $p = 0.000 < 0.001$ ) than patients with lymph node-negative (53.6%).

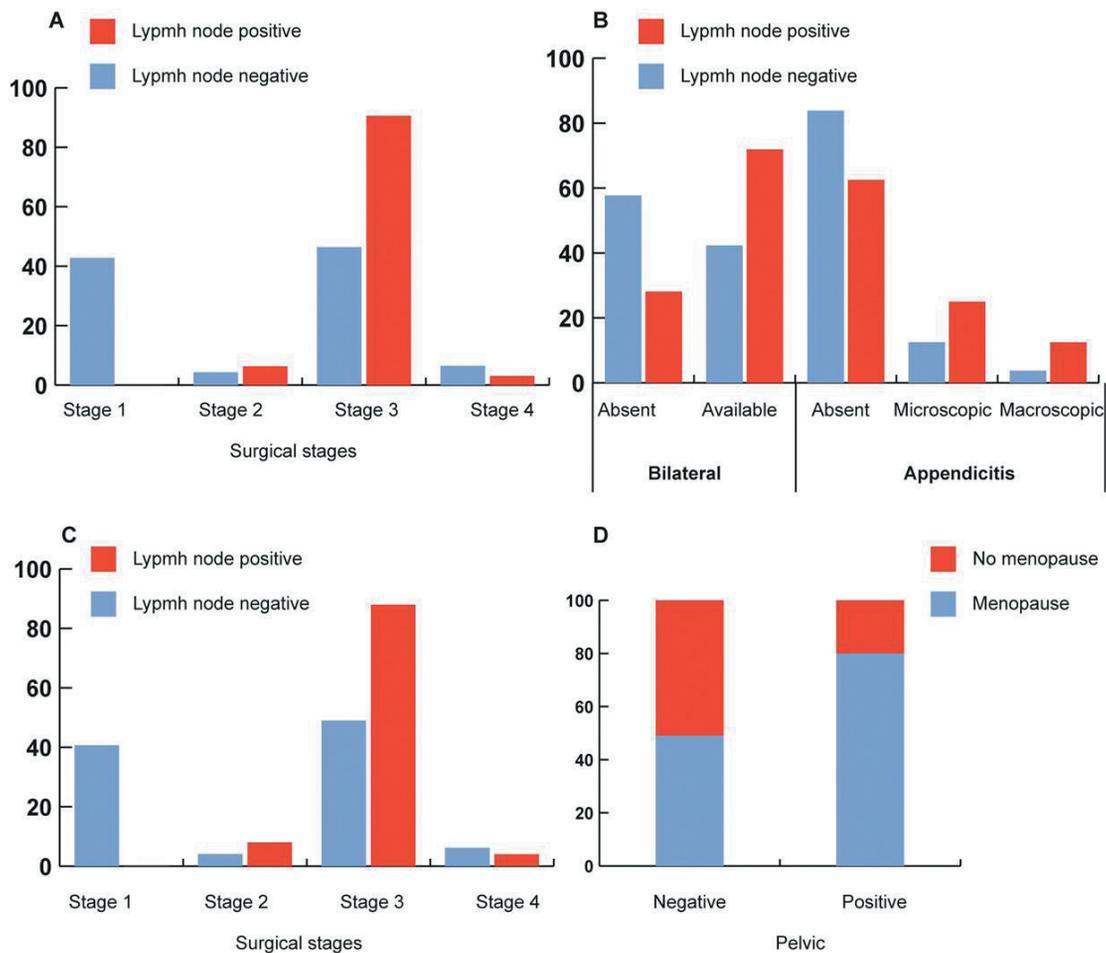
CA19.9, CEA level, cyst diameter, the presence of ascites, capsule inv, abdominal fluid, omentum, residual tumor, intraoperative and postoperative complication rates indicated no significant difference in patients with pelvic lymph node positive and negative ( $p > 0.05$ ). The CA125 value of patients with lymph node-negative ( $469 \pm 954$ ) was significantly lower ( $p = 0.004 < 0.05$ ) than patients with lymph node-positive ( $1307 \pm 2937$ ). The rate of being bilateral (71.9%) in patients with lymph node-positive was significantly higher ( $p = 0.003 < 0.05$ ) than patients with lymph node-negative (42.3%). The rate of omentum involvement (67.7%) in patients with lymph node-positive was significantly

higher ( $p = 0.026 < 0.05$ ) than patients with lymph node- negative (45.6%). The rate of appendix involvement (62.5%) in patients with lymph node-positive was significantly lower ( $p = 0.007 < 0.05$ ) than patients with lymph node- negative (Figure 2b)

The mean age ( $50.6 \pm 12.2$ ) of the patients with pelvic lymph node- negative was significantly higher than the patients with pelvic lymph node-positive ( $46.3 \pm 7.0$ ) ( $p = 0.016 < 0.05$ ). Family history, past history, complaints, smoking, number of cigarettes per day and duration of cigarette consumption did not show a significant difference ( $p > 0.05$ ) in patients with pelvic lymph node positive and negative. The grades of patients with pelvic lymph node negative and positive did not indicate a significant difference ( $p > 0.05$ ). In patients with pelvic lymph node-positive, the stages were significantly higher than patients with pelvic lymph node-negative ( $p = 0.000 < 0.001$ ) (Figure 2c)

The presence of grvida, number of grvida, presence of parity, number of parity, duration of menopause, having infertility treatment or not did not differ significantly ( $p > 0,05$ ) in patients with pelvic lymph node positive and negative. The menopausal rate (20%) was significantly lower in patients with pelvic lymph node-positive (20%) than in patients with pelvic lymph node-negative (51%) ( $p=0,004 < 0,05$ ) (Figure 2d)

CA19.9, CEA level, cyst diameter, the presence of ascites, presence of capsule invasion, abdominal fluid, omentum, residual tumor, intraoperative and postoperative complication rates indicated no significant difference in patients with pelvic lymph node positive and negative ( $p > 0.05$ ). CA125 value of patients with pelvic lymph node-negative ( $485 \pm 947$ ) was significantly lower ( $p = 0.028 < 0.05$ ) than in patients with pelvic lymph node-positive ( $1399 \pm$



**Figure 2.** The parameters: A. The relationship between lymph node positivity and surgical stage; B. The relationship between Lymph node involvement and appendix involvement and bilaterality; C. Relationship between pelvic lymph node positivity and the stage; D. Relationship between pelvic lymph node involvement and menopausal status.

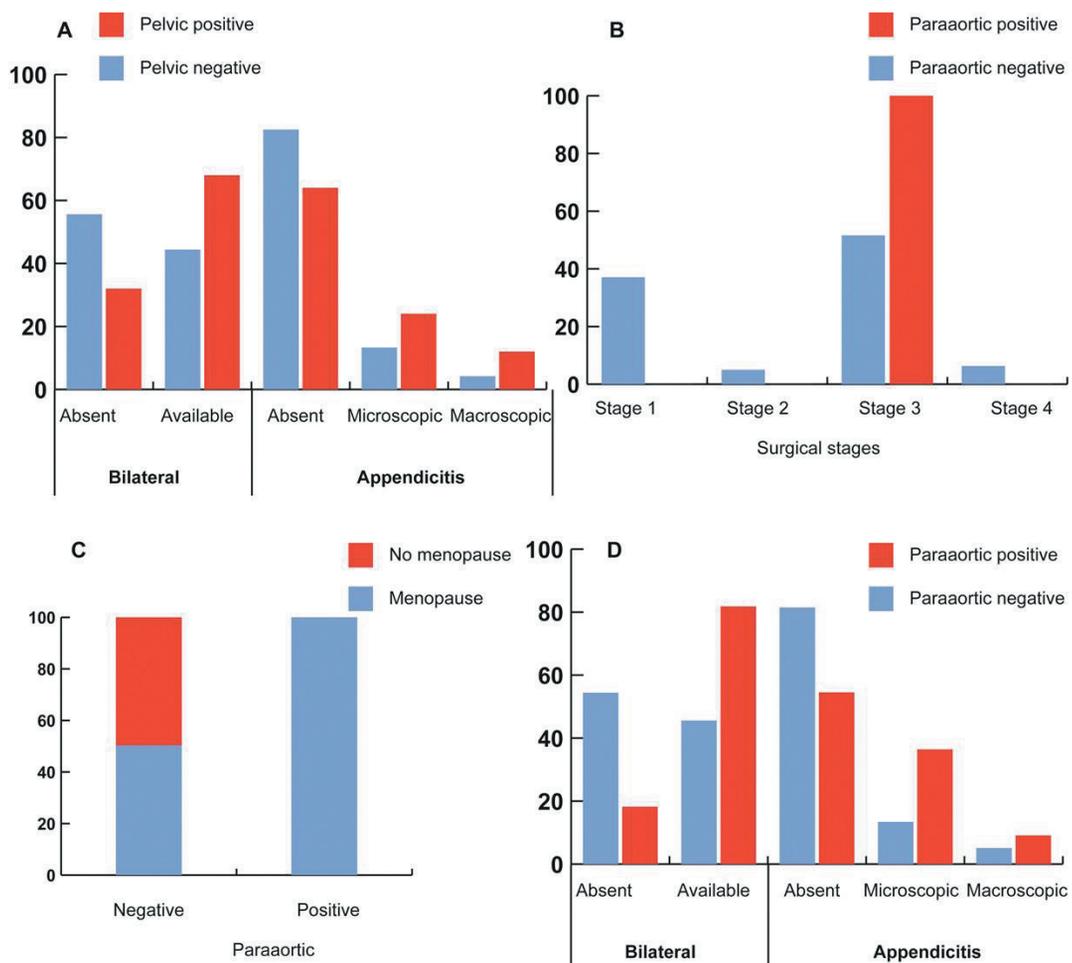
3231). The rate of being bilateral (68%) in patients with pelvic lymph node-positive was significantly higher ( $p = 0.030 < 0.05$ ) than in patients with pelvic lymph node-negative (%44,4). The rate of appendix involvement (64.0%) in patients with pelvic lymph node- positive was significantly lower ( $p = 0.030 < 0.05$ ) than in patients with pelvic lymph node-negative (82.5%) (Figure 3a)

The mean age ( $50,7 \pm 11,6$ ) of the patients with para-aortic lymph node-negative was significantly higher ( $p = 0,005 < 0,05$ ) than the patients with para-aortic lymph node-positive ( $40,5 \pm 8,4$ ). Family history, past history, complaints, smoking, number of cigarettes per day and duration of cigarette consumption did not indicate a significant difference in patients with para-aortic lymph node positive and negative ( $p > 0.05$ ).

The grades of patients with para-aortic lymph node negative and positive did not show a significant

difference ( $p > 0,05$ ). Stages in patients with para-aortic lymph node-positive were significantly higher ( $p = 0.000 < 0.001$ ) than in patients with para-aortic lymph node-negative (Figure 3b).

The presence of grvida, number of grvida, presence of parity, number of parity, duration of menopause and having infertility treatment or not did not indicate a significant difference ( $p > 0,05$ ) in para-aortic lymph node positive and negative patients. The menopausal rate (0%) in patients with para-aortic lymph node-positive was significantly lower ( $p = 0.001 < 0.05$ ) than in patients with para-aortic lymph node-negative (49.7%). The mean parity number ( $2.9 \pm 2.4$ ) of the patients with para-aortic lymph node-negative was significantly lower ( $p = 0.036 < 0.05$ ) than in patients with para-aortic lymph node-positive ( $1.6 \pm 0.8$ ) (Figure 3c).



**Figure 3.** The parameters: A. The relationship between pelvic lymph node involvement and appendix involvement and bilaterality; B. Relationship between para-aortic lymph node involvement and the stage; C. Relationship between para-aortic lymph node involvement and menopausal status.; D. The relation between involvement of para-aortic lymph nodes and involvement of the appendix and bilaterality.

CA125, CA19.9, CEA levels, cyst diameter, presence of ascites, capsule inv, positivity of abdominal fluid, omentum involvement, residual tumor, postoperative complication rates did not show a significant difference ( $p > 0,05$ ) in para-aortic lymph node positive and negative patients. The rate of being bilateral (81.8%) in patients with para-aortic lymph node-positive was significantly higher ( $p=0,020 < 0,05$ ) than in patients with para-aortic lymph node-negative (45.6%). The rate of appendix involvement (54.5%) in patients with para-aortic lymph node-positive was significantly lower ( $p = 0.031 < 0.05$ ) than in patients with para-aortic lymph node-negative (81.5%). The rate of intraoperative complications (36.4%) in patients with para-aortic lymph node-positive was significantly higher ( $p = 0.018 < 0.05$ ) than in patients with para-aortic lymph node-negative (8.8%) (Figure 3d).

The relationship between tumor histologies and lymph node, pelvic, para-aortic lymph node is indicated in Figure 4.

### Discussion

Ovarian cancers are of distinctive importance due to the fact that they have the highest mortality rates among gynecological cancers, and their initial symptoms are often nonspecific causing that they spread to the pelvic and abdominal cavity in 60% of patients and are detected in the advanced stage (11). Ovarian cancers were mostly observed in the perimenopausal and postmenopausal period and it was emphasized that the period in which the incidence was peaked was in the 60s (12). The mean age of the cases operated in our clinic was 51.2 years in the lymph node-negative group and 44.7 in the lymph node-positive group.

In a study conducted by Merino MJ et al., it was emphasized that approximately 85% of ovarian cancer cases were 50 years or older (13). In a study conducted by Scholz HS et al. that Stage IV ovarian cancers were evaluated retrospectively, the mean age was determined to be 59.9 (37-76) years (14). In the study conducted by Panici PB et al. that the systemic lymphadenectomy

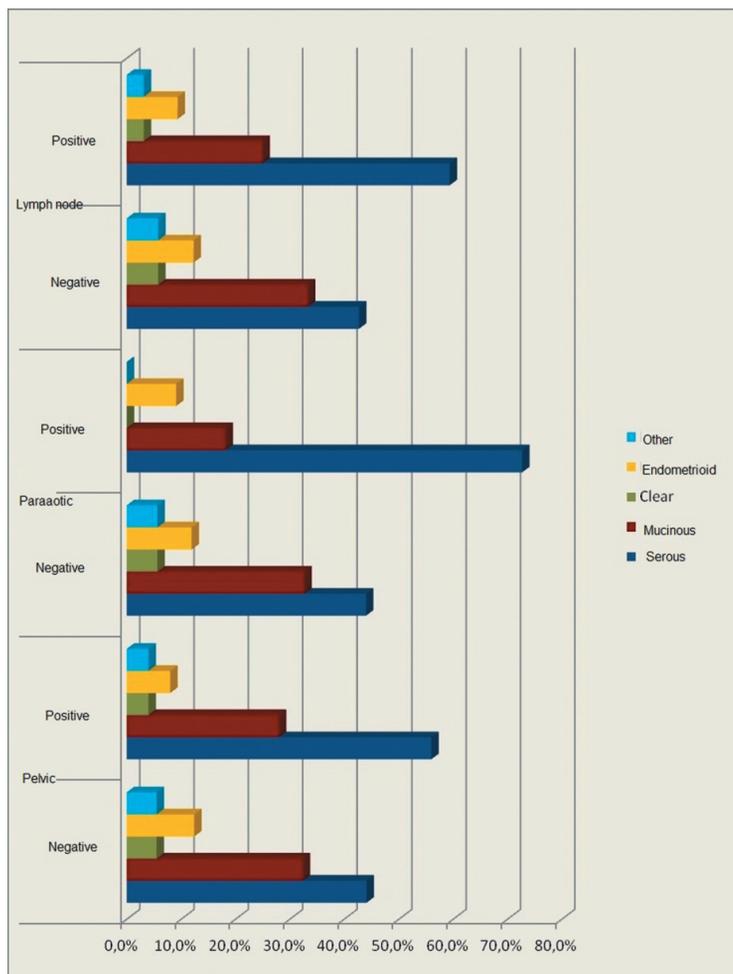


Figure 4. The relationship between tumor histology and lymph, pelvic, para-aortic lymph nodes.

of patients were argued, the mean age was determined to be close to our study, as 53 and 56 (15).

As a result, demographics characteristics of the patients operated in our clinic in terms of age were found similar to other studies, but the fact that the age group in which lymph node-positive cases were most frequently observed was lower than the age group in the sixth decade reported in the literature may be due to the proportional differences in the population of the relevant age group in developing and developed western countries.

Although the etiology of ovarian cancer is not clear, it was emphasized that hormonal and reproductive factors were also important (16). In our study, it was revealed that the cases who did not give birth was in 13% in the lymph node-negative group and in 12.5% in the lymph node-positive group when patients were grouped according to their birth numbers. The presence of one or more gravida was 87.5% in both groups. The mean number of gravida did not indicate a significant difference between the lymph node negative and the positive group and it was found to be 3.7 and 3.2.

The protective effect of pregnancy, lactation and oral contraceptives can be explained by Falhalla's (17) theory indicating the mutations that may occur in the physiological process of the damage and repair mechanism on the surface of uninterrupted ovulation may lead to a higher rate of ovarian cancer. In addition, the hypothesis that increased progesterone levels during pregnancy increased the clearance of the transitional epithelium in the ovarian epithelium and induction has also been supported (18). In our study, no decrease in the age distribution of ovarian cancer with increased parity has been observed, but this data is required to be evaluated by comparing the population data of each country, fertility characteristics and the number of new ovarian cancer cases. Likewise, it is not surprising that the cases detected due to the more number of children in developing countries have also given birth to a large number.

When the symptoms were evaluated, it was observed that 100% of the patients in the lymph node-positive group applied to the doctor on a complaint and this rate was 88% in the lymph node-negative group. It was observed that ovarian cancer was detected only in the lymph node-negative group of patients in routine controls.

Vine et al.(18) emphasized in their studies that they detected ovarian cancer in routine controls in 12% of patients, and reported that the remaining cases applied to a doctor on a complaint. In our study, among the complaints of the patients, abdominal distention ranked the first with 59.1%, followed by abdominal

pain with 20.8%. It was detected that vaginal bleeding was in 8.7% and groin pain was in 8.7%. Similarly to our study, Olson SH et al. (19) emphasized the feeling of fullness, swelling and pressure in abdomen as the first complaint (71%) and reported that the second frequent complaint was observed as abdominal pain (52%). Although the number of patients in our study was limited and there was no comparison with healthy individuals in the similar age group, the most common complaints of abdominal distention and abdominal pain were observed in 79.9% and these were frequently evaluated as nonspecific. On the other hand, without complaints, the lack of cases detected in routine controls can be explained with the habit of not applying to the doctor without a complaint in the overall society.

When analyzed the distribution of patients according to the histopathology, in our study, the most common epithelial tumors of serous ovarian cancer was encountered, as the rate of these cancers was 44% in the lymph node-negative group and 56% in the lymph node-positive group. The endometrioid type ranked second with 18.2%, the mucinous type ovarian cancers ranked third with 11.6%.

In the study Levi F et al conducted, serous epithelial type ovarian cancer was found in 41%, while endometrioid type was observed in 13% and mucinous type in 12% (20). Similarly in the study carried out by Katsubee Y et al., unlike our study, it was reported that mucinous type ovarian cancers (7-15%) were at the second rank and endometrioid type ovarian cancers (10-20%) were at the third rank while the most common serous cancer was encountered (40-50%) (21). Considering the number of patients and case distribution in our study, the results can be interpreted as compatible with the literature.

When the patients were evaluated according to the surgical stages, 42% of the patients in the lymph node-negative group were in stage I. The rate of lymph node-positive cases detected in stage II, stage III and stage IV was 4.4%, 46.4% and 6.5%.

Bast et al. (22) described CA-125 for the first time in ovarian cancer patients and since then many studies have been conducted to investigate the prognostic value of CA-125. In our study, the CA-125 value of the patients with negative lymph node ( $469 \pm 954$ ) was significantly lower than those with positive lymph node ( $1307 \pm 2937$ ) when preoperative CA-125 values were evaluated ( $p=0,004 < 0,05$ ). A statistically significant relationship was detected between the CA-125 value and the surgical stage of the disease and it was determined that the increase in CA-125 level increased the lymph node involvement ( $p < 0.04$ ).

In the literature, similarly to our study, Saygılı U et al. emphasized that the CA-125 was found in higher levels in the higher group when preoperative CA-125 levels were evaluated according to the stages of the patients (23).

Chi DS et al. emphasized that there was a relationship between the most appropriate surgery and preoperative CA-125 levels. In this study, 43 (78%) of 55 cases with suboptimal surgery were detected to have CA125 levels at 500U/ml or higher, and its specificity was found to be 73% (24).

In the study conducted by Kimura T et al., it was pointed out that the increase in para-aortic lymph node involvement in undifferentiated and grade 3 tumors was higher than in other histological types and grade 1, 2 tumors. In the same study, it was detected that the para-aortic lymph node involvement was 18,48 times higher than the tumors not having these properties if grade 3 tumors, tuba, uterus and omentum spread (25). Similarly, in our study lymph node involvement was present in 67% of patients with omentum involvement. In our study, we observed that pelvic, para-aortic lymph node involvement increased with stage increase, but there was no such relationship between tumor grade and histological type.

In the retrospective studies of Ayhan A. et al. in which they examined 420 epithelial ovarian cancers, they detected lymphatic spread in 48.3% of patients. This rate was 44.7% in our study. In the study conducted by Ayhan A. et al, it was reached that there was a significant relationship between stage, histological type (higher in serous, brenner and mixed cell tumors) and CA-125 more than 500 U/ml., with lymphatic spread. In the same study, a significant relationship was also determined between age and grade and para-aortic lymph node involvement. ( $P=0.003$  and  $P=0.02$ , respectively). In the study, it was reported that there was an increase in the risk of lymph node involvement with stage increase, but no lymphatic metastasis in stage IA, grade 1, 2 tumors (26).

In our study, unlike the study of Ayhan et al., we could not detect a significant relationship in terms of increase in age, histological grade and pelvic and para-aortic lymph node involvement.

In the study carried out by Morice P et al., 276 patients who underwent systematic pelvic and para-aortic lymphadenectomy were investigated, and lymphatic involvement rate was determined to be 20% in stage I, 40% in stage II, and 55% in stage III + IV. In our study, these ratios were 0% in stage I and 6.3% in stage II and 90.6% in stage III. No lymphatic spread was detected in 15 patients with stage IA grade 1. In our study, no lymphatic metastasis was detected in 37

patients with stage IA grade 1. In the study Morice P et al. conducted, they emphasized that there was an increase in the risk of lymphatic expansion by stage and grade increase. It has been stated that lymphadenectomy should be performed even for ovarian cancer stage IA, and lymphadenectomy may not be performed if tumor is stage IA grade 1 or mucinous tumor is stage I (4).

In a study in which 112 patients were evaluated between stage I and IV, Bidzinski et al. revealed that age, tumor grade, and histological type were correlated in terms of lymph node involvement, and that there was more lymph node involvement in clear cell and mixed cancers as histological type. In the same study, it was noted that lymph adenectomy is necessary in patients as lymph node involvement may occur even in early stages because of lymph node involvement in early stages (27). We also perform lymphadenectomy for all patients in our hospital even for stage IA.

In the study conducted by Chen et al., the effect of stage, tumor grade, and histological type on lymph node involvement in 61 patients was investigated. Para-aortic lymph node involvement was determined to be 18.2% in stage I, 20% in stage II, 41.9% in stage III, and 66.7% in stage IV. The most common nodal involvement was detected in Grade 3 tumors and in these cases, the involvement of para-aortic lymph node was determined to be 52.5%. In the histological type, the most nodal involvement was observed in serous, undifferentiated and clear cell type (28). In the literature, the relationship between lymph node involvement and stage, grade, age and histological type were investigated (27,28). Lymphatic metastasis was most frequently detected in clear cell, mixed type, and undifferentiated tumors. In our study, we could not detect any significant difference between the histological types in terms of lymph node involvement.

In another study conducted by Tsurichi et al.,(19) the effect of para-aortic lymph node involvement on 5-year survival and the risk factors for para-aortic lymphatic spread were investigated. In the study in which a total of 125 patients were evaluated, 26% para-aortic lymph node metastasis was detected. The 5-year survival rate was determined higher patients with no para-aortic lymph node metastasis (71% versus 17%). It was detected that the involvement of parenchymal-aorta lymph node, the tumor's spread to the omentum, uterus, and tuba and histologic type of the tumor were correlated in logistic regression. In cases with these risk factors, it was emphasized that para-aortic lymphadenectomy should be certainly performed (29). When the literature was reviewed, the conditions such as stage, grade, histological type, age, and tumor's spread to surrounding tissues were frequently examined as

factors affecting the presence of lymphatic involvement. In addition, the effects of parity, presence of ascites, tumor size and tumor markers were also evaluated in our study. A significant relationship was detected only between the increase in stage and preoperative CA-125 and pelvic and para-aortic lymph node involvement. The presence of lymphatic involvement in epithelial ovarian cancer is important for 5-year survival.

## Conclusion

As stated in the literature, lymphadenectomy is important even in early stage epithelial ovarian cancers. Many factors can be effective in the increase in the risk of lymphatic spread of the tumor. In order to determine these factors, we believe that it is important to determine the factors affecting lymph node involvement by conducting large series studies in which all risk factors are evaluated together.

## Declaration of interest

The authors have no financial associations or any other conflicts of interest to declare. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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