

# Assessment on Cases Operated Due to Postmenopausal Adnexal Masses

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**OBJECTIVE:** The objective was to evaluate the clinical traits, as well as preoperative and postoperative histopathologic findings of patients who are operated due to adnexal mass during postmenopausal period.

**STUDY DESIGN:** Our study incorporates 204 patients who were operated at our hospital due to adnexal masses during postmenopausal period. Clinical details (age, parity, personal and family history, oral contraceptive and smoking status) of all patients are recorded. Measurement of serum ca 125 values and trans-vaginal or trans-abdominal ultrasonography findings are recorded, as well as morphological features of each adnexal mass. The tissue material removed in operation was analyzed in histopathologic terms. Preoperative findings are compared with histopathologic diagnosis.

**RESULTS:** According to pathologic examinations, the results for 76.5% of 204 patients (n=156) operated due to postmenopausal adnexal mass were benign, whereas the remaining 48 patients (23.5%) had malign results. The most common pathological examination result in the patients was serous cystadenoma (n=62; %30.4) (p<0.05). In malign cases, serous adenocarcinoma was encountered the most (n=24; %50.1) (p<0.05). The analyses on adnexal masses which are evaluated via preoperative ultrasonography showed that cyst diameter, its capsule thickness and - if any - septa thickness was more common in malign cases. In addition, multilobulation, the septa formation, papillary formation, semisolid formation, the presence of bilaterality and ascites were more common in masses in malign group (p<0.05). Average ca 125 level was 27.9 IU/ml and 699.6 IU/ml (p<0.05) in benign and malign groups, respectively.

**CONCLUSION:** Serum ca 125 levels and TVUSG are useful diagnostic procedures in evaluating especially postmenopausal adnexal masses, however, the definitive diagnosis regarding adnexal masses should be made via histopathologic analysis.

**Key Words:** Postmenopause, Adnexal mass

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## Introduction

Adnexal masses are the fourth most common gynecological reason of applying to a hospital and 90% of them are benign.<sup>1</sup> The ovaries become smaller and quieter in postmenopausal women. In late postmenopausal period, physiological growth and functional cysts do not occur in ovaries and

the gonads suffer atrophy. While only 7% of the epithelial ovarian tumors are malign in premenopausal patients, the rate of malignancy increases to 30% in postmenopausal period.<sup>2</sup>

Epithelial cancers of ovaries are seen in postmenopausal period with a proportion of 81%.<sup>3</sup>

All adnexal masses should be evaluated carefully in postmenopausal period due to the high potential of malignancy.

In this study, the preoperative findings (age, parity, personal and family history, oral contraceptive and smoking status, ca 125 level, ultrasonography findings) and postoperative histopathological findings of the patients who were operated due to adnexal mass in postmenopausal period were evaluated in our hospital.

## Material and Method

Our study incorporates 204 patients who were operated at

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our hospital due to adnexal masses during postmenopausal period between September 2008 and March 2010. The patients who hasn't gone through menopause with adnexal masses and patients whose adnexal masses were diagnosed and who didn't want to have operation were not included in the study. The clinical characteristics and preoperative findings (age, parity, self and family history, oral contraceptive and smoking, ca 125 value, ultrasonography findings) and postoperative histopathological findings were recorded. The size and morphological features of adnexal masses were examined by ultrasonography. The largest diameter in the mass measurements detected by transabdominal and transvaginal ultrasonography was evaluated. The results of histopathological evaluation of the operation materials and ultrasonographic findings were compared.

The ca 125 value limit was appointed as 35 IU/ml.

In the statistical studies, independent t test was used in the intergroup comparison of independent groups in terms of parametric methods. Mann U test and Moses were used in the intergroup comparison of independent groups in terms of nonparametric methods and Kendall's Tau-b test was used in order to examine the relationship between the non-categorical variables. The data were evaluated at a level of 95% confidence and it was considered meaningful if the p value was less than 0.05.

Informed consents were obtained from all participants. Approval of Education Planning Committee of the hospital was obtained for the study.

## Results

The ages of 204 patients participated in our study ranged from 46 to 85. The average age was  $58.8 \pm 8.2$ . The parity of the patients ranged from 0 to 8 and the average parity was 2.7. The average menarche age of 204 patients was  $13.4 \pm 1.7$ , menopause age was  $48.4 \pm 3.1$ . The average reproductive age of the patients were calculated as  $34.8 \pm 3.7$  years, the average duration in menopause was calculated as  $10.2 \pm 8.1$  years.

When the patients were asked in terms of the use of at least 1 year of oral contraceptives (OC) in a lifetime, 58 patients (28.4%) responded positively and 45 patients (21.1%) stated that they smoke. The patients were questioned whether there is anyone who suffers breast and ovarian cancer in their families. The first degree relatives of 15 patients (7.4%) had breast cancer and the first degree relatives of 4 patients (2%) had ovarian cancer.

According to the results of ultrasonographic examination, the cyst diameter of the patients was approximately  $92 \pm 49$  mm, capsule thickness was  $3.2 \pm 0.2$  mm and the average septa thickness of the cyst which have septa was  $4 \pm 0.2$  mm.

Multilobulation in 73 patients (35.8%), septa formation in 68 patients (33.3%), papillary formation in 58 patients (28.4%) and semisolid formation in 87 patients (42.6%) were diagnosed in ultrasonographic examination. While bilateral adnexal mass was diagnosed in 33 patients (16.2%), 30 patients (14.7%) had evidence of ascites.

Ca 125 level for all the preoperative patients ranged from 2 to 8206 IU/ml. The average ca 125 level was determined as  $185.9 \pm 72.9$  IU/ml.

While the results of pathologic examination of 76.5% of 204 patients (n=156) were benign, the results of 48 patients (23.5%) were malign. The average age of the patients who are benign was 58.1, and the average age of those who are malign was 61.3 ( $p > 0.05$ ). The most common pathological examination result in the patients was serous cystadenoma (n=62; %30.4) ( $p < 0.05$ ). In malign cases, serous adenocarcinoma was encountered the most (n=24; %50.1) ( $p < 0.05$ ) (Table I and 2).

When we divide our patients into two groups as younger than 70 (84.8% n=73) and as equal to and older than 70 (15.2% n=31), we concluded that while 38 patients in the first group were malign (22.8%), 10 patients in the second group were malign (%32.3) ( $p > 0.05$ ) (Table 3).

When the benign and malign groups were examined, while the use of OC is 35.9% in the first group, it is 4.2% in the second ( $p < 0.05$ ).

Smoking was 25% in benign group and 12.5% in malign group ( $p > 0.05$ ). When 7 patients who have mucinous adenocarcinoma and borderline mucinous tumor are compared to other malign patients, the smoking rate in the first group was 71.4% and 24.3% in the second group ( $p < 0.05$ ).

The analyses on adnexal masses which are evaluated via preoperative ultrasonography showed that cyst diameter, its capsule thickness and – if any – septa thickness was more common in malign cases. In addition, multilobulation, the septa formation, papillary formation, semisolid formation, the presence of bilaterality and ascites were more common in masses in malign group ( $p < 0.05$ ) (Table 4).

Preoperative Ca 125 level was obtained from every patient. The average Ca 125 level was 27.9 IU/ml in the benign group and was 699.6 IU/ml in the malign group ( $p < 0.05$ ) (Table 5).

The patients were divided into two groups according to their Ca 125 levels. 5.6% malignancy was diagnosed in the group whose Ca 125 level was under 35 IU/ml (8/144), whereas malignancy was 66.7% in the group whose Ca 125 level was over 35 IU/ml (40/60) ( $p < 0.05$ ).

Table 1: Pathologic evaluation results of the benign 156 cases who were operated due to postmenopausal adnexal mass

Pathologic evaluation results	%	n
Serous cystadenoma	39.7	62
Follicle cyst	8.3	13
Mucinous cystadenoma	7.7	12
Mature cystic teratoma	7.1	11
Serous cystadenofibroma	6.4	10
Fibroma	5.8	9
Endometrioma	4.5	7
Paratubal serous cyst	3.8	6
Inclusion cyst	3.2	5
Hydrosalpinx	2.6	4
Brenner tumor	1.3	2
Hydatic cyst	1.3	2
Lutein cyst	1.3	2
Corpus albicans	0.6	1
Mature cystic teratoma+mucinous adenofibroma	0.6	1
Mixed type cystadenoma (endometrioid+serous type)	0.6	1
Mucinous cystadenofibroma	0.6	1
Mucinous cystadenoma+endometrioma	0.6	1
Mature cystic teratoma+mucinous cystadenoma	0.6	1
Struma ovarii	0.6	1
Tubaovarian abscess	0.6	1
Torsioned ovarian cyst	0.6	1
<b>TOTAL</b>	<b>100</b>	<b>156</b>

Table 2: Pathologic evaluation results of the malign 48 cases who were operated due to postmenopausal adnexal mass

Pathologic evaluation results	%	n
Serous adenocarcinoma	50.1	24
Mucinous adenocarcinoma	12.5	6
Endometrioid adenocarcinoma	12.5	6
Mixed type adenocarcinoma (serous+ endometrioid)	8.3	4
Undifferentiated adenocarcinoma	4.2	2
Clear cell adenocarcinoma	2.1	1
Granuloza cell tumor	2.1	1
Carcinosarcoma	2.1	1
Borderline serous tumor (micropapillary type)	2.1	1
Borderline mucinous tumor	2.1	1
Metastatic tumor (breast cancer)	2.1	1
<b>TOTAL</b>	<b>100</b>	<b>48</b>

Table 3: Pathologic evaluation results of the cases according to the age groups (benign- malign)

	Benign	Malign	TOTAL
Cases younger than 70	77.2% (n=135)	22.8%(n=38)	100%(n=173)
Cases equal to and older than 70	67.7%(n=21)	32.3%(n=10)	100%(n=31)

Table 4: Ultrasonographic features of the masses

Ultrasonographic features	Benign group (n=156)	Malign group (n=48)
Average (av.) cyst diameter	85 mm	114 mm
Av. capsule thickness	2 mm	6 mm
Av. septa thickness	2 mm	5 mm
Multilobulation	19.9%	87.5%
Septa formation	16%	89.6%
Papillary formation	12.2%	81.3%
Semisolid formation	28.2%	89.6%
Bilateral mass formation	8.3%	41.7%
Ascites formation	0%	62.5%

Table 5: Average Ca 125 levels of benign and malign cases

	Average Ca 125 levels	minimum	maximum
Benign group(n=156)	27.9 IU/ml	2 IU/ml	1041 IU/ml
Malign group (n=48)	699.6 IU/ml	3 IU/ml	8296 IU/ml

## Discussion

Postmenopausal adnexal masses are the masses that must be considered carefully due to their high potential of malignancy. A woman who is diagnosed to have adnexal mass is evaluated with anamnesis, symptoms, pelvic examination, pelvic or transvaginal ultrasonography, computed tomography or magnetic resonance imaging if necessary. Examination with laparoscopy or laparotomy is decided according to the characteristics of diagnosed mass. It should be noted that final diagnosis of the mass can only be diagnosed by histopathological examination.

Luxman et al. diagnosed malignancy at the rate of 28% in 102 patients with postmenopausal mass.<sup>4</sup> Kaymak et al. examined 114 postmenopausal patients who had laparotomy because of adnexal mass in a study. The ages of the patients ranged from 45 to 72 and the average age of the patient was 50.7. They diagnosed nonneoplastic, mostly simple cyst in 89 patients, benign mass in 21 patients and malign mass in 4 patients. Two of the malign patients were determined as serous cystadenocarcinoma whereas serous cystadenoma was diagnosed the most between benign masses.<sup>5</sup> In our study, the results of 48 patients (23.5%) were diagnosed as malign whereas the results of 204 patients (76.5% n=156) were diagnosed as benign. Serous cystadenoma (39.7%) and serous ade-

nocarcinoma (50.1%) were diagnosed the most in benign and malign groups, respectively ( $p < 0.05$ ).

In the studies in which the results of ultrasonographic findings and histopathological examination is compared in the literature, the findings such as mass over 5 cm, bilaterality, thick septa formation, irregular limited masses, presence of papillary formation, presence of ascites support malignancy. Rulin et al. diagnosed 1 malignancy in 32 patients with <5cm mass (3.1%), 6 malignancy in 55 patients with 5-10 cm mass (10.9%) and malignancy in all of the patients with over 10 cm mass (100%) in their study in which they examined the patients who had laparotomy because of postmenopausal adnexal mass.<sup>6</sup> Ovadia et al. stated in their study that as the size of the mass increases, malignancy increases too.<sup>7</sup> Haberal et al. diagnosed malignancy in 52.1% of the patients with >10 cm mass, 42.8% of the patients with 5-10 cm mass and 16.6% of the patients with <5 cm mass.<sup>8</sup>

Bailey et al. screened 7705 postmenopausal women with transvaginal ultrasonography and diagnosed complex cystic ovarian mass in 250 patients (3.2%). All of these masses is under 10 cm, 89% of which is under 5 cm. After 60 days, the mass persisted in 115 patients and these patients were taken to laparotomy. Ovarian cancer in 7 of these patients, peritoneal cancer in 1, metastatic breast cancer in 1 were diagnosed. Unilocular cystic tumors were detected in 256 of 7705 patients (3.3%). Malignancy wasn't found in 45 of these 256 patients who were operated due to persistence of unilocular cyst.<sup>9</sup> In a study in which Ekerhovd et al. examined 927 premenopausal and 377 postmenopausal women, they determined that the risk for malignancy in cysts containing papillary formations or solid parts was 3 to 6 times higher than that in unilocular echo-free cysts.<sup>10</sup> In our study, when the features of adnexal mass evaluated by preoperative ultrasonography were examined, cyst diameter, capsule thickness of the cyst and the thickness of septa-if there is any- were found higher in malign cases ( $p < 0.05$ ). In addition, multilobulation, septa formation, papillary formation, semisolid formation, bilaterality and presence of ascites were more common in the masses in malign group ( $p < 0.05$ ).

In the study of Ovaida et al, the malignancy was determined as 25.1% in the age group of 50-60, 16.3% in the age group of 60-80 and 58.6% in the age group of 80 and older.<sup>7</sup> Rulin et al. determined that the number of malign patients increases as the age increases.<sup>6</sup> In the study of Kaymak et al, the average age of malign patients was 60 and the average age of non-neoplastic and benign patients was 48 and 51, respectively.<sup>5</sup> In our study, the average age of benign patients was 58.1 and average age of malign patients was 61.3. It was determined that malignancy increases as the age increases, but it was not statistically significant ( $p > 0.05$ ).

In the study in which Rivas - Corchado et al examined 40 patients with ovarian cancer, 60% of the patients were detected in postmenopausal period. The use of oral contraceptives (OC) was present in 40% of the patients. The average menarche age of the patients was 12.7.<sup>11</sup> Tsilidis et al had compared patients used OC for 10 years and more with the patients used OC for 1 year and less; they determined a reduction in the risk of ovarian cancer in the first group. When multiparous patients were compared with the nulliparous, a reduction at the rate of 29% was determined and it was stated the reduction continued at a rate of 8% for each parity. It was determined that the risk of ovarian cancer increases as the age of menopause increase and no relation with the menarche age was found.<sup>12</sup> In the study of Velkovic et al. it was stated that the use of OC is prophylactic from ovarian cancer especially in nulliparous and this effect continues for years after giving up the medicine.<sup>13</sup> In our study, when the patients were questioned in terms of oral contraceptive use for at least 1 year, 58 patients answered positively (28.4%). When benign and malign groups were examined separately, while the use of OC was 35.9% in the first group, it was 4.2% in the second group ( $p < 0.05$ ).

When the relationship between smoking and ovarian cancer is investigated, Tworoger et al in their study couldn't find any relationship between smoking and ovarian cancer but stated that smoking increases the formation of mucinous tumors.<sup>14</sup> Terry et al emphasized that the risk of epithelial ovarian cancer is doubled by smoking for a long time and that the risk of mucinous ovarian cancer is doubled by smoking for a less time.<sup>15</sup> Jordan et al. examined 910 mucinous and 5564 nonmucinous ovarian cancer patients in their study, they determined that smoking doubles the risk of mucinous ovarian cancer compared to never smokers.<sup>16</sup>

The most important risk factor for ovarian cancer is the presence of ovarian or breast cancer in the family. BRCA1 or 2 mutation can be predicted by the presence of this feature in anamnesis.<sup>17</sup> The risk of ovarian cancer specified as 1.6% for a 35-year-old woman becomes 5% on the condition that there is a relative with ovarian cancer and it increases to 7% in the condition the there are two relatives with ovarian cancer. In case of presence of hereditary ovarian cancer in the family, the lifetime risk of ovarian cancer can be up to 50%.<sup>18</sup> Hemminki et al. determined in their study that the presence of ovarian or breast cancer in mother or sister increases the incidence of ovarian cancer and the mortality rates.<sup>19</sup> In our study, when 204 patients were questioned in terms of family history, the presence of breast cancer in the first-degree relatives was 10.4% in malign cases, and 6.4% in benign cases ( $p > 0.05$ ). Ovarian cancer was encountered in 2.1% of the relatives of malign patients and 1.9% of the relatives of benign patients ( $p > 0.05$ ).

Ca 125 is an indicator of tumor widely used for predicting the difference of benign and malign and in the follow-up of ovarian cancer. Ca 125 level is important especially for postmenopausal patients in differentiation of benign and malign. The specificity is lower in women of reproductive age. The highly preoperative ca 125 level predicts that the disease would continue mortally in stage 1a ovarian cancer.<sup>20</sup> In the study of Kaymak et al. in which they examined 114 postmenopausal patients, ca 125 level was high in 3 of 4 malign patients (ca 125> 35 IU/ml). The average ca 125 levels of simple cyst, functional cyst, benign and malign masses were determined as 13.4, 13.07, 12.07 and 143.07 IU/ml respectively. While the malignancy rate was determined as 16.6% in the patients whose ca 125 levels were high, it was 1.96% in the other group.<sup>5</sup> In the study of Reimer et al. in which they examined 58 patients older than 47, ca 125 level was significantly high in the group of malign patients.<sup>21</sup> In our study, the average ca 125 level was 27.9 IU/ml in benign group and 699.6 IU/ml in malign group (p<0.05).

In conclusion, serum ca 125 levels and TVUSG are useful diagnostic procedures in evaluating especially postmenopausal adnexal masses, however, the definitive diagnosis regarding adnexal masses should be made via histopathologic analysis.

### Postmenopozal Adneksiyal Kitle Nedeni ile Opere Edilen Olguların Değerlendirilmesi

**AMAÇ:** Postmenopozal dönemde adneksiyal kitle nedeni ile opere olan hastaların klinik özellikleri ve preoperatif bulguları ile postoperatif histopatolojik bulgularının değerlendirilmesi amaçlanmıştır.

**GEREÇ VE YÖNTEM:** Çalışmamıza hastanemizde postmenopozal dönemde adneksiyal kitle nedeni ile opere olan 204 hasta dahil edildi. Tüm hastaların klinik özellikleri (yaş, parite, öz ve soygeçmiş, oral kontraseptif ve sigara kullanımı) kaydedildi. Serum ca 125 değerleri ölçümü ve transvajinal ya da transabdominal ultrasonografi bulguları kaydedildi. Her adneksiyal kitlenin morfolojik özellikleri kaydedildi. Operasyonda çıkarılan doku materyali histopatolojik olarak incelendi. Preoperatif bulgular ile histopatolojik tanımlar karşılaştırıldı.

**BULGULAR:** Postmenopozal adneksiyal kitle nedeni ile opere edilen 204 hastamızın %76,5'inin (n=156) patolojik inceleme sonuçları benign iken 48 (%23,5) hastanın sonuçları malign olarak değerlendirildi. Olgularda en sık rastlanan patolojik inceleme sonucu seröz kistadenom oldu (n=62;%30,4) (p<0,05). Malign vakalarda en sık seröz adenokarsinom patolojisi görüldü (n=24; %50,1) (p<0,05). Preoperatif ultrasonografi ile değerlendirilen adneksiyel kitleye ait özellikler incelendiğinde kist çapı, kistin kapsül kalınlığı ve septa var ise kalınlığı malign vakalarda daha fazla izlendi (p<0,05). Ayrıca malign grupta kitlelerde multilobulasyon, septa oluşumu, papiller oluşum, semisolid oluşum, bilateralite ve asit varlığına daha sık rastlandı (p<0,05). Benign grupta ca 125 düzeyi ortalama 27,9 IU/ml, malign grupta ise 699,6 IU/ml olarak tespit edildi (p<0,05).

**SONUÇ:** Serum ca 125 değerleri ve TVUSG özellikle postmenopozal adneksiyal kitlelerin değerlendirilmesinde faydalı tanısal yöntemlerdir ancak adneksiyal kitlelerin kesin tanısı histopatolojik inceleme ile konulmalıdır.

**Anahtar Kelimeler:** Postmenopoz, Adneksiyal kitle

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