Araştırma Makalesi (Research Article)

Immunhistochemical Expression of Estrogen, Progesteron Receptors, C-Erb B-2, P53 and BRCA1 in Ovarian Carcinoma and Their Prognostic Value

Over Karsinomlarında Östrojen, Progesteron Reseptörleri, C-Erb B-2, P53 ve BRCA1'in İmmünhistokimyasal Ekspresyonu ve Prognostik Önemleri

Didar GURSOY[1], Iclal GURSES[2], Vedia Bennu GILAN[3], Bahar TASDELEN[4], Ali ARICAN[5], Celalettin Ekrem TOK[6]

[1] Hatay Mustafa Kemal University Faculty of Medicine, Department of Pathology, Hatay, Turkey
[2] Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Department of Pathology, Istanbul, Turkey
[3] Mersin University, Erdemli School of Applied Technology and Management, Computer Technology Information Systems, Mersin, Turkey
[4] Mersin University Faculty of Medicine, Biostatistics and Medical Informatic, Mersin, Turkey
[5] Acibadem Atakent Hospital, Medical Oncology, Istanbul, Turkey
[6] Mersin City Hospital, Gynecology and Obstetrics, Mersin, Turkey

Özet

Amaç: Çalışmamız over karsinomlarında ER, PR, C-erbB-2, p53 ve BRCA1 genlerinin immünohistokimyasal ekspresyonunu ve bunların klinikopatolojik özellikler ile ilişkisini ve prognostik önemini belirlemeyi amaçlamaktadır.

Gereç ve Yöntemler: Çalışmamıza bir fakülte hastanesinde 2002-2012 yılları arasında epitelyal over kanseri tanısı konulan ve takip edilen 85 hasta dahil edildi. ER, PR, C-erbB-2, p53 ve BRCA1'in immünohistokimyasal ekspresyonu ve bunların klinikopatolojik parametrelerle ilişkisi değerlendirildi.

Bulgular: Seröz karsinomlarda, ER ekspresyonu ile fallop tüpüne metastaz, PR ekspresyonu ile hastanın yaşı, p53 ekspresyonu ile progresyonsuz sağkalım (PFS), BRCA1'in sitoplazmik ekspresyonu ile genel sağkalım (OS) ve PFS arasında anlamlı bir ilişki vardı. Patogenez gruplarında 55 tümör tip 1 ve 30 tümör tip 2 idi. İki grup arasında ER, PR ve p53 ekspresyonları ile anlamlı korelasyonlar vardı.

Sonuç: Çalışmamızda PR ve p53 seröz karsinomda prognostik faktörlerdi. Bu beş immünohistokimyasal belirtecin prognostik değerini belirlemek için her histolojik grupta daha fazla vaka içeren kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: C-erbB-2, BRCA1, Hormon reseptörleri, Over kanseri, p53

Abstract

Objectives: Our study aimed to determine immunohistochemical expression of ER, PR, C-erbB-2, p53 and BRCA1 genes and their relationship with clinicopathological features and prognostic significance in ovarian carcinoma.

Material and Methods: The present study included 85 patients that were diagnosed with epithelial ovarian carcinoma, treated and followed-up between 2002 and 2012 at a faculty hospital. Immunohistochemical expression of ER, PR, C-erbB-2, p53 and BRCA1 and their relationship with clinicopathological parameters were evaluated.

Results: In serous carcinomas, expression of ER was significantly associated with metastasis to the fallopian tube, expression of PR was significantly associated with patient's age, expression of p53 was significantly associated with the progression-free survival (PFS), and cytoplasmic expression of BRCA1 was significantly associated with the overall survival (OS) and PFS. In pathogenesis groups, 55 tumors were type 1, and 30 tumors were type 2. There were significant correlations with ER, PR and p53 expressions between the two groups.

Conclusion: In our study, PR and p53 were prognostic factors in serous carcinoma. Extensive studies that contain more cases in each histological group are needed to determine the prognostic value of these five immunohistochemical markers.

Key words: C-erbB-2, BRCA1, Hormone receptors, Ovarian cancer, p53

Yazışma Adresi: Didar GURSOY, Hatay Mustafa Kemal University Faculty of Medicine, Department of Pathology

Telefon: 0505 271 85 09, **Mail:** gursoydidar@gmail.com

ORCID No (Sırasıyla): 0000-0002-0674-7047, 0000-0002-0115-2124, 0000-0002-7119-221X, 0000-0001-8146-4912, 0000-0002-6099-2000, 0000-0002-1197-6039

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INTRODUCTION

Worldwide, ovarian cancers (OCs) is the seventh most common cancer type in females and also the eighth leading cause of cancer-related deaths. Several factors such as FIGO stage, residual disease status after the surgery, patient age, cell type, histopathological grade, capsule rupture, peritoneal cytology status affect its prognosis (1,2). Serous carcinoma (SC) is the most common histological type of ovarian cancer (3).

The estrogen receptor (ER) is related with the nuclear hormone receptor family. It is found in the cell cytoplasm and acts as a ligand-dependent transcription factor (4). The progesterone receptor (PR) is an intracellular protein (5) and stimulates cell proliferation (6). ER and PR are not included in the oncogene or tumor suppressor gene class but can be considered as the cancer genes because they play a critical role in both onset and progression of breast cancer. Recent studies have shown that the expressions of these receptors have a positive effect on the survival of patients with OC (7,8).

The "tumor protein p53 gene", also known as p53 gene, is a tumor suppressor gene located at the locus 17p13.1 (9). More than 75% of cancers involve Tp53 mutation (10,11). It has been debated by many researchers that insignificant mutations in the Tp53 gene were associated with high-stage disease and poor prognosis. However, there are various conclusions about to what extent the type of mutation affects prognosis (12). The p53 mutations have been reported in more than 75% cases with Type 2 OCs (2).

C-erythroblastic oncogene B-2 (C-erbB-2), also known as human epidermal growth receptor 2 (Her2/neu), is a transmembrane glycoprotein of the tyrosine kinase receptor family that controls cell growth. It acts as a co-receptor for a large number of growth factors and also shows tyrosine kinase activity. It is considered as an oncogene when overexpressed (13,14). There is usually an inverse relationship between C-erbB-2 positivity and survival (15).

Breast cancer susceptibility gene 1 (BRCA1) encodes a protein of 1863 amino acids, located in the 21st band on the long arm of chromosome 17. The intracellular localization of BRCA1 has been defined in different ways. It has been shown to be totally or predominantly localized in the nucleus by many studies. All humans carry these genes as part of the genetic structure. The females with a BRCA mutation carry a high risk for high-grade SC (16).

Our study aimed to determine immunohistochemical expression of ER, PR, C-erbB-2, p53 and BRCA1 genes and their relationship with clinicopathological features and prognostic significance.

MATERIALS AND METHODS

Study Design and Samples

The present study included 85 patients that were diagnosed with epithelial OC, treated and followed-up between 2002 and 2012 at a faculty hospital. This study was approved by Clinical Research Ethics Committee (Decision No: 2013/191) of University. SC was diagnosed in 51 of the cases as well as 34 cases with non-serous surface epithelial cancer [endometrioid carcinoma (EC), mucinous carcinoma (MC), clear-cell carcinoma (CCC), undifferentiated carcinoma (UC) and transitional cell carcinoma (TCC) in 11, 10, 7, 5 and 1 cases, respectively] in morphology. The clinical information of the patients was obtained from medical records

Pathological Evaluation

Hematoxylin-Eosin (H&E) stained preparations were examined by two researchers regarding grade of tumors, the presence of capsule rupture, metastasis to uterus and fallopian tubes, lymphovascular invasion and lymph node metastasis and presence of omental implants were independently evaluated based on the pathology reports (DG, IG). The clinical information such as tumor size, laterality of the tumor and presence of malignant cells in peritoneal washing or acid fluid were obtained from the pathology reports.

Immunohistochemical Staining Technique

Immunohistochemical staining procedure was performed with a standard avidin-biotin-immunoperoxidase technique. Paraffin-embedded sections of 4-µm thickness were taken to poly-L-lysine slides. The slides were kept in the 60-degree incubator for 120 minutes (min) for deparaffinization procedure and applied with three different xylol solutions for 30 minutes each after taking from the incubator. The sections rehydrated by applying with absolute alcohol for 5 min, 96% alcohol for 5 min, 90% alcohol for 5 min and 70% for 5 min were washed off with distilled water and phosphate buffered saline (PBS) at ph 7.2 for 1 min each. For accomplishment of antigen retrieval; the sections prepared for the antibodies of ER, PR, C-erb B2 and p53 in pH=6 1:10 citrate buffer solution and for the antibody of BRCA1 in pH=9 EDTA solution (1/10) were placed into the microwave oven and kept for 7 min under high temperature, for 5 min under moderate-high temperature and for 5 min under moderate temperature. The preparations were kept for 20 min under room temperature and washed off with PBS. The borders of the tissues were drawn with tissue counturing pen (PAP Pen). The slides were dropped with 3% H2O2 to inhibit the activity of endogeneous peroxidase in the tissue and kept for 10 min, thereby the tissues became ready for primary antibody. The slides re-washed off with PBS and applied with protein block (to prevent non-specific staining) for 10 mins and washed off with PBS. The slides were placed into the chamber dropped with the primary antibodies of ER (Novocastra, 6F11, dilution 1/100), PR (Novocastra, 16, dilution 1/100), C-erbB-2 (Bio-care, EP1045Y, dilution 1/40), p53 (Novocastra, DO7, dilution 1/40), BRCA1 (Abcam, MS13, dilution 1/100), the basement of the chamber was applied with boiled water to obtain humid environment and kept for 60 minutes after covering. The sections were washed off with PBS and unbounded antibodies were removed. The sections were drop-

Table 1. Histopathological findings of cancers

	Capsular rupture (n)	Uterin metastasis (n)	Fallopian tube metastasis (n)	Omental metastasis (n)	Lymphovascular invasion (n)	Lymph node metastasis (n)	Malignant cytology (n)
Yes	35	37	41	46	46	38	29
No	41	46	43	39	39	42	56
Unknown	9	2	1	0	0	5	0

* Two patients underwent organ-sparing surgery due to their age (1 patient had uterus and tuba, and one patient had uterine preservation).

ped with biotinylated secondary antibody and awaited for 30 min. The sections were washed off with PBS for 5 mins. Streptavidin peroxidase solution was dropped onto the slides and awaited for 30 min. The slides were washed off with PBS for 5 min. To visualize the peroxidase activity, 3 3'-diaminobenzidine tetrahydrochloride (DAB) solution as a chromogen was dropped onto the slides, awaited for 3 minutes and then slides were washed off with distilled water. Mayer's hematoxylin was used to obtain counterstaining in all the slides. The slides were washed off with running tap water and applied with 70%, 90% and 96% ethyl alcohol concentrations and also xylol to obtain transparency. The sections were covered with Entellan and and examined under a light microscope.

Immunohistochemical Analysis

ER and PR: A hundred cells were counted and the number of stained cells was expressed as a percentage (17).

C-erbB-2: ASCO/CAP guideline prepared for breast cancer was used (18).

P53: The preparations were evaluated for nuclear positivity and 100 cells were counted. The number of stained cells was expressed as a percentage.

BRCA1: The preparations were evaluated in terms of nuclear and cytoplasmic staining. The cases were scored between 0 to 3 based on the presence and intensity of nuclear/cytoplasmic staining. 0: no nuclear/cytoplasmic staining, 1: <50% of tumor cells stained, 2: 50%≤ tumor cells stained.

As the positive control staining; ER and PR positive invasive ductal carcinoma tissue of the breast were used for ER and PR while 3+ positive invasive ductal carcinoma tissue of the breast, serous OC tissue and healthy breast tissue were used as the positive control staining for C-erbB-2, P53 and BRCA1, respectively.

Statistical Analysis

Data were expressed as number, percentage, means, standard deviation (SD), median value (MV) and minimum-maximum (min-max) values. The normality assessment for numerical data was performed by Shapiro Wilk test. The correlation of IHC staining with histopathological and clinical variables was evaluated by correlation analysis, Chi-Square test, Mann-Whitney U test, Kruskal Wallis and ANOVA methods. A p-value of less than 0.05 was accepted as statistically significant.

RESULTS

The mean ages of the patients at diagnosis for SC, EC, MC, CCC and UC were 57.88±10.94, 44.73±10.18, 42.40±15.36, 53.57±5.41 47.8±9.68 years, respectively. High grade SC was encountered in 50 of the cases. Right, left and bilateral ovarian tumors were detected in 26 (30.5%), 17 (20%) and 42 (49.5%) of the cases, respectively. The histopathological tumor findings were summarized in **Table 1**. The distribution of the stages according to histological types was shown in **Table 2**. The residual tumors were monitored in 57 patients whereas 27 patients had no residual tumor tissue. Data related with residual tumor information for one patient could not be obtained from the hospital records.

ER (+) nuclear staining was determined in 43 (84.3%), 9 (81.8%) and 3 (60%) cases with MVs of 70.00, 60.00 and 25.00 in the SC, EC and UC groups **(Figure 1A, 1B, 1C)**, respectively. No ER (+) staining was observed in the other groups. A statistically significant correlation was detected between ER (%) variable and fallopian tube metastasis in SC group (p=0.037). The patients with fallopian tube metastasis (80.00) indicated a higher MV than those without metastasis (50.00). The intergroup comparison between the SC-CCC, SC-MC, CCC-EC, EC-MC groups showed statistically significant differences with respect to ER (%) nuclear staining (p<0.00001) **(Table 3)**.

Table 2. Stage distribution according to histological types of tumors

Histological type	Stage I	Stage II	Stage III	Stage IV
SC (n=51)	3	2	40	6
EC (n=11)	6	5	0	0
MC (n=10)	8	1	1	0
CCC (n=7)	5	1	1	0
UC (n=5)	0	2	2	1
TCC (n=1)	0	0	0	1

SC= Serous carcinoma, EC=Endometrioid carcinoma, MC=Mucinous carcinoma, CCC=Clear cell carcinoma, UC=Undifferentiated carcinoma, TCC=Transitional cell carcinoma

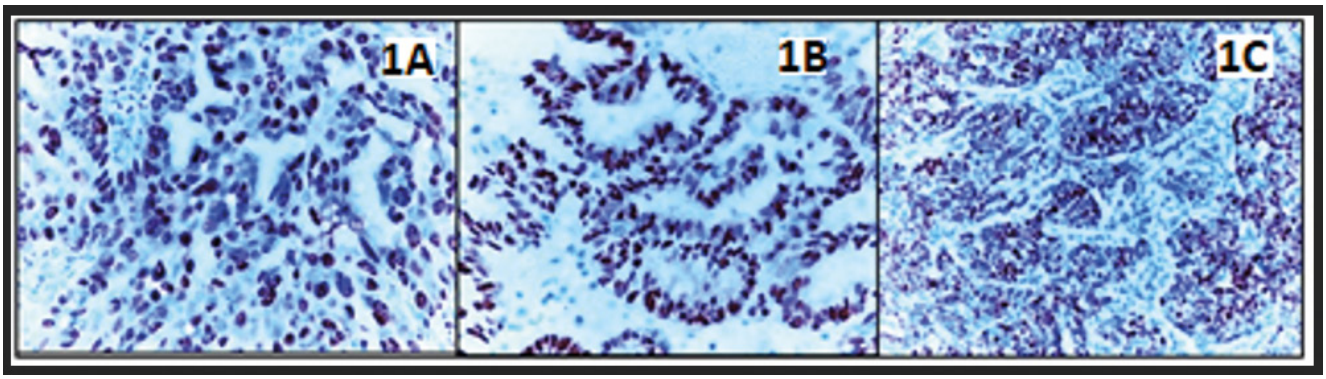

Figure 1A. 70% nuclear staining with ER in a SC case (ER, x200)

Figure 1B. 90% nuclear staining with ER in an EC case (ER, x200)

Figure 1C. 60% nuclear staining with ER in an UC case (ER, x200)

Table 3. The min, max and median values (MVs) in the histological groups of ER, PR and p53

Histological type	SC (n=51)		EC (n=11)		MC (n=10)		CCC (n=7)		UC (n=5)		P
	Min-max.	MV	Min-max.	MV	Min-max.	MV	Min-max.	MV	Min-max.	MV	
ER - %	0-97	70.00	0-97	60.00	0-0	0.00	0-0	0.00	0-80	25.00	<0.00001
PR - %	0-99	40.00	0-99	95.00	0-0	0.00	0-0	0.00	0-90	0.00	<0.00001
p53 - %	40-100	95.00	0-15	2.00	0-70	0.00	0-4	1.00	0-99	92.00	<0.00001

SC= Serous carcinoma, EC=Endometrioid carcinoma, MC=Mucinous carcinoma, CCC=Clear cell carcinoma, UC=Undifferentiated carcinoma, ER=Estrogen receptor, PR=Progesterone receptor

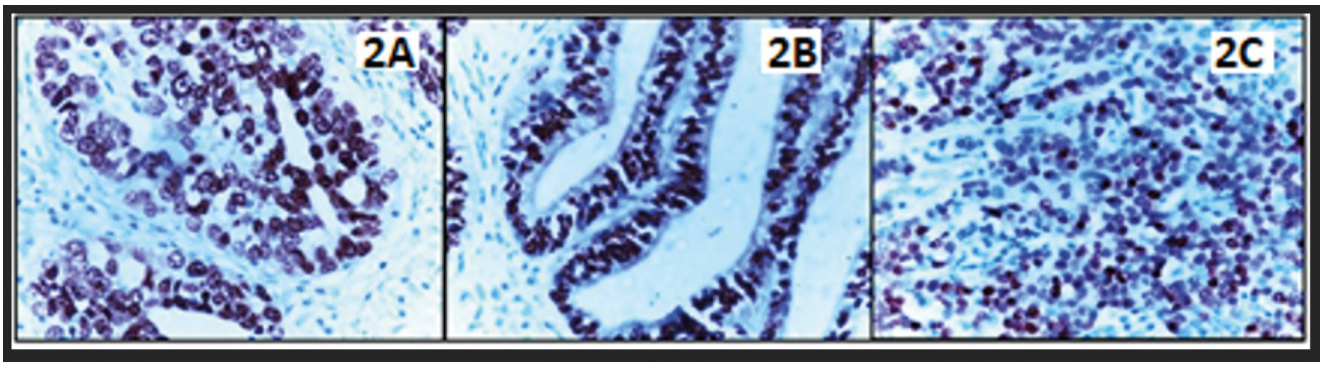

Figure 2A. 95% nuclear staining with PR in a SC case (PR, x400)

Figure 2B. 99% nuclear staining with PR in EC case (PR, x400)

Figure 2C. 60% nuclear staining with PR in UC case (PR, x400)

PR (+) nuclear staining was observed in 39 (76.4%), 10 (90.9%) and 2 (40%) cases in the SC, EC and UC groups with MVs of 40.00, 95.00 and 0.00 **(Figure 2A, 2B, 2C)**, respectively. No staining was observed with PR in the other groups. PR (%) variable and ages in the SC group (p=0.008) demonstrated a statistically significant negative correlation was present between. A reduced PR expression was observed as age increased (R=-0.36). The intergroup comparison between the SC-EC, SC-MC, SC-CCC, CCC-EC, EC-MC and EC-UC groups showed statistically significant differences regarding PR (%) nuclear staining (p<0.00001) **(Table 3)**.

All the cases in the SC group displayed positive nuclear staining with p53 **(figure 3A)** with a MV of 95.00 while 6 (54.5%) **(figure 3B)**, 4 (40.00%) **(figure 3C)**, 4 (57.1%) and 3 (60%) (figure 3D) patients in the EC, MC, CCC and UC groups with MVs of 2.00, 0.00, 1.00 and 92.00, respectively. There was no staining in the TCC group. A statistically significant negative correlation was detected between the p53 (%) variable and PFS (Progression-Free Survival) in the SC group (p= 0.019). PFS value decreased as the expression of p53 increased (R=-0.32). The intergroup comparison manifested statistically significant differences between the SC-EC,

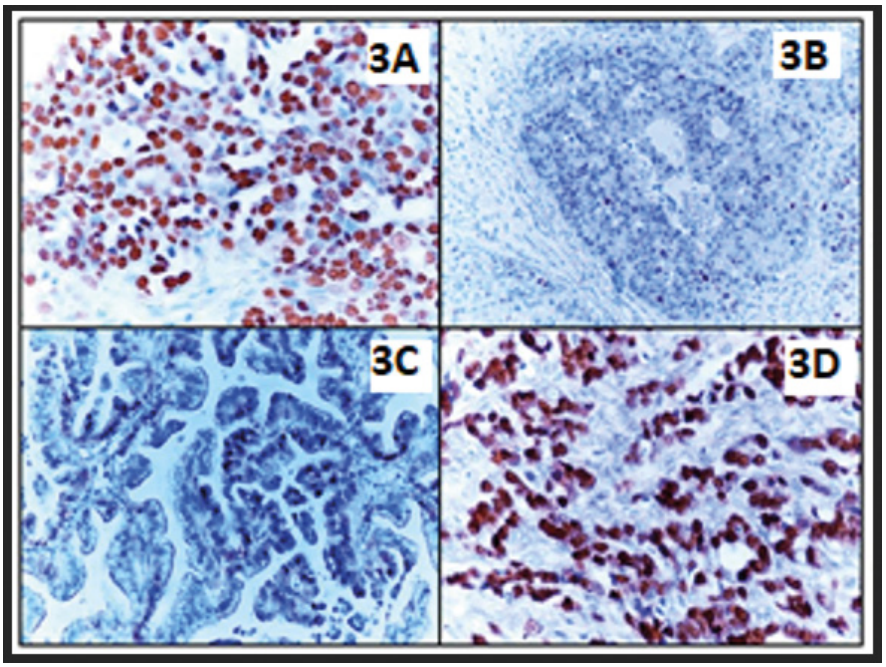

Figure 3A. 95% nuclear staining with p53 in a SC case (p53, x400)
Figure 3B. 5% nuclear staining with p53 in an EC case (p53, x200)
Figure 3C. 30% nuclear staining with p53 in a MC case (p53, x200)
Figure 3D. 96% nuclear staining with p53 in an UC case (p53, x400)

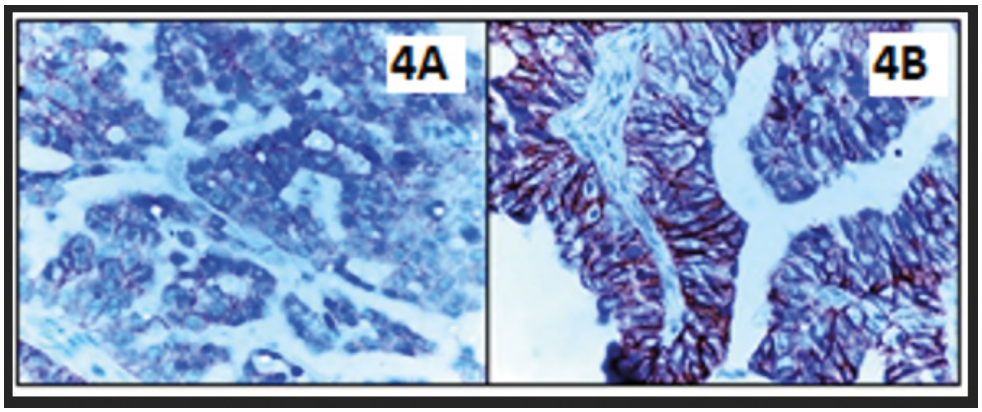

Figure 4A. 2+ membranous staining with C-erbB-2 in the SC case (C-erbB-2, x200)

Figure 4B. 3+ membranous staining with C-erbB-2 in the SC case (C-erbB-2, x400)

SC-CCC, SC-MC, SC-UC, CCC-UC, EC-UC and MC-UC groups regarding p53 (%) nuclear staining ($p<0.00001$) **(Table 3)**.

Since other groups included limited number of cases, no statistical comparison between the groups in terms of ER-%, PR-%, p53-% variables and parameters mentioned could be performed.

C-erbB-2 positivity was detected in only 3 of 85 study patients. These 3 cases indicated SC morphology with score 2 **(figure 4A)** and score 3 **(figure 4B)** in 2 and 1 cases, respectively. Score 2 and Score 3 correspond to Stage II and Stage III according to FIGO Classification, respectively. Because of the limited number of membranous stained cases in the SC group beside the absence of any positive staining in the other groups; the relationships between the variables and the groups were not statically comparable.

Nuclear BRCA1 staining was positive in only 3 of the cases with SC and all the cases showed Score 1 positivity was determined in all the cases. These 3 cases were Stage III according to FIGO Classification. Since the number of cases with positive nuclear BRCA1 staining was limited in the SC group, the relationships between the variables and these groups were not statistically comparable. According to pre-

Table 4. The prevalence of cytoplasmic staining of BRCA1 in the histological groups

Histological type /BRCA1	SC (n=51)		EC (n=11)		MC (n=10)		CCC (n=7)		UC (n=5)	
	Number	%	Number	%	Number	%	Number	%	Number	%
Score 0	20	39.2	8	72.7	2	20.0	4	57.1	2	40.0
Score 1	21	41.2	2	18.2	7	70.0	3	42.9	3	60.0
Score 2	10	19.6	1	9.1	1	10.0	0	0.0	0	0.0

SC= Serous carcinoma, EC=Endometrioid carcinoma, MC=Mucinous carcinoma, CCC=Clear cell carcinoma, UC=Undifferentiated carcinoma, BRCA1=Breast cancer susceptibility gene 1

valence analysis in terms of BRCA1 cytoplasmic staining in the groups; Score 0, 1 and 2 were encountered in 37, 36 and 12 cases **(Table 4)**, respectively.

In the SC group, a statistically significant correlation was identified between the cytoplasmic expression of BRCA1 and OS (p= 0.03), and patients with Score 1 had a longer OS than those with Score 2. Also, a statistically significant relationship was found between the cytoplasmic expression of BRCA1 and PFS (p= 0.005), and Score 1 patients had a longer PFS than those with Score 0 and Score 2. Since the other groups included a limited number of cases, we could not perform a comparative evaluation between the cytoplasmic expression of BRCA1 and the parameters mentioned.

DISCUSSION

The incidence of ovarian tumors increases with age (2). In our study, the mean ages of the patients with SC, EC, MC, CCC and UC were 57.88±10.94, 42.75±10.18, 42.40±15.36, 53.57±5.41 and 47.8±9.68 years, respectively. Our results were consistent with the literature. Sieh et al. have comparatively evaluated hormone receptor expression and OS in the 2933 patients with OC. They have encountered ER positivity in 87.5%, 80.7%, 76.6%, 20.8% and 19.4% of the patients with low-grade SC, high-grade SC, EC, MC and CCC, respectively, and PR positivity in 57.4%, 31.1%, 67.4%, 16.4% and 8% of the patients with low-grade SC, high-grade SC, EC, MC and CCC, respectively (7). The results of gene expression analysis in our SC and EC groups were partially similar with this study; however, we encountered no staining in the MC and CCC groups. In the same study, ER expression was found higher than in PR expression in all groups (7). Our findings were similar except the EC group. As a comprehensive multidisciplinary evaluation, MALignant OVArian Cancer Study (MALOVA) was conducted on 582 OC and 191 borderline ovarian tumors in Denmark. In that study, ER nuclear expression positivity was found in 43%, 59%, 4%, 2% and 36% of the patients with SC, EC, MC, CCC and UC, respectively, while PR positivity was detected in 19%, 41%, 6%, 4% and 9% of the patients with SC, EC, MC, CCC and UC, respectively (8). In that study, SC, EC and UC groups showed lower ER (+) and PR (+) staining than our groups. Hormone receptor expression was encountered in CCC and MC groups, however, at lower rates compared with the study of Sieh et al. (7, 8).

Positive ER and PR expressions were demonstrated in the patients with MC in some studies in the literature (7,8,19). In our study, ER and PR expressions were negative in the patients with MC. These differences between the studies may be related with number of the cases, differences between IHC methods and primary antibody clones, differences between tissue follow-ups, type of MC tumor such as endocervical or intestinal type MC tumor and different assessments of the observers.

It is known that hormone receptors are typically negative in the cases with CCC. Fujimura et al. have investigated ER on 28 CCC, 36 SC, 12 EC, and 10 MC cases; they have detected no ER expression in the cases with CCC similarly with our study. They have stated that the OC phenotype will shift to CCC in the absence of ER expression because other three groups (SC, EC and MC) had ER expression (20).

In the MALOVA study, the prognostic values of ER and PR expression were investigated in OCs and ER and PR expressions were found to increase as OS prolonged. In that study, the level of ER expression was high in the high-stage disease and absence of residual disease; the level of PR expression was high in the high grade tumor and absence of residual disease (8).

Sieh et al. have determined a statistically significant correlation between OS and PR nuclear expression in the high-grade SCs, and the patients with high PR expression were found to have longer OS. In the same study, a similar correlation was found between ER expression and OS in the EC group. They attributed elongated lifetime to the direct intrinsic biological properties of hormone receptors or better treatment response in the hormone receptor positive cases. In the same study, they have suggested that PR is a more important prognostic factor in OCs based on the evidence that apoptosis is induced by PR and transactivated by ER as well as the fact that the presence of PR assures an intact ER signaling pathway (7).

In our study; there was a statistically significant negative correlation between PR (%) and patient age in the SC group and age increased as PR expression decreased. Age is a prognostic factor in the OCs and is longer in the patients below 45 years of age. This outcome of our study showed that PR may have a prognostic significance.

The studies have determined p53 expression ranging between 32-84% (mean 51%) in the OCs, mostly in the SCs (21). We detected a p53 expression in 80% of our patients compatibly with the literature.

The rationales for our results closer to upper limits are the heterogeneous distribution between our cases and the fact that 60% of our cases are SCs. High correlation between Tp53 mutation and Anti-p53 antibody [DO-7] clone number was mentioned (22) in the literature; we also used the this clone in our study.

Skirnisdottir et al. have found positive p53 staining in 25% of the patients in their study that they assessed the prognostic significance of p53 expression. The assessment of all the cases without differentiation regarding histological type, both statistically significant positive and negative correlation of p53 expression with tumor grade and PFS were found such that high p53 positive expression was found in less differentiated tumors while a longer PFS was determined in the p53 negative group. They have detected a statistically significant correlation of p53 expression with PFS and recurrent disease in the SC group such that the patients with p53 negative expression indicated a longer PFS whereas a higher disease recurrence rate was encountered in the patients with p53 positive expression. Several authors have concluded that PFS is an independent prognostic factor (22). In our study, there was a statistically significant correlation between the p53 variable and PFS; and we have concluded that this variable could be an independent prognostic factor. Besides, a high number of the cases with positive p53 expression in UCs suggest that UCs are the endpoint of the high-grade SC spectrum (23).

There are studies in the literature that investigated the possible prognostic impact of C-erbB-2 over-expression. Hogdall et al. (24) and Berchuck et al. (25) have found that the group with C-erbB-2 overexpression had a worse prognosis whereas De Graeff et al. (26) and Saxena et al. (27) have found no adverse effect of C-erbB-2 overexpression on prognosis. Buller et al. (28) have detected C-erbB-2 expression in 6 of 11 patients with familial OC and determined that 5-year survival rates were 67% and 17% in the C-erbB-2 negative and positive expression groups, respectively. Broet et al. detected C-erbB-2 expression in 16% of the patients in their study that involved 164 patients with advanced OC and observed a shorter OS and PFS in the C-erbB-2 positive expression group (29). In our study, we could not perform a statistical comparative analysis because of the limited number of the positively stained cases.

Thrall M et al. have analysed the expression of BRCA1 in 230 spontaneous patients with OC and reported that BRCA1 expression decreased in advanced cancers. Totally 152 patients with a postoperative residual tumor <1 cm were included in their study and they have detected that low levels of BRCA1 expression were associated with statistically significantly longed OS and PFS durations (30).

Swisher et al. have conducted a study on 155 patients with primary sporadic OC, they have found that BRCA1 protein loss was associated with longed OS and that a high level of BRCA1 expression was detected in 62% of recurrent cancer cases (31). On the other hand, some studies reported inconsistent outcomes with that study. Deloia et al. have found that no significant correlation was present between BRCA1 expression and patient survival in their study that analysed the prevalence of BRCA1 in 99 OC patients (32). In our study, we could not compare the correlation between BRCA1 nuclear expression and prognostic factors statistically since the number of the BRCA1 positive cases was limited.

Our study has some limitations. These limitations include limited number and heterogeneous distribution of the cases according to the groups. Since the numbers of the cases in the non-SC groups were limited, no statistical analysis could be performed in these groups.

CONCLUSION

We have found in our study that expression of estrogen receptor, expression of progesterone receptor and expression of p53 were statistically significantly correlated with metastasis to the fallopian tube, patient age and progression-free-survival, respectively, while cytoplasmic expression of BRCA1 was significantly correlated with both overall and progression-free survival in serous carcinomas. As a conclusion of our study, PR and p53 functioned as prognostic factors in serous carcinoma. The studies are currently carried out to determine the prognosis and chemotherapy responses in these patients. Taking the reported impact of ER, PR, C-erbB-2, p53 and BRCA1 on the prognosis and treatment of patients with OC into consideration, we conclude that further comprehensive studies should be carried out to confirm and improve the outcomes on that subject.

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Ethical Approval: This study was approved by Clinical Research Ethics Committee (Decision No: 2013/191) of University.

Author Contribution: All authors contributed equally to the article.

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