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Research Article

CORRELATION OF GATA3, E-CADHERIN, P53, AND KI-67 EXPRESSION WITH HISTOLOGICAL TYPE/MOLECULAR SUBTYPE AND CLINICOPATHOLOGICAL PARAMETERS IN BREAST CANCER

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Abstract: *The purpose of our study is to examine immunohistochemically the correlation of GATA binding protein 3 (GATA3), E-cadherin, p53, and Ki-67 expression with histological type/molecular subtype and clinicopathological parameters in breast cancer. 120 patients diagnosed with breast cancer were retrospectively investigated between 2018 May and 2021 January. We used the GATA3, E-cadherin, P53, Ki67 antibodies by immunohistochemical analysis in breast tumors. GATA3 was positive in 100% (107/107) of the luminal A, luminal B, and HER2 overexpressing groups and 79.9% (10/13) of the triple-negative (TN) group. It is less common in the TN group (p <0.001). Ki67 of >20% was higher in human epidermal growth factor receptor 2 (HER2) overexpressing and TN groups compared to luminal A and luminal B subtypes (p <0.05). Estrogen receptor (ER) and progesterone receptor (PR) were more frequently observed in the group with Ki67≥20% than that with Ki67 <20% (71/120, 59.2%) (p <0.05).ER/PR hormone receptors were observed more in the p53-negative group than in the p53-positive group (66/117, 56.4%) (p <0.05). There is no significant difference between molecular subtypes in terms of the incidence of E-cadherin and p53 immunoexpressions (p> 0.05). Our study demonstrated that the presence of GATA3 was found to be associated with the ER/PR receptor and tumors associated with these receptors, lumen-type breast carcinomas. In addition to its proper use for diagnostic purposes in routine surgical pathology, GATA3 will have a developmental role in breast carcinomas and prognostic significance in different molecular subtypes of tumors at the same clinical stage. Ki67 is observed at a higher rate in high-grade tumors and has a prognostic significance. No significant correlation was reported between E-cadherin and p53 and prognostic factors.*

Keywords*: breast cancer, molecular classification, GATA3, p53, Ki67, e-cadherin*

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1. Introduction

Breast cancer (BC) is the most common malignancy in women and is the leading cause of cancer-related mortality in women in developing countries [1]. In 2018, 2,088,849 (11.6%) new cases and

626,679 (6.6%) mortalities occurred because of BC around the world [2]. In Turkey, BC constitutes 22.4% of cancer cases in women with a new case number of 22,345 in 2018 and is by far the most common type of cancer. BC cases are estimated to reach 3.2 million annually by 2050 worldwide [3]. Although it is still a major cause of cancer, morbidity and mortality have largely decreased because of early detection and more effective treatments [4]. GATA3 is a transcription factor with two conserved Zinc finger DNA binding domains, encoding a protein member of the GATA family, involved in basic processes such as luminal cell differentiation, adhesion, and proliferation [5]. GATA3 has also been indicated to play a role in the development of breast, urothelial and salivary gland carcinomas [6,7][7].

E-cadherin is known as Cadherin 1 and is encoded by the CDH1 gene. Cadherin-1 is a classic member of the cadherin superfamily [8]. E-cadherin, a Ca2-dependent adhesion molecule, plays an important role in maintaining intercellular connections in normal epithelial cells in most organs [9]. In such tumors, cell separation is usually accomplished by expression or loss of E-cadherin function, which is an epithelial cell adhesion molecule [10]. Mutations in this gene are associated with gastric, breast, colorectal, thyroid, and ovarian cancers. The loss of function is considered to contribute to cancer progression by increasing proliferation, invasion, and/or metastasis [8].

P53 is a tumor suppressor gene. P53 functions to eliminate and inhibit proliferation, preventing abnormal cells, thus neoplastic development. P53 is the most common gene mutation in many cancers. P53 inactivation plays an important role in breast carcinogenesis [11]. Overall, 30%–35% of primary invasive BC are mutated. However, among BC, the prevalence of TP53 mutations depends on the molecular subtype of the disease. It is observed in ~80% of patients with the triple-negative (TN) subtype, 30% of those with Luminal A and Luminal B subtypes, and 70% of those with HER2 overexpressing types [12,13].

Ki-67, a marker of cell proliferation that is observed in all stages of the cell cycle except the G0 phase is a specific nuclear antigen. Ki67 expression is closely associated with tumor growth and prognosis. Some guidelines and international groups have concluded that the Ki-67 measurement may be important in both standard clinical practice and clinical trials [14].

The purpose of our study is to examine immunohistochemically the correlation of GATA-3, E-cadherin, p53, and Ki-67 expression with histological type/molecular subtype and clinicopathological parameters in BC. This will help predict the patient's prognosis and contribute to treatment management.

2. Materials and Methods

2.1. Cases

In this study, 120 patients diagnosed with BC at Pamukkale University Medical Faculty Pathology Department between 2018 May and 2021 January were retrospectively investigated. Demographics and other data such as age, gender, tumor diameter, and tumor localization were recorded using the descriptions in the pathology reports of the cases. Distant organ metastasis, clinical stage of the disease, family history, neoadjuvant chemotherapy status were obtained from the hospital automation system and patient follow-up files in General Surgery clinics. Information such as the clinical stage of the disease, family history, neoadjuvant chemotherapy status was obtained from the hospital automation system and General Surgery patient follow-up files.

Ethical Statement: This work was approved by Pamukkale University Ethics Committee of Non-Interventional Clinical Research. Approval number and date: 03; 02.02.2021.

2.2. Histopathological evaluation

Histopathological evaluations are based on the World Health Organization (WHO) histological classification of breast tumors [15] and Rosen's breast pathology [16]. Histological/nuclear grade and mitosis rate in all breast tumors were determined based on the modified Bloom–Richardson grading system. The histological grade was scored as follows: Score 1 (>75% the tumor area contains tubular or glandular structures), Score 2 (10% to 75% glandular/tubular structures), and Score 3 (<10% glandular/tubular structures). The nuclear atypia was scored between 1 and 3 (1 for low-grade atypia, 2 for moderate atypia, and 3 for high-grade atypia). The mitosis rate was scored based on mitotic figures per 10 high-magnification fields (40 objective lenses, Nikon Eclips E200 microscope) (1 for 0–7 mitosis, 2 for 7–14 mitosis, and 3 for>15 mitosis). The histological grade was scored as 1, 2, and 3, when the sum of scores for nuclear atypia and those for mitotic counts were 3-4-5, 6-7, and 8-9-10, respectively [15,16]

2.3. Classification of molecular subtypes

BC is a heterogeneous disease; therefore, molecular subtypes have been established based on genetic tests and/or immunohistochemical analyses. The molecular subtypes are based on the presence of ER/PR/HER-2 oncogene expression and the Ki-67 index [17]. Last updated in 2013 by the St. Gallen consensus, five subtypes have been determined:

- Luminal A (ER positive, PR>20%, HER2 negative, and Ki-67 index<20%),
- Luminal B/HER2 negative (ER positive, PR<20%, HER2 negative and Ki-67 index>20%),
- Luminal B/HER2 positive (ER positive, any PR, HER2 positive, and any Ki-67 index),
- HER2 positive (ER negative, PR negative, HER2 positive, and any Ki-67 index)
- TN (Basal-like) (ER negative, PR negative, HER2 negative, and any Ki-67 index) [18].

2.4. Immunohistochemistry (IHC):

A sample that best reflects the tumor tissue of the cases was determined. One 5-µm-sized section was taken from selected paraffin blocks to positively charged slides to study GATA3, E-cadherin, P53, and Ki67 antibodies for each case. Tissue samples taken were maintained in the incubator at 60°C for one night for deparaffinization and then stained automatically by VENTANA, Benchmark XT device using the routine procedure. The target proteins were made visible by applying GATA3 antibody (L50-823, Mouse monoclonal, Cell Marque, USA, prediluted), P53 antibody (DO-7, mouse monoclonal, Ventana, USA, prediluted) Ki67 antibody (30-9, rabbit monoclonal, Ventana, USA, prediluted), and E-cadherin antibody (36, mouse monoclonal, Ventana, USA, prediluted) on the stained sections.

Immunohistochemical expression of GATA3, E-cadherin, P53, Ki67 applied to the tumor-rich block of the cases was evaluated under optical microscopy. The nuclear expression of ≤5% of GATA3 was considered positive. The cut-off value for Ki67 was considered to be 20%. The higher value was considered positive [7]. Homogeneously stained cellular membrane positivity for e-cadherin was considered positive [19] and P53>10% nuclear staining was considered positive [20].

2.5. Statistical analysis

All analyses were conducted using the SPSS program (version 17.0, SPSS Inc., Chicago, IL, USA). Demographics and clinical data were determined and presented as a mean ± standard deviation

or frequency (percentage). The statistical significance level was set at 0.05. Mann–Whitney U test and Chi-square test were used for statistical analysis.

3. Results

3.1. Clinicopathological Findings

The study included 120 BC patients. Moreover, 117 (97.5%) were female and 3 (2.5%) were male. The age of the patients was between 31 and 92 years. The mean age was 55 ± 12.25 years. The tumor is 0.1–8 cm in diameter. Tumor diameter is 2.3 ± 1.56 cm on average. Furthermore, 64 (53.3%) were in the left breast, 53 (44.2%) in the right breast, and 3 (2.5%) in the bilateral breast. 88 (73.3%) of these patients were located in the upper outer quadrant, and 14 (11.7%) in the lower outer quadrant, 5 (4.2%) in the lower inner quadrant, and 1 (0.8%) in the retroareolar region. Note that 24 (20%) were multicentric, whereas 100 (83.3%) underwent mastectomy and 20 (16.7%) underwent breast-conserving surgery.

74 (61.7%) patients had ductal carcinoma in situ around the tumor. 48 (40%) had lymph node invasion. In fact, 22 (18.3%) were stage 1, 61 (50.8%) stage 2, 27 (22.5%) stage 3, and 8 (6.7%) stage 4. 83 (69.2%) were early stage (stage 1-2) and 35 (29.2%) were late stage (stage 3-4). Table 1 lists the distribution of the patients based on clinicopathological characteristics.

Table 1. Clinicopathological data of 120 breast carcinoma patients.

Clinicopathologic characteristics		**Total**
Age (X+sd)	55 ± 12.25	n=120
	N(%)	
Histologic type		n=120
Microinvasive carcinoma	1(%0.8)	
Invasive ductal carcinoma	92(%76.7)	
Invasive lobular carcinoma	7(%5.8)	
Tubular carcinoma	1(%1.7)	
Nöroendokrin carcinom	4(%3.3)	
Invasive micropapillary carcinoma	4(%3.3)	
Metaplastic carcinoma	1(%0.8)	
Mixed carcinoma	9(%7.5)	
Surgery type		n=120
Modified radical mastectomy	100(%83.3)	
Breast conserving surgery	20(%16.7)	
Tumour grade		n=120
Grade 1	20(%16.7)	
Grade 2	61(%50.8)	
Grade 3	37(%30.8)	
Tumour stages		n=118
pT1	22(%18.3)	
pT2	61(%50.8)	
pT3	27(%22.5)	
pT4	8(%6.7)	
Lymph node stages		n=120
pN0	55(%45.8)	
pN1	41(%34.2)	
pN2	17(%14.2)	
pN3	7(%5.8)	
Lymphovascular invasion		n=120
Yes	23(%19.2)	
No	97(%80.8)	
Neoadjuvant chemotherapy		n=119
Yes	42(%35)	
No	77(%64.2)	
Recurrence	3(%2.5)	

3.2. Comparisons of the expressions of GATA3, E-cadherin, p53, and Ki67 among different histological types of breast cancer

GATA3 was reported to be positive in 117 (97.5%) patients. The immune expression has not been observed in three patients diagnosed only with invasive ductal carcinoma. E-cadherin was reported to be positive in 110 (%95.7) patients. Positivity was observed in all tumor types (100%). However, only 7 (77.8%) patients were positive for mixed carcinoma and 4 (57.1%) for lobular carcinoma ($p < 0.05$). P53 was positive in 43 (36.8%) patients. It was negative in microinvasive carcinoma, tubular carcinoma, and metaplastic carcinoma ($p > 0.05$). Ki67 was ≤20% in 90(75%) of patients. Ki67 was<20% in microinvasive carcinoma (1, 100%) and tubular carcinoma (2, 100%). Ki67 was also ≤20% in metaplastic carcinoma (1, 100%), mixed carcinoma (4, 4.44%), invasive micropapillary carcinoma (3,75%), invasive ductal carcinoma (74, 80.4%) and invasive lobular carcinoma (5, 71.4%) ($p<0.05$).

3.3. Classification of molecular subtypes in breast cancer patients

Among the 120 patients with BC, 77 patients had Luminal A subtype, accounting for 64,2% (77/120), 26 had Luminal B subtype, accounting for 21,7% (26/120), 4 had HER-2 overexpression subtype, accounting for 3,3% (4/120), and 13 had triple-negative subtype, accounting for 10,8% (13/120).

3.4. Comparisons of the expressions of GATA3, E-cadherin, p53, and Ki67 among different molecular subtypes of breast cancer

GATA3 was positive in 100% (107/107) of the luminal A, luminal B, and HER2 overexpressing groups and 79.9% (10/13) of the TN group. It is less common in the TN group ($p < 0.05$). Ki67 of >20% was higher in HER2 overexpressing and triple-negative groups compared to luminal A and luminal B subtypes ($p < 0.05$). There is no significant difference between molecular subtypes in terms of the incidence of E-cadherin and p53 immunoexpressions ($p > 0.05$) (Table 2).

Table 2. Comparisons of the expressions of GATA3, E-cadherin, p53 and Ki67 among different molecular subtypes of breast cancer

Subtype	n	GATA3(n=120)		E-cadherin(n=115)		p53 (n=117)		Ki67	
	120	+	-	+	-	+	-	≥%20	<%20
Luminal A	77	77(%100) **	0(0)	70(%9.6)	4(%5.4)	23(%30.3)	53(%69.7)	52(%67.5)*	25(%32.5)
Luminal B	26	26(%100) **	0(0)	24(%96,0)	1(%4.0)	10(%40.0)	15(%60.0)	21(%80.8)*	5(%19.2)
HER-2 overekspressing	4	4(%100) **	0(0)	3(%100)	0(0)	2(%50.0)	2(%50.0)	4(%100) *	0(0)
Triple-negatif	13	10(%79.9) **	3(%23.1)	13(%100)	0(0)	8(%66.7)	4(%33.3)	13(%100) *	0(0)

*p<0.05 **p<0.01

3.5. Correlation between GATA3 expression and clinical pathology

GATA3 was applied to 120 patients, which was positive in 117 (97.5%). ER/PR hormone receptors were observed more in the GATA3 positive group than in the negative group (99/120, 82.5%). There was no significant correlation between GATA3 expression and age, grade, tumor size, lymph node invasion, stage, lymphovascular invasion, HER2 status, and neoadjuvant chemotherapy ($p > 0.05$) (Table 3).

3.6. Correlation between E-cadherin expression and clinical pathology

E-cadherin was applied to 115 patients. E-cadherin expression was observed in 110 (91.7%) patients. All patients with loss of E-cadherin expression were grade 2, which was not statistically significant (5/5, p>0.05). There was no significant correlation between E-cadherin and age, tumor size, ER / PR hormone receptors, lymph node invasion, stage, lymphovascular invasion, HER2 status, and neoadjuvant chemotherapy (p > 0.05) (Table 3).

Table 3. Relationship between the expression of GATA3 , E-cadherin and clinical pathology

Clinicopathologic type	GATA3 expression				E-cadherin expression			
		positive	negative			positive	negative	
	n	n(%)	n(%)	p	n	n(%)	n(%)	p
Age (years)	120			0.259	115			0.869
<50 years		41(34.2)	2(1.7)			40(34.8)	2(1.7)	
≥50 years		76(63.3)	1(0.8)			70(60.9)	3(2.6)	
Tumour grade	118			0.719	114			0.087
Grade 1		20(16.9)	0(0)			20(17,5)	0(0)	
Grade 2		59(50.0)	2(1.7)			54(47.4)	5(4.4)	
Grade 3		36(30.5)	1(0.8)			35(30.7)	0(0)	
Tumor size, cm	116			0.834	113			0.703
≤2		65(56.0)	2(1.7)			61(54.0)	3(2.7)	
2-5		36(31.0)	1(0.9)			36(31.9)	1(0.9)	
>5		12(10.3)	0(0)			11(9.7)	1(0.9)	
Lymph node stages	120			0.304	115			0362
pN0		52(43.3)	3(2.5)			52(45.2)	2(1.7)	
pN1		41(34.2)	0(0)			37(32.2)	1(0.9)	
pN2		17(14.2)	0(0)			14(12.2)	2(1.7)	
pN3		7(5.8)	0(0)			7(6.1)	0(0)	
Stage	120			0.255	114			0.131
I-II		80(67.8)	3(2.5)			78(68.4)	2(1.8)	
III-IV		35(29.7)	0(0)			31(27.2)	3(2.6)	
Lymphovascular invasion	120			0.393	115			0.226
Yes		23(19.2)	0(0)			22(19.1)	0(0)	
No		94(78.3)	3(2.5)			88(76.5)	5(4.3)	
ER/PR Status	120			**0.019***	115			0.309
Positive		99(82.5)	1(0.8)			91(79.1)	5(4.3)	
Negative		18(15.0)	2(1.7)			19(16.5)	0(0)	
HER-2 Status	120			0.322	115			0.817
Positive		29(24.2)	0(0)			83(72.2)	1(0.9)	
Negative		88(73.3)	3(2.5)			27(23.5)	4(3.5)	
Neoadjuvant chemotherapy	119			0.943	115			0.478
Yes		41(34.5)	1(0.8)			39(33.9)	1(0.9)	
No		75(63.0)	2(1.7)			71(61.7)	4(3.5)	

*p<0.05

3.7. Correlation between p53 expression and clinical pathology

P53 was applied to 117 patients, which was positive in 43 (%35.8). ER/PR hormone receptors were observed more in the p53-negative group than in the p53-positive group (66/117, 56.4%) ($p<0.05$). It was seen in 37.4% (34/91) of invasive ductal carcinoma, 42.9% (3/7) of invasive lobular carcinoma, and 31.6% (6/19) of others ($p=0.842$). There was no significant correlation between P53 expression and age, grade, tumor size, lymph node invasion, stage, lymphovascular invasion, HER2 status, and neoadjuvant chemotherapy ($p > 0.05$) (Table 4).

3.8. Relationship between the expression of Ki67 and clinical pathology

Ki67 was applied to 120 patients, which was more frequently observed in grade 2 and grade 3 tumors than grade 1 tumors (45/120, 38.1%; 34/120, 28.8%) ($p = 0.002$). ER/PR hormone receptors were more frequently observed in the group with Ki67≥20% than that with Ki67 <20% (71/120, 59.2%) ($p <0.05$). There was no significant correlation between Ki67 expression and age, tumor size, lymph node invasion, stage, lymphovascular invasion, HER2 status, and neoadjuvant chemotherapy ($p < 0.05$) (Table 4).

Table 4. Relationship between the expression of p53, Ki67 and clinical pathology

Clinicopathologic type	p53 expression				Ki67 expression			
		positive	negative			positive	negative	
	n	n(%)	n(%)	p	n	n(%)	n(%)	p
Age (years)	117			0.239	120			0.227
<50 years		18(15.4)	23(19.7)			35(29.2)	8(6.7)	
≥50 years		25(21.4)	51(43.6)			55(45.8)	22(18.3)	
Tumour grade								
Grade 1		5(4.3)	15(13.0)			10(8.5)	10(8.5)	
Grade 2		20(17.4)	40(34.8)			45(38.1)	16(13.6)	
Grade 3		18(15.7)	17(14.8)			34(28.8)	3(2.5)	
Tumor size, cm	113			0.664	116			0.143
≤2		24(21.2)	41(36.3)			47(40.5)	20(17.2)	
2-5		13(11.5)	23(20.4)			32(27.6)	5(4.3)	
>5		6(3.5)	6(5.3)			8(6.9)	4(3.4)	
Lymph node stages	117			0.191	120			0.631
pN0		16(13.7)	37(31.6)			45(35.8)	12(10.0)	
pN1		15(12.8)	25(21.4)			28(23.3)	13(10.8)	
pN2		7(6.0)	10(8.5)			13(10.8)	4(3.3)	
pN3		5(4.3)	2(1.7)			6(5.0)	1(0.8)	
Stage	115			0.222	118			0.453
I-II		27(23.5)	53(46.1)			61(51.7)	22(18.6)	
III-IV		16(13.9)	19(16.5)			28(23.7)	7(5.9)	
Lymphovascular invasion	117			0.087	120			0.141
Yes		12(10.3)	11(9.4)			20(16.7)	3(2.5)	
No		31(26.5)	63(53.8)			70(15.8)	27(22.5)	

Table 4 *continued.*

Clinicopathologic type	p53 expression				Ki67 expression			
		positive	negative			positive	negative	
	n	n(%)	n(%)	p	n	n(%)	n(%)	p
ER/PR Status	117			**0.037***	120			**0.024***
Positive		32(27.4)	66(56.4)			71(59.2)	29(20.0)	
Negative		11(9.4)	8(6.8)			19(15.8)	1(0.8)	
HER-2 Status	117			0.442	120			0.268
Positive		12(10.3)	16(13.7)			24(20.0)	5(4.2)	
Negative		31(26.5)	58(49.6)			66(55.0)	25(20.8)	
Neoadjuvant chemotherapy	116			0.053	119			0.058
Yes		20(17.2)	21(18.1)			36(30.3)	6(5.0)	
No		23(19.8)	52(44.8)			54(45.4)	23(19.3)	

*p<0.05

4. Discussion

In our study, the presence of GATA3 was found to be associated with the ER/PR receptor and tumors associated with these receptors. Unlike GATA3, ER/PR hormone receptors were more common in the p53-negative group than the p53-positive group. Moreover, Ki67 proliferation was observed in higher-grade tumors. High expression of GATA3 in primary invasive BC has been confirmed by the limited number of studies showing that it is associated with smaller tumor size and lower nuclear grade, ER/PR positive tumors. Consequently, the loss of GATA3 expression was reported to be associated with adverse prognostic outcomes [5].

GATA3 and ER are closely associated and have a positive correlation between GATA3 and ER expression in breast cancers. Although some studies have suggested a prognostic or predictive role for GATA3 expression, it can be considered as a marker to prove the breast origin of metastatic cancer. The frequency of GATA-3 expression ranges from 47% to 100% in all breast adenocarcinomas [21]. It was reported to be positive in 117/120 (97.5%) of our patients.

E-cadherin expression is mostly observed in epithelial cells [9]. At the end of the previous century, the essential role of E-cadherin during normal epithelial function as a tumor suppressor has been demonstrated. In the important studies of Birchmeier and Van Roy groups, it was shown that inhibition of E-cadherin induces dissociation and invasion of cancer cells [22]. Another study showed clinical relevance by demonstrating that the BC subtype called invasive lobular carcinoma is characterized by loss of expression of E-cadherin, whereas most other BC subtypes are expressed E-cadherin [23].

There is a limited number of data on differentiated E-cadherin status in BC subtypes in molecular systems. Most of the available studies are studies that refer to the classical histopathology of breast cancer, not molecular classification [8]. The study by Margan et al. [8] demonstrated that the loss of E-cadherin is associated with the grade of Luminal A-type tumors [8]. In our study, the loss of E-cadherin expression was observed in luminal A and luminal B types, and all of these cases were grade 2. E-cadherin, interfering with other metastasizing factors such as EGFR- or Akt/STAT-mediated pathway, has been reported as the main cause of induction of epithelial mesenchymal transmission in TN cancers and has been tested in vitro as a potential therapeutic target [12]. In our study, the loss of E-cadherin expression was not observed in TN tumors.

Abnormal p53 expression was detected in 29% (193/673) of tumors, respectively [25]. Overall, 30%–35% of primary invasive BC are mutated. However, among BC, the prevalence of TP53 mutations depends on the molecular subtype of the disease. It is observed in ~80% of patients with the TN subtype, 30% of those with luminal A and luminal B subtypes, and 70% of those with HER2 overexpressing types [12, 24]. In our study, although it was not statistically significant, p53 was more common in HER2 positive and TN groups than in luminal groups. Breast cancers with high p53 expression detected by IHC are characterized by a poor prognosis and a metastatic phenotype [12].

The absence of a targeted therapy combined with intrinsic aggressiveness means that patients with TNBC tend to have a poor outcome [25]. Another attractive feature of mutant p53 as a therapeutic target in breast cancer is that the gene is mutated in almost 90% of patients with BC metastases in the brain [26,27]. In our study, although it was not statistically significant, p53 was more common in HER2 positive and TN groups than in luminal groups.

In the literature review, the high index Ki67 is considered an unfavorable factor affecting tumor progression and is associated with a poorer prognosis [14, 28, 29]. The study by Li et al reported that higher expression of Ki67 was associated with a higher degree of malignancy, a faster growth rate of tumor cells, a higher degree of invasion and metastasis, and poorer clinical prognosis [30]. In our study, the higher expression of Ki67 was found to be associated with high-grade tumors.

Clinical studies confirmed that BC is characterized by high heterogeneity, and disease prognosis can significantly differ, even if the clinical stage and treatment method used for patients are the same. Therefore, it is particularly important to determine how to predict prognosis in patients during treatment [30]. Detection of GATA3, E-cadherin, p53, and Ki67 protein expressions in BC patients helps to evaluate the treatment effect and prognosis. Therefore, multiple biological markers detected through immunohistochemistry provide additional reference standards for the clinical treatment of patients with BC. Thus, it comprises a solid scientific basis for the correct estimation of its prognosis.

The limitation of our study is that it included the patients with breast carcinoma diagnosed in the last 2 years because GATA3 immunohistochemistry has been performed in our routine practice for the last two years. Therefore, the survival times of the patients could not have been examined. However, prognostic factors affecting survival time have been evaluated. These cases can be re-evaluated by considering their survival times with a higher number of cases in the future.

5. Conclusion

As a result, GATA3 is specifically expressed in lumen-type breast carcinomas. It can also be seen in TN and HER-2 positive breast carcinomas. In addition to its diagnostic use, GATA3 has a developmental role in breast carcinomas and prognostic importance in different molecular subtypes of tumors. Ki67 is seen at a higher rate in high-grade tumors and has prognostic significance. No significant relationship was reported between E-cadherin and p53 and prognostic factors.

Conflict of interest: The authors declare that they have no conflict of interest.

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Ethical Statement: This work was approved by Pamukkale University Ethics Committee of Non-Interventional Clinical Research. Approval number and date: 03; 02.02.2021. The study protocol was conducted according to the Declaration of Helsinki.

The compliance to the Research and Publication Ethics: This study was carried out in accordance with the rules of research and publication ethics.

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