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Mutation-Associated P53 Immunohistochemical Patterns in Invasive Breast Carcinoma: Clinicopathological Correlations

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Abstract:

Objective: TP53 mutations are the most common genetic changes in human malignancies. Recent studies suggest that specific p53 immunohistochemical staining patterns may reflect underlying TP53 mutations and have prognostic significance. This study aimed to evaluate the predictive and prognostic importance of p53 immunohistochemical staining patterns in invasive breast carcinoma.

Methods: A total of 345 patients with invasive breast carcinoma were included in the present study. p53 immunohistochemistry was evaluated and categorized as wild-type, overexpression, null, cytoplasmic or equivocal. Clinicopathological variables were compared statistically.

Results: Wild-type p53 staining was observed in 243 (70.4%)cases, whereas abnormal p53 staining were detected in 90 (26.1%) cases. Abnormal p53 expression were associated with a younger patient age (median 48 vs. 52 years, P=0.041), larger tumor size (29 vs. 22 mm, P<0.001), higher histological grade (P<0.001) and higher Ki-67 levels (P<0.001). Hormone receptor negativity was significantly more frequent in tumor with abnormal p53 staining (ER negativity: 63.3% vs. 9.1%; PR negativity: 65.6% vs. 21.0%; both P<0.001). HER2 positivity was also more prevalent in the abnormal p53 group (P<0.001). Triple-negative breast cancer was significantly more prevalent in tumor with abnormal p53 expression (43.3% vs. 6.6%, P<0.001). Additionally, lymph node metastasis was significantly more prevalent in the abnormal p53 group (75.6%vs.56.8%, P=0.003).

Conclusion: Abnormal p53 staining patterns are strongly associated with adverse clinicopathological features and aggressive molecular subtypes in invasive breast carcinoma. These results suggest that p53 staining patterns could be used as a practical surrogate marker to reflect tumor aggressiveness and provide prognostic information in routine pathological evaluations.

Keywords: Breast Carcinoma, P53 Staining, Immunochemistry, Mutation

Breast cancer is among the most common malignancies in women worldwide, representing an important cause of morbidity and mortality in the world [1]. Because of marked heterogeneity of breast cancer due to clinical course and treatment response, there is an increasing recognition of the importance of molecular markers in diagnosis, prognosis and treatment planning. Classic markers such as the estrogen receptor (ER), progesterone receptor (PgR), human epidermal growth

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factor receptor 2 (HER2), and Ki-67 play as key role in guiding treatment; however, the complexity of tumor biology requires the necessity of searching additional markers [2]. It is expected that these markers will contribute to be understood breast cancer pathogenesis and contribute to the classification of the disease according to its molecular subtypes.

TP53, one of the tumor suppressor genes, is located at the 17p13.1 locus and is approximately 16–20 kb in length [3–5]. The p53 protein, encoded by this gene, is a transcription factor that plays an essential role in regulating the cell cycle, the response to DNA damage, apoptosis, senescence, and genomic stability [6, 7]. It is due to these characteristics that p53 is frequently referred to as the "guardian of the genome". p53 mutations are the most common gene mutations in human malignancies, and they are reported in approximately 20–35% of breast cancers [8-10]. The frequency of p53 mutation varies according to breast cancer molecular subtype; they are notably higher in triple-negative and HER2-enriched tumor [7, 9, 10]. In the absence of cellular abnormalities p53 is expressed at low levels as an immunohistochemical marker, and its detection is difficult [5]. However, in the presence of mutation, the protein's half-life increases, and as a result of nuclear accumulation, it becomes detectable by immunohistochemistry [3, 4]. Nevertheless, the correlation between p53 immunohistochemical expression and gene mutation is unclear, with particular staining patterns demonstrating a strong association with mutation [11]. In recent years, increasing research proposed that the evaluation of p53 immunohistochemical staining patterns should not be limited to a binary classification as either positive or negative. Instead, a more comprehensive approach proposes the categorization of patterns into various groups, including wild-type, overexpression, null pattern, cytoplasmic, and equivocal staining [12, 13]. These staining patterns have been studied in ovarian, endometrial, and vulvar carcinomas; while Köbner standardized this classification for ovarian serous carcinomas, the classification remains unclear outside of ovarian carcinoma [12-14]. While the predictive and prognostic value of p53 mutations has been investigated in breast cancer, predictive and prognostic value of immunohistochemical staining patterns remains limited [15, 16]. The objective of this study was to investigate the predictive and prognostic value of previously defined abnormal p53 staining patterns in breast carcinoma.

METHODS

A total of 520 cases of breast cancer diagnosed between January 2020 and July 2025 were reviewed. Subsequently, cases lacking a mastectomy specimen, those for which clinical and radiological data were unavailable, and those in which the immunohistochemical markers specified in the methods section were not applied were excluded from the study. The study incorporated a total of 345 cases that satisfied the specified criteria. In each patient, both diagnostic tru-cut biopsy specimens and subsequent mastectomy specimens were available for analysis. Three to four micron thick sections were obtained from formalin-fixed, paraffin embedded tissue (FFPE) samples, and stained with hematoxylin and eosin (H&E). The H&E-stained slides were then subjected to review by two pathologists. Initial evaluation of the cases was conducted to ascertain their histological type and grade, utilizing the Nottingham histological scoring system. The clinical information pertaining to the patients' age, tumor size, tumor location, axillary lymph node involvement, and distant metastasis was obtained from the hospital information system.

For the purpose of immunohistochemical analysis, 4 micrometer thick sections were taken from FFPE breast tru-cut biopsies and mounted on slides. The tissue sections were incubated at a temperature of 95°C. The sections were then subjected to an antigen retrieval procedure for 52 minutes (Cell Conditioning 1; Ventana). Following this procedure, the specimens were analyzed using an automated staining system (Ultra-Benchmark, Ventana, Roche Diagnostics) to determine the expression of ER (clone SP1; Ventana Medical Systems), PgR (clone 1E2; Ventana Medical Systems), HER2 (clone 4B5; Ventana Medical Systems), Ki-67 (MIB-1, Ventana Medical Systems), and p53 (clone DO-7, Ventana Medical Systems). Consequently, a 16-minute counterstaining process was conducted using hematoxylin, subsequently followed by background staining with diaminobenzidine (DAB). The results of the ER, PgR,

HER2, Ki-67, and p53 immunohistochemistry tests for the cases were evaluated by two pathologists.

ER, PR, and HER2 were evaluated in accordance with the criteria delineated in the 5th Edition of the WHO Breast Tumours [1]. Accordingly, staining more than 1% was considered as positive result for both ER and PR.

The following criteria were used for HER2:

•3+: Complete, intense circumferential membrane staining in >10% of tumor cells;

•2+: Weak to moderate complete membrane staining was observed in >10% of tumor cells.

•1+: Incomplete membrane staining faint/barely in >10% of tumor cells.

•Ultra-low: Incomplete membrane staining faint/barely in <10% of tumor cells.

•0: No staining is observed.

Cases with equivocal (2+) HER2 staining were confirmed using the HER2 Dual-Silver in situ hybridization (SISH) method (Ventana Medical Systems).

The P53 immunohistochemical evaluation was conducted in accordance with the classification system delineated by Kobel *et al*. [12]. Accordingly;

1. Wild-type staining pattern: variable nuclear positivity (Figure 1).

2. Abnormal staining pattern: Overexpression: manifestation of strong nuclear positivity in >80% of tumor cells (Figure 2a).

3. Null pattern: absence of staining in tumor cells in tissue containing an internal control (Figure 2b).

4. Cytoplasmic: cytoplasmic staining without widespread strong nuclear positivity (Figure 2c).

5. Equivocal: The presence of strong nuclear positivity was observed in a proportion of tumor cells that ranged from 50% to 80% (Figure 2d).

Statistical Analysis

The relationship between p53 staining patterns and various clinicopathological parameters was examined. These parameters included patient age, tumor size, histological grade, and the immunohistochemical staining of ER, PgR, HER2, and Ki-67. Molecular subtype, axillary lymph node involvement and distant metastasis were also considered. Statistical analyses were conducted using R statistical software (version 4.5.0, R Foundation for Statistical Computing, Vienna, Austria). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. As most continuous variables did not follow a normal distribution, they were summarized as median values with interquartile ranges (IQRs). Categorical variables were reported as frequencies and percentages. Patients

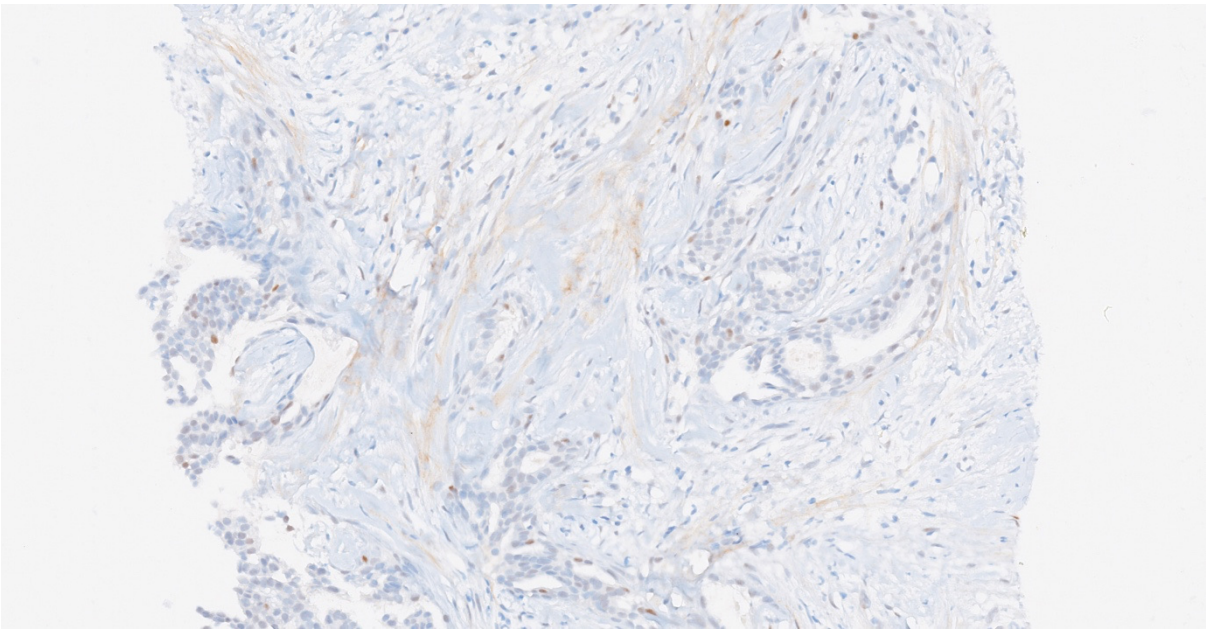

FIGURE 1. Wild-type staining pattern on p53 immunohistochemistry (×20).

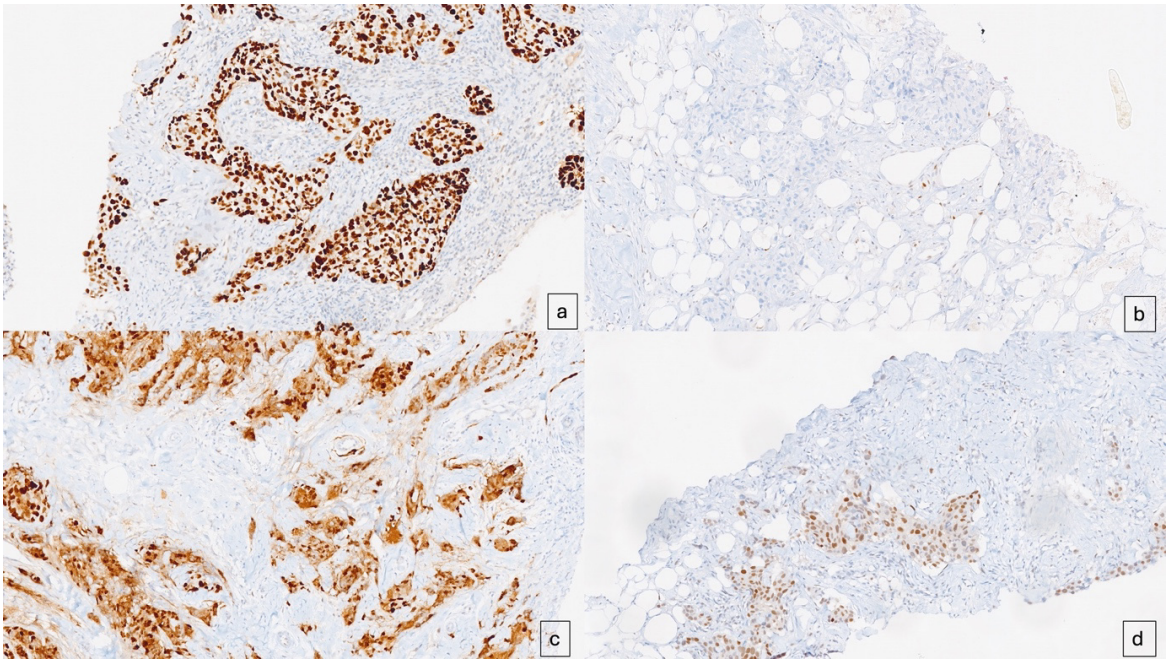

FIGURE 2. Abnormal p53 staining patterns. (a) Overexpression (×20), (b) Null pattern (×10), (c) Cytoplasmic staining pattern (×20) and (d) Equivocal staining pattern (×10).

were divided into two groups according to their p53 expression status: wild-type and abnormal. The abnormal p53 category comprised overexpression, complete absence (null pattern) and cytoplasmic staining. Equivocal cases were excluded from further comparative analyses. The Mann–Whitney U test was used to analyze continuous variables between groups for statistical comparisons. Categorical variables were evaluated using chi-squared test or Fisher's exact test. A P-value of less than 0.05 was considered statistically significant.

RESULTS

The study comprised a total of 345 patients diagnosed with invasive breast carcinoma. In accordance with the results of p53 immunohistochemical staining patterns, 243 (70.4%) cases demonstrated wild-type expression, 67 (19.4%) cases revealed overexpressions, 19 (5.5%) cases exhibited a null staining pattern, 4 (1.2%) cases displayed cytoplasmic staining, and 12 (3.5%) cases were categorized as equivocal (Table 1). The median age of patients was found to be similar across p53 staining pattern groups. Cases exhibiting abnormal p53 staining were found to have a significantly higher histological grade in comparison to those cases with wild-type p53 staining. Tumors with abnormal p53 staining patterns tended to demonstrate larger tumor size (22 mm vs. 29 mm) and higher Ki-67 levels compared with tumors showing wild-type p53 expression. A marked divergence in hormone receptor status was observed between the groups. ER negativity and PR negativity were more frequently observed in tumors with abnormal p53 staining patterns, whereas the majority of tumors with wild-type p53 expression were hormone receptor positive (Table 1).

When molecular subtypes were evaluated, Luminal A tumors were predominantly associated with wild-type p53 expression, while triple-negative and HER2-enriched subtypes were more frequently observed among tumors with abnormal p53 staining patterns.

Lymph node metastasis was observed in 56.8% of tumors with wild-type p53 expression, whereas higher proportions of lymph node involvement were observed among tumors with abnormal p53 staining patterns (Table 1).

For the purpose of comparative analysis, cases were grouped as wild-type p53 (n=243) and abnormal p53 expression (n=90), with the exclusion of cases that were equivocal.

TABLE 1. Clinicopathological Characteristics According to p53 Staining Pattern

Variable	Wild type (n=243)	Overexpression (n=67)	Null (n=19)	Cytoplasmic (n=4)	Equivocal (n=12)
Age (years)	52 (44–61)	48 (41–56)	48 (44–58)	52 (47–53)	53 (42–64)
Tumor size (mm)	22 (15–30)	29 (20–45)	30 (23–43)	27 (20–35)	32 (25–40)
Histological grade					
Grade I	56 (23%)	2 (2.9%)	0	0	0
Grade II	107 (44%)	13 (19.4%)	2 (10.5%)	0	4 (33.3%)
Grade III	80 (33%)	52 (77.7%)	17 (90.5%)	4 (100%)	8 (66.7%)
Ki-67 (%)	0 (0–0)	0 (0–0)	1 (0–1)	0 (0–1)	1 (0–1)
ER status					
Negative	22 (9.1%)	39 (58.2%)	16 (84.2%)	2 (50.0%)	7 (58.3%)
Positive	221 (90.9%)	28 (41.8%)	3 (15.8%)	2 (50.0%)	5 (41.7%)
PR status					
Negative	51 (21.0%)	41 (61.2%)	16 (84.2%)	2 (50.0%)	8 (66.7%)
Positive	192 (79.0%)	26 (38.8%)	3 (15.8%)	2 (50.0%)	4 (33.3%)
HER2 (CERB-2)					
Negative	181 (74.5%)	37 (55.2%)	14 (73.7%)	2 (50.0%)	6 (50.0%)
1+	10 (4.1%)	2 (3.0%)	0	0	0
3+	25 (10.3%)	26 (38.8%)	5 (26.3%)	2 (50.0%)	6 (50.0%)
Ultra-low	27 (11.1%)	2 (3.0%)	0	0	0
Molecular subtype					
Luminal A	88 (36.2%)	1 (1.5%)	0	1 (25.0%)	0
Luminal B HER2−	114 (46.9%)	15 (22.4%)	2 (10.5%)	1 (25.0%)	2 (16.7%)
Luminal B HER2+	18 (7.4%)	12 (17.9%)	2 (10.5%)	0	3 (25.0%)
HER2-enriched	7 (2.9%)	14 (20.9%)	3 (15.8%)	0	3 (25.0%)
Triple-negative	16 (6.6%)	25 (37.3%)	12 (63.2%)	2 (50.0%)	4 (33.3%)
Lymph node status					
Positive	138 (56.8%)	51 (76.1%)	13 (68.4%)	4 (100%)	8 (66.7%)
Negative	105 (43.2%)	16 (23.9%)	6 (31.6%)	0	4 (33.3%)

Data are shown as median (interquartile range [IQR]) or n (%) where appropriate. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

In this analysis, tumors exhibiting abnormal p53 expression were associated with a younger patient age (P=0.041), larger tumor size (P<0.001), higher histological grade (P<0.001), and higher Ki-67 levels (P<0.001) (Table 2).

Furthermore, ER-negative and PR-negative status were found to be significantly more prevalent in tumors exhibiting abnormal p53 expression (both P<0.001). The HER2 expression status exhibited significant variation between the groups (P<0.001). With regard to molecular subtypes, triple-negative breast cancer was significantly more prevalent in the abnormal p53 group (43.3%) in comparison with the wild-type group (6.6%), whereas Luminal A tumors were predominantly observed in the wild-type group (36.2%) (P<0.001).

Finally, lymph node metastasis was shown to be significantly more prevalent in tumors exhibiting

TABLE 2. Association Between Abnormal p53 Expression and Clinicopathological Variables

Variable	Wild type (n=243)	Abnormal p53 (n=90)	P-value
Age (years)	52 (44–61)	48 (41–56)	**0.041**
Tumor size (mm)	22 (15–30)	29 (20–45)	**<0.001**
Histological grade			
Grade I	56 (23%)	2 (2.2%)	**<0.001**
Grade II	107 (44%)	15 (16.6%)	
Grade III	80 (33%)	73 (81.2%)	
Ki-67 (%)	0 (0–0)	0 (0–1)	**<0.001**
ER status			**<0.001**
Negative	22 (9.1%)	57 (63.3%)	
Positive	221 (90.9%)	33 (36.7%)	
PR status			**<0.001**
Negative	51 (21.0%)	59 (65.6%)	
Positive	192 (79.0%)	31 (34.4%)	
HER2 (CERB-2)			**<0.001**
Negative	181 (74.5%)	54 (60.0%)	
1+	10 (4.1%)	2 (2.2%)	
3+	25 (10.3%)	32 (35.6%)	
Ultra-low	27 (11.1%)	2 (2.2%)	
Molecular subtype			**<0.001**
Luminal A	88 (36.2%)	1 (1.1%)	
Luminal B HER2−	114 (46.9%)	18 (20.0%)	
Luminal B HER2+	18 (7.4%)	15 (16.7%)	
HER2-enriched	7 (2.9%)	17 (18.9%)	
Triple-negative	16 (6.6%)	39 (43.3%)	
Lymph node status			**0.003**
Positive	138 (56.8%)	68 (75.6%)	
Negative	105 (43.2%)	22 (24.4%)	

Data are shown as median (interquartile range [IQR]) or n (%) where appropriate. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.
Statistically significant P-values in bold.

abnormal p53 expression in comparison to those demonstrating wild-type p53 expression (75.6% vs. 56.8%, P=0.003).

DISCUSSION

The p53 mutation has been identified as the most prevalent mutation in human cancers, with prevalence rates of up to approximately 30% in breast cancers being reported. The role of p53 in tumor development is explained by two mechanisms: the loss of the tumor -suppressor function of the mutated p53 (loss of function) or the acquisition of oncogenic activity (gain of function) [6, 8]. The majority of p53 mutations are associated with the DNA-binding domain of the gene,

often resulting in missense mutations [8, 17]. Missense mutations are most commonly found in exons 5–8 (81%) [10]. P53 mutations have been associated with poor clinical and pathological features in various human cancers, including breast cancer [11, 18]. However, the implementation of genetic testing in routine laboratory practice is challenging due to the complexity, cost, and specific infrastructure requirements. Consequently, the potential of p53 immunohistochemistry in detecting p53 mutations, and its subsequent application in predicting prognosis and clinical-pathological characteristics, has become a subject of interest.

Despite the utilization of a broad spectrum of threshold values for p53 staining patterns (1–90%) [19-23], Köbel *et al*. [12] have standardized them for ovarian high grade serous carcinoma, delineating overexpression, null, and cytoplasmic staining patterns as being associated with p53 mutations. While an 80% threshold is conventionally employed for expression analysis, a recent study has proposed the use of this threshold for cytoplasmic staining as well [24]. While the majority of cases exhibiting p53 mutations are characterized by overexpression, cytoplasmic staining has been documented in 2–3% of cases in studies conducted on various tumors [13, 25]. In the present study, 74.4% of cases exhibiting abnormal p53 staining were found to be overexpressing, while cytoplasmic staining was observed in a mere 4.4% of cases. The null pattern was observed in 22% of cases. In studies comparing p53 mutations with immunohistochemical expression, the overexpression pattern has frequently been associated with missense mutations, while the null pattern has been associated with truncating mutations that involves frameshift, nonsense, and splice-site mutations. The results of this study demonstrate that the functional consequences of p53 mutations can be reflected at the immunohistochemical level [13]. As is well documented in the relevant literature, mutant p53 proteins resulting from missense mutations accumulate in the nucleus, creating an overexpression pattern, whereas truncating mutations prevent the synthesis of functional protein, resulting in a null pattern [26]. Despite the clarity of these patterns, certain cases of over-expression, typically exceeding 50% but falling short of the 80% threshold, have been described as equivocal in some studies. Genetic studies have indicated that the majority of these cases are characterized by missense mutations, and this discrepancy can be explained by the degradation of mutant p53 due to poor or insufficient stabilization [11, 12]. It has also been reported that the fact that the regions bound by mutant p53 differ from those bound by immunohistochemistry may contribute to this result [11, 12, 24, 27]. In the present study, 12 cases were deemed to be equivocal. The majority of these cases were ER- and PR-negative, the majority exhibited a high histological grade, none were Luminal A cases, and the average tumor size was similar to that of cases showing abnormal staining. These findings support the hypothesis that cases exhibiting equivocal staining demonstrate biological behaviour similar to those showing abnormal staining.

In the present study, the abnormal staining pattern was found to be significantly associated with high Nottingham grade, negative ER and PR results, HER2 positivity, and higher Ki-67. An examination of the relationship between molecular subtypes and p53 revealed that abnormal p53 staining was more prevalent, particularly in the HER2-enriched and triple-negative subtypes. In the extant literature, p53 mutations have been reported as being common in the triple-negative subtype [7, 9, 10]. It has been reported that 80% of triple-negative cancers, 10% of Luminal A cases, 70% of Luminal B cases, and 70% of HER2-enriched cases exhibit p53 mutations. In the course of the present study, an investigation was conducted into the association between abnormal p53 expression subpatterns and the triple-negative subtype, in comparison to other staining patterns. The null pattern was found to be more frequently associated with the triple-negative subtype than other staining patterns. It has been established through previous studies that the null pattern is associated with high Nottingham grade and the triple-negative subtype. This suggests that this staining pattern may indicate a more unfavourable biology compared to overexpression from a prognostic perspective [11]. Another study demonstrated that the null pattern is associated with PR negativity; in our study as well, the null pattern showed a higher association with ER and PgR negativity compared to other abnormal staining patterns.

In our study, when abnormal p53 staining was

compared to wild-type staining, it was found to be significantly associated with larger tumor size, axillary lymph node metastasis at diagnosis, and distant metastasis, and studies in the literature have also reported that mutant p53 staining in tru-cut biopsies can predict lymph node and distant metastasis [10, 11, 18]. When examining the subtypes of abnormal staining patterns, it has been reported that the null staining pattern may be associated with a poorer prognosis compared to cases showing overexpression and is more frequently associated with BRCA mutations [11, 28].

From a clinical perspective, it has been reported that p53 mutations are associated with treatment resistance in Luminal cancers [17, 29]. Consequently, it is hypothesized that the presence of an abnormal p53 staining pattern in biopsies conducted at the time of diagnosis may serve as a prognostic indicator for treatment response. In the context of Luminal A cancers, the presence of p53 mutations has been demonstrated to be associated with a poor prognosis and a tendency towards treatment resistance. Furthermore, the high prevalence of p53 mutations in various human cancer types has led to the suggestion that it could serve as a therapeutic target [30]. For triple-negative breast cancer, the limited availability of targeted treatment options and the poor prognosis increase the significance of p53 as a potential biomarker and therapeutic target in this group [9, 10, 31]. Studies demonstrate that p53 is almost always as mutated in metastatic foci of triple-negative breast cancer, because of that establishing p53 as a promising therapeutic target for further investigation [31].

Strengths and Limitations

The study's most significant strength is its extensive sample size, which encompassed 345 cases, including a sufficient number of cases from each molecular subtype. Additionally, it employed a standardized methodology, which enhances the study's internal validity. The retrospective and single-centre study design may limit the generalizability of the findings. P53 immunohistochemical staining patterns were utilized as an indirect marker for TP53 mutation status, with molecular validation (e.g. sequence analysis) not being performed. Despite the evaluation of staining patterns by two pathologists, the possibility of interobserver variability remains unresolved.

CONCLUSION

In conclusion, p53 immunohistochemical expression patterns provide significant insights into tumor biology in breast cancer. The correlation of expression levels with specific mutation types and aggressive clinicopathological features lends further support to the value of p53 as a prognostic and potentially predictive biomarker. Nevertheless, the standardization of evaluation criteria, in conjunction with the interpretation of immunohistochemistry alongside molecular analyses, will render the clinical use of p53 more reliable.

Ethics Approval and Consent to Participate

This study was approved by the Gaziantep University Non-Interventional Clinical Research Ethics Committee. (Decision No: 2025/290; date: 08.10.2025). All procedures were conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments. Informed consent was waived because of the retrospective nature of the study and the analysis used anonymous clinical data.

Data Availability

All data generated or analyzed during this study are included in this published article. The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

Authors' Contribution

Study Conception: EU, EBG; Study Design: EU; Supervision: EU; Funding: EU; Materials: EU, EBG; Data Collection and/or Processing: EU, EBG, TE; Statistical Analysis and/or Data Interpretation: EU, İT; Literature Review: EU, EBG; Manuscript Preparation: EU, EBG, İT; and Critical Review: EU.

Conflict of Interest

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Generative Artificial Intelligence Statement

The author(s) declare that no artificial intelligence-based tools or applications were used during the preparation process of this manuscript. The all content of the study was produced by the author(s) in accordance with scientific research methods and academic ethical principles.

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REFERENCES

1. World Health Organization. WHO classification of tumours of the breast. 5th ed. Lyon: IARC; 2019.
2. Zeng L, Li W, Chen CS. Breast cancer animal models and applications. Zool Res. 2020;41(5):477-494. doi: 10.24272/j.issn.2095-8137.2020.095.
3. Wang H, Zhang H, Zhou J, et al. Study on the correlation between Ki-67, P53, and CA153 and axillary lymph node metastasis in breast cancer. Chin Gen Med. 2019;17(9):1518-1522. doi: 10.16766/j.cnki.issn.1674-4152.000985.
4. Mantovani F, Walerych D, Sal GD. Targeting mutant p53 in cancer: a long road to precision therapy. FEBS J. 2017;284(6):568-572. doi: 10.1111/febs.13948.
5. Sullivan KD, Galbraith MD, Andrysik Z, Espinosa JM. Mechanisms of transcriptional regulation by p53. Cell Death Differ. 2018;25(1):133-143. doi:10.1038/cdd.2017.174.
6. Wang H, Guo M, Wei H, Chen Y. Targeting p53 pathways: mechanisms, structures, and advances in therapy. Signal Transduct Target Ther. 2023;8(1):92. doi: 10.1038/s41392-023-01347-1.
7. Børresen-Dale AL. TP53 and breast cancer. Hum Mutat. 2003;21(3):292-300. doi:10.1002/humu.10174.
8. Marvalim C, Datta A, Lee SC. Role of p53 in breast cancer progression: an insight into p53-targeted therapy. Theranostics. 2023;13(4):1421-1442. doi: 10.7150/thno.81847.
9. Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumors. Nature. 2012;490:61-70. doi: 10.1038/nature11412.
10. Shah SP, Roth A, Goya R, et al. The clonal and mutational evolution spectrum of primary triple-negative breast cancers. Nature. 2012;486:395-399. doi: 10.1038/nature10933.
11. Alsner J, Jensen V, Kyndi M, et al. A comparison between p53 accumulation determined by immunohistochemistry and TP53 mutations as prognostic variables in tumors from breast cancer patients. Acta Oncol. 2008;47(4):600-607. doi: 10.1080/02841860802047411.
12. Kobel M, Piskorz AM, Lee S, et al. Optimized p53 immunohistochemistry is an accurate predictor of TP53 mutations in ovarian carcinoma. J Pathol Clin Res. 2016;2(4):247-258. doi: 10.1002/cjp2.53.
13. Matsumoto N, Manrai P, Rottmann D, et al. Correlative assessment of p53 immunostaining patterns and TP53 mutation status by next-generation sequencing in high-grade endometrial carcinomas. Int J Gynecol Pathol. 2023;42(6):567-575. doi: 10.1097/PGP.0000000000000930.
14. Tessier-Cloutier B, Kortekaas KE, Thompson E, et al. Major p53 immunohistochemical patterns in in situ and invasive squamous cell carcinomas of the vulva and correlation with TP53 mutation status. Mod Pathol. 2020;33(8):1595-1605. doi: 10.1038/s41379-020-0524-1.
15. Bertheau P, Lehmann-Che J, Varna M, et al. p53 in breast cancer subtypes and new insights into response to chemotherapy. Breast. 2013;22(Suppl 2):S27-S29. doi: 10.1016/j.breast.2013.07.005.
16. Duffy MJ, Synnott NC, Crown J. Mutant p53 in breast cancer: potential as a therapeutic target and biomarker. Breast Cancer Res Treat. 2018;170(2):213-219. doi: 10.1007/s10549-018-4753-7.
17. Ungerleider NA, Rao SG, Shahbandi A, et al. Breast cancer survival predicted by TP53 mutation status differs markedly depending on treatment. Breast Cancer Res. 2018;20(1):115. doi: 10.1186/s13058-018-1044-5.
18. Li JP, Zhang XM, Zhang Z, et al. Association of p53 expression with poor prognosis in patients with triple-negative invasive ductal breast carcinoma. Medicine. 2019;98(18):e15449. doi: 10.1097/MD.0000000000015449.
19. Holstege H, Joosse SA, van Oostrom CT, et al. High incidence of protein-truncating TP53 mutations in BRCA1-related breast cancer. Cancer Res. 2009;69(8):3625-3633. doi: 10.1158/0008-5472.CAN-08-3426.
20. Anderson SA, Bartow BB, Harada S, et al. P53 protein expression patterns associated with TP53 mutations in breast carcinoma. Breast Cancer Res Treat. 2024;207(1):213-222. doi: 10.1007/s10549-024-07357-z.
21. Guarneri V, Barbieri E, Piacentini F, et al. Predictive and prognostic role of p53 according to tumor phenotype in breast cancer patients treated with preoperative chemotherapy. Int J Biol Markers. 2010;25(2):104-111. doi: 10.1177/172460081002500208.
22. Rabban JT, Garg K, Ladwig NR, et al. Cytoplasmic pattern of p53 immunoexpression in pelvic and endometrial carcinomas with TP53 mutations involving nuclear localization domains. Am J Surg Pathol. 2021;45(11):1441-1451. doi: 10.1097/PAS.0000000000001713.
23. Darb-Esfahani S, Denkert C, Stenzinger A, et al. Role of TP53 mutations in triple-negative and HER2-positive breast cancer treated with neoadjuvant chemotherapy. Oncotarget. 2016;7(42):67686-67698. doi: 10.18632/oncotarget.11891.
24. Vermij L, Leon-Castillo A, Singh N, et al. P53 immunohistochemistry in endometrial cancer: clinical and molecular correlates in the PORTEC-3 trial. Mod Pathol. 2022;35(10):1475-1483. doi: 10.1038/s41379-022-01102-x.

25. Köbel M, Kang EY. The Many Uses of p53 Immunohistochemistry in Gynecological Pathology: Proceedings of the ISGyP Companion Society Session at the 2020 USCAP Annual9 Meeting. Int J Gynecol Pathol. 2021;40(1):32-40. doi: 10.1097/PGP.0000000000000725.
26. Roszkowska KA, Piecuch A, Sady M, Gajewski Z, Flis S. Gain of Function (GOF) Mutant p53 in Cancer-Current Therapeutic Approaches. Int J Mol Sci. 2022;23(21):13287. doi: 10.3390/ijms232113287.
27. Köbel M, Ronnett BM, Singh N, Soslow RA, Gilks CB, McCluggage WG. Interpretation of P53 Immunohistochemistry in Endometrial Carcinomas: Toward Increased Reproducibility. Int J Gynecol Pathol. 2019;38 Suppl 1:S123-S131. doi: 10.1097/PGP.0000000000000488.
28. Holstege H, Horlings HM, Velds A, et al. BRCA1-mutated and basal-like breast cancers have similar aCGH profiles and a high incidence of protein-truncating TP53 mutations. BMC Cancer. 2010;10:654. doi: 10.1186/1471-2407-10-654.
29. Grote I, Bartels S, Kandt L, et al. TP53 mutations are associated with primary endocrine resistance in early-stage luminal breast cancer. Cancer Med. 2021;10(23):8581-8594. doi: 10.1002/cam4.4376.
30. Salim KY, Maleki Vareki S, Danter WR, Koropatnick J. COTI-2, a novel small molecule active against multiple human cancer cell lines in vitro and in vivo. Oncotarget. 2016;7(27):41363-41379. doi: 10.18632/oncotarget.9133.
31. Duffy MJ, McGowan PM, Crown J. Targeted therapy for triple-negative breast cancer: where are we? Int J Cancer. 2012;131(11):2471-2477. doi: 10.1002/ijc.27632.