RESEARCH ARTICLE

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MCM2 and *p53* Expression Correlate with the Spectrum of Mucinous Ovarian Tumor

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Abstract

Objective: The objective was to analyze the expression of *p53* and *MCM2* across the spectrum of mucinous ovarian tumor (MOT) and to identify potential diagnostic markers for distinguishing benign, borderline, and malignant. **Methods:** A cross-sectional study was conducted on 60 cases of MOT, comprising mucinous cystadenoma (MCA), mucinous borderline tumor (MBT), low-grade mucinous carcinoma (LG-MC, grade 1), and high-grade mucinous carcinoma (HG-MC, grades 2 and 3). The expressions of *p53* and *MCM2* were evaluated by immunohistochemistry. Statistical analyses were performed to assess expression patterns and determine their associations across the tumor spectrum. **Result:** *p53* expression in MCA demonstrated a normal staining pattern in all samples. In contrast, abnormal (mutant-type) staining was observed in MBT, LG-MC, and HG-MC at frequencies of 13.33%, 40%, and 80%, respectively. *p53* expression were found significant differences between MCA and LG-MC, MCA and HG-MC, MBT and HG-MC, and LG-MC and HG-MC. Furthermore, *MCM2* expression is not significantly different from the spectrum of MOT. Both *p53* and *MCM2* expression correlated with the spectrum of MOT (r = 0.632 (strong) and r = 0.274 (weak), respectively). Furthermore, *p53* expression showed a moderate positive correlation with *MCM2* expression across the spectrum of MOT (r = 0.393). **Conclusion:** The abnormal (mutant-type) *p53* staining pattern increased progressively with tumor grade in MOT, indicating its association with tumor progression. Both *p53* and *MCM2* expressions showed positive correlations with the spectrum of MOT, reflecting their relationship with increasing malignancy. These findings suggest that *p53* could serve as a complementary markers for distinguishing benign, borderline, and malignant mucinous ovarian tumors.

Keywords: Cancer, mucinous borderline tumors, *p53*, ovarian carcinoma, *MCM2*

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Introduction

The Global Cancer Observatory (GLOBOCAN) 2022 data showed the global incidence of ovarian cancer was 324,603 cases, with nearly half (178,223 cases; 54.9%) occurring in Asia [1]. The global mortality from ovarian cancer was estimated at 206,956 deaths in the same year [1]. In Indonesia, ovarian cancer ranks as the third most common malignancy among women, with 15,130 new cases (8.5%) and 9,673 deaths reported in 2022 [1]. Ovarian cancer originates from different cell types, including epithelial, germ, and stromal cells. Epithelial ovarian carcinoma, which are the most common, comprises four main histological subtypes: serous carcinoma (the most common), endometrioid carcinoma, clear cell carcinoma, and mucinous carcinoma [2].

Based on histopathological criteria, mucinous ovarian tumor (MOT) is classified along a spectrum from benign to malignant forms, including mucinous cystadenoma and adenofibroma (MCA), mucinous borderline tumor (MBT), and mucinous carcinoma of the ovary, which is further subdivided into low-grade mucinous carcinoma (LG-MC) and high-grade mucinous carcinoma (HG-MC) types [3]. The incidence of primary mucinous carcinoma has been reported to be approximately 3% of all epithelial ovarian carcinomas [4, 5] and relatively higher in Asian populations, particularly in Indonesia, Singapore, and Korea [3]. In Brunei Darussalam (2007-2017), mucinous carcinoma accounted for 31% (64/207) of ovarian carcinoma cases, followed by serous carcinoma at 28% (58/207) [6]. Data from the Anatomical Pathology Laboratory of Dr. Soetomo General Hospital, Surabaya (2016–2020), demonstrated that mucinous carcinoma accounted for 25% of all MOT, and MBT represented 85% of all borderline ovarian tumors [7]. In addition, data of MOT during 2018-2021 were 46 (39%) MCA, 17 (14%) MBT, and 55 (47%) LG-MC [8]. Overall, the prognosis for patients with mucinous carcinoma is more favorable

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compared to other epithelial ovarian carcinoma subtypes, with a five-year overall survival rate exceeding 90% [9].

The diagnosis of MOT remains challenging because of their wide morphological spectrum, from benign to malignant lesions, including MCA, MBT, LG-MC, and HG-MC. Mucinous borderline tumor exhibit epithelial proliferation resembling well-differentiated adenocarcinomas but are distinguished by the absence of stromal invasion [10]. Overlapping cellular features among benign, borderline, and malignant lesions further hinder accurate diagnosis, potentially leading to misclassification of borderline tumors as cystadenomas, borderline tumors as carcinomas, or carcinomas as borderline tumors. Such diagnostic inaccuracies may result in suboptimal treatment and affect clinical outcomes and survival. Borderline ovarian tumors are usually treated surgically [11], while mucinous carcinoma require surgical resection followed by adjuvant chemotherapy as the standard treatment approach [12]. Therefore, the identification of reliable differentiation markers among MCA, MBT, and mucinous carcinoma is critical for guiding optimal clinical management.

Among the potential biomarkers, *p53* has gained attention as a critical regulatory in tumorigenesis. Functioning as a transcription factor, the *p53* protein modulates the expression of downstream target genes that regulate key cellular processes, including cell cycle control, DNA damage repair, and apoptosis [13]. *TP53* is frequently mutated genes in human cancers, with present in over half of all cases and commonly altered in ovarian cancer. In ovarian carcinoma, approximately 70% of *TP53* mutations are missense mutations, and these alterations often occur early in tumor development, suggesting a role in ovarian carcinogenesis [14, 15].

In addition to *p53*, minichromosome maintenance protein 2 (*MCM2*) is one of the biomarkers involved in tumorigenesis, reflecting the regulation of proliferation. It has recently been recognized as a novel proliferation marker with significant prognostic relevance across various cancer types [16]. *MCM2* belongs to the MCM protein complex or pre-replication complex, which consists of six highly conserved proteins (*MCM2*-MCM7) that collectively interact to initiate DNA replication. This complex is considered a convergence point connecting growth signaling pathways with DNA replication initiation [17]. *MCM2* initiates DNA replication and is a surrogate marker for *Ki-67*, which is active in all phases of cell division, while *Ki-67* is only active in the S phase [17]. Recent studies have shown that overexpression of *MCM2* is associated with cancers of the stomach, colon, and skin. In addition, *MCM2* is a promising proliferative marker in various cancers, including thyroid, rectal, and breast cancers, and is frequently upregulated in ovarian carcinoma, where it is associated with advanced stage, high-grade tumors, and poor prognosis [18]. Although *p53* and *MCM2* have been widely studied as individual biomarkers in various cancers, limited data are available regarding their relationship in MOT. Therefore, this study aims to evaluate the expression of *p53* and *MCM2* across the spectrum of MOT and to identify potential diagnostic markers for distinguishing benign, borderline, and malignant ovarian tumors.

Materials and Methods

An analytical cross-sectional study was conducted on patients diagnosed with MOT by histopathological examination at Dr. Soetomo General Hospital between 2018 and 2021. Ethical approval was obtained from the Health Research Ethics Committee (No. 0913/KEPK/II/2024; February 6, 2024).

Study samples

The samples consisted of formalin fix paraffin-embedded tissue (FFPE) from patients who fulfilled the inclusion criteria, including tissue blocks of adequate quality with tumors cells sufficiently preserved and representative for immunohistochemical analysis. Cases with coexisting tumors of the gastrointestinal tract or other organs were excluded.

The sample size was determined according to the formula $n = Z\alpha^2 . p . q/d^2$, where n represents the minimum required sample size; α was set at 0.05 (Zα = 1.96); p was assumed to be 0.5; q = 1 − p = 0.5; and d (margin of error) was set at 0.14. Based on this calculation, each group required 14 samples, resulting in a minimum total of 48 samples. After applying a 10% correction factor, the total was adjusted to 53 and subsequently rounded to 60 samples, including MCA (n = 15), MBT (n = 15), LG-MC (mucinous carcinoma grade 1, n = 15), and HG-MC (mucinous carcinoma grades 2 and 3, n = 15).

Immunohistochemistry assessment

All slides were independently examined by two pathologists using a binocular light microscope (Olympus CX41RF). In this study, *p53* expression was evaluated by immunohistochemistry (IHC) using a mouse monoclonal anti-*p53* antibody (clone DO-7, dilution 1:100; Diagnostic Biosystems). *p53* expression is interpreted as either a normal staining pattern, indicating the wild-type, or an abnormal staining pattern, indicating the mutant-type. The normal staining pattern is characterized by heterogeneous (patchy) nuclear staining with variable intensity, ranging from negative to weak and strong positivity. In contrast, the abnormal staining pattern can be classified into three types: overexpression, complete absence, and cytoplasmic staining. Overexpression is characterized by diffuse, strong nuclear staining observed in more than 80% of tumor cells. Complete absence shows negative nuclear staining, while internal control cells remain positive, confirming the validity of the test. Cytoplasmic staining is defined by unequivocal, strong cytoplasmic positivity with or without accompanying nuclear staining [19, 20].

MCM2 expression was evaluated by IHC using a mouse monoclonal anti-*MCM2* antibody (clone 1E7, #12079; Cell Signaling Technology, dilution 1:100). Nuclear or cytoplasmic staining was considered positive. Immunohistochemical results were quantified based on two parameters such as the percentage of positively stained tumor cells (A) and staining intensity (I). The proportion score (A) was defined as follows: 0 = no tumor cells stained (0%), 1 = <35% positive cells, and 2 = >35–100%

positive cells. The intensity score (I) was graded as 0 = no staining, 1 = weak, 2 = moderate, and 3 = strong. The immunoreactive score (IRS) was obtained by multiplying A × I, and classified as: 0 = negative, 1–2 = weak, 3–4 = moderate, and 5–6 = strong expression.

Statistical analysis

Differences in *p53* and *MCM2* expression were analyzed using the Kruskal–Wallis test, followed by the Mann–Whitney U test for pairwise comparisons and correlations were evaluated using Spearman's rank correlation test.

Results

Patient characteristics

Sample characteristics included histopathological diagnosis, patient age, and tumor location. The mean age was 43.2 years (range 16–69), with the highest proportion aged 46–55 years (23%), followed by 56–65 years (21.7%), and 50% of patients were under 45 years. Tumors were most commonly located in the right ovary (48.3%), followed by the left ovary (41.7%) and bilateral cases (10%) (Table 1).

p53 expression

Immunohistochemical staining for *p53* is presented in Figure 1 for MCA and MBT, and in Figure 2 for LG-MC and HG-MC. Overall, *p53* expression was predominantly of the normal staining pattern (66.7%). All MCA samples exhibited a normal staining pattern, which was also observed in 86.67% of MBT, 60% of LG-MC, and 20% of HG-MC cases. Statistical analysis demonstrated a significant difference in *p53* expression across the MOT spectrum (p = 0.000) (Table 2). The results of the Mann–Whitney test showed significant differences in *p53* expression between MCA and LG-MC (p=0.007), MCA and HG-MC (p=0.000), MBT and HG-MC (p=0.000, and LG-MC and HG-MC (p=0.028). There were no significant differences in *p53* expression observed between MCA and

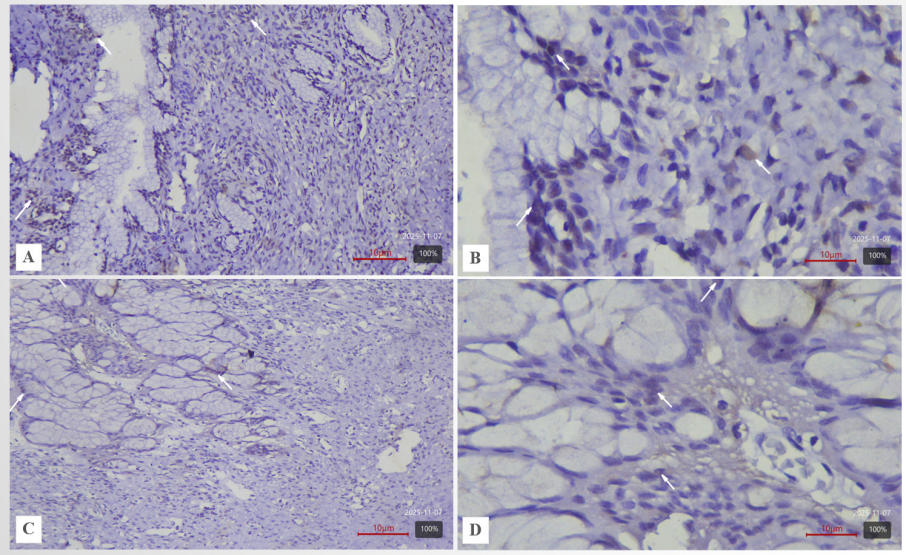

Figure 1. Immunohistochemical Staining of *p53* in Mucinous Cystadenoma and Mucinous Borderline Tumor. *p53* expression showed variable nuclear staining patterns, ranging from negative to weak and strong positivity, consistent with normal (wild type) expression. Mucinous cystadenoma was showed at 100× (A) and 400× (B), and in mucinous borderline tumor at 100× (C) and 400× (D) magnification.

Table 1. Characteristics of Samples

Characteristics	MCA	MBT	LG-MC	HG-MC	N (%)
Age					
16-25 years	6	3	1	2	12 (20)
26-35 years	1	3	3	2	9 (15)
36-45 years	1	3	1	4	9 (15)
46-55 years	3	2	5	4	14 (23.3)
56-65 years	2	4	4	3	13 (21.7)
65-75 years	2	0	1	0	3 (5)
Tumor location					
Left ovary (ovarium sinistrum)	9	7	5	4	25 (41.7)
Right ovary (ovarium dextrum)	6	8	10	5	29 (48.3)
Bilateral ovaries (ovarium bilateral)	0	0	0	6	6 (10)

MCA, Mucinous Cystadenoma; MBT, Mucinous Borderline Tumor; LG-MC, Low Grade Mucinous Carcinoma; HG-MC, High-Grade Mucinous Carcinoma.

Table 2. Differences in *p53* and *MCM2* Expression among the Spectrum of Mucinous Ovarian Tumors

	MCA	MBT	LG-MC	HG-MC	Total	p value
	N (%)	N (%)	N (%)	N (%)	N (%)	
p53 expression						p = 0.000*
Normal (wild type) staining	15 (100)	13 (86.67)	9 (60)	3 (20)	40 (66.67)	
Abnormal (mutant type) staining	0	2 (13.33)	6 (40)	12 (80)	20 (33.33)	
MCM2 expression						p = 0.118
IRS interpretation						
0=Negative	6 (10)	8 (13.33)	4 (6.67)	2 (3.330	20 (33.33)	
1-2=Weak	7 (11.67)	4 (6.67)	9 (15)	8 (13.33)	28 (46.67)	
3-4=Moderate	2 (3.33)	2 (3.33)	2 (3.33)	1 (1.67)	7 (11.67)	
5-6=Strong	0	1 (1.67)	0	4 (6.67)	5 (8.33)	

Note, *, significant difference; MCA, Mucinous Cystadenoma; MBT, Mucinous Borderline Tumor; LG-MC, Low Grade Mucinous Carcinoma; HG-MC, High-Grade Mucinous Carcinoma; IRS, Immunoreactive Score

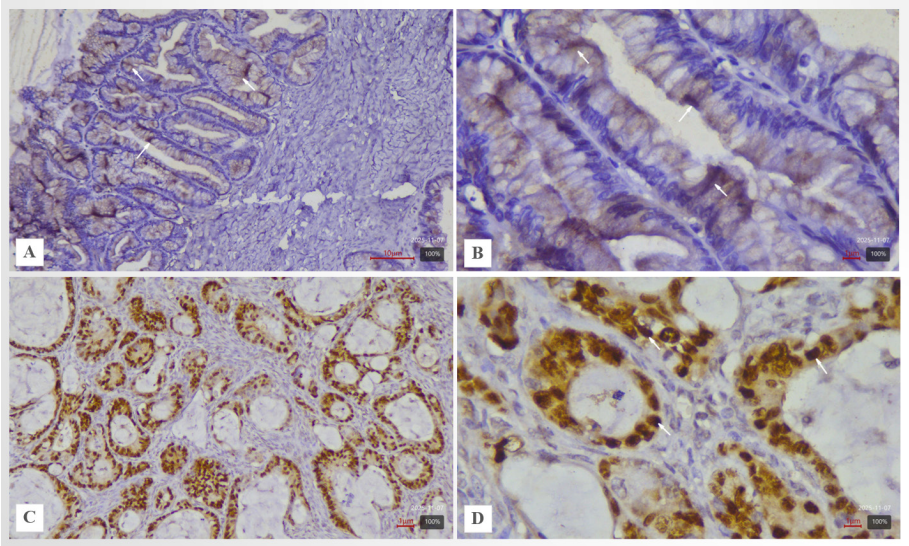

Figure 2. Immunohistochemical Staining of *p53* in Low Grade and High Grade Mucinous Carcinoma. *p53* expression shows unequivocal, strong cytoplasmic staining with or without nuclear staining, as well as diffuse, strong nuclear overexpression in more than 80% of tumor cells, consistent with abnormal (mutant type) expression. Low grade mucinous carcinoma was showed at 100× (A) and 400× (B), and high grade mucinous carcinoma at 100× (C) and 400× (D) magnification.

MBT, or between MBT and LG-MC (Table 3).

MCM2 expression

Immunohistochemical staining for *MCM2* is shown in Figure 3. *MCM2* expression in MCA was predominantly weak (11.67%), while in MBT was mostly negative (13.33%). LG-MC and HG-MC predominantly showed weak expression, observed in 15% and 13.33% of cases, respectively (Table 2). *MCM2* expression did not differ significantly across the MOT spectrum based on the Kruskal–Wallis test (p = 0.118) (Table 2).

Table 3. Mann-Whitney Test of *p53* Expression among the Spectrum of Mucinous Ovarian Tumors

Spectrum of mucinous ovarian tumors	p value
MCA and MBT	0.150
MCA and LG-MC	0.007*
MCA and HG-MC	0.000*
MBT and LG-MC	0.104
MBT and HG-MC	0.000*
LG-MC and HG-MC	0.028*

Note: *, significant difference; MCA, Mucinous Cystadenoma; MBT, Mucinous Borderline Tumor; LG-MC, Low Grade Mucinous Carcinoma; HG-MC: High-Grade Mucinous Carcinoma.

Correlation between MCM2 and p53

Spearman analysis revealed a strong positive correlation between *p53* expression and the MOT spectrum ($p < 0.05$; $r = 0.632$) and a weak positive correlation between *MCM2* expression and the MOT spectrum ($p < 0.05$; $r = 0.274$). Furthermore, a significant moderate positive correlation was also found between *MCM2* and *p53* expression in MOT ($p < 0.05$; $r = 0.393$).

Discussion

Mucinous ovarian tumors are a distinct subtype of epithelial ovarian carcinoma, accounting for 3–10% of

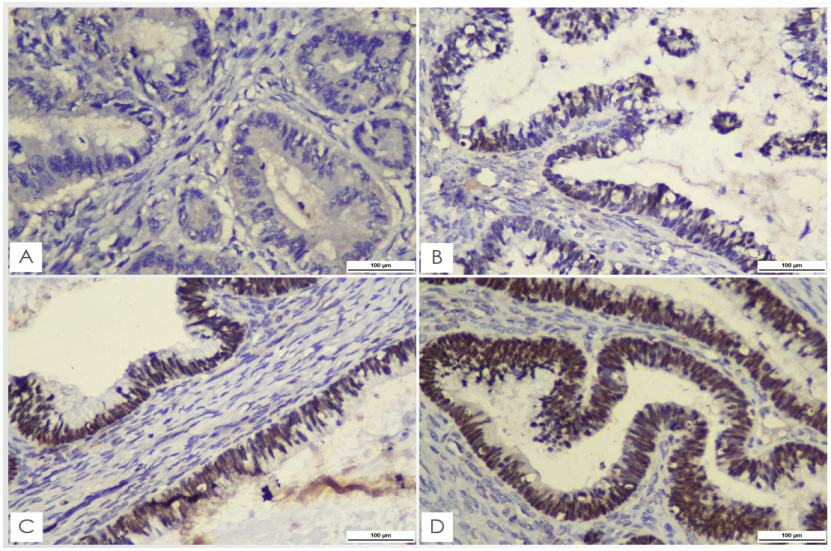

Figure 3. Immunohistochemical Detection of Minichromosome Maintenance Protein 2 (*MCM2*) in Mucinous Ovarian Tumors (Original Magnification ×400; scale bar = 100 µm). Positive *MCM2* expression is visualized as brown staining in the nuclei and cytoplasm of tumor cells. (A) negative; (B) weakly positive; (C) moderately positive; (D) strongly positive.

cases and commonly diagnosed at an early stage [4]. They are typically unilateral, large size and approximately 65–80% are diagnosed at an early stage [5, 9]. This is consistent with the present study, in which most tumors were unilateral, involving either the right ovary (48.3%) or the left ovary (41.7%). In addition, it tends to occur in younger individuals, with 50% of patients under 45 years, indicating a predilection for premenopausal women. In contrast, high-grade serous carcinoma of the ovary (HG-SC) predominantly occurs in postmenopausal women, with a median age at diagnosis of approximately 61 years [5, 9]. This result is consistent with previous reports showing that mucinous carcinoma typically arises in younger patients compared to HG-SC, with approximately 17% of cases diagnosed before age 40 and 37% before age 50 [5, 9].

This tendency is thought to be associated with genetic alteration such as *KRAS*, *HER2*, *TP53*, etc. The *KRAS* oncogene plays a pivotal role in the development and progression of epithelial ovarian carcinoma, from benign to malignant forms. Previous studies have reported *KRAS* mutations in approximately 40–65% of mucinous carcinoma [9]. Moreover, *KRAS* mutations have been detected in carcinoma foci and also in adjacent borderline and benign areas [4, 9]. The frequency of *KRAS* mutations varies among histological subtypes, with the highest prevalence observed in mucinous carcinoma (50%), followed by endometrioid ovarian carcinoma (10%), serous ovarian carcinoma (5%), and clear cell ovarian carcinoma (0%) [21]. Another study reported *KRAS* mutations in 57% of mucinous adenomas (4/7), 90% of MBT (9/10), and 75.61% of mucinous carcinoma cases (31/41), while no *KRAS* mutations were identified in normal ovarian tissue [22]. In comparison with serous ovarian tumors, primary MOT shows a higher frequency of *KRAS* mutations and a lower incidence of BRCA and *p53* alterations [4]. Moreover, *TP53* and *KRAS* co-mutations occur in approximately 53% of cases and are associated with poorer progression-free and overall survival [23, 24].

This study showed that all benign tumors exhibited normal (wild-type) *p53* expression, while 87% of borderline tumors demonstrated normal staining. In contrast, malignant tumors mainly exhibited abnormal pattern, indicating increased mutant-type *p53* expression with higher tumor grade. The abnormal staining patterns observed included overexpression, complete absence, and cytoplasmic staining [19, 20]. Moreover, in this study found that *p53* expression strongly correlate with the spectrum of MOT. These findings are consistent with previous reports describing *p53* overexpression in approximately 70% of malignant tumors and 33% of MBT, as well as in 85% of HG-SC and 16% of mucinous carcinoma [4, 25]. These data imply that *p53* alteration represents an early molecular event in the neoplastic transformation from benign to malignant [24]. *p53* mutations occur in approximately 50–60% of mucinous carcinomas but are less frequent in borderline tumors (~11.5%) [26].

This study found that *MCM2* expression in MOT tended to be weak, with no statistically significant differences observed across the spectra of MOT and weak positive correlation with the spectrum of MOT. In addition, a moderate positive correlation was found between *MCM2* and *p53* expression across the spectrum of MOT. Consistent with previous studies in epithelial ovarian carcinoma subtypes, particularly clear cell carcinoma. *MCM2* expression has been associated with poor prognosis, and its immunoreactivity has been detected in both the nucleus and cytoplasm of tumor cells [18]. Additionally, *MCM2* expression increases significantly with higher tumor grade and stage [27]. Cytoplasmic *MCM2* expression has been associated with excellent long-term survival (up to 100% at 15 years), whereas nuclear expression correlates with lower 5-year overall survival (~78%) [18].

In normal cells, DNA damage can induce mutant *p53* to upregulate *MCM2* and poly (ADP-ribose) polymerase (PARP), facilitating binding to chromatin. Both *MCM2* and PARP play essential roles in DNA repair by activating repair pathways. However, in cancer cells, mutant *p53* interacts aberrantly with *MCM2* and PARP, leading to defective DNA repair mechanisms. This failure promotes the accumulation of mutations in oncogenes and tumors suppressor genes, resulting in uncontrolled cell proliferation, migration, and invasion, which contribute to tumors progression [13, 28-30]. *MCM2* can promote increased cancer cell migration and invasion. *MCM2* activates Cdc42 and Rho, which disrupt filopodia formation and induces stress fiber development, thereby enhancing cellular invasion and migration. In addition, Rhotekin (RTKN), an effector protein of Rho, can also upregulate *MCM2* expression, further promoting cell proliferation, migration, and invasion [28, 29]. In addition, *MCM2* has been implicated in cancer progression, showing positive correlations with TNM stage and lymph node metastasis in several cancers, where it promotes cell proliferation and inhibits apoptosis [17].

This study is limited by a relatively small sample size (60 cases), which may reduce statistical power and generalizability, particularly for high-grade tumors with diverse genetic profiles. The cross-sectional design precludes assessment of temporal changes, causality, prognostic value, recurrence, and survival outcomes. Additionally, molecular analysis was restricted to *p53* and *MCM2* without evaluating other relevant oncogenic pathways (e.g., EMT-related proteins, Wnt/β-catenin signaling components, MMPs, or VEGF) that may influence tumor behavior. Future prospective longitudinal studies with clinical follow-up and expanded molecular profiling are needed to clarify the temporal and clinical utility of these biomarkers across the spectrum of mucinous ovarian tumors.

Despite its limitations, this study offers valuable insights into *p53* and *MCM2* expression across the MOT spectrum, demonstrating a strong association between mutant-type *p53* and tumor progression, as well as a moderate correlation between *p53* and *MCM2*. These findings suggest that *p53* may serve as complementary to support the distinction between benign, borderline, and malignant mucinous carcinoma of the ovary.

In conclusion, this study showed significant differences in *p53* expression across the spectrum of MOT, particularly between MCA and LG-MC, MCA and HG-MC, MBT and HG-MC, and LG-MC and HG-MC, but not between MCA and MBT or between MBT and LG-MC. *p53* expression in MCA demonstrated a normal staining pattern in all samples, whereas abnormal (mutant-type) staining increased across the spectrum of MOT. Moreover, *p53* expression have a strong positive correlation with the spectrum of MOT. The increasing frequency of abnormal *p53* staining with higher tumor grade indicates a strong association between mutant-type *p53* expression and tumor progression. These findings enhance our understanding of the molecular alterations underlying mucinous ovarian tumors and may inform future diagnostic and prognostic strategies.

Author Contribution Statement

All authors are responsible for the content of this article and contributed to the critical review and approval of the final manuscript. Alphania Rahniayu: conseptual idea, writing the manuscript, and critical revisions. Gondo Mastutik: the main conceptual framework, manuscript writing, and critical revisions. Anny Setijo Rahaju: histopathological analysis and manuscript editing. Radianto Chandra Wijaya Oey: specimen diagnosis and sample collecting. Aditya Sari: specimen diagnosis and histopathological analysis. Heru Fajar Trianto: statistical analysis.

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General

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Ethical Declaration

Ethical approval for this study was obtained from the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, No. 0913/KEPK/II/2024, issued on February 6, 2024.

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Conflict of Interest

The authors declare that there is no conflict of interest

References

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, et al. Global cancer observatory: Cancer today. Lyon: International Agency for Research on Cancer. 2024. Available from: https://gco.iarc.who.int/today
2. Lheureux S, Braunstein M, Oza AM. Epithelial ovarian cancer: Evolution of management in the era of precision medicine. CA Cancer J Clin. 2019;69(4):280-304. https://doi.org/10.3322/caac.21559.
3. Herrington CS. WHO Classification of Tumours Editorial Board. WHO classification of tumours: Female genital tumours. 5th ed. Lyon: International Agency for Research on Cancer; 2020.
4. Frumovitz M, Schmeler KM, Malpica A, Sood AK, Gershenson DM. Unmasking the complexities of mucinous ovarian carcinoma. Gynecol Oncol. 2010;117(3):491-6. https://doi.org/10.1016/j.ygyno.2010.02.010.
5. Barbier de Reulle C, Rebotier M, Chopin N, Rossi L, Treilleux I, Meeus P, et al. Mucinous ovarian carcinoma: Impact of ovarian stimulation, hormonal contraception, and hormone replacement therapy. Eur J Obstet Gynecol Reprod Biol. 2025;307:13-20. https://doi.org/10.1016/j.ejogrb.2025.01.036.
6. Leong E, Ong SK, Jali F, Naing L. Incidence, mortality and survival analysis of epithelial ovarian cancer in brunei

darussalam. Asian Pac J Cancer Prev. 2022;23(4):1415-23. https://doi.org/10.31557/apjcp.2022.23.4.1415.
7. Takaria M, Sugianto YM,, Chotimah C, Iwantono HS, Ariani G. Profile of ovarian tumor in anatomical pathology laboratory of dr. Soetomo general academic hospital surabaya period 1 january 2016 - 31 december 2020. Int J Health Sci. 2022;6(55):495-500. https://doi.org/10.53730/ijhs.v6nS5.7976.
8. Oey RCW, Rahniayu A, Mastutik G. Differences in the expression of CD44 and EMMPRIN in various spectra of mucinous ovarian tumors. J Med Chem Sci.2023;6(12):3221-30. https://doi.org/10.26655/JMCHEMSCI.2023.12.35.
9. Morice P, Gouy S, Leary A. Mucinous ovarian carcinoma. N Engl J Med. 2019;380(13):1256-66. https://doi.org/10.1056/NEJMra1813254.
10. Sahraoui G, Fitouri A, Charfi L, Driss M, Slimane M, Hechiche M, et al. Mucinous borderline ovarian tumors: Pathological and prognostic study at Salah Azaiez Institute. Pan Afr Med J. 2022;41:349. https://doi.org/10.11604/pamj.2022.41.349.32332.
11. Kipp B, Vidal A, Lenick D, Christmann-Schmid C. Management of borderline ovarian tumors (BOT): Results of a retrospective, single center study in Switzerland. J Ovarian Res. 2023;16(1):20. https://doi.org/10.1186/s13048-023-01107-3.
12. Algera MD, Van de Vijver KK, van Driel WJ, Slangen BFM, Lof FC, van der Aa M, et al. Outcomes of patients with early stage mucinous ovarian carcinoma: A Dutch population-based cohort study comparing expansile and infiltrative subtypes. Int J Gynecol Cancer. 2024;34(5):722-9. https://doi.org/10.1136/ijgc-2023-004955.
13. Xiao G, Lundine D, Annor GK, Canar J, Ellison V, Polotskaia A, et al. Gain-of-function mutant *p53 R273H* interacts with replicating DNA and PARP1 in breast cancer. Cancer Res. 2020;80(3):394-405. https://doi.org/10.1158/0008-5472.CAN-19-1036
14. Köbel M, Kang EY. The many uses of *p53* immunohistochemistry in gynecological pathology: Proceedings of the ISGyP companion society session at the 2020 USCAP annual meeting. Int J Gynecol Pathol. 2021;40(1):32-40. https://doi.org/10.1097/PGP.0000000000000725.
15. Zhang Y, Cao L, Nguyen D, Lu H. *TP53* mutations in epithelial ovarian cancer. Transl Cancer Res. 2016;5(6):650-63. https://doi.org/10.21037/tcr.2016.08.40.
16. Deng M, Sun J, Xie S, Zhen H, Wang Y, Zhong A, et al. Inhibition of *MCM2* enhances the sensitivity of ovarian cancer cell to carboplatin. Mol Med Rep. 2019;20(3):2258-66. https://doi.org/10.3892/mmr.2019.10477.
17. Abe S, Kurata M, Suzuki S, Yamamoto K, Aisaki K, Kanno J, et al. Minichromosome maintenance 2 bound with retroviral gp70 is localized to cytoplasm and enhances DNA-damage-induced apoptosis. PLoS One. 2012;7(6):e40129. https://doi.org/10.1371/journal.pone.0040129.
18. Aihemaiti G, Kurata M, Nogawa D, Yamamoto A, Mineo T, Onishi I, et al. Subcellular localization of *MCM2* correlates with the prognosis of ovarian clear cell carcinoma. Oncotarget. 2018;9(46):28213-25. https://doi.org/10.18632/oncotarget.25613.
19. 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(Iss 1 Suppl 1):S123-31. https://doi.org/10.1097/PGP.0000000000000488.
20. Chang YW, Kuo HL, Chen TC, Chen J, Lim L, Wang KL, et al. Abnormal *p53* expression is associated with poor outcomes in grade i or ii, stage i, endometrioid carcinoma: A retrospective single-institute study. J Gynecol Oncol. 2024;35(6):e78. https://doi.org/10.3802/jgo.2024.35.e78.
21. Gemignani ML, Schlaerth AC, Bogomolniy F, Barakat RR, Lin O, Soslow R, et al. Role of *KRAS* and braf gene mutations in mucinous ovarian carcinoma. Gynecol Oncol. 2003;90(2):378-81. https://doi.org/10.1016/s0090-8258(03)00264-6.
22. Lee YJ, Lee MY, Ruan A, Chen CK, Liu HP, Wang CJ, et al. Multipoint *KRAS* oncogene mutations potentially indicate mucinous carcinoma on the entire spectrum of mucinous ovarian neoplasms. Oncotarget. 2016;7(50):82097-103. https://doi.org/10.18632/oncotarget.13449.
23. Zhang Y, Barkdull S, Kontoyiannis PD, Legarreta AF, Gershenson DM, Ramalingam P, et al. *TP53* and *KRAS* co-mutations are associated with worse outcomes in mucinous ovarian carcinomas. Front Oncol. 2025;15:1573801. https://doi.org/10.3389/fonc.2025.1573801.
24. Dundr P, Hájková N, Kendall Bártů M, Cibula D, Drozenová J, Fabian P, et al. Refined criteria for *p53* expression in ovarian mucinous tumours are highly concordant with *TP53* mutation status, but *p53* expression/*TP53* status lack prognostic significance. Pathology. 2023;55(6):785-91. https://doi.org/10.1016/j.pathol.2023.04.008.
25. Dergham AP, Vaz de Paula CB, Nagashima S, Olandoski M, de Noronha L, Sotomaior VS. Immunohistochemical profiling of pd-1, pd-l1, cd8, msi, and *p53* and prognostic implications in advanced serous ovarian carcinoma: A retrospective study. J Pers Med. 2023;13(7). https://doi.org/10.3390/jpm13071045.
26. Rechsteiner M, Zimmermann AK, Wild PJ, Caduff R, von Teichman A, Fink D, et al. *TP53* mutations are common in all subtypes of epithelial ovarian cancer and occur concomitantly with *KRAS* mutations in the mucinous type. Exp Mol Pathol. 2013;95(2):235-41. https://doi.org/10.1016/j.yexmp.2013.08.004.
27. Gakiopoulou H, Korkolopoulou P, Levidou G, Thymara I, Saetta A, Piperi C, et al. Minichromosome maintenance proteins 2 and 5 in non-benign epithelial ovarian tumours: Relationship with cell cycle regulators and prognostic implications. Br J Cancer. 2007;97(8):1124-34. https://doi.org/10.1038/sj.bjc.6603992.
28. Sun Y, Cheng Z, Liu S. *MCM2* in human cancer: Functions, mechanisms, and clinical significance. Mol Med. 2022;28(1):128. https://doi.org/10.1186/s10020-022-00555-9.
29. Fei L, Xu H. Role of *MCM2*-7 protein phosphorylation in human cancer cells. Cell Biosci. 2018;8:43. https://doi.org/10.1186/s13578-018-0242-2.
30. Zheng F, Zhang Y, Chen S, Weng X, Rao Y, Fang H. Mechanism and current progress of poly(ADP-ribose) polymerase (PARP) inhibitors in the treatment of ovarian cancer. Biomed Pharmacother. 2020;123:109661. https://doi.org/10.1016/j.biopha.2019.109661.