UDC: 616.33-006.6-091.8-071 DOI: 10.52532/2663-4864-2024-1-71-22-29

CORRELATION OF Ki-67 CELL PROLIFERATION MARKER EXPRESSION WITH AGE, SEX, DISEASE STAGE, AND TUMOR DIFFERENTIATION IN GASTRIC CANCER

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ABSTRACT

Relevance: *Gastric cancer continues to lead the cancer incidence structure.*

One of the directions of a comprehensive plan to reduce the incidence of malignant neoplasms is the development of a highly efficient early diagnostics based on the relationship between the expression of the Ki-67 cell proliferation marker in gastric cancer with age, sex, stage of the disease and the degree of tumor differentiation according to the results of the immunohistochemical method.

The study aimed to *study the relationship between the expression of the Ki-67 marker in gastric cancer and age, sex, stage of the disease, and the degree of tumor differentiation.*

Methods: *The research design is a comparative descriptive study. For the study, surgical material was used from 109 patients with gastric cancer stages 0-IIIC, obtained during gastric cancer operations from the pathology department of the West Kazakhstan Marat Ospanov Medical University Medical Center from 2021 to 2022. Histological and immunohistochemical studies were conducted at the morphological laboratory of the Department of Histology of West Kazakhstan Marat Ospanov State Medical University (WKMOMU). The obtained data was statistically processed.*

Results: *The present study showed a significant statistical correlation between the Ki-67 level and the histopathological grade of gastric cancer (p=0.039).*

The indicators such as 'pTNM stage' (p=0.894), 'Age' (p=0.664), 'Sex (F – 1, M – 2)' (p=0.928), and 'Tumor localization (cardia – 1, body – 2, antrum and pylorus – 3)' (p=0.866) did not statistically significantly correlated with the Ki-67 expression level.

Conclusions: *The relationship between Ki-67 expression and histopathological grade (p=0.039) in gastric cancer helps identify patients with aggressive tumors that need adjuvant therapy.*

Keywords: *gastric cancer, morphology, histology, immunohistochemistry, Ki 67, proliferation.*

Introduction: The International Agency for Research on Cancer expects about 1.8 million new cases of gastric cancer and about 1.4 deaths from this disease in the world in 2040 [1]. About 1 million cases of gastric cancer are registered in the world each year, and the annual mortality exceeds 700,000 cases. In 2020, gastric cancer ranked fifth in the world in frequency among other malignancies [2]. Cancer incidence studies in different countries observe a downward trend in gastric cancer incidence. Still, gastric cancer continues to lead the cancer incidence structure. In particular, early detection of gastric cancer at stage I is growing, while late detection at stages III-IV decreases [1]. Gastric cancer is more common in East Asia, mostly in Japan, Korea, and China, and in Eastern Europe, including Russia. Its incidence is low in Northern America and Australia. Precancers and early cancer are heterogeneous diseases whose incidence varies greatly by territory [3].

The incidence and mortality of gastric cancer is high in the Republic of Kazakhstan, with a 2.6-fold higher incidence in men [4]. According to the Global Cancer Observatory, 35,366 new cases of gastric cancer were registered, and 20,959 people died of this disease in the RK in 2020. Gastric cancer ranks third in cancer incidence in both sexes (9.5%) after lung cancer (13.1%) and breast cancer (12.4%). In men, gastric cancer follows lung cancer; in women, it follows breast cancer, colon cancer, and cervical cancer. Gastric cancer is second in mortality after lung cancer.

Measures to improve national cancer care were carried out as part of the implementation of the objectives of the Comprehensive Plan for Cancer Control in the Republic of Kazakhstan for 2018-2022, approved by the Decree of the Government of the Republic of Kazakhstan dated 29 June 2018 No. 395, aimed at reducing the burden of cancer with six other diseases and developing early detection of malignancies [5]. It should be noted that there are low early detection indicators in Aktobe – 17.4 % – the national worst result (vs 16.2% in 2021), Atyrau – 17.5% (14.1%) and Turkestan – 19.0% (16.0%) regions. These regions do not follow the patient's route within the framework of the "Standard for organizing the provision of oncological care to the population of the Republic of Kazakhstan." These regions underperform in diagnostic examinations due to the lack of equipment required by

the Comprehensive Plan for Cancer Control in the RK for 2023-2027 [6]. Considering the results of the implementation of a comprehensive plan for the Aktobe region in 2018-2022, 55.8% of patients are people of working age (18-64 years).

Today, morphological criteria for tumor process malignancy, such as tumor size, depth of invasion, and macroscopic and histological types, are widely used to predict the clinical course of gastric cancer [7]. The course of the disease can vary significantly within one histological type. Immunohistochemical (IHC) techniques can predict the clinical course of cancer in different individuals. Therefore, it is necessary to select the most informative markers [8] and consider various complications of other organs in cancer [9].

Early detection of cancer pathologies at stages 0-I is a key indicator of efficient cancer care. In Kazakhstan, the early detection of gastric cancer increased from 27.1% in 2019 to 29.0% in 2021 and 2022; however, it did not reach the planned 33.5% [6]. This requires a comprehensive analysis of the use of tumor markers for a more in-depth study of gastric cancer, comparing the results of simultaneous macroscopic, histological, and IHC studies in gastric cancer using the expression of Ki-67 cell proliferation marker.

The study aimed to study the relationship between the expression of the Ki-67 marker in gastric cancer and age, sex, stage of the disease, and the degree of tumor differentiation.

Materials and Methods:

For the study, surgical material was used from patients with gastric cancer, obtained during gastric cancer operations from the pathology department of the West Kazakhstan Marat Ospanov Medical University (WKMOMU Medical Center (Aktobe, RK), from 2021 to 2022.

Data on the age and sex of the patients, the location of the anatomical tumor, as well as the results of the macroscopic examination have been obtained from case histories and postmortem reports.

Study design: This comparative descriptive study was conducted according to the protocol of the Biostatistics and Clinical Epidemiology Sector of "West Kazakhstan Marat Ospanov State Medical University" (WKMOMU).

Sampled population: The initial population included unselected samples of surgical material collected from 109 patients with various forms of GC stage 0-IIIC.

Inclusion criteria: patients of all ages operated at stage 0-IIIC of GC.

Exclusion criteria: stage IV GC; the presence of any other malignant neoplasms.

Histological and immunohistochemical studies were conducted at the morphological laboratory of the Department of Histology of WKMOMU. The study followed the instruction on standard operating procedures (WKMOMU 65-03, 10.01.2020).

After cutting the material out, fixation was performed in a 10% buffered formalin solution. A sledge microtome was used to prepare the histological sections. After the paraffinization stage, histological sections of the stomach with a thickness of 4-5 μm have been prepared from paraffin blocks [10]. To confirm that the cutouts were gastric tissues, microslide staining was carried out with hematoxylin-eosin. The material was reviewed with the use of an AxioLab A1 laboratory medical video microscope (Carl Zeiss Microscopy GmbH, Germany) at different magnifications (×50; ×100; ×400; ×1000).

The study, including the determination of the anatomical location area of the tumor (cardia, fundus, corpus, antrum and pylorus), followed the WHO recommendations and the clinical protocol on GC (No. 174 dated 11/21/2022) of the Joint Commission on the Quality of Medical Services of the Ministry of Health of the Republic of Kazakhstan. The studied GC cases were compared based on histopathological classification of gastric tumors: G1 (highly differentiated), G2 (moderately differentiated), G3 (poorly differentiated), and G4 (undifferentiated). Monoclonal rabbit antibodies (RMab (clone: EP5)) to Ki-67 and the Mouse/Rabbit PolyDetector Plus DAB HRP Brown Detection System (ImmunoDNA Washer 20x, Tinto Deparaffinator EDTA 20x (Bio SB, Santa Barbara, CA, USA) have been used to study proliferative activity. All reagents were stored at a temperature of 4 ° C before use. The IHC study was conducted according to the manual IHC protocol according to the manual IHC staining protocol using the detection system. The stained sections were evaluated at a high magnification microscope 400 times and 100 cells were counted in each field. At the same time, five fields were randomly selected and examined for each section, the number and intensity of positively stained cells were recorded and averaged. The proliferative activity of gastric cells was assessed by the Ki-67 marker expression index; see Table 1 for details.

Table 1 – Proliferative activity of Ki-67 in gastric cancer by positive cell detection

Sign of activi-ty	Proliferation activity	Share of Ki-67-positive cells (%)
Negative «-»	Very low	<25%
Positive «+»	Low	25-50%
Positive «++»	Moderate	50-75%
Positive «+++»	High	>75%

Statistical processing of the study results was carried out using a special package of the Statistica 10 computer software system (StatSoft Inc., USA) using the program library and SPSS 25. All results were presented in the form of a 95% confidence interval (CI). The studied groups were independent of each other, i.e. nonparametric, and therefore, the comparative assessment was carried out using the Mann-Whitney test, the Student's t-test, and Pearson's chi-squared test. Statistical analysis was also carried out using the StatTech v.3.0.9 program (Stattech LLC, Russia). Quantitative indicators with normal distribution were described using the arithmetic mean (M) and standard deviations (SD), 95% CI. In the absence of normal distribution, quantitative data were described using the median (Me), lower and upper quartiles (Q1-Q3). The categorical data were described with the indication of absolute values and share in percentage terms. Comparison of two groups on a quantitative indicator with normal distribution under the condition of equality of dispersions was performed using the Student's t-test. Comparison of two groups on a quantitative indicator, whose distribution was different from normal, was performed using the Mann-Whitney U test. Comparison of percentages in the analysis of four-field contingency tables was performed using Pearson's chi-square test (with values of expected phenomenon higher than 10). Comparison of percentages in the analysis of multi-field contingency tables was performed using Pearson's chi-square test.

The approval of the Local Commission on Bioethics of WKMOMU (Protocol No.8 dated 10/15/2021) on the selection of the material and research methods has been obtained.

Results: The study involved 109 gastric cancer patients, including 77 men (70.6%) and 32 women (29.4%). At diagnosis, the age of the patient varied from 27 to 81 years (median 63 years, Q_1-Q_3: 59-70, min – 27, max – 81).

The tumors were located mainly in the corpus (47.7% of cases) compared to the cardiac (38.5%) and antral (13.8%) sections (Table 2).

Table 2 – Clinical-pathological data and expression of the Ki-67 marker (descriptive statistics of categorical variables)

№	Indicator	Category	Abs.	Percent (%)	Confidence interval (95% CI)
1	Sex (F – 1, M – 2)	female	32	29.4	21.0-38.8
		male	77	70.6	61.2-79.0
2	Tumor localization by stomach section	Cardia	42	38.5	29.4-48.3
		Corpus	52	47.7	38.1-57.5
		Antrum and pylorus	15	13.8	7.9-21.7
3	Histopathological differentiation (high – G1, medium – G2, low – G3, undifferentiated – G4)	G1	4	3.7	1.0-9.1
		G2	27	24.8	17.0-34.0
		G3	46	42.2	32.8-52.0
		G4	32	29.4	21.0-38.8
4	pTNM stage (I, II, III)	I	6	5.5	2.0-11.6
		II	45	41.3	31.9-51.1
		III	58	53.2	43.4-62.8
5	Ki-67 expression	negative (-; +)	32	29.3	19.4-36.9
		positive (++; +++)	77	70.7	63.1-80.6

According to the histopathological classification of cancer, the highest percentage consisted of cases of poorly differentiated cancer (n=46; 42.2%), second were cases of undifferentiated tumors (n=32; 29.4%). Furthermore, cases of medium differentiation (n=27; 24.8%) and high differentiation tumor of GC (n=4; 3.7%) were identified. In our study, according to the TNM classification, the distribution of GC cases was as follows: stage I – 6 (5.5%), stage II – 45 (41.3%), stage III – 58 (53.2%). IHC analysis of gastric tumors by Ki-67 proliferative activity showed 70.7% of positive cases (77) and 29.3% of negative cases (32).

As a result of the study of the proportions of Ki-67 negative and positive cells, 11 negative cases ("-", 10.1%) have been revealed. Furthermore, low proliferation activity with a proportion of Ki-67-positive cells has been detected in 21 patients ("+", 21%), moderate activity observed in 58 patients ("++", 53.2%), and high activity found in 19 patients ("++ +", 17.4%) (Table 2).

The Student's t-test revealed no statistically significant differences (p=0.664) between 'Age' and 'Ki-67 expression (negative – 1, positive – 2)' (Table 3, Figure 1).

The Pearson's Chi-square test revealed no statistically significant differences (p=0.928) between 'Sex' and 'Ki-67 expression (negative – 1, positive – 2)' (Table 4, Figure 2).

Table 3 – Ki-67 expression (negative, positive) in GC depending on the patient's age

Indicator	Category	Age			p
		M±SD	95% CI	n	
Ki-67 expression	negative	64±10	60-67	30	0,664
	positive	63±10	60-65	79	

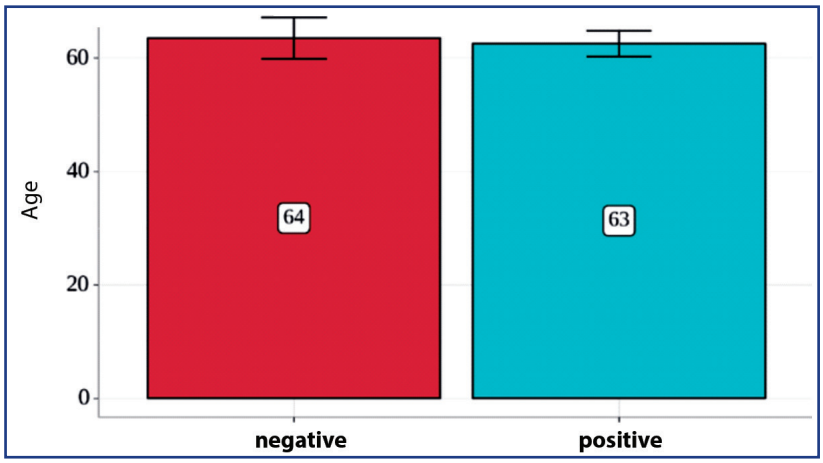

Figure 1 – Analysis of the 'Age' indicator depending on the 'Ki-67 expression'

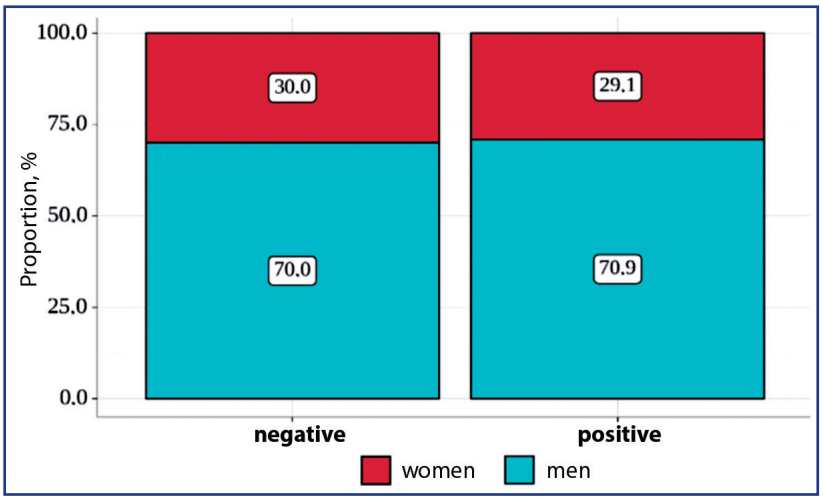

Figure 2 – Analysis of the 'Sex (Female, Male)' indicator depending on the 'Ki-67 expression (negative, positive)'

Table 4 – 'Ki67 expression (negative, positive)' in gastric cancer, depending on the 'Sex (Female, Male)' indicator

Indicator	Category	Ki-67 expression (negative, positive)		*p*
		negative	positive	
Sex	female	9 (30.0)	23 (29.1)	0.928
	male	21 (70.0)	56 (70.9)	

The Pearson's Chi-square test revealed no statistically significant differences (p=0.840) between 'Tumor localization (cardia, corpus, antrum and pylorus)' and 'Ki-67 expression (negative, positive)' (Table 5, Figure 3).

Table 5 – 'Ki-67 expression (negative, positive)' in gastric cancer depending on the tumor localization (cardia, corpus, antrum and pylorus)

Indicator	Category	Ki-67 expression (negative, positive)		*p*
		negative	positive	
Localization (cardia, corpus, antrum and pylorus)	cardia	11 (36.7)	31 (39.2)	0.860
	corpus	14 (46.7)	38 (48.1)	
	antrum and pylorus	5 (16.7)	10 (12.7)	

The evaluation revealed significant differences (p=0.039) in 'Histopathological differentiation (high – G1, medium – G2, low – G3, undifferentiated – G4)' depending on 'Ki-67 expression (negative, positive)" (method used: Pearson's Chi-square) (Table 6, Figure 4).

No statistically significant dependance was established between 'pTNM stages' and 'Ki-67Ki-67 expression (negative, positive)' indicators was established (p=0.894) (method used: Pearson's Chi-square) (Table 7, Figure 5).

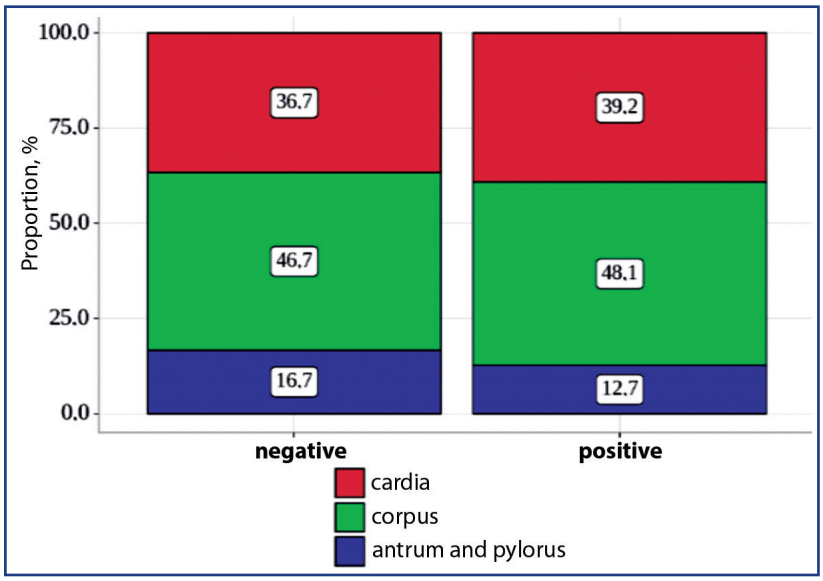

Figure 3 – Analysis of the 'Localization (cardia, corpus, antrum and pylorus)' indicator dependance on 'Ki-67 expression (negative, positive)'

Table 6 – "Ki-67 expression (negative, positive)" in gastric cancer, depending on tumor histopathological differentiation (high – G1, medium – G2, low – G3, undifferentiated – G4)

Indicator	Category	Ki67 expression (negative, positive)		*p*
		negative	positive	
Histopathological differentiation (high – G1, medium – G2, low – G3, undifferentiated – G4)	G1	2 (6,7)	2 (2,5)	0,039*
	G2	12 (40,0)	15 (19,0)	
	G3	7 (23,3)	39 (49,4)	
	G4	9 (30,0)	23 (29,1)	

*Note: * The differences in indicators were statistically significant (p<0.05)*

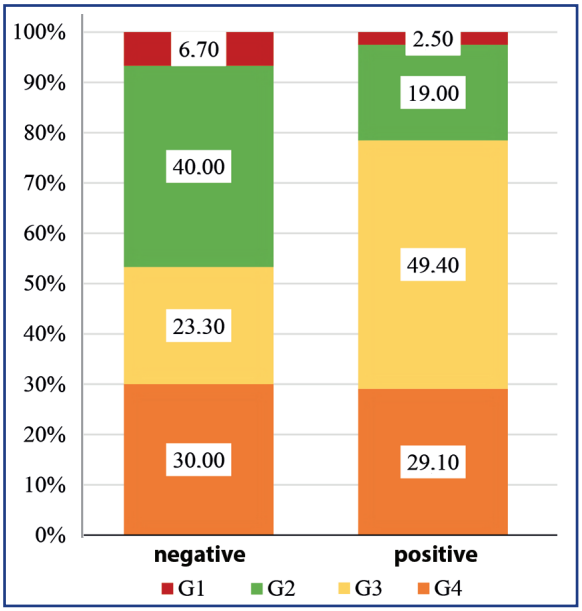

Figure 4 – Analysis of tumor histopathological differentiation (high – G1, medium – G2, low – G3, undifferentiated – G4), depending on the indicator 'Ki-67 expression (negative, positive)'

Table 7 – "Ki-67 expression (negative, positive)" in gastric cancer, depending on tumor stage according to pTNM classification

Indicator	Category	Ki-67 expression (negative, positive)		*p*
		negative	positive	
pTNM stages	I	2 (6.7)	4 (5.1)	0.894
	II	13 (43.3)	32 (40.5)	

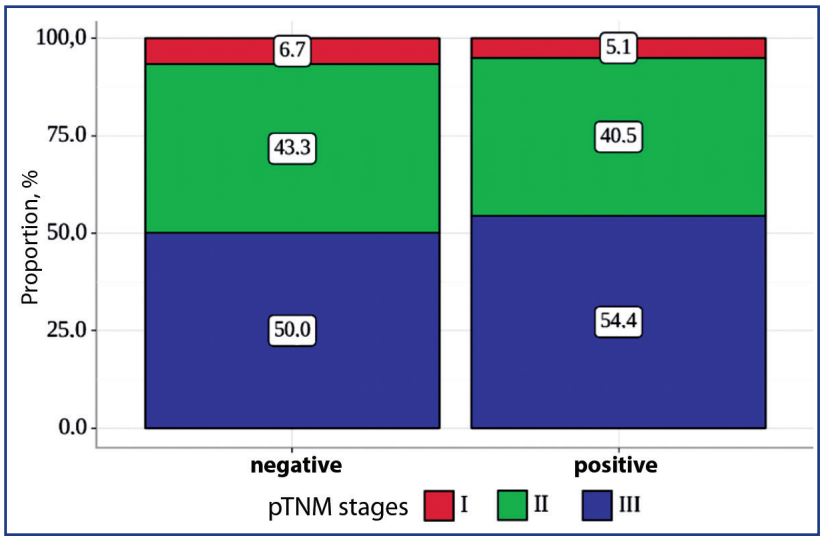

Figure 5 – Analysis of the 'pTNM stages' indicator depending on the 'Ki-67 expression (negative, positive)'

Discussion: In the present study, the expression of the Ki-67 proliferative activity marker in patients with GC was reviewed to obtain information on the pathogenesis and search for a prognostic biomarker for this aggressive carcinoma.

IHC methods occupy an important place in modern diagnostic oncomorphology and represent a fundamental molecular method. IHC provides information on the expression of various genes of proliferation and apoptosis in tissue morphology, peculiarities of tumor histogenesis, and determination of the prognosis of 25 diseases. At the same time, IHC is an auxiliary method, which requires a high level of critical interpretation in the context of many other data, including clinical data [10, 11].

The consensus diagnosis with the use of the Ki-67 surface expression marker as an adjunct marker in low-grade malignancy dysplasia facilitates the identification of patients with high-risk progression of dysplasia to high-grade and esophageal adenocarcinoma.

Prevention of GC remains a priority, so higher risk patients should be evaluated for early detection and chemoprophylaxis. Researchers briefly summarized the most important aspects of GC, including epidemiology, risk factors, classification, diagnosis, prevention, and treatment [12]. However, many tactics and strategy issues remain the subject of active debates and clinical studies. As noted by Liu et al., the new indicator of IHC assessment by markers: microsatellite instability marker (MSI), cell cycle regulatory transcription factor (P53), and proliferative activity protein (Ki-67) (MSI-P53-Ki-67) can effectively predict postoperative general survival and relapse-free survival in patients with GC, stratify postoperative patients by risk and identify high-risk postoperative patients for more accurate patient management [13].

There is a close correlation between the degree of tumor differentiation and the Ki-67 indicator ($p<0.001$) [14]. In studies by Solhjoo et al., the relationship between Ki-67 and the disease grade was significant ($p=0.03$), but the relationship between Ki-67 and tumor location ($p=0.3$), pathological type ($p=0.3$) and tumor stage ($p=0.4$) was not significant [15]. In our studies, the highest number of tumors was located in the corpus (47.7%), followed by the cardia (38.5%) and then the antrum (13.8%). This is not consistent with the publication by Pranjali et al., where the tumor was located mainly in the antral or pyloric region. The study involved 57 patients with gastric adenocarcinoma, with a mean age of 56.12 years. There was no significant correlation between CDX2 and Ki-67 with clinical, total, and microscopic parameters, except for tumor location and depth of invasion. They found a significant correlation between CDX2 ($p=0.04$) and Ki-67 ($p=0.03$) with tumor location. The depth of tumor invasion was significantly associated with Ki-67 ($p=0.013$). No significant association was observed between CDX2 and Ki-67 expression [16].

The present study revealed a significant statistical correlation between the Ki-67 level and the histopathological degree of GC differentiation ($p=0.039$). These findings are consistent with those of El-Gendi et al. [17], who found that a high level of Ki-67 expression was significantly associated with a higher grade of tumor malignancy. Similarly, Luo et al. reported that high expression of Ki-67 may serve as a prognostic biomarker of a poor prognosis in patients with GC. Stratification by Ki-67 expression may be the choice factor for therapeutic regimen and complex treatment [18].

The study of Almabrouk et al. showed a statistically significant correlation of increased Ki-67 expression with the tumor location in the gastric fundus and corpus, as well as with the presence of distant metastases. A statistically significant correlation was also established between a higher mean percentage of Ki-67 positive cells and the presence of pT1 adenocarcinoma with locoregional recurrence ($p<0.001$, $p=0.02$). A high-

er percentage of Ki-67 expression was found in grade III adenocarcinoma and positive perineural invasions, compared to other cases; however, the correlation was not statistically significant [19]. This is consistent with our findings. Our studies did not reveal any statistically significant dependance between the 'pTNM stage' and 'Ki-67 expression' indicators (p=0.894), while grade III GC was associated with a higher Ki-67 expression.

Conclusions: As a result of the analysis of Ki-67 expression in GC, the relationship between Ki-67 expression and histopathological grade degree (p=0.039) in gastric cancer helps identify patients with aggressive tumors that need adjuvant therapy. However, we did not establish a statistically significant dependance on age (p=0.664) or sex of the patients (p=0.928), tumor location (p=0.8660), or disease stage (p=0.8494). Therefore, the rationale for using targeted therapy in GC is based on the results of histological and IHC studies of the tumor material. At the same time, cell proliferation demonstrates the tumor malignancy grade.

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АҢДАТПА

АСҚАЗАН ҚАТЕРЛІ ІСІГІНДЕГІ ЖАСУША ПРОЛИФЕРАЦИЯСЫНЫҢ МАРКЕРІ (Ki-67) МЕН ЖАСЫ, ЖЫНЫСЫ, АУРУДЫҢ САТЫСЫ ЖӘНЕ ДИФФЕРЕНЦИАЦИЯ ДӘРЕЖЕСІ АРАСЫНДАҒЫ БАЙЛАНЫС

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Өзектілігі: *Асқазанның қатерлі ісігі (АҚІ) қатерлі ісік ауруының құрылымында жетекші орынды иеленуін жалғастыруда. Қатерлі жаңа түзілімдермен сырқаттанушылықты төмендету бойынша кешенді жоспардың бағыттарының бірі – жас, жыныс, аурудың сатысымен асқазан ісігіндегі Ki-67 жасушалық пролиферация маркерінің экспрессиясының арасындағы байланыс негізінде жоғары тиімді ерте диагностиканы әзірлеу. және иммуногистохимиялық әдістің нәтижелері бойынша ісіктердің дифференциациялану дәрежесі.*

Зерттеудің мақсаты: *асқазан қатерлі ісігіндегі Ki-67 маркерінің экспрессиясы мен жасы, жынысы, аурудың сатысы және ісіктердің дифференциация дәрежесі арасындағы байланысты зерттеу болды.*

Әдістері мен материалдары: *Зерттеу дизайны салыстырмалы сипаттамалық зерттеу болды. Зерттеуге 2021-2022 жылдар аралығында Батыс Қазақстан медицина университетінің Марат Оспанов атындағы медициналық орталығының патология бөлімшесінен асқазан обырына операция жасау кезінде алынған асқазан обырының 0-IIIC сатысы бар 109 науқастың хирургиялық материалы қолданылды. Марат Оспанов атындағы БҚМУ гистология кафедрасының морфологиялық зертханасында гистологиялық және иммуногистохимиялық зерттеулер жүргізілді. Алынған мәліметтер статистикалық өңдеуден өтті.*

Нәтижелері: *Осы зерттеу Ki-67 деңгейі мен асқазан обырының гистологиялық дәрежесі арасында маңызды статистикалық корреляцияны көрсетті (p=0,039). «pTNM сатысы» (p=0,894), «Жасы» (p=0,664), «Жынысы (F – 1, M – 2)» (p=0,928), «Орналасу (кардиальды – 1, дене – 2, антральды және пилорикалық – 3)» (p=0,860) Ki67 көрсеткіштерін салыстыру кезінде өрнек деңгейімен статистикалық маңызды корреляцияны орнату мүмкін болмады.*

Қорытынды: *Асқазан қатерлі ісігіндегі Ki-67 экспрессиясы мен гистологиялық дифференциация дәрежесі (p=0,039) арасындағы байланыс адъювантты терапияны қажет ететін агрессивті ісіктері бар науқастарды анықтауға көмектеседі.*

Түйінді сөздер: *Асқазан қатерлі ісігі, морфология, гистология, иммуногистохимия, Ki-67, пролиферация.*

АННОТАЦИЯ

СВЯЗЬ ЭКСПРЕССИИ МАРКЕРА КЛЕТОЧНОЙ ПРОЛИФЕРАЦИИ KI-67 ПРИ РАКЕ ЖЕЛУДКА С ВОЗРАСТОМ, ПОЛОМ, СТАДИЕЙ ЗАБОЛЕВАНИЯ И СТЕПЕНЬЮ ДИФФЕРЕНЦИРОВКИ ОПУХОЛИ

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Актуальность: *Рак желудка (РЖ) продолжает занимать лидирующее положение в структуре онкозаболеваемости. Одним из направлений комплексного плана по снижению заболеваемости злокачественными новообразованиями является развитие высокоэффективной ранней диагностики на основании связи экспрессии маркера клеточной пролиферации Ki-67 при раке желудка с возрастом, полом, стадией заболевания и степенью дифференцировки опухоли по результатам иммуногистохимического анализа.*

Цель исследования *– изучить взаимосвязь экспрессии маркера Ki-67 при раке желудка с возрастом, полом, стадией заболевания и степенью дифференцировки опухоли.*

Методы: Дизайн исследования – сравнительное описательное исследование. Для исследования использовался операционный материал 109 пациентов с раком желудка стадий 0-IIIC, полученный при операциях по поводу рака желудка из патологоанатомического отделения Медицинского центра ЗКМУ имени Марата Оспанова в период с 2021 по 2022 гг. Гистологические и иммуногистохимические исследования проводились в морфологической лаборатории кафедры гистологии ЗКМУ им. Марата Оспанова. Полученные данные были подвергнуты статистической обработке.

Результаты: *Настоящее исследование показало значимую статистическую корреляцию между уровнем Ki-67 и гистопатологической степенью дифференцировки рака желудка (p=0,039). При сравнении показателей «Стадия pTNM « (p=0,894), «Возраст» (p=0,664), «Пол (Ж – 1, М – 2)» (p=0,928), «Локализация (кардиальный – 1, тело – 2, антральный и пилорический – 3)» (p=0,860) не удалось установить статистически значимых корреляций с уровнем экспрессии Ki-67.*

Заключение: *Взаимосвязь между экспрессией Ki-67 и степенью гистопатологической дифференцировки (p=0,039) при раке желудка помогает выявлять пациентов с агрессивными опухолями, нуждающихся в адъювантной терапии.*

Ключевые слова: *рак желудка (РЖ), морфология, гистология, иммуногистохимия (ИГХ), Ki-67, пролиферация.*

Transparency of the study: *Authors take full responsibility for the content of this manuscript.*
Conflict of interest: *The authors declare no conflict of interest.*
Funding: *The authors declare no funding for the study.*
Authors' contributions: *The authors contributed equally to the conception, scientific design, execution, and interpretation of the submitted scientific research and the preparation of this scientific paper.*
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