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ABSTRACT

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THE ROLE OF TP53 GENE MUTATION IN THE SURVIVAL OF NON-SMALL CELL LUNG CANCER PATIENTS

Protein p53 is a surrogate but a highly informative marker for determining a TP53 gene mutation. The primary roles of this protein include the preservation of genome stability and the inhibition of cancer development. Alterations in p53 function and TP53 gene mutations are common in different cancer types, including non-small cell lung cancer (NSCLC). Although a mutation in a major suppressor gene should have catastrophic consequences, the effect on survival is highly ambiguous.

The aim of our study was to establish the prognostic role of TP53 gene mutation in radically treated NSCLC patients.

Materials and methods. The study included 42 patients who received radical surgical treatment at the Sumy Regional Clinical Oncology Center. All patients had I-IIIB pathological stages of NSCLC and did not receive preoperative radiation therapy or chemotherapy. The follow-up period continued for at least five years. To detect TP53 gene mutation, the immunohistochemistry of NSCLC tissue samples with antibodies against the p53 protein was performed. Pearson $\chi 2$ test, log-rank test, and Kaplan-Meier method were used for statistical evaluation. The results were considered statistically significant at $p < 0.05$. Statistical analysis was performed using Stata V.18.0 software (StataCorp, Texas, USA; https://www.stata.com; 2024).

Results. When analyzing the relationship between p53 expression and histological variants of NSCLC, a higher frequency of p53-mut was found in patients with squamous cell lung carcinomas (p=0.012). Other clinicopathological characteristics, including age, sex, tumor stage, category N, and smoking status, did not correlate with p53 expression. The expression of p53-mut was determined in 19 (45.2%) of 42 tumor tissue samples and included 14 (73.7%) samples of squamous cell carcinomas and 5 (26.3%) samples of adenocarcinomas. Univariate analysis showed that NSCLC patients with stages IA-IIA, category N0, p53-mut, never smokers, female gender, and age younger than 60 had better recurrence-free and overall survival. However, no statistically significant difference between the groups was found. Evaluation by histological variant showed that patients with squamous cell carcinoma and TP53 gene mutation had better recurrence-free survival than patients with wild-type TP53 (Log-rank p=0.0490), while adenocarcinoma patients did not demonstrate difference in survival (Log-rank p=0.8003).

Conclusions. TP53 gene mutation is present in 45.2% of patients with NSCLC, 25.0% with adenocarcinomas, and 63.6% with squamous cell lung carcinomas. Although patients of the studied cohort with squamous cell carcinomas and mutant p53 had better recurrence-free survival, we cannot conclude that a mutation in the TP53 gene is associated with a favorable prognosis. The obtained results only confirm that the mutation in the TP53 gene does not always have a negative impact on survival. Next-generation sequencing and the application of the evolutionary action of the p53 approach may provide more effective clinical decisions for predicting survival in patients with NSCLC.

Keywords: p53, TP53, lung cancer, survival, immunohistochemistry, squamous cell carcinoma, prognosis.

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РОЛЬ МУТАЦІЇ ГЕНУ TP53 У ВИЖИВАННІ ХВОРИХ НА НЕДРІБНОКЛІТИННИЙ РАК ЛЕГЕНІ

Сурогатним, але високоінформативним маркером для визначення мутації гена TP53 є білок p53. Основні ролі цього білка включають збереження стабільності геному та пригнічення розвитку раку. Зміни у функції p53 і мутації гена TP53 є поширеними при різних типах раку, включаючи недрібноклітинний рак легені (НДКРЛ). Хоча мутація в головному супресорному гені повинна мати катастрофічні наслідки, вплив на виживання дуже неоднозначний.

Метою нашого дослідження було встановити прогностичну роль мутації гена TP53 у радикально пролікованих пацієнтів, хворих на НДКРЛ.

Матеріали та методи. Обстежено 42 хворих, які отримали радикальне хірургічне лікування в Сумському обласному клінічному онкологічному центрі. Усі пацієнти мали I-IIIB патологічні стадії НДКРЛ і не отримували передопераційну променеву та хіміотерапію. Період спостереження тривав щонайменше п'ять років. Для виявлення мутації гена TP53 проводили імуногістохімічне дослідження зразків тканин НДКРЛ з антитілами до білка p53. Для статистичної оцінки використовували критерій Пірсона, логарифмічний ранговий критерій та метод Каплана-Мейєра. Результати вважалися статистично значущими при p < 0,05. Статистичний аналіз проводили за допомогою програмного забезпечення Stata V.18.0 (StataCorp, Техас, США; https://www.stata.com; 2024).

Результати. При аналізі зв’язку між експресією p53 та гістологічними варіантами НДКРЛ виявлено більш високу частоту мутантного p53 у пацієнтів із плоскоклітинним раком легень (p=0,012). Інші клініко-патологічні характеристики, включаючи вік, стать, стадія захворювання, категорія N і статус паління, не корелювали з експресією p53. Експресію мутантного p53 встановлена в 19 (45,2%) з 42 зразків пухлинної тканини і включала 14 (73,7%) зразків плоскоклітинних карцином і 5 (26,3%) зразків аденокарцином. Однофакторний аналіз показав, що пацієнти з НДКРЛ зі стадіями IA-IIA, категорією N0, мутантним p53, жіночої статі, віком до 60 років та ті, що ніколи не палили мали кращу безрецидивну та загальну виживаність. Однак статистично значущої різниці між групами не виявлено. Оцінка за гістологічними варіантами показала, що пацієнти з плоскоклітинною карциномою та мутацією гена TP53 мали кращу безрецидивну виживаність, ніж пацієнти з диким типом TP53 (Log-rank p=0,0490), тоді як пацієнти з аденокарциномою не продемонстрували різниці у виживаності (Log-rank p=0,8003).

Висновки. Мутація гена TP53 присутня у 45,2% пацієнтів з НДКРЛ, 25,0% з аденокарциномами і 63,6% з плоскоклітинними карциномами легень. Хоча пацієнти досліджуваної когорти з плоскоклітинними карциномами та мутантним p53 мали кращу безрецидивну виживаність, ми не можемо зробити висновок, що мутація в гені TP53 пов’язана зі сприятливим прогнозом. Отримані результати лише підтверджують, що мутація в гені TP53 не завжди негативно впливає на виживання. Секвенування наступного покоління та застосування підходу еволюційної дії p53 можуть забезпечити більш ефективні клінічні рішення для прогнозування виживаності пацієнтів з НДКРЛ.

Ключові слова: p53, TP53, рак легень, виживаність, імуногістохімія, плоскоклітинна карцинома, прогноз.

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INTRODUCTION / ВСТУП

The p53 protein is the product of the TP53 gene, which is located on human chromosome 17. The primary roles of this protein include the preservation of genome stability and the inhibition of cancer development [1]. P53 stimulates gene transcription by binding to DNA sequences and controlling the cell cycle. P53 regulates cellular metabolism and acts as a key metabolic sensor through indirect mechanisms [2]. In response to DNA damage or various triggers like metabolic or ribosomal stress, p53 undergoes post-translational modifications. The alterations in the protein structure facilitate the activation of genes that either repair a damaged cell or induce programmed cell death [3].

TP53 gene mutation leads to the negative regulation and loss of function of the wild-type p53 (p53-wt), which has protective effects. As a result, mutant p53 (p53-mut) demonstrates tumorigenic properties and stimulates tumor progression and metastasis [4, 5].

A surrogate marker that determines a mutation in the TP53 gene is the expression of the p53 protein. In the past, immunohistochemical interpretation of p53 expression was based on the percentage of stained tumor cell nuclei with different threshold values ranging from 5 to 10% [6]. However, the modern approach considers the percentage of positively stained cells and the staining intensity. In addition, three staining patterns are considered: overexpression, negative expression, and cytoplasmic expression. This approach allows the detection of the TP53 gene mutation with an accuracy of up to 95% and covers all possible variants of this gene mutation [7].

Alterations in p53 function and TP53 gene mutations are common in different cancer types, including non-small cell lung cancer (NSCLC). Several studies have demonstrated that p53-mut correlates with poor survival and unfavorable outcomes in patients with lung cancer [8, 9]. Restoration of p53 protein structure and activation of the p53 signaling pathway, on the contrary, suppresses carcinogenesis [10, 11].

Recent studies show that the TP53 gene mutation does not impact survival in patients with lung adenocarcinomas. Conversely, patients with squamous cell carcinomas demonstrate a surprisingly long survival, which can be related to fundamentally different ways of suppression and activation [12]. Deeping knowledge related to the impact of p53 on the survival and progression of adenocarcinoma and squamous cell lung carcinomas will enable the development of a targeted therapeutic approach, potentially leading to improved patient outcomes. **The aim** of our study was to establish the prognostic role of TP53 gene mutation in radically treated NSCLC patients.

MATERIALS AND METHODS

Selection of patients. The study included 42 patients who received radical surgical treatment at the Sumy Regional Clinical Oncology Center. All patients had I-IIIB pathological stages of NSCLC and did not receive preoperative radiation therapy or chemotherapy. Patients with IB-IIIB stages received 2 to 4 courses of postoperative platinum-based chemotherapy. In the case of the N2 category, patients were involved in adjuvant radiation therapy. The follow-up period continued for at least five years. The most recent survival data evaluation occurred on July 1, 2024. Data about the patients' death were obtained from the Cancer Registry of the Sumy Regional Clinical Oncology Center. The study was approved by the Local Ethics Committee of the Sumy Regional Clinical Oncology Center (protocol №21, dated December 25, 2023). All patients signed informed consent forms before the study began.

Immunohistochemistry. For immunohistochemistry (IHC) analysis of non-small cell lung carcinoma tissues, 4 μm thick serial histological sections of lung tissue were affixed to SuperFrost adhesive slides (Thermo Scientific, Waltham, MA, USA). The tissue sections were deparaffinized and underwent antigen unmasking through heat treatment in 0.1 M citrate buffer (pH 6.0) at 95–98 ◦C. The IHC results were visualized using the "In Vitro" detection system from Master-Diagnostica, Spain. Antibodies against p53 from Master-Diagnostica, Spain (ready to use) were utilized in the studies. Active and passive control of the obtained results was carried out as quality control of IHC studies. For each sample, 6 different fields of view with a diameter of 1 mm were analyzed. A pathologist carried out the p53 IHC staining. The scoring system was based on multiplying the percentage of positively stained nuclei (0-4) by the staining intensity (0-3). The percentage of positively stained nuclei was assessed on a scale (0 – absent, 1 – <25%, 2 – 25%-50%, 3 – 50%-75%, and 4 – 75%-100%. Negative expression (score 0) or overexpression of p53 (score 4 and above) indicated the presence of the TP53 gene mutation.

Statistical analysis. The relationship between p53 expression and age, sex of patients, pathological stage, N category, smoking, and histological variants of NSCLC was evaluated using the Pearson χ2 test. The Kaplan-Meier method was used to visualize survival curves. The Log-rank test determined the difference in survival between groups. The results were considered statistically significant at $p < 0.05$. Statistical analysis was performed using Stata V.18.0 software (StataCorp, Texas, USA; https://www.stata.com; 2024).

Table 1 – The relationship between type of p53 and clinicopathological characteristics

Baseline clinicopathological characteristics	Total (%) n=42	p53-wt (%) n=23	p53-mut (%) n=19	χ2 (p)
Age, n (%):				
Median	58	60	56	
Range	29–75	44–73	29–75	
< 60	22 (52.4)	10 (43.5)	12 (63.2)	1.6155
≥ 60	20 (47.6)	13 (56.5)	7 (36.8)	(0.204)
Sex, n (%):				
Female	8 (19.0)	5 (21.7)	3 (13.0)	0.2389
Male	34 (81.0)	18 (78.3)	16 (87.0)	(0.625)
Stage, n (%):				
IA-IIA	15 (35.7)	9 (39.1)	6 (31.6)	0.2584
IIB-IIIB	27 (64.3)	14 (60.9)	13 (68.4)	(0.611)
Histology, n (%):				
Adenocarcinoma	20 (47.6)	15 (65.2)	5 (26.3)	6.3127
Squamous cell carcinoma	22 (52.4)	8 (34.8)	14 (73.7)	(0.012)
Category N, n (%):				
N0	24 (57.1)	15 (65.2)	9 (47.4)	1.3535
N1-2	18 (42.9)	8 (34.8)	10 (52.6)	(0.245)
Smoking status, n (%):				
Never smokers	8 (19.0)	5 (21.7)	3 (13.0)	0.2389
Current or former smokers	34 (81.0)	18 (78.3)	16 (87.0)	(0.625)

RESULTS

Patient characteristics. Among the 42 patients whose tumors were evaluated for p53 expression, there were 8 females and 34 males. Their average age was 58 years (range 29 to 75). Lung adenocarcinoma was confirmed in 20 patients, squamous cell carcinoma in 22. In the investigated cohort, 34 patients (81%) were former or current smokers. When analyzing the relationship between p53 expression and histological variants of NSCLC, a higher frequency of p53-mut was found in patients with squamous cell lung carcinomas (p=0.012). Other clinicopathological characteristics did not correlate with p53 expression (Table 1).

Immunohistochemistry results

Immunohistochemical visualization of the p53 protein showed its localization in the nuclei of tumor cells. Also, single p53-positive nuclei belonged to normal epithelium cells and the tumor microenvironment cells, thus demonstrating a wild-type reaction. We identified two main variants of the distribution of p53-positive cells: diffuse and patchy. In samples with a diffuse variant, the expression of p53 was homogeneous and followed throughout the area. The patchy variant of p53 expression was heterogeneous, with dense areas of p53-positive cells and large areas of tissue where the reaction was negative. The diffuse variant was more common in squamous cell carcinomas, while the patchy variant was more common in adenocarcinomas. In general, the expression of mutant p53 was determined in 19 (45.2%) of 42 samples of tumor tissue of NSCLC, 14 (63.3%) samples of squamous cell carcinomas, and 5 (25.0%) adenocarcinomas (Fig. 1).

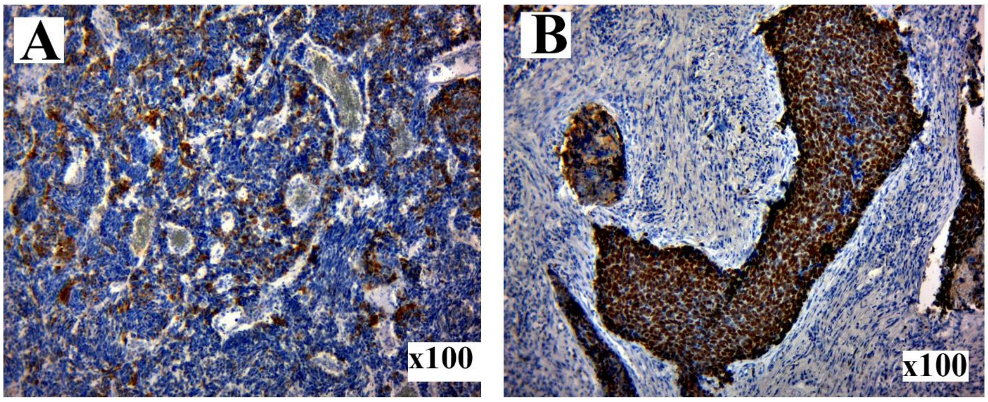

Figure 1 – IHC staining with antibodies against p53 protein in non-small cell lung cancer tissue. A – patchy variant of staining in adenocarcinoma tissue; B – a diffuse variant of staining in squamous cell carcinoma tissue. Staining of cell nuclei with Mayer's hematoxylin. Magnification is indicated in the lower right corner of the image

Prognostic factors of recurrence-free and overall survival in patients with NSCLC. During the follow-up period, disease recurrence was registered in 19 (45.2%) of 42 patients. The median follow-up period before disease recurrence was 54.0 months. Univariate analysis showed that patients with stages IA-IIA, category N0, p53-mut, never smokers, female gender, and age younger than 60 years had better recurrence-free survival. However, no statistically significant difference between the groups was found (Table 2).

Eighteen patients (42.9%) of the study cohort died due to NSCLC progression. One patient (2.4%) died due to causes unrelated to disease recurrence. The median follow-up period until death was 57.9 months. Patients with stages IA-IIA, category N0, p53-mut, those who had never smoked, had a female gender and were younger than 60 years had better overall survival. However, no statistically significant difference between the groups was found (Table 3).

Survival of patients with lung adenocarcinomas depends on the type of p53. Univariate analysis demonstrated that p53 type did not impact recurrence-free and overall survival in patients with NSCLC. Given the correlation between p53 expression and histological variants of NSCLC (Table 1), we investigated the survival of patients with adenocarcinomas and squamous cell carcinomas.

Among 20 patients with lung adenocarcinomas, disease recurrence and death were registered in 8 (40%) patients. Mutant p53 type was present in 2/8 (25%), wild type - 6/8 (75%) patients. No significant difference in survival was found (Log-rank p=0.8003, Fig. 2 and Fig. 3).

Survival of patients with squamous cell lung carcinomas depends on the type of p53. Among 22 patients with squamous cell lung carcinomas, disease recurrence and death were reported in 11 (50%) patients. 5/11 (45.5%) patients had p53-mut and 6/11 (54.5%) patients had p53-wt. Patients with p53-mut had statistically significant better recurrence-free survival than patients with p53-wt (Log-rank p=0.0490; Fig. 4).

Table 2 – Univariate analysis of recurrence-free survival

Baseline clinicopathological characteristics	Patients without disease recurrence, n	Patients with disease recurrence, n	Median follow-up period (months)	Log-rank p
Age:				0.9224
< 60	12	10	55.0	
≥ 60	11	9	52.8	
Sex:				0.2210
Female	6	2	70.8	
Male	17	17	50.0	
Stage:				0.1095
IA-IIA	11	4	64.2	
IIB-IIIB	12	15	48.3	
Histology:				0.7117
Adenocarcinoma	12	8	56.5	
Squamous cell carcinoma	11	11	51.7	
Category N:				0.7117
N0	16	8	61.9	
N1-2	7	11	43.4	
Smoking status:				0.2127
Never smokers	6	2	71.8	
Current or former smokers	17	17	49.8	
Type of p53:				0.2756
Wild type	11	12	48.6	
Mutant	12	7	60.5	
Total	23	19	54.0	

Table 3 – Univariate analysis of overall survival

Baseline clinicopathological characteristics	Alive patients, n	Dead patients, n	Median follow-up period (months)	Log-rank p
Вік:				0.6443
< 60	13	9	61.0	
≥ 60	10	10	54.7	
Sex:				0.0776
Female	7	1	75.0	
Male	16	18	54.0	
Stage:				0.1210
IA-IIA	11	4	69.2	
IIB-IIIB	12	15	51.8	
Histology:				0.7197
Adenocarcinoma	12	8	58.4	
Squamous cell carcinoma	11	11	57.6	
Category N:				0.3263
N0	15	9	62.5	
N1-2	8	10	52.0	
Smoking status:				0.0729
Never smokers	7	1	76.3	
Current or former smokers	16	18	53.7	
Type of p53:				0.2890
Wild type	11	12	53.6	
Mutant	12	7	63.3	
Total	23	19	57.9	

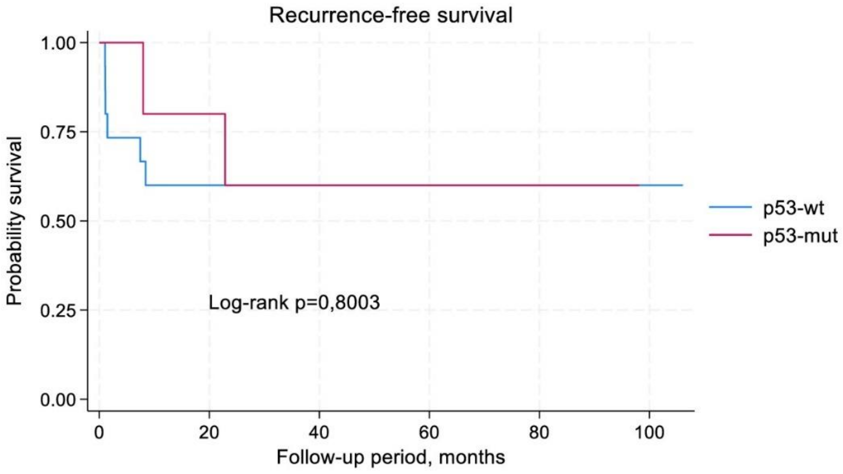

Figure 2 – Kaplan-Meier curves showing recurrence-free survival in patients with lung adenocarcinomas depending on p53 type

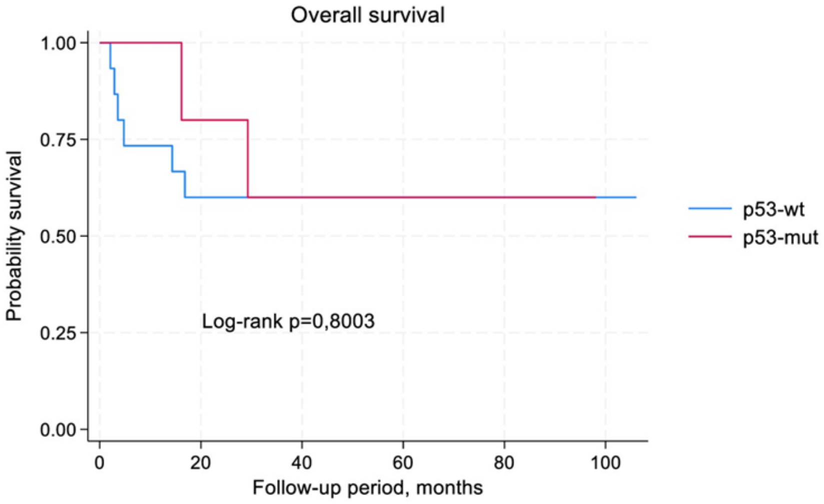

Figure 3 – Kaplan-Meier curves showing overall survival in patients with lung adenocarcinomas by p53 type

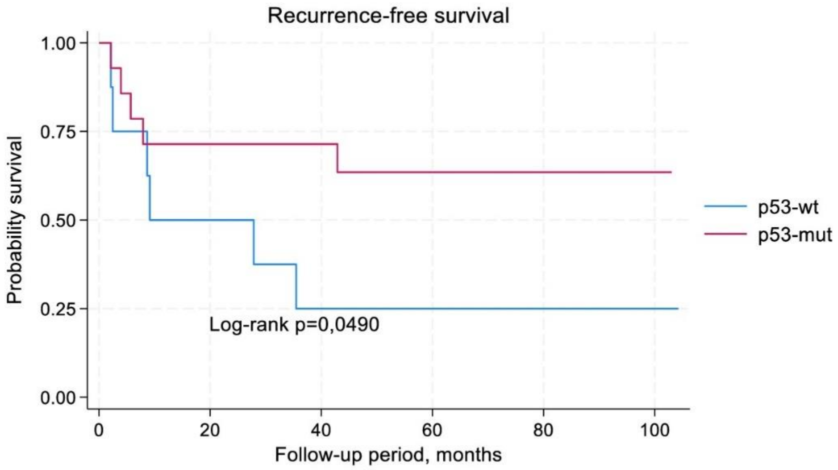

Figure 4 – Kaplan-Meier curves showing recurrence-free survival in patients with squamous cell lung carcinomas by p53 type

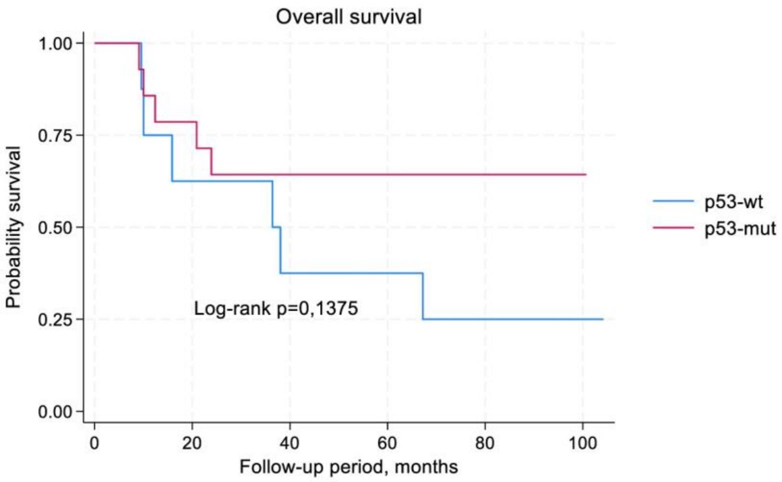

Figure 5 – Kaplan-Meier curves showing overall survival in patients with squamous cell lung carcinomas by p53 type

Patients with p53-mut also tended to have better overall survival, but no significant difference between groups was registered (Log-rank p=0.1375; Fig. 5).

DISCUSSION

TP53 gene mutation is one of the most common in NSCLC and can be detected in approximately 77% of squamous cell carcinomas and 47% of adenocarcinomas [13]. In the current study, the prevalence of TP53 mutation was 45.2% for NSCLC, 26.3% for adenocarcinoma, and 73.7% for lung squamous cell carcinoma. Patients with squamous cell carcinomas and TP53 gene mutation had better recurrence-free survival than patients with TP53-wt. For adenocarcinomas, the difference in survival was unreliable.

Traditionally, patients with TP53 gene mutation have been thought to have poor clinical outcomes primarily due to resistance to platinum-based chemotherapy. However, recent studies suggest that TP53 plays different biological roles in survival patients with adenocarcinomas and squamous cell carcinomas and has different prognostic significance [14].

The isolated effect of TP53 gene mutation is not considered a prognostic factor for survival in patients with NSCLC. More and more attention is paid to the combined effect of mutations (co-mutations) [15]. Depending on the histology, lung tumors have a different mutational landscape. For adenocarcinoma, the most common combination of a mutation in the TP53 gene and classic mutations, such as ALK, EGFR, RET, and BRAF. Squamous cell carcinomas that carry the TP53 mutation are often associated with rarer mutations such as CSMD, TTN, RYR2, DNAH5, and LRP1B. Co-mutations have a powerful effect on carcinogenesis and determine the clinical, molecular heterogeneity, and poor survival of patients with NSCLC [16, 17].

In the current study, we did not perform molecular genetic testing of tumor tissue, so we cannot assess the presence of co-mutations in the studied cohort. However, Qin et al. [18] demonstrated that co-mutation frequency varies significantly by geographic region. For example, the prevalence of TP53 and EGFR mutations in the European population is 25.91%. In the Asian population, this prevalence is much higher and reaches 60%. Shajani-Yi et al. [19] found that in the Netherlands, only every tenth patient with an EGFR mutation has a co-mutation with the TP53 gene. The main factors of poor survival in patients with mutations are genomic instability and insensitivity to targeted therapy with tyrosine kinase inhibitors. The number of co-mutations in our cohort was probably low, so no significant difference in the survival of patients with mutant and wild-type TP53 was observed.

The findings from our research on the impact of p53-mutation on the survival rates of patients diagnosed with squamous cell lung carcinomas were remarkably unexpected. It was found that patients with p53-mut have better recurrence-free survival. This discrepancy could be explained by the small sample and the impossibility of obtaining statistically reliable results. However, Fan et al. [20] obtained similar results while studying 487 patients with lung squamous cell carcinomas. Mutant p53 was recognized as an independent predictor of overall survival and a factor of favorable prognosis.

Although a mutation in a major suppressor gene should have catastrophic consequences, the effect on survival is highly ambiguous. Perhaps that is why the mutational status of the TP53 gene is not taken into account during the clinical evaluation of patients with NSCLC. The results we obtained in the current study allow us to agree with the conclusions of Zengin et al. [21], who established that a mutation in the TP53 gene in adenocarcinomas and squamous cell carcinomas is associated with fundamentally different pathways of suppression and activation. Squamous cell carcinomas are more likely, up to 94%, to carry TP53 mutations. However, this mutation does not consistently impact the prognosis of certain cancers, including lung squamous cell carcinoma.

Squamous cell carcinomas mostly develop in heavy smokers. Tabaco carcinogens cause the formation of DNA adducts, which in turn disrupt the function of various genes associated with cancer. Chromosomal abnormalities in squamous cell carcinomas can be broadly categorized, leading to not only the loss of cell cycle regulation (RB1, TP53, MYC, CDKN2A) but also affecting the expression of squamous cell differentiation pathways (SOX2, NOTCH, TP63), the upregulation of oncogenic signaling through the PI3K and RAS pathways, and abnormalities in epigenetic regulators (NSD1, KMT2D and KDM6A). A wide range of biological pathways may impact lung squamous cell carcinoma. So, not only TP53 gene mutation determines the loss of p53 function [22].

We hypothesize that the superior survival rates observed in patients with TP53 gene mutations may be attributed to inadequacies in the TP53 mutation assessment system. Truncating mutations, deletions, and missense mutations can lead to the loss of function of the TP53 gene. A missense mutation is the most common variant of the TR53 gene mutation. A point mutation leads to the replacement of a nucleotide and the formation of a codon, which begins synthesizing a new amino acid. The result of this process is a change in the protein structure. However, not all missense mutations significantly alter the p53 protein. An amino acid can be substituted by one with comparable chemical properties, allowing the protein to continue functioning normally; this is referred to as a neutral, "silent," or conservative mutation. Alternatively, substituting the amino acid could happen in a part of the protein that does not substantially impact its secondary structure or function. As a result, we observed the TP53 gene mutation, but p53 preserved its protective effect [23].

Additionally, some of the p53-mut retain the function of the p53-wt. For example, truncated mutations of the TP53 gene lead to the expression of a protein that retains the ability to induce apoptosis. Moreover, p53-mut can retain the ability to induce cell senescence and still has the ability to block the cell cycle but can not induce apoptosis. Therefore, a mutation in the TP53 gene is not necessarily associated with a complete loss of the function of the p53 protein [24].

In recent years, more and more scientific works have been devoted to studying the prognostic value of TR53 gene mutations. The new approach is called the evolutionary action of p53 (EAp53) and is based on the theory of the impact of point mutations on human health in the short term and on the process of evolution in the long term. EAp53 is considered to be the most accurate prognostic method, which allows stratification of TP53 missense mutations of high (EAp53 score >75) and low risk (EAp53 score ≤75). High-risk TP53 mutations impair p53 protein function and have a negative prognostic value. Low-risk TP53 mutations, in contrast, do not result in loss of p53 protein function, and the effect on survival is similar to p53-wt [25].

This approach has been used in several studies. Zhao et al. [26] evaluated the prognostic value of EAp53 in patients with stage I lung adenocarcinoma. Patients with high-risk EAp53 TP53 mutations had lower recurrence-free and overall survival. On the other hand, NSCLC patients with low-risk EAp53 mutations had a 70% and 48% lower risk of death than patients with high-risk EAp53 or TP53-wt, respectively. Jiang et al. [27] obtained similar results, indicating a negative effect of high-risk EAp53 mutation on overall survival in patients with metastatic NSCLC.

Therefore, the prognosis of patients with NSCLC largely depends on the TP53 gene polymorphism. Next-generation sequencing is the appropriate method for determining the type of TP53 mutation. The EAp53 algorithm identifies high- and low-risk mutations that differentially impact survival. A significant limitation of the present study is the absence of molecular genetic analyses of the tumor tissue samples. We believe the main reason for the better prognosis in patients with TP53 gene mutation was the predominance of low-risk TP53 gene mutations. Next-generation sequencing and application of the EAp53 approach may provide more effective clinical decisions for predicting survival in patients with NSCLC.

CONCLUSIONS

TP53 gene mutation is present in 45.2% of patients with NSCLC, 26.3% with adenocarcinomas, and 73.7% with squamous cell lung carcinomas. Although patients of the studied cohort with squamous cell carcinomas and mutant p53 had better recurrence-free survival, we cannot conclude that a mutation in the TP53 gene is associated with a favorable prognosis. The obtained results only confirm that the mutation in the TP53 gene does not always have a negative impact on survival.

AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

Conceptualization O.V.; methodology O.V.; investigation O.V. and Y.M.; resources O.V.; data curation O.V.; writing—original draft preparation O.V.; writing—review and editing O.V. and Y.M.; visualization Y.M.; supervision R.M.; project administration R.M.; funding acquisition O.V. All authors have read and agreed to the published version of the manuscript.

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CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

ARTIFICIAL INTELLIGENCE DISCLOSURE / ВИКОРИСТАННЯ ШТУЧНОГО ІНТЕЛЕКТУ

The authors confirm that no artificial intelligence-based technologies were utilized in the writing or editing of the manuscript.

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