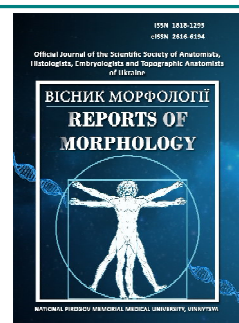




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## GLUT1 expression in patients with non-small cell lung cancer and its impact on survival

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### CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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### DATA SHARING

Data are available upon reasonable request to corresponding author.

GLUT1 is an essential glucose transporter, the expression of which increases in tumor cells, especially under conditions of hypoxia, and correlates with their active proliferation. This study aimed to investigate the relationship between GLUT1 expression and biological parameters and to evaluate the potential impact on survival in patients with radically treated non-small cell lung cancer (NSCLC). Forty-two patients who received radical treatment for NSCLC were involved in the study. Gender, age, smoking history, disease stage, and tumor histological type were considered when analyzing the data. GLUT1 antibodies were used to assess the degree of hypoxia. A semi-quantitative immunohistochemical score ranging from 0 to 12 was used for calculation. The  $\chi^2$  and Student's t-test were used to compare categorical and parametric variables. The Cox proportional hazards model, the Kaplan-Meier method, and the Log-rank test were used to evaluate the effect of GLUT1 expression on survival. The results were considered statistically significant at  $p < 0.05$ . A moderate correlation was found between GLUT1 expression and histological type of NSCLC ( $r = 0.432$ ,  $p < 0.0001$ ), sex ( $r = 0.336$ ,  $p < 0.0009$ ), and smoking ( $r = 0.325$ ,  $p < 0.0009$ ). GLUT1 overexpression was observed more in squamous cell carcinomas than in adenocarcinomas ( $p = 0.0001$ ). In patients with adenocarcinomas, the level of GLUT1 expression depended on age and T category. In patients with squamous cell carcinomas, GLUT1 expression was not associated with the studied clinicopathological characteristics. Patients with T1b-2a categories, without regional lymph node metastases, younger than 60, and non-smokers have better survival. Kaplan-Meier curves demonstrated no statistically significant differences in recurrence-free survival and overall survival between the patients with high and low GLUT1 (Log-rank  $p = 0.3284$  and Log-rank  $p = 0.7161$ , respectively). In conclusion, GLUT1 overexpression is associated with squamous cell lung carcinomas. GLUT1 expression has no prognostic value and does not correlate with recurrence-free and overall survival in radically treated patients with NSCLC.

**Keywords:** GLUT1, lung cancer, survival, adenocarcinoma.

### Introduction

At the beginning of the 20th century, Otto Warburg described a specific pattern of changes in the metabolism of tumors called the Warburg effect. Its essence is that even with sufficient oxygen concentration, malignant cells use glycolysis as the main pathway for adenosine

triphosphate production. Unlike tumor cells, normal cells metabolize glucose by oxidative phosphorylation (OXPHOS) [25]. Hypoxia is the key factor determining tumor cells' metabolic reprogramming and shifting from OXPHOS to anaerobic glycolysis [26]. At the same time, tumor cells

demonstrate increased glucose utilization due to increased transport inside cells with glucose transporters (GLUT) involvement. Members of the glucose transporter family (GLUT1-14) are widely represented on the surface of most cells in the human body and are involved in maintaining cellular homeostasis. Among them, GLUT1 is considered an essential transporter, the expression of which increases in tumor cells, especially under conditions of hypoxia. It correlates with the acceleration of the proliferation of malignant cells [3].

Glucose metabolism is closely related to the state of immune cells in the tumor microenvironment. X. Lai et al. [18] established that an elevated glucose level weakens the primary effector functions of human CD4<sup>+</sup> T cells. C. C. Yao et al. [28] demonstrated that reprogramming of glucose metabolism promotes antitumor immunity and effector function of CD8<sup>+</sup> T cells.

GLUT1 may be a promising biomarker indicating the energy supply of the tumor and its aggressiveness [8]. In recent years, a topical issue has been the development of drugs that affect tumor metabolism, particularly energy consumption by tumor cells. More and more authors consider GLUT1 an attractive target for targeted therapy and are actively investigating the relationship with survival [20, 24]. L. Wu et al. [27] established that the deficiency of glucose-6-phosphate isomerase and GLUT1 leads to the activation of the antitumor effect of cytotoxic T cells. Blocking GLUT1 stimulates the transition from glycolysis to oxidative phosphorylation. As a result, there is hyperproduction of reactive oxygen species and death of tumor cells mediated by tumor necrosis factor alpha.

GLUT1 overexpression has been reported in a significant number of malignancies, including oral cancer [1], triple-negative breast cancer [21], gallbladder [9], liver [23], and non-small cell lung cancer (NSCLC) [30]. Previous studies have shown that depending on the stage of the disease [17], mutation burden, and histological variant [15], the prognostic role of GLUT1 in patients with NSCLC differs significantly. These factors identify a possible impact of GLUT1 expression on NSCLC aggressiveness and patient outcomes, but data on this issue are limited.

*This study aimed* to investigate the relationship between GLUT1 expression and biological parameters and assess the potential impact on survival in patients with radically treated NSCLC.

## Materials and methods

**Research design.** The study involved 42 patients who received radical treatment for NSCLC at the Sumy Regional Clinical Oncology Center from 2015 to 2018. Inclusion criteria were age over 18 years, stages IA-IIIB of NSCLC, absence of severe cardiovascular and pulmonary pathology, and radical surgery in medical history ((bi)lobectomy or pneumonectomy). Exclusion criteria were comorbidities that could lead to the patient's death in the coming years, neoadjuvant chemotherapy or radiation therapy, and

postoperative complications. In addition to surgical treatment, patients with IB-IIIB stages received adjuvant chemotherapy according to the histological variant of the primary tumor. Radiation therapy with a total dose of 30 Gray was performed for patients with category N2. Pathological stages were evaluated according to the 8th edition of the TNM tumor staging system (AJCC, 2017). Sex, age, smoking history, and histological type of tumor were also considered when analyzing the data.

**Follow-up period.** Thirty-six patients received adjuvant chemotherapy, and five patients received radiation therapy. After the radical treatment of NSCLC was completed, all patients moved to the follow-up phase. According to local practice, in the first two years after surgery, computed tomography scans were repeated every three months and every six months in the next three years. After a 5-year follow-up period, a chest X-ray was performed every year. In case of suspicion of disease recurrence, imaging examinations were performed unscheduled. Recurrence-free survival was considered the period from the surgery to the registration of the recurrence of the disease. Overall survival was considered the interval between the surgery and the patient's death. In general, the interval of the follow-up period was from 2 to 106 months. Data on the death of patients were obtained from the cancer registry of the Sumy Regional Clinical Oncology Center. The data collection end date was July 1, 2024.

The study was approved by the Local Ethics Committee of the Sumy Regional Clinical Oncology Center (protocol № 20, dated December 21, 2023). All alive patients signed an informed consent before the start of the study.

**Histology and immunohistochemistry.** Lung cancer tissue samples were fixed in a 10 % neutral formalin solution for 24 hours. The processing of biological material and production of paraffin blocks was carried out according to the generally accepted method. For immunohistochemical examination (IHC) of NSCLC tissues, serial sections with a thickness of 4 µm were applied to SuperFrost slides (Thermo Scientific, Waltham, MA, USA). Deparaffinized sections were subjected to antigen unmasking by heat treatment in 0.1 M citrate buffer (pH 6.0) at 95-98 °C. The "In Vitro" detection system (Master-Diagnostica, Spain) was used to visualize IGH results. Antibodies to GLUT1 (polyclonal, Cell Marque, Rocklin, CA, USA) were used to assess the degree of hypoxia. A semi-quantitative immunohistochemical staining score (IHS) with a range from 0 to 12 was used to evaluate GLUT1 expression, where 0 points indicated the absence of immunoreactive cells, 1-4 points weak, 5-8 moderate, and 9-12 high expression of the biomarker). The IHS was calculated as the multiplication of the percentage of immunoreactive cells and the intensity of staining (0 - no staining, 1 - weak, 2 - moderate, 3 - strong). Less than 5 % of stained cells meant 0; 6-25 % - 1; 26-50 % - 2; 51-75 % - 3; ≥75 % - 4. As a positive control, we focused on erythrocytes [13].

**Statistical analysis.** Statistical analysis was performed

using Stata V.18.0 software (StataCorp, Texas, USA; <https://www.stata.com>; 2024). The normality of the distribution was determined by the Shapiro-Wilk test. Spearman's rank correlation coefficient was used to establish the relationship between GLUT1 expression level and clinicopathological characteristics. The significance of the difference between the two studied groups was assessed by the Student's t-test (for parametric variables). The Chi2 test was used to compare categorical variables. The Cox proportional hazards model was used to study the influence of clinicopathological characteristics on patients' recurrence-free and overall survival. The Kaplan-Meier method was used to compare survival depending on GLUT1 expression. The Log-rank test assessed the significance of the difference in survival in patients with low and high GLUT1. The results were considered statistically significant at  $p < 0.05$ .

## Results

**Histology and immunohistochemistry.** Adenocarcinoma tissue was characterized by the presence of atypical

glandular structures that infiltrated the interstitial lung tissue. Tumor cells, which consist of glandular and pseudo-glandular structures, had signs of cellular atypia. Some tumors have a papillary structure and contain mucin. When adenocarcinoma tissue was stained with anti-GLUT1 antibodies, a focal membrane reaction was detected in tumor cells (Fig. 1 A-B).

Squamous cell carcinoma is represented by layers of atypical flat epithelium with pathological mitoses and cell polymorphism. Tumor cells and complexes are surrounded by fibrous tissue with lymphohistiocytic inflammatory infiltration. Staining of squamous cell carcinoma tissue with antibodies against GLUT1 showed the presence of a distinct membrane reaction in layers of tumor cells (Fig. 1 C, D).

**Characteristics of the studied group of patients.** Among the patients involved in the study, 22 had squamous cell carcinomas (52.4 %) and 20 - adenocarcinomas (47.6 %). The median age of patients in the studied cohort was  $58.52 \pm 1.334$  years. The median age of patients with

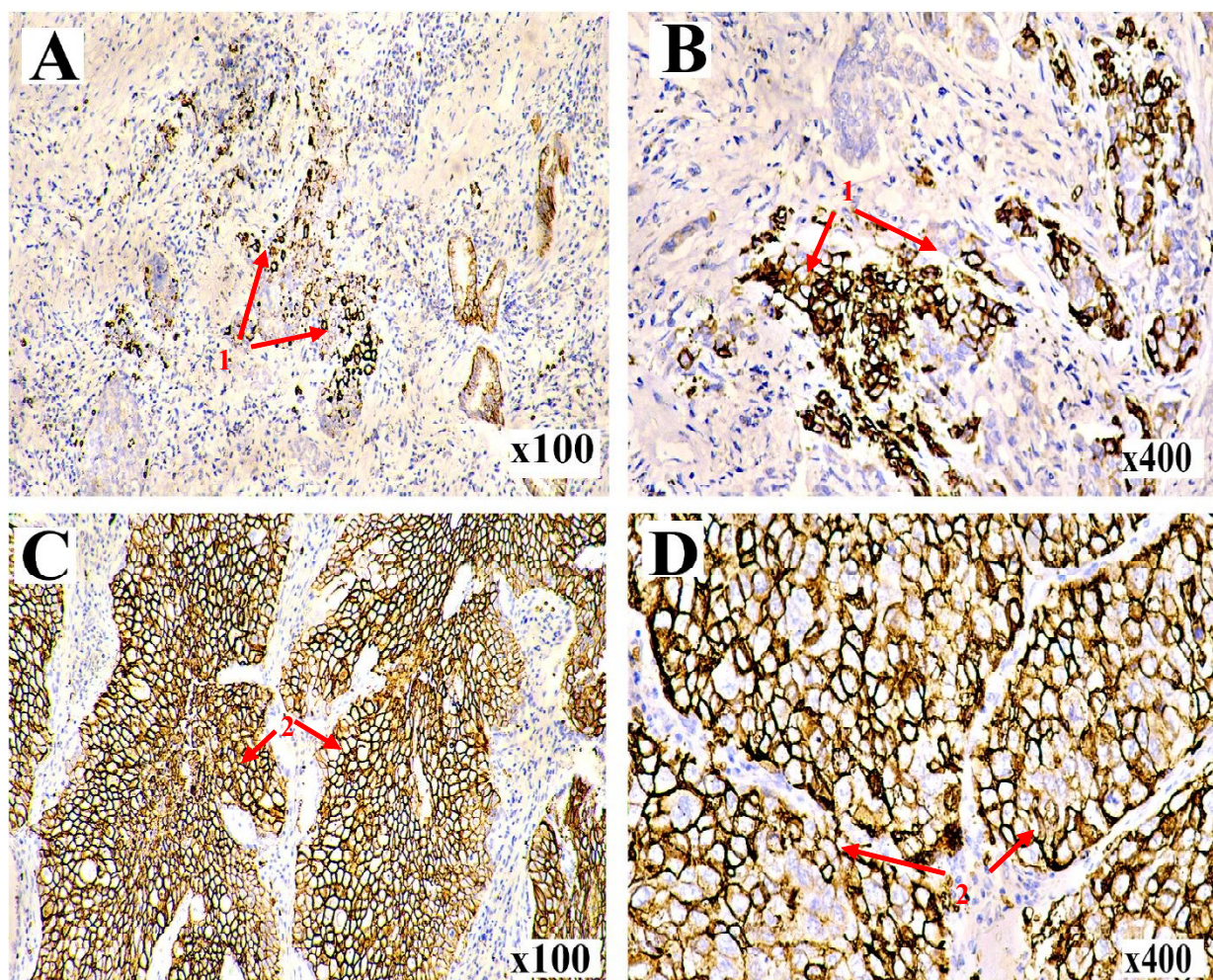


**Fig. 1.** Immunohistochemistry of NSCLC tissue with antibodies against GLUT1. A, B - adenocarcinoma, membrane staining (1), C, D - squamous cell carcinoma, membrane staining (2). Staining of nuclei with Mayer's hematoxylin. Magnification is indicated in each image's lower right corner.

adenocarcinoma is  $59.53 \pm 1.861$ , and squamous cell carcinoma is  $57.54 \pm 1.852$ . Among them, 34 patients were current or former smokers, and eight patients had no history of smoking.

According to GLUT1 expression, all patients were divided into 2 study groups:  $<9$  IHS (low GLUT1) and  $\geq 9$  IHS (high GLUT1). A moderate correlation was found

between GLUT1 expression and histological type of NSCLC ( $r=0.432$ ,  $p<0.0001$ ), sex ( $r=0.336$ ,  $p<0.0009$ ), and smoking ( $r=0.325$ ,  $p<0.0009$ ). The patients' other clinical and pathological characteristics did not demonstrate a statistically significant correlation with GLUT1. The results are presented in more detail in Table 1.

**Table 1.** Clinical and pathological characteristics of the studied cohort.

| Baseline clinicopathological characteristics                         | Total (%) n=42                     | Low GLUT1 (%) n=29                 | High GLUT1 (%) n=13              | r, p-value         |
|----------------------------------------------------------------------|------------------------------------|------------------------------------|----------------------------------|--------------------|
| Age, n (%):<br>Median<br>Range <60<br>≥60                            | 58 29-75<br>22 (52.4)<br>20 (47.6) | 59 29-75<br>14 (48.3)<br>15 (51.7) | 58 40-69<br>8 (61.5)<br>5 (38.5) | -0.123<br>(0.2647) |
| Sex, n (%):<br>Female<br>Male                                        | 8 (19.0)<br>34 (81.0)              | 8 (27.6)<br>21 (72.4)              | 0 (0.0)<br>13 (100.0)            | 0.336<br>(0.0009)  |
| Stage, n (%):<br>IA-IIA<br>IIB-IIIIB                                 | 15 (35.7)<br>27 (64.3)             | 10 (34.5)<br>19 (65.5)             | 5 (38.5)<br>8 (61.5)             | -0.038<br>(0.7221) |
| Category T, n (%):<br>T1b-2a<br>T2b-4                                | 19 (45.2)<br>23 (54.8)             | 11 (37.9)<br>18 (62.1)             | 8 (61.5)<br>5 (38.5)             | -0.219<br>(0.0463) |
| Category N, n (%):<br>N0<br>N1-2                                     | 24 (57.1)<br>18 (42.9)             | 16 (55.2)<br>13 (44.8)             | 8 (61.5)<br>5 (38.5)             | -0.060<br>(0.5920) |
| Histology, n (%):<br>Adenocarcinoma<br>Squamous cell carcinoma       | 20 (47.6)<br>22 (52.4)             | 18 (62.1)<br>11 (37.9)             | 2 (15.4)<br>11 (84.6)            | 0.432<br>(0.0001)  |
| Smoking status, n (%):<br>Never smokers<br>Current or former smokers | 8 (19.0)<br>34 (81.0)              | 8 (27.6)<br>21 (72.4)              | 0 (0.0)<br>13 (100.0)            | 0.325<br>(0.0009)  |

**Table 2.** Association between GLUT1 expression in adenocarcinomas and squamous cell carcinomas and clinicopathological characteristics.

| Baseline clinicopathological characteristics                  | Adenocarcinoma             | p-value       | Squamous cell carcinoma     | p-value |
|---------------------------------------------------------------|----------------------------|---------------|-----------------------------|---------|
| Age:<br><60<br>≥60                                            | 3.837±1.686<br>0.291±0.247 | <b>0.0089</b> | 8.428±0.828/<br>8.100±1.587 | 0.2192  |
| Sex:<br>Female<br>Male                                        | 1.528±0.878<br>1.807±1.117 | 0.1220        | 2.601±0.321<br>8.580±0.744  | 0.1480  |
| Stage:<br>IA-IIA<br>IIB-IIIIB                                 | 1.762±1.384<br>1.675±0.954 | 0.6670        | 8.785±1.434<br>8.086±0.920  | 0.5170  |
| Category T:<br>T1b-2a<br>T2b-4                                | 3.171±1.983<br>0.923±0.502 | <b>0.0040</b> | 9.091±0.834<br>7.370±1.727  | 1.0000  |
| Category N:<br>N0<br>N1-2                                     | 1.307±0.855<br>2.457±1.599 | 0.5070        | 9.136±0.982<br>7.481±1.149  | 0.0700  |
| Smoking status:<br>Never smokers<br>Current or former smokers | 0.657±0.450<br>2.276±1.152 | 0.1220        | 2.611±0.102<br>8.815±0.742  | 0.1480  |

*Relationship between GLUT1 expression, NSCLC histology, and patients' clinicopathological characteristics.* GLUT1 overexpression was observed more in squamous cell carcinomas than in adenocarcinomas ( $p=0.0001$ ). Among patients with lung adenocarcinomas and squamous cell carcinomas, 10 % (2 of 20) and 50 % (11 of 22) of patients had high GLUT1, respectively. The average IHS of the studied cohort was  $5.161 \pm 0.721$ . In patients with adenocarcinomas, the level of GLUT1 expression depended on age and T category. It is worth noting that GLUT1 expression in all patients with adenocarcinomas was low and did not reach the mean value of IHS for the studied cohort. However, higher GLUT1 expression was reported in patients younger than 60 and with categories T1b-2a. In patients with squamous cell carcinomas, GLUT1 expression was not associated with the studied clinicopathological characteristics (Table 2).

*Relationship between GLUT1 expression and survival in patients with radically treated NSCLC.* The median follow-up period was  $57.92 \pm 4.23$  months. The recurrence of the disease was registered in 19 patients. Nineteen patients died. In eighteen patients, death was related to lung cancer

recurrence. One patient died of other causes. Cox regression analysis demonstrated that the T category, N category, and smoking impact recurrent-free survival. Patients with categories T1b-2a, without metastases in the lymph nodes, and non-smokers have better recurrence-free survival (Table 3).

Multivariable analysis showed that independent predictors of overall survival were category T, category N, age, and smoking status. Patients with categories T1b-2a, without lymph node metastases, younger than 60, and non-smokers have better overall survival (Table 4).

Kaplan-Meier curves showed a trend toward better recurrence-free survival in patients with high GLUT1. However, no statistically significant differences were found between the groups with high and low GLUT1 (Log-rank  $p=0.3284$ ; Fig. 2).

Similar results were obtained during the analysis of overall survival. Patients with high GLUT1 tend to have a better prognosis. However, no statistically significant differences were found between the groups with high and low GLUT1 (Log-rank  $p=0.7161$ ; Fig. 3).

**Table 3.** Multivariable analysis of the impact of clinical and pathological characteristics on recurrence-free survival.

| Clinicopathological characteristic                              | Hazard ratio | 95 % CI     | p-value            |
|-----------------------------------------------------------------|--------------|-------------|--------------------|
| Age (<60 versus $\geq 60$ )                                     | 2.23         | 0.89-5.56   | 0.0860             |
| Sex (female versus male)                                        | 2.08         | 0.06-1.28   | 0.5710             |
| Stage (IA-IIA versus IIB-IIIB)                                  | 0.29         | 0.6670      | 0.1050             |
| Category T (T1b-2a versus T2b-4)                                | 30.62        | 3.03-309.43 | <b>0.0040</b>      |
| Category N (N0 versus N1-2)                                     | 37.74        | 5.07-280.74 | <b>0.0001</b>      |
| Histology (adenocarcinoma versus squamous cell carcinoma)       | 2.70         | 0.86-8.42   | 0.0870             |
| Smoking status (never smokers versus current or former smokers) | 11.18        | 1.12-111.13 | <b>1.12-111.13</b> |
| GLUT1 (low versus high)                                         | 1.96         | 1.96        | 0.3740             |

**Table 4.** Multivariable analysis of the impact of clinical and pathological characteristics on overall survival.

| Clinicopathological characteristic                              | Hazard ratio | 95 % CI     | p-value            |
|-----------------------------------------------------------------|--------------|-------------|--------------------|
| Age (<60 versus $\geq 60$ )                                     | 3.21         | 1.29-8.02   | 0.0120             |
| Sex (female versus male)                                        | 2.22         | 0.08-58.22  | 0.6310             |
| Stage (IA-IIA versus IIB-IIIB)                                  | 0.39         | 0.09-1.61   | 0.1960             |
| Category T (T1b-2a versus T2b-4)                                | 98.51        | 9.10-1065.6 | <b>9.10-1065.6</b> |
| Category N (N0 versus N1-2)                                     | 29.85        | 3.93-226.33 | 3.93-226.33        |
| Histology (adenocarcinoma versus squamous cell carcinoma)       | 3.16         | 0.89-11.16  | 0.0740             |
| Smoking status (never smokers versus current or former smokers) | 28.96        | 1.43-584.99 | <b>0.0280</b>      |

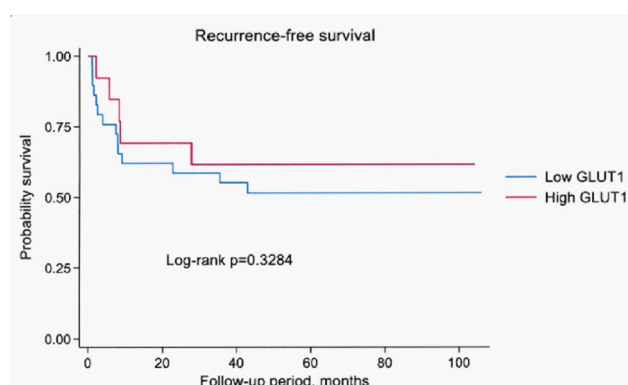


**Fig. 2.** Kaplan-Meier curves show recurrence-free survival of patients with low and high GLUT1 expression.

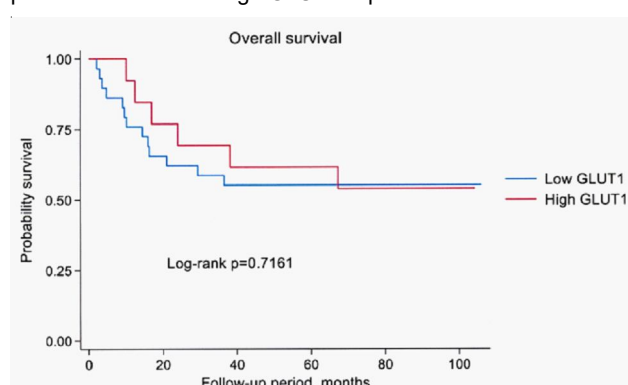


**Fig. 3.** Kaplan-Meier curves show patients' overall survival with low and high GLUT1 expression.

During the follow-up period, eight patients with adenocarcinoma and eleven patients with squamous cell carcinomas died. 7 of 8 patients with adenocarcinoma and 6 of 11 with squamous cell carcinoma had low GLUT1. Kaplan-Meier curves show a trend toward better overall survival in patients with low GLUT1 and adenocarcinoma. However, no statistically significant difference in the survival of patients was found (Log-rank  $p=0.8881$ ; Fig. 4).

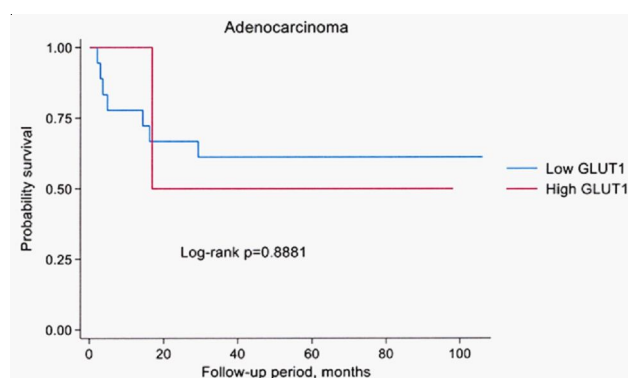


**Fig. 4.** Kaplan-Meier curves showing overall survival in patients with lung adenocarcinomas depending on GLUT1 expression.

For squamous cell carcinomas, there is a trend toward better survival in patients with high GLUT1, although there is also no significant difference between groups (Log-rank  $p=0.3160$ ; Fig. 5).

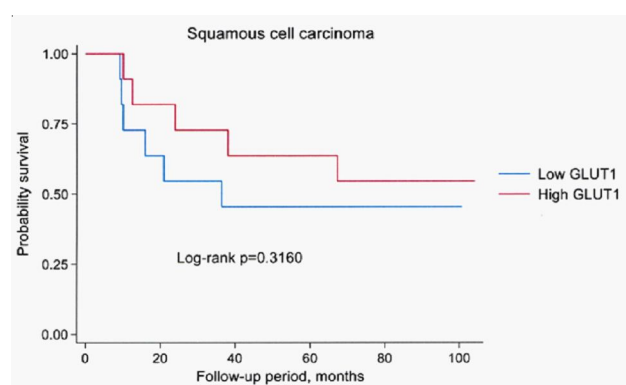


**Fig. 5.** Kaplan-Meier curves showing overall survival in patients with squamous cell carcinomas depending on GLUT1 expression.

## Discussion

The current study found that GLUT1 expression correlates with NSCLC histology, sex, and smoking status. GLUT1 overexpression is significantly more common in squamous cell carcinomas than in adenocarcinomas. We have shown that GLUT1 expression does not impact recurrence-free and overall survival in patients with radically treated NSCLC.

Our results coincide with the findings of Tan Z. et al. [22], who, in their meta-analysis, found that GLUT1 overexpression is more associated with squamous cell carcinomas and correlates with gender. GLUT1 overexpression was correlated with poor survival in patients with lung adenocarcinomas. It is worth noting that most of the studies devoted to the impact of GLUT1 expression on survival were conducted on the Asian population [5, 11, 14]. At the same time, no statistically significant difference in patient survival was found in Caucasians [4]. The current study also found no correlation between GLUT1 expression and survival. This may be due to the ethnic characteristics and limitations of this study, such as the small sample size and heterogeneity of patients concerning histological diagnosis and tumor stage.

This study found a correlation between smoking and GLUT1 expression. Q. Zhang et al. [29] attributed this phenomenon to the stimulatory effect of nicotine on hypoxia-inducible factor- $\alpha$  (HIF-1 $\alpha$ ), which closely enhances GLUT1 expression. It is believed that through the activation of acetylcholine receptors, nicotine causes metabolic reprogramming of cells and affects the redox balance in the tumor, changing the pH in NSCLC cells [16].

It is essential that, in addition to influencing the metabolism of tumor cells, GLUT1 and HIF1 $\alpha$  are also co-expressed in cells of the immune microenvironment, including in tumor-associated macrophages. HIF-1 $\alpha$  can induce macrophage polarization. Suppression of GLUT1 expression, on the contrary, can block this process. In addition, SLC2A1 (the gene encoding GLUT1) is negatively associated with other immune checkpoints, including PD-1, T cell receptor to Ig and ITIM domains (TIGIT), cytotoxic T lymphocyte-associated protein 3 (CTLA4) and LAG3, but

positively correlated with the level of CD44 expression [10].

The heterogeneity of GLUT1 expression in adenocarcinomas has both genetic and epigenetic determinants. S. K. Do et al. [7] showed that single-nucleotide variants significantly affect the overall survival of patients with squamous cell lung carcinomas but do not affect this indicator in adenocarcinomas. In addition, Contact C. et al. [6] found that lung adenocarcinoma is characterized by the presence of two glucose transporters, GLUT1 and GLUT3; therefore, when searching for predictive markers and vectors for the targeted action of new drugs, it is essential to take into account the expression of both glucose transporters. Y. Nakanishi et al. [19] also showed that GLUT4 can influence GLUT3 expression and survival in patients with NSCLC.

Given the expression of different GLUT types in NSCLC cells, it seems logical that regression analysis did not

identify GLUT1 as an independent prognostic factor for recurrence-free and overall survival. However, it is promising to study the influence of GLUT1 gene expression and polymorphism on the effectiveness of chemotherapy, radiation therapy, and targeted therapy with tyrosine kinase inhibitors [2, 12].

## Conclusions

1. GLUT1 overexpression is associated with squamous cell lung carcinomas. In patients with adenocarcinomas, the level of GLUT1 expression depended on age and T category, while GLUT1 expression in squamous cell carcinomas was not associated with the studied clinicopathological characteristics.

2. GLUT1 expression has no prognostic value and does not correlate with recurrence-free and overall survival in radically treated patients with NSCLC.

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## ЕКСПРЕСІЯ GLUT1 У ПАЦІЄНТІВ З НЕДРІБНОКЛІТИННИМ РАКОМ ЛЕГЕНЬ ТА ЇЇ ВПЛИВ НА ВИЖИВАНІСТЬ

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GLUT1 є ключовим транспортером глюкози, експресія котрого збільшується в пухлинних клітинах, особливо за умов гіпоксії, і корелює з прискоренням їх проліферації. Метою даного дослідження було вивчити зв'язок між експресією GLUT1 та біологічними параметрами та оцінити потенційний вплив на виживаність у пацієнтів з радикально пролікованим недрібноклітинним раком легень (НДКРЛ). Для проведення дослідження було залучено 42 пацієнта, котрі отримали радикальне лікування НДКРЛ. При аналізі даних враховували стать, вік, історію паління, стадію захворювання та гістологічний тип пухлини. Для оцінки ступеня гіпоксії застосовували антитіла до GLUT1. Для підрахунку використовували напівкількісну імуногістохімічну шкалу з діапазоном від 0 до 12. Chi2 тест та t-критерій Стьюдента використовували для порівняння категоріальних та параметричних змінних. Модель пропорційних ризиків Кокса, метод Каплана-Майєра та Log-rank тест застосовували для оцінювання впливу експресії GLUT1 на виживаність. Результати вважали статистично значущими при  $p < 0,05$ . Кореляція середнього ступеня виявлена між експресією GLUT1 та гістологічним типом НДКРЛ ( $r = 0,432$ ,  $p < 0,0001$ ), статтю ( $r = 0,336$ ,  $p < 0,0009$ ) та палінням ( $r = 0,325$ ,  $p < 0,0009$ ). Гіперекспресію GLUT1 спостерігали здебільшого в плоскоклітинних карциномах, ніж в аденокарциномах ( $p = 0,0001$ ). У пацієнтів з аденокарциномами рівень експресії GLUT1 залежав від віку та категорії Т. У пацієнтів з плоскоклітинними карциномами експресія GLUT1 не була пов'язана з досліджуваними клініко-патологічними характеристиками. Краще виживаність мали пацієнти з категоріями T1b-2a, без метастазів у регіонарних лімфатичних вузлах, віком молодше 60 років та ті, що не палили. Криві Каплана-Майєра продемонстрували відсутність статистично достовірних відмінностей у безрецидивній виживаності та загальній виживаності між групами з високим та низьким GLUT1 (Log-rank  $p = 0,3284$  та Log-rank  $p = 0,7161$  відповідно). Таким чином, гіперекспресія GLUT1 асоційована з плоскоклітинними карциномами легень. Експресія GLUT1 не має прогностичного значення та не корелює з безрецидивною та загальною виживаністю у радикально пролікованих пацієнтів з НДКРЛ.

**Ключові слова:** GLUT1, рак легень, виживаність, аденокарцинома.

## Author's contribution

Vynnychenko O. I. – conceptualization, research, methodology and original project writing.

Moskalenko Yu. V. – data visualization, software.

Yazykov O. V. – data visualization, software.

Seleznev O. O. – validation.

Sulaieva O. M. – review writing and editing.

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