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ABSTRACT

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ANALYSIS OF ASSOCIATION BETWEEN *MALAT1* GENE RS619586-POLYMORPHISM AND DISEASE-FREE SURVIVAL IN KIDNEY CANCER AND BLADDER CANCER PATIENTS

MALAT1 (Metastasis Associated Lung Adenocarcinoma Transcript 1) is an oncogenic long non-coding RNA, the overexpression of which is detected in many types of malignant tumors, including urinary tract cancer, and is often correlated with tumor progression and poor prognosis. Specific polymorphic loci within the *MALAT1* gene are known to be associated with the development of urinary tract cancer and their impact on patient survival. Therefore, the aim of our work was to study the distribution of the *MALAT1* rs619586-genotypes and alleles in patients with clear cell renal cell carcinoma (CCRCC) and transitional cell carcinoma of the urinary bladder (TCCUB), and to evaluate the potential association of this genetic locus with patient survival.

Material and methods. The study included 342 individuals: 101 patients with CCRCC, 141 patients with TCCUB, and 100 cancer-free controls. Genotyping for the *MALAT1* rs619586-locus was performed using real-time polymerase chain reaction (RT-PCR) with the TaqMan Assay C___1060479_10. Statistical analysis of the results was performed using the Prism (version 10.4.1) and R (version 4.4.2) software.

Results. In CCRCC patients, the minor G-allele of the *MALAT1* rs619586-polymorphism was significantly more frequent than in the control group (P = 0.03). No significant difference was found in the allele distribution for this locus among TCCUB patients (P = 0.09). A significant difference in the distribution of rs619586 genotypes was observed between men with CCRCC and male controls: carriers of the minor G-allele were more common among affected men (P = 0.01). Furthermore, among women with TCCUB, carriers of the minor G-allele were more frequent compared to female controls (P = 0.01). Sex-specific differences in the rs619586 genotype distribution were also revealed within the TCCUB group: female patients carried the minor allele more

frequently than male patients (P = 0.0001). A decrease in survival was demonstrated in CCRCC patients who were carriers of the minor G-allele compared with major allele homozygotes (P = 0.0101). No association was detected between the *MALAT1* rs619586-genotype and the overall survival of TCCUB patients (P = 0.8479).

Conclusions. The minor G-allele of the *MALAT1* rs619586-polymorphism is more frequent in CCRCC patients than in the control group. Furthermore, CCRCC patients carrying the G-allele exhibit lower survival rates compared to major allele homozygotes.

Keywords: gene polymorphism, long non-coding RNA MALAT1, clear cell renal cell carcinoma, transitional cell carcinoma of the urinary bladder.

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РЕЗЮМЕ

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АНАЛІЗ ЗВ'ЯЗКУ RS619586-ПОЛІМОРФІЗМУ ГЕНА *MALAT1* З ВИЖИВАНІСТЮ ПАЦІЄНТІВ ІЗ РАКОМ НИРКИ ТА РАКОМ СЕЧОВОГО МІХУРА

Вступ. MALAT1 (Metastasis Associated Lung Adenocarcinoma Transcript 1) є онкогенною довгою некодуючою RNA, гіперекспресія якої виявляється в багатьох типах злоякісних пухлин, включно з раком сечовидільної системи, і часто корелює з прогресуванням пухлинних захворювань та поганим прогнозом. Відомий зв'язок деяких поліморфних локусів гена *MALAT1* з розвитком онкологічних захворювань сечовидільної системи та їх вплив на виживаність пацієнтів. Тому, метою нашої роботи стало вивчення розподілу rs619586-генотипів і алелів гена *MALAT1* у хворих на світлоклітинний рак нирки (СКРН) і перехідноклітинний рак сечового міхура (ПКРСМ), а також оцінка можливого зв’язку даного генетичного локусу із виживаністю пацієнтів.

Матеріал і методи. У дослідженні взяли участь 342 особи: 101 пацієнт із СКРН, 141 хворий на ПКРСМ та 100 осіб без онкологічних захворювань. Генотипування за rs619586-локусом гена *MALAT1* здійснювали методом полімеразної ланцюгової реакції у режимі реального часу (Real-time PCR) за наявності TaqManAssay C___1060479_10. Статистичну обробку отриманих результатів проводили за допомогою програм Prism (версія 10.4.1) та R (версія 4.4.2).

Результати. У пацієнтів з СКРН мінорний G-алель за rs619586-поліморфізмом гена *MALAT1* зустрічався частіше, ніж у осіб контрольної групи (P = 0,03). Різниці у розподілі алелів за вивченим поліморфним локусом серед пацієнтів з ПКРСМ не виявлено (P = 0,09). Існує достовірна різниця у розподілі rs619586-генотипів гена *MALAT1* між чоловіками, хворими на СКРН і особами чоловічої статі, що не мають цієї недуги: серед хворих чоловіків носії мінорного G-алеля зустрічалися частіше (P = 0.01). Показано, що серед осіб жіночої статі, хворих на ПКРСМ носії мінорного G-алеля за rs619586-поліморфізмом гена *MALAT1* зустрічалися частіше, ніж серед жінок, що не мають ПКРСМ (P = 0.01). Виявлені статеві особливості розподілу rs619586-генотипів гена *MALAT1* у хворих на ПКРСМ: серед осіб жіночої статі носії мінорного алеля

зустрічалися частіше, ніж серед осіб чоловічої статі (P = 0,0001). Показано зниження виживаності осіб, що є носіями мінорного G-алеля, порівняно з гомозиготами за основним алелем у групі хворих на СКРН (P = 0,0101). Впливу генотипу за rs619586-поліморфізмом гена *MALAT1* на загальну виживаність пацієнтів із ПКРСМ не виявлено (P = 0,8479).

Висновки. У пацієнтів із СКРН мінорний G-алель за rs619586-поліморфізмом гена *MALAT1* зустрічається частіше, ніж у осіб контрольної групи. Виживаність осіб хворих на СКРН, що є носіями G-алеля є нижчою, ніж гомозигот за основним алелем.

Ключові слова: поліморфізм генів, довга некодуюча РНК MALAT1, світлоклітинний рак нирки, перехідноклітинний рак сечового міхура.

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INTRODUCTION

Urinary tract cancer represents a significant challenge in modern oncology and are one of the leading causes of mortality worldwide [1]. Despite advances in diagnosis and treatment, disparities in the prognosis and survival rates of patients with urinary tract cancer remain substantial. This highlights the urgent need to identify new, reliable biomarkers that could aid in risk stratification and the personalization of therapeutic approaches.

In recent years, attention has increasingly focused on the role of long non-coding RNAs (lncRNAs) in carcinogenesis. These molecules, which exceed 200 nucleotides in length and are not translated into protein, act as critical regulators of gene expression at various levels, influencing proliferation, apoptosis, metastasis, and treatment resistance [2]. Among them, the lncRNA MALAT1 (Metastasis Associated Lung Adenocarcinoma Transcript 1) holds a special place [3; 4; 5; 6]. Numerous studies have confirmed that MALAT1 is an oncogenic lncRNA, the hyperexpression of which is found in many types of malignant tumors, including urinary tract cancer, and often correlates with disease progression and poor prognosis [7]. Overexpression of the *MALAT1* gene has been detected in bladder cancer cells [8]. It has been shown that the production level of MALAT1 in primary bladder cancer tumors of patients with metastases is significantly higher compared to tumors of patients without metastases. MALAT1 has been demonstrated to promote tumor cell invasion by inactivating miR-125b [9]. A correlation has been established between the MALAT1 expression level and the degree of differentiation of bladder cancer cells, the cancer stage, and the presence of distant metastases [10]. Furthermore, overall survival in bladder cancer patients with high MALAT1 expression is significantly lower than in patients with low MALAT1 production [10]. Considering the accumulated scientific data, it can be concluded that MALAT1 is a promising biomarker for early-stage kidney and bladder cancer [11; 12], as well as other kidney diseases [13].

Genomic polymorphism, particularly single nucleotide polymorphisms (SNPs), in lncRNA genes can affect their stability, expression, processing, and functional activity, thus modifying individual cancer susceptibility and disease prognosis [2; 14]. Some polymorphisms of the *MALAT1* gene and their associations with the risk of developing certain types of urological cancer have been investigated [15; 16; 17]. However, the effect of the rs619586-polymorphic locus on the survival of patients with clear cell renal cell carcinoma and transitional cell carcinoma of the urinary bladder remains unexplored. Data on this could broaden the understanding of the molecular mechanisms underlying the variability in the prognosis of urological malignancies and contribute to the development of new prognostic models and personalized therapy strategies. Given the key role of MALAT1 in the development of urinary tract cancer and the potential functional impact of the rs619586 polymorphism, the aim of our study was to investigate the distribution of rs619586-genotypes and alleles of the *MALAT1* gene in patients with clear cell renal cell carcinoma (CCRCC) and transitional cell carcinoma of the urinary bladder (TCCUB), as well as to evaluate the association of this genetic locus with patient survival.

MATERIALS AND METHODS

Study Population

The study involved 342 individuals: 101 patients with CCRCC, 141 patients with TCCUB and 100 individuals without an oncological history (Table 1). Comparative clinical characteristics of patients by sex

Table 1. General clinical characteristics of patients with CCRCC and TCCUB

Indicator	CCRCC	TCCUB	Control group	P_1	P_2
Age, years	61.62±10.32	67.60±12.12	77.38±8.499	<0.000001	<0.000001
Body weight, kg	78.49±12.15	79.04±11.84	74.31±11.38	0.021	0.002
Height, cm	170.7±7.954	171.5±7.349	165.8±10.26	0.000561	<0.0001
BMI, kg /m^2	27.01±4.24	27.01±4.34	27.13±4.3	0.852	0.852
Blood glucose, mmol/L	5,50±1,58	5,52±1,59	5,27±0,80	0.239	0.138
Sex, f/m	42/59	27/114	34/66	0.309	0.011
Smokers, n (%)	49 (48.5)	70 (49.6)	27 (27.0)	0.002	0.001
Obesity, n (%)	30 (29.7)	31 (22.0)	18 (18.0)	0.068	0.517

Note: n – number of patients; f – female; m – male; P_1 – statistical significance of differences between patients with CCRCC and control group; P_2 – statistical significance of differences between patients with TCCUB and control group. Categorical variables were compared using the χ^2-test, and quantitative variables were compared using the t-test

are provided in Table 2. The final morphological diagnosis of CCRCC and TCCUB was verified in accordance with the European Association of Urology Guidelines [18]. All patients had clinical stage II cancer according to the TNM classification of malignant tumors, which was established based on histological examination or MRI results. Individuals with tumors of other locations, hereditary pathologies, or diseases of unclear etiology were excluded from the main study group. The research protocol received approval from the Ethics Committee of the Educational and Scientific Medical Institute at Sumy State University (protocol no. 5/07.2022) and was conducted in line with the principles outlined in the Declaration of Helsinki. All participants provided informed written consent before their personal data was processed and blood samples were collected for genetic analysis.

Genotyping

For the investigation of the *MALAT1* gene rs619586-polymorphism, venous blood was collected under sterile conditions into 2.7 mL monovettes containing potassium ethylenediaminetetraacetic acid (11.7 mM) as an anticoagulant (Sarstedt, Germany). Blood samples were frozen and stored at -20°C. DNA was isolated from whole blood leukocytes using the GeneJET Whole Blood Genomic DNA Purification Mini Kit (Thermo Fisher Scientific, USA). Genotyping for the rs619586 polymorphic locus of the *MALAT1* gene was performed in the Scientific Laboratory of Molecular Genetic Research at Sumy State University using Real-time Polymerase Chain Reaction (Real-time PCR) on a Quant Studio 5 DX Real-Time instrument (Applied Biosystems, USA). The study utilized TaqMan assays (TaqMan®SNP Assay C___1060479_10) and a real-time PCR reagent kit (Thermo Fisher Scientific, USA). Amplification consisted of initial denaturation at 95ºC for 10 minutes, followed by 45 cycles, each consisting of a 15-second step at 95ºC and a 30-second step at 60°C.The resulting curves were analyzed using the software provided with the Quant Studio 5 DX Real-Time.

Statistical Analysis

Statistical processing of the obtained results was carried out using Prism (version 10.4.1) and R (version 4.4.2) software. The analysis of the distribution of rs619586-genotypes between the comparison groups was performed using Pearson's χ^2-test. Hardy-Weinberg equilibrium for genotype distribution was tested using the online resource Equilibrium WpCalc (https://wpcalc.com/en/equilibrium-hardy-weinberg/). Overall survival was analyzed using the Kaplan-Meier method. All tests were two-sided, and P-value < 0.05 were considered statistically significant.

RESULTS

As a result of the genotyping performed for the *MALAT1* rs619586-polymorphism, the distribution of A and G alleles and AA, AG, GG genotypes was obtained in the main and control groups (Table 3). Due to the low number of patients with the GG genotype, carriers of the minor allele AG and GG were combined into a common group AG + GG.

The obtained data show that in patients with CCRCC, there is a statistically significant difference in the ratio of A and G alleles between the comparison groups. In the main group, this ratio was 189 (93.6%) and 13 (6.4%), while in the control group it was 196 (98%) and 4 (2%). The minor G-allele was found more frequently in the CCRCC patient group than in the control individuals (P = 0.03). In patients with TCCUB, no statistically significant difference in allele distribution was found. The ratio was 264 (95%) and 14 (5%) in the main group and 196 (98%) and 4 (2%) in the control (P = 0.09). The distribution of genotypes

Table 2. Clinical characteristics of individuals of different sexes with CCRCC and TCCUB

Indicator	Women	Men	P
CCRCC			
Age, years	62.55±9.94	60.97±10.6	0.450
Body weight, kg	75.64±13.7	80.51±10.6	0.047
Height, cm	165.2±5.71	174.5±7.02	<0.000001
BMI, kg /m^2	27.67±4.77	26.54±3.98	0.199
Blood glucose, mmol/L	5,40±1,7	5,57±1,49	0.588
Leukocytes	6,21±22.9	6,16±19.3	0.910
Erythrocyte sedimentation rate, mm/h	18.6±15.5	16.5±12.8	0.460
Smokers, n (%)	6 (12.3)	43 (87.7)	<0.0001
Obesity, n (%)	15 (35.7)	15 (25.4)	0.278
Alcohol consumption, n (%)	15 (35.7)	49 (83)	<0.0001
Diabetes, n (%)	8 (19)	14 (23.7)	0.632
Arterial hypertension, n (%)	23 (54.8)	36 (61)	0.546
TCCUB			
Age, years	69.19±13.55	67.22±11.79	0.451
Body weight, kg	77.67±15.11	79.36±10.98	0.506
Height, cm	164.2±5.936	173.3±6.549	<0.0001
BMI, kg /m^2	28.85±5.8	26.49±3.75	0.010
Blood glucose, mmol/L	5,75±16.33	5,47±15.79	0.417
Leukocytes	6,39±20.25	7,14±24.17	0.134
Erythrocyte sedimentation rate, mm/h	17.63±11.58	15.83±13.96	0.537
Smokers, n (%)	2 (7.4)	68 (59.6)	<0.0001
Obesity, n (%)	11 (40.74)	20 (17.5)	0.018
Alcohol consumption, n (%)	12 (44.4)	88 (77.2)	0.002
Diabetes, n (%)	5 (18.6)	26 (22.8)	0.798
Arterial hypertension, n (%)	20 (74.1)	62 (54.4)	0.083

Note: n – number of patients; P – statistical significance of differences. Categorical variables were compared using the χ^2-test, and quantitative variables were compared using the t-test

Table 3. Frequency of alleles and genotypes for the rs619586-polymorphism of the *MALAT1* gene in the compared groups

	Main group		Control group		P (χ^2)
	n	%	n	%	
CCRCC					
Genotypes					
AA	89	88.1	96	96	0.39 (4.260)
AG+GG	12	11.9	4	4	
Alleles					
A	189	93.6	196	98	0.03 (4.882)
G	13	6.4	4	2	
TCCUB					
Genotypes					
AA	127	91.4	96	96	0.16 (1.999)
AG+GG	14	8.6	4	4	
Alleles					
A	264	95	196	98	0.09 (2.958)
G	14	5	4	2	

Note: n – number of patients; P – statistical significance of differences

among homozygotes for the major allele (AA) and minor allele carriers (AG + GG) in the CCRCC patient group was as follows: 89 (88.1%) and 12 (11.9%), while in the control group it was 96 (96%) and 4 (4%), respectively. No statistically significant difference in genotype distribution was found between the comparison groups (P = 0.39). Similar results were obtained for TCCUB patients. The ratio was 127 (91.4%) and 14 (8.6%) in the main group, 96 (96%) and 4 (4%) in the control, and this difference was not statistically significant (P = 0.16).

Sex-specific characteristics of the distribution of *MALAT1* gene rs619586-polymorphic variants in patients with CCRCC are presented in Table 4.

Table 4. Frequency of alleles and genotypes of the rs619586-polymorphism of the *MALAT1* gene in patients with CCRCC and control group of different sexes

Group	Genotypes				P_1 (χ^2)
	AA		AG+GG		
	n	%	n	%	
Men					
CCRCC	49	83	10	17	0.01 (6.954)
Control	64	97	2	3	
Women					
CCRCC	40	95.2	2	4.8	0.83 (0.047)
Control	32	94.1	2	5.9	
P_2 = 0.06 (3.481); P_3= 0.49 (0.475)					

Note: n – number of patients; P_1 – statistical significance of differences between patients with CCRCC and control group; P_2 – statistical significance of differences between patients with CCRCC of different sexes; P_3 – statistical significance of differences between individuals in the control group of different sexes

Among male patients with CCRCC, the genotype ratio was as follows: AA – 49 (83%) and AG + GG – 10 (17%). In contrast, for male control subjects, the ratios were AA – 64 (97%) and AG + GG – 2 (3%). These results indicate a statistically significant difference in the distribution of *MALAT1* rs619586-genotypes between men with CCRCC and male control subjects: carriers of the minor allele are found more frequently among affected men (P = 0.01). In the group of female patients with CCRCC, the ratio of homozygotes for the major allele (AA) and minor allele carriers (AG + GG) was 40 (95.2%) and 2 (4.8%). Among female control subjects, the ratio was 32 (94.1%) to 2 (5.9%) respectively. No statistically significant difference in the genotype ratio was found between the groups of women with CCRCC and female control subjects (P = 0.83). Furthermore, no significant differences were observed in the genotype distribution between affected patients of different sexes (P = 0.06) or between control subjects of different sexes (P = 0.49).

Sex-specific characteristics of the distribution of *MALAT1* gene rs619586-polymorphic variants in patients with TCCUB are presented in Table 5. Among female patients with TCCUB, the genotype ratio was as

Table 5. Frequency of alleles and genotypes of the rs619586-polymorphism of the *MALAT1* gene in patients with TCCUB and control group of different sexes

Group	Genotypes				P_1 (χ^2)
	AA		AG+GG		
	n	%	n	%	
Men					
TCCUB	108	94.7	6	5.3	0.48 (0.491)
Control	64	97	2	3	
Women					
TCCUB	19	70.4	8	29.6	0.01 (6.192)
Control	32	94.1	2	5.9	
P_2 = 0.0001 (14.49); P_3 = 0.49 (0.475)					

Note: n – number of patients; P_1 – statistical significance of differences between patients with CCRCC and control group; P_2 – statistical significance of differences between patients with CCRCC of different sexes; P_3 – statistical significance of differences between individuals in the control group of different sexes

follows: AA – 19 (70.4%) and AG + GG – 8 (29.6%). In contrast, for female control subjects, the ratios were AA – 32 (94.1%) and AG + GG – 2 (5.9%). These results indicate a statistically significant difference in the distribution of *MALAT1* rs619586-genotypes between women with TCCUB and female control subjects: carriers of the minor allele are found more frequently among affected women (P = 0.01). In the group of male patients with TCCUB, the ratio of homozygotes for the major allele (AA) and minor allele carriers (AG + GG) was 108 (94.7%) and 6 (5.3%). Among male control subjects, the ratio was 64 (97%) and 2 (3%). No statistically significant difference in the genotype ratio was found between the groups of men with TCCUB and male control subjects (P = 0.48). No significant differences were observed in the genotype distribution between control subjects of different sexes (P = 0.49). However, a significant difference was shown in the genotype ratio between TCCUB patients of different sexes. Among female TCCUB patients, the ratio of AA and AG + GG genotypes was 19 (70.4%) to 8 (29.6%), while among male patients it was 108 (94.7%) and 6 (5.3%). Minor allele carriers are found significantly more frequently among female TCCUB patients than among male TCCUB patients (P = 0.0001).

To assess the impact of the *MALAT1* gene rs619586-polymorphism on the overall survival of patients with CCRCC and TCCUB, survival analysis was performed using the Kaplan-Meier method. Among CCRCC patients, a reduced survival was shown in individuals who are carriers of the minor allele (AG + GG) compared to homozygotes for the major allele (AA) (P = 0.0101) (Fig. 1). Statistical analysis revealed no significant association between the rs619586-genotype of the *MALAT1* gene and the overall survival of TCCUB patients (P = 0.8479) (Fig. 2).

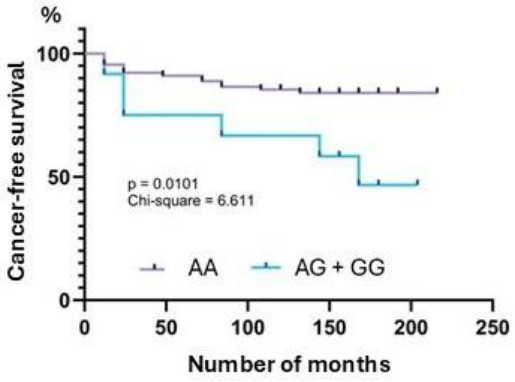

Figure 1. Overall survival of patients with CCRCC depending on MALAT1 rs619586-genotype

Note: Survival curves were generated using the Kaplan-Meier method

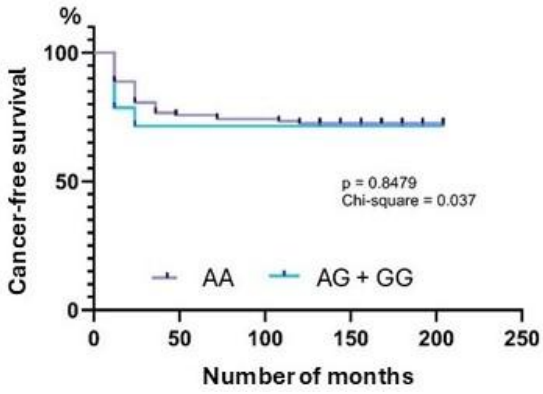

Figure 2. Overall survival of patients with TCCUB depending on MALAT1 rs619586-genotype

Note: Survival curves were generated using the Kaplan-Meier method

DISCUSSION

Long non-coding RNAs are crucial regulators of gene expression, which determines their influence on proliferation, apoptosis, metastasis, and treatment resistance [2]. As stated by the meta-analysis data from W. Ni [19] and L. Cao [20], the *MALAT1* gene rs619586 polymorphic locus is significantly associated with cancer risk. The authors supported the idea that the long non-coding RNA MALAT1 is a potential biological marker for the diagnosis and prognosis of various types of cancer.

The *MALAT1* gene was first identified in 2003 in non-small cell lung cancer cells, where its expression level was observed to be elevated [21]. The *MALAT1* gene is localized on chromosome 11 (11q13.1). It consists of 8708 base pairs and contains 2 exons [14]. According to the NCBI (National Center for Biotechnology Information), as of October 2025, 8369 polymorphic sites of the *MALAT1* gene are known [22]. The rs619586-polymorphism is characterized by the substitution of adenine (A) with guanine (G) in the non-coding region of the gene.

In our study, we report the first investigation of the distribution of genotypes and alleles for the *MALAT1* gene rs619586-polymorphic locus in patients CCRCC and TCCUB in the Ukrainian population. We showed that in CCRCC patients, the minor G allele is encountered more frequently than in control subjects, whereas no difference in allele distribution was found in TCCUB patients. As noted, there are no existing studies dedicated to investigating the association of the rs619586-polymorphic site with the occurrence of CCRCC and TCCUB. Regarding the role of the *MALAT1* rs619586-polymorphism in the development of other types of cancer, an association has been shown between this genetic marker and the development of

cervical cancer [23], lung cancer [24], prostate cancer [25], thyroid cancer [26], gastric cancer [27], colorectal cancer [28], melanoma [29], and others.

Our results revealed sex-specific differences in the distribution of rs619586-genotypes in TCCUB patients. Specifically, carriers of the minor G-allele were found more frequently among female patients than among male patients. Furthermore, interesting data were obtained within the groups. Among men with CCRCC, the minor allele was encountered more frequently than among men without CCRCC. Among women, the genotype ratio did not differ between the main and control groups. However, among women with TCCUB, the minor allele was found more frequently than among women without TCCUB, while the genotype ratio in the main and control groups of male subjects did not differ. Other data on the sex-specific association of the *MALAT1* gene rs619586-polymorphic locus with the development of urological or other cancers are absent.

In our study, reduced survival was demonstrated in individuals who are carriers of the minor G-allele compared to homozygotes for the major allele in the CCRCC patient group. In the TCCUB patient group, no impact of the rs619586-genotype on the overall survival of patients was found. Data on the survival of CCRCC and TCCUB patients depending on the *MALAT1* gene rs619586-polymorphism genotype are lacking. Regarding other polymorphic sites, the influence of the *MALAT1* gene rs3200401 polymorphism on the survival of patients with bladder cancer [16], lung cancer [30], and breast cancer [31] is known.

It should be noted that our study has a limitation related to the small sample size. Perhaps an increase in the number of patients with clear cell renal cell carcinoma and transitional cell carcinoma of the urinary bladder, together with a functional analysis of the rs619586-polymorphism, will allow a final conclusion to be drawn about the possibility of using this genetic factor as a diagnostic marker for the development of oncological diseases of the urinary system. Alongside this, it should be noted that this was the first study to study the distribution of genotypes and alleles at the polymorphic locus rs619586 of the MALAT1 gene in patients with clear cell renal cell carcinoma and transitional cell bladder cancer in the Ukrainian population and in the global population, as well as to assess the association of this genetic marker with patient survival.

Thus, the scientific search for genetic markers of urological malignancies, which is currently an active area of research in oncology, is an important direction in addressing the issues of early diagnosis, personalized treatment, and prognosis of these diseases. Similar approaches to determining risk markers and syntropy indices are already used to optimize early detection measures for non-communicable diseases (NCDs) and are effective in their prevention strategies [32]. The proposed approaches constitute a significant contribution to achieving Sustainable Development Goal 3 "Good Health and Well-being" which aims to improve access to quality healthcare [33].

CONCLUSIONS

1. The minor G-allele of the *MALAT1* gene rs619586-polymorphism is found more frequently in CCRCC patients than in control subjects (P = 0.03). No difference in allele distribution for the polymorphic locus studied was found among TCCUB patients (P = 0.09).

2. A statistically significant difference exists in the distribution of *MALAT1* rs619586-genotypes between men with CCRCC and male control subjects: carriers of the minor G allele are found more frequently among affected men (P = 0.01).

3. It is shown that among female patients with TCCUB, carriers of the minor G-allele of the *MALAT1* gene rs619586-polymorphism are found more frequently than in women without TCCUB (P = 0.01).

4. Sex-specific differences in the distribution of *MALAT1* rs619586-genotypes were detected in TCCUB patients: carriers of the minor allele are found more frequently among female patients than among male patients (P = 0.0001).

5. A reduced survival was shown in individuals who are carriers of the minor G-allele compared to homozygotes for the major allele in the CCRCC patient group (P = 0.0101). No impact of the *MALAT1* gene rs619586-genotype on the overall survival of TCCUB patients was found (P = 0.8479).

PROSPECTS FOR FUTURE RESEARCH

Further work will be carried out to expand the research group and search for other genetic factors in the progression of urinary tract cancer.

AUTHOR CONTRIBUTIONS

Author substantively contributed to the drafting of this paper. They take full responsibility for the integrity of all aspects of the work.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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