Reference

1. Dorofeikov V.V., Zazerskaya I.V., Khazova E.L. Vitamin D i reproduktivnoe zdorov'e zhenshchiny [Vitamin D and women's reproductive health. Saint Petersburg: Jeko-Vektor; 2017. 151 p. (In Russ.).]
2. Gromova O.A., Torshin I.Y., Tomilova I.K. [et al.]. Metabolity vitamina D: rol' v diagnostiki i terapii vitamin D-zavisimoj patologii [Vitamin D metabolites: a role in the diagnosis and therapy of vitamin D-dependent pathology. Practical Medicine. 2017;5 (106): 4-10. (In Russ.).]
3. Nacional'naya programma «Nedostatochnost' vitamina D u detej i podrostkov Rossijskoj Federacii: sovremennye podhody k korrekcii» [National program 'Vitamin D Deficiency in children and adolescents of the Russian Federation: modern approaches to correction'. Pediatricians' union of Russia. Moscow: 'Pediatr' Publ., 2018; 96 p. (In Russ.).]
4. Lesnyak O.M., Yershova O.B., Belova K.Y. [et al.]. Epidemiologiya osteoporoticheskih perelomov v Rossijskoj Federacii i rossijskaya model' FRAX [Epidemiology of osteoporotic fractures in the Russian Federation and the FRAX Russian model. Osteoporosis and osteopathy. 2014;3:3-8. (InRuss.).]
5. Bae S.C., Lee Y.H. Association between Vitamin D level and/or deficiency, and systemic lupus erythematosus: a meta-analysis. Cell Mol Biol (Noisy-le-grand). 2018;64(1):7-13. DOI: 10.14715/cmb/2018.64.1.2.
6. Clinician's Guide to Prevention and Treatment of Osteoporosis. F. Cosman, S. de Beur, M. LeBoff [et al.]. Osteoporos Int. 2014 Oct;25(10):2359-81. doi: 10.1007/s00198-014-2794-2.
7. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Kanis J.A., Cooper C., Rizzoli R. [et al.]. Osteoporos Int. 2019 Jan;30(1):3-44. doi: 10.1007/s00198-018-4704-5.
8. Pavic R., Hnatesen D., Margetic P. Epidemiology of Adult Fractures in Eastern Croatia by Cause of Injury, Fracture Location and Type of Treatment. Acta Clin Croat. 2017;56(3):494-504.
9. Vitamin D levels in systemic sclerosis patients: a meta-analysis. L. An, M.H. Sun, F. Chen [et al.]. Drug Des Devel Ther. 2017;11:3119-25. DOI: 10.2147/DDDT. S144860.
10. Vitamin D supplementation in elderly or postmenopausal women: a 2013 update of the 2008 recommendations from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Rizzoli R., Boonen S., Brandi M.-L. Current Medical Research & Opinion 2013;29(4):1–9.

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DIFFERENTIAL INFORMATIVENESS OF SERUM ONCOMARKERS FOR DETECTION OF RARE FORMS OF UTERINE BODY CANCER

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Aim. The aim of the study was to conduct a comparative analysis of the preoperative level of the concentration of tumor markers CA-125, HE4 and DJ-1 in the blood serum in endometrial and non-endometrial cancer of the uterine body.

Materials and methods. 249 patients with endometrial carcinoma (EC), 33 patients with serous (SC) and 24 patients with clear cell carcinoma (CCC) of the uterine body of stages II-IV according to FIGO were examined. Prior to the start of specialized antitumor treatment, the concentration of CA-125, HE4 and DJ-1 proteins was determined in blood serum by enzyme immunoassay.

Results. In patients with EC, SC and CCC the blood levels of CA-125 and HE4 tumor markers were elevated relative to the reference normal range, but did not differ significantly between the groups (p>0,05). A comparative analysis showed that a statistically significant difference between the groups was found only for the DJ-1 marker. In patients with EC, the mean blood level of DJ-1 corresponded to 521,4±12,8 pg/ml and in rare forms of uterine body cancer it was higher. With CCC the concentration DJ-1 was 984,2±19,2 pg/ml and in SC – 998,5±23,7 pg/ml.

Conclusion. For the differential diagnosis of endometrial and non-endometrial cancer of the body of the uterus, preoperative measurement of the concentration of DJ-1 in the blood is informative.

Key words: uterine body cancer, endometrial carcinoma, serous uterine body cancer, clear cell uterine body cancer, tumor markers.

Introduction. In the practice of oncologists, the determination of serum levels of tumor markers CA-125 (Cancer Antigen-125) and HE4 is used in the screening and prognosis of uterine cancer. An elevated level of CA-125 before surgery is accompanied by a poor prognosis for patients with endometrial carcinoma, which requires a higher frequency of postoperative examination of patients [6]. The HE4 (Human epididymis protein 4) marker is highly sensitive and specific in detecting early forms of endometrial cancer; its level has been correlated with the lethality of patients with poorly differentiated RTM [5]. In recent years, there has been encouraging information about the promise of protein deglycase DJ-1, also known as PARK7 (Parkinson's disease-associated protein 7), for the diagnosis of uterine cancer. DJ-1 is a multifunctional protein that activates proliferative cell processes and plays an important role in the pathogenesis and progression of cancer by modulating the tumor suppressor PTEN. The association of the level of DJ-1 in the blood with the course of the disease is associated by the authors with an increase in the expression of genes encoding this

protein in cells of poorly differentiated uterine body cancer and in non-endometrial carcinomas [3,7]. As is known, type II uterine cancer has a poor prognosis due to the high degree of malignancy [1]. Information about the degree of differentiation and the histological type of EC is mainly obtained from the morphological study of endometrial biopsy specimens before surgery. However, the results of histological examination of preoperative biopsy specimens of the endometrium and surgical specimens of uterine cancer in patients at high risk (G3 or non-endometrial forms of uterine cancer) do not match in a third of cases [4,8]. This mismatch can lead to incorrect surgical tactics. In this regard, oncologists need laboratory preoperative support in assessing the risk of progression of uterine cancer by determining the concentration of molecular markers in the blood. This will expand the possibilities of identifying patients with an unfavorable prognosis regarding the course of the disease. The aim of the study was to conduct a comparative analysis of the preoperative level of the concentration of tumor markers CA-125, HE4 and DJ-1 in the blood serum in endometrial and non-endometrial cancer of the uterine body.

Materials and methods. 249 patients with endometrial carcinoma (EC), 33 patients with serous (SC) and 24 patients with clear cell carcinoma (CCC) of the uterine body of stages II-IV according to FIGO were examined. The stages of uterine body cancer were determined based on the results of the revision of the organs during the operation and the results of the histological examination of surgical tissue samples according to the FIGO classification. The inclusion criteria for the study were: a histologically confirmed diagnosis of endometrial adenocarcinoma, clear cell or serous uterine body cancer; lack of specialized anticancer treatment before surgery. Exclusion criteria: decompensation of concomitant somatic diseases, oncological diseases of other localization, hormonal treatment before hysterectomy. All patients signed a voluntary informed consent to participate in the study. The study was approved by the Local Ethics Committee of the National Medical Research Center for Oncology of the Russian Ministry of Health.

All patients underwent extirpation of the uterus with appendages. Pelvic and lumbar lymph node dissection, omentectomy were performed according to indications.

Blood samples were collected the day before surgery by venipuncture of the cubital vein on an empty stomach. Blood was placed into test tubes with S-Monovette® Serum Gel (Sarstedt). Blood coagulation occurred at room temperature, samples were centrifuged at 3000 g for 10 minutes. Next, three aliquots of 300 µl were taken from the serum from each patient and stored at -80°C until the laboratory step.

Determination of DJ-1 concentration was carried out using enzyme immunoassay using specific test systems CircuLex Human DJ-1/PARK7 ELISA Kit (CycLex Co., Ltd. Japan) on an iMARK apparatus (Bio-Rad Laboratories, USA). Serum levels of CA-125 and HE4 were measured using electrochemiluminescence immunoassay using UniCel DxI 800 (Beckman Coulter, USA) and Roche Cobas e411 (Roche Group Ltd, Switzerland), respectively. The ARCHITECT Ca125 II diagnostic kit (CN 2K45-24, Abbott) was used to measure CA-125, and the ARCHITECT HE4 test system (CN 2P51-25, Abbott) was used to determine HE4.

Immunohistochemical evaluation of DJ-1 protein expression in the tissue of tumor samples was performed on paraffin sections 5 µm thick using standard technology. Anti-DJ-1 antibodies (Anti-DJ-1 antibody, 1:500, Cell Signaling Technology, Danvers, USA, 5933) were used for protein identification. Nuclear and nuclear/cytoplasmic staining was assessed using ranks 0,1,2,3: 0 - no staining, 1 point - the number of stained cells less than 10%, 2 points - 10-50%, 3 points - ≥50%.

Statistical data analysis was performed using Statistica 12.0 software (StatSoft, USA). We used descriptive statistics, analysis of variance, ROC analysis, comparison of shares using Pearson's test with a nonparametric correction.

Results and discussion. General characteristics of patient clinical groups are presented in Table 1.

The mean age of patients with EC corresponded to 64,5±1,9 years, with a diagnosis of CCC – 63,4±2,4 years and SC – 65,7±2,1 years. The diagnosis of uterine body cancer in most patients, regardless of the histological type, was first made in the postmenopausal period. Groups of patients were formed with a similar distribution of stages of the disease, mainly included patients with stages II-III according to FIGO. Obesity was a common comorbidity and occurred in EC in 87,1% (n=217), CCC – 83,3% (n=20) and SC – 78,8% (n=26), which affected the high values of the index body weight. In the majority of observations in the three groups of patients, a moderate degree of differentiation of tumor cells was noted. However, in rare forms of uterine body cancer, low differentiation of tumor cells was more common (CCC –

Table 1

General characteristics of patients with uterine body cancer

Indicator	EC (n=249)	SC (n=24)	CCC (n=33)	p
Menopausal status, abs.(%): pre-/perimenopausa postmenopausa	31 (12.4) 218 (87.6)	1 (4.2) 23 (95.8)	2 (6.1) 31 (93.9)	0.29
Body mass index, kg/m^2 (M±m)	31.4±1.8	29.7±1.5	29.4±1.9	0.83
Stage FIGO, abs.(%): II III IV	134 (53.8) 75 (30.1) 40 (16.1)	9 (37.5) 10 (41.7) 5 (20.8)	16 (48.5) 12 (36.4) 5 (15.1)	0.61
Degree of differentiation, abs.(%): G1 G2 G3	40 (16.1) 173 (69.5) 36 (14.4)	1 (4.2) 16 (66.6) 7 (29.2)	1 (3.1) 21 (63.6) 11 (33.3)	0.01
Myometrial invasion, abs.(%): <50% ≥50%	65 (26.1) 184 (73.9)	4 (16.7) 20 (83.3)	2 (6.1) 31 (93.9)	0.027
Metastases to lymph nodes, abs.(%): -yes -no	96 (38.6) 153 (61.4)	15 (62.5) 9 (37.5)	17 (51.5) 16 (48.5)	0.037

Note: Confidence probability p was determined by comparing three shares according to the Pearson test with Yates correction for continuity, quantitative indicators - according to the Kruskal-Wallis test.

Table 2

Concentration of tumor markers in blood serum before surgery in patients with uterine body cancer

Disease	Statistic	CA-125, U/ml	HE4, pmol/ml	DJ-1, pg/ml
EC (n=249)	M±m	37.9±1.2	77.8±2.6	521.4±12.8
	Me	36	79	513
	[25-75]	33-41	74-83	451-592
CCC (n=24)	M±m	40.9±1.5	87.4±2.9	984.2±19.2
	Me	41	88	985
	[25-75]	37-43	84-92	897-1124
SC (n=33)	M±m	42.5±1.6	88.3±3.3	998.5±23.7
	Me	44	90	1005
	[25-75]	39-47	86-95	864-1207
p_{EC-CCC}		0.24	0.10	<0.001
p_{EC-SC}		0.09	0.08	<0.001
p_{CCC-SC}		0.82	0.91	0.87
p_{all}		0.27	0.31	0.004

Note: M - the mean sample value, m - the error of the mean, Me - the median, [25-75] - the interquartile range, the confidence probability in multiple comparison between groups (p min) was determined using the Kruskal-Wallis test, pairwise comparison between groups were performed according to the Mann-Whitney test, adjusted for the number of compared pairs.

Table 3

Evaluation of DJ-1 expression in surgical tumor specimens taking into account the histological type of uterine body cancer

Tumor expression DJ-1, points	EC (n=249) abs.(%)	CCC (n=24) abs.(%)	SC (n=33) abs.(%)	p
0	81 (32.5)	4 (16.7)	4 (12.1)	p<0.001 ($\chi2$=51.3)
1	56 (22.5)	1 (4.2)	1 (3.0)	
2	75 (30.1)	9 (37.5)	7 (21.2)	
3	37 (14.9)	10 (41.6)	21 (63.7)	

Note: Confidence probability p was determined by comparing three shares of Pearson's test with Yates' correction for continuity.

29,2%, SR – 33,3%) compared with EC (14,4%). This circumstance affected the formation of statistically significant differences (p=0,01) depending on the degree of tumor differentiation. In rare forms of uterine body cancer, the tumor was more invasive compared to endometrial cancer (p=0,027). Metastases to the lymph nodes in CCC (62,5%) and SC (51,5%) were more common (p=0,037) compared with patients with EC (38,6%).

The values of the initial concentration of oncomarkers in the blood serum of patients with cancer of the uterine body are presented in Table 2.

The concentration of CA-125 and HE4 did not differ significantly in patients depending on the histological type of uterine cancer (p>0,05). Comparative analysis showed that the difference between the groups was found only in relation to the marker DJ-1 (p=0,004). In patients with EC, the mean blood level of DJ-1 corresponded to 521,4±12,8 pg/ml, and in rare forms of uterine body cancer it was higher. With CCC, the concentration of DJ-1 was 984,2±19,2 pg/ml, and with SC – 998,5±23,7 pg/ml.

The use of ROC analysis made it possible to clarify that before surgery, if the concentration of DJ-1 in the blood of patients with cancer of the uterine body exceeded the differential separation level of 852 pg/ml, the risk of detecting a rare form of cancer in the histological examination of surgical samples of the endometrium was high (diagnostic sensitivity 86,7 %, diagnostic specificity 81,3%, p=0,001).

Differences in the content of DJ-1 in the blood in endometrial and non-endometrial carcinoma may be due to different intensity of protein expression in the tumor tissue. Immunohistochemical study revealed that the nuclear expression of DJ-1 in tumor cells was observed more often (p=0,003) in EC (n=141, 56,6%) compared with patients with CCC (n=8, 33,3%) and SC (n=10, 30,3%). On the contrary, cytoplasmic localization of the DJ-1 protein was more common (p=0,02) in SC (n=29, 87,9%) and CCC (n=20, 83,3%) in contrast to patients with EC (n= 168, 67,5%). Overexpression of the DJ-1 protein in surgical tumor samples was more often observed in SC (63,7%), CCC (41,6%) compared with patients diagnosed with EC (14,9%) (Table 3).

DJ-1 activates the PI3K/Akt/mTOR signaling pathway, promoting tumor growth, metabolism activation, cancer cell proliferation, enhancing their viability, increasing metastatic potential, and avoiding cancer cells from apoptosis [2]. In rare forms of cancer of the body of the uterus, which differ from endometrial carcinoma in high metastatic potential and poor prognosis, the concentration of DJ-1 in the blood was higher. The difference in serum DJ-1 concentration in patients depending on the histological type of tumor is associated with different intensity of protein expression in the tumor tissue. The differential informativeness of the preoperative assessment of the level of DJ-1 in the blood before surgery in relation to the detection of forms of uterine body cancer with a high degree of malignancy complements the diagnostic capabilities of endometrial biopsy before the start of specialized treatment and makes it possible to rationally determine the tactics of surgical intervention until a final conclusion about the histological type of tumor is obtained.

Conclusions

1. For the differential diagnosis of endometrial and non-endometrial types of uterine body cancer, it is informative to measure the concentration of DJ-1 protein deglycase in the blood serum.

2. In patients with an excess of DJ-1 concentration in the blood above 852 pg/ml, the risk of detecting a rare form of uterine body cancer with a high malignant potential is increased, which requires surgical treatment in specialized centers by a multidisciplinary team of qualified oncogynecologists and morphologists to develop the correct surgical tactics.

Reference

1. Braun M.M., Overbeek-Wager E.A., Grumbo R.J. Diagnosis and Management of Endometrial Cancer. Am. Fam. Physician. 2016; 93: 468–474.

2. Wang W, Wang H, Xiang L, et al. DJ-1 is a new prognostic marker and predicts chemot-

herapy efficacy in colorectal cancer. Oncol. Rep. 2020; 44: 77–90. doi: 10.3892/or.2020.7593.
3. Di Cello A, Di Sanzo M, Perrone F.M., et al. DJ-1 is a reliable serum biomarker for discriminating high-risk endometrial cancer. Tumor Biol. 2017; 39(6): 1010428317705746. doi: 10.1177/1010428317705746.
4. Di Cello A, Rania E, Zuccala V, et al. Failure to recognize preoperatively high-risk endometrial carcinoma is associated with a poor outcome. Eur J Obstet Gynecol Reprod Biol. 2015; 194: 153–160. doi: 10.1016/j.ejogrb.2015.09.004.
5. Abbink K, Zusterzeel PL, Geurts-Moespot AJ, et al. HE4 is superior to CA125 in the detection of recurrent disease in high-risk endometrial cancer patients. Tumor Biol. 2018; 40(2): 1010428318757103. doi: 10.1177/1010428318757103.
6. Reijnen C, Visser NC, Kasius JC, et al. Improved preoperative risk stratification with CA-125 in low-grade endometrial cancer: A multicenter prospective cohort study. J. Gynecol. Oncol. 2019; 30: e70. doi: 10.3802/jgo.2019.30.e70.
7. Benati M, Montagnana M, Danese E, et al. The clinical significance of DJ-1 and HE4 in patients with endometrial cancer. J. Clin. Lab. Anal. 2018; 32: e22223. doi: 10.1002/jcla.22223
8. Matsuo K, Opper NR, Ciccone MA, et al. Time interval between endometrial biopsy and surgical staging for type I endometrial cancer: association between tumor characteristics and survival outcome. Obstet Gynecol. 2015; 125: 424–433. doi: 10.1097/AOG.0000000000000636.

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DNA COPY NUMBER VARIATIONS (14 CANCER-ASSOCIATED GENES) IN NON-SMALL CELL LUNG CANCER

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Non-small cell lung cancer (NSCLC) accounts for 85% of all lung cancers, 15-30% of which is squamous cell carcinoma, 54% is adenocarcinoma. The copy number variations (CNVs) as one of the factors affecting gene transcription activity is necessary to assess the role of genetic variation in pathological processes. The purpose of our study was to research the relative number of copies of 14 onco-associated genes: *APC, AURCA, CCND1, GKN1, PIK3CA, NKX2-1, ERBB2, SOX2, EGFR1, BRCA1, BRCA2, TP63, CDKN2A, MDM2,* in lung tissue samples as tumor markers of lung cancer. The study included 72 patients with Slavic and Crimean Tatar (Crimean) population, aged 46-78 (median 64) years with a diagnosis of lung cancer T1-1aN0-2M0-1 (stage I-IV). The relative copy number variation of genetic loci was assessed by the RT-qPCR method. In our study, statistically significant CNV change events ($p<0.05$) were recorded for the *CCND1*, *GKN1*, *PIK3CA*, *EGFR1*, *SOX2*, *BRCA2*, *TP63*, *MDM2* genes in squamous cell carcinoma samples and NKX2-1 in lung adenocarcinoma samples. Thus, these genes can be used as differentiating and diagnostic biomarkers in NSCLC.

Keywords: lung cancer, copy number variations, squamous cell lung cancer, lung adenocarcinoma, biomarkers.

Introduction. Lung cancer is associated with poor prognosis and is the leading cause of cancer death [4]. Non-small cell lung cancer (NSCLC) accounts for 85% of all types of lung cancer, 15-30% of which is squamous cell lung cancer, 54% is lung adenocarcinoma [16]. Despite studies of various treatment options, patients diagnosed with NSCLC (all stages) have a mortality rate of over 50% at 1 year and an overall 5-year survival rate of less than 18% [20].

The molecular basis of lung cancer is the gradual accumulation of genetic and epigenetic changes in the cell nucleus. These changes lead to a weakening of the DNA structure and its greater susceptibility to subsequent mutations. Due to the tumor process in the cells, the mechanisms that control their division and location are violated. This is caused by disturbances in the regulation of the cell cycle (mutations of proto-oncogenes and suppressor genes) and disturbances in the processes of repair of damaged DNA. Further changes, such as increased expression of growth factors, sustained angiogenesis, avoidance of apoptosis (mutations of anti-apoptotic and pro-apoptotic genes), limitless replicative potential and tissue invasion and metastasis, affect tumor progression [14].

Among other changes, lung cancer is characterized by genomic instability leading to a high frequency of somatic mutations and extensive genomic changes in individual genomes [9]. Change in the number of copies (English copy number variations, CNV) means a change in genomic DNA, characterized by a change in the DNA sequence numbers in the normal (diploid) genome. These DNA changes can affect individual genes, chromosomal regions, or entire chromosomes. CNVs have been shown to be associated with lung cancer as well as a number of other malignancies [7]. Generally, in cancer, a decrease or increase in DNA copy number can affect tumor suppressor genes and oncogenes, respectively. CNVs play an important role in the etiology of the disease. Understanding the association of CNV with diseases will help in the early detection and prognosis of the outcome of these diseases, and will also determine the most effective treatment strategies for patients.

Purpose of the study. To study the copy number of 14 cancer-associated genes APC, *AURCA*, *CCND1*, *GKN1*, *PIK3CA*, *NKX2-1*, *ERBB2*, *SOX2*, *EGFR1*, *BRCA1*, *BRCA2*, *TP63*, *CDKN2A*, *MDM2* in lung tumor tissue relative to conditionally healthy tissue as potential lung cancer tumor markers.

Materials and methods. The study included 72 Caucasoid patients living in the Republic of Crimea, aged 46-78 years (median 64) diagnosed with lung cancer T1-1aN0-2M0-1 (stage I-IV), who underwent planned treatment at the Medical Academy named after S.I. . Georgievsky, Federal State Autonomous Educational Institution of Higher Education "KFU named after W.I. Vernadsky" in 2015-2020 (Table 1). All patients voluntarily signed an informed consent to the processing of personal data and the transfer of information constituting a medical secret, as well as to the transfer of biological material. The study was carried out in accordance with the ethical principles of biomedical research, reflect-

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