DOI 10.26724/2079-8334-2025-3-93-88-94
UDC 616.61-006:616.65+576.367

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EXTRACELLULAR VESICLES OF STEM CELLS AS DIAGNOSTIC BIOMARKERS IN LIQUID BIOPSY OF SOMATIC AND ONCOLOGICAL DISEASES

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The purpose of the study was to investigate the prognostic value of extracellular vesicles (CD63 expression) in oncological and somatic diseases by liquid biopsies. To test our hypothesis, this case-control study consisted of the indicators of CD63 expression in the blood plasma of 20 healthy donors (control group); 18 patients with a positive diagnosis of COVID-19 according to PCR analysis; 33 patients with critical limb ischemia; 38 patients with renal cell carcinoma; 11 patients with uterine sarcoma. Extracellular vesicle was isolation from human plasma samples. Our studies have shown that the CD63 expression correlates with the progression of the deseases and lower survival. Thus, we performed this analysis to better understand the prognostic value of CD63 expression in somatic and oncologic diseases. Levels of circulating extracellular vesicles (CD63 expression) showed healthy donors group has the lowest mean value; uterine sarcoma group shows the highest mean value; groups with COVID-19 and renal cell cancer demonstrate similar mean values; group with critical limb ischemia shows an intermediate value. The results suggest that the CD63 can be a universal valuable marker in predicting complications and survival in somatic and oncological diseases.

Key words: extracellular vesicles. renal cell carcinoma, uterine sarcoma, COVID-19, critical limb ischemia.

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ПОЗАКЛІТИННІ ВЕЗИКУЛИ СТОВБУРОВИХ КЛІТИН ЯК ДІАГНОСТИЧНІ БІОМАРКЕРИ В РІДИННІЙ БІОПСІЇ СОМАТИЧНИХ ТА ОНКОЛОГІЧНИХ ЗАХВОРЮВАНЬ

Метою дослідження було вивчення прогностичної цінності позаклітинних везикул (експресія CD63) при онкологічних та соматичних захворюваннях за допомогою рідинної біопсії. Для перевірки нашої гіпотези це дослідження випадок-контроль включало показники експресії CD63 у плазмі крові 20 здорових донорів (контрольна група); 18 пацієнтів з позитивним діагнозом COVID-19; 33 пацієнти з критичною ішемією кінцівок; 38 пацієнтів з нирково-клітинною карциномою; 11 пацієнтів із саркомою матки. Позаклітинні везикули були виділені зі зразків плазми крові людини. Наші дослідження показали, що експресія CD63 корелює з прогресуванням захворювань та нижчою виживаністю. Таким чином, ми провели цей аналіз для кращого розуміння прогностичної цінності експресії CD63 при соматичних та онкологічних захворюваннях. Рівні циркулюючих позаклітинних везикул (експресія CD63) показали, що група здорових донорів має найнижче середнє значення; група з саркомою матки показує найвище середнє значення; групи з COVID-19 та раком нирки демонструють подібні середні значення; група з критичною ішемією кінцівок показує проміжне значення. Результати свідчать про те, що CD63 може бути універсальним цінним маркером у прогнозуванні ускладнень та виживаності при соматичних та онкологічних захворюваннях.

Ключові слова: позаклітинні везикули, нирково-клітинна карцинома, саркома матки, COVID-19, критична ішемія кінцівок.

The study is a fragment of the research project "Development and implementation of innovative technologies for the diagnosis of oncogynecological and oncourological diseases based on liquid biopsy data of extracellular DNA and stem cells", state registration No. 0123U101248.

In recent years, the tumor microenvironment (TME) has gained attention for its critical role in shaping tumor behavior, where small extracellular vesicles (small EVs) have emerged as key mediators of intercellular communication. These vesicles carry a diverse cargo of proteins, lipids, DNA, and various non-coding RNAs-such as miR-21, miR-155, and miR-1246-mirroring the molecular status of their originating cells [3].

Cells release extracellular vesicles (EVs) of different sizes and intracellular origin. The heterogeneity of EVs and presence of non-vesicular extracellular nanoparticles pose major obstacles to our understanding of the composition and functional properties of distinct secreted components [14]. Greater precision in assigning RNA, DNA and protein to their correct extracellular compartments and identifiying their mechanisms of secretion is crucial for identification of biomarkers and design of future drug interventions. Exosomes are 40–150 nm, endosome-derived, small extracellular vesicles (sEVs) secreted by most, if not all, cells. RNA (including mRNA, miRNA and other non-coding RNA), DNA and lipids are reported to be

actively and selectively incorporated into intraluminal vesicles (ILVs), which reside within multivesicular endosomes (MVEs) and are the precursor of exosomes [15]. In addition to accounting for the presence of membrane proteins in exosomes, inward budding of endosomal membranes is thought to result in the engulfment of cytosolic proteins and other components to the lumen of ILVs [12, 15]. Fusion of MVEs with the plasma membrane then releases ILVs into the extracellular space as exosomes. In contrast, microvesicles are 150–1000 nm large extracellular vesicles (lEVs) generated by shedding from the plasma membrane [12, 15]. However, specific markers that distinguish microvesicles from exosomes are lacking [6].

Exosomes are small membrane-bound vesicles that are released from various cells into the extracellular spaces. Such vesicles contain proteins, lipids and nucleic acids, which can be taken up by neighboring or distant cells and subsequently modulate recipient cells. Recently, it has been reported that exosomes from tumor cells might be involved in tumor progression by modulating the tumor microenvironment, e.g. metastatic niche formation and angiogenesis [2, 9, 10].

The tetraspanin protein CD63 has been described as a key factor in extracellular vesicle production and endosomal cargo sorting [10]. CD63 is expressed on almost all cell and tissues types and is located not only on the cytoplasmic membrane, but also in late endosomes, lysosomes, and multivesicular bodies (MVBs) [7]. In most cells, the CD63 pool is present on the membrane of late endosomes and lysosomes due to the lysosome targeting signal sequence present in its structure (YXXX). CD63 is also present in MVBs of platelet granules, melanosomes of melanocytes, cytotoxic granules of T cells, Weibel-Palade bodies of endothelial cells, and Major Histocompatibility Complex II (MHC-II) compartments of dendritic cells. The stimulation of these cells leads to the fusion of these multivesicular bodies with the cell surface, resulting in the release of microvesicles, called exosomes, in the extracellular microenvironment. For this reason, CD63 is highly enriched in exosomes derived from different cell types [7].

CD63 have been reports evaluating the association between CD63 expression and tumor existense. Moreover, some studies have suggested that CD63 expression is associated with survival in patients with tumors. However, the prognostic value of CD63 expression remains contradictory or inconclusive [10].

The purpose of the study was to investigate the prognostic value of extracellular vesicles (CD63 expression) in oncological and somatic diseases by liquid biopsies.

Materials and methods. The studies were carried out on the basis of city and regional hospitals of the Luhansk region between 2009 to 2024. In accordance with the provisions of the Declaration of Helsinki by the World Medical Association of the last revision (1964–2013) and informed consent for the use of biological material was obtained in all patients prior to inclusion in the study. Research permission was obtained from the Bioethics Committee of the Lugansk State Medical University (Luhansk, Ukraine, number 12/2009, Rubizhne, 25/2015, Rivne, 1/26.09.2022). The patients' epidemiological data, laboratory examination, complications, clinical outcomes, CT imaging data, and treatment plan were extracted from medical records.

To test our hypothesis, this case-control study consisted of the indicators of extracellular vesicles (CD63 expression) in the blood plasma of 20 healthy donors (control group); 18 patients with a positive diagnosis of COVID-19 according to PCR analysis; 33 patients with critical limb ischemia (CLI); 38 patients with renal cell carcinoma (RCC); 11 patients with uterine sarcoma (US). The clinical diagnosis in all patients was confirmed by morphological examination of the tumor according to the classification of kidney tumors of the World Health Organization (WHO/ISUP) [1]. According to the TNM classification, patients with malignant kidney tumors had stages of the tumor process:renal cell carcinoma $T_1N_0M_0$ – 8 (21 %), $T_2N_0M_0$ – 25 (66 %), $T_3N_0M_0$ – 4 (10 %), $T_4N_2M_0$ – 1 (3 %). According to the WHO International Classification of Diseases for Oncology, third edition (ICD-O-3) morphology codes [5]; histological subtypes of uterine sarcoma were defined as follows:

– Carcinosarcoma: Mullerian mixed tumor (n=0), Mesodermal mixed tumor (n=2),

– Carcinosarcoma, not otherwise specified (NOS) (n=1).

– Leiomyosarcoma: Leiomyosarcoma, NOS (n=2), Epithelioid leiomyosarcoma (n=2), Myxoid leiomyosarcoma (n=0).

– Stromal sarcoma: Endometrial stromal sarcoma (n=2), Endometrial stromal sarcoma, low-grade (n=0), Stromal sarcoma, NOS (n=0).

– Adenosarcoma (n=1).

– Sarcoma, NOS (n=1).

We determined the extent of disease at diagnosis using the International Federation of Gynecology and Obstetrics (FIGO) staging system.

Tumor grade was defined as follows: grade I, well differentiated; grade II, moderately differentiated; grade III, poorly differentiated; and grade IV, undifferentiated, anaplastic.

Extracellular vesicle isolation from human plasma samples [6].

Blood was drawn into BD Vacutainer Blood Collection Tubes (BD Bioscience) containing either Acid Citrate Dextrose Solution A or Buffered Sodium Citrate as anticoagulants. The first tube drawn was discarded. Further processing of samples was initiated within 20 min of blood draw. Plasma was generated by first centrifugation of the blood at 3000 × g for 15 min and then a second round of centrifugation of the supernatant at 3000 × g for 15 min tube to ensure that no platelets remained. The resulting plasma samples were immediately diluted ~1:20 in ice cold PBS and spun at 15,000 × g for 40 min to pellet and remove lEVs and microparticles. The supernatant was filtered through a 0.22 μm pore PES filter (Millipore). Clarified supernatants were subjected to ultracentrifugation at 120,000 × g for 4h (Beckman Coulter, Fullerton, CA) to sediment sEVs. Pellets of crude sEVs (P120) were resuspended in ice-cold PBS, tubes filled with PBS, and then subjected to ultracentrifugation at 120,000 × g for 4h. The washed pellet was resuspended again and subjected to a second wash step, again at 120,000 × g for 4h. The washed pellet was resuspended in ice-cold PBS. Crude plasma sEV samples were further purified by high-resolution iodixanol density gradients fractionation. At no time during the process were plasma or plasma sEVs subjected to temperatures below 4°C. A 40 μl of sample from serum eluate is taken from the plasma sEVs.

Table 1

Level of circulating extracellular vesicles (CD63 expression)

Groups	n	CD63 ng/ml	p level
healthy control	20	2.7±0.01	
patients with renal cell carcinoma	38	13.39±0.27	p=0.0000001
patients with uterine sarcoma	11	15.58±0.5	p=0.0000001
patients with COVID-19	18	13.63±0.47	p=0.0000001
patients with critical limb ischemia	33	7.67±0.25	p=0.0000001

Note: Data are means ± SEM for Gaussian variables. Intergroup by the T-test Students. p – significant differences between group healthy control with test other groups.

CD63 was determined using sandwich Enzyme-Linked Immunosorbent Assay (sELISA) from Human CD63 ELISA Kit (A310656) (Antibodies.com Europe AB, Sweden), following the manufacturer's instructions.

Data Processing. Statistical and graphical analyses were done using STATISTICA 7.0 (StatSoft Inc. USA, version 7.0) and MedCalc Version 20.218 64-bit (MedCalc Software, Ostend, Belgium). Parametric data were summarized as mean (standard error) (Mean±SEM). Kolmogorov-Smirnov test was applied to examine the normality of data distribution. To examine group-wise differences, unpaired Student's t-test was used. Receiver operating characteristics (ROC) curve analysis was performed to estimate optimal cut-off values, maximizing sensitivity and specificity according to the Youden index. Survival (patients with RCC and US), the development of respiratory failure (patients with COVID-19) and time to treatment failure (patients with CLI) analysis was performed using the Kaplan–Meier method. The Cox proportional hazards regression model was used to assess the effect of the value of extracellular vesicles (CD63 expression) on the diagnostic, prognosis and clinical outcomes in survival analysis. A p-value below 0.05 was considered statistically significant.

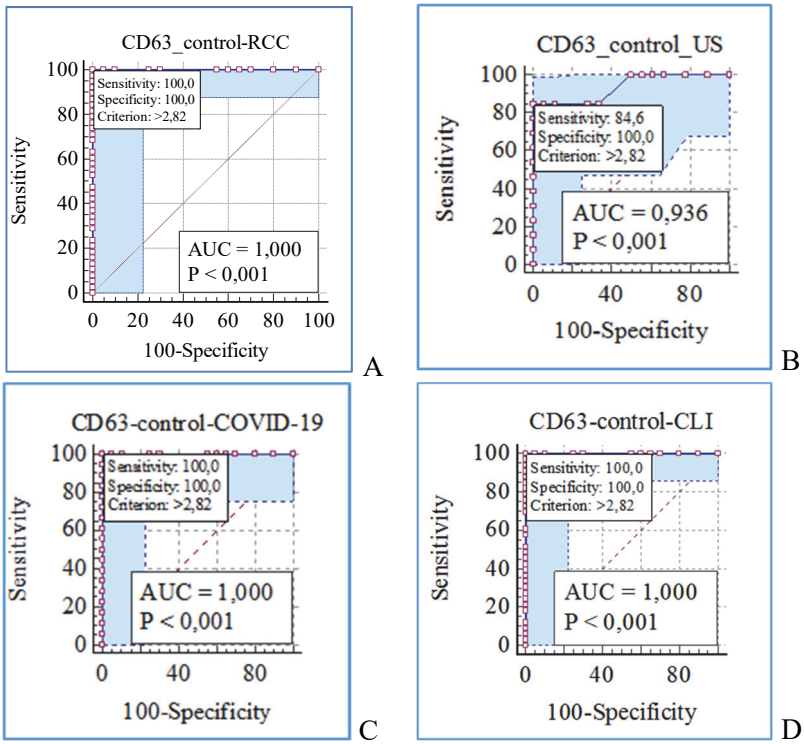

Fig. 1. ROC analysis: receiver operating characteristic (ROC) curves for for the CD63 measured in patients with: A – renal cell carcinoma; B – uterine sarcoma; C – COVID-19; D – critical limb ischemia.

Note: Here and in the following figures: p<0.001 – calculated by univariate logistic regression analysis.

Results of the study and their discussion. During the study, we divided patients into groups: healthy donors (control group); patients with a positive diagnosis of COVID-19; patients with critical limb ischemia; patients with renal cell carcinoma; patients with uterine sarcoma, in which we studied the level of circulating extracellular vesicles (CD63 expression) in the blood plasma (Table 1).

As our results showed control group has the lowest mean value (2.7±0.01); uterine sarcoma group shows the highest mean value (15.58±0.5); groups with COVID-19 and renal cell cancer demonstrate similar mean values (13.63±0.47 and 13.39±0.27 respectively); group with critical limb ischemia shows an intermediate value (7.67±0.25).

ROC-analysis was used to evaluate the diagnostic performance of plasma CD63 profile in the differentiation between control group (healthy donors) and patients with renal cell carcinoma and uterine sarcoma, COVID-19 and critical limb ischemia (Fig. 1).

Fig. 1A shows the ROC curve for the CD63 marker in patients with renal cell carcinoma. Let's analyze its main characteristics: Area Under the Curve (AUC) = 1.000 (0.938 to 1.000, p< 0.0001); optimal cut-off point = 2.82 ng/ml provides optimal separation between groups. At this point, CD63 appears to be an excellent biomarker with perfect discrimination between positive and negative endpoints. Higher CD63 levels are significantly associated with shorter survival times. The difference in survival between high and low CD63 groups is statistically significant (p<0.001).

With respect to survival, the optimal cut-off values identified by ROC analysis were as follows: CD63 of patients with uterine sarcoma – 2.82 ng/ml; like patients with COVID-19 and critical limb ischemia. The values of area under the curve (AUC) were 0.936 (0.786 to 0.992, p< 0.0001) for CD63 of patients with uterine sarcoma. Analysis of the ROC curve in patients with COVID-19 showed CD63 as a predictor of the development of respiratory failure (I or II) within 30 days of hospitalization. The area under ROC curve of CD63 was AUC=1.000 (0.933 to 1.000, p< 0.0001) in patients with COVID-19. The ROC curve in patients with critical limb ischemia showed CD63 as a predictor of the time to treatment failure, AUC=1.000 (0.933 to 1.000, p< 0.0001).

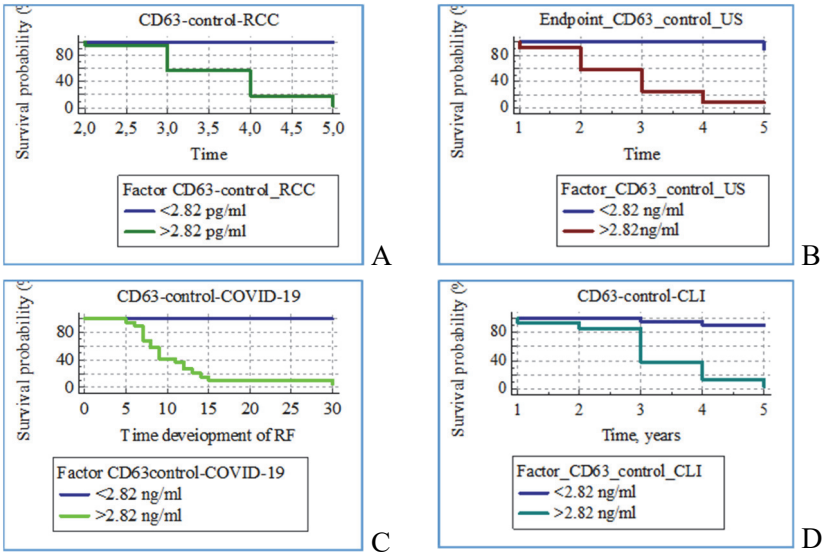

Fig. 2. Kaplan–Meier curves of the survival (A – patients with RCC and B – US), the development of respiratory failure (C – patients with COVID-19) and the time to treatment failure (D – patients with CLI). p value by Long-rank test.

Note: Here and in the following figures: p<0.0001 – calculated by univariate logistic regression analysis.

The Kaplan–Meier survival curves (Fig.2), after classifying the patients on the basis of Youden cut-offs obtained by ROC curves, showed Mean survival 3.69±0.13 (95 % CI for the mean 3.43 to 3.95) in patients with renal cell carcinoma;2.83±0.3 (95 % CI for the mean 2.23 to 3.44) in patients with uterine sarcoma.

Analysis of the development of severe acute respiratory syndrome within 30 days of hospitalization, as a function of CD63 levels, was carried out using the Kaplan-Meier method in patients with COVID-19. The mean duration was 11.5±1.63 days (95 % CI for the mean, 8.34 to 14.72). Kaplan-Meier survival plot of time (Mean=3.28±0.18 years,95 % CI for the mean 2.93 to 3.64) to treatment failure (major amputation of leg, all-cause mortality, doubling of total wound surface area from baseline, de novo gangrene) for all patients with critical limb ischemia (endpoint).

Next, we performed a Cox proportional hazards regression analyses of predictors for the development of respiratory failure (patients with COVID-19), the time to treatment failure (patients with CLI) and cancer-specific mortality in patients with renal cell cancer and uterine sarcoma are presented in Fig. 3 and Table 2.

In Cox regression (as in logistic regression), the null hypothesis (the predictor has no relationship with the dependent variable, i.e. its regression coefficient is not significantly different from zero) is tested using the Wald criterion. If the regression coefficient is significantly different from zero, then the independent variable makes a significant contribution to the predictive ability of the model, which is what

our results show. Coefficient Exp(B), which shows how many times the risk of an outcome occurring changes if the value of the predictor changes by one. If the value of Exp(B) or the risk ratio is greater than one, then the positive value of this factor will be a factor associated with the risk of developing the outcome, if less than one, then it will be associated with an increase in survival time (that is, it will act as a protective factor with respect to the outcome). The Cox model shows that CD63 is a significant predictor of 5-year survival in the patients with RCC, ($p<0.0001$), with Exp(b) (Hazard Ratio) =2.03 (95 % CI=1.41 – 2.9, $p<0.0001$); Harrell's C-index =0.867, as values close to 1, which indicate high performance of the Cox-model. In univariate analysis, CD63 was significantly associated with an increased risk of cancer-specific mortality in patients with uterine sarcoma with Exp(b) (Hazard Ratio) = 1.56 (95 % CI=1.13 – 2.16, $p=0.0063$); Harrell's C-index =0.869, and the development of complications in patients with COVID-19 (Exp(b) (Hazard Ratio) =1.32 (95 % CI=1.17 – 1.48, $p<0.0001$); Harrell's C-index =0.812) and critical limb ischemia (Exp(b) (Hazard Ratio) =2.41 (95 % CI=1.77 – 3.26, $p<0.0001$); Harrell's C-index =0.892). All models show good predictive ability (C-index > 0.8). All results are statistically significant ($p < 0.05$). Most significant results ($p < 0.0001$) in CLI, RCC, and COVID-19 groups. All studied factors are significant risk predictors in their respective groups.

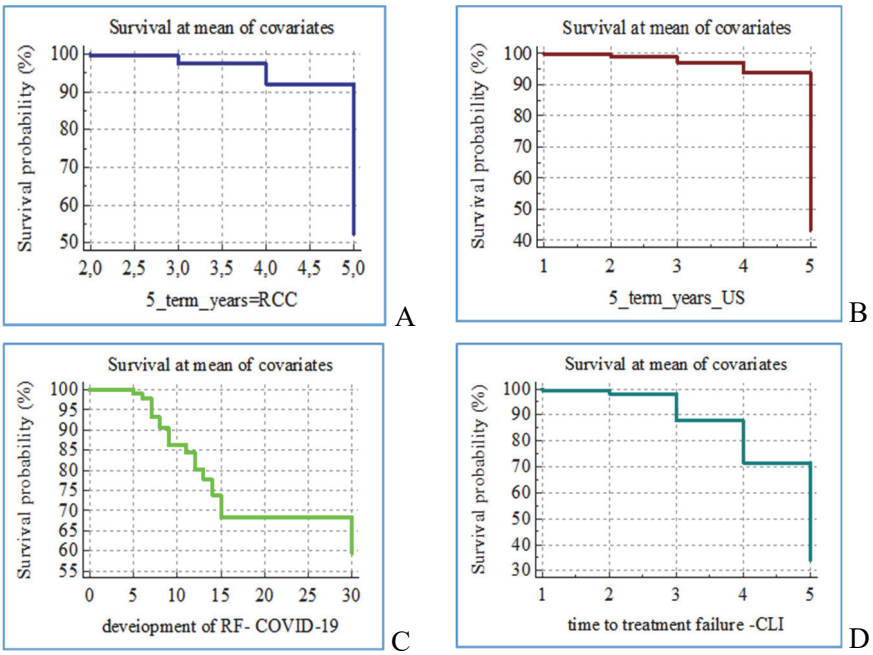

Fig. 3. A Cox proportional hazards regression analysis of predictors for the cancer-specific mortality in patients with renal cell cancer (A) and uterine sarcoma (B); development of respiratory failure (patients with COVID-19) (C), the time to treatment failure (patients with CLI) (D).

Liquid biopsy involves the analysis of biofluids, such as blood or urine, to identify molecular biomarkers that provide significant information about disease characteristics. This method has already been used for the diagnosis and monitoring of various malignancies. In RCC, potential biomarkers encompass circulating tumor cells (CTCs), cell-free tumor DNA (ctDNA) or circulating free DNA (cfDNA), exosomes, tumor-derived metabolites, as well as proteins found in blood and urine [13].

Table 2

Unadjusted and adjusted hazard ratios (HR) for respective univariate Cox proportional hazard models for survival (patients with RCC and US), the development of respiratory failure (patients with COVID-19) and the time to treatment failure (patients with CLI) analysis

Covariate	Harrell's C-index	b	SE	Wald	p	Exp(b) (Hazard Ratio)	95 % CI of Exp(b)
patients with renal cell carcinoma	0.867	0.71	0.183	14.84	<0.0001	2.03	1.41–2.9
patients with uterine sarcoma	0.869	0.45	0.164	7.45	=0.0063	1.56	1.13–2.16
patients with COVID-19	0.812	0.27	0.061	20.33	<0.0001	1.32	1.17–1.48
patients with critical limb ischemia	0.892	0.88	0.156	31.78	<0.0001	2.41	1.77–3.26

In our previous study, we found the role of the biomarker of circulating cell-free DNA in the the development of pregnancy-associated renal cell carcinoma and pregnancy-associated uterine sarcoma within 1 years after childbirth. We have established a high level of circulating cell-free DNA in sick women, both renal cell carcinoma and uterine sarcoma, as well as the pregnancy-associated renal cell carcinoma and pregnancy-associated uterine sarcoma, at all stages of the tumor process. in our study [11].

A negative relationship between CD63 expression and increased malignancy is reported in various tumors, including ovarian, lung, breast, and colon cancer [8-10]. Koh HM. et al. (2020) revealed that CD63

expression is associated with prognosis in patients with solid tumors (HR=1.34, 95 % CI=0.92 – 1.97, p=0.129). In the subgroup analysis, the HRs of lung cancer and other tumors were 0.50 (95 % CI=0.32 – 0.77, p=0.002) and 2.16 (95 % CI=1.93 – 2.42, p<0.001) respectively. The results suggested that CD63 expression may have a different effect on each tumor. Further research should reveal the effects of CD63 expression on the type of tumor. CD63 expression was significantly associated with disease-specific survival (HR=1.69, 95 % CI=1.15 – 2.49, p=0.008) and sample size more than 150 (HR=2.15, 95 % CI=2.92 –2.41, p<0.001) [9].

Our data showed similar dynamics and indicate significant differences in CD63 expression between the control group and pathological conditions, with the most pronounced changes observed in uterine sarcoma and COVID-19. Patients with critical limb ischemia has the highest risk: event probability is 141 % higher compared to the control group (HR=2.41 (95 % CI=1.77 – 3.26, p<0.0001). RCC group shows the second highest risk: event probability is 103% higher (HR =2.03 (95 % CI=1.41 – 2.9, p<0.0001). Patients with uterine sarcoma demonstrates moderate risk increase: probability is 56% higher than control group (HR) =1.56 (95 % CI=1.13 – 2.16, p=0.0063). COVID-19 group has the lowest but still significant risk increase: probability is 32% higher than control group (HR =1.32 (95 % CI=1.17 – 1.48, p<0.0001). Even the smallest risk increase (32 % for COVID-19) is clinically significant. Percentage risk calculation helps better understand the clinical significance of results and more clearly presents differences between groups.

Some studies, like ours, have shown that the CD63 expression correlates with the progression of the tumor and lower survival [4, 9, 10]. Thus, we performed this analysis to better understand the prognostic value of CD63 expression in somatic and oncologic diseases.

Conclusions

1. Levels of circulating extracellular vesicles (CD63 expression) showed healthy donors group has the lowest mean value; uterine sarcoma group shows the highest mean value; groups with COVID-19 and renal cell cancer demonstrate similar mean values; group with critical limb ischemia shows an intermediate value.

2. The results suggest that the CD63 can be a universal valuable marker in predicting complications and survival in somatic and oncological diseases. The optimal cut-off values for CD63 identified by ROC analysis were – 2.82 ng/ml for all groups. Each case was classified to a low (< 2.82) or high (≥ 2.82) expression group based on the median value.

3. A univariate Cox proportional hazards regression analysis determined high CD63 expression to be an independent factor for 5-year **s**urvival in the patients with renal cell cancer; associated with an increased risk of cancer-specific mortality in the patients with uterine sarcoma; the development of complications in the patients with COVID-19l the time to treatment failure in the patients with critical limb ischemia.

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Стаття надійшла 19.08.2024 р.

DOI 10.26724/2079-8334-2025-3-93-94-99
UDC 616.12-008.331.1+616.12-005.4+616.12-009.72

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COMPARATIVE EVALUATION OF MYOCARDIAL REMODELING IN PATIENTS WITH HYPERTENSIVE DISEASE AND COMORBIDITY WITH CORONARY HEART DISEASE

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231 patients by hypertensive disease with II stages were inspected, 105 men and 126 women, the average ages of 52.3±1.2 years. Duration of arterial hypertension was the average 9.7±0.45 years. At 121 from 231 inspected patient's ischemic heart disease – stable angina of II-III of functional class was diagnosed. Chronic heart failure of II-III FC (NYHA) was present at 90 from the inspected patients: at 39 (35.5 %) from 110 patients in a group with hypertensive disease and at 51 (42.1 %) from 121 – in the group of hypertensive disease in combination with coronary heart disease. Research purpose: estimation of deposit of coronary heart disease in the processes of remodeling and functional states of myocardium for the patients of hypertensive disease II the stages. It was set that tacking of coronary heart disease to hypertensive disease increases the degree of pathological remodeling of myocardium, mainly, due to dilatation of heart, and instrumental in progress of systole and diastolic dysfunction. Combination of hypertensive disease and coronary heart disease is instrumental in the increase of number of patients with violations of cardiac rhythm, including with ventricular extrasystoles of high gradation of Lown. Arterial hypertension and coronary heart disease make worse each another, and their combination results in the increase of cardiovascular risk.

Key words: hypertensive disease, coronary heart disease, structurally-functional indexes of myocardium, remodeling of myocardium, systolic dysfunction, diastolic dysfunction.

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ПОРІВНЯЛЬНА ОЦІНКА РЕМОДЕЛЮВАННЯ МІОКАРДА У ХВОРИХ НА ГІПЕРТОНІЧНУ ХВОРОБУ ТА ПРИ КОМОРБІДНОСТІ З ІШЕМІЧНОЮ ХВОРОБОЮ СЕРЦЯ

Проведене обстеження 231 пацієнта з гіпертонічною хворобою II стадії, 105 чоловіків і 126 жінок, середній вік 52,3±1,2 років. Тривалість артеріальної гіпертонії склала в середньому 9,7±0,45 років. У 121 з 231 обстежених хворих діагностована ішемічна хвороба серця – стабільна стенокардія II-III функціонального класу. Хронічна серцева недостатність II-III ФК (по NYHA) була у 90 з обстежених пацієнтів: у 39 (35,5 %) з 110 хворих в групі з гіпертонічною хворобою і у 51 (42,1 %) з 121 – в групі пацієнтів з гіпертонічною хворобою у поєднанні з ішемічною хворобою серця. Мета дослідження: оцінка внеску ішемічної хвороби серця в процеси ремоделювання і функціональний стан міокарда у хворих на гіпертонічну хворобу II стадії. Встановлено, що приєднання ішемічної хвороби серця до гіпертонічної хвороби збільшує ступінь патологічного ремоделювання міокарда, переважно, за рахунок дилатації серця, і сприяє прогресуванню систолічної і діастолічної дисфункції. Поєднання гіпертонічної хвороби та ішемічної хвороби серця сприяє збільшенню числа хворих з порушеннями серцевого ритму, у тому числі, і з шлуночковою екстрасистолією високої градації за Лауном. Артеріальна гіпертензія та ішемічна хвороба серця мають взаємообтяжливу дію і їх поєднання призводить до підвищення кардіоваскулярного ризику.

Ключові слова: гіпертонічна хвороба, ішемічна хвороба серця, структурно-функціональні параметри міокарда, ремоделювання міокарда, систолічна дисфункція, діастолічна дисфункція.

The work is a fragment of the research project "Cardiovascular remodeling, structural and functional state of the liver and kidneys, and their relationship with cardiometabolic risk factors in patients with cardiac pathology and comorbidities. Possibilities of treatment optimization", state registration No. 0124U002036.

Arterial hypertension (AH) is one of the most common diseases of the cardiovascular (CV) system. Numerous studies have convincingly demonstrated the significance of AH as a risk factor for coronary heart disease (CHD), stroke, and chronic heart failure (CHF). The prognosis of the disease worsens and the complexity of therapy increases when AH and CHD are combined, especially in elderly people [1, 7, 10].