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NOVEL BIOMARKERS: THE RENIN-ALDOSTERONE AND ENKEPHALINERGIC SYSTEMS IN DIAGNOSTIC OF KIDNEY CANCER, KIDNEY STONE AND NEPHROPATHY OF RHEUMATOID ARTHRITIS GENESIS

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The renin-angiotensin system and endogenous opioids are important bioactive neuropeptides, which are widely distributed in the brain and peripheral regions to produce diverse biological and neurobiological activities. Research evidence demonstrates significant positive as well as negative interactions between the renin-angiotensin system and endogenous opioids. The purpose of the study was to investigate the association between the renin-aldosterone and enkephalinergic systems in patients with kidney cancer, kidney stone and nephropathy of rheumatoid arthritis genesis. Survival and decline in eGFR ≤ 40 % analysis was performed using the Kaplan–Meier method; univariate and multivariate analyses were undertaken using log rank test and Cox's regression model, respectively. Met-enkephalin has a high prognostic efficacy for assessing the development of end-stage kidney disease in patients with nephrolithiasis. Level activity renin plasma was an independent predictor of decline in glomerular filtration rate in patients with ureteral stones, patients with nephropathy on the background of rheumatoid arthritis and cancer-specific mortality in .patients with renal cell cancer.

Key words: renin-aldosterone system, methionine-enkephalin, kidney disease.

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НОВІ БІОМАРКЕРИ: РЕНІН-АЛЬДОСТЕРОНОВА ТА ЕНКЕФАЛІНЕРГІЧНА СИСТЕМА В ДІАГНОСТИЦІ РАКУ НИРКИ, СЕЧОКАМЕННОЇ ХВОРОБИ ТА НЕФРОПАТІЇ РЕВМАТОЇДНО-АРТРИТНОГО ГЕНЕЗУ

Ренін-ангіотензинова система та ендогенні опіоїди є важливими біологічно активними нейропептидами, які широко поширені в головному мозку та периферичних тканинах для забезпечення різноманітної біологічної та нейробіологічної діяльності. Дані досліджень демонструють значну позитивну, а також негативну взаємодію між ренін-ангіотензиновою системою та ендогенними опіоїдами. Мета дослідження — вивчити зв'язок ренін-альдостеронової та енкефалінергічної систем у хворих на рак нирки, сечокам'яну хворобу та нефропатію на тлі ревматоїдного артриту. Аналіз виживаності та зниження швидкості клубочкової фільтрації проводили за методом Каплана–Мейєра; однофакторний та багатофакторний аналізи були проведені з використанням логарифмічного рангового тесту та регресійної моделі Кокса відповідно. Мет-енкефалін мав високу прогностичну ефективність для оцінки розвитку термінальної стадії ниркової недостатності у пацієнтів із нефролітіазом. Рівень активності реніну плазми був незалежним предиктором зниження швидкості клубочкової фільтрації у пацієнтів з каменями сечоводу, пацієнтів з нефропатією на тлі ревматоїдного артриту та онкоспецифічної смертності у хворих на нирково-літинний рак.

Ключові слова: ренін-альдостеронова система, метіонін-енкефалін, захворювання нирок.

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 and "Biomarker diagnostics of oncourological diseases", state registration No. 0118U001025.

Hormones at the level of the whole organism, and cytokines - at the paracrine level, carry out humoral regulation of not only the physiological activity of cells, but also the number of cell populations in various organs and tissues. By maintaining viability and proliferation or, conversely, by inducing cell death, hormones and cytokines regulate cellular homeostasis in tissues [1, 8].

Enkephalins, like all regulatory peptides, have a wide spectrum of biological activity. Performing the functions of neuromodulators, neurotransmitters and hormones in the body, enkephalins affect many body systems, including neurotransmitter, neuroendocrine, immunoreactive, emotional and mental state of the organism, are characterized by high analgesic activity, as well as anti-stress effect [13]. Such a variety of biological properties of enkephalins allows us to consider them as endogenous regulators of many physiological and pathological processes in the body. However, the mechanisms of manifestation of this kind of polyfunctionality of regulatory peptides and the features of their action under various physiological and pathological conditions of the body are still the subject of discussion [7, 15]. Enkephalins, like other endogenous opioids, belong to the central regulatory system. However, recently, more and more data have appeared on their paracrine level of regulation and even cytokine-like. So, [Met5]-enkephalin was renamed opioid growth factor (OGF) after discoveries of its growth-modulating characteristics in mouse neuroblastoma cells and developing rat brains, and to distinguish its pharmacological function from neurotransmission [15].

Interesting relationships develop in the enkephalinergic system with the renin-angiotensin and aldosterone systems, not only in terms of the interaction of effects, but also at the level of the metabolic link of endogenous opioids. According to modern concepts, one of the mechanisms for changing the level of biologically active peptides in the body, their multifunctionality and biological action is the intensity of their metabolism - the rate of processing and degradation of peptides. The role of the angiotensin-converting enzyme in the metabolism of enkephalins attracts attention: the enzyme takes part both in the processing of enkephalins and in their inactivation, while exhibiting dipeptidylcarboxypeptidase and endopeptidase activities. Angiotensin-converting enzyme is involved in the degradation of enkephalins, playing the role of one of the regulatory factors in the metabolism of enkephalins [3]. From the position of modern ideas about the role of humoral factors in the regulation of the pathophysiology of the kidneys, we studied the main links of the neurohormonal axis in the urological sphere: pituitary hormones - the renin-aldosterone system.

The purpose of the study was to investigate the association between the renin-aldosterone and enkephalinergic systems in patients with kidney cancer, kidney stone and nephropathy of rheumatoid arthritis genesis.

Materials and methods. The studies were carried out on the basis of city and regional hospitals in Svatovo, Severodonetsk, and Rubizhne of the Luhansk region in 2013–2021. 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 (Rubizhne, Ukraine, number 25/2015). The patients' epidemiological data, laboratory examination, complications, clinical outcomes, CT imaging data, and treatment plans were extracted from medical records.

To test our hypothesis, this case-control study consisted of 20 healthy donors (control group), 15 patients with nephrolithiasis, 62 patients with ureteral stones, 103 patients with renal cell cancer, and 27 patients with nephropathy in patients with rheumatoid arthritis. The material for the study was the peripheral blood from the cubital vein of patients and healthy control. Methionine-enkephalin, plasma renin activity (ARP), plasma aldosterone were measured by radioimmunoassay using Kits Incstar (USA), CIS (France). The baseline serum creatinine was measured directly on hospital admission in the laboratory. The primary endpoint of this study was incident chronic kidney disease (CKD), defined as the incident-estimated glomerular filtration rate (eGFR) < 40 mL/min/1.73 m^2 during the follow-up period. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to calculate eGFR [9].

Statistical and graphical analyses were done using STATISTICA 7.0.61.0 (StatSoft, Inc., Tulsa, OK, USA; serial number: AXF003C775430FAN7) and MedCalc Version 20.218 64-bit (MedCalc Software, Ostend, Belgium). Parametric data are presented as a mean±standart deviation (SD). Kolmogorov–Smirnov test was applied to examine the normality of data distribution. To examine group-wise differences, unpaired Student's t-test was used. Frequency calculations were performed using Fisher's exact test. The difference between study groups was tested by a nonparametric Mann–Whitney U test was used. A p-value below 0.05 was considered statistically significant. Receiver operating characteristics (ROC) curve analysis was performed to estimate optimal cut-off values, maximizing sensitivity and specificity according to the Youden index. Survival and decline in eGFR < 40 mL/min/1.73 m^2 analysis was performed using the Kaplan–Meier method; univariate and multivariate analyses were undertaken using log-rank test and Cox's regression model, respectively [2]. A *p*-value below 0.05 was considered statistically significant. The Cox proportional hazards regression model was used to assess the effect of the activity of renin plasma, aldosterone and met-enkephalin levels on clinical outcomes in survival analysis.

Results of the study and their discussion. The study included 207 patients. The mean follow-up period for patients with nephrolithiasis was 40.0 months, [95 % CI 30.4862 to 49.5]; for patients with ureteral stones was 50.9 months, [95 % CI 46.9; 54.9]; for patients with renal cell cancer was 55.9 months, [95 % CI 54.06; 57.8]; for patients with nephropathy with rheumatoid arthritis was 53.6 months, [95 % CI 48.9; 58.1] with a maximum follow-up period of 60 months.

Descriptive statistics and results of comparison of groups of patients according to the studied parameters included in the analysis of predictors of survival and the development of chronic renal failure are presented in Table 1.

Table 1

The results of the renin-aldosterone system and methionine-enkephalin in patients with kidney diseases and nephropathy with rheumatoid arthritis

Clinical groups	Activity renin plasma, ng/ml/h	Aldosterone, pg/ml	Methionine-enkephalin, pg/ml
healthy donors (control group) (n=20)	4.93±0.6	169. 7±26.9	92.5±11.4
patients with nephrolithiasis (n=15)	6.07±0.23	199.71±21.78	408.27±40.0
	p < 0.00001 *	p = 0.001271 *	p < 0.00001 *
patients with ureteral stones (n=62)	4.68±0.88	256.39±19.45	594.7±23.3
	p > 0.05 *	p < 0.00001 *	p < 0.00001 *
patients with renal cell cancer (n=103)	8.74±1.01	91.85±10.13	601.2±31.6
	p < 0.00001 *	p < 0.00001 *	p < 0.00001 *
	p < 0.00001 *	p < 0.00001 *	p < 0.00001 *
nephropathy in patients with rheumatoid arthritis (n=27)	2.76±0.5	231.54±15.83	337.59±60.3
	p < 0.00001 *	p < 0.00001 *	p < 0.00001 *

Notes: Data are means ± SD for Gaussian variables. Intergroup by the T-test Students. * – p – significant differences between control (healthy donors) and test groups

As can be seen from the table, the patients of the three comparison groups differed significantly in many laboratory parameters. So, for example, the renin activity plasma in patients with nephrolithiasis was higher (p< 0.00001), in patients with ureteral stones the value did not differ from the control group (p>0.05), in patients with renal cell cancer was a significantly higher (2-fold higher) than in healthy donors (p< 0.00001). In a subgroup of patients who developed nephropathy on the background of rheumatoid arthritis, lower values (2-fold lower) were found of the renin activity plasma (p< 0.00001).

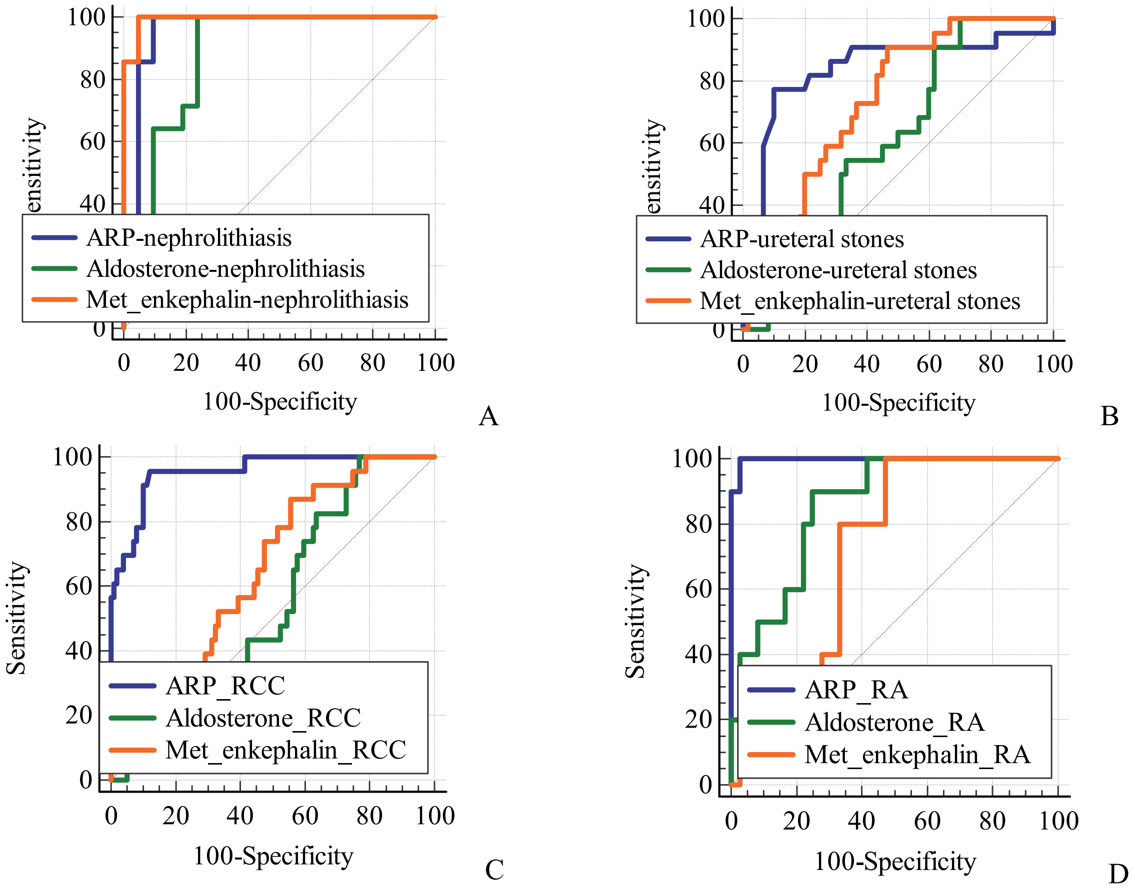

Fig. 1. ROC analysis: receiver operating characteristic (ROC) curves for Activity renin plasma. Aldosterone and Met-enkephalin measured in patients with a) nephrolithiasis and b) ureteral stones, c) renal cell cancer and d) nephropathy in patients with rheumatoid arthritis. Note: Here and in the following figures: p<0.001 – calculated by univariate logistic regression analysis.

Differences were observed in aldosterone levels, and in methionine-enkephalin levels between all subgroup of patients and control groups. Thus, in the groups of patients with nephrolithiasis (p=0.001271), ureteral stones (p<0.00001), nephropathy on the background of rheumatoid arthritis (p<0.00001) we observed hyperaldosteronism, while in patients with renal cell cancer, hypoaldosteronism occurred (p<0.00001). Patients of all subgroups displayed increased levels of methionine-enkephalin (p<0.00001).

Analysis of the ROC curve in patients with nephrolithiasis (Fig. 1) showed that met-enkephalin has the largest area under the ROC curve (0.993), which reflects the high predictive effectiveness of these indicators for assessing the development of end-stage renal disease (ESRD) (eGFR<40 mL/min/1.73 m^2). The optimal cut-off values were >116.9 pg/ml for met-enkephalin with excellent accuracy for aldosterone >176.17 pg/ml and for plasma renin activity >5.7 ng/ml/h.

The area under ROC curve of studied parameters were ranging between 0.836 for activity renin plasma, 0.611 for aldosterone and 0.643 for met-enkephalin in patients with ureteral stones, indicating a high prognostic value for decline in eGFR<40 mL/min/1.73 m^2. Activity renin plasma was the strongest predictor biomarkers of decline in eGFR<40 mL/min/1.73 m2. The statistically optimal cut-off value for activity renin plasma was >5.3 ng/ml/h with excellent accuracy. In patients with renal cell cancer the strongest predictor biomarkers of mortality were activity renin plasma, the statistically optimal cut-off value for activity renin plasma was >9.12 ng/ml/h. The values of area under the curve (AUC) were 0.997 for activity renin plasma of patients with nephropathy on the background of rheumatoid arthritis. The strongest predictor biomarkers of decline in eGFR<40 mL/min/1.73 m^2 were activity renin plasma (cut-off level ≤2.7 ng/ml/h).

The Kaplan–Meier survival curves, after classifying the patients on the basis of Youden cut-offs obtained by ROC curves, showed significant decline in eGFR<40 mL/min/1.73 m^2 with higher values of met-enkephalin of patients with nephrolithiasis (Fig. 2) (HR=2289; 95 % CI 653 to 8024; p<0.0001).

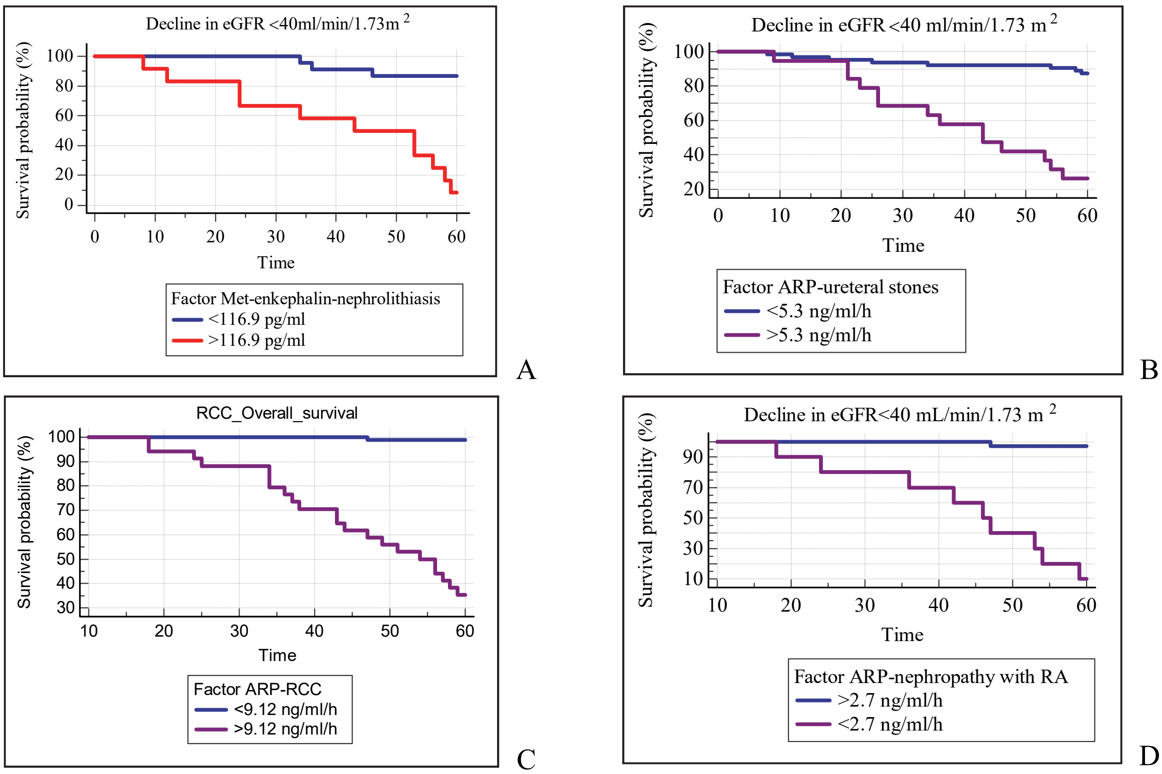

Fig. 2. Kaplan–Meier curves of decline in eGFR<40 mL/min/1.73 m^2 of A – nephrolithiasis patients (predictor – met-enkephalin); B – ureteral stones patients (predictor – activity renin plasma); C – Kaplan–Meier survival curves of renal cell cancer patients (predictor – activity renin plasma) with different cut-off values of the of indices investigated. p value by Long-rank test; D – patients with nephropathy on the background of rheumatoid arthritis (predictor – activity renin plasma). Note: Here and in the following figures: p<0.0001 – calculated by univariate logistic regression analysis.

To compare the cumulative incidences of ESRD among the subjects with ureteral stones, patients with nephropathy on the background of rheumatoid arthritis Kaplan–Meier analyses were conducted, which visualized that the risks of ESRD are significantly increased in the subjects with cut-off level activity renin plasma >5.3 ng/ml/h and ≤2.7 ng/ml/h respectively (p < 0.0001, by Log-rank test).

The Kaplan–Meier survival curves showed significant lower survival with higher values of cut-off value for activity renin plasma (>9.12 ng/ml/h). of patients with renal cell cancer (HR=102.09, 95 % CI 36.96 to 281.98; p<0.0001).

In nephrolithiasis patients activity renin plasma and aldosterone were not independently associated with progression to ESRD. Met-enkephalin and aldosterone were not independently associated with progression to ESRD in ureteral stones patients and patients with nephropathy on the background of rheumatoid arthritis and progression to cancer-specific mortality in renal cell cancer patients. Next, we performed a Cox proportional hazards regression analyses of predictors for progression to decline in eGFR<40 mL/min/1.73 m^2 in nephrolithiasis patients, ureteral stones patients, patients with nephropathy on the background of rheumatoid arthritis and cancer-specific mortality in patients with renal cell cancer are presented in Table 2.

Table 2

Unadjusted and adjusted hazard ratios (HR) for respective univariate and multivariate Cox proportional hazard models for progression to decline in eGFR<40 mL/min/1.73 m^2 and overall survival

Factor	Univariable			Multivariable		
	HR (95 % CI)	Harrell's C-index	p-Value	HR 95 % CI	Harrell's C-index	p-Value
	Nephrolithiasis patients					
activity renin plasma	46.98 (6.07–63.49)	0.624	p<0.0002	98.7605 (5.17–1887.84)	0.839	p=0.0023
aldosterone	17.09 (5.2–56.23)	0.618	p<0.0001			
met-enkephalin	12.9 (3.5–47.49)	0.781	p<0.0001			
	Ureteral stones patients					
activity renin plasma	3.79 (2.0–7.14)	0.791	p<0.0001	7.87 (3.17–19.58)	0.800	p<0.0001
aldosterone	4.61 (1.08–19.74)	0.616	p=0.0394			
met-enkephalin	5.41 (1.6 –18.3)	0.658	p=0.0066			
	Renal cell cancer					
activity renin plasma	88.82 (11.9–661.3)	0.879	p<0.0001	75.78 (9.94–577.58)	0.896	p<0.0001
aldosterone	7.52 (1.01–55.82)	0.607	p=0.0484			
met-enkephalin	4.41 1.31–14.85	0.635	p=0.0166			
	Nephropathy on the background of rheumatoid arthritis					
activity renin plasma	68.0 (8.4–550.3)	0.893	p<0.0001	124.7 (6.95– 2237.2)	0.953	p=0.0011
aldosterone	20.02 (2.5–158.7)	0.804	p=0.0046			
met-enkephalin	7.4 (0.94–58.5)	0.674	p=0.0511			

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

In univariate analysis, met-enkephalin >116.9 pg/mL (p<0.0001) was significantly associated with an increased risk of decreased eGFR<40 mL/min/1.73 m^2 in patients with nephrolithiasis. In patients with ureteral stones, patients with nephropathy secondary to rheumatoid arthritis, the predictor of plasma renin activity (cut-off level of plasma renin activity >5.3 ng/ml/h and ≤2.7 ng/ml/h, respectively) increases the risk of ESRD progression, in patients with renal cell carcinoma (cut-off value for activity renin plasma >9.12 ng/ml/h) increases the risk of a poor prognosis of overall survival.

Harrell's C-index, also known as the concordance index, is a goodness of fit measure for models which produce risk scores [11]. As the C index is a proportion, it can assume any value from 0 to 1. Values near 1 indicate high performance and a value of 0.5 indicates that the discrimination performance of the model is the same as a coin flip (random concordance) in predicting which patient will live longer [11]. Values below 0.5 indicate that the model output is worse than a coin flip; therefore, concluding the opposite of what the model output indicates would be better for a more accurate prediction.

All parameters that were significant at a p value less than 0.10 could predict decline in eGFR<40 mL/min/1.73 m^2 in nephrolithiasis patients (with C-indexes ranging from 0.618 to 0.781), ureteral stones patients (with C-indexes ranging from 0.616 to 0.791), patients with nephropathy on the background of rheumatoid arthritis (with C-indexes ranging from 0.674 to 0.893) and in patients with renal cell carcinoma (with C-indexes ranging from 0.607 to 0.879) increases the risk of a poor prognosis of overall survival.

On multivariate analyses, level activity renin plasma was an independent predictor of decline in eGFR<40 mL/min/1.73 m^2 and cancer-specific mortality. On multivariate analyses, another independent indicator that was used as a potential predictor of the occurrence of ESRD or mortality (level aldosterone) was not included in the model and, accordingly, has no prognostic value.

Angiotensin and endogenous opioids are important bioactive neuropeptides, which are widely distributed in the brain and peripheral regions to produce diverse biological and neurobiological activities. Data from our study and others demonstrate significant positive as well as negative interactions between the renin-angiotensin system (RAS) and endogenous opioids [3, 7].

Our studies of ARP in patients with kidney diseases have shown that ARP is increased in kidney diseases that cause ischemia of the renal parenchyma, namely, renal cell carcinoma, and to a lesser extent in urolithiasis, when surrounding tissues are compressed by a calculus localized in the pelvis. It is now well-recognized that multiple RAAS axes are working concomitantly to regulate blood pressure and tissue perfusion. The circulating or classical RAAS including all major components that have well-recognized endocrine effects [10]. By contrast, the RAAS in the kidney may represent an important paracrine/autocrine/intracrine system, eliciting a more local and intracellular effect within the kidney tissue, especially within the proximal tubules [10]. Notably, the intrarenal RAAS has been found to have markedly higher concentrations of Ang II when compared to circulating plasma concentrations. Immunohistochemical studies of kidney tumors have shown that autonomous renin production occurs in the tumor tissue, exceeding the level of renin secretion by the parenchyma of the contralateral kidney [4, 5].

Given the reciprocal relationship between the renin-angiotensin system and the aldosterone system, it would be logical to expect a synchronous increase in plasma aldosterone levels with ARP [6]. In particular, we observed such dynamics in patients with kidney stones and urolithiasis. Aldosterone levels rise with urolithiasis (regardless of the localization of the stone), which may be due to an imbalance of electrolytes (in particular potassium) [4].

However, in patients with kidney cancer, the level of aldosterone in plasma was completely opposite to the level of aldosterone in urolithiasis, its concentration in blood plasma was low. In other words, hyperreninemic hypoaldosteronism develops in kidney cancer. This syndrome is quite rare. In most cases, isolated hypoaldosteronism is due to insufficient production of renin (so-called hyporeninemic hypoaldosteronism). Hypoaldosteronism is a clinical condition characterized by a deficiency of aldosterone or a violation of its action at the tissue level. The disease may be the result of impaired production and secretion of renin by the kidneys, the conversion of angiotensin I to angiotensin II, the synthesis and secretion of aldosterone by the adrenal glands, or an abnormal response of target tissues to aldosterone [12].

The diverse actions of Ang II are possibly mediated indirectly through endogenous opioids, while opioids have also been shown to activate components of the RAS, suggesting upregulation of each system associated with each other.

On the contrary, there are reports suggesting a negative correlation between the RAS and the opioid system [3 14]. We obtained such data in patients with nephropathy on the background of rheumatoid arthritis. Research data also supports the notion that Ang II acts as an anti-opioid peptide, reducing the effects of opioids. In addition, decreased angiotensin release and function induced by opioids have also been reported [3]. In the present study, the complexities of positive and negative interactions between RAS and opioids, as well as the possible mechanisms responsible for these interactions, are obtained.

Conclusions

1. The kidney diseases we studied had different plasma renin activity: normoreninemic - patients with ureteral stones, hyperreninemic – patients with nephrolithiasis and patients with renal cell cancer, hyporeninemic – patients with nephropathy on the background of rheumatoid arthritis, which is determined by the ischemic effect of volumetric structures (stone or tumor) on the intrarenal renin-angiotensin system.

2. Met-enkephalin has a high prognostic efficacy for assessing the development of end-stage kidney disease in patients with nephrolithiasis. (eGFR<40 mL/min/1.73 m^2).

3. Level activity renin plasma was an independent predictor of decline in eGFR<40 mL/min/1.73 m^2 in patients with ureteral stones, patients with nephropathy on the background of rheumatoid arthritis and cancer-specific mortality in patients with renal cell cancer.

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CLINICAL AND INSTRUMENTAL FEATURES OF DIAGNOSTICS OF COMBAT SURGICAL CHEST INJURY WITH TISSUE DEFECTS

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Retrospective analysis of the results of comprehensive diagnostic examination of 127 injured persons with combat surgical chest injuries and their complications (bronchopleural fistula and pleural empyema) was conducted. Injured military servicemen with thoracic wall tissue defects in combat thoracic trauma at the III and IV levels of medical care were analyzed. Two clinical groups were defined: the main group and the comparator group. Clinical, laboratory, microbiological and instrumental research methods were used to examine injured servicemen and monitor clinical course of traumatic disease. To identify anatomical and morphological features of chest injuries, instrumental methods were used, with preference given to X-ray and ultrasound methods. During diagnostic examination of lungs and pleural cavities using computed tomography, compared to chest X-ray examination, 8.6 % more cases of pneumothorax/pneumohydrothorax, 14.1 % more cases of hydrothorax, 22.8 % more cases of pneumonia were identified, as well as new syndrome categories were identified: subpleural hematoma, pleural thickening.
Key words: combat thoracic trauma, thoracic wall defects.

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КЛІНІКО-ІНСТРУМЕНТАЛЬНІ ОСОБЛИВОСТІ ДІАГНОСТИКИ БОЙОВОЇ ХІРУРГІЧНОЇ ТРАВМИ ГРУДНОЇ КЛІТИНИ З ДЕФЕКТАМИ ТКАНИН

Проведено ретроспективний аналіз результатів комплексного діагностичного обстеження 127 поранених з бойовою хірургічною травмою грудної клітини та її ускладнень (бронхо-плевральні нориці та емпієма плеври). Аналізу підлягали поранені військовослужбовці з дефектами тканин грудної стінки при бойовій торакальній травмі на III та IV рівнях медичного забезпечення. Визначено дві клінічні групи: основну та групу порівняння. Для діагностики поранених та моніторингу перебігу травматичної хвороби застосовували клінічні, лабораторні, мікробіологічні та інструментальні методи дослідження. Для визначення анатомо-морфологічних особливостей ушкоджень грудної клітини, застосовували інструментальні методи, перевагу надавали рентгенологічним та ультразвуковим методам. Під час діагностичного обстеження легень та плевральних порожнин за допомогою комп'ютерної томографії, у порівнянні з рентгенографією грудної клітини, виявлено та визначено більше випадків пневмотораксів/пневмогідротораксів на 8.6 %, гідротораксів на 14.1 %, пневмоній на 22.8 %, а також визначити нові синдромальні категорії: субплевральна гематома, плевральні нашарування.
Ключові слова: бойова торакальна травма, дефекти грудної стінки.

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Specific features of diagnostic examination and treatment of injured persons with combat thoracic trauma (CTT) with soft tissue injuries are one of the most important issues in modern military field surgery and are the critical point of study for various experts [1, 2]. Over the last year, during the full-scale invasion of Russia with the use of modern aggressive weapons, a large number of injured persons have been reported