

**Резюмета на статиите на английски език на доц. Атанас Кундурджиев  
след НОС „доцент“**

1. **A. Kundurdzhiev**, A. Markova. Methods for ultrasound screening of cardiovascular diseases in type 2 diabetic patients. ActaMedicaBulgarica. Vol. XLV. 1/2018. (IF-0,21)

**Abstract.** *Diabetes mellitus is a chronic disorder that affects predominantly the carbohydrate metabolism, but also the biotransformation of proteins and fat. Many intra- and extracellular metabolic mechanisms are impaired which leads to structural changes in the vascular wall and the heart muscle. This eventually causes their functional deterioration and the end result is clinical manifestation of macrovascular incidents or heart failure. People with perturbations of the glucose metabolism (impaired fasting glucose, impaired glucose tolerance and insulin resistance) are also with a higher risk of cardiovascular diseases, even before the diagnosis of diabetes. Nowadays we have a cheap, easy and non-invasive method for early diagnosis of cardiovascular disorders, way before their clinical manifestation, and that is the ultrasound methodology. The echocardiography is a valuable technique for the detection of changes in the myocardial structure and its contractility. The tissue Doppler ultrasound is a more precise method that can detect the slightest aberrations in the heart muscle function, that could not be seen with the conventional echocardiography. Subclinical atherosclerotic changes can be determined with a Doppler scan of the big arteries (carotids, renal arteries), and the subsequent calculation of their resistive index and of the intima-media thickness. There are a lot of studies in this field which show that the structural and functional impairment could be diagnosed in diabetic patients without any complaints and with otherwise healthy hearts. This means that these diagnostic methods should be used in the routine clinical examination of every diabetic individual in order to predict and possibly prevent major cardiovascular events and severe heart failure.*

**Key words:** *diabetes mellitus, cardiovascular complications, transthoracic echocardiography, tissue Doppler imaging, Intima-media thickness, resistive index*

2. DiyanGenov, **AtanasKundurdgiev**, VentsislavaPencheva. Resistive Index for the Evaluation of Renal Damage in Diabetes Mellitus Type 2. Open Journal of Internal Medicine, 2018, 8, 160-166

## Abstract

**Background:** One of the most common causes of renal impairment and development of chronic kidney disease is diabetes mellitus type 2 (DM 2). The aim of this prospective study was to determine the role of Resistive Index (RI) as a non-invasive marker for the evaluation of renal impairment in patients with DM 2. **Material and Methods:** 47 patients with DM 2 in mean age  $62.66 \pm 10.081$  years were included in the study for the period of one year. All of them were with well-compensated diabetes mellitus ( $HbA1c < 7.0\%$ ) and optimal control of arterial hypertension. Hematological analysis of blood were carried out. Serum and urine biochemical parameters were tested, glomerular filtration rate (GFR) was calculated, and abdominal ultrasound with measure of RI was done. **Results:** Patients with  $RI < 0.7$  and those with  $RI \geq 0.7$  did not differ significantly in terms of their age, sex, body mass index (BMI), duration of DM 2 and arterial hypertension, use of antihypertensive drugs and HbA1c ( $p > 0.05$  for all). There was significant difference between the groups according to serum creatinine ( $p = 0.026$ ), GFR ( $p = 0.044$ ) and the degree of proteinuria ( $p = 0.001$ ). There was a positive correlation between RI and serum creatinine ( $r = 0.418$ ;  $p = 0.001$ ) and between RI and proteinuria ( $r = 0.396$ ;  $p = 0.004$ ). A negative correlation relationship between RI and GFR values was found ( $r = -0.413$ ;  $p = 0.011$ ). **Conclusions:** RI may be used as an indicator for the assessment of the severity of renal impairment in patients with DM 2. It correlates well with serum creatinine, GFR and proteinuria, which are proven biochemical parameters indicating the degree of renal damage in patients with DM 2.

## Keywords

Diabetes Mellitus Type 2, Resistive Index, Serum Creatinine, Proteinuria, Glomerular Filtration Rate

3. R. Gancheva<sup>1</sup>, At. Kundurdjiev<sup>2</sup>, M. Ivanova<sup>1</sup>, T. Kundurzhev<sup>3</sup>, Zl. Kolarov. Obesity, Echocardiographic changes and Framingham risk score in spectrum of gout: a cross-sectional study. Arch Rheumatol. 2019; 34;(2) 176-185; doi: 10. 5606

#### ABSTRACT

**Objectives:** This study aims to establish cardiovascular risk in obese and non-obese patients in stages of gout by using Framingham risk score (FRS) and transthoracic echocardiography.

**Patients and methods:** This single-center cross-sectional study encompassed 201 patients (160 males, 41 females; mean age 56.9±13 years; range 20 to 89 years) including 52 asymptomatic hyperuricemia, 86 gouty arthritis without tophi, and 63 gouty tophi patients. body mass index (BMI) and FRS were calculated. Left atrium (LA), interventricular septum, posterior wall (PW) of the left ventricle, fractional shortening (FS), mitral annular systolic velocity (S'), mitral annular early diastolic velocity (E') and transmitral to mitral annular early diastolic velocity ratio (E'/E') were measured. Data were analyzed by Kolmogorov-Smirnov test, Shapiro-Wilk test, t-test, Mann-Whitney U test, analysis of variance test and multiple linear regression models.

**Results:** There was no significant difference in FRS, FS, S', E' and E'/E' between obese and non-obese patients with asymptomatic hyperuricemia, gouty arthritis without tophi or gouty tophi. Obese patients in the three disease gradations had larger LA (p=0.007, p=0.004, p=0.039) and thicker PW (p=0.002, p=0.037, p=0.007). Increased BMI independently predicted the thickening of the PW in asymptomatic hyperuricemia (R<sup>2</sup>=0.319), gouty arthritis without tophi (R<sup>2</sup>=0.093) and gouty tophi (R<sup>2</sup>=0.068).

**Conclusion:** Despite the lack of difference in FRS and functional systolic and diastolic parameters between obese and non-obese patients in the spectrum of gout, morphological heart changes were more pronounced in obese patients. In gouty tophi, it is possible that higher urate load together with chronic inflammation contribute for the alterations, as obesity worsens them.

**Keywords:** Cardiovascular risk, gout stages, obesity.

4. V. Grozeva, **A. Kundurzhiev**. Calcium-Phosphate metabolism disorders in patients with renal failure. Clinical significans, diagnosis and treatment. ActaMedicaBulgarica. Vol. XLVI, 2019, pp-50-56, N1. (IF-0,21)

**Abstract.** *Chronic kidney diseases (CKD) are commonly associated with calcium and phosphorus metabolism disorders. The general term of "renal osteodystrophy" (ROD) encompasses a complex spectrum of abnormalities in bone and mineral metabolism in CKD. This is one of the most serious and debilitating complications of CKD. It is related to disproportionately high direct and indirect costs of healthcare, thus posing a major burden on society. The development of ROD begins too early in the course of CKD. Some mechanisms involved in the pathogenesis of ROD are reduced calciferol production, calcium deficiency and hyperphosphatemia. Clinically, ROD occurs with varied manifestations – osteomalacia, osteoporosis, adynamic bone disease. The diagnosis and the treatment are a challenge for the physician and effort should be made to prolong the duration and quality of life of the affected patients.*

**Key words:** *calcium-phosphate metabolism, chronic kidney diseases, hyperparathyroidism*

5. R. Gancheva<sup>1</sup>, **At. Kundurdjiev**<sup>2</sup>, T. Kundurzhiev<sup>3</sup>, Zl. Kolarov. Cardiovascular risk in type 2 diabetic patients with asymptomatic hyperuricemia and gout. ActaMedicaBulgarica. Vol. XLVI, 2019, pp-13-20, N2. (IF-0,21)

**Abstract. Aim:** To study the differences in cardiovascular risk between type 2 diabetic and non-diabetic patients with asymptomatic hyperuricemia and gout using the Framingham Risk Score (FRS) and complex multimodal ultrasonography. **Patients and methods:** A total of 201 patients participated, divided into two groups: 1/ patients with asymptomatic hyperuricemia (n = 52), and 2/ patients with gout (n = 149). FRS was determined as well as ultrasound parameters, independent predictors of cardiovascular risk: left atrial size (LA), intima-media thickness (IMT) and common carotid artery resistive index (CCARI). **Results:** The patients in the two groups were age-matched and conventional cardiovascular risk factors were equally distributed. In the asymptomatic hyperuricemia group, 12 patients (23.1%) had diabetes. In this group, there was no difference in FRS between diabetic and non-diabetic individuals. However, diabetic patients had larger LA, thicker intima-media and higher CCARI. In the gout group 18 subjects (12%) had diabetes, but the FRS, LA, IMT and CCARI values were similar among diabetic and non-diabetic patients. Furthermore, when gout subjects were subdivided according to the presence of tophi, we found that the subgroup having gouty tophi and diabetes had larger LA (p = 0.014) compared to those with gouty tophi without diabetes. **Conclusion:** In diabetic patients with asymptomatic hyperuricemia and gouty tophi, a more complex approach for estimation of cardiovascular risk is needed. Our work suggests that diabetes and tophi might potentiate their action on the cardiovascular system.

**Key words:** cardiovascular risk; type 2 diabetes; asymptomatic hyperuricemia; tophi

6. **AtanasKundurjdjiev**, Iva Angelova, Milena Nikolova\*, TsvetelinaVutova, Antonia Hadjiiska, JuriTodorov, Marin Penkov, TsvetelinaDobrova, BorislavKochmalarski, KalinaChupetlovska, YordanVlahov. Mesenteric Panniculitis – A Rare Diagnosis. ARC Journal of Immunology and Vaccines Volume 4, Issue 2, 2019, PP 3-6 [www.arcjournals.org](http://www.arcjournals.org)

**Abstract:** Mesenteric panniculitis (MP, also known as sclerosing mesenteritis, mesenterial lipodystrophy, retractile mesenteritis) is a rare immune-mediated inflammatory and fibrosing condition with unknown etiology that affects the mesenteric lipocytes. MP is characterized by degeneration and necrosis of the fat tissue, chronic inflammation and the development of fibrosis within the mesenterium. The most common clinical symptoms are abdominal discomfort and pain, nausea and vomiting, palpable tumor formation in the abdomen, weight loss, fever, and symptoms of bowel obstruction. Some patients are asymptomatic and MP is detected incidentally during imaging studies for other reasons. We present a 62-years-old male patient with tumor formation in the abdomen discovered during ultrasound examination for other reasons and diagnosed on magnetic-resonance imaging as mesenteric panniculitis and discuss the etio-pathogenesis, diagnosis and treatment of this rare disease.

**Keywords:** mesenteric panniculitis, mesenteric lipodystrophy, rare disease, abdominal ultrasound, magnetic-resonance imaging.

**Abbreviations:** CRP = C-reactive protein, CT = computed tomography, ESR = erythrocyte sedimentation rate, IgG = immunoglobulin G, MP = mesenteric panniculitis, MRI = magnetic resonance imaging

7. <sup>1</sup>Rada Gancheva, <sup>2</sup>**Atanas Koundurdjiev**, <sup>3</sup>Galina Nikolova, <sup>1</sup>Mariana Ivanova, TodorKundurzhiev, <sup>1</sup>Zlatimir Kolarov, <sup>3</sup>Veselina Gadjeva. Serum oxidative stress markers do not associate with renal and common carotid arteries arteriosclerotic vascular changes in patients with gout. Acta Med Bulg 2019 Vol. XLVI №3 pp. 37-43(IF-0,21)

**Abstract. Objective:** To establish the association between serum levels of reactive oxygen species (ROS) products, nitric oxide (NO) radicals and ascorbate radicals with renal resistive index (RRI), common carotid artery resistive index (CCARI) and intima-media thickness (IMT) in gout patients, and to find out whether the connection is more pronounced when tophi are present. **Methods:** A cross-sectional study including 71 consecutive gout patients, divided into two groups according to the presence of subcutaneous tophi. Serum concentrations of ROS products, NO radicals and ascorbate radicals were determined by ex vivo electron paramagnetic resonance (EPR) study. RRI was measured in both kidneys at the level of interlobar arteries with 3.5 MHz transducer. By applying ultrasound of the common carotid arteries, conducted with 10 MHz linear transducer CCARI and IMT were measured. **Results:** Gouty arthritis without tophi and gouty tophi subjects were age-matched. Serum uric acid and distribution of conventional cardiovascular risk factors was equal in the groups. However, in tophi patients CRP and the number of individuals who had suffered a cardiovascular event were higher. In the two stages of the disease serum levels of ROS products, NO radicals, ascorbate radicals, as well as RRI and CCARI were comparable but intima-media was thicker in gouty tophi. Serum concentrations of ROS products, NO radicals and ascorbate radicals did not correlate with RRI, CCARI and IMT. Among untreated and treated with Allopurinol or Febuxostat patients the means of ROS products, NO radicals, ascorbate radicals, RRI, CCARI and IMT were similar. **Conclusions:** In the earlier and advanced stage of the disease we found no difference in oxidative stress level but the degree of inflammation was higher in tophi subjects. No connection was established between serum ROS products, NO radicals and ascorbate radicals with renal and carotid arteries arteriosclerotic vascular changes. We suggest that in gout individuals intrinsic inflammation has a leading role in the process of atherogenesis.

**Key words:** gout, serum oxidative stress markers, arteriosclerotic vascular alterations

8. E. Natchev, A. Kundurdjiev, N. Zlatareva, S. Vandeva, G. Kirilov, T. Kundurzhiev, S. Zacharieva. 2019. Echocardiographic myocardial changes in acromrgaly& a cross-sectional analysis in a tertiary center in Bulgaria. ActaEndocrinologica (Buc), vol. XV15:52-61doi: 10.4183/aeb.2019.52(IF-0,411)

## **Abstract**

**Context.** Cardiomyopathy is the most frequent cardiovascular complication in acromegaly.

**Objective.** We aimed to compare some echocardiographic markers in acromegaly patients with controls and find a correlation with disease duration, disease activity, levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-1).

**Design.** We conducted a cross-sectional case-control study for the period of 2008-2012.

**Subjects and methods.** Acromegaly patients altogether 146 (56 men and 90 women), were divided into four groups according to disease activity and the presence of arterial hypertension (AH). The control group included 83 subjects, matching the patient groups by age, gender and presence of AH. GH was measured by an immunofluorometric method, while IGF-1 by IRMA method. All patients and controls were subjected to one- and two-dimensional transthoracic echocardiography, color and pulse Doppler.

**Results.** We found a thickening of the left ventricular walls and an increase in the left ventricular mass. However, these changes were not statistically significant in all groups and no correlation with disease duration could be demonstrated. As markers of diastolic dysfunction, increased deceleration time and isovolumetric relaxation were registered, which were dependent mainly on age in a binary logistic regression analysis, but not GH or IGF-1. Using absolute values, ejection and shortening fractions were increased in some groups. Using cut-off values, a higher percentage of systolic dysfunction was demonstrated in patients compared to their corresponding controls. Engagement of the right heart ventricle was also found – increased deceleration time and decreased  $e/a$  tric ratio.

**Conclusions.** In conclusion, functional impairments of both ventricles were present, with a predominance of left ventricular diastolic dysfunction.

**Key words:** acromegaly, acromegaly cardiomyopathy, echocardiography, GH, IGF-1.

9. Diyan Genov, Irena Ivanova, Ventsislava Pencheva, **Atanas Kundurdgiev**. Serum uromodulin - a marker for diagnosis of chronic kidney diseases. *Acta Medica Mediterranea*, 2019, 35: 3249-3253 (IF-0,751)

**ABSTRACT**

**Introduction:** Chronic kidney disease is one of the most frequent chronic diseases causing disability and a significant decrease in quality of life. A major role in its diagnosis plays the clinical laboratory because it provides fast, easy and relatively cheap methods. Although there are well-established markers such as serum creatinine and cystatin C, the search for new reliable biomarkers to help assess kidney function and to predict the evolution of the disease continues. One of them can be Uromodulin, also known as Tamm-Horsfall protein. However, its exact function still needs to be clarified.

The aim of the study was to evaluate the role of serum uromodulin as a marker of the renal impairment in patients with chronic renal diseases.

**Materials and methods:** A total of 68 patients were enrolled in this prospective observational study in the Clinic of Nephrology of the University Hospital "St. Ivan Rilski" for a period of two years (2017-2018). The mean age of the patients was  $62.21 \pm 11.869$  years with the male/female ratio 31/37 (45.6% / 54.4%). Laboratory blood and urine tests, abdominal ultrasound with resistive index measurement and serum uromodulin investigations were performed in all patients.

**Results:** Serum uromodulin levels were significantly negatively correlated with serum creatinine ( $r = -0.720, p < 0.0001$ ), urea ( $r = -0.717, p < 0.0001$ ), uric acid ( $r = -0.296, p = 0.017$ ), cystatin C ( $r = -0.353, p = 0.004$ ) and resistive index ( $r = -0.353, p = 0.004$ ). Correspondingly, a positive relationship with estimated glomerular filtration rate ( $r = 0.692, p < 0.0001$ ) was found.

**Conclusion:** Serum uromodulin levels significantly correlate with the resistive index and all already established laboratory parameters used for evaluation of renal impairment. It can be used as a potential marker for diagnosis and early assessment of chronic kidney disease progression.

**Keywords:** serum uromodulin, chronic kidney disease, biomarker, cystatin C, resistive index.

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10. R. Gancheva<sup>1</sup>, Ts. Velikova<sup>2</sup>, T. Kundurzhev<sup>3</sup>, Zl. Kolarov<sup>1</sup>, A. Koundurdjiev<sup>4</sup>. Serum concentration of IL-1 $\beta$  and IL-18 in gaut patients and cardiovascular alterations. *Rheumatology*. Vol. XXVII, № 4/2019. ISSN 1310-0505

**Резюме.** В литературата има данни, че ключовите за иницирането и поддържането на подагрозното възпаление интерлевкини – IL-1 $\beta$  и IL-18, се асоциират с бъбречни и сърдечно-съдови нарушения. Имат главна регулаторна функция в първичния имуен отговор и в съдовата патология. Поставихме си за цел да изследваме серумното ниво на IL-1 $\beta$  и IL-18 при контроли с неактивирана остеоартроза, при пациенти с асимптомна хиперурикемия, подагрици без тофи и болни с тофи извън пристъп и да установим дали серумните им концентрации се асоциират с ехографски промени на бъбреците и сърцето. Проучването е с кроссекционен дизайн. Включени са общо 83 последователни болни: 18 с неактивирана остеоартроза, 29 с асимптомна хиперурикемия, 22-ма подагрици без тофи и 18 подагрици с тофи в междупристъпен период. Серумната концентрация на интерлевкините е определена чрез ензимно-свързан имуносорбентен метод (ELISA) с Human IL-1 $\beta$  и IL-18 ELISA китове (Platinum, eBioscience, Vienna, Austria). Ехографски са измерени: бъбречният резистивен индекс (RRI) с 3.5 MHz трансдюсер, работещ с пулсова доплерова честота 2.5 MHz, и индексът на левокамерната мускулна маса (LVMI), с 2.5 MHz трансдюсер Phased Array. Данните са анализирани чрез One-Sample Kolmogorov-Smirnov, ANOVA, Tukey HSD, Kruskal Wallis, Mann-Whitney и точният тест на Fisher. Корелационните анализи са извършени чрез корелационния коефициент на Spearman. При пациентите с тофи серумното ниво на IL-1 $\beta$  беше недектируемо в сравнение с останалите три групи ( $p < 0.001$ ), докато в серумната концентрация на IL-18 не се установи разлика между изследваните групи ( $p = 0.154$ ). Имайки предвид, че нивото на IL-1 $\beta$  беше недектируемо при подагриците с тофи, корелационен анализ при тези болни със серумното ниво на пикочната киселина, RRI и LVMI не се проведе. В останалите три групи, в които имаше стойности на IL-1 $\beta$  над нулата, не установихме връзка със споменатите показатели. Корелация не се откри и между концентрацията на IL-18 със серумната пикочна киселина, RRI и LVMI. Смятаме, че серумното ниво на IL-1 $\beta$  и IL-18 не отразява тежестта на болестта и сърдечно-съдовия риск при изследваните болни от подагра.

**Ключови думи:** болни от подагра в междупристъпен период, серумни нива на IL-1 $\beta$  и IL-18, сърдечно-съдови промени

**Abstract.** In the literature, there are reports that the key interleukins, IL-1 $\beta$ , and IL-18, for the initiation and maintenance of gouty inflammation are associated with renal and cardiovascular disorders. They have a major regulatory function in the innate immune response and vascular pathology. We aimed to determine serum levels of IL-1 $\beta$  and IL-18 in controls with inactivated osteoarthritis, patients with asymptomatic hyperuricemia, gouty arthritis without tophi subjects and gouty tophi individuals out of flare, and to establish whether their serum concentrations are connected to ultrasound alterations of the kidneys and heart. The study is cross-sectional in design. A total of 83 consecutive patients were included: 18 with inactivated osteoarthritis, 29 with asymptomatic hyperuricemia, 22 gouty arthritis without tophi, and 18 gouty tophi individuals out of flare. Serum interleukin concentrations were determined by enzyme-linked immunosorbent assay (ELISA) with Human IL-1 $\beta$  and IL-18 ELISA kits (Platinum, eBioscience, Vienna, Austria). By applying ultrasound were measured: renal resistive index (RRI) with 3.5 MHz transducer working with the pulse-Doppler frequency of 2.5 MHz and left ventricular mass index (LVMI), determined with 2.5 MHz transducer Phased Array. Data were analyzed by One-Sample Kolmogorov-Smirnov, ANOVA, Tukey HSD, Kruskal Wallis, Mann-Whitney and Fisher's exact test. Correlational analyzes were performed using the Spearman correlation coefficient. In gouty tophi subjects serum IL-1 $\beta$  level was undetectable compared to the other three groups ( $p < 0.001$ ). The serum concentration of IL-18 was comparable across the groups ( $p = 0.154$ ). Given that the level of IL-1 $\beta$  was undetectable in gouty tophi patients, correlation analysis in this group with serum uric acid concentration, RRI and LVMI was not performed. In the remaining three groups, which had values of IL-1 $\beta$  above zero, we did not detect an association with the parameters mentioned above. No correlation was found between IL-18 concentration and serum uric acid, RRI and LVMI in the groups. : We suggest that serum IL-1 $\beta$  and IL-18 levels do not reflect the severity of the disease and cardiovascular risk in the examined gout patients.

**Key words:** gout patients out of flare, serum concentrations of IL-1 $\beta$  and IL-18, cardiovascular alterations



11. R. Gancheva<sup>1</sup>, **At. Kundurdjiev**<sup>2</sup>, M. Ivanova<sup>1</sup>, T. Kundurzhev<sup>3</sup>, Zl. Kolarov<sup>1</sup>. Renal, Heart and Vascular Changes in Fifty-Three Gout Patients: a Follow-up Study. *Comptes rendus de l'Academie bulgare des Sciences* (in press). (IF-0,32)

12.

**Objective:**The study aimed to determine renal, heart and vascular changes developing in gout patients over time and to find out whether they are more pronounced in the presence of tophi.**Materials and methods:** Fifty-three gout subjects, 31 gouty arthritis without tophi and 22 gouty tophi, underwent multimodal ultrasound examination at the study entry and 18 months thereafter. Renal resistive index (RRI), aorta (Ao), left atrium (LA) size, thickness of the interventricular septum (IVS) and of posterior wall (PW) of the left ventricle, end-diastolic volume index (EDVi), end-systolic volume index (ESVi), stroke volume index (SVi), fractional shortening (FS), ejection fraction (EF), intima-media thickness (IMT) and common carotid artery resistive index (CCARI) were measured. **Results:**There were no apparent changes from baseline in serum uric acid levels, eGFR, RRI, EDVi, ESVi, SVi, FS and CCARI. Results over time, reflecting both assessment time points revealed that Ao (p=0.008), LA (p=0.001), IVS (p=0.007), IMT (p=0.009) increased and EF decreased (p=0.026). In both groups Ao, LA, IVS and IMT changed similarly over time, but the worsening of EF was more pronounced in gouty tophi (p=0.031). **Conclusions:** In the follow-up of gouty arthritis without tophi and gouty tophi patients, comparable alterations in the heart and carotid arteries morphology develop, however the pumping function of the heart seems to be more affected in the later stage of the disease.

**Key words:** multimodal ultrasound; gout; follow-up study

13. Vlahov Y, Borisova A-M, Nikolova M, Kundurdjiev A, et al. Subacute thyroiditis – an underestimated diagnosis. *Acta Med Bulg* 2019 (in press). (IF-0,21)

**Abstract**

Subacute thyroiditis is a relatively rare thyroid disease that develops after acute viral upper respiratory tract infection and manifests with neck pain, fever and transient hyperthyroidism. The diagnosis is often delayed due to the non-specific presentation and laboratory findings. It is misdiagnosed with upper respiratory tract infections, cervical lymphadenitis, even with acute pyelonephritis. The authors present a series of 12 patients with subacute thyroiditis and discuss the main steps in the diagnosis, differential diagnosis and treatment of this disease.

**Key words:** subacute thyroiditis, diagnosis, differential diagnosis, treatment.



## Резюмета на статии в български списания на доц. Атанас Кундурджиев

1. Д-р Рада Ганчева, **доц. Атанас Кундурджиев**, проф. Златимир Коларов. Хиперурикемия: Мозъчно-съдови инциденти и паркинсонова болест. Топмедика. Брой 3. 2018 г. стр. 2-4, ISSN 1314-0434

*Предполага се, че съществува патогенетична връзка между мозъчния инсулт, Паркинсоновата болест и серумното ниво на пикочната киселина. Проучванията в тази насока подкрепят тази теза. Извънклетъчно пикочната киселина е антиоксидант и е част от протективните механизми на организма срещу предизвиканата от оксигираните радикали токсичност. Предполага се, че понижава оксидативния стрес в невроните, потиска липидната пероксидация и намалява оксидативната увреда [25]. Теоретично би могла да бъде протектор срещу оксидативна и исхемична увреда в мозъка. При определени условия в мощен прооксидант [3]. Повишеното ѝ ниво се свързва с повишена артериална ригидност, ендотелна дисфункция и нарушен вазодилататорен отговор [23]. Пикочната киселина допринася за ендотелната дисфункция като стимулира оксигирането на LDL, стимулира гранулоцитната адхезия и макрофагвалната инфилтрация в съдовата стена [38]. Оксидативната увреда допринася за мозъчната исхемия като увеличава зоната, ангажирана от инфаркта [23].*

2. **Доц. Атанас Кундурджиев**, д-р Рада Ганчева. Антикоагулация при хронични бъбречни заболявания. Наука кардиология.. Бр. 6. 2018 г. стр. 271-275, ISSN 1311-459X

*Резюме: В статията се обсъжда възможността при хроничните бъбречни заболявания да има едновременно риск от повишена съсирваемост и повишена скланноск към кървене, защото бъбреците участват във фибринолизата, в обмяната на хепарина, в каликреин-кининовата система, през тях може да настъпи загуба на някои естествени антикоагуланти и др. С напредването на възрастта и при влошаването на бъбречната функция риска от предсърдно мъждене се увеличава. В статията се обсъждат възможностите за определяне на риска от кървене и повишена съсирваемост и антикоагулацията при хронични бъбречни заболявания.*

3. **А. Кундурджиев**, Н. Колева, Д. Генов, Ц. Вутова, А. Костадинова, В. Минкова, А. Андреева. Клиничен случай на пациент със системен лупус изявил се със синдром на Гилен-Баре – диагностични и теапевтични проблеми. Медицински преглед. Vol. LV. №4. 2019 г. стр. 57-61, ISSN 1312-2193

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| <b>Резюме:</b>                  | Представяме случай на пациент със системен лупус, изявил се в началото като синдром на Гилен–Баре. Заболяването започва с бързо развиваща се типична клинична картина на синдром на Гилен–Баре, при нетипична находка от гръбначномозъчния ликвор и негативна имунология за системно заболяване. Започнато е лечение с имуновенин и нивалин с частичен резултат. Около една година след старта на болестта се появяват кожни обриви, протеинурия, ставни болки и рентгенови данни за засягане на белия дроб. Проведена е консултация с нефролог. Назначени са имунологични изследвания и е направена пункционна бъбречна биопсия, които са положителни за системен лупус. Започнато е патогенетично лечение с кортикостероиди и имunosупресори с положителен ефект върху бъбречното, кожното, ставното и белодробното засягане и върху промените в гръбначномозъчния ликвор. Авторите обсъждат причините за по-късната изява на симптоматиката на системен лупус и особеностите на клиничната картина. |
| <b>Ключови думи:</b>            | системен лупус еритематозус, синдром на Гилен–Баре, невролупус, хронична възпалителна демиелинизираща полиневропатия   |
| <b>Адрес за кореспонденция:</b> | Д-р Нели Колева, e-mail: rosseneli@yahoo.com   |
| <b>Abstract:</b>                | We present a female patient with systemic lupus (SLE) with initial clinical manifestation of the Guillain–Barre syndrome. The disease manifested with fast progressing typical Guillain–Barre syndrome with atypical cerebrospinal fluid findings and negative autoantibodies. Treatment with intravenous immunoglobulins and nivaline was started, with incomplete effect. Approximately one year after the disease onset the patient developed skin rash, proteinuria, arthralgiae and lung involvement. The patient was referred to nephrologist, immunological investigations and renal biopsy were performed and revealed laboratory and histological data for SLE. Treatment with corticosteroids and immunosuppressors was started and positive effect on the renal, skin, articular and lung involvement was observed, along with positive dynamics in cerebrospinal fluid findings. The authors discuss the late onset of SLE and the peculiar clinical picture of SLE.                       |
| <b>Key words:</b>               | SLE, Guillain-Barre syndrome, neurolupus, chronic inflammatory demyelinating polyneuropathy  |

4. Ива Петкова, Атанас Златев, Гергана Димитрова, Мадлен Стоянова, **Атанас Кундурджиев**, Милена Николова, Мария Христова, Диян Генев, Анна Костадинова, Н. Колева, Жулиета Христова. Амилоидоза – трудности при поставяне на диагнозата. Наука пулмология. Брой 3. 20019 г. стр. 28-33. ISSN 1312-8302

*Резюме: Амилоидозата е рядко заболяване, което се дължи на отлагане на неразтворим протеин (амилоид) в различни тъкани и органи предизвиквайки структурни и функционални увреди. Заболяването засяга редица жизнено важни органи, което го прави изключително значимо. Най-често засегнати са бъбреци, сърце, черен дроб, слезка, нервна система, бял дроб и гастроинтестинална система. Съществува голямо разнообразие на симптомите и белезите характеризиращи заболяването, което го прави трудно за диагностициране. В статията се представят два клинични случая с доказана амилоидоза. Ключови думи: амилоидоза, симптоми, клинични форми, диагноза.*

*Abstract: Amiloidosis a rare disease that results from deposition of insoluble fibriler protein (amiloid) in varies tissue and organs, causing structural and functional changes. It covers a number of vital organs wich makes it exstremly important. Most commonly affected are: kidney, heart, liver, spleen, nervous system, lung and gastrointestinal tract. There is a great deal of diversity in the symptoms and features that characterize the disease wich often results in difficult diagnose. The*

article presents two clinical cases with amyloidosis and different organ affected. Key words: amyloidosis, clinical forms, symptoms, diagnose.

5. Д. Генов, А. Кундурджиев. Уромодулин – маркер за хронична бъбречна увреда. сп. "Медицински преглед" vol. LV;2019; брой 6; стр. 5-12, ISSN 1312-2193

Резюме:

Уромодулин (Tamm-Horsfall протеин) е най-изобилният протеин, екскретиран в урината при физиологични условия. Биологичната му функция все още не е напълно изяснена. Предполага се, че той има роля в баланса между вода и електролит, изпълнява защитна функция срещу инфекции на пикочните пътища, участва във вродения имунитет на бъбреците. Мутациите в гена на уромодулина причиняват заболявания, свързани с алелни нарушения, наречени с общото наименование уромодулин-асоциирано бъбречно заболяване. Хроничното увреждане при различни други ренални патологии води до промяна в уринния и серумния уромодулин. Това показва, че той играе важна роля в развитието на хроничните бъбречни заболявания, а определянето му дава възможност за ранно откриване на реналното увреждане при различни болести. Това от своя страна води до започване на ранно лечение, а при началните стадии на бъбречно увреждане – и до спиране развитието на болестта. Ролята на уромодулина обаче все още подлежи на задълбочени проучвания.

уромодулин, хронични бъбречни заболявания, биомаркер, уромодулин-асоциирано бъбречно заболяване

Abstract:

Uromodulin (Tamm-Horsfall protein) is the most abundant protein excreted in the urine under physiological conditions. Its biological function is unclear. It is believed that uromodulin has a role in the balance between water and electrolyte, has a protective function against urinary tract infections, takes a part in the innate immunity of the kidneys. Mutations in the uromodulin gene cause diseases associated with allelic disorders called uromodulin-associated kidney disease. Chronic damage in various other renal pathologies leads to a change in urinary and serum uromodulin. This indicates that uromodulin plays an important role in the development of chronic kidney disease, and its study makes possible early detection of renal impairment in different diseases. This allows early treatment and ending the development of the disease at earlier stages. However, its role is still subject to in-depth research.

uromodulin, chronic kidney disease, biomarker, uromodulin-associated kidney disease

6. М. Николова, **Ат. Кундурджиев**, И. Ангелова, Хр. Пенчев, С. Драгнева, П. Николов, З. Спасова, М. Рангелова, К. Давидов. Бъбречни увреждания при болести, свързани с натрупване на желязо – хемохроматоза и таласемия майор. Диагностичен и терапевтичен ултразвук. Брой 2, 2019, стр. 69-75, ISSN 1310-1153

**Резюме.** Хомозиготната бета-таласемия и хемохроматозата са две заболявания, свързани с натрупване на желязо в тъканите. Бъбречните увреждания и при двете могат да настъпят вследствие токсичните ефекти на желязото върху бъбречната тъкан, развитието на захарен диабет или съпътстващото лечение на основното заболяване, както и по други механизми. Авторите представят случай на хомозиготна бета-таласемия (таласемия майор) и хемохроматоза с бъбречно засягане, механизмите на развитие на тези усложнения и основните стратегии за тяхното лечение.

**Ключови думи:** болести на натрупване на желязо, таласемия майор, хемохроматоза, нефрокалциноза, захарен диабет, хелатори на желязо, лечение.

**Abstract.** Homozygous beta-thalassemia and hemochromatosis are both associated with increased iron storage. The renal changes in both diseases may develop due to iron toxicity, secondary to diabetes mellitus, drug toxicity of the medications used for the underlying disease, and via other mechanism. The authors present patients with homozygous beta-thalassemia (thalassemia major) and hemochromatosis with renal involvement and the current knowledge on the mechanisms of development and major therapeutic strategies in these complications.

**Key words:** iron storage diseases, thalassemia major, hemochromatosis, nephrocalcinosis, diabetes, iron chelators, treatment

7. М. Христова, **Ат. Кундурджиев**. Хиперурикемия. Pro Medic. Брой 6. 2019 г. стр. 4-11. ISSN 2603-4727

*Резюме:* Хиперурикемията представлява абнормно повишаване на нивата на пикочна киселина в кръвта, при което тя може да кристализира и да се отложи в различни тъкани и органи. В организма тя съществува основно под формата на уратни йони. Отлагането на уратните кристали в тъканите започва да се появява, когато концентрацията на пикочна киселина надвиши референтните граници. Въпреки наличието на популационни и възрастови различия е прието, че това се случва при стойности над 360  $\mu\text{mol/L}$  (6  $\text{mg/dL}$ ) за жени и над 400  $\mu\text{mol/L}$  (6.8  $\text{mg/dL}$ ) за мъже.

8. **А. Кундурджиев**, Р. Ганчева. Хиперурикемия, подагра и сърдечно-съдов риск. *Medical Magazine*. Брой 73. Февруари 2020 г. стр. 58-64, ISSN 1314-9709

*Резюме: В статията се прави исторически преглед на познанията за подаграта и хиперурикемията. Проследяват се публикациите за връзката на хиперурикемията и подаграта с сърдечно-съдовия риск. Отчита се, че ретроспективните проучвания доказват връзка на хиперурикемията с повишен сърдечносъдов риск, докато проспективните показват противоречиви резултати. Споделя се собствен опит чрез използването на комплексната мултимодална сонография. Доказва се, че много от показателите, които имат самостоятелно значение като индикатори за сърдечносъдов рик са сигнификантно променени и показват по-висок такъв при подаграта с тофи, отколкото при подаграта без тофи и асимптомната хиперурикемия. Тези доказателства подкрепят тезата, че подагрозните тофи не са обикновени структури а грануломи, поддържащи провъзпалително състояние на организма.*

9. Н. Колева, **Ат. Кундурджиев**, М. Николова, М. Христова, А. Костадинова, Д. Генов, Ц. Вутова, Т. Тодоров, Ж. Христова. Два клинични случая с комбинация MGUS и гломеруллопатия – диагностични и терапевтични проблеми. *Медицински преглед*, брой №2 2020 г. ISSN 1312-2193

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| <p><b>Резюме:</b></p> <p><b>Ключови думи:</b></p> <p><b>Адрес за кореспонденция:</b></p>   | <p>Представяме 2 клинични случая на съчетание на моноклонална гамапатия с неясно значение (MGUS) и гломерулопатия: бързо прогресиращ полулуноен ГН – ANCA позитивен, и амилоидоза. Макар MGUS да протича доброкачествено, в конкретния случай наблюдавахме злокачествен ход с развитие на амилоидоза и влошаване на бъбречната функция и необходимост от диализно лечение. Пациентите бяха изследвани хистологично, имунологично, проведоха се имунофиксация, ехокардиография и рентген на бял дроб и сърце. Хистологично се потвърдиха типичните находки при полулуноен гломерулонефрит и амилоидоза. Типизира се амилоидозата и се определи имунохистохимично като AL. Вторият случай е демонстрация на типичното представяне на MGUS със злокачествено протичане на заболяването и развитие на амилоидоза: бързо влошаване на бъбречната функция с анемичен синдром и започване на ренозаместително лечение. Провеждането на активно патогенетично лечение подобри бъбречната функция, но и в двата случая имаме прогресивен ход с усложнения.</p> <p>моноклонална гамапатия с неясно значение, мултиплен миелом, амилоидоза, бързопрогресиращ гломерулонефрит, ANCA асоцииран гломерулонефрит</p> <p><i>Д-р Нели Колева, Клиника по нефрология, УМБАЛ „Св. Ив. Рилски“, e-mail: rosseneli@yahoo.com</i></p>  |
| <p><b>Abstract:</b></p> <p><b>Key words:</b></p> <p><b>Address for correspondence:</b></p> | <p>We present two clinical cases of association of monoclonal gammopathy of unknown significance (MGUS) and glomerulopathy: rapidly progressing semilunar GN – ANCA positive, and Amyloidosis. Although the MGUS has a benign course, in the present case, a malignancy was observed with the development of amyloidosis and impaired renal function and the need for dialysis treatment. Patients were examined histologically, immunologically, immunofixation was conducted, echocardiography and roentgenology of the lung and heart were performed. The typical findings of semi-lunar glomerulonephritis and amyloidosis were histologically confirmed. Amyloidosis was typed and immunohistochemically identified as AL. The second case is a demonstration of the typical presentation of MGUS with a malignant course of progression and the development of amyloidosis: rapid deterioration of renal function with anemic syndrome and initiation of replacement therapy. Active pathogenetic treatment improved kidney functionality, however, in both cases a progression of the course with accompanying complications is seen.</p> <p>monoclonal gammopathy of unknown significance, multiple myeloma, amyloidosis, rapidly progressive glomerulonephritis, ANCA-associated vasculitis</p> <p><i>Neli Koleva, MD, Clinic of Nephrology, University Hospital „Sv. Ivan Rilski“, e-mail: rosseneli@yahoo.com</i></p> |

10. М. Николова, Л. Маринчев, М. Христова, Р. Ганчева, Зл. Коларов, М. Балева, Р. Стойчев, **Ат. Кундурджиев**. Blue toe синдром. Медицински преглед, брой №2, 2020 г. ISSN 1312-2193



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| <p><b>Резюме:</b></p> <p><b>Ключови думи:</b></p> <p><b>Адрес за кореспонденция:</b></p>   | <p><i>Blue toe</i> синдром представлява остра исхемия и последваща цианоза на пръст на крака вследствие съдова оклузия на артериален кръвоносен съд с малък калибър от тромбоза, емболия, вазоспазм или възпаление и при липса на предхождаща травма, студово увреждане или подлежащо заболяване, свързано с генерализирана цианоза (например хипоксия или метхемоглобинемия). Често появата на симптомите се предхожда от съдова интервенция. Понякога може да се развият оток и цианоза и на съседни тъкани. При някои пациенти се наблюдава засягане и на други органи и системи. Изключително важно е да се осигури бърза реперфузия на засегнатите тъкани поради висок риск от тъканна некроза и гангрена. Настоящият обзор разглежда съвременните познания за <i>blue toe</i> синдром.</p> <p>blue toe синдром, атероемболия, съдови интервенции, васкулити, лечение</p> <p>Д-р Милена Николова, Клиника по нефрология, УМБАЛ „Св. Ив. Рилски“, София, e-mail: milena_i_dani@abv.bg</p>           |
| <p><b>Abstract:</b></p> <p><b>Key words:</b></p> <p><b>Address for correspondence:</b></p> | <p><i>Blue toe</i> syndrome is acute ischemia and cyanosis of a toe due to vascular occlusion of arterial branch of small caliber – thrombosis, embolism, vasospasm or inflammation of the vascular wall in the absence of preceding trauma, cold-induced tissue injury or underlying condition with generalized cyanosis (i.e., hypoxia or methemoglobinemia). Frequently the appearance of blue toe syndrome is preceded by vascular intervention. Sometimes edema and cyanosis of the adjacent tissues are present. In some patients involvement of other organs and tissues is observed. The fast reperfusion of the affected tissues is crucial due to the high risk for tissue necrosis and gangrene. This review is focused on the current knowledge on blue tow syndrome.</p> <p>blue toe syndrome, atheroembolism, vascular interventions, vasculitis, treatment</p> <p>Milena Nikolova, MD, Clinic of Nephrology, University Hospital Sv. Iv. Rilski, Sofia, e-mail: milena_i_dani@abv.bg</p> |

11. М. Николова<sup>1</sup>, Ат. Кундурджиев<sup>1</sup>, М. Христова<sup>1</sup>, Й. Влахов<sup>2</sup>, В. Тенев<sup>3</sup>. Синдром на Segliker и депресия: две тежки усложнения при хронична бъбречна недостатъчност. Сп. Обща медицина брой 1. 2020 г. стр. 92-99, ISSN 1311-1817

**Резюме.** Синдромът на Sagliker е едно от тежките хронични усложнения на диализното лечение, свързано с мутилация на лицевия череп, промени в костите на крайниците, зъбите, неврологични и психологични прояви, развиващи се в резултат от появата на вторичен хиперпаратиреоидизъм вследствие на продължителни нарушения в калциево-фосфорната обмяна и нивата на дихидрокси витамин D при пациенти с терминална хронична бъбречна недостатъчност. Описан е през 2004 г. от Y. Sagliker и сътр. и оттогава в литературата се натрупват много данни за клиничните, рентгенологичните и генетичните основи на заболяването. Депресията е друго тежко усложнение на хроничната бъбречна недостатъчност, свързано със сериозна инвалидизация на пациентите. Авторите представят съвременните познания за синдрома на Sagliker и депресията при хронична бъбречна недостатъчност.

**Ключови думи:** синдром на Sagliker, терминална хронична бъбречна недостатъчност, хиперпаратиреоидизъм, мутилация на лицевия череп, GNAS1, FGF23, FGFR3, депресия

**Abstract.** The Sagliker syndrome is a severe chronic complication of dialysis treatment presenting with facial skull mutilation (uglifying), changes in limb bones, teeth, and neurological and psychological changes, developing in association with secondary hyperparathyroidism due to long-standing calcium-phosphate metabolism and dihydroxy vitamin D abnormalities in patients with end-stage renal disease. It was described in 2004 by Y. Sagliker et al. Many clinical, radiological and genetic abnormalities have been described in such patients. Depression is another serious complication of chronic kidney disease, leading to disability. Different mechanisms have been proposed for its development. The authors present the recent knowledge on Sagliker syndrome and depression in chronic kidney disease.

**Key words:** Sagliker syndrome, end-stage renal disease, hyperparathyroidism, facial mutilation (uglifying), GNAS1, FGF23, FGFR3, depression