Results: We studied 369 participants with increased CV risk: 63 with CAD equivalent (47 diabetes mellitus type II/DM and 16 end-stage renal disease), 92 with chronic inflammatory disorders and 73 with essential hypertension/EH. We further included 53 subjects with CAD as positive and 87 otherwise healthy as negative controls. All MVs were lower in patients with increased CV risk as compared to positive controls ($p < 0.001$ for all). In addition, PMVs ($p = 0.045$) and EMVs ($p = 0.028$) were increased in patients with increased CV risk as compared to negative controls. Between patients with increased CV risk, those with CAD equivalent had increased EMVs versus EH ($p = 0.002$) and chronic inflammatory disorders ($p = 0.021$).
In the whole cohort, RMVs were associated only with the presence of EH (beta = 0.119/p = 0.029). In univariate analysis, PMVs were significantly associated with body mass index/BMI (beta = 0.192/p < 0.001), office and central systolic BP (beta = 0.114/p = 0.031 and beta = 0.131/p = 0.015, respectively). EMVs were associated with age (beta = 0.195/p < 0.001), BMI (beta = 0.108/p = 0.042), office and central systolic BP (beta = 0.159/p = 0.003 and beta = 0.172/p = 0.001, respectively), DM (beta = 0.302/p < 0.001), EH (beta = 0.171/p = 0.002), and dyslipidemia (beta = 0.176/p = 0.001).
In multivariate analysis, central systolic BP (beta = 0.150/p = 0.006) predicted PMVs, independently of BMI. Age (beta = 0.141/p = 0.011), central systolic BP (beta = 0.219/p < 0.001), and diabetes mellitus (beta = 0.236/p < 0.001) predicted EMVs, independently of age and dyslipidemia.

Conclusions: In a large cohort of patients with divergent CV risk, MVs emerge as potential biomarkers. Central systolic BP is a strong predictor of MVs levels highlighting its predictive value for CV outcomes.

SERUM HEPATOCYTE GROWTH FACTOR CONCENTRATION IS ASSOCIATED WITH BLOOD PRESSURE IN SUBJECTS WITH PREHYPERTENSION

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Objective: Hepatocyte growth factor (HGF) is a pleiotropic factor that regulates cellular processes such as cell survival, proliferation, migration, and differentiation. Serum HGF concentration is associated with systolic blood pressure (BP) and is higher in hypertensive than in normotensive individuals, especially if complications of arterial hypertension are developed. Our aim was to determine the association of serum HGF concentration in subjects with prehypertension.

Design and method: Data from 612 subjects (57,8% women, average age 41 years) was nalysed. After clinical examination, fasting blood and urine samples were drawn. HGF was measured using a commercial test. BP was measured according to the ESC/ESH guidelines. Based on BP values, subjects were divided into two groups: OBP - subjects with optimal blood pressure (BP < 120/80 mmHg, N = 295), and PHT (subjects with BP 120/80–140/90 mmHg N = 317).

Results: Subjects with PHT were significantly older and had higher values of body mass index, waist circumference, serum total cholesterol levels, triglyceride levels, and fasting glucose levels (all $p < 0.001$). The prevalence of metabolic syndrome was significantly higher in PHT group (4.3% vs. 30.4%, $p < 0,001$). Serum HGF concentrations were higher in PHT subjects, but the difference was not significant (270.8 vs. 277.9 pg/ml, $p = 0.651$). Serum HGF concentration showed a significant positive correlation to systolic and diastolic BP in PHT ($r = 0,226$, $p < 0,05$ and $r = 0,232$, $p < 0,01$, respectively), but not in OBP group ($p > 0.05$).

Conclusions: Serum HGF is associated with BP in prehypertensive subjects, but not in subjects with optimal BP. In our cohort, the correlation is more pronounced for diastolic blood pressure.

MID-REGIONAL PROADRENOMEDULLIN (MR-PROADM) AS A BIOMARKER IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND HYPERTENSION - STUDY CONTINUATION

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Objective: Assessment of MR-proADM serum concentration as a biomarker in patients with CKD and arterial hypertension.

Variable	Study group
Age,y, (median)	72 (19-93)
Sex (M/F), n(%)	83/77 (51,9/ 48,1)
CKD stage, n(%)	1-7 (4,3)
	2-18 (11,3)
	3a-16 (10)
	3b-33 (20,6)
	4-58 (36,3)
	5-28 (17,5)
mSBP, mmHg (median)	136
mDBP, mmHg (median)	76
Control of BP, n (%)	Yes 87(54,4)
	no 73 (45,6)
Comorbidities, n(%)	
Diabetes mellitus	1- 5(3.1)
	2- 66 (41,3)
Myocardial infarction	22 (13,8)
Heart failure	54 (33,4)

Design and method: Our study included a single-center cohort of 160 patients admitted to the Second Department of Nephrology and Hypertension with Dialysis Unit Medical University of Bialystok with CKD treated conservatively. The concentration of MR-proADM were measured in the serum of patients and the control group (27 healthy volunteers). The statistical analysis included past medical history, the stages of CKD, the presence and degree of control of arterial hypertension, and the presence of cardiovascular diseases.

Results: Patients with CKD had higher serum MR-proADM concentrations compared to the control group (62,61 [45,67–81,39] vs 224 [143,95–293,35] pg/mL, $p < 0,0001$). The median MR-proADM concentration in each stage was not statistically different.
There was a significant positive correlation between MR-proADM and the dimension of the left ventricle ($R = 0,25$; $p = 0,009$) with glucose concentration ($R = 0,19$; $p = 0,017$) and a negative correlation with serum iron concentration ($R = -0,20$; $p = 0,03$). There were no significant differences in the plasma concentration of MR-proADM depending on the degree of hypertension control.

Conclusions: In larger group of CKD patients, an increased serum concentration of MR-proADM was confirmed. Left ventricular hypertrophy found in echocardiography was associated with higher serum concentrations of MR-proADM. To assess the usefulness of this hormone as a prognostic biomarker of CKD or cardiovascular risk, further studies in larger groups still are required.

UTILITY OF IRISIN AND APELIN IN PREDICTION OF HEART FAILURE PHENOTYPES IN TYPE 2 DIABETES MELLITUS PATIENTS

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Objective: The aim of the study was to investigate whether serum levels of both irisin and apelin predict HF with preserved ejection fraction (HFpEF) in patients with type 2 diabetes mellitus (T2DM).

Design and method: One hundred and eight HF patients with T2DM having HFpEF (n = 58), HF with mildly reduced ejection fraction (HFmrEF, n = 22), HF with reduced ejection fraction (HFrEF, n = 28) aged from 41 to 62 years and 20 non-HF patients with T2DM. Healthy control group was consisted of 25 individuals matched with age and sex. All patients gave voluntary written informed consent to participate in the study. We polled at baseline demographic and anthropometric information, data for hemodynamic performances by B-mode echocardiography, Doppler and TDI, and the levels of biomarkers including irisin, apelin, N-terminal pro-brain natriuretic peptide (NT-proBNP) by ELISA.

Results: Using ROC curve we revealed that cut-off points for irisin and apelin that distinguished HFpEF from HFrEF/HFmrEF were (6.50 ng/mL; AUC = 0.78; 95% confidence interval [CI] = 6.85 - 10.66 ng/mL and 4.12 ng/mL, AUC = 0.72;

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95% CI = 3.90–5.75 ng/mL, respectively). Then we divided all patients with HF having elevation of NT-proBNP > 750 pmol/mL into three subgroups depending on the biomarkers' levels. Patients from subgroup A had both irisin and apelin levels higher cut-off points, individuals from group B had higher concentration of one of two biomarkers, and patients from subgroup C demonstrated levels of both peptides lower cut-off points. Multivariate logistic regression analysis revealed that discriminative value of irisin and apelin to predict HFpEF in subgroup B (Odds Ratio [OR] = 2.18; 95% CI = 1.26–3.14; P = 0.001) were substantially higher compared with subgroups A and C (OR = 1.03; 95% CI = 1.00–1.05; P = 0.64 and OR = 0.92; 95% CI = 0.89–1.01; P = 0.62, respectively). Adding irisin and apelin to NT-proBNP as independent variables to the predictive model sufficiently improved discriminative ability of whole model for HFpEF.

Conclusions: Multidirectional changes in the levels of irisin and apelin in T2DM patients had better predictive value for HFpEF that simultaneous increase and decrease in the circulating levels of these peptides.

ANALYSIS OF RAAS BIOMARKERS TO CLASSIFY ANTI-HYPERTENSIVE DRUG TREATMENTS IN THE GENERAL POPULATION: THE CHRIS STUDY

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Objective: Hypertension is a leading cause of death worldwide. Large-scale population-based epidemiological studies are an opportunity to assess the effectiveness of anti-hypertensive drug (AHD) treatment. However, these studies often lack treatment documentation, especially in situations where linkage to electronic health records is not established, with consequent recall and classification biases. When relevant biomarkers are measured, it should however be possible to attribute individuals to the most likely AHD treatment, limiting information loss.
We investigate whether unsupervised cluster analysis applied to measured RAAS biomarkers may help to classify different AHD treatments in a general population sample.

Design and method: In the Cooperative Health Research in South Tyrol (CHRIS) study, automated drug barcode scans allowed classification of AHD specific treatment among participants. We measured angiotensin I, angiotensin II and aldosterone levels on 800 participants using liquid chromatography combined with tandem mass spectrometry (LC-MS/MS) analysis, as implemented in the RAAS Triple-A assay. Age and sex matched participants (age: 43–90 years; 54% females) were split into 8 balanced groups: normotensive (n = 101); untreated hypertensive (n = 100); non-AHD (n = 100); ACEi (n = 99); ARB (n = 98); ACEi+diuretic (n = 100); ARB+diuretic (n = 102); and beta-blockers (n = 100).
We performed unsupervised cluster analysis based on the three biomarkers ignoring the known AHD treatment. We evaluated the extent of agreement between the automated drug recognition system and RAAS based classification.

Results: We identified three clinically heterogeneous clusters. Cluster 1 (n = 444) was characterized by participants not receiving any AHD and having high systolic blood pressure. Cluster 2 (n = 235) identified the use of ARB with or without diuretics. These individuals were more likely to present diabetes. Cluster 3 (n = 121) identified ACEi with or without diuretics and included older and overweight participants. The inter-classification agreement between the automated recognition system and RAAS clusters was highest for ACEi and ARB.

Conclusions: In the absence of specific information, unsupervised cluster analysis applied to RAAS biomarkers can reliably identify individuals under ACEi and ARB treatment.

ROLE OF SERUM URIC ACID LEVELS AND CRP IN THE EXISTENCE OF ATRIAL FIBRILLATION IN HYPERTENSIVE PATIENTS

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Objective: The inflammatory effect of the serum uric acid and C-reactive protein (CRP) is evident, as well as the role and significance, of inflammation in the presence of atrial fibrillation.
The aim of this study was to investigate a possible association between the serum uric acid levels with the existence of atrial fibrillation in hypertensive patients and the possible role of CRP in this status.

Design and method: We studied 1196 hypertensive patients (45,1% female), treated or newly diagnosed untreated, of mean age: 63,1 ± 13,3 years, without any known cardiovascular disease and with mean office systolic/diastolic arterial blood pressure (S/DBPo): 142,1 ± 19.3/86.5 ± 12,6 mmHg, mean office heart rate (HRo): 73,7 ± 10,7 bpm, average body mass index (BMI): 28.5 ± 5,8 kg/m^{2}and average waist circumference (WC) 96.1 ± 12.9 cm
The levels of serum uric acid (SUA), C-reactive protein (CRP), urea, creatinine,were recorded. eGFR was calculated according Cockcroft-Gault Equation and the atrial fibrillation (AF) status was recorded. The study population was separated in two groups, according the existence or not of any evidence for AF
Group A: with PAF or PEAF
Group B: without AF
By using the ANOVA statistic method we registered the SUA and CRP values in both groups.
Using Pearson correlation method we correlated SUA with CRP serum levels.

Results: Table 1: Differences of serum uric acid and CRP levels between group A and group B

	SUA (mg/dl)	CRP (mg/L)
Group A (N = 319)	5,9 ± 1,7	3,16 ± 3,24
Group B (N = 877)	5,2 ± 1,6	2,4 ± 3,4
p	< 0,001	0,019

Table 2: Correlation between serum uric acid levels with C-reactive protein levels

	CRP
SUA	r = 0.158
	p < 0,001

SUA: serum uric acid
CRP: C-reactive protein

Conclusions: In hypertensive patients treated or not, the presence of PAF or PEAF was associated with significantly higher serum uric acid levels and CRP levels, while a significant positive correlation exists between SUA and CRP levels in this population. possibly indicating their importance in the inflammatory status of hypertensive patients with atrial fibrillation.

PROGNOSTIC SIGNIFICANCE OF RISK FACTORS AND BIOMARKERS IN PATIENTS HOSPITALIZED FOR CARDIORENAL SYNDROMES

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Objective: Cardiorenal syndromes (CRS), involving the heart-kidney cross-talk and the activation of neurohumoral and inflammatory pathways, is an entity characterized by high morbidity and mortality. Our study aimed to evaluate the prognostic role of risk factors and biomarkers in patients ospitalised for CRS.

Design and method: In this observational cohort study, 100 consecutive patients ospitalised for CRS were enrolled. Socio-demographic characteristics, personal medical history, and prior medication use were recorded upon admission, and echocardiography was performed. Moreover, an array of blood markers was measured. The endpoint of interest was a composite of death or dialysis dependence at discharge.

Results: Patients were classified into two groups; Group 1 (N = 52): discharged being dialysis-independent, Group 2 (N = 48): death/dialysis dependence at discharge. No significant differences were detected in baseline characteristics between the two groups. Group 2 patients used ospit-angiotensin-aldosterone system blockers (RAASb) less often (Group 1: 71.2% vs. Group 2: 41.7%, p = .003) and more frequently presented with oliguria/anuria (Group 1: 28.8% vs. Group 2: 66.7%, p < .001). Group 2 patients had significantly lower hemoglobin, serum albumin, and 25-hydroxy-vitamin D [25(OH)D] (Figure). At the same time, serum phosphate, potassium, N-terminal-pro hormone brain natriuretic peptide, and parathyroid hormone (PTH) were significantly higher in Group 2 patients (Figure). In a multivariate regression analysis, lack of prior RAASb (Odds ratio: 22.0, 95% confidence interval: 2.7–179.5, p = .004) and lower 25(OH)D levels (Odds ratio: 0.90, 95% confidence interval: 0.82–0.99, p = .03) were independently associated with an increased risk of death or dialysis dependence at discharge. 25(OH)D/PTH ratio was the most accurate predictor of the composite endpoint (area under receiver operating characteristics curve: 0.81), with a cutoff of equal or less than 97.9 having a sensitivity and specificity of 79.4% and 70.4%, respectively.

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