An association of biomarkers of cardiac remodeling, myocardial fibrosis and inflammation with the parameters of heart function and structure in the patients with arterial hypertension

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Background and study objective

- Backround: An early evaluation of the cardiac remodeling may be usefull in prediction of heart failure in arterial hypertension (AH)

- Study objective: to evaluate the association of cardiac biomarkers levels with the parameters of cardiac structure and function in patients with AH

Patients and methods

- Patients with arterial hypertension, normal LV EF and absence of symptoms and signs of heart failure were included in the study.

- The levels of biomarkers: NT-proBNP, sST2, Galectin-3, GDF-15, Cystatin C, TIMP-1 and ceruloplasmin were measured and assessed together with other biochemical and echocardiographic parameters.

- *Pearson's correlation* coefficients and in the case of not-normal distributed variables the non-parametric *Spearman's correlation* coefficients were calculated

Results - Patients

- Total number of 92 patients, 56 males (61 %) and 36 females (39 %) mean
age 61.5 years met criteria for the study.
- Commorbidities: of 73 % dyslipidaemia, 29 % type 2 diabetes mellitus
and 15 % CAD.
- The mean number of drugs for AH was 2.34.
- Betablockers and diuretics in 52 (57 %) patients, ACEIs 42 (46 %)
ARBs 43 (47 %), CCBs 42 (46 %) MRAs 16 (17 %).

Other medication:

ASA (32 %), statins (64 %), oral antidiabetics (21 %), alopurinol (14 %).

Results – laboratory parameters

Parameter	Mean ± SD	Median [Min – Max]
GDF-15* [ng/L]	1608.1 ± 1351	1133.6 433.7 – 8478.0
Galectin-3* [ng/L]	1689.4 ± 2323	503.1 19.2 – 9903.0
Cystatin C [ng/L]	18802.6 ± 5717	17283.6 9046.9 – 32866.3
sST2 [ng/L]	298.9 ± 178	258.3 41.4 – 817.7
TIMP-1 [µg/L]	299456.0 ± 106527	276400.1 140685.8.- 589331.0
NT-proBNP* [pg/mL]	20.9 ± 7.78	11.0 1.0 – 197.0
Cp [g/L]	0.3 ± 0.07	0.2 0.1 – 0.5

** Variables that do not fulfill conditions of a normal distribution were marked with an asterisk*

Results – echocardiographic parameters

Parameter	Mean ± SD	Median [Min – Max]
LV EF* [%]	64.7 ± 5.3	65 45 – 75
EDD [mm]	49.2 ± 4.2	49 40 – 58
LA [mm]	38.9 ± 6.2	38 29 – 73
RV [mm]	27.4 ± 3.1	28 21 – 35
E/A	1.1 ± 0.46	1.0 0.5 – 3.1
E/E´	7.1 ± 3.5	6.3 2.8 – 21.6

** Variables that do not fulfill conditions of a normal distribution were marked with an asterisk*

Results – echocardiographic parameters

Parameter	Mean ± SD	Median [Min – Max]
ACT RVOT [ms]	119.1 ± 17.7	116 83 – 160
ePAP [mmHg]	15.3 ± 2.4	15 11 – 20
LVM [g]	189.9 ± 52.2	184 113 – 357
LVMi [g/m²]	91.7 ± 15.8	90.8 15.8 – 154.1
RWT	0.4 ± 0.05	0.4 0.3 – 0.5
LAi [mm/m²]	19 ± 2.7	18.8 14.3 – 31. 1

Results

- NT-proBNP level correlated with LV diastolic function:

velocity of E wave (r = 0.377, P < 0.002),

E/A ratio, (r = 0.455, P < 0.0001), E´ lat (r = -0.354, P = 0.006),

E/E´ ratio, r = 0.393, P < 0.002, ePAP (r = 0.390, P = 0.014),

and age (r = 0,384, P < 0.0001).

- sST2 level correlated with parameters of cardiac structure:

LV mass (r = 0.290, P < 0.01) and LVM index (r = 0.307, P = 0.012)

and with posterior wall thickness PW (r = 0.380, P < 0.001).

Results

- The patients were divided into two groups according to presence of LVH. LVH was defined by LVMi > 95 g/m^2 in females or > 115 g/m^2 in males **and** RWT > 0.42 for both genders.

- Two multivariate logistic regression models for patients LVH vs. non-LVH were developed.

1. Model: Patients LVH vs. non- LVH: only NT-proBNP, GDF-15, Galectin-3, Cystatin C, sST2, and TIMP-1 were used as predictive variables.
2. Model: Patients LVH vs. non-LVH: the next predictive variables were added: age, LV EF, LA, RV, E/A, E/E', Na, K, urea, creatinine, and eGFR.

Results

Odds ratios (OR), 95% Confidence Intervals (CI) and levels of significances of Wald's statistic (*P*) of differences in predictive values between patients with LVH (N=31) and without LVH (N=47).

Variable	OR	95% CI	P
Model 1 – Predictive variables: NT-proBNP, GDF-15, Galectin-3, Cystatin C, sST2, and TIMP-1			
sST2	**1.0033**	**1.0001 – 1.0066**	**0.041***
TIMP-1	1.0001	0.9999 – 1.0001	0.161
Model 2 – Predictive variables: NT-proBNP, GDF-15, Galectin-3, Cystatin C, sST2, and TIMP-1 + age, LV EF, LA, RV, E/A, E/E', Na, K, urea, creatinine, and eGFR			
Cystatin C	0.9998	0.9996 – 1.0001	0.141
sST2	1.0057	0.9992 – 1.0122	0.086
TIMP-1	**1.0001**	**1.0001 – 1.0002**	**0.012**
LA	1.1356	0.9710 – 1.3281	0.112
Age	1.0566	0.9712 – 1.1494	0.200

** Statistically significant predictors are marked in bol*

Conclusion

- In patients with arterial hypertension and no signs of HF NT-proBNP level correlated with LV diastolic function.
- Biomarker sST2 level correlated with parameters of cardiac structure.
- Biomarkers sST2 and TIMP-1 were associated with the presence of left ventricular hypertrophy.

Thank you for your attention