development of adverse outcomes in patients with myocardial infarction seems relevant. One of the most important directions in this field is the study of biomarkers of endothelial dysfunction as predictors of adverse outcome.
Purpose: the aim of the study was to evaluate the levels of biomarkers associated with endothelial dysfunction in patients after myocardial infarction (MI) depending on the outcome.
Methods: 223 patients with MI at the age of 57.35±10.09 years was included in the study. The observation period was 18-24 months. Depending on the outcome, the patients were divided into 2 groups: 1st–55 patients (24,7%) with an adverse outcome (all-cause mortality, recurrent acute coronary syndrome, decompensate chronic heart failure); 2nd–168 patients (75,3%) with favorable outcome. We determined the levels of interleukin-6 (IL), matrix metalloproteinase-2 (MMP), high-sensitivity C-reactive protein (hsCRP) by immunoenzyme method on the 3rd and 14th days in blood, circulating endothelial cells (CEC) by flow cytometry, antigen von Willebrand factor (vWF:Ag) by immunoturbidimetric method, endothelin-1 (ET-1) and superoxide dismutase (SOD) was determined by immunoenzyme method at day 14 and after 3 months MI. Statistical data are presented as the median and interquartile scale.
Results: Concentrations of IL-6, MMP2 and hsSRP on day 3 were significantly higher in group 1 (14,9 [7,9;53,5] pg/ml vs 10,4[5,1;16,1] pg/ml, 29,8 [24,3;of 32.6] ng/ml vs 21,5 [18,4;24,3]ng/ml, and 18.1 [10,7;40,7] mg/l vs 11,5 [6,1;28,2] mg/l, respectively ($p<0.05$). At day 14 the concentrations of IL-6 and hsSRP decreased and were not significantly different. Thus, elevated levels of IL-6, hsSRP and MMP-2 on day 3, are most likely related with activity of inflammatory reaction and necrosis of the myocardium. The levels of CEC and ET-1 at day 14 was increased in both groups (5[5;8]C/3x10ã çleucocytes vs 5[1;10]C/3x10ã çleucocytes, 0,7[0,3;1,7]fmol/ml vs 0,3[0,2;0,6]fmol/ml, respectively, in 1st and 2nd groups) and remained increased after 3 months (6[2;10]C/3x10ã ç leucocytes vs 3[2;4] C/3x10ã ç leucocytes ($p=0.048$) and 1,8[0,7;3.7 V] vs 0,6[0,4;1,0] ($p=0,033$) in 1st and 2nd group, respectively). We have analyzed the prognostic value of biomarkers at 3, 14 days and 3 months after MI. The greatest prognostic value was determined for the high levels of IL-6 (AUC of 0.63 with 95% CI from 0.54 to 0.72), MMP-2 (AUC of 0.83 with 95% CI from 0.75 to 0.89), hsSRP (AUC of 0.65 with 95% CI from 0.54 to 0,73), ET-1 (AUC of 0.73 with 95% CI from 0.53 to 0.88) after 3 months of MI.
Conclusions: High activity of inflammation, necrosis of the myocardium in the early stages of MI and persisting endothelial dysfunction associated with a poor prognosis in long term period in patients after MI.

P300

Features of catestatin in patients with essential hypertension

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Funding Acknowledgements: Samara Region Governor Grant 2017

Currently, close attention is paid to the study of catestatin as a potential prospective marker, the routine definition of which would improve cardiovascular complications risk stratification in hypertensive patients. Being a derivate of chromogranin A, catestatin participates in the blood pressure regulation mechanism.
The study included 78 men, whose average age was 42 years. Patients were divided into 4 groups according to a cardiovascular risk: group 1 – medium risk (n=17), group 2 – high risk (n=40), group 3 – very high risk (n=2), control group selected 18 men without hypertension matched for age.
Echocardiography, the brachiocephalic arteries ultrasound duplex scanning, blood pressure daily monitoring and catestatin enzyme immunoassay of blood serum were performed in all groups. Statistical data processing was performed using specialized package «Statistica 6,0».
The concentration of catestatin in the first group of subjects was 10.88±4,09 ng/ml, 10.42±3,65 ng/ml in the second group, 8±2,83 ng/ml in the third group and 11,87±7,33 ng/ml in the control group. Were identified correlations between catestatin the thickness of the lefr ventricle posterior wall of the left ventricle in diastole (r=-0,308, p=0,013), interventricular septum in diastole (r=-0,307, p=0,014), indexed myocardial mass (r=-0,280, p=0.035), relative wall thickness of left ventricle (r=-0,326, p=0,013), KIM the common carotid artery on the right (r=-0,260, p=0.035) and left (r=-0,269, p=0,023), morning rise in blood pressure (r=0,370, p=0.003).
Thus, significant associations indicate the involvement of catestatin in the cardiovascular risk formation in hypertensive patients that should be considered in further studies.

P301

Inflammatory signaling is activated in association with differential expression of lncRNAs in heart failure with preserved systolic function

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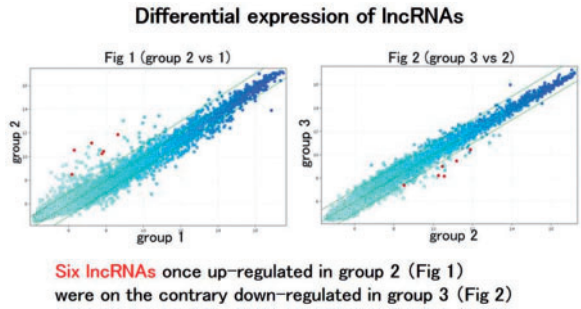
Introduction/ Background: Chronic inflammation of the myocardium is focused as the crucial mechanism of the cardiac remodeling. Long noncoding RNAs (lncRNAs) have been demonstrated to play a pivotal role in the pathogenesis of cardiac hypertrophy and failure, but the mechanism of their contribution is still unclear.
Purpose: We investigated the changes in the pro- and anti-inflammatory gene expression and tried to identify the associating lncRNAs in the process of cardiac remodeling.
Methods: Dahl salt-sensitive rats (n=21, 6 week-old) were divided to two groups. Group 1 (n=9) was fed with diet containing 0.3%NaCl and group 2 (n=12) with 8%NaCl. Echocardiography was performed every one week. Three rats of each group were sacrificed every one week after 12 week-old for histological examination and investigation of total RNA of the heart. Microarray profiling and real-time PCR analysis of mRNA and lncRNA was performed.
Results: The hearts of group 2 showed preserved left ventricular ejection fraction (EF) with significant increase in wall thickness and myocardial cell hypertrophy by 14 week-old. After then EF progressively decreased leading to sudden death. Group 2 were again divided to two groups according to EF at the time of sacrifice. Three rats showed preserved EF (70±8%, group 2) and another three showed significantly decreased EF (38±9%, group 3). Microarray profiling analysis following confirmation with real-time PCR of the myocardial mRNA revealed significant up-regulation of coding genes related to inflammation in addition to ANF, BNP and embryonic type of contractile proteins. They were interferon lambda3, interleukin 1 beta, interleukin 1 receptor kinase 3, TNF receptor superfamily 1b 11b 12a, Relt, and complement components 1qa, 1qb, 1qc 1s, 2, 3, 4a. In PPAR axis Ppara and Ppargc1a were down- and Pparg and Ppargc1b were up-regulated. Anti-inflammatory genes Sirt1, 4 and 5 were down-regulated. 13,611 lncRNAs were detected among which 344 significantly up- or down-regulated. Strict filtration narrowed down 344 to 74. 43 lncRNAs were significantly up-regulated and 31 down-regulated, and each had one to five near-by coding genes. The lncRNA overlapping with the exon of Sirt4 was down-regulated. Six of those 43 lncRNAs once significantly up-regulated (Figure 1: group 2 vs group 1) were on the contrary down-regulated in group 3 compared with group 2 (Figure 2). The most significantly enriched GOs targeted by up-regulated lncRNAs was associated with immune system process and down-regulated was with single-organism metabolic process.
Conclusion: Pro-inflammatory genes were up-regulated and sirtuins were down-regulated during hypertrophic remodeling. LncRNAs related to immune and inflammatory systems were up-regulated. Furthermore, the expression of several lncRNAs was suppressed as the systolic function deteriorated.



Abstract P301 Figure. Figures 1 and 2

P302

Cathepsin B induced cardiomyocyte hypertrophy requires activation of the Na+/H+ exchanger isoform-1

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Funding Acknowledgements: Qatar University Internal Grant
Background: Multiple studies have demonstrated that Na+/H+ exchanger isoform-1 (NHE1), cathepsin B (Cat B) and matrix metalloproteinase-9 (MMP-9) contribute to the progression of cardiac hypertrophy (CH). Cat B is activated under acidic conditions, a key stimuli of NHE1, suggesting that NHE1 and Cat B activities are related. Although the inhibition of NHE1 reduces hypertrophy, the mechanisms underlying this effect remain unknown.
Purpose: and Methods: To understand the mechanistic bases for Cat B in the anti-hypertrophic effect of NHE1 inhibition, H9c2 cardiomyoblasts were stimulated with Angiotensin (Ang) II in the presence and absence of N-[2-methyl-4,5-bis(methylsulphonyl)-benzoyl]-guanidine, hydrochloride (EMD, EMD 87580), an NHE1-specific inhibitor or CA-074Me, a Cat B inhibitor and characterized for changes in the cell surface area, protein content and atrial natriuretic peptide (ANP) mRNA, indices of hypertrophy.
Results: EMD significantly suppressed markers of hypertrophy and inhibited the Ang II stimulated Cat B protein and gene expression. Cat B is localized primarily within the acidic environment of lysosomes. The loss of integrity of the lysosomes releases Cat B proteases into the cytosol. EMD or CA-074Me prevented the dispersion of the lysosomes induced by Ang II and reduced the ratio of LC3-II to LC3-I, a marker of autophagy. Moreover, Cat B protein expression and MMP-9 activity in the extracellular space were significantly reduced upon the inhibition of NHE1.
Conclusion: Our study demonstrates a novel mechanism for attenuation of the hypertrophic phenotype by NHE1 inhibition that is mediated by a reduction in Cat B expression, the autosomal-lysosomal pathway and MMP-9 activation.

P303

Female gender-specific dysregulation of miR-29b and its target AKT-3 in experimental and clinical cardiac hypertrophy under pressure overload

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Funding Acknowledgements: Ministerio de Economía y Competitividad [Fondo de Investigaciones Sanitarias (PI15/01224), Fundació La Marató de TV3 (101/C/2015). IDIVAL-NextVAL1504
Introduction: Sustained pressure overload (PO) stress can elicit in the left ventricle (LV) from aortic stenosis (AS) patients a harmful remodelling, characterized by cardiomyocyte hypertrophy and interstitial fibrosis. Regression of LV hypertrophy after aortic valve replacement (AVR) surgery exhibits sex-related differences. Repression of miR-29 and the consequent aberrant activity of the AKT pathway are key elements in the maladaptive LV remodelling. Both miR-29 and AKT exhibit gender-related dysregulation under different pathological conditions.