Methods: The study included 150 patients from the Cardiology Unit in King Khalid University Hospital. The severity of CAD was determined by Gensini scoring. The enzyme-linked immunosorbent assay was applied to measure plasma levels of CTRP-3, and real-time polymerase chain reaction to detect gene expression. Immunohistochemical studies determined the expression of CTRP-3 in human peripheral atherosclerotic vessels.
Results: Circulating CTRP-3 levels were significantly lower in CAD patients, and levels declined as the severity of the disease increased. CTRP-3 gene expression was upregulated in CAD, and human atherosclerotic arteries highly expressed CTRP-3.
Conclusions: CTRP-3 could be a useful biomarker for CAD, and may help in assessing CAD severity. Moreover, CTRP-3 levels may have important therapeutic and preventive implications for reducing acute coronary events, and its expression in atherosclerotic plaque may contribute to plaque stability.

P1.7.113.
IGF-1 REGULATES CARDIAC HYPERTROPHY AND INOS EXPRESSION IN OBESE MALE RATS THROUGH ERK1/2 SIGNALING PATHWAY

A. Panic, J. Stanimirovic, M. Obradovic, E. Sudar-Milovanovic, E.R. Isenovic. *Vinca Institute of Nuclear Sciences, Department of Radiobiology and molecular genetics, Belgrade, Serbia*

Aim: High-fat (HF) diet-induced obesity is accompanied by inflammation and myocardial dysfunction. Inducible nitric oxide synthase (iNOS) represents an important inflammatory mediator, also involved in the development of heart hypertrophy. IGF-1 regulates cardiac metabolism and hypertrophy through different signaling pathways, including ERK1/2 kinase pathway. We explored whether ERK1/2 is involved in IGF-1-mediated regulation of cardiac hypertrophy and iNOS protein expression in obese rats.

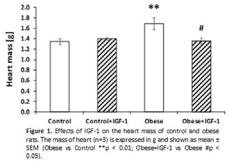

Figure 1. Effects of IGF-1 on the heart mass of control and obese rats. The mass of heart (n=3) is expressed in g and shown as mean ± SEM (Obese vs Control **p < 0.01; Obese+IGF-1 vs Obese #p < 0.05).

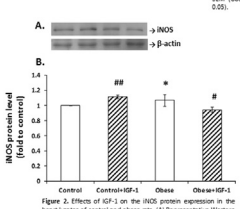

Figure 2. Effects of IGF-1 on the iNOS protein expression in the heart lysates of control and obese rats. (A) Representative Western blot of iNOS protein expression. (B) Western blot analysis showing relative iNOS protein level (n=3). Results are expressed as a percentage of the value obtained for control and represent mean ± SEM (Obese vs Control *p < 0.05; Control+IGF-1 vs Control ##p < 0.01; Obese+IGF-1 vs Obese#p < 0.05).

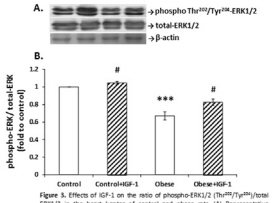

Figure 3. Effects of IGF-1 on the ratio of phospho-ERK1/2 (Thr^{202}/Tyr^{204})/total ERK1/2 in the heart lysates of control and obese rats. (A) Representative Western blot of ERK1/2 phosphorylation and total ERK1/2 protein expression. (B) Western blot analysis showing the ratio of phospho-ERK1/2/total-ERK1/2 (n=3). Results are expressed as a percentage of the value obtained for control and represent mean ± SEM (Obese vs Control ***p < 0.001; Control+IGF-1 vs Control #p < 0.05; Obese+IGF-1 vs Obese#p < 0.05).

Methods: The half of male Wistar rats fed a standard laboratory diet or a HF diet (42% of fat) for 12 weeks were treated with IGF-1 (50 μg/kg, I.P) as bolus injection, 24h before sacrifice. Hearts were excised and weighed. Protein level of iNOS and ERK1/2 phosphorylation level were determined by Western blot method.
Results: After 12 weeks, HF diet induced obese phenotype ($p<0.05$) and increased heart mass ($p<0.01$) in rats, while IGF-1 treatment of obese rats decreased heart mass ($p<0.05$) compared with untreated control. In obese rats, protein level of iNOS increased ($p<0.05$) compared with control rats. IGF-1 treatment of non-obese rats led to the increase of iNOS protein level ($p<0.01$), while in obese rats IGF-1 decreased iNOS ($p<0.05$) protein level, compared with respective controls. The phosphorylation of ERK1/2 was decreased ($p<0.001$) in obese rats compared with control. Treatment with IGF-1 increased ERK1/2 phosphorylation in both non-obese rats ($p<0.05$) and in obese rats ($p<0.05$) compared with untreated rats.
Conclusions: Our results show that IGF-1 exerts beneficial effects on heart by regulation of cardiac hypertrophy and iNOS expression, probably through the mechanism involving ERK1/2.

P1.7.114.
IGF-1 AMELIORATES DETRIMENTAL EFFECTS OF OBESITY IN RAT HEART BY PROMOTING AKT AND FOXO1

J. Stanimirovic, A. Panic, M. Obradovic, S. Zafirovic, E.R. Isenovic. *Vinca Institute of Nuclear Sciences, Department of Radiobiology and Molecular Genetics, Belgrade, Serbia*

Aim: Obesity contributes to the increasing prevalence of cardiovascular diseases (CVD). Decreased level of insulin like growth factor-1 (IGF-1) could be one of the possible mechanisms explaining the development of vascular dysfunction and ischemic heart disease in obesity. Akt/FoxO1 appears to be a common signaling pathway which mediates metabolic and vasorelaxation effects of IGF-1 in heart. Akt regulates FoxO1 which has a central role in promoting cardiac dysfunction by inducing cell death, inhibiting myocardial proliferation, and decreasing myocardial glucose utilization. We propose that IGF-1 may contribute to amelioration of detrimental effects of obesity in heart through regulation of Akt/FoxO1 signaling pathway.

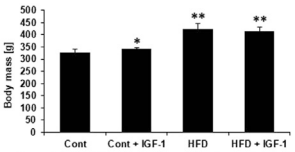

Figure 1. Effect of IGF-1 on body mass in obese and control rats. The body mass is expressed in g and represents the mean ± SEM (n=3); *p<0.05; **p<0.01; #fold to control; Cont – control rats; HFD – high fat diet rats.

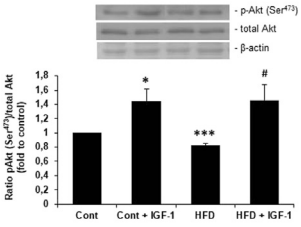

Figure 2. Effect of IGF-1 on Akt phosphorylation in obese and control rats. The data shown represent the mean ± SEM (n=3); */#p<0.05; ***p<0.001; #fold to control; #fold to HFD; Cont – control rats; HFD – high fat diet rats.

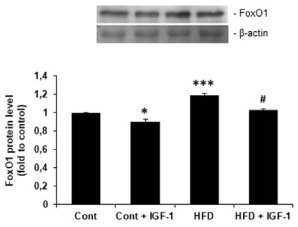

Figure 3. Effect of IGF-1 on FoxO1 protein level in obese and control rats. The data shown represent the mean ± SEM (n=3); */#p<0.05; ***p<0.001; #fold to control; #fold to HFD; Cont – control rats; HFD – high fat diet rats.

Methods: Male Wistar rats were normally fed (controls, n=6) or fed with high-fat diet (HFD) for 12 weeks (HFD, n=6). Half of the normally fed (controls + IGF-1, n=3) and obese rats (HFD + IGF-1, n=3) were treated with a single dose of IGF-1 (50 μg/kg, intraperitoneally) and 24 hours after the treatment all rats were sacrificed. Cardiac Akt and Foxo1 were detected by Western blot.
Results: Results show that HFD increased body mass ($p<0.01$) and decreased phosphorylation of Akt ($p<0.001$) in HFD rats compared to control rats. Treatment with IGF-1 increased Akt phosphorylation in normally fed ($p<0.05$) and obese ($p<0.05$) rats. FoxO1 ($p<0.001$) expression was markedly elevated in obese rats compared to control. In contrast, IGF-1 treatment decreased FoxO1 expression in normally fed ($p<0.05$) and obese ($p<0.01$) rats.
Conclusions: Our findings suggest that Akt/FoxO1 appears to be a common signaling pathway which mediates positive effects of IGF-1 in obesity.

P1.7.115.
THE ROLE OF LIPID, SEX HORMONE AND INFLAMMATION PATHWAY GENES POLYMORPHIMS ON CORONARY ARTERY DISEASE IN TURKS

A.S. Ozuynuk [1], N. Coban [1], A.F. Erkan [2], B. Ekicl [2], E. Vurgun [1], N. Erginel-Unaltuna [1], I.Y. Diker [1]. [1] *Department of Genetics, Institute for Experimental Medicine, Istanbul University, Istanbul, Turkey;* [2] *Department of Cardiology, Medical Faculty, Ufuk University, Ankara, Turkey*

Aim: Coronary artery disease (CAD) is under influence of both environmental and genetic factors, therefore it is important to identify polymorphisms on the candidate genes which are related in the development of this disease. In this study, some of the polymorphisms on APOA5,

APOC1, APOD, APOE, CH25H, CLU, LDLR, SORL1 and ESR1 genes are selected.
Methods: Unselected 493 Turkish CAD patients and controls were genotyped for selected nine genes polymorphisms using hydrolysis and hybridization probes in Real-Time PCR LC480 device. Blood samples were drawn before coronary angiography. Gensini and SYNTAX scores and myocardial blush grade (MBG) were assessed.
Results: A significant association was found between CLU T allele carriers and non-CAD group (p=0.05). Furthermore, risk for CAD was lower (OR=0.67, [95% CI 0.246–0.99] p= 0.04) in these carriers, after adjustment for sex and other confounders. In addition, APOE ε2 allele carriers were found to be associated with non-CAD group in women using the Chi-squared test (p=0.07). Logistic regression analysis showed the ε2 allele carriage was protective for CAD (OR=0.24, [95% CI 0.067-0.85] p=0.027), additively to age and other confounders in women. In contrast, logistic regression analysis showed the ESR1 rare allele carriage tend to predict CAD (OR = 2.12, [95% CI 1.01–4.1] p=0.025), additively to age, HLD-C, LDL-C, age and smoking status in men.
Conclusions: In especially sex-specific, compared to non-carriers, carriers of the CLU T allele and APOE ε2 allele carriers show a degree of protection against developing the CAD. ESR1 polymorphisms associated with CAD risk in men.

P1.7.116.
TELOMERE LENGTH AND THE AGE-RELATED FACTORS GDF-11 AND SIRT-1 IN CAD

T.B. Opstad [1], A.A. Kalstad [1,2,3], A.A. Pettersen [1,3], H. Arnesen [1,2,3], I. Seljeflot [1,2,3]. [1] *Center for Clinical Heart Research, Dept. of Cardiology, Oslo University Hospital Ullevål, Oslo, Norway;* [2] *Faculty of Medicine, University of Oslo, Oslo, Norway;* [3] *Center for Heart Failure Research, Oslo University Hospital Ullevål, Oslo, Norway*

Aim: Telomere length (TL), growth and differentiation factor (GDF)-11 and sirtuin (SIRT)-1 are markers of ageing and cell senescence and have been related to age-related diseases, possibly influenced by lifestyle. We aimed to investigate the associations between leukocyte TLs (LTLs), chronological age and comorbidities in patients with CAD. Any covariations between LTL, GDF-11 and SIRT-1 were further assessed.
Methods: In 300 patients with stable CAD (age 36-81 years, 20% females), DNA and RNA were isolated from whole blood for PCR analysis and relative quantification of LTLs and GDF-11 and SIRT-1 gene-expression, respectively.
Results: Patients who previously had suffered MI presented with 20% shorter LTLs vs. those without (p=0.015), however, only in men (p=0.009, n=115) in which the upper quartile associated with 60% lower frequency of MI (p=0.008, adjusted) versus the 3 lowest quartiles. LTLs were not differently distributed according to sex or comorbidities, such as hypertension, T2DM and Mets.
LTLs and GDF-11, not SIRT-1, were inversely correlated to age (r=-0.17 and r=-0.16, respectively, p<=0.01 both), only LTL in women (r=-0.37) and GDF-11 in men (r=-0.19) (p =0.006, both). Gene-expression of GDF-11 and SIRT-1 were strongly inter-correlated (r=0.56, p<0.001). LTLs were moderately correlated to GDF-11 and SIRT-1, however, only in overweight women (BMI >=25) (r=0.41 and 0.43, respectively, p<0.03, both).
Conclusions: In men, LTLs associated with the severity of CAD shown by previous MI. In women, LTLs were more related to age. The results may indicate gender-related differences in regulatory mechanisms of TLs and possibly obesity-influenced associations between LTLs and GDF-11and SIRT-1.

P1.7.117.
PHYSIOLOGICAL STUDIES OF CARDIAC CONTRACTILITY OF RABBIT HEART WITH EXPERIMENTAL HYPERTHYROIDISM

C.R. Revnic [1], F. Revnic [2], B. Paltineanu [3], S. Voinea [1]. [1] *UMF Carol Davila, Bucharest, Romania;* [2] *NIGG Ana Aslan, Bucharest, Romania;* [3] *UMF Tg Mures, Targu Mures, Romania*

Aim: The aim of this study was to evaluate physiological parameters of cardiac contractility in rabbit heart with experimental hyperthyroidism induced with Tyroxine (T4).
Methods: We used 6 adult rabbits treated with T4(i.p. injections 4.5mg/kg body weight) for 4 weeks. After treatment the hearts were excised and mounted in a Langendorf retrograde perfusion system and perfused for 25 minutes with Krebs-Henseleit buffer(stabilization period), and then applying 45 minutes ischemia followed by 120 minutes reperfusion at 37C,pH 7.6 supplimented with 10mM glucose. Physiological parameters :Left ventricular developed pressure(LVDP),heart rate(H.R.) and coronary flow(C.F.) have been measured. We measured also, biochemical parameters of cardiac metabolism in hyperthyroid rabbit heart : CK,LDH,GSH,GGT,SOD,plasma cholesterol, and total lipids.
Results: There was a decrease in coronary flow in hyperthyroid rabbit heart versus controls.In both cases there was a decrease of this parameter during reperfusion with lower values in controls and a tendency of reaching a plateau value. Hyperthyroidism is reflected by changes in plasma LDH enzyme values i.e. 3 times higher than in controls accounting for an increase in plasma and myocardial CK,values .There was a decrease in SOD activity in the myocardium which may account as an energy support for accelerated metabolism and installing oxidative stress at this level.There was a decrease in GGT and an increase in total lipids.
Conclusions: Because of low levels of total plasma cholesterol and of absence of a significant modification of lipid peroxides,hyperthyroid rabbit heart seems not to be a target for the atherogenic factors present in other forms of arterial hypertension.

1.8 Imaging atherosclerosis

P1.8.118.
NON-CORONARY ATHEROSCLEROSIS: IS IT FEASIBLE TO USE IT FOR NON-INVASIVE PREDICTION OF CORONARY RISK?

N. Gavrilova [1], V. Metelskaya [2], M. Zhatkina [3]. [1] *National Research Center for Preventive Medicine-Department of Clinical cardiology, Moscow, Russia;* [2] *National Research Center for Preventive Medicine-Department of Biochemistry, Moscow, Russia;* [3] *National Research Center for Preventive Medicine-Department of Biostatistics, Moscow, Russia*

Aim: Bakground: Atherosclerosis is a systemic disease, and detection of its clinical manifestation at multiple, rather than single, vascular sites may provide greater insight on the overall burden and risk associated with subclinical atherosclerosis. Subclinical atherosclerosis develops slowly over several decades, but there are no diagnostic protocols for its non-invasive detection.
Aim: To assess feasibility of estimation of coronary atherosclerosis risk by detection of non-coronary lesions.
Methods: Patients admitted to the National Research Centre for Preventive Medicine for coronary angiography and ultrasound dopplerography of carotid and femoral arteries were enrolled into the study (n=50; M/F 20/30; 60.0,8±0.5 yrs).
Results: Total cohort was split into groups with unaffected coronary arteries (stenosis 0-20%), and with subclinical coronary atherosclerosis (stenosis 21-50%). Visual Score, including intima-media thickness (IMT) (<0,9;>0,9mm), atherosclerotic plaques number (ASP) (<3;>3) and degree of stenosis (<45%;>45%), with values >/=2 points with a sensitivity of 66.0% detected patients with subclinical coronary atherosclerosis. The analysis carried out in groups differed by carotid or femoral Visual Score revealed the higher number of points in patients with subclinical coronary atherosclerosis as compared to those with unaffected arteries (1 vs 2 points in carotid, p<0.001; 1 vs 3 points in femoral, p<0.001, respectively). Moreover, patients with subclinical coronary atherosclerosis had higher number of points estimated by femoral Visual Score than that estimated by carotid Visual Score (3 vs 2 points, p<0.05).
Conclusions: Carotid and femoral Visual Scores can be useful tool to improve the prediction of coronary risk by non-invasive identifying subjects with subclinical coronary atherosclerosis.