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May 2018 Vol 48 Supplement

European Journal of Clinical Investigation

52nd Annual Scientific Meeting of the
European Society for Clinical Investigation

Barcelona, Spain
30th May – 1st June 2018

ABSTRACT BOOK

ESCI
Official journal of the European Society for Clinical Investigation

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examined. Bootstrap and jackknife cross-validation approaches were performed.

Results: CMI (hs-TnT ≥ median), MIF (PICP≥ or CITP: MMP-1 ≤ median) and EDI (VCAM-1 ≥ median) presence was determined in the Generation Scotland patients. Twenty-nine (40·8%), 24 (33·8%) and 18 (25·4%) patients had zero or one, two or three biomarker alterations, respectively, the latter showing higher risk of outcome ($P < 0·05$). A similar median-based categorization confirmed higher risk of outcome ($P < 0·05$) in the Leizaran patients with the three alterations ($n = 50$ [25·4%]). This combination added incremental predictive value as demonstrated by Harrell's *C*-statistic, integrated discrimination and net reclassification improvements ($P \leq 0·04$).

Conclusions: A panel combining biomarkers of CMI, MIF and EDI identifies HF patients at higher risk of HHF or CVD over and beyond established risk factors. These findings reinforce the necessity for a holistic view of myocardial remodelling and hold promise for personalizing risk prediction and treatment of HF patients.

P094-T | Contraction (retraction) of blood clots as a pathogenic factor in thrombosis

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Background: Contraction or retraction of a blood clot may approximate the wound edges and restore blood flow past obstructive intravascular thrombi. Despite its potential clinical significance, the pathogenic importance of contraction of clots and thrombi remains unknown.

Materials and methods: We studied kinetics of contraction of clots formed from the blood of patients with ischemic stroke (IS) and venous thromboembolism (VTE), including patients with pulmonary embolism (PE). Patients were excluded from this study if they were given antiplatelet drugs at least 2 weeks prior to examination. Functionality of isolated platelets was assessed using flow cytometry and scanning electron microscopy.

Results: The velocity and degree of clot contraction in the blood from patients with IS and VTE was reduced compared to that of healthy subjects. In venous thrombosis associated with PE contraction was significantly impaired compared to the isolated thrombosis, suggesting that decreased clot compaction could increase the risk of embolization. The reduced ability of clots to contract correlated with pronounced platelet dysfunction. Platelets from IS and VTE patients were spontaneously activated as revealed by the more frequent shape change and formation of filopodia in electron micrographs compared to the less common morphologically altered platelets from healthy subjects. In response to chemical stimulation, platelets from the blood of IS and VTE patients had a significantly lower expression of P-selectin and fibrinogen-binding capacity compared to activated normal platelets, suggesting that reduced platelet contractility is a result of exhaustion.

Conclusion: The results suggest that contraction of clots and thrombi is an underappreciated pathogenic mechanism that may affect the course and outcomes of IS and VTE. The clinical importance of reduced clot contraction in IS and VTE as well as the diagnostic and prognostic value of the clot contraction assay is worth further exploration. Work supported by the Program of Competitive Growth of KFU.

P095-T | Vegetative regulation of heart activity in conditions of electrical stimulation of the spinal cord

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The method of transcutaneous electrical stimulation of the spinal cord (tSCS) is widely used for the rehabilitation of locomotor functions in patients with spinal cord injury. In order to predict undesirable changes in cardiac activity, which can presumably be induced by electric current, it is necessary to take into account the changes in the regulatory mechanisms of the circulatory system. The aim of this work was to study the variability of the heart rate in conditions of transcutaneous electrical stimulation of the spinal cord. The tSCS was performed at the level of T11–12 vertebrae in healthy persons using monophasic rectangular electrical stimuli with duration of 1 ms and frequency of 30 Hz for 1 minute. After the tSCS we observed a decrease in the mean heart rate (M), an increase in the standard deviation (σ). Prior to the tSCS the normotonia of the tested persons was assessed by the mode index (Mo) and the variation in the range (MxDMn). After tSCS the vegetative activity was assessed as a vagotonic. The tSCS did not cause an increase in sympathetic influences: we did not observe an increase in the amplitude of the mode (Amo) and the decreased of the stress index after the tSCS. Thus, the tSCS at the lower thoracic level of stimulation increased the degree of variability of the cardiointervals, which indicates an increase in the tonicity of the parasympathetic system. The results suggested that the application of this method leads to an increase in the processes of self-

regulation and activation of the autonomic circuit regulation of the rhythm of the heart.

This work was funded by the subsidy allocated to Kazan Federal University for the state assignment in the sphere of scientific activities no. 17.9783.2017/8.9.

P096-T | Determinants of thrombosis: activation of canonical Wnt pathway

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Background: Platelets are responsible of atherothrombosis. They can interact with different proteins and coagulation factors in very complex ways to generate thrombus. The activation of platelets intracellular signaling pathways defines the fate of the event, and the study of the different signaling pathways may help to separate thrombosis from bleeding. We aimed to define the role of LRP5 and the canonical Wnt pathway in platelet function.

Materials and methods: Platelet deposition, thrombus formation, platelet adhesion and platelet secretion were studied in blood from Wt and Lrp5 depleted mice. Downstream signaling of the collagen receptors GPVI, $\alpha 2\beta 1$ and FcRγ and of the ADP receptors P2Y12, P2Y1 and P2X1 were analyzed in platelets of Wt and Lrp5$^{-/-}$ mice.

Results: Platelet deposition on collagen coated surfaces in Wt and Lrp5$^{-/-}$ mice was significantly different. Platelets from Lrp5$^{-/-}$ animals had a highly reduced deposition with respect to Wt mice. Platelet GPVI protein expression was lower in Lrp5$^{-/-}$ mice than in Wt platelets. However, GPVI downstream signaling after collagen stimulation showed no differences in platelets from Wt and Lrp5$^{-/-}$ mice. ADP platelet stimulation induced a reduction in platelet release of α- and dense granules in Lrp5$^{-/-}$ mice with respect to Wt mice platelets. Platelet P2Y12 receptor levels were significantly lower in Lrp5$^{-/-}$ mice as well as VASP phosphorylation confirming that the downstream signaling pathway of P2Y12 is downregulated in Lrp5$^{-/-}$ mice.

Conclusion: Our data demonstrate that LRP5 regulates thrombosis because genetic deletion of LRP5 reduces the thrombotic potential of platelets. Activation of the canonical Wnt pathway acts as a positive regulator of platelet function in vitro and in vivo.

P097-T | The human heart post-translational proteome: modified proteins as markers of aging and type 2 diabetes in the context of cardiovascular disease

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Background: Cardiovascular disease (CVD) is the leading cause of death in the world. Its increase has been exacerbated by the combined effect of aging, lifestyle changes and the epidemic rising of obesity and type 2 diabetes (T2DM) during the last years. A growing body of evidence indicates that modified proteins are the main effectors in metabolic and CVD as well as important sensors of damage and cellular stress suggesting that post-translational modifications (PTMs) could potentially be used as biomarkers.

Material and methods: Here, we have evaluated the complete landscape of PTMs in protein extracts of the heart right atrial appendage from a set of individuals matched by age, CVD and T2DM clinical history ($n = 31$). We have resorted to mass spectrometry (MS) approaches using an innovative algorithm (Comet-PTM) for its analysis. This ad-hoc algorithm bypasses the main limitations of current open search approaches allowing a comprehensive analysis of all PTMs detectable by MS and the simultaneous quantification of them and their belonging proteins.

Results: Our preliminary analysis has identified near 100 000 modified peptides in the human heart proteome. Our results highlight the significant abundance of PTMs such as oxidations, methylations, phosphorylations, deamidations, carbonylations or advanced glycation end-products (AGEs), highlighting an important role of these modifications in aging, T2DM and CVD. Particularly, we have uncovered more than 1000 significantly modified peptides with aging ($P < 0{\cdot}05$). Interestingly, some of these PTMs belong to proteins previously implicated in cardiovascular and metabolic homeostasis like the natriuretic peptide (NPPA) as well as glycolytic, mitochondrial or collagen proteins.

Conclusions: We have characterized the comprehensive landscape of modifications in the human heart proteome. Our findings advance in the understanding of the mechanisms underlying physiological aging and its interplay with CVD and T2DM, and pave the way towards the use of PTMs as novel biomarkers in the clinical setting.