Methods and Materials: 60 hypertensive patients, aged 20-45, with fasting HI or/and HI after glucose stress test, without diabetes mellitus, glucose intolerance or high fasting glycemia and regular antihypertensive therapy were examined. Fasting glucose and immunoreactive insulin (IRI) during glucose stress test were determined. All patients were randomized in 2 groups, comparable by age, sex, glucose and insulin levels. 1st group (n = 30) received candesartan (7,46 ± 1,38 mg daily), 2nd group - bisoprolol (6,0 ± 1,93 mg daily). HOMA indexes and area under insulin curve before treatment and in 12 weeks were calculated.

Results: All patients achieved target blood pressure levels. In candesartan group HOMA index as well as fasting IRI level did not change ($p > 0,05$). Significant decrease of IRI in 30, 60, 90, 120 minutes and area under insulin curve after glucose stress test was identified. In bisoprolol group increase of HOMA index (p=0,001), fasting IRI (p=0,000), IRI levels in 30, 60, 90, 120 minutes and area under the insulin curve (p=0,033) were detected. IRI concentration in candesartan group was 33% less (p=0,044) in 90 minutes and 54,4% less (p=0,000) in 120 minutes after glucose stress than in bisoprolol group. With similar baseline data in hypertensive patients with HI in 12 weeks of treatment in 1st group insulin production to support carbohydrate homeostasis decreased in response to glucose stress, as opposite to the 2nd group where this index increased and fluctuation was 17,86% as compared to baseline data, what with normal glycemia indicates IR decrease in candesartan patients and IR strengthening with compensatory IRI levels increase to support normal glycemia in bisoprolol patients.

Conclusions:

1. Candesartan has positive effect on the carbohydrate metabolism, leads to insulin level decrease while maintaining glycemia after the glucose stress.
2. Bisoprolol doesn't decrease IR in this category of patients and in 12 weeks stimulates compensatory increase of IRI for saving normal glycemia after the glucose stress test.

P188

Identification of new matrix metalloproteinase targets in the vasculature

C. Stegemann; A. Didangelos; M. Mayr
King's College London, James Black Centre, London, United Kingdom

Matrix metalloproteinases (MMPs) play a key role in vascular remodeling and cardiovascular disease. MMPs degrade and reorganize the vascular extracellular matrix (ECM). In atherosclerosis MMP activity is associated with plaque rupture leading to heart attacks and stroke. Surprisingly little is known about the targets of MMPs in the vasculature. In the present study, we used a proteomics approach to identify vascular targets for three members of the major classes of MMPs: MMP-3 - a member of matrilysins, MMP-9 - a gelatinase and MMP-14 - a member of the membrane—bound MMPs. We incubated human radial arteries with MMP-3, -9 and -14 and analyzed the released proteins by gel-LC-MS/MS. New substrates were confirmed by digestion of recombinant proteins with the same MMPs. Further analysis focused on the identification of new MMP cleavage sites of ECM proteins by searching for non-tryptic peptides. Finally, the newly identified degradation products were validated in human aortic tissue with high MMP-9 activity to relate protein degradation in vitro with exogenous MMPs to endogenous proteolytic activity in vivo. Using this innovative approach, we identified 17 novel targets, including ECM proteins associated with the basement membrane (collagens, nidogen-1, agrin), elastic fibers (emilin-1, transglutaminase-2, TGF β-induced protein ig-h 3) and other extracellular proteins (galectin-1, tenascin-X, tenascin-C). In total, we detected 74 cleavage sites for MMP targets, many of which were shared among different MMPs. Thus, our current classification of MMPs based on few selected targets (collagenases, elastase, etc) is an oversimplification of a complex area of biology, and our study is a first attempt to contribute to a better understanding about the role of MMPs in the vasculature.

P189

Development of biological small diameter vascular grafts

D. Byzov; I. Mikhaylova; N. Chizh; E. Pushkova; O. Synchykova; B. Sandomirsky
Institute for Problems of Cryobiology and Cryomedicine, Kharkiv, Ukraine

There is progressive need in small diameter (≤ 6mm) vascular prostheses caused by increased number of peripheral arteries' pathology worldwide and coronary arteries diseases as well. Commonly used autological vessels are considerably limited and have some serious short-comings including traumaticity of their deriving, increased infections and inflammatory complications. One of the most perspective alternatives of autovessels is using biological prostheses based on xenogeneic arteries. However the technologies of their treatment to reduce immunogenicity and prevent early occlusion have been uneffective till now.

The research aim. The goal of our study was to devitalize the xenogeneic arteries by using two physical factors: low temperatures and electron beam irradiation to create non-immunogenic biological vascular prostheses.

Methods: The research objects were porcine intrathoracic arteries, derived from mature animals with meeting all the bioethical rules. Isolated vessels were deeply frozen and after thawing on water bath they were subjected to ionizing irradiation in the experimental doses. Morphological structure of devitalized arteries was estimated by optical and electron microscopies. Biomechanical properties of treated arteries were also estimated. Immunogenicity and biocompatibility of devitalized arteries were studied in vivo at subcutaneous xenoimplantation. Experimental vascular surgeries of xenoprosthetic repair have been also done with using devitalized arteries as vascular grafts.

Results: Freezing led to initial damages of cells which were mainly noted in endothelial layer as desquamation areas. The following ionizing irradiation resulted in a complete deendothelization and significant destruction of smooth muscle cells. However the connective tissue structure of devitalized arteries was mainly preserved and internal elastic membrane has no considerable structural disorders. Combined influence of freezing and ionizing irradiation increased strength parameters of arteries. Xenoimplantation demonstrated the absence of any rejections on the devitalized arteries for all the observation terms. Performed experimental vascular surgeries have shown adequate functioning and high-grade patency of the treated arteries for 10 months at least, there were no signs of occlusion and inflammation reactions.

Conclusion: The proposed treatment allows to design integrally functioning biological vascular grafts basing on xenogeneic arteries. Positive results of experimental transplantation testify that devitalized arteries are promising to be studied in clinic as biological vascular grafts.

P190

Telomere length in metabolic disorders in group of survivors of Leningrad Siege

O. Freylikhman; O. Rotar; N. Chromova; E. Moguchaya; V. Ivanenko; E. Kolesova; A. Erina; M. Boyarinova; A. Kostareva; A. Konradi
V. A. Almazov Federal Heart, Blood and Endocrinology Center, Saint-Patersburg, Russian Federation

Purpose: The impairment of perinatal nutrition could promote the development of metabolic disorders and cardiovascular complications in the adult life. Contradictive results have also been reported on intrauterine starvation influence on telomere length what is one of the discussed markers of metabolic disorders and it has been found to be shortened in subjects with obesity, insulin resistance, arterial hypertension. The aim of our study was to assess the metabolic state and telomere length in subjects who survived of Leningrad Siege during second World War (1941-1944) comparing to control group of the same age.

Methods: 189 survivors of Leningrad Siege (54 males, 135 females) were examined on EVA syndrome. In 36 of Siege survivors (13 males, 23 females) and 12 controls (6 males, 6 females) the telomere length was also examined. The patients were divided in two groups: born before the Leningrad Siege (157 subjects) and during the Leningrad Siege (32 subjects). Informed consent was obtained from all participants. All participants were interviewed by special questionnaire regarding lifestyle and risk factors. Blood pressure was measured on right arm in the sitting position after 5 minute of rest two times. Anthropometry were performed according to standard procedures. Fasting serum lipids and plasma glucose were measured on Hitachi-902. Relative telomere lengths were measured by qRT-PCR, the ratio of telomere repeat copy number to single gene copy number (T/S) was calculated for each DNA sample.

Results: The telomere lengths in the survivors of Leningrad Siege group was significantly shorter compared to the controls: relative T/S values was 0,78 (± 0,05) vs. 0,69 (± 0,04) for controls group; $p < 0,005$.

Conclusions: Survivors who were born during the Leningrad Siege had higher prevalence of metabolic disorders. Starvation in late gestation and early perinatal period predict short telomere length and promote the development of metabolic syndrome.

Rate prevalens of metabolic parameters

Parameters	Rate prevalence		
	Subjects were born before siege	Subjects were born after siege	p
Hypertriglyceridemia > 1,7 mmol/l	17 %	25 %	p < 0,05
Obesity	60 %	75 %	p < 0,05
Glucose > 5,6 mmol/l	34 %	37 %	p < 0,05
Patients withhypertension	79 %	87,5 %	p < 0,05

P191

Mitral valve prolapse and sudden cardiac death. Is there a cardiomyopathy linked to floppy mitral valve?

S.D. Preston[1]; D. Baskaran[2]; A.M. Plonczak[2]; K. Norita[2]; S.V. De Noronha[2]; M.N. Sheppard[1]
[1]*Royal Brompton and Harefield NHS Trust Hospital, Imperial College London, London, United Kingdom;*
[2]*CRY Centre for Cardiac Pathology, Imperial College London, London, United Kingdom*

Background: Mitral valve prolapse (MVP) is a relatively common disorder of the mitral valve and most cases take a benign clinical course. This condition is common in the elderly but also recognised in the young, rarely leading to a sudden cardiac death (SCD). The aim of our study was to assess the frequency, demographics and histologic myocardial abnormalities in patients with MVP and SCD.

Design: A retrospective study of MVP and SCD referred to our tertiary referral centre during the period of 1994-2010.

Results: A total of 39 cases of sCD with MVP were identified with a similar distribution by gender; 1:1.3 (M:F), median age 37, range 19-79 years. MVP was associated with left ventricular myocardial fibrosis in over half of the cases (n = 22, 56%) predominately in females (63%, n=14). Left ventricle hypertrophy (LVH) (n = 11, 28%) alone (n = 2) or with fibrosis (n = 9) was also common with MVP. The myocardium was normal in 6 cases.

Conclusions: Abnormalities of the myocardium, of which fibrosis was the most common, were present in 85% of cases raising the question of a possible link of MVP to cardiomyopathy. It is also possible that the floppy valve change is secondary to the cardiomyopathy.

P192

Cancer induced cardiac cachexia displays a shift of metabolic genes

A. Haghikia; B. Stapel; M. Hoch; D. Hilfiker-Kleiner
Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany

Purpose: Patients suffering from heart failure or advanced cancer share several clinical features including limitation in exercise capacity, shortness of breath, early fatigue, and the development of cachexia. One of the major factors in both populations that reduces quality of life and is associated with an unfavorable prognosis is cachexia. The underlying mechanisms of cancer-mediated cardiac cachexia are poorly understood. To investigate putative metabolic alterations, we evaluated the expression of genes involved in fatty acid oxidation in a mouse cancer model associated with cardiac cachexia.