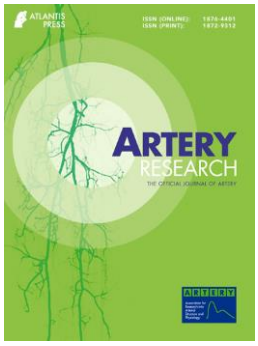

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P4.31: ARTERIAL STIFFNESS AND HAEMOSTASIS CHANGES IN OBESE ZUCKER RATS

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pulse wave velocity (cf-PWV) by applanation tonometry were measured in all participants by a single trained operator, who was blind to clinical features of participants.
Results: Compared with those with alcohol-related liver disease, patients with HCV had markedly lower FMD (4.57±1.50 vs. 9.84±3.60%, $p<0.0001$) (Table 1). They also had significantly lower total cholesterol level (4.60±1.34 vs. 5.87±1.40 mmol/L, $p<0.05$), lower serum liver enzymes (AST/ALT ratio: 0.87±0.3 vs. 1.26±0.6U/L, $p<0.05$; GGT: 54±42 vs. 137±117 U/L, $p<0.01$) and higher urea nitrogen (4.98±1.5 vs. 3.69±1.0 mmol/L, $p<0.05$). No significant differences were found in CIMT, cf-PWV, age, sex, body mass index, waist circumference, smoking status, blood pressure, serum triglycerides, creatinine, glucose and insulin resistance (as estimated by HOMA-IR score) between the two groups. Notably, as shown in Figure 1, the marked differences in FMD observed between the groups were only slightly weakened after adjustment for potential confounding variables.
Conclusions: Our results suggest that chronic HCV infection is strongly associated with endothelial dysfunction.

P4.31
ARTERIAL STIFFNESS AND HAEMOSTASIS CHANGES IN OBESE ZUCKER RATS

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Objectives: The metabolic syndrome (MetS), a cluster of risk factor including abdominal fat, hypertension, dyslipidemia and raised fasting plasma glucose, is associated with modifications in the arterial wall, endothelial dysfunction and atherothrombosis. To explore the course of events we characterized the coagulation, fibrinolysis and vascular phenotypes in 25 and 80-week-old Zucker rats, that mimics human MetS.
Methods: Arterial phenotype was assessed using ultrasonic echo-tracking. Thrombin generation was monitored using calibrated automated thrombography. Fibrinolysis was measured by a clot lysis assay.
Results: Endothelial dysfunction was evidenced by a high plasma concentration of von Willebrand factor at both ages. The arterial wall stress/modulus curves were superimposed at 25 weeks and shifted towards the left with age, the shift being more pronounced in obese rats. Media thickness was not modified with MetS but was increased with aging in obese and lean rats. *In vitro* thrombin generation was higher in 25-week-old obese rats than in age-matched control lean rats (428±29 versus 328±27 nM.min) and still higher at 80 weeks (422±30 versus 306±11 nM.min). Regarding fibrinolysis, half-time lysis clot was increased in obese rats compared to control lean rats (46.5±1.2 versus 41.5±0.7 min at 25 weeks) and increased with age (54.1±1.1 versus 49.3±1.8 min at 80 weeks).
Conclusions: We have shown that thrombin generation increased and fibrinolysis decreased *in vitro* with obesity as early as 25 weeks of age. Theses alterations of hemostasis may participate to the accelerated arterial aging as assessed by increased arterial stiffness triggered by obesity and metabolic disorders in SMet.

P4.32
INACTIVATION OF SERUM RESPONSE FACTOR CONTRIBUTES TO DECREASE VASCULAR MUSCULAR TONE AND ARTERIAL STIFFNESS IN MICE

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Rationale: Vascular smooth muscle cell (VSMC) phenotypic modulation plays an important role in arterial stiffening associated with ageing. Serum response factor (SRF) is a major transcription factor regulating smooth muscle (SM) genes involved in maintenance of the contractile state of VSMCs.
Objective: We investigated whether SRF and its target genes regulate intrinsic SM-tone and thereby arterial stiffness.
Methods and results: The SRF gene was inactivated (SRF^{SMKO}) specifically in VSMCs by injection of tamoxifen into adult transgenic mice. Fifteen days later, arterial pressure and carotid thickness were lower in SRF^{SMKO} than in control mice. The carotid distensibility/pressure and elastic modulus/wall stress curves showed a greater arterial elasticity in SRF^{SMKO} without modification in collagen/elastin ratio. In SRF^{SMKO}, vasodilation was decreased in aorta and carotid arteries whereas a decrease in contractile response was found in mesenteric arteries. By contrast, in mice with inducible SRF overexpression, the *in vitro* contractile response was significantly increased in all arteries. Without endothelium, the contraction was reduced in SRF^{SMKO} compared with control aortic rings due to impairment of the NO pathway. Contractile components (SM-actin and myosin light chain), regulators of the contractile response (myosin light chain kinase, myosin phosphatase target subunit 1 and protein kinase C-potentiated myosin phosphatase inhibitor) and integrins were reduced in SRF^{SMKO}.
Conclusion: SRF controls vasoconstriction in mesenteric arteries via VSMC phenotypic modulation linked to changes in contractile protein gene expression. SRF-related decreases in vasomotor tone and cell-matrix attachment increase arterial elasticity in large arteries.

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P5.01
ASSESSMENT OF THE EFFICACY OF TREATMENT OPTIONS IN CRITICAL LIMB ISCHAEMIA ACCORDING TO PATIENT-ORIENTED OUTCOMES

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Objectives: Traditional outcomes after vascular intervention include vessel patency, limb salvage rates and mortality but correlate poorly with functional goals. Patent-oriented outcomes are patient-reported functional outcomes. The aim of this study is divided into 2 complementary parts: Part A: To define patient-oriented outcomes by performing a patient survey. Part B: Systematic review of treatment options in lower limb CLI according to patient-oriented outcomes, defined by part A.
Methods: Part A: CLI patients ranked 10 outcomes according to importance. Part B: A systematic review of randomised control trials assessing angioplasty, stenting and bypass surgery according to patient-oriented outcomes.
Results: Part A: A patient survery indicates that QOL, symptom relief, living status, amputation-free survival and mobility should be considered patient-oriented outcomes. Patients place little importance is placed on vessel patency and reintervention. Part B: 6 RCTs involving 1166 patients assessed QOL, symptom relief, and amputation-free survival following vascular intervention. There is no significant difference in QOL between bypass surgery and angioplasty. There is no difference in symptom relief between sirolimus-eluding stents and angioplasty. Bare-metal stents and angioplasty were not significantly different in providing symptom relief. There was poor correlation between traditional outcomes and patient-oriented outcomes.
Conclusion: There is no evidence supporting a single superior treatment between angioplasty, stenting and bypass surgery when assessed by patient-oriented outcomes.

P5.02
RELATIVE CONTRIBUTION OF PRE AND AFTER-LOAD IN REDUCTION OF TIME-VARYING MYOCARDIAL STRESS BY NITROGLYCERIN

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Background: Nitroglycerin (NTG) reduces cardiac pre-load and after-load through venodilation and arterial dilation respectively but the relative contributions of these effects to reduction in myocardial wall stress is unknown.
Methods: We estimated myocardial wall stress from transthoracic echocardiographic imaging of the left ventricle (LV) and LV pressure estimated from carotid tonometry during systole. Nineteen subjects aged 43.3 ± 2.7 (mean ± SE) years were studied before and 7-12 min after NTG (400 ig sublingually). Carotid pressure calibrated by mean and diastolic blood pressure (BP) was used to calculate time-varying LV wall stress from endocardial and epicardial volumes obtained from Tomtec wall tracking analysis. The relative contributions of reductions in systolic pressure and in LV volumes and to overall reduction in LV wall stress were calculated assuming that volume or pressures after NTG were identical to baseline values.
Results: NTG decreased peak LV stress (pre: 387±22; post: 329±22kdynes/cm^2, $P<0.001$), mean stress (pre: 335±19; post: 277±20 kdynes/cm^2, $P<0.001$) and peak stress time over ejection time (pre: 0.37±0.03; post: 0.30±0.01, $P<0.05$) due to reduction of LV end-diastolic volume (pre: 107±7.3; post: 95.6±7.3ml, $P<0.01$), end-systolic volume (pre: 47.9±4.4; post: 40.1±3.7ml, $P<0.01$) and central systolic BP (pre: 138±5.9; post: 122±4.8 mmHg, $P<0.001$). Percentage change in mean stress attributable to reductions in pressure and volume were 11.2% and 9.5% respectively