



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

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

H. Gu, H. Fok, B. Jiang, M. Sinha, J. Simpson, P. Chowienczyk

To cite this article: H. Gu, H. Fok, B. Jiang, M. Sinha, J. Simpson, P. Chowienczyk (2013) P5.02: RELATIVE CONTRIBUTION OF PRE AND AFTER-LOAD IN REDUCTION OF TIME-VARYING MYOCARDIAL STRESS BY NITROGLYCERIN, Artery Research 7:3_4, 144–145, DOI: <https://doi.org/10.1016/j.artres.2013.10.152>

To link to this article: <https://doi.org/10.1016/j.artres.2013.10.152>

Published online: 14 December 2019

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. $9.84 \pm 3.60\%$, $p < 0.0001$) (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 ± 0.6 U/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

J. L. Lagrange¹, L. W. Walton², S. B. Bloemen³, K. C. Cruickshank⁴, A. B. Benetos¹, P. L. Lacolley¹, V. R. Regnault¹

¹INSERM 1116, Université de Lorraine, Nancy, France

²School of medicine, Manchester, United Kingdom

³Synapse BV, Maastricht, Netherlands

⁴King's College of London, London, United Kingdom

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. These 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

G. Galmiche¹, V. Regnault², Z. Li¹, P. Lacolley²

¹UR4, UPMC, Paris, France

²Inserm U1116, Université de Lorraine, Nancy, France

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 over-expression, 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.

P5 Clinical Science 2

P5.01

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

B. L. Phillips, J. Tsui

Royal Free Hospital, London, United Kingdom

Objectives: Traditional outcomes after vascular intervention include vessel patency, limb salvage rates and mortality but correlate poorly with functional goals. Patient-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 survey 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-eluting 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

H. Gu¹, H. Fok¹, B. Jiang¹, M. Sinha², J. Simpson², P. Chowienzyk¹

¹King's College, London, United Kingdom

²Evelina Children's Hospital, London, United Kingdom

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 \pm SE) years were studied before and 7-12 min after NTG (400 μ g 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 ± 22 kdynes/cm², $P < 0.001$), mean stress (pre: 335 ± 19 ; post: 277 ± 20 kdynes/cm², $P < 0.001$) 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 ± 7.3 ml, $P < 0.01$), end-systolic volume (pre: 47.9 ± 4.4 ; post: 40.1 ± 3.7 ml, $P < 0.01$) 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

demonstrating that pre-load and after-load contributed approximately equally to the reduction of LV wall stress.

Conclusions: NTG reduces myocardial stress and increases myocardial contraction efficiency as a result of similar contributions from reductions in pre- and after-load.

P5.03 Withdrawn by author

P5.04

ARTERIAL STIFFNESS AND WAVE REFLECTIONS DECREASE DURING PREGNANCY

J. Bossuyt¹, I. Fabry¹, S. Vermeersch^{1,2}, J. Kips^{1,2}, K. Roelens³, L. Van Bortel¹

¹Heymans Institute of Pharmacology, Ghent, Belgium

²Institute Biomedical Technology, Ghent, Belgium

³Department of Obstetrics and Gynaecology, Ghent, Belgium

Objective: Studies on changes in arterial stiffness and wave reflections during pregnancy are limited to cross-sectional studies. Our aim was to investigate maternal hemodynamic and cardiovascular adaptations at each trimester of pregnancy in a prospective longitudinal case-control study.

Methods: Cardiovascular measurements were performed at 12, 20 and 35 weeks of gestation, and included peripheral (Omron M6) and central (Sphygmocor) blood pressures, wave reflection and arterial stiffness measures (Sphygmocor and Esaote AU5 Wall track system).

Results: 109 healthy women with a normal pregnancy (mean age 29.3y, range 21-42) and 26 healthy non-pregnant control subjects (mean age 28.4y, range 21-40) were included. Except for peripheral and central systolic blood pressure, all cardiovascular parameters showed significant ($p < 0.05$) changes during pregnancy. Heart rate increased linearly during pregnancy. In contrast, diastolic blood pressure (DBP), mean arterial pressure (MAP), augmentation index ($Alx@75$) and aortic stiffness (PWV) showed a typical V-shaped pattern, characterized by a significant drop from 12 to 20 weeks of gestation (DBP: -2.6 mm Hg; MAP: -1.6 mm Hg; $Alx@75$: -10.0%; PWV: -0.6 m/s), followed by a rise (DBP: +4.2 mm Hg; MAP +4.0 mm Hg) or smaller drop ($Alx@75$: - 7.8 %; PWV: -0.4 m/s) at 35 weeks compared to 12 weeks of gestation.

Conclusions: The present longitudinal case-control study confirms the results of previous cross-sectional studies on peripheral and central hemodynamics. In addition, it shows a drop in wave reflection and arterial stiffness which may be due to vasodilation in the second and third trimester of pregnancy.

P5.05

EXERCISE- INDUCED ALBUMINURIA IS A MANIFESTATION OF EXERCISE AORTIC RESERVOIR FUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

R. E. D. Climie¹, V. Srikanth², L. J. Keith¹, J. E. Davies³, J. E. Sharman¹

¹Menzies Research Institute Tasmania, Hobart, Australia

²Stroke and Ageing Research Group, Monash Medical Centre, Monash University, Melbourne, Australia

³International Centre for Circulatory Health, Imperial College, London, United Kingdom

Objectives: Patients with type 2 diabetes (T2DM) are susceptible to exercise-induced albuminuria even at submaximal exercise, but the mechanisms are unknown. Recent data indicates that T2DM patients have raised central blood pressure (BP) during submaximal exercise and this could contribute to renal dysfunction independent of upper arm BP. This study sought to determine the relationship between exercise central haemodynamics and exercise-induced albuminuria in T2DM.

Methods: Forty T2DM patients (62±9 years; 50% male) and 40 healthy controls (53±9 years; 50% male) were examined at rest and during a 20-minute bout of light cycle exercise (40W; 50RPM). Haemodynamics recorded included, aortic reservoir function (excess pressure integral [xSP] and aortic reservoir pressure), aortic stiffness, augmented pressure (AP), brachial and central BP. Albuminuria was assessed by albumin/creatinine ratio (ACR) at rest and within 20 minutes after exercise.

Results: There was no difference between groups in resting ACR ($p > 0.05$). Exercise induced a significant ACR rise in T2DM patients but not controls (0.39±0.89 vs 1.05±1.38 mg/mol, $p = 0.017$). All central haemodynamic variables indicative of systolic stress were significantly higher during exercise in T2DM participants (i.e. xSP, systolic BP and AP; $p < 0.01$ all). For T2DM patients, exercise xSP was independently associated with increased ACR ($\beta = 0.003$, $p = 0.001$), independent of age, sex, body mass index, and 24-hour ambulatory SBP.

Conclusions: Aortic reservoir function, as determined by excess pressure during submaximal exercise, is independently associated with exercise-induced albuminuria in T2DM patients. These novel findings suggest that aortic reservoir function could be important for appropriate renal function in patients with T2DM.

P5.06

NATURAL TIME COURSE OF AORTIC STIFFNESS AND WAVE REFLECTIONS IN NORMAL PREGNANCY AND IN GESTATIONAL DIABETES: A LONGITUDINAL STUDY

F. Battista¹, G. Pucci¹, C. F. Sorrentino², E. Torlone³, S. Gerti², G. Schillaci¹

¹Università di Perugia, Medicina Interna, Terni, Italy

²Università di Perugia, Ginecologia, Perugia, Italy

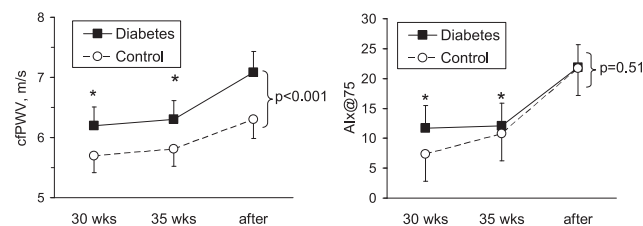
³Azienda Ospedaliera di Perugia, MISEM, Perugia, Italy

Pregnancy is associated with profound vascular adaptive changes. Cross-sectional studies show greater arterial stiffness in gestational diabetes than in normal pregnancy. However, the time course of maternal cardiovascular hemodynamics in normal and diabetic pregnancy can only be appreciated in longitudinal studies.

Thirty-six women with gestational diabetes (34±5 years, BP 111/69±13/8 mmHg) and 36 with normal pregnancy (33±3 years, BP 111/68±10/8 mmHg) were examined 3 times, at a gestational age of 30 and 35 weeks, and 12 weeks after delivery. On each occasion, tonometry-based carotid-femoral pulse wave velocity (cfPWV) and heart-rate corrected aortic augmentation index ($Alx@75$) were obtained (SphygmoCor).

Compared to women with normal pregnancies, women with gestational diabetes had a higher age- and mean arterial pressure-adjusted cfPWV ($p < 0.001$, Figure), both during pregnancy (6.2±0.9 vs 5.7±0.8 m/s at week 30, 6.3±0.9 vs 5.8±0.9 at week 35) and after delivery ($p = 7.1±1.0$ vs 6.3±1.1 m/s). Alx did not differ between the two groups ($p = 0.51$). In both groups, cfPWV was significantly lower at 30 and 35 weeks than after delivery (Figure, both $p < 0.001$). $Alx@75$ and central SBP were markedly lower during pregnancy than after delivery (both $p < 0.001$), despite unchanged brachial SBP.

Conclusions: (1) compared with normal pregnancy, gestational diabetes is associated with a higher aortic stiffness, which remains elevated 3 months after delivery; (2) no significant differences in wave reflection are present in normal and diabetic pregnancies; and (3) aortic stiffness and augmentation are lower during the third trimester of gestation than after delivery, both in normal pregnancies and in gestational diabetes.



P5.07

DIFFERENT EFFECTS OF AGEING AND BP ON SEVERAL AORTIC AND CAROTID SEGMENTS

F. Tosello^{1,2}, M. Bensalah³, H. Ketthab¹, N. Kachenoura³,

P. Boutouyrie¹, S. Laurent¹, E. Mousseaux³

¹Descartes University, Pharmacology Dpt, Paris, France

²Turin University, Medical Sciences Dpt, Turin, Italy

³Descartes University, Radiology Dpt, Paris, France

Objective: Carotid-femoral PWV (cfPWV) is a regional marker of vascular ageing: our aim was to take advantage of Magnetic Resonance (MRI) and High resolution Echotracking (HRE) in order to non-invasively investigate the effect of age and blood pressure (BP) on different segments of large arteries.

Methods: Regional stiffness was measured as cfPWV using Sphygmocor and as aortic arch PWV using MRI (ArchPWV). Local stiffness was measured at the carotid artery site using HRE (carPWV), and at the ascending and