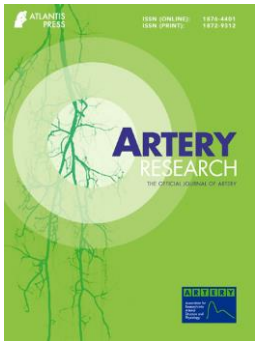

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5.1: MILD REDUCTION OF GLOMERULAR FILTRATION RATE IS ASSOCIATED WITH INCREASED SYSTEMIC VASCULAR RESISTANCE INDEPENDENT OF CHANGES IN CARDIAC AUTONOMIC TONE

Ilkka Porsti, Kati Vaaraniemi, Pauliina Kangas, Antti Tikkakoski, Jenni Koskela, Anna Tahvanainen, Arttu Eraranta, Jukka Mustonen

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4.2±0.6 L/min meanSD p<0.001), higher Ctot (2.7±1.0 vs 2.0±0.4 ml/mmHg p<0.001), lower AIx (13±10 vs 32±11 % p<0.001) and lower GALA (41±15 vs 68±6 ° p<0.001). GALA was associated with Ctot and AIx. After vasopressors, MAP increase was associated with a decrease in Ctot (2.4±0.9 vs 1.7±0.7 ml/mmHg p<0.001), and an increase in AIx (21±14 vs 25±14 % p<0.001) and GALA (53±18 vs 61±16 ° p<0.001). Changes in GALA and Ctot after vasopressors were strongly associated (p=0.004).
Conclusions: PU Loop assessment from routine hemodynamic optimization management during GA and especially our novel GALA parameter could monitor cardiac afterload continuously in anesthetized patients, and may help clinicians to titrate vasopressor therapy.

4.7
MEASUREMENT OF ARTERIAL STIFFNESS USING A CONNECTED BATHROOM SCALE: CALIBRATION AGAINST SPHYGMOCOR

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Background: Measurement of arterial stiffness (AS) is still considered difficult. We developed a non-invasive technique to assess AS from a connected bathroom scale, based on ballistocardiography (BCG) and impedance plethysmography (IPG).
Methods: We included 198 subjects and patients, 111 for calibration study (cal), 88 for validation study (val), 34% hypertensives, mean age 48±17 years, 50% women. The scale pulse transit time (WS-PTT) was calculated as the difference between BCG systolic signals and IPG blood flow in the foot. Distance was estimated from body height and PWV was calculated. Carotid to femoral transit time (CF-PTT) was measured using Sphygmocor. Spearman and robust multivariate regressions were used.
Results: The WS-PTT correlated well with CF-PTT with R=0.69 in pooled population (cal 0.73, val 0.60). WS-PWV correlated with CF-PWV with R=0.73 (cal 0.67, val 0.59). The standard deviation of difference was 1.19 m/s with no significant bias compared with CF-PWV. Correlations of WS-PWV with age and blood pressure were similar (R= 0.69 and 0.60, resp.) to those of CF-PWV (R=0.67 and 0.60, resp.). These good correlations were non-trivial given the differences in wave paths, the fact that measurements are made in orthostatic position and totally investigator-free.
Conclusion: We show in two distinct populations that a simple user-oriented instrument such as a connected bathroom scale can estimate arterial stiffness with accuracy close to healthcare-oriented systems. Because these devices will be used by the general population, the availability of arterial stiffness data on very large, non-medicalized populations will change our management of well-being and health.

4.8
INCREASED CARDIAC WORKLOAD IN THE UPRIGHT POSTURE IN MALE SUBJECTS: NON-INVASIVE HEMODYNAMICS IN MEN VERSUS WOMEN

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Background: Men and women differ in the risk of cardiovascular disease, but the underlying mechanisms are not completely understood. We examined possible sex-related differences in supine and upright cardiovascular regulation.
Methods: Hemodynamics were recorded from 167 men and 167 women of matching age (~45 years) and body mass index (~26.5 kg/m2) during passive head-up tilt. None had diabetes, cardiovascular disease other than hypertension, or antihypertensive medication. Whole-body impedance cardiography, tonometric radial blood pressure, and heart rate variability were analyzed. Results were adjusted for height, smoking, alcohol intake, mean arterial pressure, plasma lipids and glucose.
Results: Supine hemodynamic differences were minor: lower heart rate (-4%) and higher stroke volume (+7.5%) in men than women (p<0.05 for both). Upright systemic vascular resistance was lower (-10%), but stroke volume (+15%), cardiac output (+16%), and left cardiac work were clearly higher (+20%) in men than women (p<0.001 for all). Corresponding results were observed in a subgroup of men and postmenopausal women (n=76, age >55 years). Heart rate variability analyses showed higher low frequency to high frequency ratio in supine (p<0.001) and upright (p=0.003) positions in men.
Conclusions: The foremost difference in cardiovascular regulation between sexes was higher upright hemodynamic workload of the heart in men, a finding not explained by known cardiovascular risk factors or hormonal differences before menopause. Heart rate variability analyses indicated higher sympathovagal balance in men regardless of body position. The deviations in upright hemodynamics could play a role in the differences of cardiovascular risk between men and women.

4.9
PROPORTIONAL PRESSURE RELATIONS IN THE PULMONARY ARTERIAL SYSTEM

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Background — Objectives: The pulmonary arterial system can be characterized by:
1. A constant product of Pulmonary Vascular Resistance (PVR) and Total Arterial Compliance (TAC) with Tau=PVRxTAC≈0.7 seconds (1).
2. A proportional relation exits between systolic and diastolic pulmonary artery pressure, sPAP, dPAP, with mean pulmonary artery pressure mPAP (2). Recently it was shown that the time constant Tau is affected by Pulmonary Arterial Wedge Pressure (PAWP), and thus not constant under all conditions (3).
We therefore questioned how the product PVRxTAC = Tau depends on PAWP.
Methods: We have studied proportionality of pressures in a group of patients (n=1054) and determined the contribution of Pulmonary Arterial Wedge Pressure.
Results: We found that sPAP=1.61mPAP and dPAP =0.62mPAP, for all PAWP between 1 and 31 mmHg. Calculating PVR and TAC in the standard way as PVR=(mPAP-PAWP)/CO and TAC=PP/SV, with CO: Cardiac Output, PP: Pulse Pressure, SV: Stroke Volume, and HR: Heart Rate, it follows that: PVRxTAC=(1-PAWP/mPAP)/HReq. 1
Comparison with Tedford's data (their fig 3C) is as follows:
PAWP Tau-TedfordTau-Eq. 1
6 mmHg 0.43s 0.48s
45 mmHg 0.18s 0.18s
Conclusions: These findings imply that for a certain PAWP and Heart Rate a hyperbolic relation remains, but the time constant Tau depends on the ratio of PAWP/mPAP and Heart Rate. A clinically measured low Tau could suggest a high PAWP.
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5.1
MILD REDUCTION OF GLOMERULAR FILTRATION RATE IS ASSOCIATED WITH INCREASED SYSTEMIC VASCULAR RESISTANCE INDEPENDENT OF CHANGES IN CARDIAC AUTONOMIC TONE

Professor Ilkka Porsti [2], Dr Kati Vaaraniemi [3], Dr Pauliina Kangas [1], Dr Antti Tikkakoski [2], Dr Jenni Koskela [2], Dr Anna Tahvanainen [2], Dr Arttu Eraranta [1], Professor Jukka Mustonen [2]
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Objective: Our aim was to evaluate the influence of mild impairment in kidney function on hemodynamics and cardiac autonomic tone.

Methods: We studied 561 (50% male) normotensive and hypertensive subjects without kidney or other cardiovascular diseases or antihypertensive treatment. Supine and upright hemodynamics were recorded using continuous pulse wave analysis, whole body impedance cardiography and heart rate variability analysis. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI cystatin C equation.
Results: Mean eGFR was 99 (range 53-152) ml/min/1.73 m^2 and one third of the patients had values below 90. After adjustments for age, sex, body mass index and low density lipoprotein cholesterol level, regression analysis indicated significant associations between lower eGFR and higher systolic ($p<0.001$) and diastolic blood pressure ($p<0.001$) and systemic vascular resistance ($p=0.001$) regardless of body position. Lower eGFR was associated with higher low frequency to high frequency ratio of heart rate variability in supine but not in upright position. The level of eGFR was not associated with the level of cardiac output.
Conclusions: Even mild kidney impairment is associated with higher systemic vascular resistance and increased supine sympathovagal balance. However, changes in autonomic tone, as based on analysis of heart rate variability, do not seem to explain the relation between lower eGFR and higher systemic vascular resistance in the upright position. The close relationship between the regulation of GFR and systemic vascular resistance may play a role in the pathogenesis of primary hypertension.

5.2
AN ASSOCIATED WITH FAMILIAL HEMIPLEGIC MIGRAINE TYPE 2 MUTATION IN THE ALPHA-2 ISOFORM NA,K-ATPASE DISTURBS VASCULAR RESPONSES IN MOUSE BRAIN

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Objectives: Migraine attack is associated with severe changes in brain perfusion vasoconstriction-induced hypoxemia during aura and rebound vasodilation in subsequent headache. Familial Hemiplegic Migraine Type 2 is associated with point mutations (including G301R) in the $\alpha 2$ isoform Na,K-ATPase. Heterozygote mice bearing G301R mutation (FHM2) were recently characterized for several behavioral and neuronal abnormalities.
Methods: Vascular function of wild type (WT) and FHM2 mice was compared in vivo (telemetry and Laser Speckle measurements of brain perfusion), in vitro (myography) and in situ (changes in astrocytic $[Ca^{2+}]_i$and parenchymal arteriole diameter in brain slices to electric field stimulation (EFS)).
Results: Vascular abnormalities were shown for cerebral circulation while only minor or no significant changes were found in peripheral arteries. Accordingly, no difference in blood pressure was seen under resting conditions. Middle cerebral artery from FHM2 mice had large inner diameter and constricted stronger to U46619, endothelin and K^+-depolarization. This was associated with increased depolarization and Src-kinase-dependent sensitization to $[Ca^{2+}]_i$.
Isolated cerebral arteries from FHM2 mice have exaggerated relaxation to elevated $[K^+]_{out}$(4-12mM) due to increased role of the inward-rectifying K^+channels. Repeated EFS (>3 times) reduced the $[Ca^{2+}]_i$responses in astrocytic endfeet and increased relaxation of parenchymal arterioles in the FHM2 in comparison with WT. Flow responses to whiskers stimulation were also potentiated in FHM2 mice.
Conclusions: A knock-out mutation of the $\alpha 2$ Na,K-ATPase leads to both elevated contractility and increased relaxation of cerebral arteries. These dysfunctions could affect the blood supply to active neurons and thus disturb neurovascular coupling.

5.3
REVERSIBILITY OF ARTERIAL STIFFNESS AFTER KIDNEY TRANSPLANTATION: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Chronic kidney disease is associated with increased arterial stiffness. Correction of the uremic milieu by kidney transplantation (KTx) may be improve arterial stiffness. However, results from clinical studies are not uniformly convincing. This could be related to small sample size of studies, heterogeneity in methods and timing of assessment of arterial stiffness after KTx. We aim to measure the reversibility of arterial stiffness after KTx.
Design and Method: Observational studies and randomized controlled trials with measurements of pulse wave velocity (PWV), pulse pressure (PP) and/or augmentation index (AIx) were extracted from MEDLINE, EMBASE, COCHRANE LIBRARY, and Web of Science from their inception to January 2016. Two reviewers independently identified eligible studies comparing PW, PP and/or AIx pre to post KTx and extracted data including population characteristics, interventions and outcomes.
Results: 13 studies of 981 met our inclusion criteria. 11 Studies (408 renal transplant) have been included in meta-analysis. There was a standard mean change of PWV by -0.45 (95% CI: - 0.68 -0.20, $I^2=58\%$) post-KTx. Both studies using aortic PWV (5 studies, 160 patients) and those using brachial-ankle PWV, showed a significant decrease of PWV by -1.58 m/s (95% CI: -2.97 - 0.19, $I^2=$ 87%) and by -1.21 m/s (95% CI: - 1.89 — 0.54, $I^2=0$ %) post-KTx, respectively. Analysis of central PP and AIx showed significant reduction post-KTx by -4.77 (95% CI: -9.19 -0.35, I2=55%) and by -11.59 (95% CI:-15.64 -7.53, I2=43%), respectively. Only two studies have reported adjusted parameters for mean arterial pressure.
Conclusions: There is a significant reduction in PWV, central PP and AIx after KTx. Heterogeneity among studies are globally moderate. Further analysis is required to examine the importance of changes in different vascular beds taking into account changes in blood pressure.

5.4
HIGH PWV IS ASSOCIATED WITH NANO-SCALE CHANGES IN THE MEDIAL LAYER OF THE INTERNAL MAMMARY ARTERY

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Background: Arterial stiffening occurs as part of the natural ageing process. Degradation of the extracellular matrix (ECM) in the medial layer is typically implicated in arterial stiffening. However, little is known about how localised changes in arteries in terms of both structure and mechanical properties contribute to the overall stiffening of arteries.
Aim: To determine localised differences in the nano-structure and mechanical properties in the medial layer of internal mammary arteries (IMA) in patients with high and low pulse wave velocity (PWV).
Methods: IMAs were collected form coronary bypass operations from 7 patients with high (13.8 3.3 m/s) and 7 patients with low (8.6 0.7 m/s) PWV. The samples were cryo-sectioned to a nominal thickness of 5 μm for atomic force microscopy (AFM) measurement. All the samples were tested hydrated. Histological analysis was used to determine collagen and elastin content. Data are presented as means SEMs.
Results: The medial layers of IMAs in the high PWV group were significant stiffer than in the low PWV group (Low 228.4 15.6 kPa, High 735.8 108.8 kPa,) ($p < 0.0001$). Topographical features as visualised with AFM were similar in both groups but the higher nanomechanical stiffness was found to correlate with histological data.
Conclusions: Nanomechanical properties of the medial layer in the IMA associate with PWV data. Changes in composition in the ECM drive the profound localized changes in tissue stiffness.

5.5
AGE-DEPENDENT TELOMERE ATTRITION, SHORT TELOMERES AND ATHEROSCLEROSIS

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Background: Short leukocyte telomere length (LTL) is associated with atherosclerosis. The prevailing view is this association exists since LTL is a biomarker of cumulative inflammation and oxidative stress during adult life. However recent studies show that LTL in adults is defined