0281
A novel device for measuring arterial stiffness using the finger-toe pulse wave velocity: validation study of the pOpmètre®

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Methods: The pOpmètre® has 2 photodiodes sensors, positioned on the finger and on the toe. The difference (Dt) between the foot of the toe pulse wave and that of the finger is measured for 20s. The travelled distance is estimated on subject’s height. Study 1 compared the cf-PWV to the carotid-femoral PWV (cf-PWV) obtained by the reference method SphygmoCor® in 86 subjects (53±20 yrs), including 69 patients with various pathologies and 17 healthy normotensives. Study 2 compared the changes of ft-PWV and cf-PWV during a cold pressure test in 10 healthy subjects. Study 3 assessed repeatability in 45 patients.

Results: ft-PWV correlated significantly with cf-PWV (r² = 0.43, p<0.0001). A better correlation was found in terms of transit time (r² = 0.61, p<0.0001). The discrepancy between the transit times was related to age. Cold pressure test induced parallel changes in cf-PWV and ft-PWV, with increased aortic stiffness reversible during recovery. The intra-session repeatability was very good with a coefficient of variation of 4.52%.

Conclusion: pOpmètre® allows measurement of arterial stiffness in routine clinical practice. The greatest advantages of ft-PWV are easiness, rapidity, feasibility and acceptability by patients, together with correct agreement with reference technique. Further studies are needed to adjust for bias and for validating the pOpmètre in larger populations.

0438
Pulse wave velocity with pOpmètre® independently correlates with glomerular filtration rate in renal transplant patients

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Aim: To evaluate the relationship between glomerular filtration rate and arterial stiffness using Pulse Wave Velocity (PWV) as an independent cardiovascular risk factor in renal transplanted patients.

Patients and methods: We studied transplanted patients followed in our outpatient clinic. After a medical examination, we measured blood pressure (Comport Cuff®-Skil-Care, USA), PWV (pOpmètre® – AxeLife sas – France) after 10 min supine resting. pOpmètre® measures the finger to toe transit time, and according to a height chart, calculates the PWV. Three measurements were performed to study the repeatability. Estimated glomerular filtration rate (eGFR) was calculated using MDRD equation.

Results: Forty-four (30 men, 14 women) renal transplant recipients were included. No significant difference between men and women were found in age (M±SEM: 53.2±2.2 years), systolic blood pressure (SBP: 138±2 mmHg), diastolic blood pressure (DBP: 81±2 mmHg), eGFR (45.9±2.4 ml/min/1.73 m²) and PWV (10.4±1 m/s) [range: 6.0-15.7]. Repeatability expressed as the SD/mean of 3 measurements was very good: 5.4%.

PWV correlated positively with age (r²=0.16, p<0.009) and negatively with eGFR (r²=0.15, p<0.009). Using a stepwise regression model (including gender, age, SBP, DBP, height, weight), only age and pOpmètre PWV remained significantly associated with eGFR.

Conclusions: Glomerular filtration rate independently correlates with pulse wave velocity in renal transplant patients, supporting the hypothesis that kidney function plays a predominant role in arterial stiffness.

0020
Role of HIF-1 in the cardiac remodeling and inotropic effects of chronic intermittent hypoxia

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Obstructive sleep apnea (OSA) is an important risk factor for cardiovascular morbidity and mortality. Chronic intermittent hypoxia (IH), a major component of OSA, has been shown to induce cardiovascular complications (hypertension, vascular remodelling, increased infarct size). We have shown that the hypoxia sensitive transcription factor HIF-1 is involved in the cardiovascular effects of IH. The α subunit of HIF-1 is degraded in normoxia (N) following prolyl hydroxylation by prolyl hydroxylase domain containing enzymes (PHD1, PHD2 and PHD3) while it is stabilized by PHD inactivation during hypoxia. The aim of the present study was to further explore the myocardial effects of IH and HIF-1 by assessing cardiac function and remodelling in mice models overexpressing or under expressing HIF-1α. For this, the response to IH was investigated in two strains of mice partially deficient for the genes encoding for PHD2 and HIF-1α, respectively. Mice were exposed in their cages, 8 h/day during 14 days, to 1-min cycles of IH (30s of 5% FiO2 followed by 30s of room air) or N (similar cycles of room air only). After exposure, the Fulton index (RV/LV+S) was evaluated in all experimental groups and cardiac contractility was assessed in heterozygous HIF-1α null mice and their respective controls. Exposure to IH induced right ventricular hypertrophy in control animals (Fulton index: 0.298 ± 0.010 vs 0.284 ± 0.008 vs 0.208 ± 0.012 in control mice). We also observed a significant increase in left ventricular developed pressure and maximal dP/dt during IH exposure in WT mice. This effect was absent in mice with partial HIF-1α deficiency.In conclusion, this study confirms the role of HIF-1 in the deleterious cardiovascular adaptation to IH leading to cardiac remodelling and increased contractility.
Sinusoidal denervated (SAD) and chemically sympathectomized (SNX) rats are characterized by a decrease in arterial distensibility without hypertension and would thus be relevant for analyzing arterial wall stiffening independently of blood pressure level. The fibronectin network, which plays a pivotal role in cell matrix interactions, is a major determinant of arterial stiffness.

We aim to determine in SAD and SNX rats the elastic properties of the arterial wall by evaluating in vivo the relationship between incremental elastic modulus by echotracking and circumferential wall stress, and the changes of cell-extracellular matrix links in the abdominal aorta, by studying fibronectin, vascular integrins receptors and ultrastructural features of the aorta by immunohistochemistry.

We observed an increase in wall stiffness in both experimental conditions associated with new modifications of cell-extracellular matrix adhesion. In SAD rats, aortic hypotrophy was coupled with an increase of muscle cell attachments to its extracellular matrix via fibronectin and its α5β1 integrin. In SNX rats, αvβ3 was also increased after discontinuous treatment compared with continuously or placebo treated rats. Nevertheless, elastin and collagen ratio was not modified between the 3 groups. The present results suggest that in our animal model, intermittent treatment with valsartan increased long-term blood pressure variability leading to increased arterial stiffness which may originate from changes in cell matrix interactions through the fibronectin-integrins pathway. Transposed to humans the present results might have important clinical implications in the treatment of hypertension, as the pharmacological mechanisms linking partial adherence to antihypertensive treatment and cardiovascular risk enhancement remain to be demonstrated.

0372
Partial adherence to antihypertensive therapy increases long-term blood pressure variability and fails to improve aortic stiffness in SHR rat
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Poor adherence to antihypertensive therapy and long-term blood pressure variability are 2 major contributors to cardiovascular damage. However, the determinants of increased long-term blood pressure variability remained scattered and incomplete. We hypothesized that intermittent treatment of spontaneously hypertensive rats by valsartan may be an animal model of partial adherence. For this purpose, height week-old spontaneously hypertensive rats were discontinuously (2 days/week) or continuously treated by valsartan (30 mg/kg/d po) or placebo during 8 weeks. We aimed to study in this model the relationship between long-term blood pressure variability and arterial stiffness and composition. Blood pressure was recorded 3 days a week by telemetry and analysed at the end of the treatment. In a second set of experiments, pulse wave velocity and aortic structure were determined in the 3 groups of rats. Long-term blood pressure variability was assessed by day-by-day standard deviation. Despite a significant reduction in systolic blood pressure, discontinuous treatment increased long-term systolic blood pressure variability but did not change pulse wave velocity. Vascular fibronectin and its integrin αvβ3 were also increased after discontinuous treatment compared with continuously or placebo treated rats. Nevertheless, elastin and collagen ratio was not modified between the 3 groups. The present results suggest that in our animal model, intermittent treatment with valsartan increased long-term blood pressure variability leading to increased arterial stiffness which may originate from changes in cell matrix interactions through the fibronectin-integrins pathway. Transposed to humans the present results might have important clinical implications in the treatment of hypertension, as the pharmacological mechanisms linking partial adherence to antihypertensive treatment and cardiovascular risk enhancement remain to be demonstrated.