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Compared to control, Pr+IS induced IL-8 gene expression in ECs (3.4 ± 1.2 fold increase, P = 0.0144) and IL-8 release from ECs (17.5 ± 7.9 pg/ml for control vs. 1.3 ± 0.2 pg/ml for Pr+IS, P = 0.0164). IL-8 addition to hASMCs under uremic exposure significantly promoted calcification in a concentration-dependent manner. Furthermore, uremic EC-CM induced hASMCs calcification was prevented by silencing of IL-8 gene in ECs. Finally, IL-8 prevented the Pr+IS-induced increase of osteopontin gene in hASMCs (wrt control, 2.2 ± 0.2 without IL-8 vs. 1.3 ± 0.3 with IL-8).

Conclusions: These results strongly suggest, for the first time, that IL-8 secreted from ECs during uremic exposure may play a critical role in vascular calcifications and thus in the cardiovascular complications of CKD.

Non-invasive measurement of heart-fermoral pulse wave velocity: correlates, reproducibility and comparison with carotid-fermoral pulse wave velocity

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Objective: Heart-fermoral pulse wave velocity (hf-PWV), estimated from the Cardio-Ankle Vascular Index device (VaSera-1500) by combining phonocardiogram with pulse signals detected by thigh cuffs, as opposite to carotid-fermoral pulse wave velocity (cf-PWV), includes the stiffness of the ascending aortic segment. We sought to investigate the repeatability and main correlates of hf-PWV, and to compare the results with cf-PWV.

Design and method: Hf-PWV and cf-PWV were obtained in 85 volunteers (n = 30 < 30 years, n = 30 30–60 years, n = 25 > 60 years), according to AR-TERY Society guidelines for validation of non-invasive devices (Artery Research 2010;4:34–40). Heart-fermoral transit time was calculated as the time lag between aortic opening to pulse arrival to the thigh cuff. Distance was taken as 0.8 x direct distance between the carotid and femoral pulses. For comparison with cf-PWV, heart-fermoral transit time was recalculated after subtracting the transit times needed to travel: (1) the distance from the femoral pulse to the top of thigh cuff; (2) the distance from the aortic valve to the carotid pulse. These two transit times were derived from age- and sex-specific values published elsewhere (Sugawara et al, J Hypertens 2014;32:881–889).

Results: Cf-PWV and hF-PWV were closely correlated (R = 0.85, p < 0.01) and showed similar degrees of association with age (R = 0.75 and R = 0.83), height (R = 0.20 and R = 0.26) and mean arterial pressure (R = 0.53 and R = 0.54). In absolute terms, after re-calculation of transit time, hf-PWV was significantly lower than cf-PWV (mean difference 2.6 ± 1.0 m/s, p < 0.01), and showed a tendency toward increasing difference at increasing PWV values (Figure 1). Hf-PWV showed high within- (coefficient of variation (CV) 4.6%) and between-observer (CV 6.0%) reproducibility.

Conclusions: Hf-PWV, measured through a semi-automated device which combines phonocardiogram with pulse detection with a thigh cuff, showed high reproducibility, was closely correlated with cf-PWV, and showed similar associations with variables classically associated with arterial stiffness. In absolute terms, hf-PWV was significantly lower than cf-PWV; such difference increased at increasing age, potentially reflecting the lower age-dependency of stiffness of the ascending aorta. Further studies aiming at evaluating the clinical and prognostic significance of hf-PWV are warranted.

Paced breathing reduces blood pressure and arterial stiffness: impact of the autonomic nervous system

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Objective: The autonomic nervous system (ANS) plays an important role in regulating blood pressure (BP), but its action on arterial stiffness (AS) is still a subject of debate. Device-guided paced breathing (DGB) has been proposed as a non-pharmacological strategy to control BP – via the effects on ANS – but its effect on AS are unknown. Therefore, we examined if DGB would affect AS in hypertensive (HT) subjects.

Design and method: Brachial BP (OMRON-705IT, Omron Corporation, Kyoto, Japan), central BP (pulse-wave analysis of the radial artery, SphygmoCor, AtCor Medical, Sydney, Australia), AS (carotid-fermoral pulse wave velocity (cfPWV), SphygmoCor) and ANS activity (high resolution heart rate variability (HRV) as log-ratio of low-frequency/high-frequency range (LF/ HF), Schiller Medilog AR-12plus, United States) were determined in HT subjects. All measurements were performed in supine position after 15 min of rest and subsequently repeated during supervised DGB therapy which allows breathing < 10 breaths/min.

Results: 25 HT patients (11 male), age (mean ± SD) 47 ± 12 years, systolic BP (SBP) 142.8 ± 19.4 mmHg, diastolic BP (DBP) 86.6 ± 8.7 mmHg and heart rate (HR) 72.4 ± 12.5 bpm were recruited. DGB decreased LF/HF by 0.09 ± 0.12 (p = 0.05) and reduced both brachial (~10.19 ± 7.89 mmHg) and central (~8.47 ± 6.80 mmHg) SBP DBP (~3.6 ± 3.0 mmHg for brachial, p < 0.01) as well as HR (~3.48 ± 6.25 bpm, p < 0.05). cfPWV decreased from 9.81 ± 1.66m/s to 8.66 ± 1.66m/s (p < 0.01) and bivariate correlation showed no associations with changes in SBP, DBP or mean BP (MBP) (β = 0.117, 0.107, 0.216 respectively; all p > 0.1). Finally, using the regression coefficient from meta-analysis and the observed decrease in MBP, we calculated the predicted reduction of cfPWV attributed to reduction in BP to be = 0.48 m/s, less than 50% of the observed reduction 1.04 (95%CI 0.65, 1.28)m/s.

Conclusions: DGB decreased central/brachial BP, an effect likely to be mediated by the reduction of sympathetic activity as indicated by HRV. Effects to reduce cfPWV were greater than those predicted from the change in BP suggesting that the ANS may play an independent role in modulating AS in HT subjects.

Renal sympathetic and sensory nerves do not drive hypertension in a polycystic kidney disease rat model

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Objective: Catherter-based renal denervation (RDN) is used to treat hypertension however recent clinical trials have cast doubt on previously reported effects. This study aims to determine if RDN improves systolic blood pressure, renal function and autonomic dysfunction in a hypertensive rodent model due to polycystic kidney disease (PKD).

Design and method: Lewis polycystic kidney rats (LPK) underwent total, selective sensory or sham RDN by periaxonal application of phenol, capsaicin or normal saline, respectively, at 6-weeks-old. Animals then underwent 1) euthanasia at 7-weeks-old, 10-weeks-old or 14-weeks-old or 2) repeat procedure at 10-weeks-old and euthanasia at 14-weeks-old. Blood pressure was measured by radiote-