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P7.2: IDENTIFICATION OF VASCULAR AND CIRCULATING BIOMARKERS TO PREDICT OUTCOME IN PATIENTS AFFECTED BY SEPTIC SHOCK

P. Vallerio, O. Belli, F. Musca, G. Monti, L. Bonacchini, M. Cazzaniga, M. Stucchi, P. Meani, L. Frigerio, M. Molteni, F. Panzeri, M. Alloni, R. Fumagalli, A. De Gasperi, C. Giannattasio

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The RI value was significantly reduced by beetroot ingestion (pre-beetroot RI=0.75±0.05 versus post-beetroot RI=0.72±0.05; pre-water RI=0.75±0.06 versus post-water RI=0.76±0.05; P=0.02).

Conclusion: Our findings suggest that the supplementation of pharmacologic therapy with dietary nitrate through beetroot juice could prevent cardiovascular events and progression of renal disease in CKD patients.

P6.10

PROPIONYL-L-CARNITINE FOR INTERMITTENT CLAUDICATION. A COCHRANE REVIEW.

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Intermittent claudication (IC) is a symptomatic form of peripheral arterial disease (PAD) (pain in the lower limbs with walking and relieved by rest). Propionyl-L-carnitine (PLC) is a drug which may lower the symptoms of PAD. Is PLC efficacious in improving clinical outcomes in IC patients?

For this Cochrane review randomized controlled trials in patients with IC receiving PLC compared with placebo or other intervention were selected. Pain-free and maximal walking performance were analyzed by standardized exercise test. ABI, quality of life and adverse events were assessed. 13 Studies were included in this review (1423 patients). The results of the selected trials were brought together in patient pools. For the maximal walking distance, the mean difference in walking performance after use of PLC compared to placebo was an absolute increase of 50.86 m (95% CI 50.34 to 51.38) or a 26% relative improvement (23 to 28%). For the pain-free walking distance, the improvement in walking performance with PLC compared to placebo was an absolute increase of 32.98 m (32.60 to 33.37) or a 31% relative improvement (28 to 34%). PLCs had an 0.09 (0.08 to 0.09) improvement in ABI over placebo. The adverse events of PLC were similar as in the control group and PLC seemed well tolerated and safe. PLC 1-2g a day costs 0.30 to 0.70 €.

PLC for IC shows a significant, though mild to moderate improvement of walking distances and ABI compared to placebo. The safety of PLC is comparable to placebo. In practice, PLC could be useful adjuvant to classic IC-therapies or when these are contra-indicated, not feasible or ineffective. This work is a Cochrane review. The data presented here presented are provisional (as the review has not yet been published).

The citation for the Cochrane protocol is: de Backer TLM, Campens L, Vander Stichele R, Van Bortel L, De Bacquer D. Propionyl-L-carnitine for intermittent claudication (Protocol). Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD010117. DOI: 10.1002/14651858.CD010117.

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P6.11

PHOSPHODIESTERASE TYPE-5 INHIBITOR USE IN TYPE 2 DIABETES IS ASSOCIATED WITH A REDUCTION IN ALL CAUSE MORTALITY

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Background: Phosphodiesterase type-5 inhibitors (PDE5is) exert cardioprotective effects in small mammal models of myocardial ischaemia. There is currently little data on whether a similar effect exists in humans. We determined whether PDE5i use in males with type 2 diabetes (T2DM) was associated with reduced mortality.

Methods: We retrospectively analysed the pseudoanonymised records of 48 GP practices in Cheshire, UK and identified all 7029 men (mean age 72.8 years) diagnosed with T2DM before 1 January 2007. Baseline clinical characteristics and PDE5i treatment data were obtained. Mean follow-up was 6.4 years (January 31, 2014) and all deaths were ascertained from GP records.

Findings: Of the 1,663 (23.7%) men prescribed a PDE5i, the proportion of deaths was significantly lower than those never prescribed (16.9% versus 29.4%). All-cause mortality rates (per 1000 person-years) were similarly lower (21.1 (19.1-24.5) versus 34.4 (32.5-36.5); P<0.0001). There was a 38% reduction in all-cause mortality (univariate Cox proportional hazards HR: 0.62 (0.54-0.71); P<0.0001) in men on a PDE5i over the period. This reduction remained but was attenuated (HR: 0.80 (0.65, 0.98); P<0.05) after multivariate regression adjusting for age (1.11 (1.09-1.12); P<0.0001 per year), smoking history (1.31 (1.16-1.47); P<0.0001), HbA1c, systolic BP, creatinine levels, prescribed statins, aspirin and beta-blocker use.

Interpretation: Around 70% of deaths in T2DM are attributable to cardiovascular disease. Our data demonstrates that PDE5i use is associated with significantly reduced mortality in men with T2DM at high risk of CVD. Further evidence is required to elucidate the role of PDE5is in cardioprotection.

P7.1

ACUTE EFFECTS OF SMOKING OVER THE ENDOTHELIAL FUNCTION AND CENTRAL ARTERIAL HEMODYNAMICS IN YOUNG HEALTHY PEOPLE

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Introduction: The aim of this study was to assess the acute effects of smoking over the endothelial function and central arterial hemodynamics, in healthy and young smokers.

Methods: Thirty healthy young individuals, were allocated into two groups, matched for gender and age, according to their smoking habits: control group (CG; n=15 non-smokers) and intervention group (IG; n=15 smokers). All the individuals were submitted to two clinical evaluations, basal and following 30 minutes (after smoking a cigar in the IG). Weight, height, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), flow-mediated dilation (FMD), aortic pulse wave velocity (PWV) and pulse wave analysis over the carotid artery (PWA) were assessed.

Results: CG and IG groups had similar baseline clinical and demographic characteristics, although the IG showed lower baseline FMD values (7.53±2.80% versus 12.47±4.63% in the CG; p=0.001). The pairwise analysis revealed significant variations in the IG, but not in the CG, with an increase in HR, brachial and central BP and PWV, and a significant decrease in FMD, revealing an important acute compromise of endothelium-dependent vasodilation after the cigar in the IG, with no changes in the CG.

Conclusion: Smoking has an acute and noteworthy pernicious effect over the vascular function in young and healthy individuals, compromising endothelium-dependent vasodilation, increasing heart rate, blood pressure and aortic stiffness.

P7.2

IDENTIFICATION OF VASCULAR AND CIRCULATING BIOMARKERS TO PREDICT OUTCOME IN PATIENTS AFFECTED BY SEPTIC SHOCK

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Introduction: Cardiovascular dysfunction is a well-recognized early complication of septic shock (SS). A hallmark of SS is a change in microvascular function and endothelial cell (EC) activation, contributing to multiple organ failure. Angiopoietin (Ang1-2) pathway has been reported associated with severity of illness and mortality.

Aim: to evaluate prognostic and clinical role of functional vascular assessment in patients with SS.

Methods: We enrolled 20 patients from intensive care units with a diagnosis of SS. Clinical, hemodynamic, instrumental evaluations and blood sample collection were obtained at hospitalization (T1), and one week later (T2). We assessed echocardiographic left ventricular systolic function (LVEF) and functional arteries evaluation with carotid-femoral PWV (Complior).

Results: During the follow-up 11 patients survived (S) and 9 died (D). S and D had similar ages (62±8vs66±11 yrs, means±SD), MAP (80±12vs81±12 mmHg, means±SD) and SOFA score (13±4vs15±4, means±SD). At T1, D had a significantly higher cf-PWV than S (12±3vs9±2 m/s, means±SD; p<0.05). Furthermore considering all patients together, we found an inverse correlation between PWV and LVEF (p<0.01). Finally, S had a significant T1-T2 increase in Ang1 (7339[4587-17010]vs47384[10658-53645] medians[25-75th]; p<0.05) and a decrease in Ang2 levels (27783±17625vs9008±5565 means±SD; p<0.01); D patients showed an inverse trend.

Conclusions: In SS endothelial dysfunction caused by EC-activation is expressed by an increase of PWV, which was significantly different depending on outcome of patients. PWV also has a correlation with LVEF. The values of PWV could express an alteration of ventricular-vascular coupling, useful

to monitor response to therapy as well as pharmacologic support of the circulation.

P7.3
IMPACT OF KIDNEY TRANSPLANTATION ON AORTIC STIFFNESS: RESULTS FROM 2-YEAR FOLLOW-UP

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Objectives: Kidney transplantation (KTx) may improve arterial stiffness. The purpose of the present study is to examine the effects of KTx on aortic stiffness after 2 years of follow-up.

Method: In this prospective, longitudinal observational study, we studied hemodynamic parameters prior to KTx and 3, 6 and 24 months after a KTx in 59 dialysis patients. Aortic stiffness was measured by carotid-femoral pulse wave velocity (cf-PWV) and heart rate adjusted central augmentation index (Alx) was measured by arterial tonometry. A successful KTx was defined by an estimated eGFR of ≥ 45 mL/min/1.73m². Linear mixed model was used to take into account the repeated measures of aortic stiffness and mean blood pressure. Values are reported as mean \pm SEM

Results: The mean age was 48 years, with 70% male, 20% with cardiovascular disease and 25% diabetes. After adjusting for mean blood pressure, cf-PWV decreased significantly from 11.2 ± 0.33 to 10.3 ± 0.30 by 3 months ($P=0.042$), but cf-PWV gradually increased to 10.8 ± 0.31 and 11.2 ± 0.33 (m/s) by 6 and 24 months and was not statistically different from the baseline. In an analysis stratified by age, the early improvement of aortic stiffness was only statistically significant for patients older than 50 years of age. However, MBP-adjusted Alx did not change significantly after KTx.

Conclusion: This study shows that there is an early reduction in aortic stiffness after KTx with a gradual return in aortic stiffness to baseline values after 2 years of follow-up. This study suggests a reduction in the rate of progression of aortic stiffness after KTx.

P7.4
AORTIC STIFFNESS IS ASSOCIATED WITH FUNCTIONAL LIMITATION (OR SIX MINUTE WALK DISTANCE) IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: THE ERICA STUDY

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Background: Six-minute walk distance (6MWD) independently predicts mortality and hospitalisation in Chronic Obstructive Pulmonary Disease (COPD) and is significantly reduced in COPD subjects with comorbidities of heart disease and hypertension. It also predicts cardiovascular events in stable coronary heart disease, and mortality in heart failure. We hypothesised that aortic stiffness is associated with 6MWD in COPD patients.

Methods: Interim analysis was performed on 354 stable subjects with COPD recruited to the ERICA (Evaluation of the role of inflammation in non-pulmonary manifestations of airways disease) study. Central haemodynamic measurements included aortic pulse wave velocity (aPWV) and augmentation index (Alx). Other measurements included carotid intima thickness, spirometry, 6MWD, fibrinogen and high-sensitivity C reactive protein (hs-CRP).

Results: 210 out of 354 subjects (59%) were male, median (range) age 67 (43-84) years, 68% were former smokers. Mean aPWV was 10.2 (2.6) m/s. Linear regression analysis indicated a significant negative association between aPWV and 6MWD ($p<0.001$). This relationship was maintained after adjustment for airflow limitation (Forced Expiratory Lung Volume in 1 second [FEV₁]), age, sex, MAP and supine HR, $p=0.011$. A 1m/s increase in PWV was associated with a 9 m decrease in 6MWD (95% CI: 4-14 m, $p=0.001$).

Conclusions: Aortic stiffness is associated with 6MWD in COPD, suggesting a link between vascular ageing and functional limitation in this patient group, which merits further investigation. Reduced 6MWD in COPD subjects with cardiovascular comorbidity, suggests aortic stiffness may be involved in the increased prevalence of cardiovascular events seen in COPD.

P7.5
PHENOTYPING OF ARTERIAL HYPERTENSION BY PULSE WAVE VELOCITY AND PLASMA RENIN ACTIVITY MEASUREMENT

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Objective: To test K.Kario hypothesis (J Am S Hypertens 2010; 4(5):215-218) that predominant "arterial stiffness" (AS) and "volume-dependent" (V) types of arterial hypertension may exist and thus evaluation of arterial stiffness and volume-dependency status may help to choice between a calcium channel blocker (as "anti-stiffness" drug) and a diuretic (as "anti-volume" drug) to achieve blood pressure (BP) control.

Methods: Pulse wave velocity (PWV, SphygmoCor, AtCor, Australia) and plasma renin activity (PRA, radioimmune assay) were measured in 124 (48 men) untreated hypertensive patients aged 50-65 years (mean 59.6 ± 5.1 years) with GFR CKD-EPI >60 mL/min/1.73 m². AS-typing was done by individual PWV interpretation (Boutouyrie P., Vermeersch S.J. Eur Heart J 2010;31:2338-2350). PRA <0.65 ng/ml/h was considered as V-type, PRA >0.65 ng/ml/h - as renin (R) type.

Results: V-type was found in 57,3%, R-type in 42,7%, AS-type in 47,6% patients. Isolated (normal PWV) types were observed in 52,4%, isolated R-type was more prevalent (38,7%) than isolated V-type (13,7%). AS+V-type was found in 43,6%, AS+R-type - in 4,0%. It means that 76,1% of patients with V-type had elevated PWV and 91,5% of patients with increased AS are volume-dependent. Multifactor analysis failed to reveal independent predictors of isolated or mixed types, but independent correlation between PRA and PWV ($\beta=-0.45$, $p<0.001$) and pulse pressure amplification ($\beta=0.76$, $p<0.001$) was found.

Conclusion: Significant over-lap in "arterial stiffness" and "volume" types of arterial hypertension argues against possibility of differential choice between a calcium channel blocker and a diuretic for BP lowering guided by evaluation of PWV and PRA

P7.6
AGE-RELATED TRENDS IN 24-PATTERNS OF AORTIC PULSE WAVE PARAMETERS

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Aim: 24-h ambulatory monitoring (AM) of central blood pressure (BP) and augmentation index (Alx) is a new method that extends understanding of the characteristics of BP and arterial properties. The aim of the study was to explore characteristics of central pulse wave and Alx on AM of brachial and central BP in age subgroups.

Methods: Successful AM of brachial and central BP was done with oscillometric BPLab VASOTENS system (OOO Petr Telegin, Russia) in 84 untreated hypertensive subjects (55,8 \pm 9,6 years, male 36,9%). Gender differences of central BP and Alx were evaluated in patients <55 years (14 men, 23 women), 55-60 years (7 men, 16 women), 61-70 years (10 men, 14 women). Differences were considered significant if $p<0.05$.

Results: Brachial day/night SBP was similar in age subgroups: <55 years $140\pm 15/130\pm 18$, 55-60 years $139\pm 17/136\pm 22$, 61-70 years $137\pm 19/132\pm 23$ mmHg. Increase in day- and night-time brachial PP was observed from younger to older patients due to the reduction of diastolic DBP: <55 years brachial PP day/night $53\pm 12/52\pm 12$, 55-60 years $57\pm 11/57\pm 13$, 61-70 years $57\pm 12/58\pm 16$ mmHg, <55 years DBP day/night $87\pm 11/78\pm 11$, 55-60 years $84\pm 9/79\pm 12$, 61-70 years $81\pm 9/73\pm 12$ mmHg. Aortic day/night PP trend was similar: <55 years $42\pm 9/43\pm 10$, 55-60 years $45\pm 10/48\pm 12$, 61-70 years $47\pm 12/50\pm 14$ mmHg. Alx@HR75 also increased with age, and this increase was observed both during day- and night-time: <55 years Alx day/night $24\pm 18/31\pm 17$, 55-60 years $28\pm 16/38\pm 16$, 61-70 years $33\pm 15/42\pm 12$ %.

Conclusion: 24-h AM of central BP revealed age-related increase in aortic PP and Alx both for day- and night-time

P7.7
GENDER-RELATED TRENDS IN 24-HOUR AMBULATORY BRACHIAL BLOOD PRESSURE AND CENTRAL PULSE WAVE MONITORING

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(Alx) is a new method that extends understanding of the characteristics of BP and arterial properties. The aim of the study was to explore gender differences on AM of central BP and Alx in different age groups.