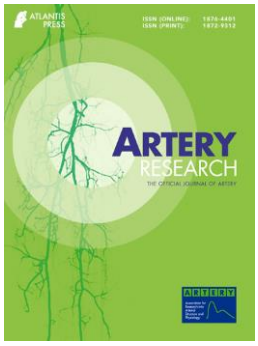

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P6.9: DIETARY NITRATE BY BEETROOT JUICE CAN LOWER RENAL RESISTIVE INDEX IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Material and Methods: 80 patients with severe untreated periodontitis were subjected to anti-infective periodontal therapy, comprising bacterial biofilm removal by scaling and root planning either with or without administration of systemic antibiotics. The following parameters were assessed at baseline and 12 month post-therapy: periodontal bleeding on probing, representing a clinical parameter for active inflammation (BoP), pulse wave velocity (PWV), augmentation index (AIx), central systolic pressure (SBPao) and central pulse pressure (PPao) using an oscillometric device (Arteriograph).
Results: Preliminary data evaluation demonstrated, that 12 months post therapy reduction of periodontal bleeding on probing correlated significantly with decreased values of PWV, SBPao, PPao, AIx, and AugP ($p<0.05$, respectively) whereas peripheral blood pressure remained unchanged.
Conclusions: Successful reduction of periodontal inflammation is associated with improved markers of arterial dysfunction.

P6.6
A DOUBLE BLIND, RANDOMISED TRIAL INVESTIGATING IF ARTERIAL STIFFNESS CAN BE REDUCED INDEPENDENTLY OF BLOOD PRESSURE IN PARTICIPANTS WITH OR AT RISK OF TYPE 2 DIABETES

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Background: Arterial stiffness (AS) as pulse wave velocity (PWV), is a powerful independent predictor of cardiovascular events, and commonly complicates Type 2 diabetes (T2D). The VaSera machine measures cardiac (by 2nd sound phonogram)-ankle PWV, expressed as a cardio-ankle vascular index (CAVI), aimed to be independent of blood pressure (BP). Our factorial trial tests whether separately randomised dietary nitrate or placebo, and an aldosterone antagonist reduce CAVI and PWV in those at risk of or diagnosed with T2D.
Method: Double-blind, randomised trial assessing AS at baseline, 3 and 6 months. Target recruitment is 120 patients, 18-90 years, excluding those with serious illness or eGFR <45mL/min. Daily interventions are spironolactone (≤50mg) or doxazosin (≤16mg), to control for BP change, with a nitrate donor (≤0.4g nitrate) or an identical nitrate-free juice.
Results: 74 participants are screened, 54 randomised and 34 completed. Mean±SD baseline age and body mass index were 59.7±12.1 years and 32.8±5.5kg/m^2, respectively; 40% female.
No differences in CAVI or PWV were observed between screening and randomisation (8.30±1.4 to 7.97±1.3 units and 9.30±2.0 to 9.17±1.8m/s, respectively). Systolic (S) and diastolic (D) BP dropped between these visits (138±17 to 133±17mmHg, $p<0.005$ and 81±12 to 71±12mmHg, $p<0.001$, respectively). Bland-Altman analysis between screening and randomisation for CAVI, PWV, SBP and DBP shows <6% of mean differences fall outside of the 95% limits; mean difference± limits of agreement; -0.13±2.12, -0.32±1.85, -5±26 and -4±19, respectively.
Conclusion: A trial focused on PWV is practical and effective within our target population, with simple recruitment and a low drop-out rate.

P6.7
SUBLINGUAL NITROGLYCERIN IN PATIENTS WITH HEART FAILURE AND PRESERVED EJECTION FRACTION: IMPACT ON CENTRAL AND REGIONAL CAROTID AND RADIAL INPUT IMPEDANCE AND HEMODYNAMICS

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Background: The systolic blood pressure lowering effect of sublingual nitroglycerin (NTG) administration is thought to primarily arise from its action on wave reflection, although recent invasive data indicate that at least part of the blood pressure reduction can be ascribed to an effect on left ventricular dynamics.
Methods: Carotid and radial pressure waveforms and aortic, carotid and radial flow were measured in 19 HFpEF patients using applanation tonometry and pulsed Doppler ultrasound, respectively. Signals were time-aligned and global systemic as well as regional impedance and wave reflection analysis was applied.
Results: NTG lowered carotid systolic (130.8±26 at baseline vs. 110.4±18.4mmHg after NTG, $P<0.01$) and mean (92.5±18.4 vs.85.4±14.3) blood pressure. Global systemic effects included a decrease in systemic vascular resistance (1.00±0.32 vs. 0.88±0.28 mmHg.ml^{-1}.s, $P<0.05$), characteristic impedance (0.133±0.089 vs. 0.089±0.034 mmHg.ml^{-1}.s, $P<0.05$) and an increase in total arterial compliance (1.20±0.58 vs. 1.52±0.53 ml.mmHg^{-1}, $P<0.01$). NTG had a major impact on the amplitude of the forward pressure wave (58±24.3 vs. 40.6±13.3 mmHg, $P<0.01$), with no significant change in reflection magnitude. Regional analysis demonstrated a large effect of NTG on carotid input impedance, lowering impedance over the entire frequency spectrum, with radial artery input impedance did not demonstrate any significant changes (despite large effects on pressure and flow waveform morphology).
Conclusions: Our data in patients with HFpEF confirm the absence of impact of NTG on reflection magnitude, and demonstrate large effects of NTG on the input impedance of the cerebral vascular district, with little effect on the distal forearm circulation.

P6.8
EFFECT OF ORGANIC NITRATES ON INTRAVENTRICULAR PRESSURE GRADIENTS IN HEART FAILURE PATIENTS WITH PRESERVED EJECTION FRACTION

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Introduction: Heart Failure with preserved ejection fraction (HFpEF) is a highly prevalent condition for which no pharmacologic therapy is available. Diastolic dysfunction is thought to be central to its pathophysiology. Organic nitrates have pharmacologic effects on preload, afterload and myocardial contraction/relaxation that may favourably influence ventricular filling. However, the effect of sublingual nitro-glycerine (NTG) on diastolic parameters in this population has not been studied. We aimed to assess the effect of NTG on intraventricular pressure gradients (IVPG) and other measures of diastolic function.
Methods: Colour M-mode Doppler (CMM) is a non-invasive ultrasound technique used to obtain left ventricular (LV) blood flow velocities during early filling and to calculate IVPG. CMM recordings of 20 patients (HFpEF) at rest and after the administration of 0.4 mg of NTG were obtained and processed. Average values of the parameters were calculated and compared (Wilconox test) at rest and after NTG.
Results: NTG induced a non-significant increase in early diastolic IVPG ($p=0.286$) due to a reduction in the early diastolic convective component ($p=0.026$). Similarly, the early diastolic reversal convective component was reduced ($p=0.009$). In contrast, the late diastolic IVPG was increased ($p=0.017$), due to an increased inertial component ($p=0.034$). There was a reduction in peak E wave velocity ($p=0.004$), E wave acceleration ($p=0.003$) and deceleration ($p=0$), while the acceleration time ($p=0.034$) and the heart rate (HR) ($p=0.016$) increased.
Conclusion: Organic nitrates exert effects on diastolic filling in HFpEF: increased HR and myocardial contractility and decreased peak E-wave velocity possibly related to a preload reduction.

P6.9
DIETARY NITRATE BY BEETROOT JUICE CAN LOWER RENAL RESISTIVE INDEX IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction: Beetroot has a high concentration of nitrate. In circulation nitrate converts to nitrite. Nitrite-derived NO is a potent vasodilatator. Increased renal resistive index (RI) are associated with higher mortality in patients with chronic kidney disease (CKD) and predict cardiovascular events in these patients. Here we investigated if the ingestion of beetroot juice can reduce RI-values.
Methods: Using a randomized cross-over study design 12 CKD patients were investigated within 4 hours (h) after one ingestion of dietary nitrate load (300 mg) by highly concentrated beetroot juice (30g beetroot powder dispended in 200 ml water) versus 200 ml water. Plasma nitrite concentration as well as renal segemental arterial RI in duplex doppler ultrasonography was measured before and 4 hours after ingestion of beetroot or water. BP was measured every 15 minutes within the 4 hours.
Results: In 12 CKD patients (7 females) the eGFR was 40.7±13.8 ml/min. Three patients had a hypertensive nephropathy, 2 diabetic nephropathy and 7 seven patients had a combined hypertensive/diabetic nephropathy.

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 diatary 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.
The authors acknowledge the Cochrane Peripheral Vascular Diseases Group.

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; p0.05). Furthermore considering all patients toghether, 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