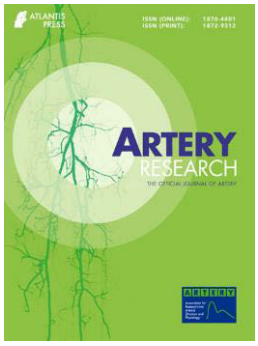

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4.6: HIPPOCAMPAL CEREBRAL BLOOD FLOW DEPENDS ON SYSTEMIC ENDOTHELIAL FUNCTION IN INDIVIDUALS WITH MILD COGNITIVE IMPAIRMENT: THE TRAIN THE BRAIN-MIND THE VESSEL STUDY

Rosa Maria Bruno, Lorenza Pratali, Rosa Sicari, Francesco Stea, Nicoletta Berardi, Gloria Tognoni, Ubaldo Bonuccelli, Lorenzo Ghiadoni, Stefano Taddei, Danilo Scelfo, Laura Biagi, Michela Tosetti, Lamberto Maffei, Eugenio Picano

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4.4
MIDDLE CEREBRAL ARTERY PULSATILITY IN HEART FAILURE AND PATIENTS WITH CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICES

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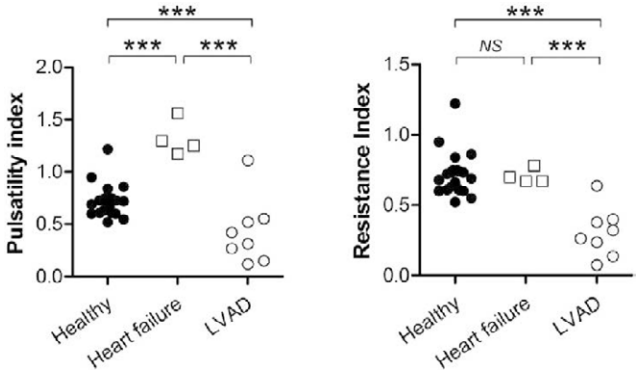
Background: High pulsatility index (PI) in the cerebral circulation has been associated with increased prevalence of stroke (1). Interestingly, heart failure (HF) patients implanted with continuous-flow left ventricular assist devices (CF-LVADs) have increased rates of stroke despite presenting with dramatically lower pulse pressures compared with healthy individuals (20 mmHg vs. 30—40 mmHg). Characterising and understanding flow velocity profiles of the middle cerebral artery (MCA) may provide a useful and local marker of pulsatile energy transmitted into the brain of HF and CF-LVAD patients.
Methods: PI and resistance index (RI) were quantified from Duplex ultrasound images (2D and pulsed-wave Doppler) of the MCA obtained in four heart failure patients (HF; 68 ± 7 yrs), eight CF-LVAD patients (59 ± 4 yrs) and 20 healthy controls (51 ± 7 yrs).
Results: Compared with healthy controls, PI of the MCA was actually higher in the HF group (0.72 ± 0.16 vs. 1.32 ± 0.17, $P < 0.0001$), but markedly lower in patients on CF-LVAD (0.36 ± 0.21, $P < 0.0001$). However, RI was similar between healthy controls and HF patients ($P > 0.05$), and only lower in CF-LVAD patients ($P < 0.0001$).



Conclusions: PI in the MCA is significantly higher in HF but markedly lower in CF-LVAD patients, relative to healthy controls. The higher PI in HF does not appear to be associated with an altered RI. Future work should examine the cerebrovascular outcomes associated with varying levels of pulsatility and resistance in both HF and CF-LVAD patients.

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4.5
THE EFFECT OF LUNG FUNCTION ON BLOOD PRESSURE AND VASCULAR INDICES FROM ADOLESCENCE TO EARLY ADULTHOOD IN A MULTI-ETHNIC COHORT

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Given the significance of lung function (LF) for vascular health in adulthood, there are surprisingly few studies that have examined the interrelationships of their developmental trajectories. Both develop and decline over the life course, though LF peaks in the 20s, and both predict cardiovascular events and mortality. We used the multi-ethnic Determinants of Adolescent Social well-being and Health (DASH) longitudinal study to test whether lung function (LF) from early adolescence to young adulthood affected vascular indices. In 2002—3, 6643 11—13 y olds from 51 London schools participated at baseline, and 4785 were seen again at 14—16 y.
Recently 665 participated in pilot follow-up at 21—23 y. Regression models examined relationships between Forced Expiratory Volume (z-scores for $zFEV_1$ derived using Global Lung Initiative equations), blood pressure (BP), aortic pulse wave velocity (PWV) and augmentation index (AIx), the latter 2 measured only at 21—23 y. At 11—13 y, 1z-score zFEV1 was associated with +1.90 mmHg (95% CI 1.11—2.68, $p < 0.001$) in systolic BP. In contrast at 21—13 y, a relationship between these measures was not evident.
Between 11—13 y and 21—23 y, 1z-score change in zFEV1 was associated with +1.38 mmHg (0.25—1.51, $p < 0.05$) SBP, adjusted for age, sex, ethnicity, waist-height ratio, employment, and reported racism, smoking and alcohol use. zFEV1 at 11—13 y or 21—23 y was not associated with PWV or central AIx (AIxao) at 21—23 y. These findings signal that whilst cross-sectionally LF is differently associated with SBP in early adolescence than in the 20s, longitudinal change in LF is positively associated with changes in SBP during this part of the life course.

4.6
HIPPOCAMPAL CEREBRAL BLOOD FLOW DEPENDS ON SYSTEMIC ENDOTHELIAL FUNCTION IN INDIVIDUALS WITH MILD COGNITIVE IMPAIRMENT: THE TRAIN THE BRAIN-MIND THE VESSEL STUDY

Rosa Maria Bruno [1], Lorenza Pratali [2], Rosa Sicari [2], Francesco Stea [2], Nicoletta Berardi [3], Gloria Tognoni [1], Ubaldo Bonuccelli [1], Lorenzo Ghiadoni [1], Stefano Taddei [1], Danilo Scelfo [4], Laura Biagi [4], Michela Tosetti [4], Lamberto Maffei [3], Eugenio Picano [2]
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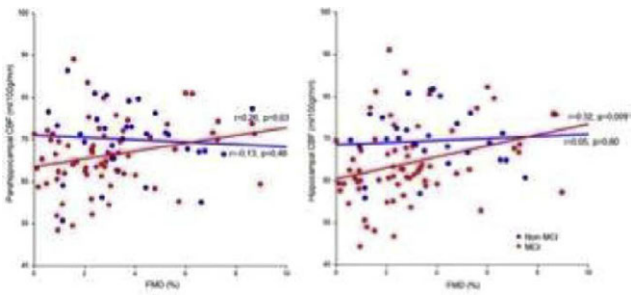
Background: Dementia has been recently viewed as a predominantly vascular disorder. Indeed, reduced brain NO availability causes increased ß-amyloid deposition by several mechanisms, including hypoperfusion.
Purpose: To investigate the relationship between cerebral blood flow in the hippocampal and parahippocampal regions (CBF-hipp and CBF-parahipp), crucial areas for memory and processing of non-verbal/spatial information, and systemic endothelial function in individuals with mild cognitive impairment (MCI), a subclinical condition predisposing to dementia.
Methods: CBF-hipp and CBF-parahipp were evaluated by magnetic resonance imaging (arterial spin labeling, GE HDxt 1.5 T Signa Neuro-optimized System) and systemic endothelial function by flow-mediated dilation (FMD) in the brachial artery.
Results: Complete data about CBF and FMD at enrollment were available for 66 individuals with MCI and 32 without (non-MCI). The two groups were matched for age (75 ± 5 vs 74 ± 5 years, $p = 0.22$), sex (men 45 vs 50%, $p = 0.18$) and mean BP (96 ± 10 vs 97 ± 9 mmHg, $p = 0.41$). FMD was significantly lower in MCI than in non-MCI (2.93 ± 2.18 vs 3.74 ± 2.03%, $p = 0.02$); CBF-hipp (64.3 ± 9.43 vs 69.5 ± 7.03 ml/100 gr/min, $p = 0.002$) and CBF-parahipp (66.3 ± 8.02 vs 70.0 ± 8.12 ml/100 gr/min, $p = 0.002$) were significantly lower in MCI as well. Among MCI, FMD was significantly correlated with CBF-parahipp ($r = 0.26$, $p = 0.03$) and CBF-hipp ($r = 0.32$, $p = 0.009$). In multiple regression models, including age, sex, mean BP, BMI, brachial artery diameter as confounders, FMD remained an independent determinant of CBF-parahipp (beta = 0.93, r2 = 0.063, $p = 0.04$) and CBF-hipp (beta = 1.31, r2 = 0.089, $p = 0.01$). Nor CBF-parahipp ($r = -0.13$, $p = 0.48$) neither CBF-hipp ($r = 0.05$, $p = 0.80$) were correlated with FMD in non-MCI group.



Conclusions: An independent association between hippocampal and parahippocampal CBF and systemic endothelial function is present in individuals with MCI.

4.7
PARAMETERS OF THE RESERVOIR-WAVE APPROACH AND MORTALITY IN DIALYSIS POPULATION

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Background: A new model has been proposed to explain hemodynamic consequences of arterial stiffness, which integrates both wave propagation and aortic reservoir function. The aim of this study was to assess the association between parameters of reservoir-wave analysis and all-cause mortality in a population with accelerated vascular ageing.
Methods: Among 311 patients with chronic kidney disease on dialysis, central arterial pressures were derived from applanation tonometry (Sphygmocor) of radial artery. Reservoir wave analysis was applied on radial pressure waveforms (without generalized transfer function) to obtain reservoir pressure (Peak RP), its integral (RP integral), excess pressure parameters (Peak XS, XS integral), and systolic (SC) and diastolic time constant (DC).
Results: During a median follow-up of 33 months, 204 (66%) deaths occurred. In Kaplan—Meier survival curves, only increasing tertiles of DC was associated with a significant decrease in survival time ($p < 0.001$). Amongst all parameters, only DC and XS integral were predictors of all-cause mortality in univariate Cox analysis as shown by hazard ratios for changes in 1-standardized deviation (HR 1-SD, Table 1). However, DC and XS integral were no longer significant when age was introduced in the model (p-value > 0.179).

Continuous variables	HR 1-SD	95% CI	p-value
Peak RP(mmHg)	1.121	0.987—1.273	0.079
RP integral(mmHg·sec)	1.050	0.920—1.197	0.470
Peak XS(mmHg)	1.112	0.966—1.281	0.138
XS integral(mmHg·sec)	1.217	1.062—1.395	0.005
SC($\times 10^{-2}$)	1.099	0.970—1.244	0.138
DC($\times 10^{-2}$)	1.186	1.60—1.328	0.003

Conclusions: Amongst all parameters of the reservoir-wave analysis, DC was the most important parameter associated with survival time and mortality. Despite its hypothetically more integrated approach to arterial tree function, none of the derived parameters showed a robust and independent association with mortality in this population. The study shows that despite its simplicity, arterial stiffness gradient remains the best predictor of mortality in this population.

4.8
ARTERIAL STIFFNESS AND ITS RELATIONSHIP TO MORTALITY IN PATIENTS WITH PERIPHERAL ARTERY DISEASE

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Background and aim: Several studies (1,2) suggest that patients with peripheral artery disease (PAD) show an increase in arterial stiffness, nevertheless the impact on mortality is less documented. (3)
Methods: 228 PAD patients mean age (68 ± 9 years) were followed-up for $4{,}8 \pm 2$ years. Anthropometric and clinical measurements were collected, ankle-brachial index (ABI) was estimated with standard protocol and hemodynamic parameters (central blood pressure, aortic pulse wave velocity [aPWV], augmentation index [Aix]) were measured using applanation tonometry. Prognostic factors of mortality were identified by Cox proportional hazards regression model.
Results: During follow-up 26 (11,6%) deaths occurred. Among them, 5 (19%) were of cardiovascular origin. The Cox analysis applied to data relative to the third tertile of aPWV (11.4—21.4, m/s), is significant for age, ($p = 0.039$), smoking history ($p = 0.0003$) non use of lipid lowering drugs ($p = 0.026$) and lower height ($p = 0.007$) but not for aPWV ($p = 0.312$), Aix ($p = 0.075$) and ABI ($p = 0.305$).
Conclusions: The present study provides further insights into the lack of association between large artery stiffness, pressure wave reflections and mortality in PAD patients.
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Oral session V — Pathophysiology and intervention

5.1
EFFECTS OF THE SGLT-2 INHIBITOR EMPAGLIFLOZIN ON VASCULAR FUNCTION AND CENTRAL HEMODYNAMICS IN PATIENTS WITH TYPE 2 DIABETES

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Background: The selective sodium-glucose cotransporter 2 (SGLT-2) inhibitor empagliflozin leads to improved cardiovascular, renal and heart failure outcome in secondary prevention. To better understand these effects, we examined vascular function and central hemodynamics.
Methods: In this prospective, double-blind, randomized, placebo-controlled, crossover study 76 patients with untreated type 2 diabetes were randomized to empagliflozin 25 mg orally once daily or placebo. After 6 weeks of treatment with either empagliflozin or placebo and 1 week washout-phase, patients crossed over to the other treatment. Central hemodynamics and vascular function were assessed by central systolic blood pressure (BP), central pulse pressure, forward and backward wave amplitude under office (Sphygmocor, AtCor, Australia) as well as ambulatory conditions (Mobilograph, IEM, Aachen).
Results: Treatment with empagliflozin reduced central systolic BP (114 ± 12 vs. 119 ± 14 mmHg, $p < 0.001$), central diastolic BP (74.4 ± 6.9 vs. 76.8 ± 8.2 mmHg, $p = 0.004$) and central pulse pressure (39.5 ± 9.9 vs. 42.2 ± 11 mmHg, $p = 0.012$) compared to placebo. Forward ($p = 0.006$) and backward ($p = 0.026$) reflection amplitude, assessed under office conditions, were also significantly lower with empagliflozin than with placebo. Under ambulatory conditions over 24-hours we also observed lower central systolic (117 ± 9 vs. 119 ± 9 mmHg, $p = 0.059$) and diastolic (79 ± 7 vs. 81 ± 7 mmHg, $p = 0.011$) BP after 6 weeks treatment with empagliflozin compared to placebo. Pulse wave velocity under ambulatory conditions was also reduced after 6 weeks with empagliflozin ($p = 0.016$).
Conclusions: Our study demonstrated consistent significant improvements of vascular function and central hemodynamics with empagliflozin under office and ambulatory conditions. Our data support the concept that empagliflozin exerts beneficial effects on cardiovascular and heart failure outcome via improved vascular function.