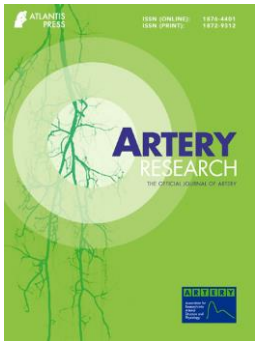

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14.5: LEVELS OF ANGIOPOIETIN-LIKE-2 ARE POSITIVELY ASSOCIATED WITH AORTIC STIFFNESS AND MORTALITY AFTER KIDNEY TRANSPLANTATION

Marie-Pier Desjardins, Nathalie Thorin-Trescases, Aboubacar Sidibe, Sacha De Serres, Richard Larivière, Eric Thorin, Mohsen Agharazii

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Methods: Non-invasive central blood pressure and flow were obtained by carotid tonometry and Doppler sonography respectively in a total of 329 women at first visit (mean SD, age 58± 8 years) and a follow-up visit approximately five years later (mean age 63± 8 years). Aortic root pulse wave velocity and reflection index (the ratio of the peak of the backward pressure wave over that of the forward pressure wave) were computed from the pressure and flow waves.
Results: Over the five year follow-up period, pulse pressure increased by 9.2%, from 43.7±73 to 47.7±0.78 mmHg (means SE, $P < 0.001$), PWV increased by 18.5 % from 4.01±0.08 m/s at first visit ($P<0.001$), the maximum value of flow velocity tended to increase (from 1.13±0.01 to 1.15±0.01 m/s) but reflection index decreased from 0.38±0.01 to 0.32±0.01 ($P<0.001$).
Conclusions: These results suggest that the increase of pulse pressure is related mainly to an increase in arterial stiffening rather than to an increase in pressure wave reflection.

14.2
LONGITUDINAL CHANGE IN VASCULAR STRUCTURE AND FUNCTION OVER A 5 YEAR PERIOD IN TWINS UK COHORT

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Background: Vascular aging is characterised by structural changes: wall thickening and an increase in lumen diameter, together with a functional increase in arterial stiffness. We investigated the longitudinal structural and functional changes that occur in the aortic wall over a 5 year follow-up period.
Methods: Subjects were 472 female twins (mean ageSD, 57.9±8.6 years at baseline). Measures of diameter and intima-media thickness (IMT), averaged from the carotid and femoral artery, and carotid-to-femoral pulse wave velocity (PWV) were made at two time-points, first between 2008-2014 and then on a second occasion an average of 4.7±3.0 years later. Young's incremental elastic modulus was estimated from the simplified Moens-Korteweg equation: $PWV = \sqrt{Eh/D}$, where h is the wall thickness and D is diameter.
Results: There was a significant increase in intima-media thickness (0.064±0.01 cm at baseline and 0.070±0.01 cm at follow-up, $P<0.0001$), diameter (0.75±0.06 cm at baseline and 0.76±0.07 cm at follow-up, $P<0.0001$) and PWV (9.15±1.8 at baseline and 9.75±1.8 m/sec at follow-up, $P<0.0001$), over the five-year follow-up period. The influence of the estimated increase in elastic modulus (10.2±4.0 and 10.7±4.1 10^6dynes/cm^2, at visit one and two respectively, $P=0.001$) on PWV was amplified by intima-media thickness increasing more than arterial diameter (10.5% versus 2.2%).
Conclusion: In our cohort of middle age to older women, increase in aortic wall thickness to lumen diameter was the most marked structural change and could potentially amplify the increase in PWV produced by intrinsic stiffening of the aortic wall.

14.3
IDEAL CARDIOVASCULAR HEALTH IS INVERSELY ASSOCIATED WITH INCREASED CAROTID-FEMORAL PULSE WAVE VELOCITY IN ITALIAN ADOLESCENTS. THE MACISTE STUDY

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Objective: Ideal cardiovascular health (ICH) among adolescents is defined as the optimal levels of three CV risk factors (SBP/DBP, fasting glucose, total cholesterol) and four behaviours (BMI, not smoking, healthy diet, physical activity)[1]. We investigated the burden of ICH among Italian adolescents, and its association with arterial stiffness (carotid-femoral pulse wave velocity,cfPWV).
Methods: 307 healthy subjects (mean age 17±2 years, 55% men) attending the High School at Terni, Italy, were evaluated. Physical activity, dietary and smoking were assessed through self-reported questionnaires. Sodium consumption was estimated by second fasting urine. Smoking was confirmed by exhaled carbon-oxyde. cfPWV was evaluated by arterial tonometry (SphygmoCor, subtracted distance). For each ICH metric, a score of 2 was also assigned if levels were ideal, 1 if intermediate, and 0 if poor.
Results: None had all 7 ICH metrics the majority (76%) had 4 or more ICH metrics. An inverse linear trend in cfPWV was observed over the number of ICH (p for linear trend <0.01). According to ICH score, after adjustment for age and sex, subjects in the lower tertile, compared to upper tertile, showed higher values of cf-PWV (5.1±1.3 m/s vs 4.6±1.8 m/s, $p<0.01$), which remained significant after further adjustment for mean BP and other confounding factors ($p=0.02$).
Conclusions: ICH is relatively uncommon among Italian adolescents, and is inversely related to cf-PWV in females. The potential adverse effects of CV risk factors and unhealthy behaviours on arterial stiffness, an early marker of vascular damage, begins to develop at an early stage of lifespan.
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14.4
A POSITIVE FAMILY HISTORY OF DIABETES IS ASSOCIATED WITH ARTERIAL STIFFNESS: THE MALMO DIET CANCER STUDY

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Objective: Arterial stiffness (AS) is known to be associated with a number of clinical conditions including hypertension, diabetes and dyslipidemia. AS may also be associated with lifestyle and early life factors, which are greatly affected by family history. The aim of this study was to investigate the association between self-reported family history (FH) and AS.
Design and method: The study population consists of 3056 individuals (mean age 72 years, 40% men) from the population-based Malmo Diet Cancer study, Sweden. Carotid-femoral pulse wave velocity (c-f PWV), a marker of AS, was measured with Sphygmocor®. Data on FH for diabetes, hypertension and cardiovascular (CV) events was retrieved from a questionnaire. Using multiple regression, adjustments were made for age, sex, mean arterial pressure (MAP) and heart rate (HR) in Model 1, and in Model 2 further adjustment made for diagnosed diabetes or hypertension, respectively.
Results: In an unadjusted model AS was associated with a FH of diabetes and CV events. These associations were significant after adjustment in Model 1 and Model 2.
Conclusion: The results indicate associations between AS and FH of both diabetes and CV-events. This shows that FH is a relevant marker of vascular ageing. There was no clear association between AS and FH for hypertension which could be explained by a lack of knowledge regarding this diagnosis even in close relatives. The associations between AS and FH will be compared to those of AS and Genetic Risk Scores (GRS) for diabetes and hypertension in ongoing analysis.

14.5
LEVELS OF ANGIOPOIETIN-LIKE-2 ARE POSITIVELY ASSOCIATED WITH AORTIC STIFFNESS AND MORTALITY AFTER KIDNEY TRANSPLANTATION

Marie-Pier Desjardins [1], Nathalie Thorin-Trescases [2], Aboubacar Sidibe [1], Sacha De Serres [1], Richard Larivière [1], Eric Thorin [2], Mohsen Agharazii [1]
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Introduction: Angiopoietin-like-2 (angptl2) is a secreted glycoprotein with homology to the angiopoietins. Through an autocrine/paracrine manner, it promotes endothelial dysfunction and atherosclerosis. Angptl2 is increased in chronic kidney disease (CKD), where the risk of cardiovascular disease (CVD) is amplified. The objectives of the present study were to 1) examine whether kidney transplantation (KTx) reduces angptl2 levels, 2) identify the determinants of angptl2 after KTx, 3) study the association of angptl2 with aortic stiffness and 4) assess the impact of angpl2 on mortality of KTx.
Methods: In 75 subjects undergoing KTx, we evaluated clinical, biochemical and aortic stiffness before and 3 months after KTx. Angptl2 levels were determined by Elisa. Aortic stiffness was assessed by carotid-femoral pulse wave velocity (cf-PWV). Logistic and Cox regressions were used for data analysis.

Results: After 3 months of KTx, angptl2 levels decreased from 71 ng/mL (IQR: 53-95) to 11 ng/mL (IQR: 9-15) P<0.001). In multivariate analysis, age, CVD, lower renal function and mean blood pressure were independently associated with higher angptl2 levels. There was a positive relationship between cf-PWV and angptl2 after KTx (r=0.260 P=0.024). After a median follow-up of 89 months, 13 deaths occurred. The group with higher angptl2 levels had a higher mortality rate (HR= 0.249 95% CI: 0.068-0.912, P=0.036).

Conclusion: There is a significant reduction in serum angptl2 levels after KTx however, our data demonstrate that after KTx, there is a positive association between angptl2, aortic stiffness and mortality, suggesting that angptl2 may play a biological role in CKD- related CVD.

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14.6
RELATIONSHIP BETWEEN 24-HOUR BLOOD PRESSURE VARIABILITY AND 24-HOUR CENTRAL ARTERIAL PRESSURE, PULSE WAVE REFLECTION AND STIFFNESS IN HYPERTENSIVE PATIENTS

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Objective: Twenty-four-hour blood pressure variability (BPV) predicts cardiovascular complications in hypertension, but its association with pulse wave indices (central arterial systolic pressure or CASP, pulse wave velocity or PWV, and augmentation index or AIx) is poorly understood. In the present study we assessed the degree of the impact of 24-hour BPV on 24-hour pulse wave indices.

Methods: Brachial BP was measured non-invasively over the 24-hours by an electronic, oscillometric, automated device (BPLab) in 661 uncomplicated, treated or untreated, hypertensive patients. Digitalized oscillometric waveforms were analyzed by a validated algorithm in order to obtain pulse wave indices. Twenty-four-hour BPV was calculated as unweighted (SDu) or weighted standard deviation (SDw) of the mean blood pressure, or as average real variability (ARV). Patients were classified in two groups according to whether the 24-hour BPV was below or above the median of the whole group.

Results: Twenty-four-hour systolic blood pressure variability (SBPV) showed a direct and significant relation with CASP (r=0.28 SDu, r=0.40 SDw, r=0.34 ARV), aortic PWV (r=0.10 SDu, r=0.21 SDw, r=0.19 ARV) and AIx (r=0.17 SDu, r=0.27 SDw, r=0.23 ARV). After adjustment for age, gender, body mass index, antihypertensive treatment and 24-hour SBP, the relationship was attenuated, but was still significant for all measures, X for AIx. Pulse wave indices were larger in patients with high than in those with low BPV: after adjustment these differences were abolished for AIx. Diastolic BPV showed a weak association with pulse wave indices.

Conclusions: In hypertensive patients 24-hour SBPV is moderately and independently associated with 24-hour CASP, wave reflection and stiffness.

14.7
HYALURONAN IS ASSOCIATED WITH AORTIC STIFFENING IN HEALTHY SUBJECTS

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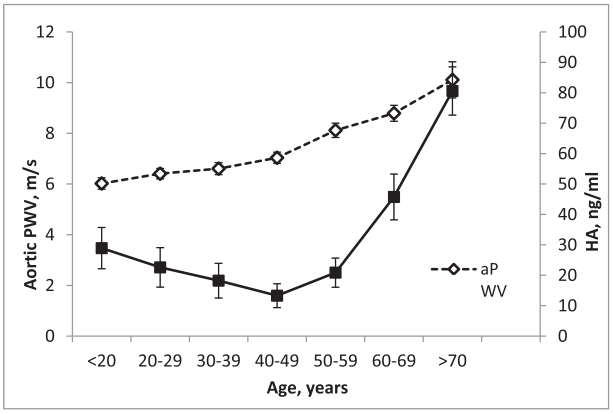
Background: Over-expression of hyaluronan (HA), glycosaminoglycan found in the extracellular matrix, results in the stiffening of the arterial wall by thinning of elastic lamellae in animal models. However, the effect in human arteries is more contentious. We aimed to study the relationship between serum HA and aortic stiffness in a cohort of healthy subjects.

Methods: Subjects were randomly selected from the Anglo-Cardiff Collaborative Trial (ACCT) database. Subjects underwent detailed haemodynamic assessment, including measurements of blood pressure (BP) and aortic pulse wave velocity (aPWV) (SphygmoCor, AtCor, Australia). Serum HA levels were measured by commercially available ELISA kit (DY3614, R&D Systems, U.K).

Results: 155 individuals (73 females and 82 males), with a mean age of 44±19 years, and a mean of BP of 134±16/86±11 mmHg were studied. HA and aPWV both increased with aging (P<0.0001 for both see the figure). Subjects were then split into tertiles of serum HA. aPWV was positively associated with HA tertile (7.03±1.42 v. 7.57±1.69 v. 8.10±2.00 m/s P=0.002). In multiple regression analysis, we found that HA remained independently associated with aPWV after adjusting for mean arterial pressure, BMI and gender (model R^2=0.233,P<0.001).



Conclusions: Our data suggests that hyaluronan may be one of the factors behind age-related aortic stiffening. However, further studies are needed to establish whether this association is causal and to understand the mechanism behind it.

14.8
VASCULAR ABNORMALITIES RELATED WITH OBESITY

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Environment and Objectives: Obesity is linked to a higher prevalence of risk factors, metabolic and inflamatory pathways conducting to increased vascular disease and CV risk.
To assess vascular disarrangements using non invasive methods in obese subjects (O) compared with matched lean (L) controls.

Methods: From the database of our Non Invasive Vascular Lab with 3964 first evaluated patients, we performed a case control study with 363 subjects, 268 obese and 95 lean age and sex matched controls. We measured IMT, Plaque analysis, PWV, Endothelial Function (EF) and arterial stiffness (CAP and Aix) (AS) using an oscillometric device (Arteriograph, Tendiomed. Hungary).

Results: Age (O 42.5+5 L 43.5+11) and sex % (O 80.6% L 78%) were similar. BMI (O 33.5+3.3 L 25+1.1Kg/m2), waist (O110.4+7.5 L 91.2+6.1cm) and BP (SBP O 139.8+16.8 L119+8.8 and DBP O 89+3.9 L 74.3+8 mmHg) were higher in O (p<0.001).CV Risk Factors in O: HTN 68% DLP 59.7% SMKG 24.2% DBT2 7.8% SED 72.4%. The proportion of abnormalities in IMT (O/L : 65.8/25.3%), Plaques (75.6/38.9%), EF (57.5/33.7%)and PWV (41.4/17.9%) were higher in O (p<0.001).Central and Peripheral PP were higher in O but not Aix.

Conclusion: Obese patients present a higher prevalence of vascular disarrangements although structural and functional explaining the role of this condition as a CV risk factor .

14.9
INCREASED ARTERIAL STIFFNESS PREDICTS LESS RECOVERY OF LEFT VENTRICULAR SYSTOLIC FUNCTION AFTER MYOCARDIAL INFARCTION

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Objective: Left ventricular (LV) remodeling may occur following myocardial infarction. Estimate the likelihood of remodeling from the state of the infarcted may with speckle tracking echocardiography (STE). Research