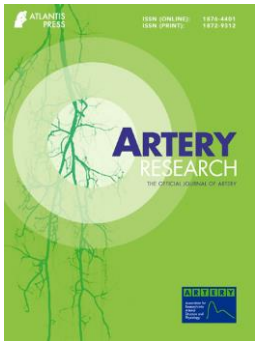

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6.6: AORTIC-BRACHIAL STIFFNESS MISMATCH IN PATIENTS WITH ARTERIAL HYPERTENSION AND TYPE 2 DIABETES MELLITUS

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Background: Arterial stiffness may provide non-invasive information about cardiovascular risk in patients with type 2 diabetes. We investigated the association between arterial stiffness and subclinical coronary atherosclerosis in patients with type 2 diabetes and healthy controls.
Methods: Patients with type 2 diabetes and controls were recruited from an on-going study on diabetes complications. Arterial stiffness (carotid-femoral pulse wave velocity [PWV]) was obtained by applanation tonometry (SphygmoCor®, Australia) whereas volumes [mm^3] of total [TP], calcified [CP], non-calcified [NCP], and low density non-calcified coronary plaques [LD-NCP]) were obtained by coronary CT-angiography and analyzed by semi-automative software (Autoplaq®, USA). A two-part model was used to describe the association between PWV and 1) the presence of plaques in all participants and 2) the extent of plaques in participants with coronary atherosclerosis.
Results: PWV and coronary atherosclerosis data were available for 49 patients and 63 controls (age 63±10 years, 49% males, diabetes duration 7.7±1.5 years). Patients had higher PWV than controls (9.6±2.4m/s vs. 8.4±1.8m/s, $p<0.01$). PWV was associated with the presence of plaques in crude analysis (odds ratio per 1m/s increase in PWV: TP 1.5, $p<0.01$, CP 1.4 $p<0.01$, NCP 1.4 $p<0.01$ and LD-NCP 1.3 $p=0.03$) but not in analysis adjusted for age, sex, blood pressure, and diabetes. In the presence of coronary plaques, PWV was associated with the extent of LDNCP (crude: 1.2 mm^3/m/s, $p<0.01$ adjusted: 1.2mm^3/m/s, $p=0.02$).
Conclusion: The presence and the extent of coronary atherosclerosis is associated with PWV in patients with type 2 diabetes and healthy controls.

6.4
LARGE AND SMALL ARTERY CROSSTALK IN PATIENTS WITH TYPE 2 DIABETES

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Background: Vascular complications to diabetes mellitus have, traditionally, been divided in to micro- and macroangiopathy. However, a growing body of evidence has put this categorical division into question, as large artery stiffness has been associated with microvascular complications in diabetics, e.g. diabetic retinopathy. The pathophysiology behind this association is poorly understood. The retinal arterioles lack sympathetic innervation and blood supply is autoregulated to accommodate changes in blood pressure and metabolic demand. Recently, dynamic vessel analysis of the retina, has made direct observation of the dynamic function of the microvascular bed of the retina feasible (spontaneous vessel oscillations). However, the crosstalk between dynamic retinal arteriole functioning and large artery stiffness remains to be elucidated.
Methods: We will include 20 type 2 diabetics and 20 sex- and age-matched controls. Arterial stiffness (carotid-femoral Pulse Wave Velocity) is assessed using applanation tonometry (SphygmoCor). Retinal blood supply regulation is examined using the Dynamic Vessel Analyzer under two conditions: i) during exposure to flickering lights which increases the metabolism of the retina, and ii) during static exercise (hand-weight lifting) which elevates systemic blood pressure.
Results: Results will be ready for presentation at the congress. Currently, 7 participants have been examined and 16 more participants have been recruited. Study completion September 2016.
Perspectives: This study provides new insight into large-small artery crosstalk. We hypothesize that large artery stiffness is associated with reduced spontaneous vessel oscillations and perturbed retinal blood flow regulation.

6.5
ASSOCIATION BETWEEN INCREASED ARTERIAL STIFFNESS AND HBA1C AND LDL CHOLESTEROL LEVEL IN TYPE 2 DIABETES PATIENTS

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Background: In patient with type 2 diabetes mellitus (T2DM) the atherosclerosis apper in younger age, in both gender and the cardiovascular risk is much higher. The aim of our study was to examine the association between pulse wave velocity (PWV) and glycated haemoglobin (HbA1c) and low density lipoprotein (LDL-C) level in patient with T2DM. (1,2)
Methods: We performed a prospective observational study, outpatient measurement included: aorta PWV measured by arteriograph, HbA1c and LDL-C level. The cut off-points are: PWV: 9 m/s, LDL-C: 2,5 mmol/l, HbA1c: 6%. In the first part of the analysis were included 169 patients with T2DM (106 men, 63 women, average age: 59 year), and were 152 patients (99 men, 53 women, average age: 59 year) in the second part. Linear regression analysis was carried using SPSS software.Values of $p<0.05$ were considered to be statistically significant.
Results: In the first investigation we found signicantly higher PWV in 87 patients (51%), mean: 9,27 m/s. The LDL-C level was higher than 2,5 mmol/l in 67% of cases, mean: 2,935 mmol/l. The second investigation underline a strict linear association between PWV and HbA1c (means: PWV: 9,286 m/s, HbA1c: 6,792 %.)
Conclusion: Our studies show parallel association between elevated HbA1c and PWV, as well as between higher LDL-C and PWV, which represent the elevated arterial stiffness (AS). Measurement of arterial stiffness can provide additional information about cardiovascular risk in patient with T2DM, which support the importance of arteriograph the only type of non-invasive method for AS measurement. (3,4)
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6.6
AORTIC-BRACHIAL STIFFNESS MISMATCH IN PATIENTS WITH ARTERIAL HYPERTENSION AND TYPE 2 DIABETES MELLITUS

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Background: Patients with type 2 diabetes have a high risk of CVD. Arterial stiffness gradient is a new prognostic predictor of mortality previously assessed only in dialysis population[1-2].
The aim of the study was to assess arterial stiffness and stiffness gradient in diabetic patients with arterial hypertension (AH).
Methods: The study included 55 patients with AH and DM (38% male, mean age 61.6±12.7 years), mean office BP 142.5±25.5/82.7±10.7mmHg. All patients receive combination antihypertensive therapy, 7.27% of patients received statins. Target BP values (<140/85 mmHg) were achieved in 52.7% of patients. Target HbA1c levels were achieved in 10.9% of patients. Carotid-femoral (CF) and carotid-radial (CR) PWV were assessed and increased arterial stiffness was defined as an elevation of pulse pressure

(PP)>60 mmHg,PWV>10 m/s. Stiffness gradient was assessed by CF-PWV/CR-PWV ratio, with values>1 indicating the stiffness mismatch.p<0.05 was considered significant.
Results: Mean PP was 47.6±12.7mmHg. PP>60mmHg was observed in 18,1%.Group with PP>60 mmHg was characterized by higher HbA1c (9.8±1.8vs8.4±2.0%) and stiffness gradient (1.4±0.4vs1.2±0.1)p<0.05 for trend. Mean CR-PWV was 7.7±1.2 m/s, mean CF-PWV was 10.3±2.0 m/s. CF-PWV>10m/s was observed in 27.2% of patients. Groups with PWV above and below 10m/s were similar by age, gender, metabolic risk factors and haemodynamic parameters. Mean stiffness gradient was 1.3±0.4, gradient >1 was observed in 92,7%. Patients with high stiffness gradient were older (63.3±11.6vs54.0±10.2,p<0.05). All other parameters were similar.
Conclusion: Patients with AH and type 2DM are characterized by aortic-brachial stiffness mismatch. Thus it can be used as early marker of vascular ageing in this patients' population.
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6.7
FIRST EVIDENCE OF PULSATILE PRESSURE INTERACTION BETWEEN THE MACRO-VASCULATURE AND MICRO-VASCULATURE: PROOF-OF-CONCEPT BY ASSOCIATION WITH KIDNEY DYSFUNCTION AMONG PATIENTS WITH TYPE 2 DIABETES

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Objectives: It is widely thought that excess pulsatile pressure energy from increased stiffness of large central arteries (macro-vasculature) is transmitted to capillary networks (micro-vasculature) and causes end-organ damage (i.e. kidneys). However, this hypothesis has never been tested, and we sought to achieve this by examining people with increased macro-vascular stiffness (patients with type 2 diabetes T2DM) compared with non-diabetic controls.
Methods: Among 13 T2DM (68±6 years) and 15 controls (58±11 years) macro-vascular function was measured by aortic stiffness and radial artery waveforms by tonometry. Forearm micro-vascular waveforms were simultaneously measured via low power laser Doppler flowmetry, with augmentation index (AIx) and augmented pressure (AP) derived on all waveforms. Kidney function was assessed by estimated glomerular filtration rate (eGFR).
Results: Aortic stiffness was higher among T2DM (9.3±2.5 vs 7.5±1.4 m/s, p=0.046). There was an obvious pulsatile micro-vascular waveform, with qualitative features similar to radial waveforms. Macro-vasculature AIx and AP were significantly related to micro-vasculature AIx (r=0.428. p=0.005 and r=0.545, p=0.004 respectively). Micro-vascular (but not macro-vascular) AIx was associated with eGFR in T2DM (r=-0.632, p=0.037).
Conclusions: This is the first in-human evidence of pulsatile pressure interaction between the macro-vasculature and micro-vasculature, and provides potential explanation for accelerated kidney dysfunction.

6.8
THE RELATIONSHIP BETWEEN DIASTOLIC FUNCTION AND CENTRAL HEMODYNAMICS IN DIABETIC HYPERTENSIVE PATIENTS

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Background: Diabetic hypertensives patients present different hemodynamic pattern than only hypertensive patients. We aimed to investigate the relationship between the diastolic function and the pulse pressure amplification (PPA), an index combining both arterial stiffness and wave reflexion, in diabetic hypertensives subjects compared to hypertensive subjects.
Methods: We examined 123 patients admitted to the one day hospital of the Hotel-Dieu Hospital (Paris, France) for cardiovascular risk assessment. Anthropometric, laboratory and clinical measurements were collected. Hemodynamic parameters (central blood pressure, aortic pulse wave velocity [PWV], augmentation index [AIx] and PPA) were measured using applanation tonometry. Standard ultrasound echocardiography was performed.
Results: Diabetic hypertensive subjects (n=44) were older than hypertensive subjects (n=79) (mean age[SD] 64[9] vs 56[14], p<0.05), and they presented similar cardiovascular risk factors frequencies. Gender was equally distributed. The diastolic function, assessed by the E/E' ratio was significantly positively correlated with PWV in total population (r=0.19, p=0.03), with no differences between the two groups. At the contrary, E/E' ratio was not correlated with PPA in total population, but it was significantly and negatively correlated with PPA only in the diabetic group (p for interaction 0.007, r= - 0.35, p=0.02). The multiregression analysis (containing all the confounding variables) in this group revealed as significant (p value<0.05) determinants of PPA: the diastolic function (partial-R2=0.14), gender (partial-R2=0.27), heart rate (partial-R2=0.26), angiotensin blockers treatement (partial-R2=0.13).
Conclusion: We confirmed that diabetic hypertensive patients have different hemodynamic behaviour than hypertensive non-diabetic patients. The results suggest that the mechanisms linking diastolic function with PPA are more prominent in diabetic patients.

6.9
ANTIPLATELET AND VASCULAR EFFECTS OF ASPIRIN IN HEALTHY PERSONS AND PATIENTS WITH TYPE 2 DIABETES

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Background: Treatment with aspirin is a cornerstone in the secondary prevention of cardiovascular disease (CVD) in diabetes, whereas its place in primary prevention remains controversial.
The effect of once-daily aspirin on platelet aggregation is unclear in patients with diabetes. Furthermore, the effects of aspirin on endothelial-dependent vasodilation and arterial stiffness, both important predictors of CVD, needs to be clarified.
Our aim is to investigate both the acute and the chronic effects of aspirin on platelet aggregation, endothelial-dependent vasodilation and arterial stiffness during 24 hours in patients with type 2 diabetes without CVD and in healthy controls.
Method: Based on power calculations, we will include 21 patients with type 2 diabetes and 21 sex and age-matched controls. Platelet aggregation is measured by impedance aggregometry, whereas arterial stiffness (carotid-femoral pulse wave velocity) is assessed by applanation tonometry. Endothelial-dependent vasodilation is assessed by peripheral arterial tonometry.
Outcome variables will be obtained at baseline and 1 hour after administration of aspirin. Participants are then treated for 6 days with once-daily aspirin and measurements are performed again 24 hours and 1 hour after aspirin intake.
Results: Preliminary results will be ready for presentation at the congress.
Perspective: This study provides new insight into whether once-daily dosing of aspirin is sufficient for effective platelet inhibition during 24 hours in patients with type 2 diabetes without CVD. Furthermore, this study will clarify if aspirin has positive effects on endothelial-dependent vasodilatation and arterial stiffness and if these effects are obtained effectively using a standard once-daily regimen of aspirin.

6.10
PERIPHERAL SENSORY NEUROPATHY AND VASCULAR ANGIOGENIC FACTORS IN TYPE 2 DIABETES PATIENTS IN GHANA

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Background: Impaired angiogenesis may be amongst the possible mechanism underlining the development of peripheral sensory neuropathy (PSN) in type