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4.1

PULSE WAVE VELOCITY CHANGES OVER A FOUR YEARS FOLLOW UP: SYNERGIC EFFECTS OF DIABETES AND HYPERTENSION

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Objective: the presence of diabetes mellitus puts hypertensive patients in high cardiovascular risk class. Diabetics patients have higher arterial stiffness but scanty data are available on its changes over time. Aim of this study was to provide information about the time course of PWV alterations in treated hypertensives and diabetics during 4 years-follow up.

Design and Method: We enrolled 348 treated hypertensive patients, among them 38 were diabetics (HTD, 61±11yrs, mean±SD) while others were only hypertensives (HT, 54±13yrs.). At baseline (t0), we collected for all of them clinical history, anthropometric parameters, clinic blood pressure (BP), cf-PWV (Complior), IMT and creatinine levels. Four years later (t1), we reassessed cf-PWV.

Results: After adjusting for age we didn't find statistical differences between HTD and HT at T0 for: BP(146.5±16/85±11 vs 140.5±19/86±10mmHg), creatinine (0.85±0.15vs0.86±0.19mg/dL), IMT (0.68±0.17vs0.65±0.18mm) and PWV (11.6±2.4vs10.6±2.4m/s). Interestingly, HTD increased their PWV significantly more than HT in 4 years (t1PWV-t0PWV= 2.36±4.4m/s vs 0.71±2.8m/s, P adjusted for age= 0.0099). Moreover, at a multivariate analysis, diabetes, age and baseline PWV were independent predictors of PWV increase, while baseline PWV was predictive of PWV decrease in four years (r2 (PWV+age+diabetes)= 0.3040, t0PWV beta:-0.65, P<0.0001; age beta: 0.074, P<0.0001; diabetes beta 1.044, P=0.0332).

Conclusions: During 4 years in a population of treated hypertensive, diabetics showed an higher increase in PWV's values this change being influenced by age and diabetes presence. Our data confirm the synergism between hypertension, diabetes and aging in inducing and increase of arterial stiffness along the time.

Funding: EU-MASCARA project -FP7/2007-2013 .

4.2

WINDKESSEL-MODEL DERIVED RESERVOIR AND EXCESS PRESSURES PREDICT CARDIOVASCULAR EVENTS IN HIGH-RISK PATIENTS

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Background and aim: It has been shown that measures derived from arterial waveforms, mostly related to wave reflection (Augmentation Index, Amplitude of backward travelling wave Pb), independently predict cardiovascular events. The aim of this work is to investigate the predictive value of parameters related to the Windkessel model (reservoir pressure - PR and excess pressure - PE).

Methods: Recently we developed an algorithm to calculate PR and PE, based on a 2-element Windkessel model, which can be applied on central waveforms derived with a transfer function from radial tonometry.

Results: We investigated 674 patients (mean age 63, 381 men, 126 diabetics, 271 coronary artery disease). After a mean follow-up duration of 1382 days, 135 patients suffered from a cardiovascular event (death, myocardial infarction, stroke, coronary, cerebrovascular and peripheral revascularization).

In univariate analysis, the areas under the reservoir and excess pressure (AR, AE) as well as their amplitudes (PR, PE) were significant predictors of cardiovascular events – Table. In multivariate Cox regression models (including among others: age, gender, mean BP, heart rate, diabetes, hypertension, smoking and coronary artery disease), PR was an independent predictor with a hazard ratio of 1.369 per 1 standard deviation (p=0.016).

Conclusions: Parameters derived from Windkessel models (reservoir and excess pressure) are associated with cardiovascular events in a cohort of high-risk patients.

Parameter	HR (per SD) (univariate)	p-value	HR (per SD) (multivariate)	p-value
PR	1.335	0.0001	1.369	0.016
PE	1.199	0.036	1.072	0.49
AR	1.214	0.014	1.257	0.11
AE	1.204	0.025	1.139	0.22
Pb	1.359	<0.0001	1.422	0.006
PP brachialis	1.349	<0.0001	1.184	0.08

4.3

SEGMENTAL AORTIC STIFFNESS DETERMINED BY THE ASSOCIATION OF ELASTIN DEGRADATION AND CALCIUM DEPOSITION IN RAT MODELS OF HYPERTENSION AND AORTIC CALCIFICATION

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Background: Aortic stiffness can be assessed by pulse wave velocity (PWV) and is determined by the integrity of elastin lamellae, elastin and collagen content and wall matrix constituents. This study investigates extracellular matrix changes in the thoracic and abdominal aorta in rat models of hypertension and aortic calcification.

Methods: PWV was determined at 110 mmHg in spontaneously hypertensive (SHR) and normotensive rats (WKY), and in WKY induced with aortic calcification by vitamin D and nicotine injection (VDN); 6 rats in each group. Thoracic and abdominal aortic segments were perfusion fixed (110mmHg) and processed for calcium quantification and histological staining for elastin and collagen. An elastin fragmentation index was obtained as a percentage of fractured lamellae.

Results: Compared with WKY, both SHR and VDN showed higher PWV in the thoracic aorta (Table), but only VDN showed higher PWV in the abdominal aorta. Both VDN and SHR showed lower density of inter-lamellar elastin but not collagen content in the thoracic aorta, resulting in lower elastin/collagen ratio in the thoracic (SHR and VDN) and abdominal aorta (VDN) compared with WKY. Greater degree of elastin lamellae fragmentation was observed in the thoracic aorta of SHR and in abdominal aorta of VDN, both associated with increased calcium content.

Conclusion. Aortic stiffness is determined by elastin degradation, in addition to blood pressure, in hypertension and aortic calcification. Findings are consistent with elastin fragmentation being a possible stimulus for trans-differentiation of smooth muscle cell phenotype, leading to increased calcium deposition in the arterial wall.

Parameter	Segment	WKY	SHR	VDN
Mean pressure (mmHg)		96 ± 9	141 ± 7*	98 ± 10
Pulse wave velocity (m/sec)				
Pulse wave velocity (m/s)	Thoracic	3.6±0.5	4.6±0.1*	4.0±0.1*
	Abdominal	5.5±2.0	5.5±1.8	8.1±2.0*
Calcium content (μmol.g ⁻¹)	Thoracic	27±6	128±20*	250±22*
	Abdominal	39±7	346±28*†	856±22*†
Inter-lamellae elastin density (%)	Thoracic	18±3	13±4*	13±4*
	Abdominal	24±5	19±3	19±4
Elastin fragmentation index (%)	Thoracic	22±14	34±21*	25±12
	Abdominal	22±11	32±8	33±23*
Elastin/collagen ratio	Thoracic	1.5±0.2	0.9±0.2*	1.3±0.3*
	Abdominal	1.8±0.6	1.3±0.4	1.0±0.3*

* P<0.05 compared to WKY. † P<0.05 compared to thoracic aorta