Determinants of inappropriately high pulse wave velocity in hypertensive patients: a retrospective cross-sectional cohort study

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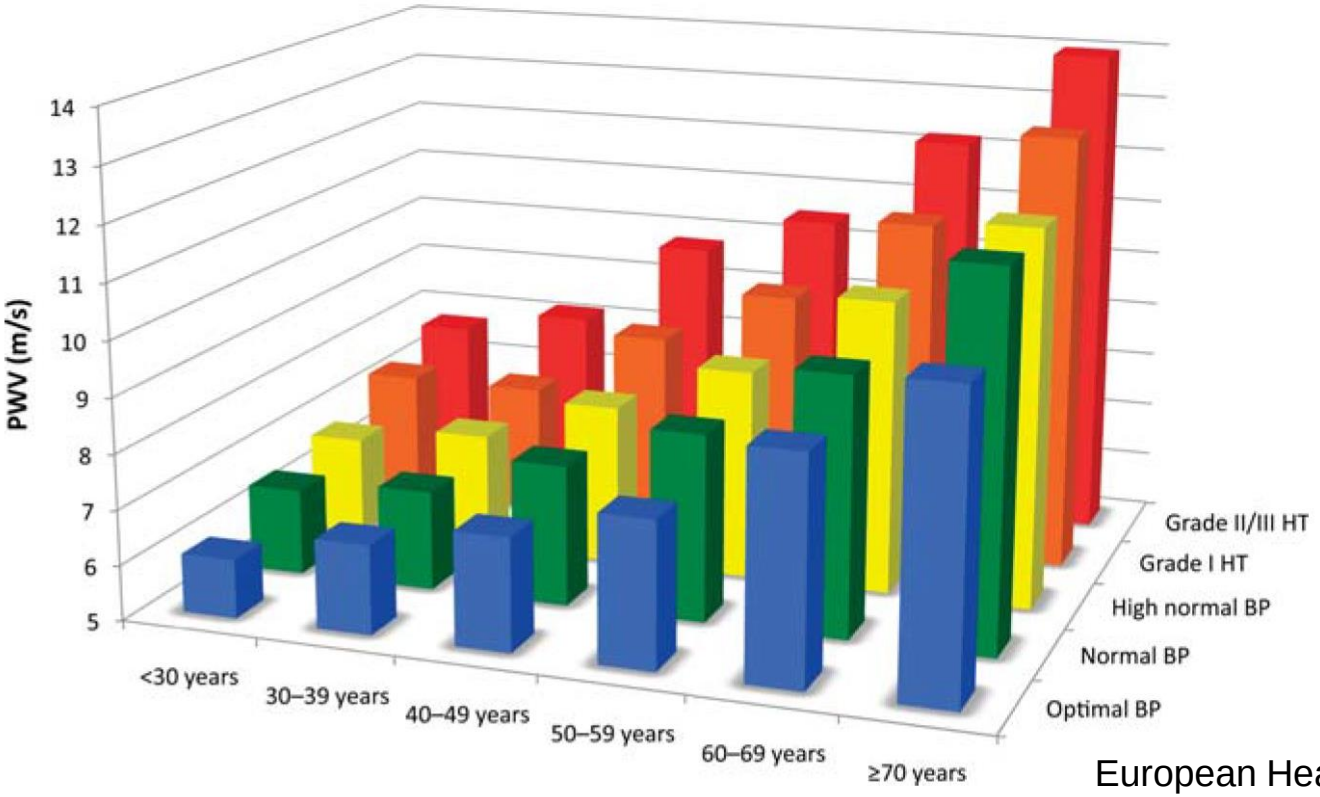
Reference values for carotid-femoral PWV

The publication of normal and reference values for PWV represented a critical step in the implementation of PWV as a clinical tool for detecting subclinical organ damage in routine patient workup

They have been cited 108 times, mainly to support the fact that age and blood pressure (BP) are the main determinants of large artery stiffness.



European Heart Journal (2010) 31, 2338–2350

Inappropriate LV mass in hypertensive patients

Inappropriate LV mass is calculated as the ratio of observed LV mass to the value predicted for an individual's gender, height, and stroke work at rest

Ambulatory Blood Pressure and Metabolic Abnormalities in Hypertensive Subjects With Inappropriately High Left Ventricular Mass

Vittorio Palmieri, Giovanni de Simone, Mary J. Roman, Joseph E. Schwartz, Thomas G. Pickering, Richard B. Devereux

Cardiac Remodeling

Inappropriate Left Ventricular Mass Changes During Treatment Adversely Affects Cardiovascular Prognosis in Hypertensive Patients

Maria Lorenza Muiesan, Massimo Salvetti, Anna Paini, Cristina Monteduro, Gloria Galbassini, Bianca Bonzi, Paolo Poisa, Eugenia Belotti, Claudia Agabiti Rosei, Damiano Rizzoni, Maurizio Castellano, Enrico Agabiti Rosei

Palmieri V et al. Hypertension. 1999;34:1032-1040
Muiesan ML et al. Hypertension . 2007;49:1077-1083

Hypothesis / aim of the study

Hypothesis:

many factors may lead to an inappropriately high pulse wave velocity (PWV) on top of age and blood pressure.

Aim of the study:

to investigate the determinants of inappropriately high PWV in hypertensive patients, and their possible role in causing organ damage accrual.

Methods: study design

- Design: retrospective, cross-sectional study
- Study population: 731 hypertensive patients aged 30-88 years seeking medical consultation in a outpatient Hypertension Unit (Pisa) during a 5-year period (2006–2011) and performing carotid-femoral PWV
- Exclusion criteria: known secondary hypertension, previous CV events
- Data collected:
  - Medical and drug history
  - Blood exams for CV risk assessment
  - Cardiac and carotid ultrasound
  - Carotid-femoral PWV

Methods: inappropriate PWV ratio oPWV/pPWV

- "Reference values" population: 11092 individuals selected from the Reference Values for Arterial Stiffness Collaboration database (13 centres across eight European countries):
  - With PWV data
  - Without overt CV disease, diabetes, secondary hypertension, treatment for hypertension and/or dyslipidemia

- Regression equations for PWV vs. mean BP according to age categories

	PWV ~ MBP
Age category (years)	
<30	PWV = 0.0472 × MBP + 2.20
30–39	PWV = 0.0423 × MBP + 2.20
40–49	PWV = 0.0646 × MBP + 1.41
50–59	PWV = 0.0731 × MBP + 1.35
60–69	PWV = 0.0715 × MBP + 3.16
≥70	PWV = 0.0676 × MBP + 5.46

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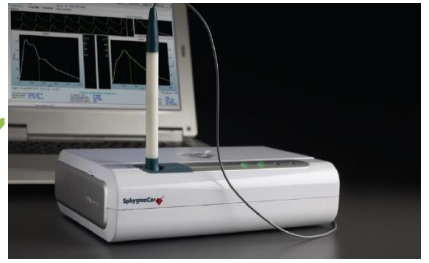
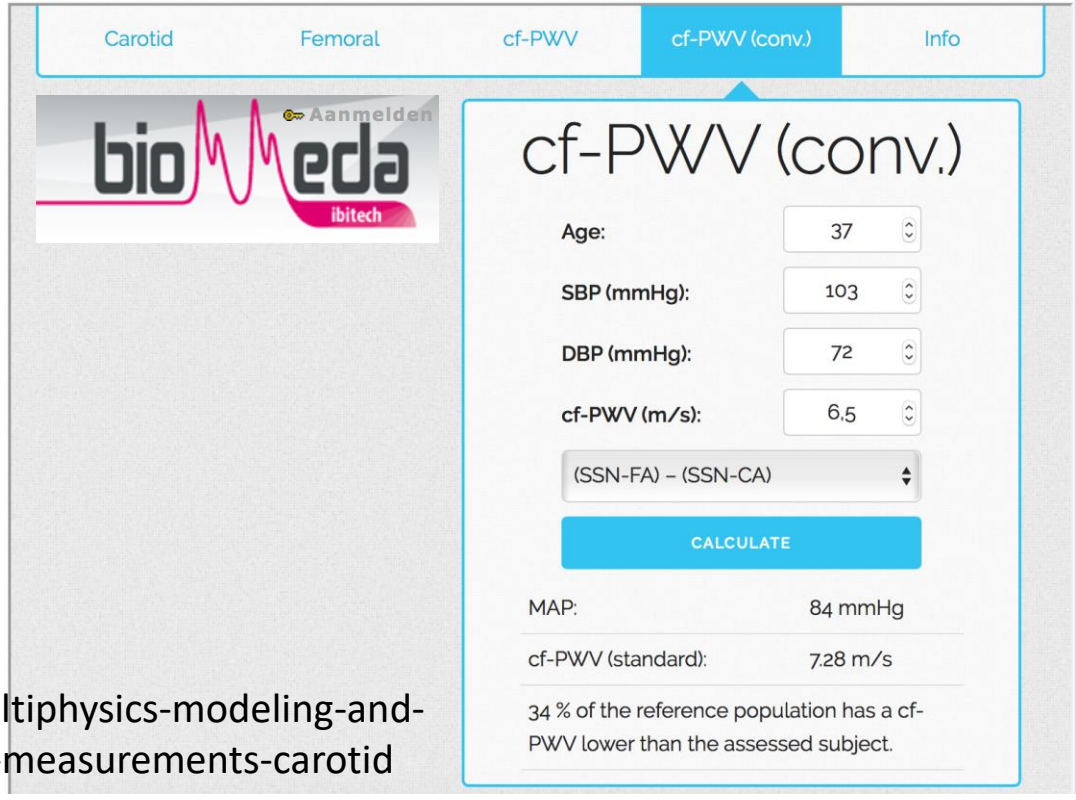
- Inappropriately high pulse wave velocity (PWV) was calculated as the ratio between the observed value and the values predicted according to the formula derived from international reference values stratified by age and mean BP (oPWV/pPWV).

Methods: Observed carotid-femoral PWV oPWV

- Device: Sphygmocor system ✔
- Transit time: detected by intersecting tangent algorithm ✔
- Path lenght: subtracted distance ✔



Conversion from (SSN-FA) – (SSN-CA) distance and direct distance*0.8 was obtained by the online calculator:

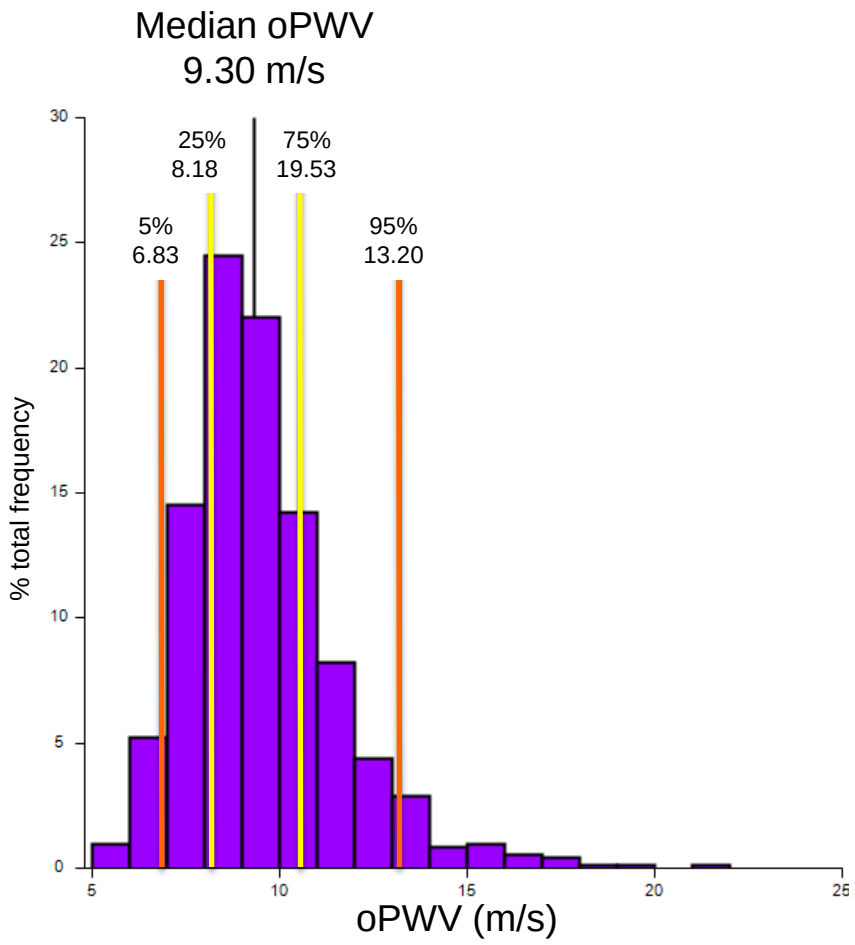


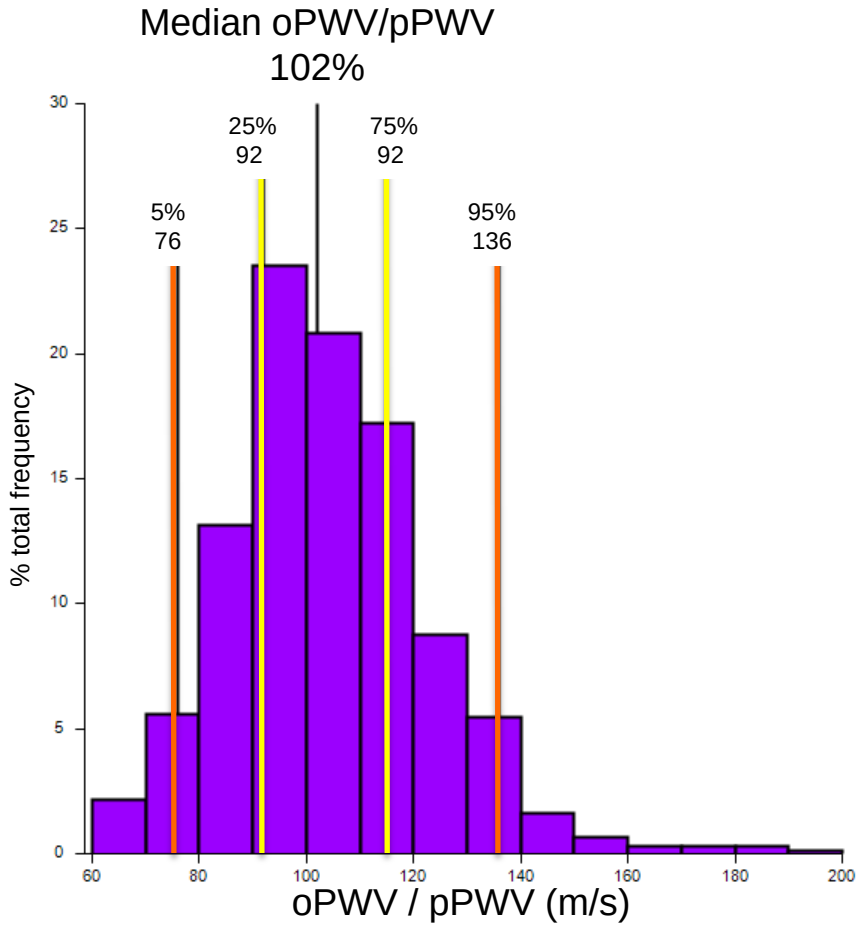
http://www.biommeda.ugent.be/research/multiphysics-modeling-and-cardiovascular-imaging/calculator-assessment-measurements-carotid

Results: study population

Variable	Overall population n= 731	Men n =425	Women n = 306	P value
Age (years)	55.7 ± 11.2	54.1 ± 11.3	57.9 ± 10.7	<.0001
Daylight hours (hours)	12.0 (9.5 – 14.8)	12.0 (9.5 – 14.8)	12.3 (9.5 – 14.8)	0.42
BMI (kg/m²)	26.8 (24.4 – 29.6)	27.1 (25.3 – 29.6)	25.8 (23.1 – 29.6)	<.0001
Waist circumference (cm)	96 (88 – 103)	98 (92 – 104)	90.0 (83.5 – 98.5)	<.0001
Smoking (%)				0.003
Yes	15%	14%	17%	
Ex	17%	20%	11%	
No	68%	65%	72%	
Antihypertensive treatment (%)	57.2%	57%	57.5%	0.88
BP-lowering drugs	2 (1 – 2)	2 (1 – 2)	2 (1 – 2)	0.80
Lipid-lowering drugs	8%	6.1%	10.5%	0.034
Antidiabetic drugs	2.6%	3.8%	1%	0.019
Antithrombotic drugs	6.7%	5.2%	8.9%	0.052

Results: oPWV and oPWV/pPWV





Determinants of inappropriate PWV ratio: Univariate analysis

	oPWV		oPWV/pPWV	
	r	p	r	p
Age	0.467	<0.001	-0.299	<0.001
BMI	0.132	<0.001	0.138	<0.001
#BP-lowering drugs	0.089	0.018	-0.086	0.080
Mean BP	0.282	<0.001	0.008	0.826
Aortic PP	0.448	<0.001	-0.071	0.058
HR	0.116	0.003	0.169	<0.001
Total cholesterol	0.046	0.223	-0.074	0.055
HDL cholesterol	0.005	0.904	-0.082	0.033
Blood glucose	0.171	<0.001	0.122	0.002
Serum creatinine	0.109	0.006	0.017	0.676
Daylight hours	-0.175	<0.001	-0.158	<0.001

	oPWV			oPWV/pPWV		
	No	Yes	p	No	Yes	p
Male sex	9.58±1.93	9.54±2.22	0.288	102.4±18.3	105.6±18.6	0.039
Current smoking	9.61±2.11	9.30±1.70	0.365	103.5±18.1	108.7±20.3	0.009

Determinants of inappropriate PWV ratio: Multiple regression analysis

Multiple regression analysis

	oPWV			oPWV/pPWV		
	beta	**r^2**	**p**	**beta**	**r^2**	**p**
Age	**0.06**	**0.08**	**<0.001**	**-0.73**	**0.12**	**<0.001**
BMI	0.04	0.01	0.036	0.49	0.01	0.013
#BP-lowering drugs	-0.06	0.00	0.392	-0.93	0.00	0.180
Mean BP	0.04	0.02	<0.001	-0.25	0.01	0.002
Aortic PP	0.03	0.03	<0.001	0.29	0.02	<0.001
HR	0.03	0.02	<0.001	0.22	0.01	0.003
Sex=F	0.18	0.00	0.312	1.75	0.00	0.336
Total chol	-0.00	0.00	0.643	-0.02	0.00	0.448
HDL chol	0.00	0.00	0.485	0.03	0.00	0.634
Current smoking	-0.00	0.00	0.975	2.35	0.00	0.248
Blood glucose	**0.01**	**0.01**	**0.011**	**0.18**	**0.02**	**<0.001**
Serum creatinine	**0.83**	**0.01**	**0.008**	**6.17**	**0.01**	**0.059**
Daylight hours	-0.16	0.03	<0.001	-1.72	0.04	<0.001
Full r^2		**0.43**			**0.24**	

- Younger age, lower BP, higher BMI, high blood glucose are associated with inappropriately elevated PWV in hypertensive patients:
  - Age is correlated positively with oPWV, inversely with o/pPWV
  - Fasting blood glucose explained a greater proportion of o/pPWV than of oPWV variance
  - Increased serum creatinine is associated with oPWV but not with o/pPWV

Is inappropriate PWV ratio associated with TOD?

Multiple linear regression, LVMI as dependent variable

	beta	r^2	p
Model 1: oPWV + age, sex, meanBP	0,29	0,00	0,46
Model 2: oPWV + all confounders	0,05	0,00	0,91
Model 3: o/pPWV + age, sex, meanBP	0,03	0,00	0,42
Model 4: o/pPWV + all confounders	-0,00	0,00	0,92

Multiple logistic regression, presence of carotid plaques as dependent variable

	beta	OR (5-95%CL)	p
Model 1: oPWV + age, sex, meanBP	0,14	1,15 (1,01-1,30)	0,02
Model 2: oPWV + all confounders	0,15	1,17 (0,99-1,37)	0,06
Model 3: o/pPWV + age, sex, meanBP	0,01	1,01 (1,00-1,02)	0,01
Model 4: o/pPWV + all confounders	0,02	1,02 (1,00-1,03)	0,03

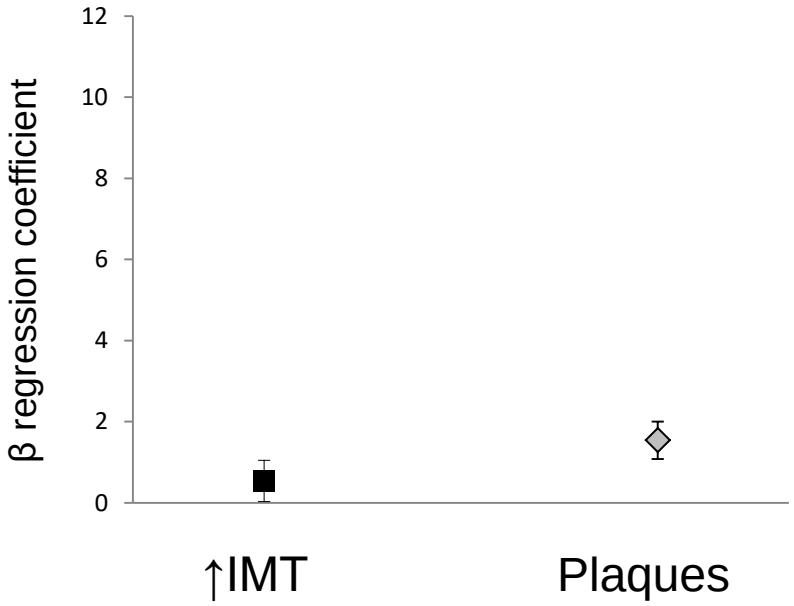
(Models 2 and 4 are adjusted for age, sex, smoking, daylight hours, BMI, blood glucose, total and HDL cholesterol, creatinine, mean BP, aortic PP, HR, #BP-lowering drugs)

Does atherosclerosis contribute to inappropriately elevated PWV ?

Multiple regression analysis, o/pPWV as dependent variable

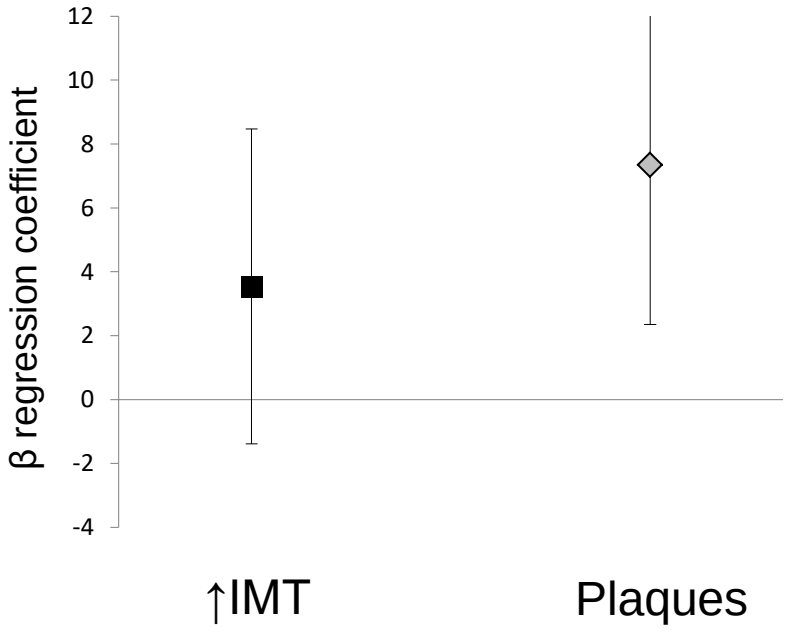
Unajusted beta (5-95%CL):

- Increased IMT 0.54 (0.03; 1.05)
- Plaques 1.54 (1.07; 2.00)



Fully adjusted beta (5-95%CL):

- Increased IMT 3.54 (-1.38; 8.47)
- Plaques 7.35 (2.36; 12.34)



(Fully adjusted model inncludes age, sex, smoking, daylight hours, BMI, blood glucose, total and HDL cholesterol, creatinine, mean BP, aortic PP, HR, #BP-lowering drugs)

Study 2: CATOD follow-up

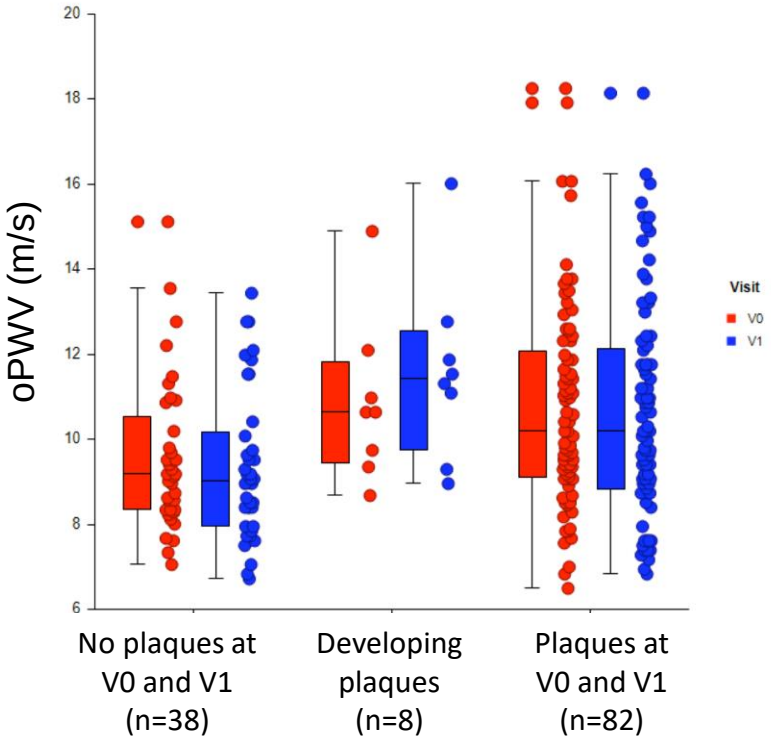
- CATOD is a cross-sectional study aimed at evaluating the relationship between carotid / aortic stiffness and hypertensive TOD and (Bruno RM et al. J Hypertens 2016, in press)
- CATOD follow-up cohort: 153 hypertensive patients, median follow-up 3 years

	No plaques at V0 and V1 (n=38)	Developing plaques (n=8)	Plaques at V0 and V1 (n=82)	P value
Age (years)	54.1	57.9	58.4	0.04
BMI (kg/m^2)	29.3	31.2	28.2	0.08
HT duration (years)	8	11	9	0.43
Mean BP (mmHg)	102	101	103	0.72
Brachial PP (mmHg)	56	63	62	0.07
Heart Rate (bpm)	70	75	67	0.13
Aortic SBP (mmHg)	127	131	134	0.09
Aortic PP (mmHg)	43	50	50	0.02
Blood glucose	118	159	109	0.009
Total cholesterol	191	191	222	0.0002
Triglycerides	161	145	150	0.76

Study 2: CATOD follow-up

oPWV

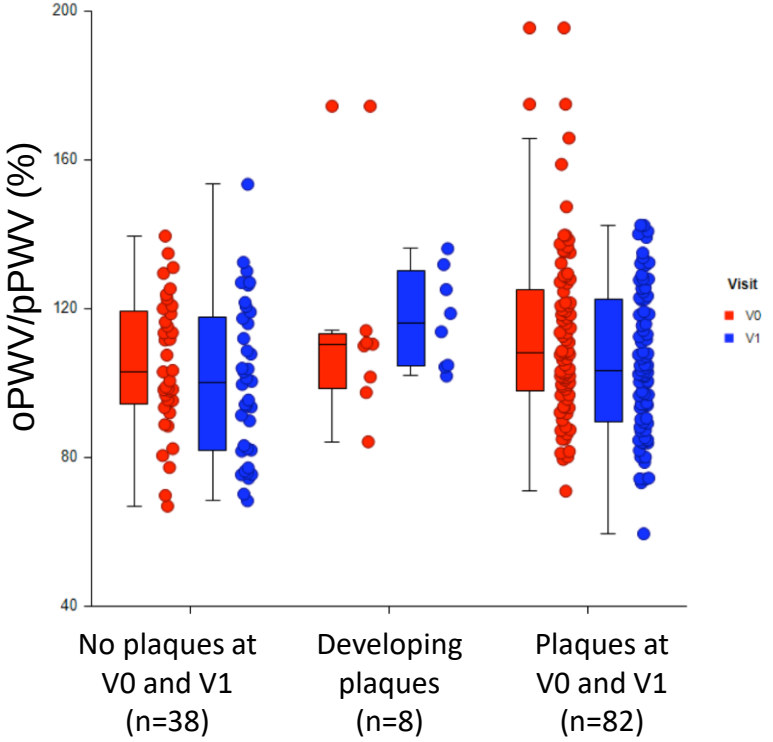
p for interaction plaques-visit = 0.45



from 10.88 to 11.61 m/s

oPWV/pPWV

p for interaction plaques-visit = 0.36



from 113.0 to 117.1 %

Conclusions (1)

In hypertensive patients, inappropriate PWV is associated with younger age and is related to high blood glucose more tightly than PWV

→ Use of inappropriate PWV instead of observed PWV might help to better depict vascular aging in younger hypertensives and in those with metabolic alterations

Increased serum creatinine is associated with oPWV but not with o/pPWV

→ Renal dysfunction in hypertension does not seem to promote arterial stiffening independent of age and BP load

There is a specific association between inappropriate PWV and carotid atherosclerosis

→ o/pPWV may favor atherosclerosis development. Conversely, a more advanced atherosclerotic process might also contribute to excess aortic stiffness than estimated by age and BP load

Perspectives

- The preliminary data from the CATOD follow-up cohort suggest that inappropriately high PWV might favor atherosclerosis development
- Whether an inappropriately high PWV translates into an increased cardiovascular risk (independent of observed PWV) is still unknown
- Longitudinal studies, adequately powered, are needed to ascertain these aspects

THANK YOU FOR THE ATTENTION !

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