Accelerated Arterial Aging in Hypertensive subjects

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HSH, March 2009



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Age-Associated Changes

in Arterial Structure and Vascular Biology during Aging

↑ Lumen size
↑ Intimal-Medial thickness
↑ Collagen, Fibronectine content
↑ Collagen non-enzymatic glycation
◆ Elastin (frayed, disorganized)
↑ Calcifications

Endothelial function
 Cytokines/ adh. molec

Phenotypes of arterial aging







Methods for evaluating Arterial Stiffness



- Peripheral and Central Pulse Pressure
- Stiffness Index (PP/MAP)
- Augmentation Index (Aul)
- Cross-Sectional Compliance (CSC)
- Flow-dependent dilation
- Pulse Wave Velocity (PWV)



Stiffness in hypertensives vs normotensives
Why hypertensives have stiffer arteries
Consequences of high art. stiffness
Can we prevent or regress stiffness



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BP and PWV in normotensive and hypertensive patients

Circulation March 12, 2002

TABLE 1. Demographic and Clinical Characteristics of Normotensive and Hypertensive Subjects During the First (1992–1993) and Second (1998–1999) Visits

	Normotensive Subjects (n=296; 64.5% male)		Treated Hypertensive Subjects (n=187; 63.1% male)	
	1st Visit	2nd Visit	1st Visit	2nd Visit
Age, y	47.6±0.6	54.1±0.6†	56.9±0.7‡	63.6±0.7†
BMI, kg/m ²	24.5±0.2	25.3±0.2†	26.6±0.3‡	27.9±0.4†
SBP, mm Hg	128.0 ± 0.7	129.5±0.9	144.5±1.0‡	149.7±1.3†
DBP, mm Hg	78.4±0.5	82.4±0.6†	88.3±0.7‡	87.2±0.7
MAP, mm Hg	94.9 ± 0.5	98.1±0.6†	$107.1 \pm 0.7 \ddagger$	108.0 ± 0.8
PP, mm Hg	49.6±0.4	47.1±0.7*	56.2±0.7‡	62.5±1.2†
HR, bpm	67.8 ± 0.7	65.5±0.5†	67.8±0.9	$65.8 \pm 0.7^*$
PWV, m/s	9.84±0.13	10.35±0.10†	11.40±0.19‡	12.23±0.18†
Cholesterol, mg/dL	228±3	231±3*	226±3	229±3
HDL, mg/dL	59.1 ± 1.0	64.8±1.1†	58.4±1.2	60.3 ± 1.6
Glucose, mg/dL	101.9 ± 1.1	97.3±0.8	106.2±1.4	102.0 ± 1.7
Triglycerides, mg/dL	89.2±4.2	100.2±4.6†	113.7±9.3‡	118.1±4.7†
Creatinine, mg/L	9.37 ± 0.09	9.95±0.08†	9.90±0.13‡	10.53±0.14†
Current smokers	20%	22%	12%‡	10%

*P<0.01 and †P<0.001, second vs first visit; $\ddagger P$ <0.001 normotensive vs treated hypertensive subjects.

Benetos A et al, Circulation 2002

PWV in subjects with Hypertension

	Women		Men	
	Normo.	Hyper.	Normo.	Hyper.
n	308	93	558	323
Age (years)	44 ± 13	$55 \pm 10^{***}$	45 ± 11	$51\pm10^{***\dagger\dagger}$
Weight (kg)	60 ± 11	$67 \pm 15^{***}$	$76\pm11^{\dagger\dagger\dagger}$	$\textbf{83} \pm \textbf{13}^{***\dagger\dagger\dagger}$
Height (cm)	161 ± 6	159 ± 7	$175\pm7^{\dagger\dagger\dagger}$	$173\pm7^{**\dagger\dagger\dagger}$
HR (beats/min)	71 ± 11	$79 \pm 12^{***}$	$67\pm10^{\dagger\dagger\dagger}$	$76 \pm 13^{***}$
SBP (mmHg)	125 ± 13	$165 \pm 14^{***}$	$132\pm12^{\dagger\dagger\dagger}$	$164 \pm 13^{***}$
DBP (mmHg)	76 ± 10	$101 \pm 9^{***}$	$81 \pm 9^{\dagger\dagger\dagger}$	$102 \pm 9^{***}$
MBP (mmHg)	91 ± 9	$122 \pm 8^{***}$	$96\pm8^{\dagger\dagger\dagger}$	$122 \pm 9^{***}$
PP (mmHa)	47 ± 8	$64 \pm 12^{***}$	$49\pm8^{\dagger\dagger}$	$62 \pm 12^{***\dagger}$
PWV (m/s)	8.5 ± 1.7	$11.0 \pm 2.4^{***}$	$8.8\pm1.6^{\dagger}$	$10.6 \pm 2.4^{***}$
l otal cholesterolaemia (mg/l)	212 ± 39	241 ± 41	219 ± 40^{1}	235 ± 43
HDL cholesterolaemia (mg/l)	66 ± 16	66 ± 16	$53\pm13^{\dagger\dagger\dagger}$	$54\pm16^{\dagger\dagger\dagger}$
Triglycerides (mg/l)	74 ± 68	$94\pm44^*$	$101\pm67^{\dagger\dagger\dagger}$	143 \pm 116***†††
Glycaemia (mg/l)	102 ± 30	106 ± 10	$107\pm14^{\dagger\dagger\dagger}$	115 \pm 25***†††

Table 1 Study 1: clinical, haemodynamic and biological parameters in women and men

Albaladejo J et al,. Hypertens. 2003

PWV in subjects with Hypertension and/or Diabetes

Table 1 Population characteristics (mean \pm SD)

	F	RVG		IDG
	Men	Women	Men	Women
n	95	111	150	99
Age (years)	66 ± 4	66 ± 4	67 ± 4	67 ± 4
BMI (kg/m²)	26 ± 3	25 ± 4	$29\pm\pm4^{\dagger\dagger\dagger}$	27 ± 4***,††
Waist (cm)	91 ± 9	84±12***	$99\pm10^{\dagger\dagger\dagger}$	87±10***
SBP (mmHg)	126 ± 9	120±13***	$144\pm17^{\dagger\dagger\dagger}$	$137 \pm 18^{***,111}$
DBP (mmHg)	72 ± 7	66±9***	$78\pm9^{\dagger\dagger\dagger}$	$73 \pm 11^{***,111}$
PP (mmHg)	54 ± 7	54 ± 10	$65\pm13^{\dagger\dagger\dagger}$	$64\pm14^{\dagger\dagger\dagger}$
MBP (mmHg)	90 ± 7	84±9***	$100\pm11^{\dagger\dagger\dagger}$	$95 \pm 12^{***,111}$
HR (beats/min)	66 ± 12	68 ± 9	66 ± 11	70±12**
Glycemia (mmol/l)	5.5 ± 1.0	5.1 ± 0.6**	$6.0 \pm 1.6^{\dagger\dagger}$	5.3±0.8***
Creatinine (µmol/l)	95 ± 13	79±9***	$102\pm14^{\dagger\dagger\dagger}$	84±14***,††
Cholesterol (mmol/l)	5.7 ± 0.9	5.9 ± 0.9	5.5 ± 1.0	5.8±0.9**
AoPWV (m/s)	8.8 ± 2.3	8.6 ± 2.2	$10.6\pm2.5^{\dagger\dagger\dagger}$	9.8±2.4**,††

Alecu et al, J. Hypertension 2008

E R A study

Progression in aortic stiffness according to the control of hypertension



Benetos et al, *Circulation 2002*

Age/aortic stiffness (PWV) relationship

The annual increase in PWV is about 70-100 mm/sec in NT 100-250 mm/sec in HT



PWV (m/sec)

personal data



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Distensibility: (Vs-Vd)/Vd/(SBP-DBP)

Stiffness is pressure dependent



Intrinsic Elastic properties preserved



Intrinsic Elastic properties modified



Chronic Hypertension

Endothelial dysfunction Increased mechanical stress Humoral factors

Accelerated Arterial Aging (Arteriosclerosis)







Arterial stiffness, and Blood Pressure regulation



Arterial hypertension and Arterial Stiffness



Brachial BP evolution with age. The Framingham Study



Franklin et al, Circulation 1997



•Why hypertensives have stiffer arteries •Associated factors

Metabolic syndrome and age-related progression of aortic stiffness (pulse wave velocity).

•Number	0	1	2	<u>></u> 3	р
•PWV (m/s)	9.4 (2.1)	10.7 (2.6)	11.2 (2.9)	12.2 (3.0)	0.0001
•∆PWVmm/sec/	year -20 (40)	90 (20)	50 (25)	145 (40)	0.003

M. Safar, F. Thomas, J. Blacher, R. Nzietchueng, JM. Bureau, B. Pannier, A. Benetos

J Am Coll Cardiol 2006, 3;47:72-5

E R A study

Progression in aortic stiffness according to the heart rate



Benetos et al, *Circulation 2002*

Arterial hypertension and large arteries





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Endothelial Dysfunction and Prognosis in Hypertensives

225 Never-Treated Hypertensives With ACh-Induced Forearm Blood Flow



Perticone F et al. Circulation. 2001;104:191-196.

PWV is an independent determinant of LV hypertrophy



Bouthier et al, Am Heart J 1985

PWV and all-cause mortality in hypertensive subjects



Arterial hypertension and large arteries





Thank you

Clinical Research GroupGeriatric Dpt Brabois Hospital

Anna Kearny-Scwartz
Cosmin Alecu
Laure Joly
Sylvie Gautier
Christine Perret
Paolo Salvi
Ghassan Watfa

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