
VASOTENS Registry

INTERNATIONAL REGISTRY FOR AMBULATORY BLOOD PRESSURE AND ARTERIAL STIFFNESS TELEMONITORING

VASOTENS Registry

Vascular health **AS**sessment **O**f **T**he hypert**ENS**ive patients

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Agenda of the start-up meeting

18:00 **Welcome**

Stefano Omboni
Igor Posokhov

18:05 **24-hour ambulatory arterial stiffness estimation: current status and perspectives**

Stefano Omboni

18:20 **The VASOTENS Registry: protocol, activities and schedule**

Stefano Omboni
Igor Posokhov

18:45 **Discussion**

24-hour ambulatory arterial stiffness estimation: current status and perspectives

Background

- ABP, central BP and PWV are parameters indicated by current hypertension guidelines as useful for better estimating BP control and vascular impairment of the hypertensive patient
- Recent advances in technology made available devices allowing combined non-invasive estimation of BP and arterial stiffness in ambulatory conditions over the 24-hours
- At present, there is limited evidence on the usefulness of such an approach in the clinical practice and much has still to be done to prove its actual benefit for hypertension management

VASOTENS Registry www.vasotens.org

European Heart Journal (2006) 27, 2588–2605
doi:10.1093/eurheartj/ehl254

Special article

Expert consensus document on arterial stiffness: methodological issues and clinical applications

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See page 2497 for the editorial comment on this article (doi:10.1093/eurheartj/ehl312)

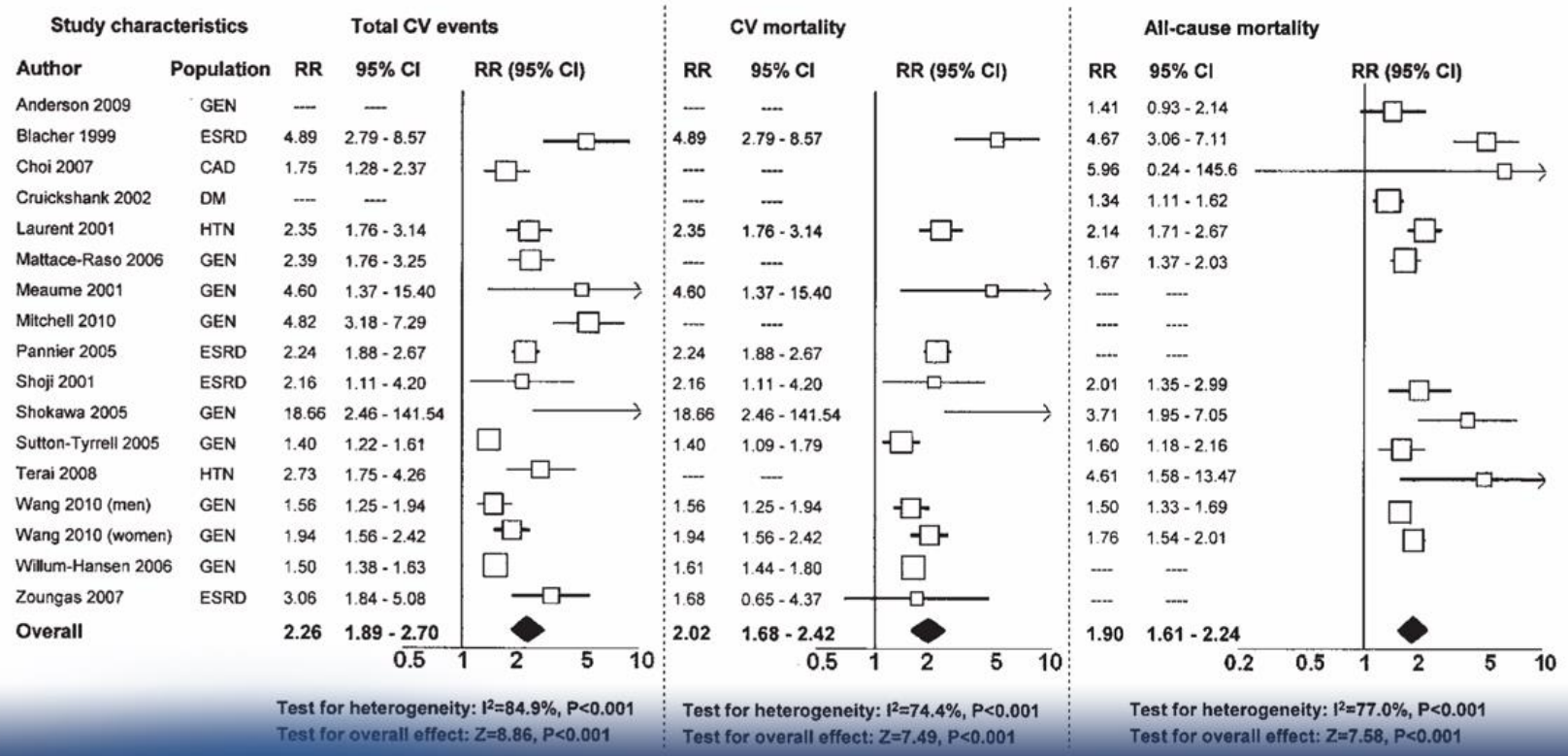
KEYWORDS

Position statement: Methods for measuring arterial stiffness in clinical practice and research

- **Carotid-femoral PWV** is considered as the **"gold standard" measurement of arterial stiffness**, has the largest amount of epidemiological evidence for its predictive value for CV events, and requires little technical expertise
- **Central pulse-wave analysis provides additional information concerning wave reflections**
- Pulse wave should be analyzed through three major parameters (central pulse pressure, **central systolic pressure and augmentation index**) and should be optimally obtained at the central level (at the site of the carotid artery or the ascending aorta, and either directly recorded or computed from the radial artery waveform using a transfer function analysis)
- Pulse wave analysis has demonstrated predictive value in ESRD, hypertensive and CAD patients, and requires little technical expertise

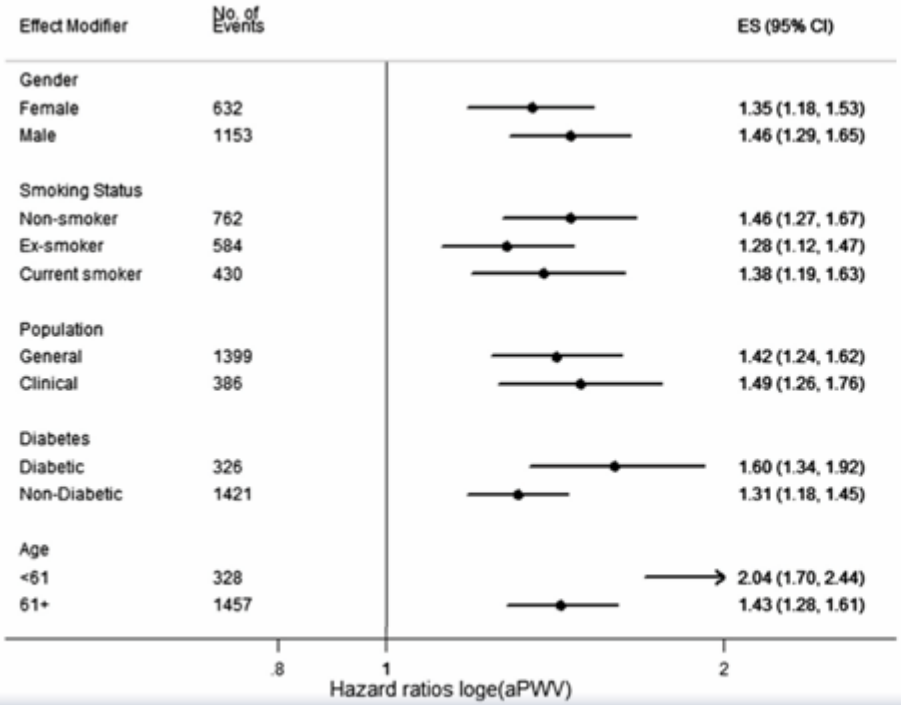
Laurent S. et al., Eur Heart J 2006;27:2588-2605

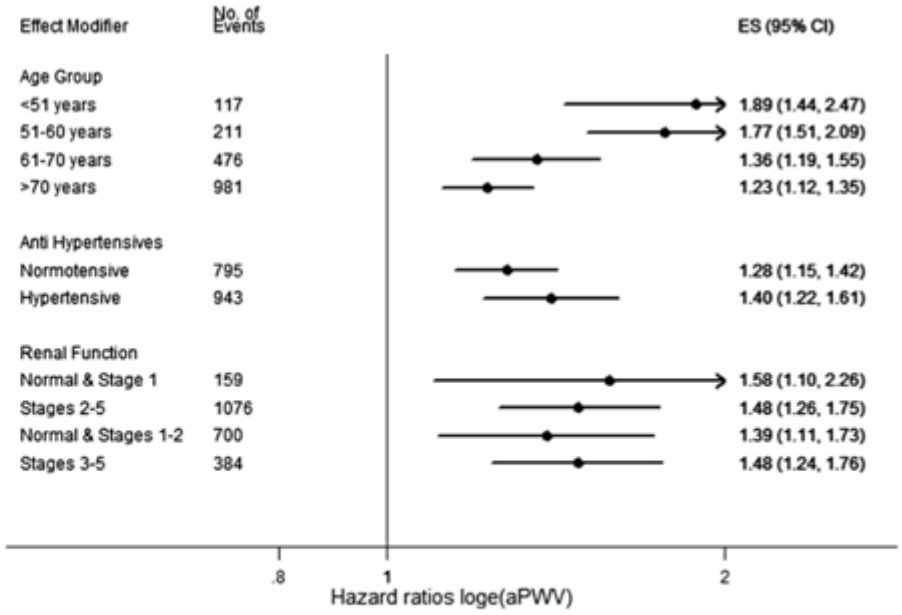
Aortic stiffness expressed as aortic PWV is a strong predictor of future CV events and all-cause mortality. The predictive ability of arterial stiffness is higher in subjects with a higher baseline CV risk



Vlachopoulos C. et al., JACC 2010;55:1318-1327

PWV may enable better identification of high-risk populations that might benefit from more aggressive CVD risk factor management (e.g. younger subjects, diabetics)



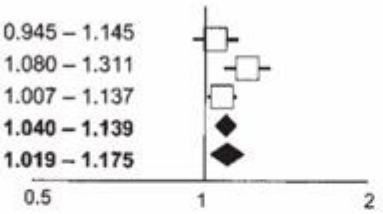


Ben-Shlomo Y. et al., JACC 2014;63:636-646

Central hemodynamic indexes are independent predictors of future CV events and all-cause mortality. AI predicts clinical events independently of peripheral pressures

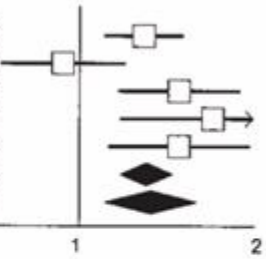
Central SBP and CV outcome

Author	Population	RR	95% CI
Dart 2006	HTN	1.040	0.945 – 1.145
Pini 2008	GEN	1.190	1.080 – 1.311
Roman 2007	GEN	1.070	1.007 – 1.137
Pooled (fixed)		**1.088**	**1.040 – 1.139**
Pooled (random)		**1.094**	**1.019 – 1.175**



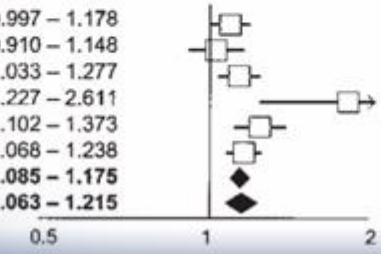
Central AIx and CV outcome

Author	Population	RR	95% CI
Chirinos 2005	CAD	1.280	1.091 – 1.502
Dart 2006	HTN	0.919	0.712 – 1.186
London 2001	ESRD	1.480	1.156 – 1.894
Ueda 2004	CAD	1.700	1.163 – 2.486
Weber 2005	CAD	1.480	1.109 – 1.976
Pooled (fixed)		**1.294**	**1.165 – 1.438**
Pooled (random)		**1.318**	**1.093 – 1.588**



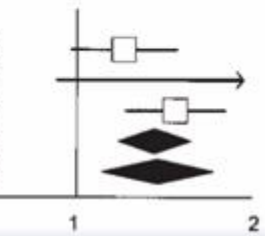
Central PP and CV outcome

Author	Population	RR	95% CI
Chirinos 2005	CAD	1.084	0.997 – 1.178
Dart 2006	HTN	1.022	0.910 – 1.148
Jankowski 2008	CAD	1.126	1.033 – 1.277
Lu 2001	CAD	1.790	1.227 – 2.611
Pini 2008	GEN	1.230	1.102 – 1.373
Roman 2007	GEN	1.150	1.068 – 1.238
Pooled (fixed)		**1.129**	**1.085 – 1.175**
Pooled (random)		**1.137**	**1.063 – 1.215**



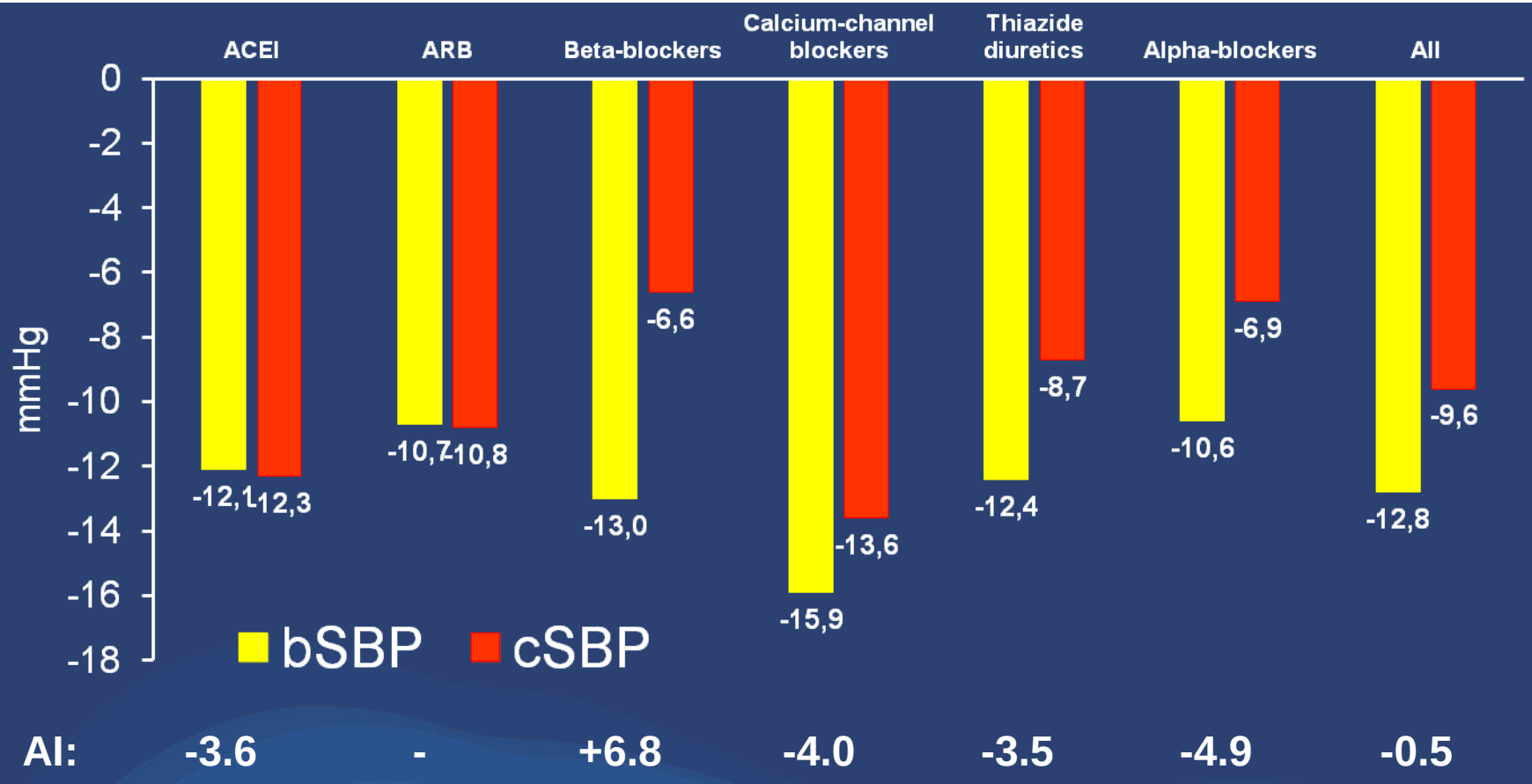
Central AIx and all-cause mortality

Author	Population	RR	95% CI
Chirinos 2005	CAD	1.220	1.098 – 1.519
Covic 2006	ESRD	2.805	0.924 – 8.517
London 2001	ESRD	1.510	1.228 – 1.857
Pooled (fixed)		**1.384**	**1.192 – 1.606**
Pooled (random)		**1.402**	**1.114 – 1.764**



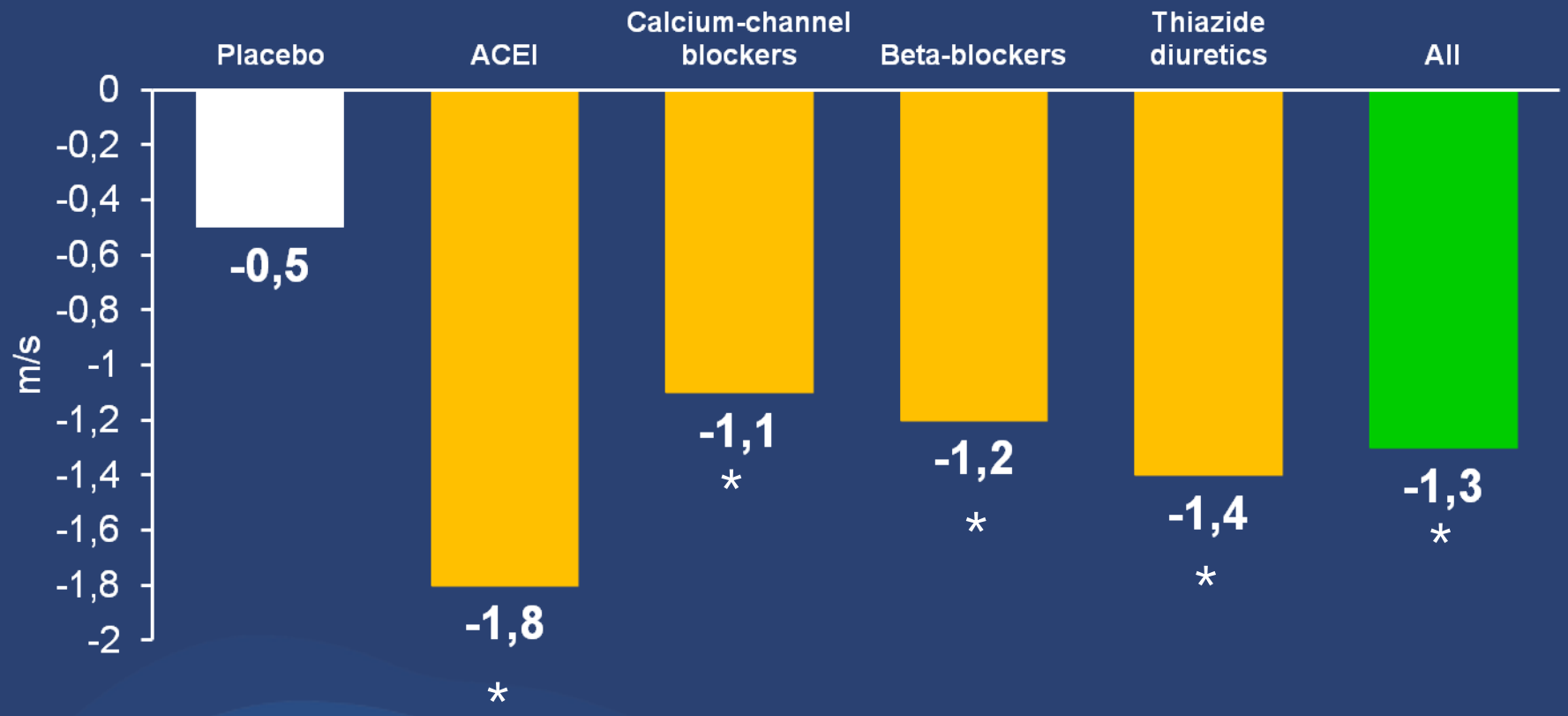
Vlachopoulos C. et al., Eur Heart J 2010;31:1865-1871

A reduction in central to brachial amplification by some classes of antihypertensive drugs (e.g. beta-blockers and thiazide diuretics) will result in lesser reductions in cSBP despite achievement of target bSBP, and in different effects on AI.



Manisty C.H. et al., Br J Clin Pharmacol 2013;75:79-92

Long-term antihypertensive treatment is associated with significant reductions in PWV vs. placebo, regardless of the magnitude of BP reduction and class of drug



*p<0.05 vs. placebo; changes are adjusted by age, gender, mean BP, HR and BMI

Ong K.T. et al., J Hypertens 2011;29:1034-1042

ESH and ESC Guidelines

2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

List of authors/Task Force Members: Giuseppe Mancia (Chairperson) (Italy)*, Robert Fagard (Chairperson) (Belgium)*, Krzysztof Narkiewicz (Section co-ordinator) (Poland), Josep Redón (Section co-ordinator) (Spain), Alberto Zanchetti (Section co-ordinator) (Italy), Michael Böhm (Germany), Thierry Christiaens (Belgium), Renata Cifkova (Czech Republic), Guy De Backer (Belgium), Anna Dominiczak (UK), Maurizio Galderisi (Italy), Diederick E. Grobbee (Netherlands), Tiny Jaarsma (Sweden), Paulus Kirchhof (Germany/UK), Sverre E. Kjeldsen (Norway), Stéphane Laurent (France), Athanasios J. Manolis (Greece), Peter M. Nilsson (Sweden), Luis Miguel Ruilope (Spain), Roland E. Schmieder (Germany), Per Anton Sirnes (Norway), Peter Sleight (UK), Margus Viigimaa (Estonia), Bernard Waeber (Switzerland), and Faiez Zannad (France)

Predictive value, availability, reproducibility and cost–effectiveness of some markers of organ damage

Marker	Cardiovascular predictive value	Availability	Reproducibility	Cost-effectiveness
Electrocardiography	+++	++++	++++	++++
Echocardiography, plus Doppler	++++	+++	+++	+++
Estimated glomerular filtration rate	+++	++++	++++	++++
Microalbuminuria	+++	++++	++	++++
Carotid intima–media thickness and plaque	+++	+++	+++	+++
Arterial stiffness (pulse wave velocity)	+++	++	+++	+++
Ankle–brachial index	+++	+++	+++	+++
Fundoscopy	+++	++++	++	+++
Additional measurements				
Coronary calcium score	++	+	+++	+
Endothelial dysfunction	++	+	+	+
Cerebral lacunae/white matter lesions	++	+	+++	+
Cardiac magnetic resonance	++	+	+++	++

Mancia G. et al., Eur Heart J 2013;34:2159-219

Sensitivity to detect treatment-induced changes, time to change and prognostic value of change by markers of asymptomatic organ damage

Marker of organ damage	Sensitivity for changes	Time to change	Prognostic value of changes
LVH/ECG	Low	Moderate (>6 months)	Yes
LVH/echo	Moderate	Moderate (>6 months)	Yes
LVH/cardiac magnetic resonance	High	Moderate (>6 months)	No data
eGFR	Moderate	Very slow (years)	No data
Urinary protein excretion	High	Fast (weeks–months)	Moderate
Carotid wall thickness	Very low	Slow (>12 months)	No
Pulse wave velocity	High	Fast (weeks–months)	Limited data
Ankle/ brachial index	Low	No data	No data

Mancia G. et al., Eur Heart J 2013;34:2159-219

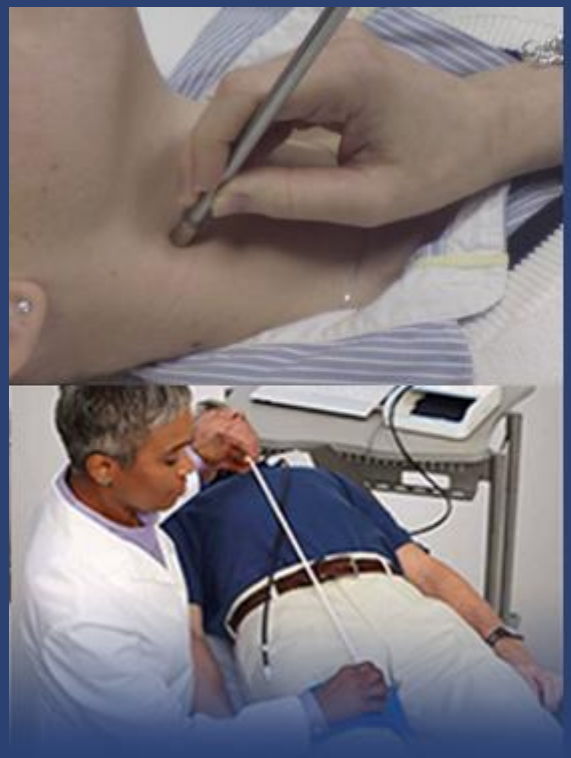
Current recommendation on PWA according to ESH/ESC guidelines

Index	Recommendation
Carotid-femoral PWV	It is the “gold standard” for measuring aortic stiffness (a PWV >10 m/s may indicate asymptomatic organ damage). It is useful for stratification of total CV risk because it has additive value of above and beyond traditional risk factors.
Central BP and AI	More investigation is needed before recommending their routine clinical use. Only exception is ISH in the young
Ambulatory PWV, central BP and AI	No recommendation

Mancia G. et al., Eur Heart J 2013;34:2159-219

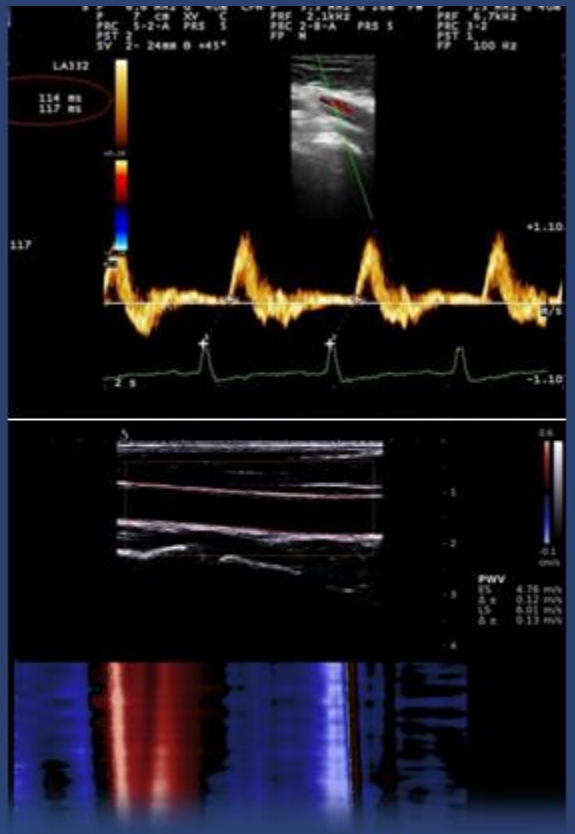
Non-invasive technologies for PWA

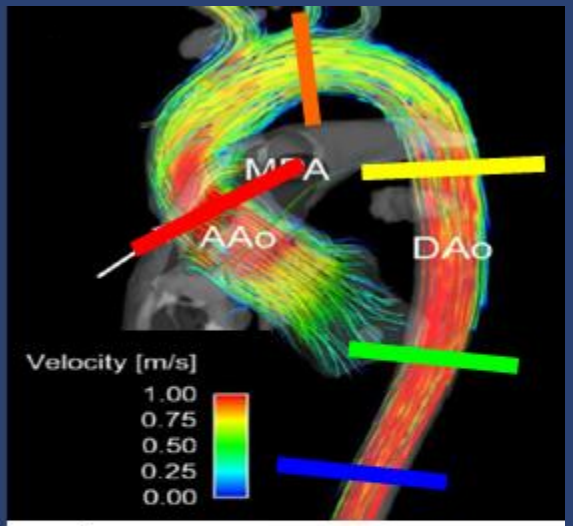
Applanation tonometry	Mechanotransducers	Finger photoplethysmography



Non-invasive technologies for PWA

Pneumosystems (oscillometry)	Ultrasonography	MRI





Techniques for 24-hour PWA

- All based on oscillometric measurements (Mobil-O-Graph, BPLab) or applanation tonometry (BPro) and transfer function analysis
- Different algorithms for the different devices
- All devices are validated against intra-arterial or SphygmoCor method
- Non-invasive estimation of central hemodynamics and arterial stiffness is device/technique dependent

Oscillometric technologies

Some studies of devices used for oscillometric pulse wave velocity measurements

Study	Number of observations	Device	Method	Result
Magometschnigg[7]	100	TensioClinic	Comparison with brachial PWV (ShygmoCor)	m: 9.1; SD: 1.8 m/second vs m: 8.4; SD: 1.5 m/second r = –0.04
Rajzer et al[17]	64	Arteriograph	Comparison with ShygmoCor and with Complior	r = 0.29 ($P = 0.043$) and r = 0.36 ($P = 0.0048$)
Baulmann et al[8]	51	Arteriograph	Comparison with ShygmoCor and with Complior	r = 0.67 ($P < 0.001$) and r = 0.69 ($P < 0.001$)
Jatoi et al[27]	254	Arteriograph	Comparison with Complior	r = 0.60 ($P < 0.001$)
Horváth et al[18]	22	Arteriograph	Comparison with invasively measured PWV	Pearson's r = 0.91 ($P < 0.001$)
Ageenkova and Purygina[10]	90	BPLab	Reproducibility and repeatability study	Reproducibility and repeatability: good
Luzardo et al[28]	35	Mobil-O-graph	Comparison with ShygmoCor at rest	m: 7.3 vs m: 7.0 m/second
Luzardo et al[28]	83	Mobil-O-graph	Comparison with ShygmoCor (ambulatory)	m: 7.9 vs m: 7.4 m/second

Abbreviations: m, mean; PWV, pulse wave velocity; r, correlation coefficient; SD, standard deviation.

Posokhov I.N. Med Devices (Auckl) 2013;6:11-15

Published clinical studies based on 24-hour PWA

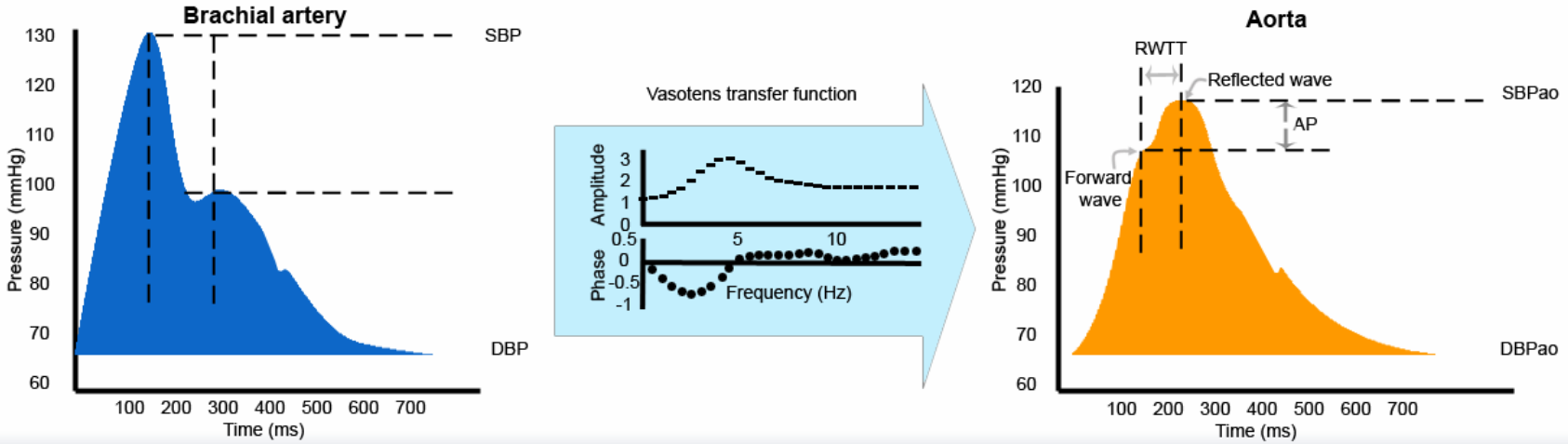
Author Study (year)	Device	Subjects	Main findings
Theilade et al. (2013)	BPro	629 type 1 diabetics and 86 controls	Aortic SBP was higher in patients and increased with diabetic complications and was stronger associated to complications than peripheral SBP
Williams et al. AmCAP Study (2013)	BPro	171 hypertensive patients treated with aliskiren (ASSERTIVE Study)	Brachial and central pressure show different diurnal patterns, which are not modulated by BP-lowering therapy, with relatively higher nigh-time central pressures
Protogerou et al. SAFAR Study (2014)	Mobil-O-Graph	229 individuals (75% hypertensives)	Aortic SBP, when compared to brachial SBP, improves the individualized assessment of the hypertension-associated heart damage (LVH)
Elsurer et al. (2014)	Mobil-O-Graph	339 hypertensive CKD patients	Serum uric acid is associated independently with AI, but not with PWV.
Kuznetsova (2014)	BPLab	467 healthy volunteers	Reference values for PWV, AI and central BP
Omboni et al. (2015)	BPLab	142 normotensives and 611 hypertensives	Non-invasive assessment of 24-hour arterial stiffness and central hemodynamics in daily life conditions may help in assessing the arterial function impairment in hypertensive patients
Maloberti (2015)	Mobil-O-Graph	119 pediatric patients and 23 controls in Williams-Beuren syndrome	Increased nigh-time AI in sick children is an early hallmarks of cardiovascular dysfunction
Karpetas (2015)	Mobil-O-Graph	153 ESRD patients during successive dialytic sessions	A gradual interdialytic increase in AI and to a less extent in PWV is observed

The Vasotens technology

A. Waveform of brachial artery

B. Amplitude and phase characteristics of the Vasotens transfer function

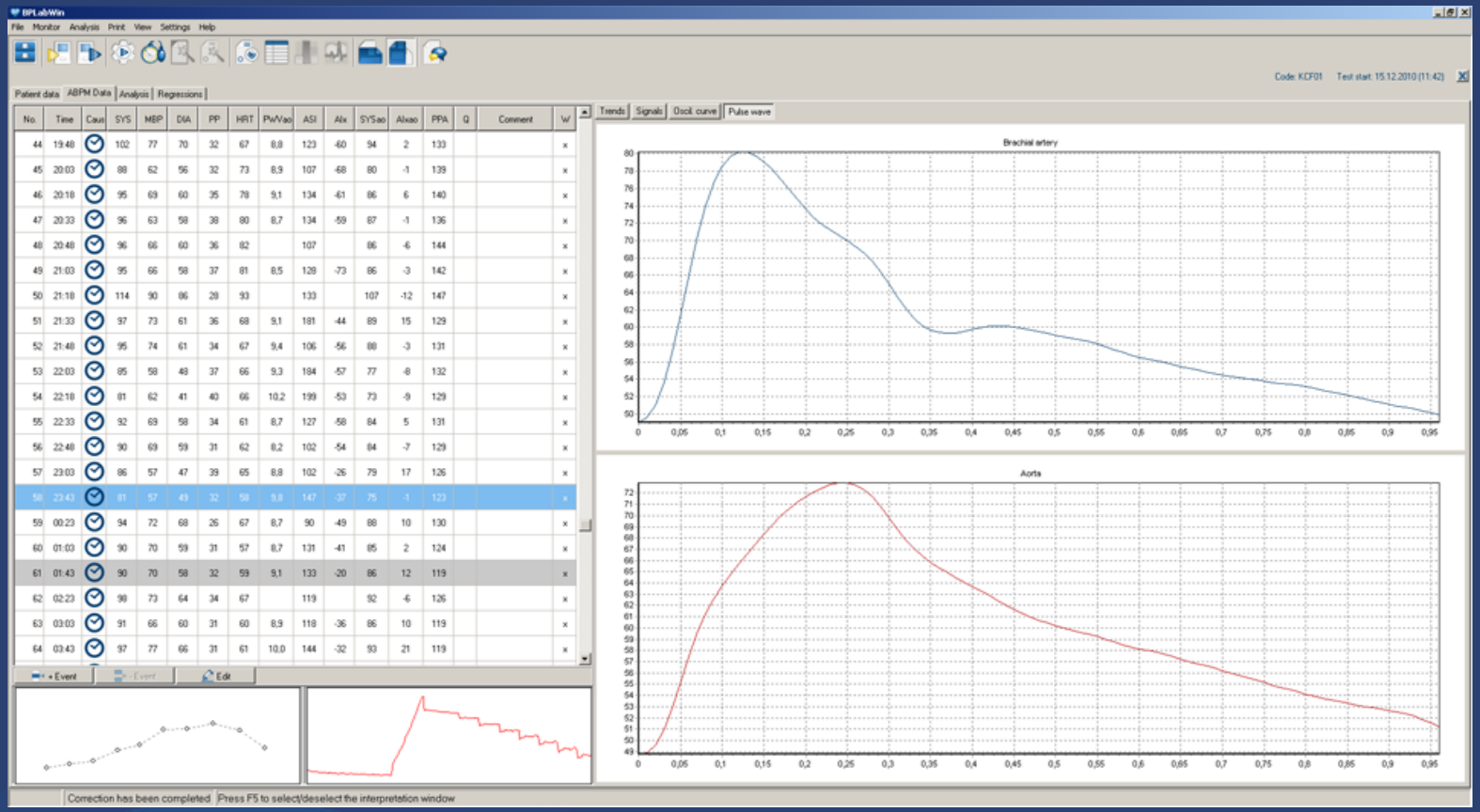
C. Waveform of aorta and main calculations



SBP, DBP = systolic and diastolic BP; SBPao, DBPao = BP in aorta; AP = augmentation pressure [AIxao = (SBPao-DBPao)/AP]; RWTT = reflected wave transit time, used in PWV formula; PWV = (k)2L/RWTT, where L = superficial morphological distance

The Vasotens technology

Screen of analysis window in BPLab / Vasotens software



A clinically validated CE and ISO technology

BP measurement

Author (year)	Subjects	BHS grade	SBP diff. Mean (SD)	DBP diff. Mean (SD)
Koudryavtcev (2011)	85 adults (18-87 years)	A / A	1.1 (6.4)	-1.2 (7.1)
Ledyaev (2015)	30 children (5-15 years)	A / A	1.6 (2.2)	0.7 (3.1)
Dorogova (2015)	30 pregnant women (20-35 years)	A / A	0.0 (2.1)	0.2 (2.2)

PWA

Author (year)	Subjects	Results (BPLab vs. SphygmoCor)
Rogoza (2012)	160 patients and healthy volunteers (18-81 years)	Aortic SBP: 122.5 vs. 121.2 (-1.3 mmHg) Aortic AI: 26.1 vs. 26.8 (-0.7%)
Kotovskaya (2014)	99 subjects (18-77 years) (ARTERY protocol)	Aortic SBP: 123 vs. 120 (2.9 mmHg) Aortic AI: 13 vs. 11 (2.6 %) Aortic PWV: 7.7 vs. 7.0 (0.7 m/s)

Accuracy of 24-hour PWA across devices

Author (year)	Mobil-O-Graph	BPro	BPLab
Aortic SBP (intra-arterial comparison)	+3.0 (6.0)[1]	-0.4 / -0.9 (6.2 / 13.0)[2]	-
Aortic SBP (Sphygmocor comparison)	-1.4 / +1.2 (3.1 / 10.0)[5]	-0.3 / -3.6 (4.4 / 4.8)[2]	+1.3 / +2.9 (2.4 / 3.5)[2]
Aortic AI (intra-arterial comparison)	-	-	-
Aortic AI (Sphygmocor comparison)	-0.7 / +1.2 (7.9 / 9.5)[3]	-	-0.8 / +2.6 (10.4 / 13.0)[2]
Aortic PWV (intra-arterial comparison)	+0.6 (1.0)[1]	-	-
Aortic PWV (Sphygmocor comparison)	-0.3 / -0.6 (1.1 / 1.3)[2]	-	+0.7 (1.4)[1]

Superscripts refer to the number of studies included in the comparison
Mobil-O-Graph: 2 studies vs. intra-arterial (n=150) and 5 studies vs. SphygmoCor (n=631)
BPro: 2 studies vs. intra-arterial (n=72) and 2 studies vs. SphygmoCor (n=781)
BPLab: 2 studies vs. SphygmoCor (n=259)

Evidence collected with BPLab

Reference	What is described
Kotovskaya YV et al, *Med Devices (Auckl). 2014;*	Validation of aortic BP and PWV vs SphygmoCor
Rogoza AN, Kuznetsov AA. *Research Reports in Clinical Cardiology. 2012*	Validation of aortic BP vs SphygmoCor
Ageenkova OA, Purygina MA. *Vasc Health Risk Manag. 2011*	Reproducibility and repeatability of CBP and RWTT
Koudryavtcev SA, Lazarev VM. *Med Devices (Auckl). 2011*	BHS – 93 validation in general population
Ledyaev MY et al, *Med Devices (Auckl). 2015*	BHS – 93 validation in children
Dorogova IV, *Vasc Health Risk Manag. 2015*	BHS – 93 validation in pregnant women
Posokhov IN et al, *Med Devices (Auckl). 2014*	Repeatability of new index, ‘pulse time index of norm’
Litvin AY et al, *Vasc Health Risk Manag. 2013*	"Vascular" risk factors in patients with OSA described with Vasotens indices.
Aksenova TA et al, *Klin Med (Mosk). 2013*	Analysis of central SBP in hypertensive patients with COPD
Minyukhina IE, *Int J Nephrol Renovasc Dis. 2013*	Analysis of 24-hour PWV in patients with renal transplantation
Kuznetsova TY et al. *Vasc Health Risk Manag. 2014*	Contribution of 24-h pulse wave velocity (day/night), aortic augmentation index and central blood pressure in normotensive volunteers
Omboni S et al, *Int J Hypertens. 2015*	Feasibility of evaluation of 24-Hour Arterial Stiffness Indices and Central Hemodynamics in Healthy Normotensive Subjects versus Treated or Untreated Hypertensive Patients

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Research Article

Evaluation of 24-Hour Arterial Stiffness Indices and Central Hemodynamics in Healthy Normotensive Subjects versus Treated or Untreated Hypertensive Patients: A Feasibility Study

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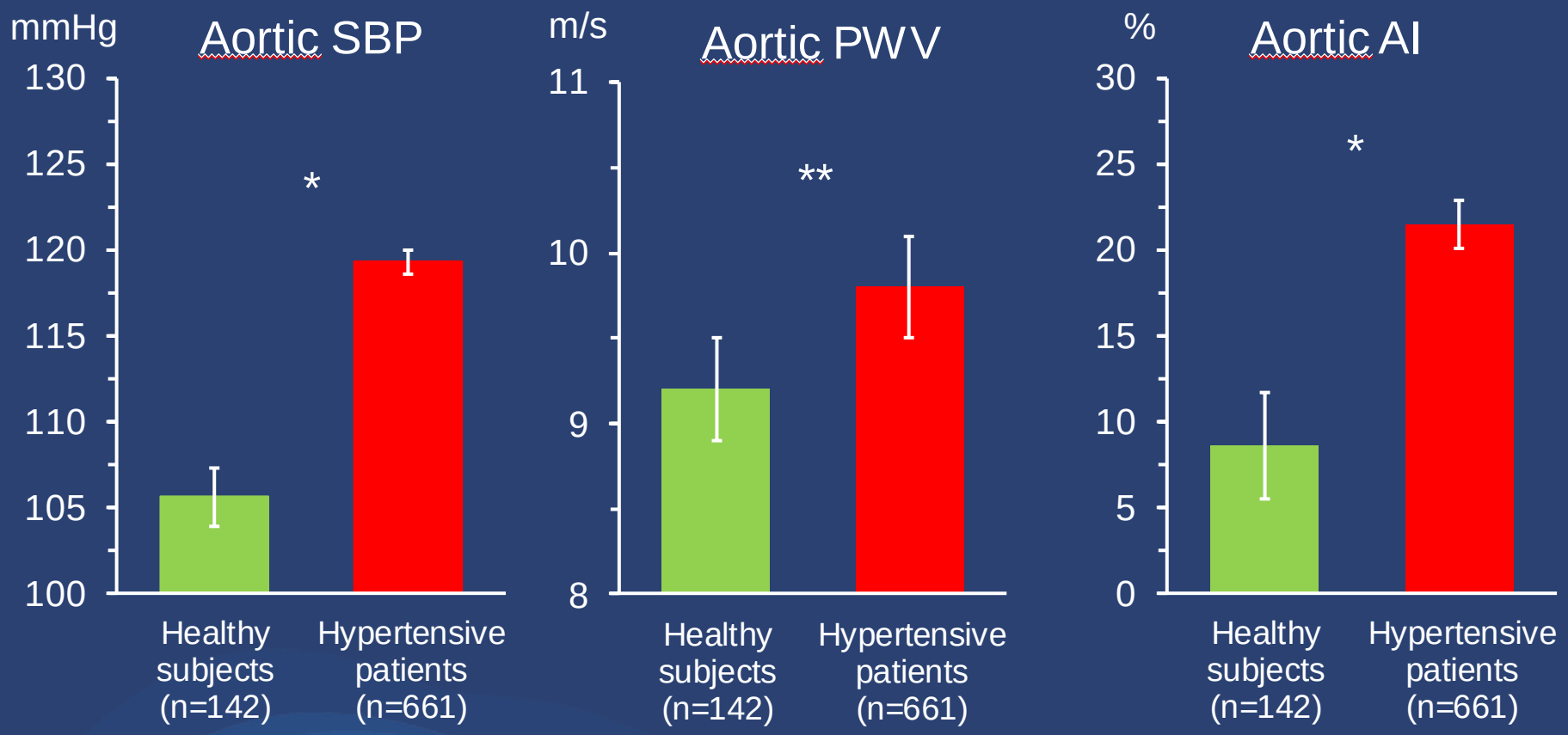
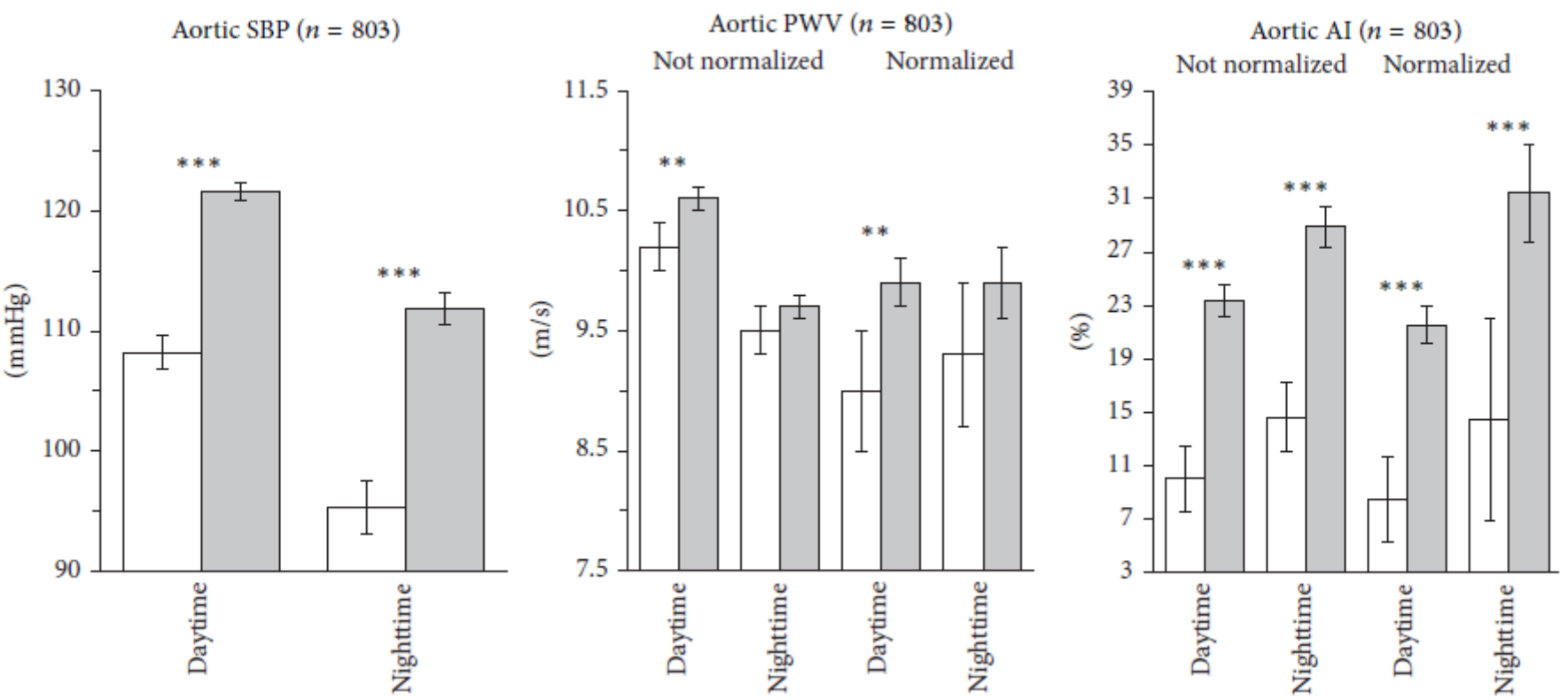
24-hour ambulatory aortic SBP, PWV and AI in a large database of normotensive and hypertensive subjects



*, p=0.0001, ** p=0.025, unadjusted

Omboni S., Posokhov I, Rogoza AN. Int J Hypertens 2015:601812

Day-time and night-time aortic SBP, PWV and AI in normotensive vs. hypertensive subjects

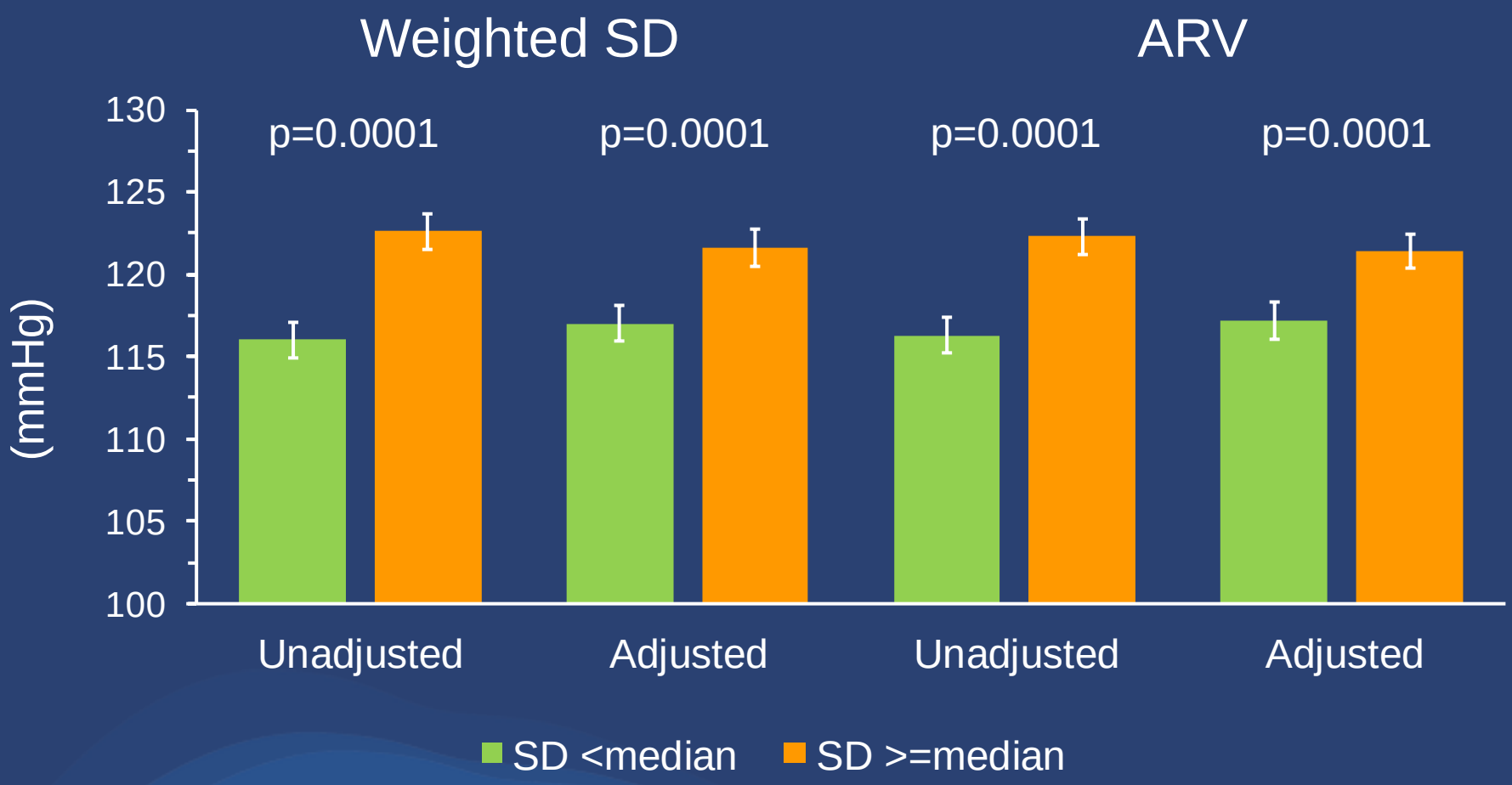


*** p<0.001; ** p<0.01

Healthy subjects (n=142)

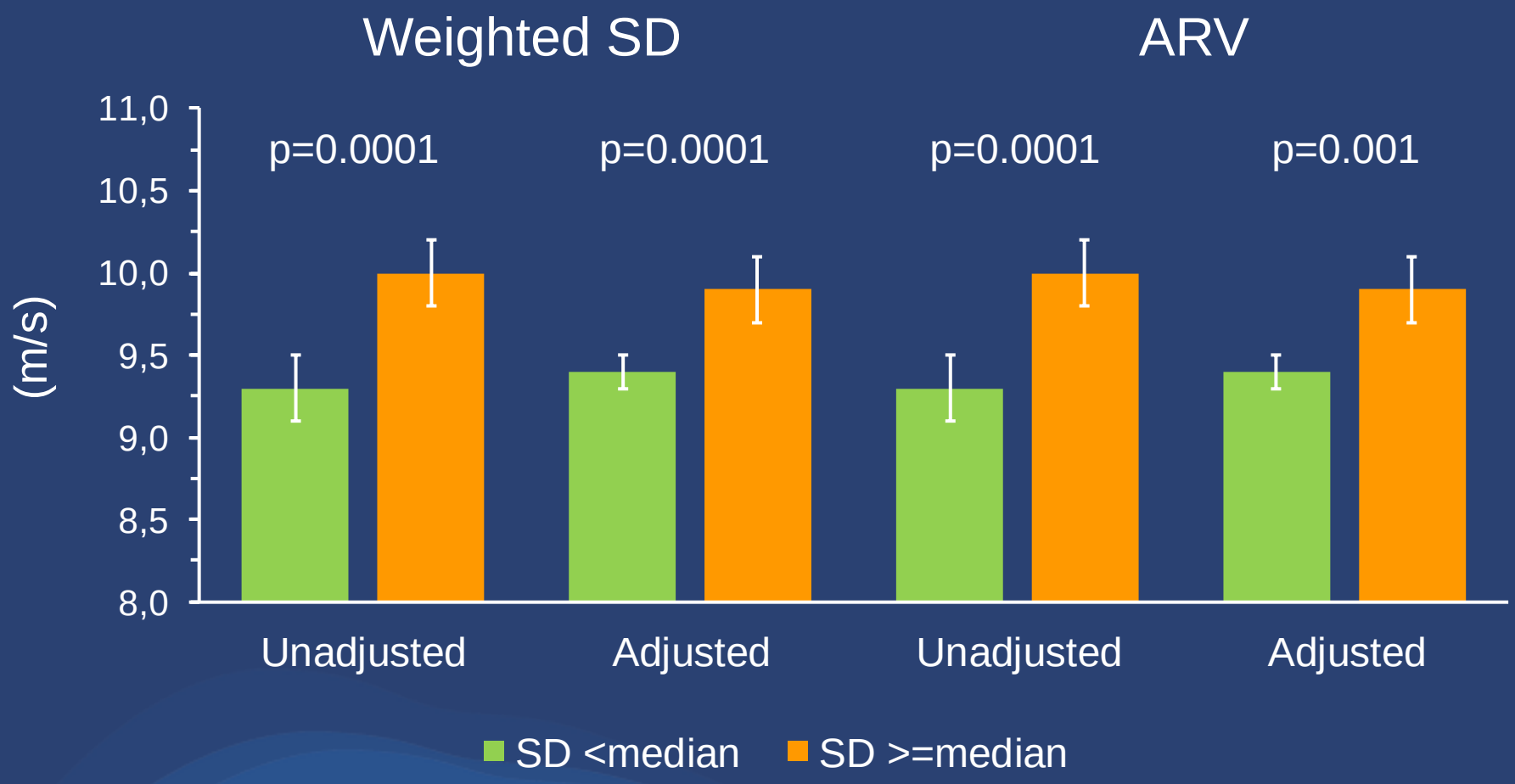
Hypertensive patients (n=661)

SBP variability vs. Aortic SBP



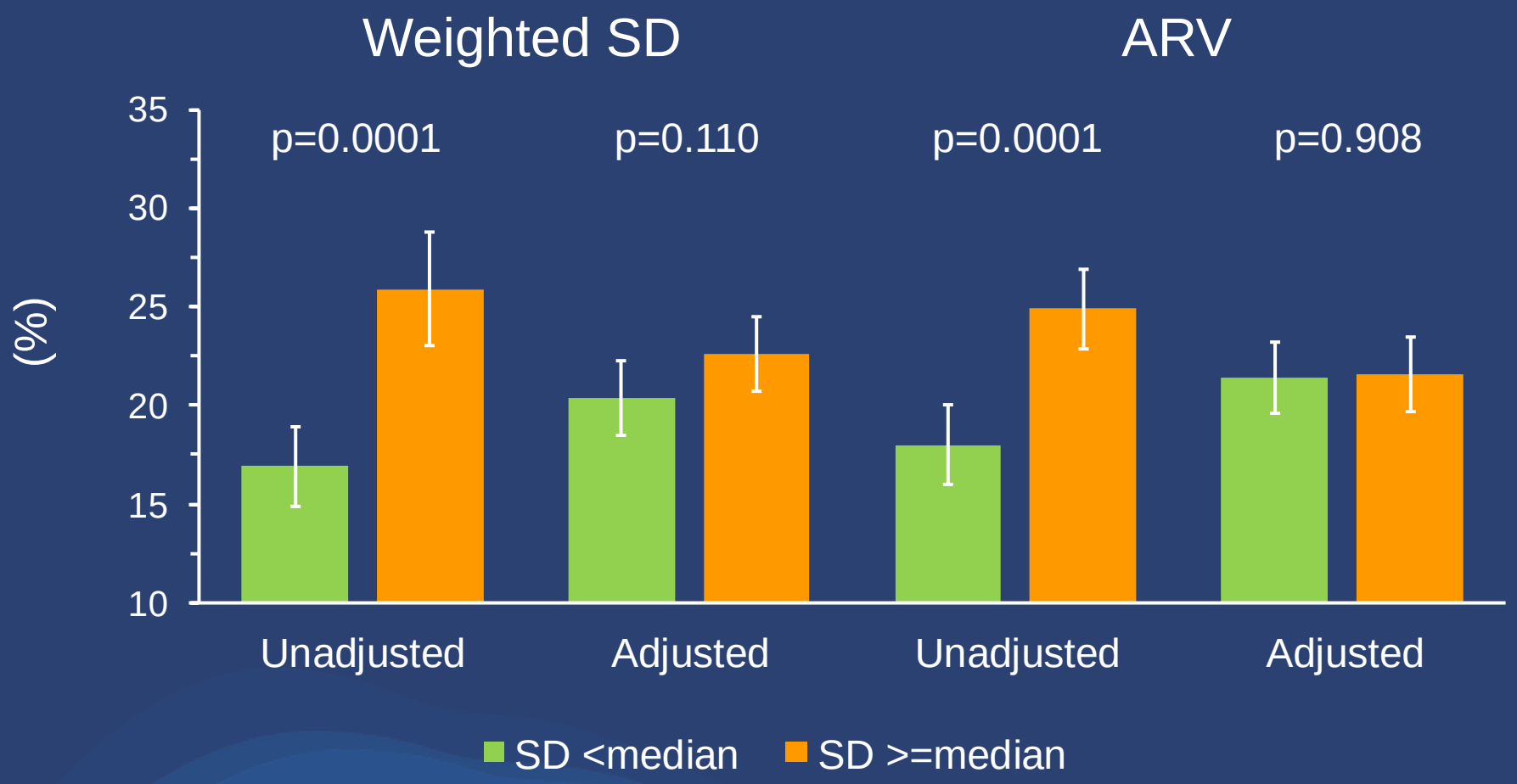
Omboni S., Posokhov I, Rogoza AN. Hypertens Res 2017;40:385-391

SBP variability vs. Aortic PWV



Omboni S., Posokhov I, Rogoza AN. Hypertens Res 2017;40:385-391

SBP variability vs. Aortic AI



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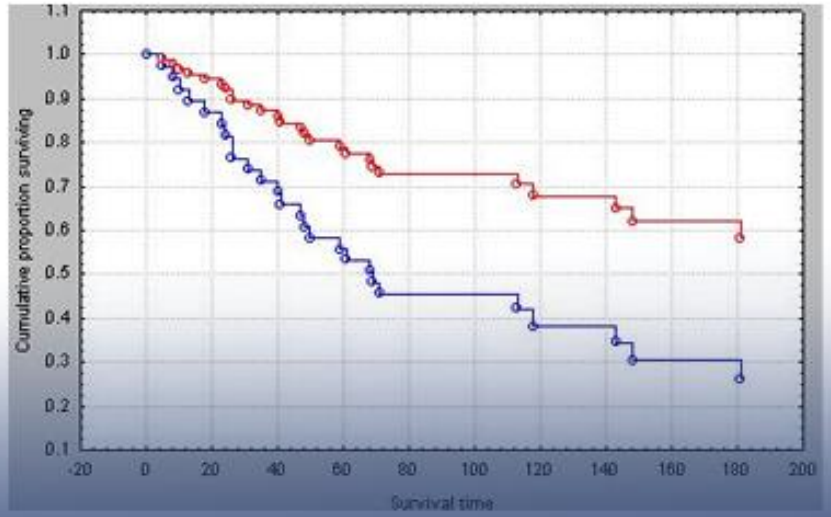


Prognostic value of ambulatory central BP and clinical value of 24-hour arterial stiffness estimation (PWV and AI)

The VASOTENS Registry Protocol, activities and schedule

Project objectives - 1

- The evaluation of non-invasive ambulatory BP and arterial stiffness estimates (through pulse wave analysis, PWA) in hypertensive subjects undergoing an ABPM for clinical reasons in the selected centers
- The evaluation of the **changes in BP and arterial stiffness estimates following treatment initiation** according to current guidelines
- The assessment of the **impact of non-invasive arterial stiffness estimation on target organ damage and patient's CV prognosis**
- The definition of the **normalcy thresholds** for pulse wave velocity (PWV), augmentation index (AI), and other current and future indices derived from PWA in hypertensive subjects, according to outcome data

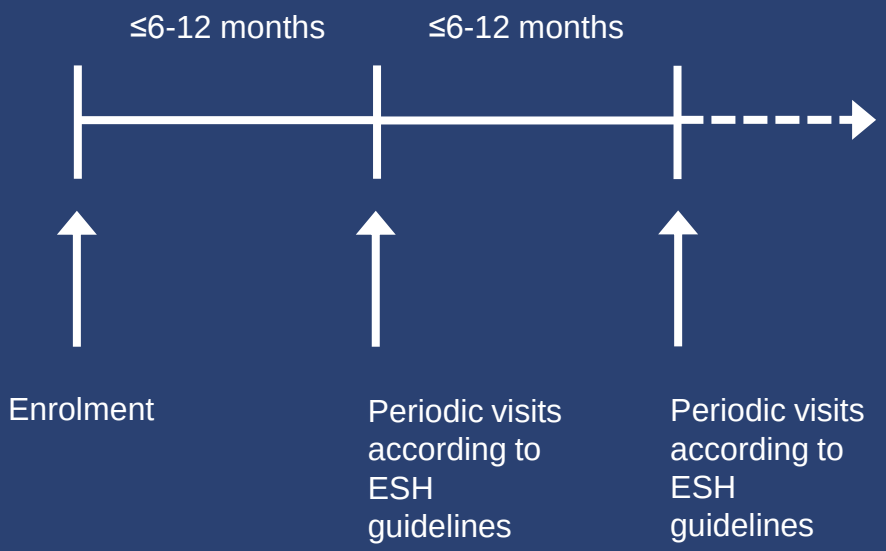
Project objectives - 2

- The definition of the **relationship between arterial stiffness, BP absolute level and variability, and outcomes**
- The setup of a worldwide network of centers performing ambulatory PWA, and the **validation and promotion of the use of such technique for hypertension screening and follow-up**
- The provision of **evidence of the clinical relevance of non-invasive arterial stiffness assessment**, in order to favor the inclusion of such evaluation in recommendations on hypertension management

Population

- Male and female subjects
- Age ≥18 years
- Subjects referred to routine diagnostic evaluation for hypertension or established hypertensive subjects
- ABPM performed for clinical reasons with a BPLab device
- Valid ABPM (interval between measurements ≤30 minutes, at least 70% of expected number of readings, at least 20 valid readings during the day-time and 7 during the nigh-time)
- Availability of individual measurements for ABPM on a .bpw file (BPLab format) or data directly uploaded on the telemedicine platform of the study

Study flow-chart



- Family history
- Anthropometric data
- Habits
- Past and current diseases
- Therapies
- Office BP
- laboratory tests, including evaluation of target organ damage
- Outcomes (adverse events)

Clinical data

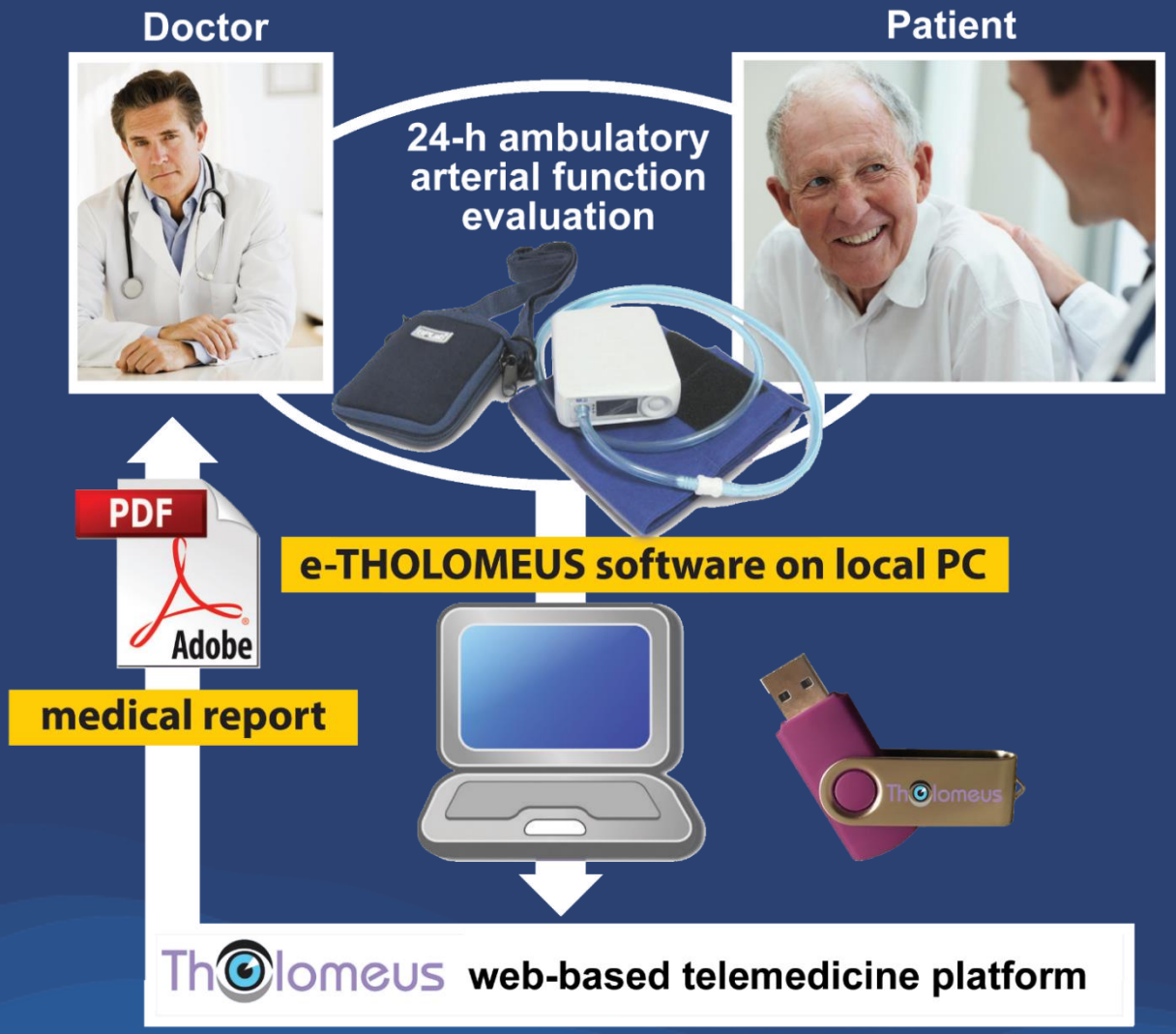
- Age and gender
- Ethnicity
- Height, weight and waist circumference
- Superficial distance between jugulum and symphysis (surrogate of aortic length)
- Smoking status, alcohol drinking, coffee or tea drinking
- Dyslipidemia (± therapy)
- Diabetes (± therapy)
- Diagnosis of hypertension (± therapy)
- Family and personal medical history for CV disease

Laboratory tests

- Office BP and heart rate obtained in the same treatment condition as ABPM
- Left ventricular mass index (LVMI) at echocardiogram
- When available, diameter of the aorta (aortic annulus, root and sinotubular junction) and/or cardiac output, assessed by the echocardiogram
- Intima-media thickness (IMT) at carotid ultrasonography
- ECG (indication on left ventricular hypertrophy, Sokolow–Lyon and Cornell index)
- When available, ankle-brachial index (ABI)
- Microalbuminuria and serum creatinine (calculation of estimated glomerular filtration rate - eGFR)
- When available, **pulse wave velocity (PWV), augmentation index (AI) and central blood pressure taken during the office visit with a validated device different for the one used in the study** (e.g. Sphygmocor or Complior)

The telemedicine system

www.tholomeus.net



Advantages of web-based telemonitoring in the study

- No need of installing software, locally
- Technology always updated
- Standardized and centralized data collection
- Data validation by experts and counselling to remote centers
- Setup and maintenance of the Registry
- Prompt data analysis

The study website

www.vasotens.org

THANK YOU FOR ATTENTION!

VASOTENS Registry

For any request or communication please e-mail to:

coordinator@vasotens.org