Simposio SIGG-SIIA
INNOVAZIONI TERAPEUTICHE NEL MANAGEMENT
DELL'IPERTENSIONE ARTERIOSA NEL PAZIENTE ANZIANO
Moderatori: Claudio Borghi (Bologna), Nicola Ferrara (Napoli)

Utilità della pressione centrale

Andrea Ungar, MD, PhD, FESC

Syncope Unit, Hypertension Centre
Geriatric Cardiology and Medicine
University of Florence, Italy

1959 Build and Blood Pressure Study
Society of Actuaries

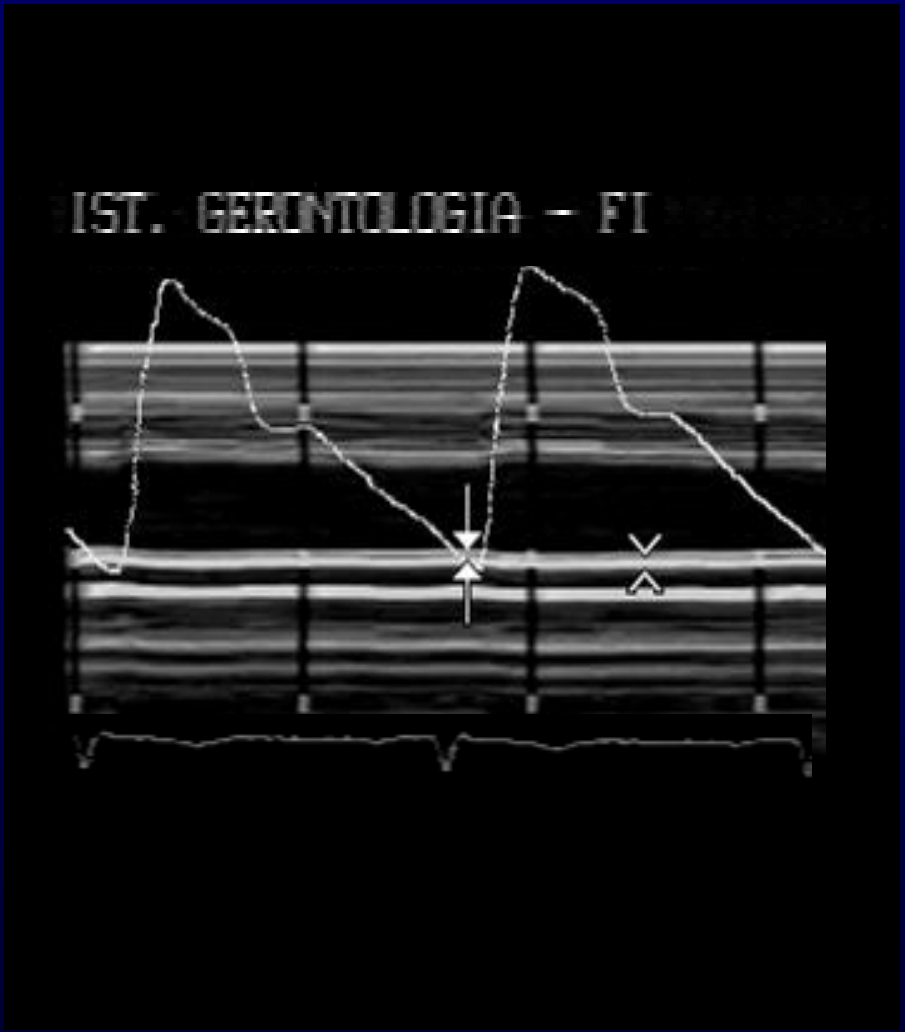
4.002.000 soggetti (15-59 anni)
(follow-up = 18 anni)

PAS	*PAD (mmHg)*				
	62-82	*83-87*	*88-92*	*93-97*	*98-102*
98-127	**83**	**103**	**109**	**-**	**-**
128-137	**106**	**116**	**137**	**160**	**160**
138-147	**136**	**144**	**166**	**164**	**208**
148-157	**150**	**185**	**189**	**231**	**272**
158-167	**211**	**180**	**215**	**249**	**307**

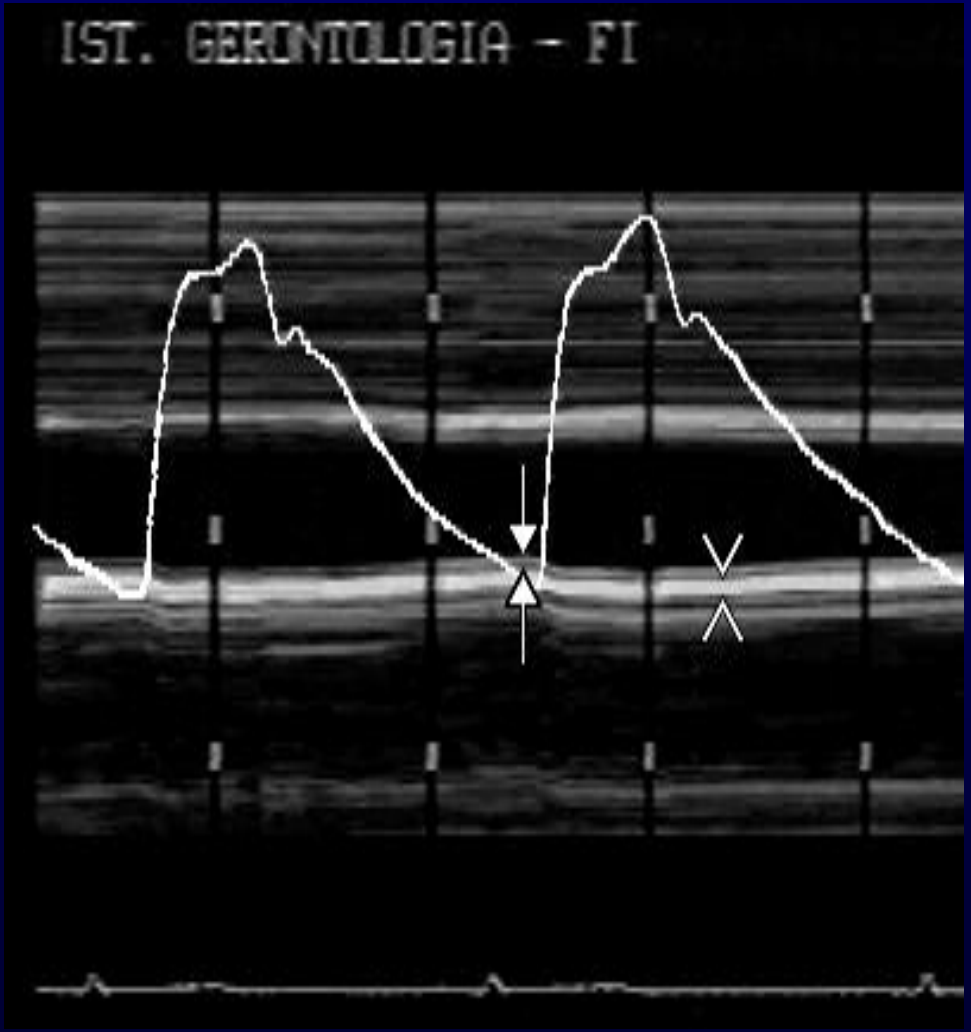
Percentuale della mortalità reale rispetto alla mortalità attesa

Gubner RS, Am J Cardiol 1962

Modificazioni dell’onda sfigmica aortica in relazione all’età

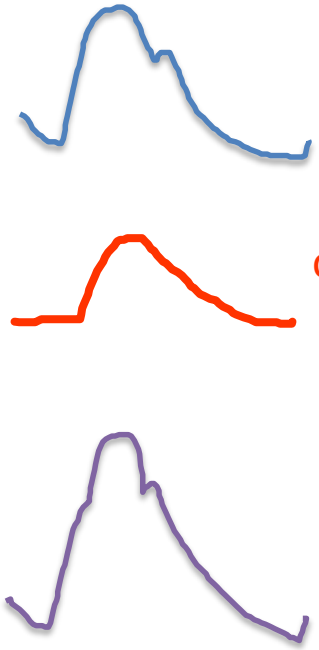


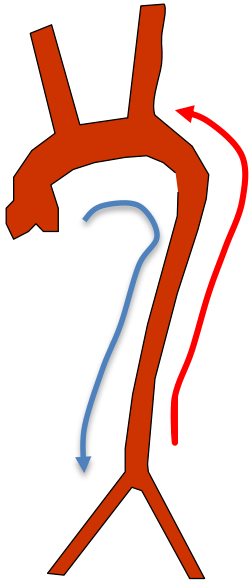
Giovane



Anziano

Invecchiamento e rigidità arteriosa/riflessione dell'onda sfigmica





↑ rigidità aortica

↓

Onde anterograda e retrograda viaggiano più velocemente

Siti di riflessione (geometria e tono del microcircolo)

↓

Riflessione più precoce dell'onda retrograda

MISURA (tonometria)

↑PVW aortica

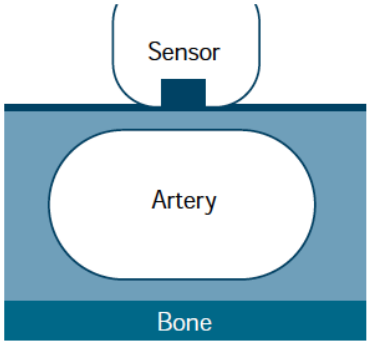
↑AIx (↑PAS/PP centrale)

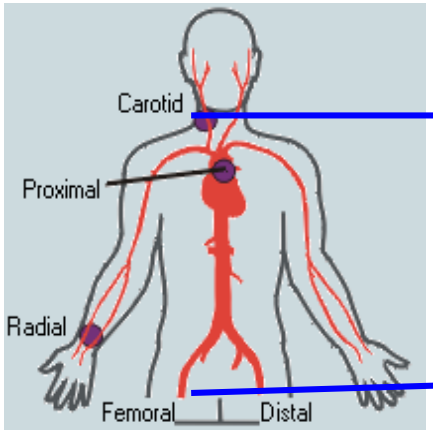
giovane

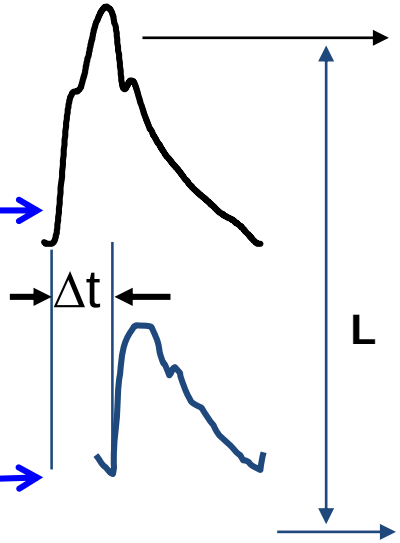
anziano

Rigidità aortica (pulse wave velocity, PWV)

Tonometria arteriosa





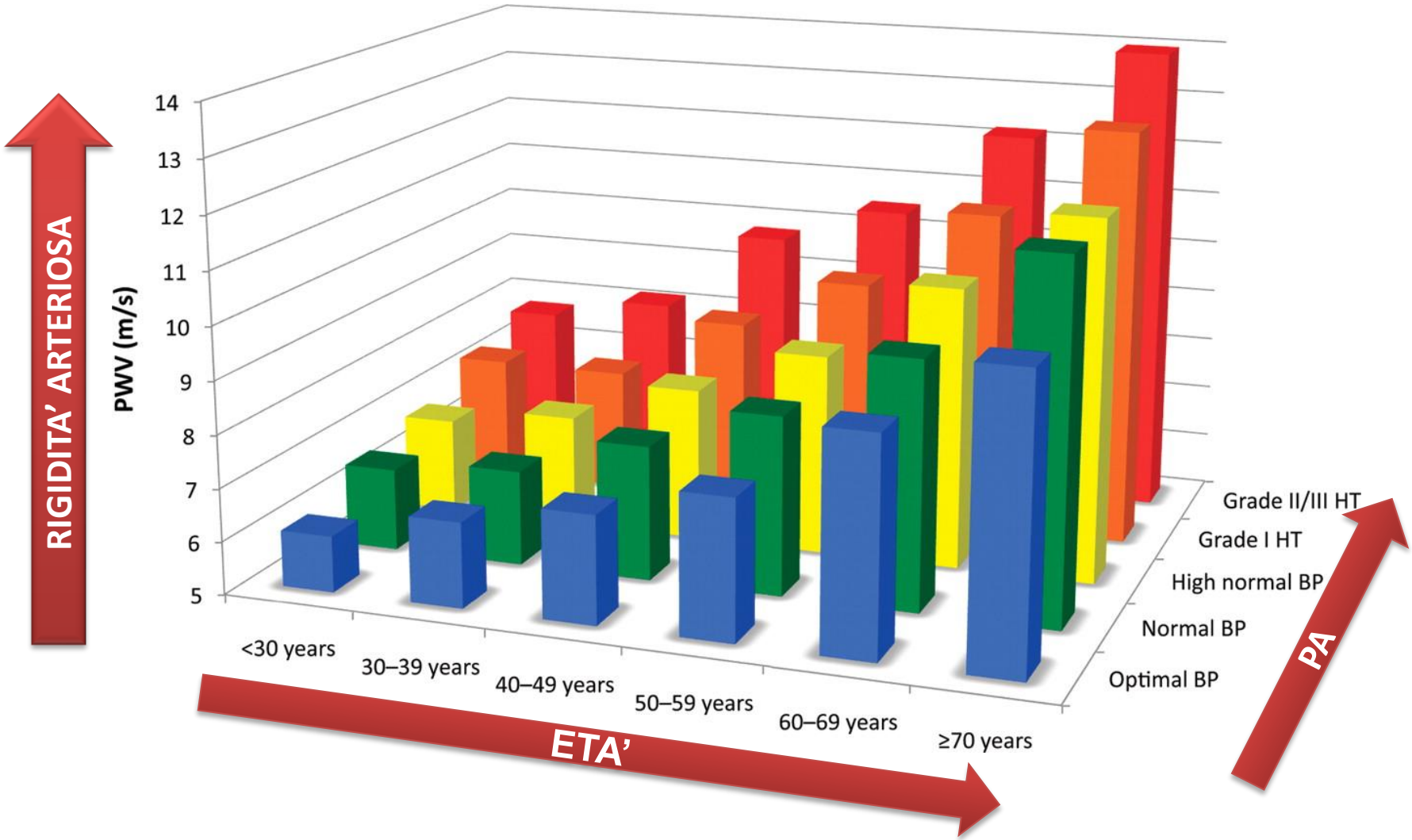


$$PWV = \frac{DL}{Dt}$$

Complior ®
ARTECH-medical
www.artechmedical.com

SphygmoCor Vx ®
Atcor Medical
www.atcormedical.com

Rigidità aortica (pulse wave velocity, PWV)



Reference Values for Arterial Stiffness' Collaboration. Eur Heart J 2010;31:2338-2350

Il “vascular aging” si può CALCOLARE

Tabelle del rischio cardiovascolare

Table 5. CVD Points for Women

Points	Age, y	HDL	Total Cholesterol	SBP Not Treated	SBP Treated	Smoker	Diabetic
−3				<120			
−2		60+					
−1		50–59			<120		
0	30–34	45–49	<160	120–129		No	No
1		35–44	160–199	130–139			
2	35–39	<35		140–149	120–129		
3			200–239		130–139	Yes	
4	40–44		240–279	150–159			Yes
5	45–49		280+	160+	140–149		
6					150–159		
7	50–54				160+		
8	55–59						
9	60–64						
10	65–69						
11	70–74						
12	75+						
Points allotted							Total

13

Rischio calcolato

Es. Donna	
Età (anni)	61
Colest. (mg/dl)	180
HDL (mg/dl)	47
PA (mmHg)	124
Fumo	Si
Diabete	No

D’Agostino RB et al, Circulation 2008

E da 61 anni si passa ad una età vascolare di 73!!!

CVD Risk for Women

Points	Risk, %
≤−2	<1
−1	1.0
0	1.2
1	1.5
2	1.7
3	2.0
4	2.4
5	2.8
6	3.3
7	3.9
8	4.5
9	5.3
10	6.3
11	7.3
12	8.6
13	10.0
14	11.7
15	13.7
16	15.9
17	18.5
18	21.5
19	24.8
20	28.5
21+	>30

Estimate for a 61-year old woman of normal risk: 6.7%

Heart Age/Vascular Age for Women

Points	Heart Age, y
<1	<30
1	31
2	34
3	36
4	39
5	42
6	45
7	48
8	51
9	55
10	59
11	64
12	68
13	73
14	79
15+	>80

Heart/Vascular age is calculated as the age of a person with the same predicted risk but will all other RF levels in normal ranges.

D'Agostino RB et al, Circulation 2008

Clinical update

European Heart Journal (2014) **35**, 1719–1725

Central blood pressure: current evidence and clinical importance

Carmel M. McEniery[1]*, John R. Cockcroft[2], Mary J. Roman[3], Stanley S. Franklin[4], and Ian B. Wilkinson[1]

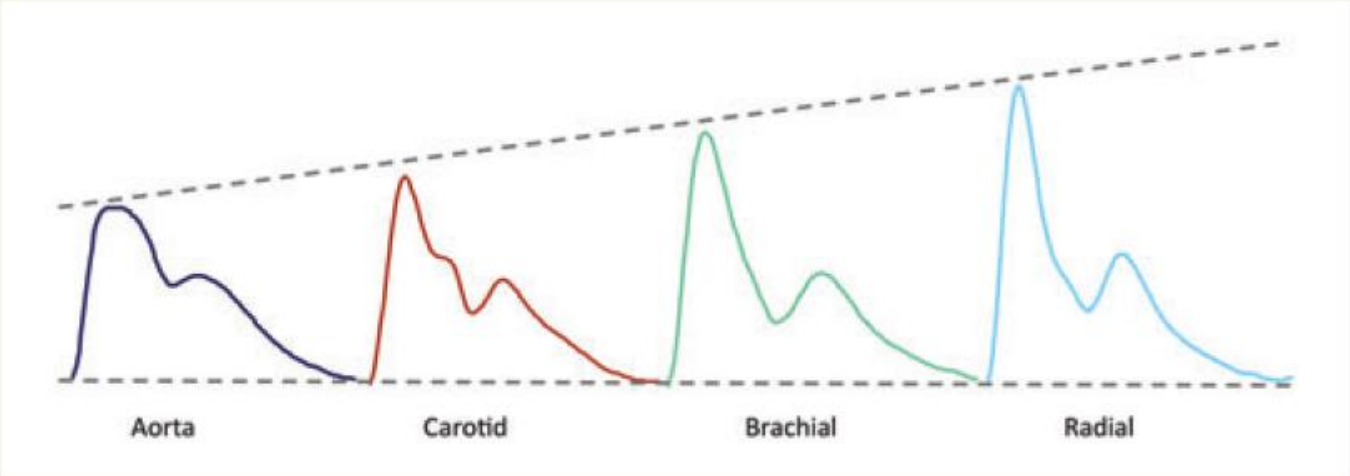


Figure 1 Amplification of the pressure waveform moving from the aorta to the radial artery.

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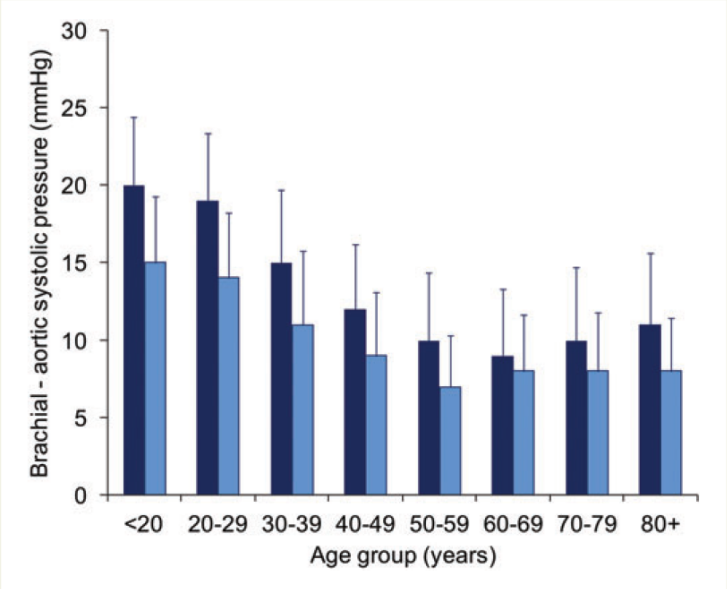

Figure 2 Difference between brachial and aortic systolic blood pressure (SphygmoCor) in healthy men (dark blue bars; $n = 2779$) and women (light blue bars; $n = 2869$). The data represent means $\pm$ SD.

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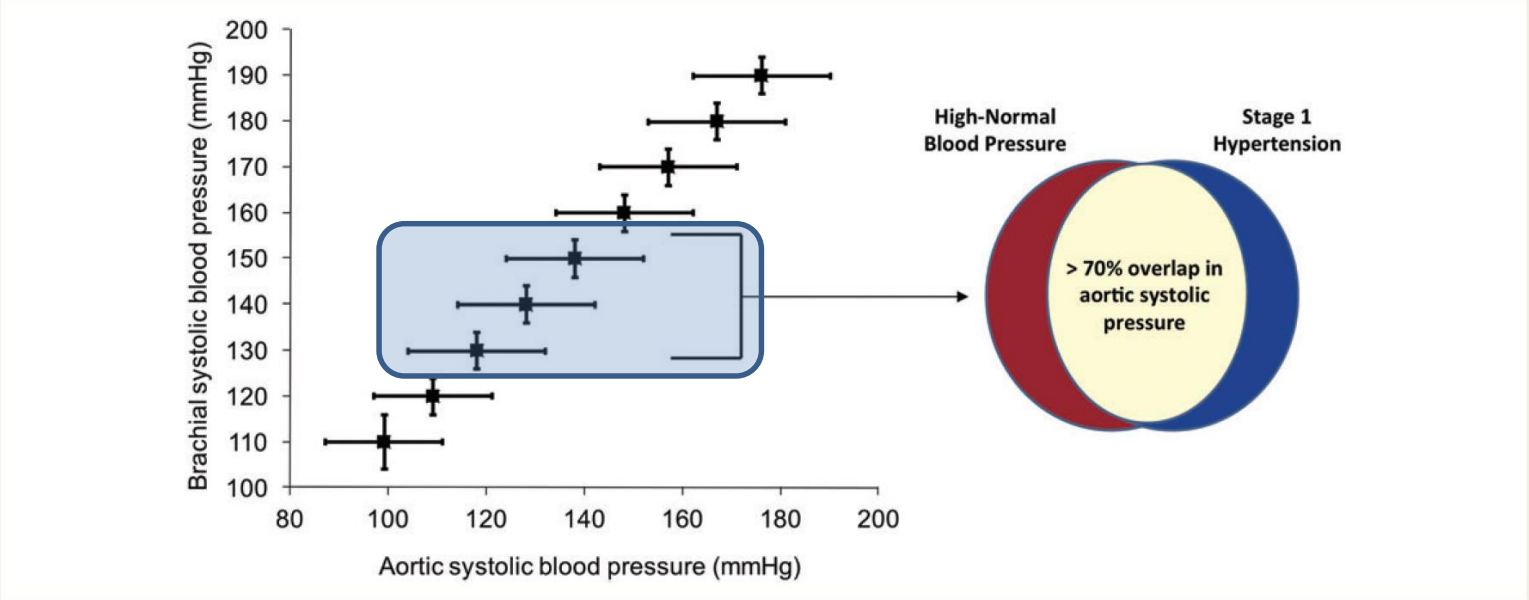

Figure 3 Overlap in aortic systolic blood pressure despite no overlap in brachial systolic pressure, in healthy men and women ($n = 5648$). Over 70% of individuals with high-normal blood pressure had aortic systolic pressures in common with individuals with stage 1 hypertension.[28]

European Heart Journal (2014) **35**, 1719–1725

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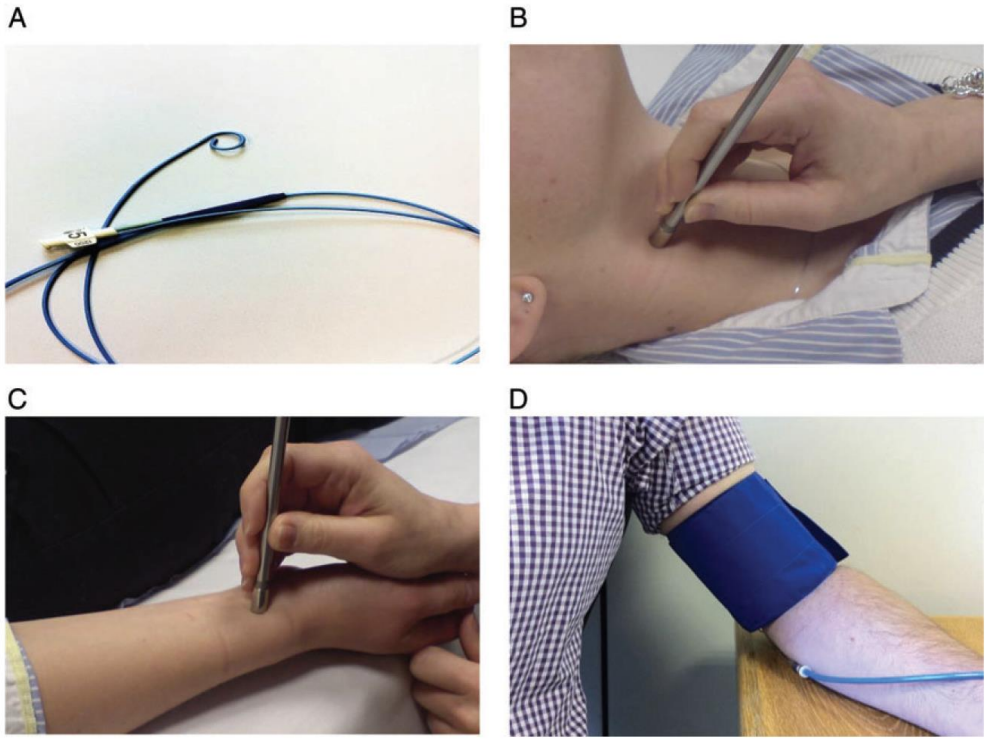

Figure 4 Techniques for assessing central blood pressure. (*A*) Invasive cardiac catheterization; (*B*) direct applanation tonometry of the carotid artery; (*C*) applanation tonometry of the radial artery; (*D*) cuff-based oscillometry at the brachial artery.

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Table 2 Comparative effect of anti-hypertensive drugs and nitrates on central systolic pressure

Class	Central systolic pressure
ACE inhibitors[61–63,95–102]	↓
Angiotensin receptor blockers[101,103–105]	↓↔
Beta-blockers[9,61–63,65,95,103,106,107]	↑↑
Calcium channel blockers[61–63,96]	↓↔
Diuretics[61–63,100,102]	↔
Nitrates[68,70,71,74]	↓↓

Clinical update European Heart Journal (2014) **35**, 1719–1725

Central blood pressure: current evidence and clinical importance

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Therefore, basing treatment decisions on **central**, rather than **brachial** pressure, is likely to have **important** implications for the future diagnosis and management of hypertension

Central But Not Brachial Blood Pressure Predicts Cardiovascular Events in an Unselected Geriatric Population

The ICARe Dicomano Study

Riccardo Pini, MD, FACC,* M. Chiara Cavallini, MD,* Vittorio Palmieri, MD, PHD,†
Niccolò Marchionni, MD,* Mauro Di Bari, MD, PHD,* Richard B. Devereux, MD, FACC,†
Giulio Masotti, MD,* Mary J. Roman, MD, FACC†
Florence, Italy; and New York, New York

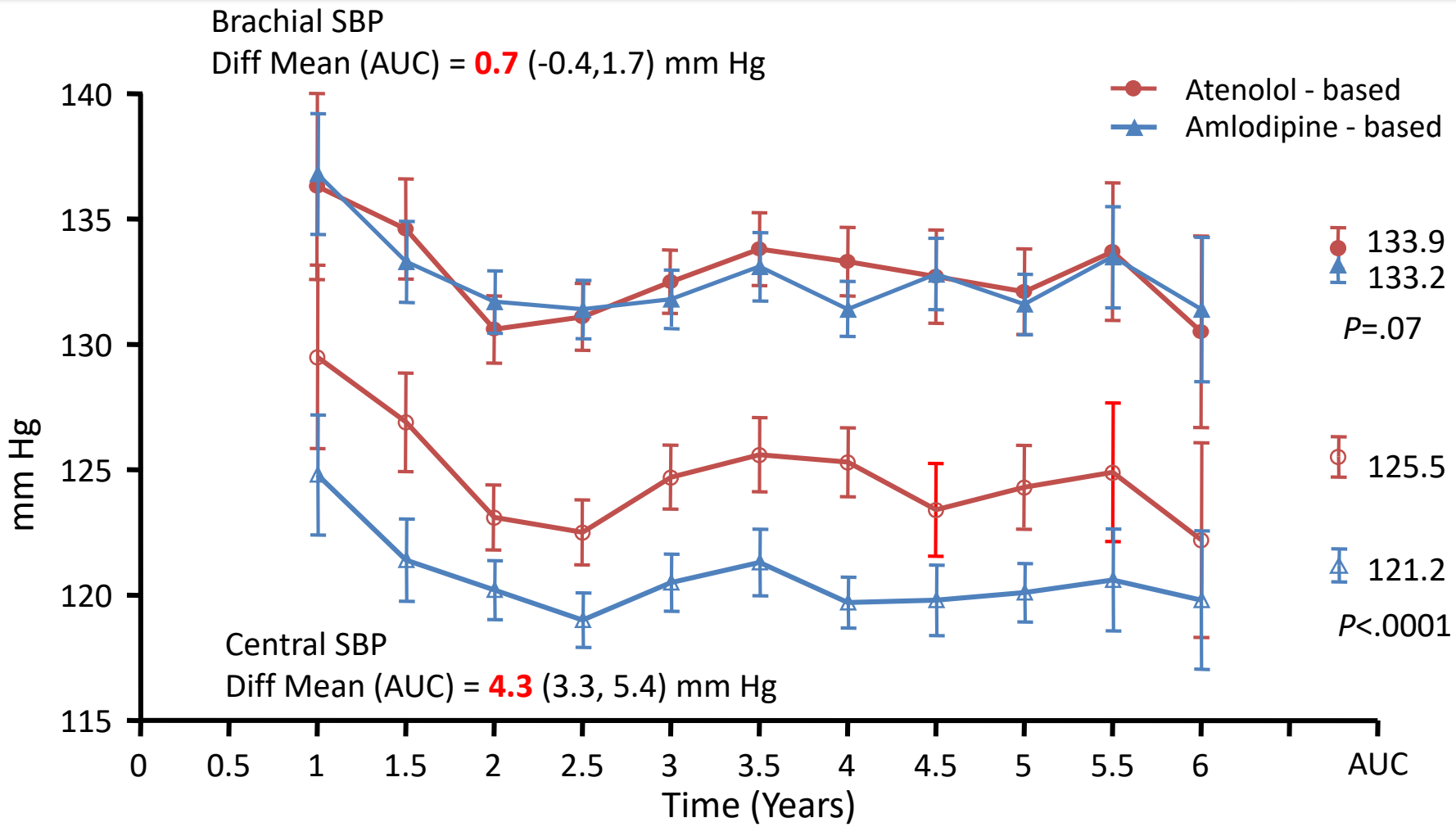
(J Am Coll Cardiol 2008;51:2432–9)

Table 6 Independent Predictors of Cardiovascular Events

	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Age (yrs)	1.09 (1.07–1.12)	<0.0001	1.09 (1.07–1.12)	<0.0001	1.10 (1.06–1.13)	<0.0001	1.09 (1.06–1.13)	<0.0001
Male gender	1.84 (1.29–1.64)	0.001	1.84 (1.29–1.64)	0.001	1.92 (1.29–2.87)	0.001	1.97 (1.32–2.94)	0.001
Brachial SBP (/10 mm Hg)		0.119						
Brachial PP (/10 mm Hg)				0.063				
Carotid SBP (/10 mm Hg)					1.19 (1.08–1.31)	<0.0001		
Carotid PP (/10 mm Hg)							1.23 (1.10–1.37)	<0.0001

Our prospective study in an unselected geriatric population of normotensive and untreated hypertensive subjects demonstrated that CV disease burden predicts CV events independent of age and BP. Moreover, we demonstrated the superior prognostic importance of carotid BP over brachial BP, indicating that central BP should be taken into account in the evaluation of the impact of therapeutic strategies on outcomes.

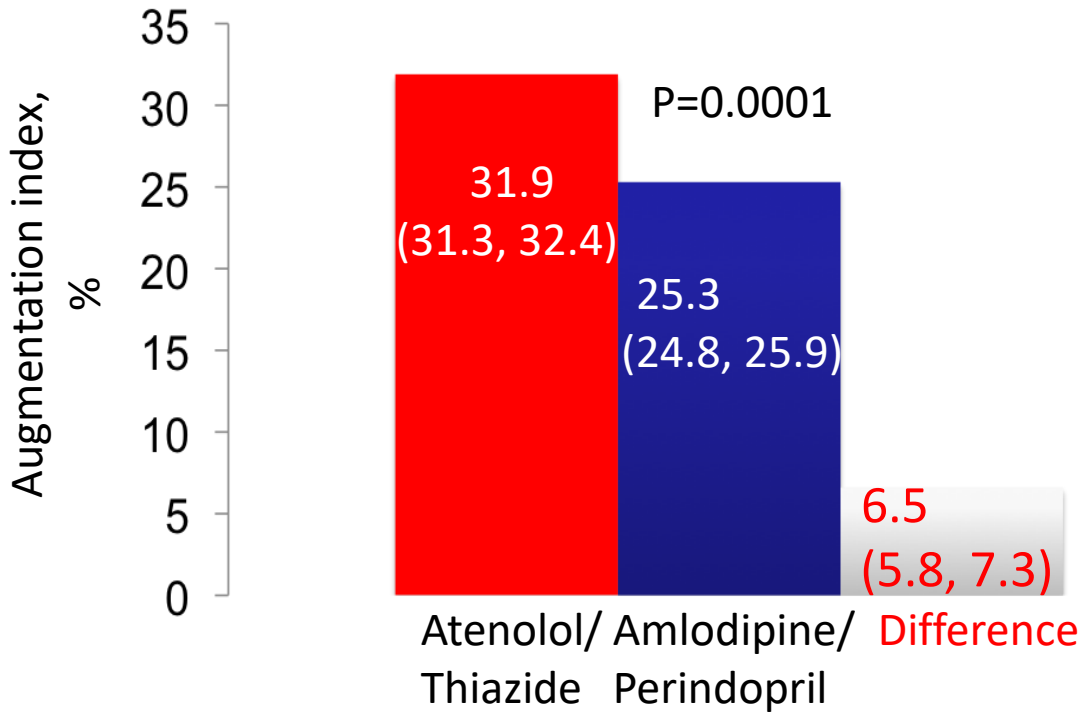
Studio CAFÉ: PA sistolica brachiale e centrale



Atenolol based	86	243	324	356	445	372	462	270	339	128	85	1031
Amlodipine based	88	248	329	369	475	406	508	278	390	126	101	1042

Williams B at al. Circulation. 2006;113:1213-1225

Studio CAFE: riflessione centrale dell'onda sfigmica



Williams B. et al Circulation. 2006;113:1213-1225

2013 ESH/ESC Guidelines for the management of arterial hypertension

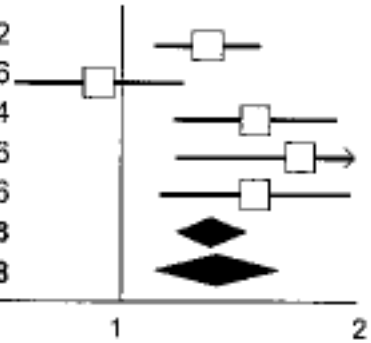
Asymptomatic organ damage
Pulse pressure (in the elderly) ≥60 mmHg
Electrocardiographic LVH (Sokolow–Lyon index >3.5 mV; RaVL >1.1 mV; Cornell voltage duration product >244 mV*ms), or
Echocardiographic LVH [LVM index: men >115 g/m^2; women >95 g/m^2 (BSA)][a]
Carotid wall thickening (IMT >0.9 mm) or plaque
Carotid–femoral PWV >10 m/s
Ankle-brachial index <0.9
CKD with eGFR 30–60 ml/min/1.73 m^2 (BSA)
Microalbuminuria (30–300 mg/24 h), or albumin–creatinine ratio (30–300 mg/g; 3.4–34 mg/mmol) (preferentially on morning spot urine)

Mancia G. et al., J. Hypertens. 2013; 31; 1281-1357

Prediction of cardiovascular events and all-cause mortality with central haemodynamics: a systematic review and meta-analysis

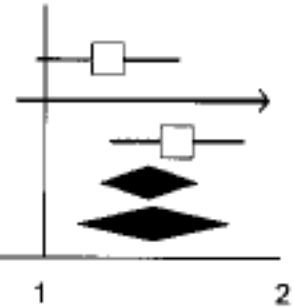
(A) **Central AIx and CV outcome**

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**



(B) **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 Heat J 2010

HYPERTENSION

B. Williams (London, UK)

Conflicts of Interest

Speaker/advisor: Novartis, Boehringer Ingelheim, Daiichi-Sankyo, Menarini, Servier

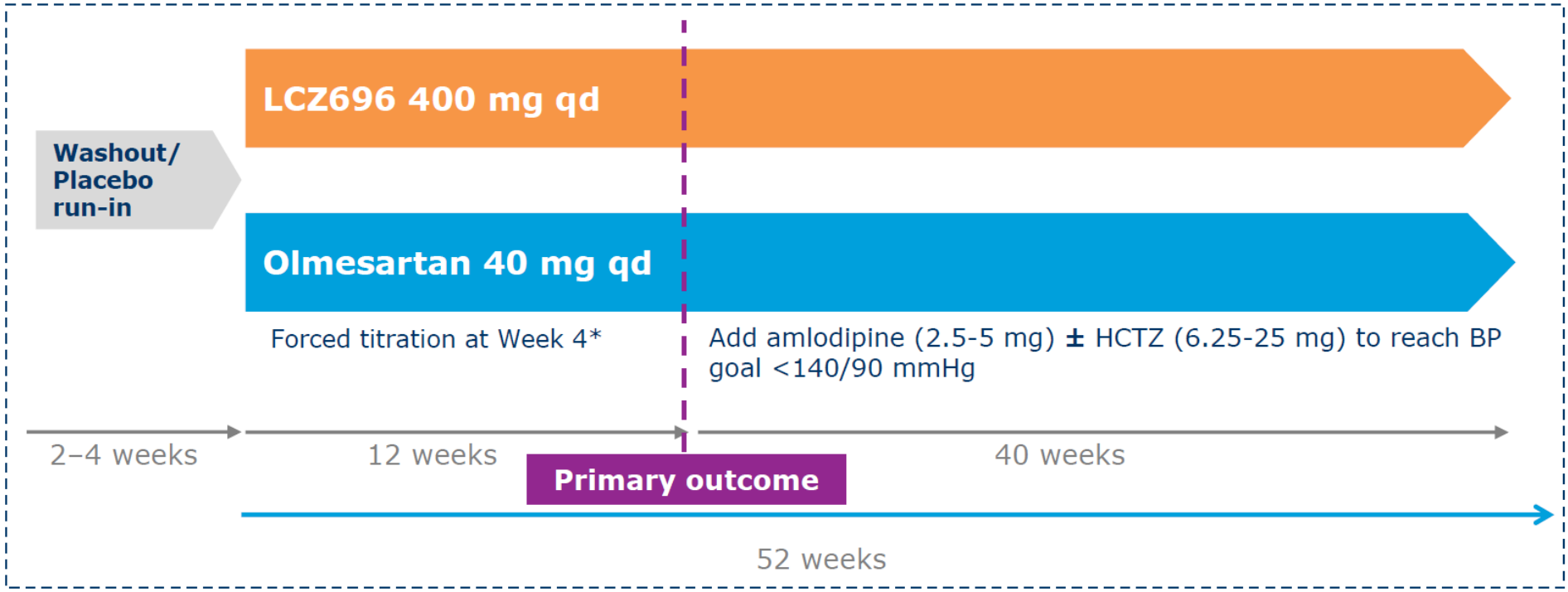
HYPERTENSION HIGHLIGHTS

ARB/NEPRILYSIN INHIBITOR (ARNI) IN PATIENTS WITH SYSTOLIC HYPERTENSION

PARAMETER Study

PARAMETER: STUDY DESIGN

Multicenter, randomized, double-blind, active-controlled, 52-week study to evaluate the safety and efficacy of an LCZ696 regimen on central aortic pressures and arterial stiffness in elderly hypertensive patients



Patient population: Isolated Systolic Hypertension with Stiff Arteries

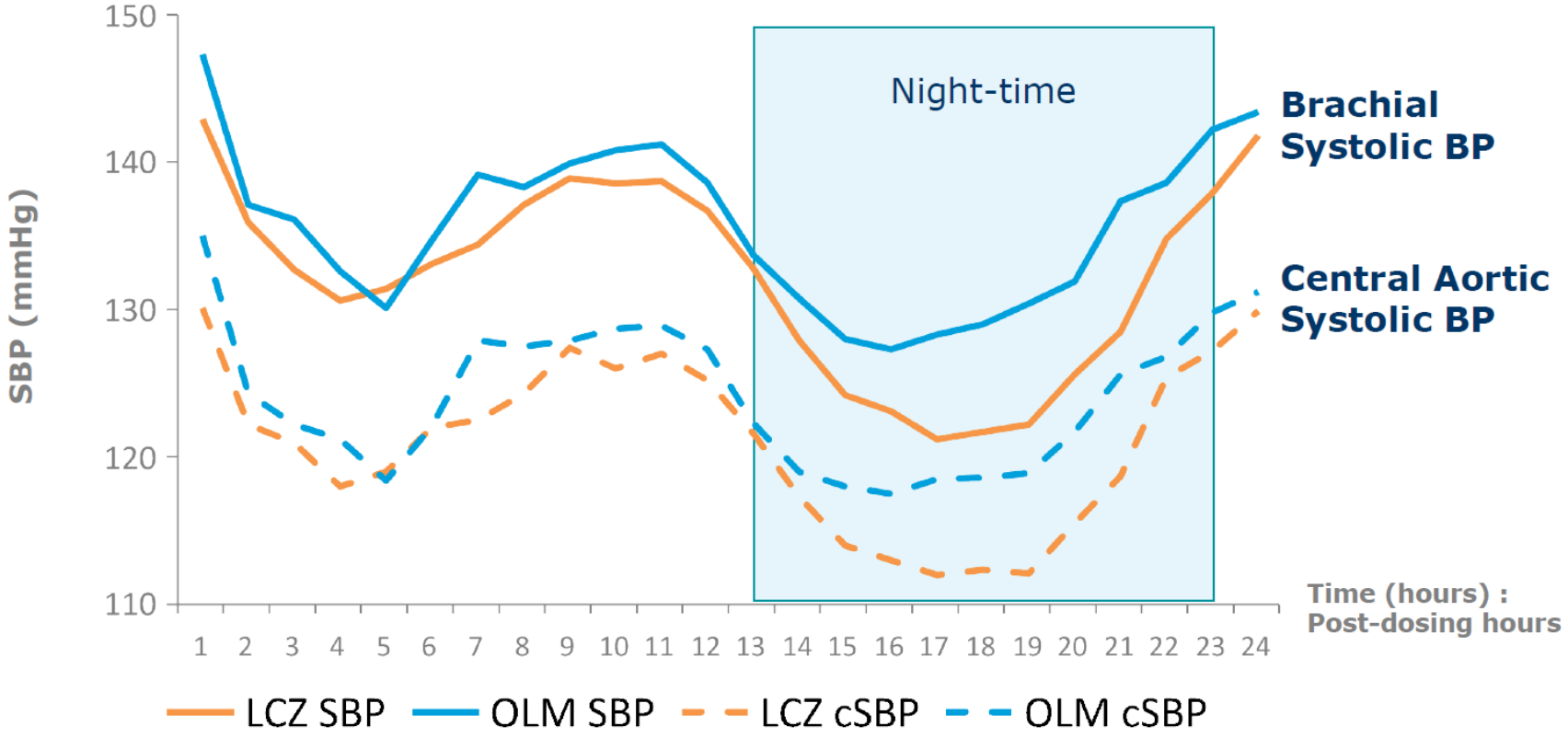
- 454 patients aged ≥60 years
- Elevated SBP (≥150 mmHg) & wide pulse pressure (>60 mmHg)

B. Williams (London, UK) FP 4143

24-HOUR BRACHIAL AND CENTRAL AORTIC SBP AT WEEK 12

Mean Δ SBP: -4.1 mmHg, p<0.001 (-13.2 (LCZ696) *vs.* -9.1 (OLM) mmHg)

Mean Δ cSBP: -3.35 mmHg, p<0.001 (-12.1 (LCZ696) *vs.* -8.7 (OLM) mmHg)



B. Williams (London, UK) FP 4143

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Hot Line
• 16:30-18
ESC Car

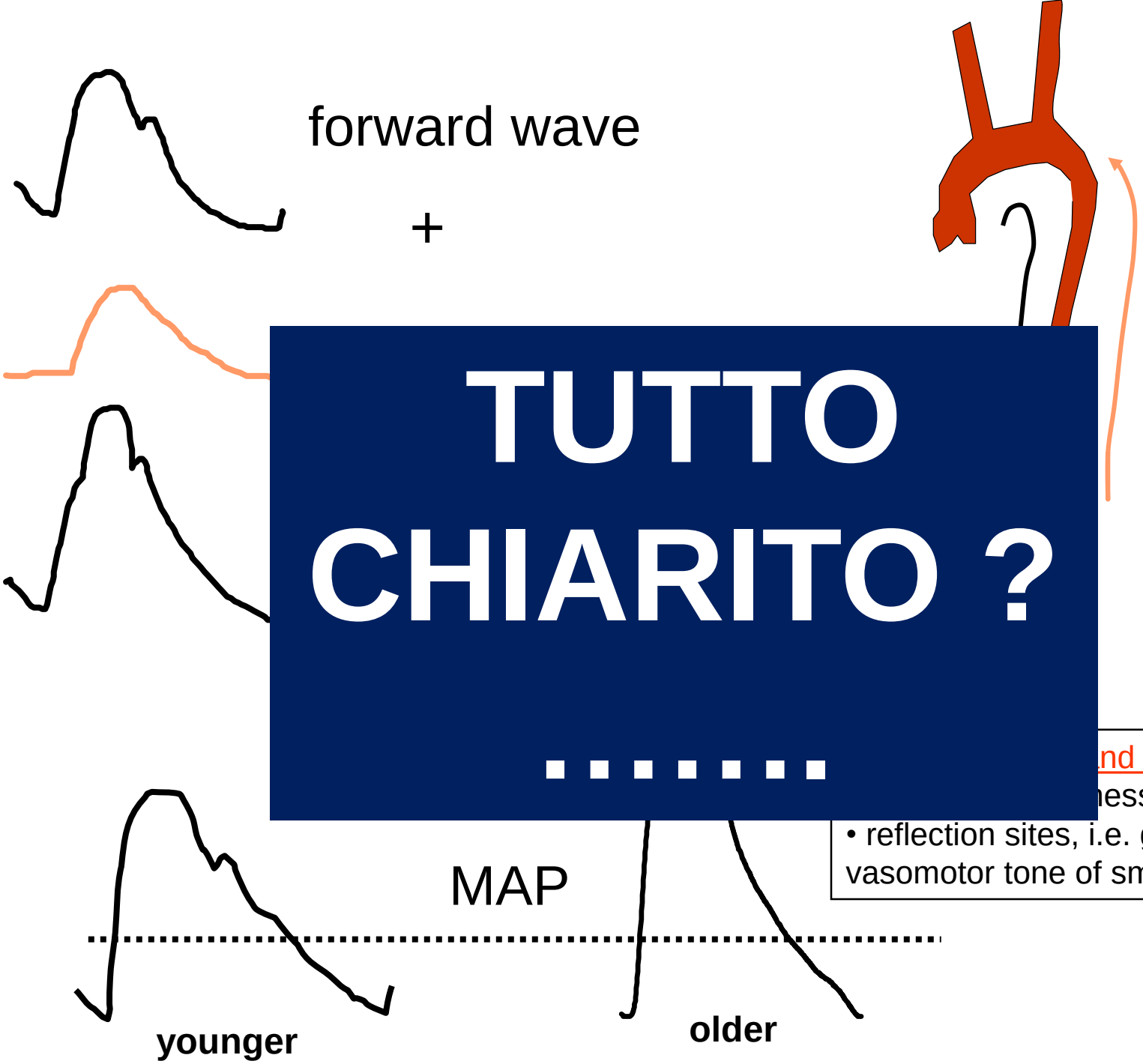
Now, in a bid to extend its indication, the PARAMETER study has shown that this same combination of sacubitril/valsartan significantly reduced central aortic systolic pressure (CASP) and central aortic pulse pressure (CPP) when compared to the standard ARB olmesartan in elderly patients with hypertension.

'An important finding of this trial,' said

r patient

400 mg qd or olmesartan 40 mg qd at 48

Continued on page 2



TUTTO CHIARITO ?

.....

nd central SBP
ness
• reflection sites, i.e. geometry and vasomotor tone of small arteries

Am J Physiol Heart Circ Physiol 298: H580–H586, 2010.
First published December 11, 2009; doi:10.1152/ajpheart.00875.2009.

The arterial reservoir pressure increases with aging and is the major determinant of the aortic augmentation index

Justin E. Davies,[1] John Baksi,[1] Darrel P. Francis,[1] Nearchos Hadjiloizou,[1] Zachary I. Whinnett,[1] Charlotte H. Manisty,[1] Jazmin Aguado-Sierra,[2] Rodney A. Foale,[1] Iqbal S. Malik,[1] John V. Tyberg,[3] Kim H. Parker,[2] Jamil Mayet,[1] and Alun D. Hughes[1]

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Submitted 15 September 2009; accepted in final form 7 December 2009

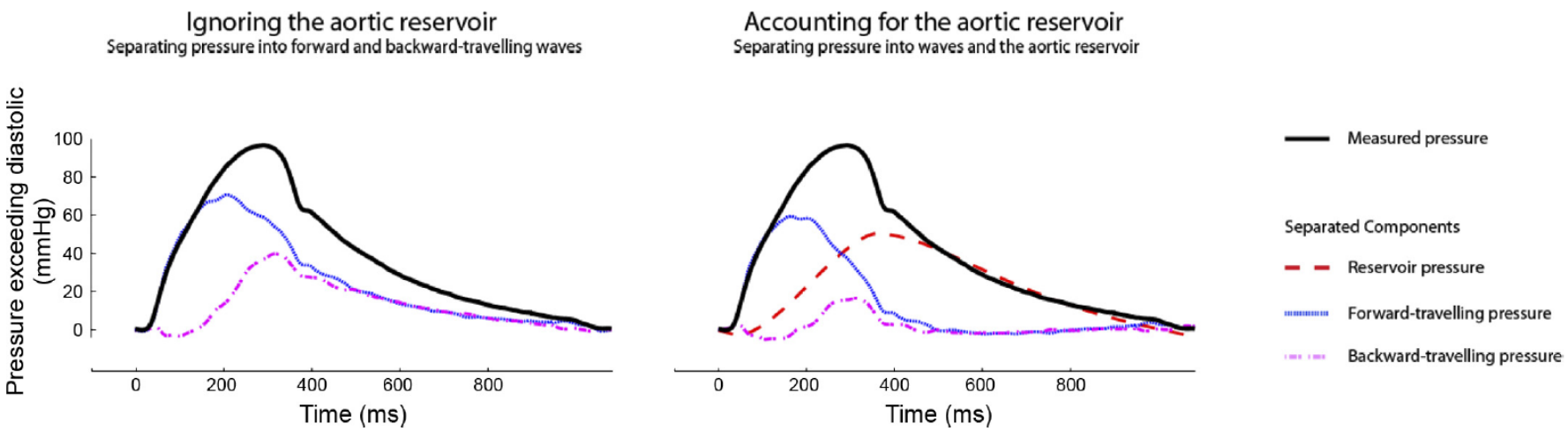

Fig. 2. Impact of accounting for the arterial reservoir pressure on the calculated forward- and backward-traveling pressure waves. The pressure wave is separated into its constituent components ignoring (*left*) and then accounting for (*right*) the aortic reservoir. When the aortic reservoir is ignored, both the forward and backward peak pressures are substantial and during diastole, they are equal and decrease slowly and continuously. When the reservoir pressure is taken into account, the backward-traveling (reflected) wave is significantly reduced and forward and backward wave pressures are absent following closure of the aortic valve.

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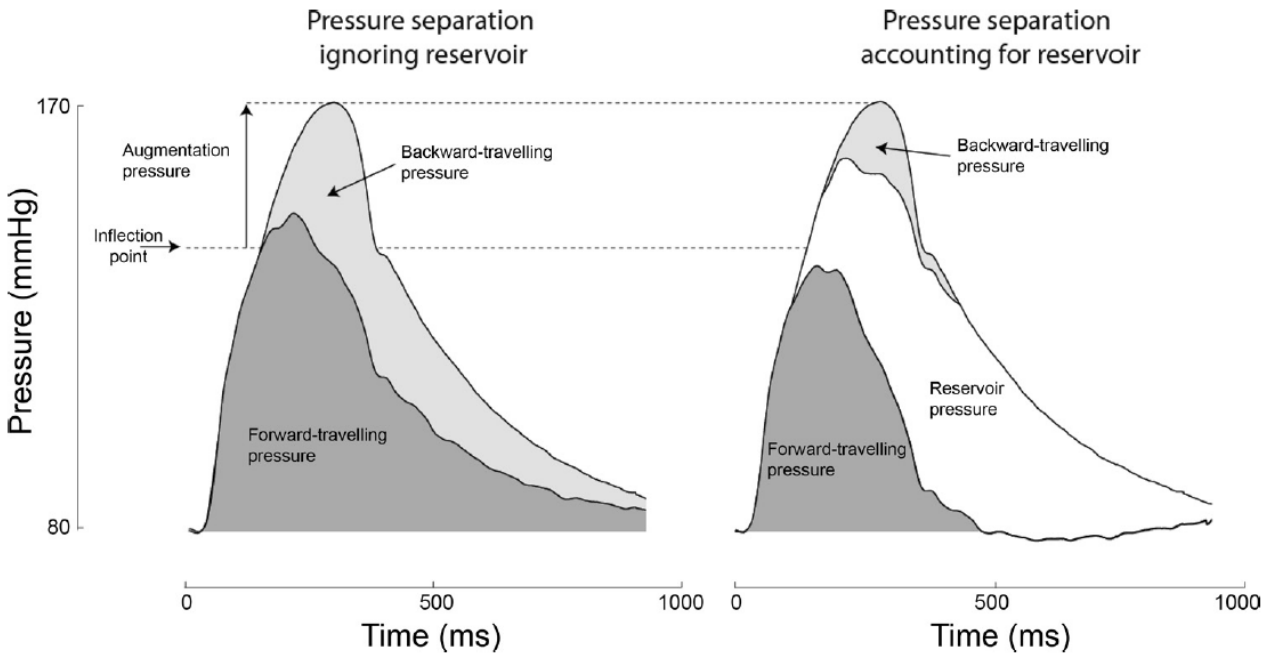
PRESSURE AUGMENTATION, RESERVOIR, WAVES, AND AGING



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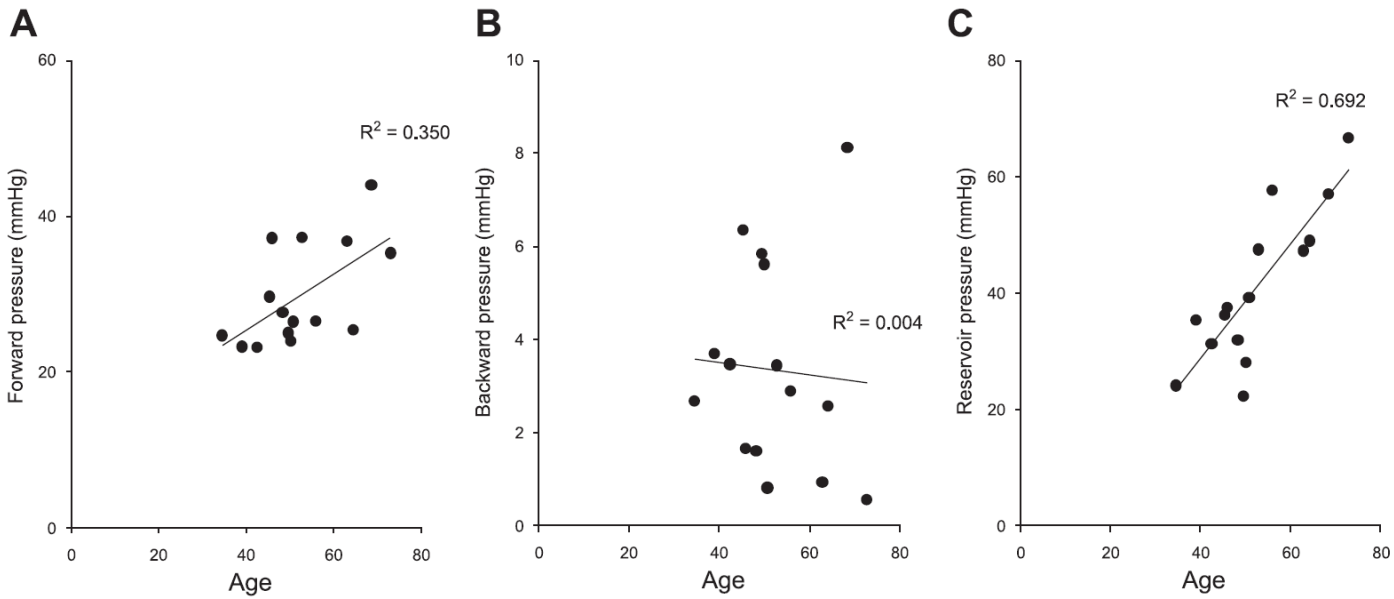

Fig. 4. Relationship between separated pressure components and aging after accounting for the aortic reservoir pressure. The pressure waveform was separated into forward (*A*) and backward (*B*) and reservoir (*C*) pressure components. With increasing age, both forward and arterial reservoir pressure increased. However, the backward pressure component was not significantly correlated with age.

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[1]*Imperial College Healthcare National Health Service Trust, International Centre for Circulatory Health, Saint Mary's Hospital Campus, London, United Kingdom;* [2]*University of Calgary, Calgary, Canada; and* [3]*Physiological Flow Unit, Department of Bioengineering, Imperial College, London, United Kingdom*

Submitted 15 September 2009; accepted in final form 7 December 2009

Conclusions. The arterial reservoir makes a large contribution to the aortic blood pressure waveform in humans and is the principal component of the AIx. In contrast, wave reflection only made a minor contribution to the AIx. This reservoir pressure is the aggregate pressure resulting from the net difference between the total arterial system inflow and outflow divided by an effective arterial compliance. Reservoir pressure increases markedly with aging, probably as a result of decreased compliance, and this is the major factor accounting for the associated change in morphology of the aortic pressure waveform. Modifying the behavior of the arterial reservoir rather than changing wave reflection may be a useful target for future therapy.

Am J Physiol Heart Circ Physiol 309: H1225–H1233, 2015.
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Associations and clinical relevance of aortic-brachial artery stiffness mismatch, aortic reservoir function, and central pressure augmentation

Martin G. Schultz,[1] Alun D. Hughes,[2] Justin E. Davies,[3] and James E. Sharman[1]

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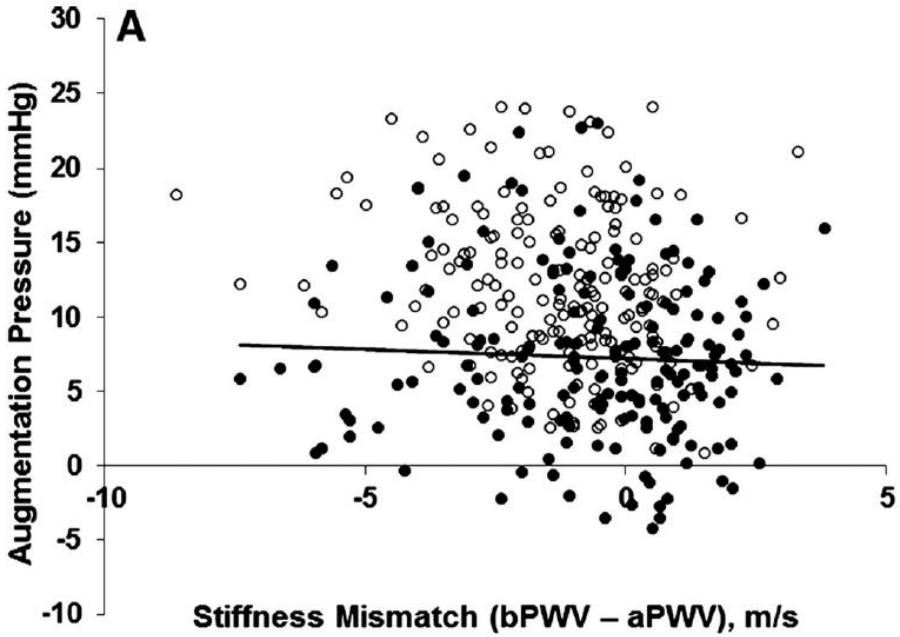

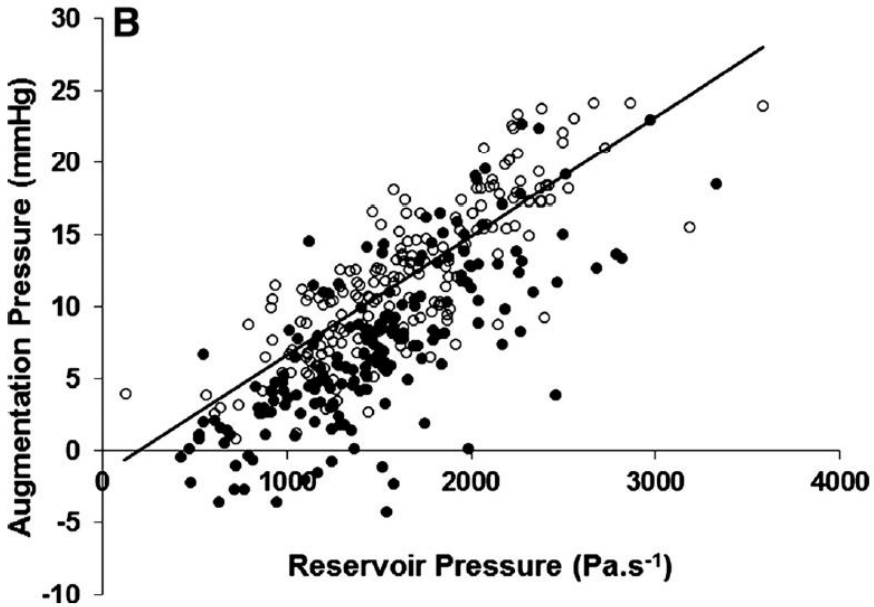

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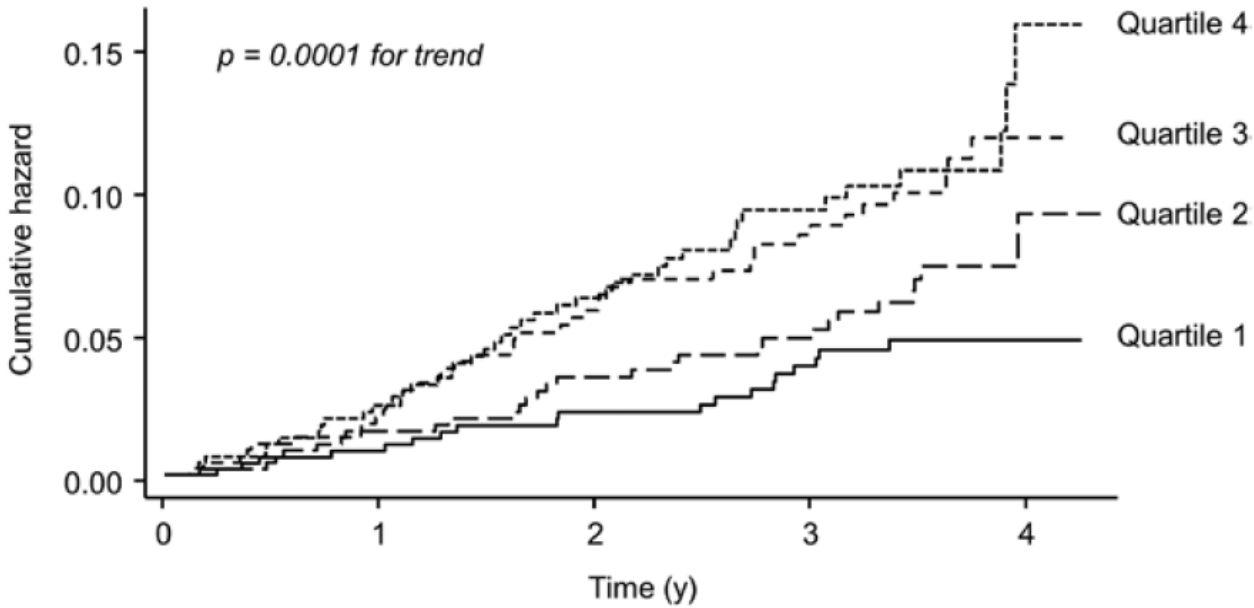
Conclusion. Although the prognostic value of wave reflection is recognized (23), our study provides persuasive evidence that central AP and AIx should not be regarded as markers of wave reflection. Reservoir pressure indexes intuitively and physiologically provide an explanation for central pressure waveform morphology and are associated to end organ damage. Since recent clinical trial data highlight the strong and independent prognostic value of reservoir pressure indexes in the prediction of cardiovascular events and mortality (10, 14), consideration of this simple model of arterial hemodynamics may provide important new and clinically relevant understanding of BP physiology.

Clinical Trial: CAFE Study

Excess Pressure Integral Predicts Cardiovascular Events Independent of Other Risk Factors in the Conduit Artery Functional Evaluation Substudy of Anglo-Scandinavian Cardiac Outcomes Trial

Justin E. Davies, Peter Lacy, Therese Tillin, David Collier, J. Kennedy Cruickshank, Darrel P. Francis, Anura Malaweera, Jamil Mayet, Alice Stanton, Bryan Williams, Kim H. Parker, Simon A. McG Thom, Alun D. Hughes

XSPI, excess pressure integral



(*Hypertension*. 2014;64:60-68.)

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Table 7. Multivariable Models of Predictors of LVMI

	Adjusted r^2=0.05		
LVMI Variables	Coefficient	(SE)	*P* Value
XSPI, mm Hg·s	7.04	2.26	0.002
PRI, mm Hg·s	9.67	2.43	<0.001
Age, y	–0.14	0.08	0.06
Male sex	–1.65	1.50	0.3
MAP, mm Hg	0.08	0.06	0.2
AP, mm Hg	–0.36	0.16	0.02
Amlodipine±perindopril	–0.35	1.18	0.8
Constant	–29.91	9.56	0.002

AP indicates augmentation pressure; LVMI, left ventricular mass index; MAP, mean arterial pressure; PRI, integral of reservoir pressure; and XSPI, excess pressure integral.

(*Hypertension*. 2014;64:60-68.)

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Excess pressure time integral predicted cardiovascular events in a moderate sized subset (10%) of the ASCOT participants and is additive to the predictive value of conventional risk factors. Finally, by differentially discriminating between different drug classes, this measurement offers a **potentially new tool for selection of pharmacological therapies on a patient-specific basis.**

(*Hypertension*. 2014;64:60-68.)

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Reservoir and excess pressures predict cardiovascular events in high-risk patients ☆

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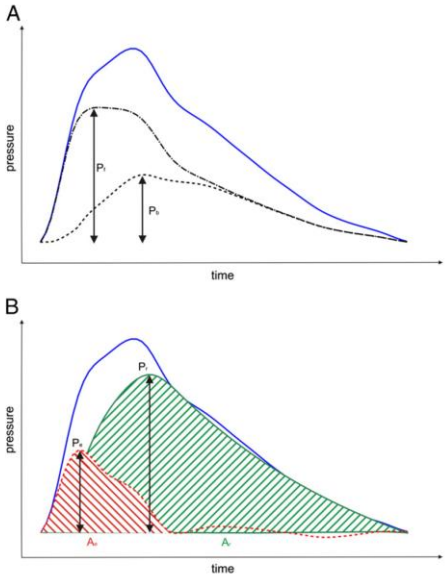

Fig. 1. Separation of the aortic pressure waveform obtained in a typical patient into: A) forward (P_f) and backward (P_b) traveling pressure waveforms; B) reservoir and excess pressure; area of reservoir pressure (A_r) and excess pressure (A_e); amplitudes of reservoir pressure (P_r) and excess pressure (P_e).

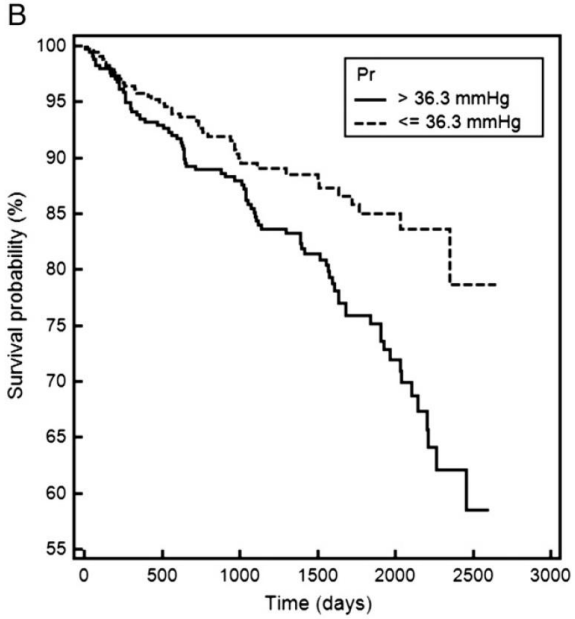

Fig. 3. Kaplan–Meier survival curves divided into two groups using the median value for: A) amplitude of backward wave pressure (P_b); B) amplitude of reservoir pressure (P_r).


PA clinica
PA centrale ?
Onda sfigmica ?
Rigidità arteriosa ?
Augmentation index?
PWW?
Reservois pressure?