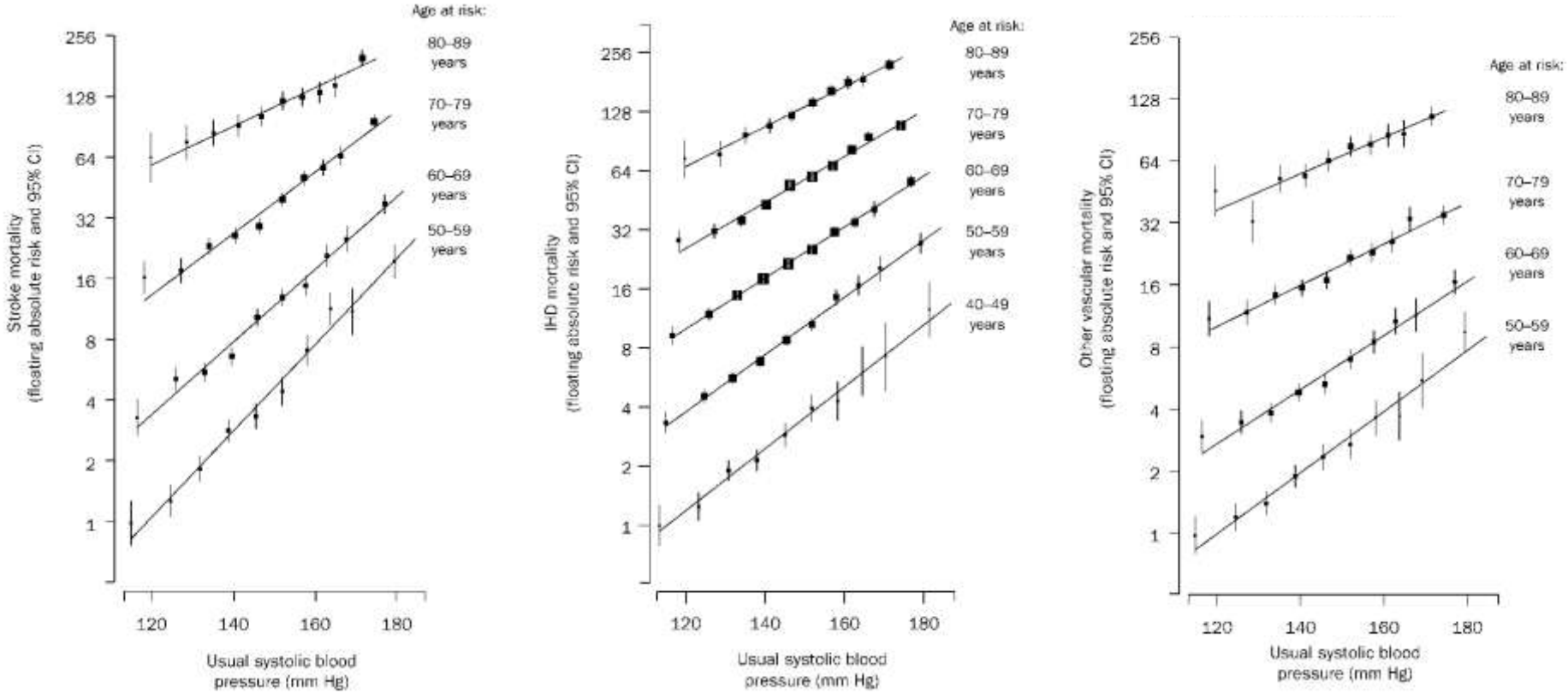
La pression artérielle comme FdR CV: Quelle pression artérielle ?

Pierre Fesler

Service de Médecine Interne - Hôpital Lapeyronie

PA et risque CDV



Une PA > 115/75 mmHg est associée à une augmentation progressive du risque CV

Prospective studies collaboration. Lancet 2002; 360: 1903

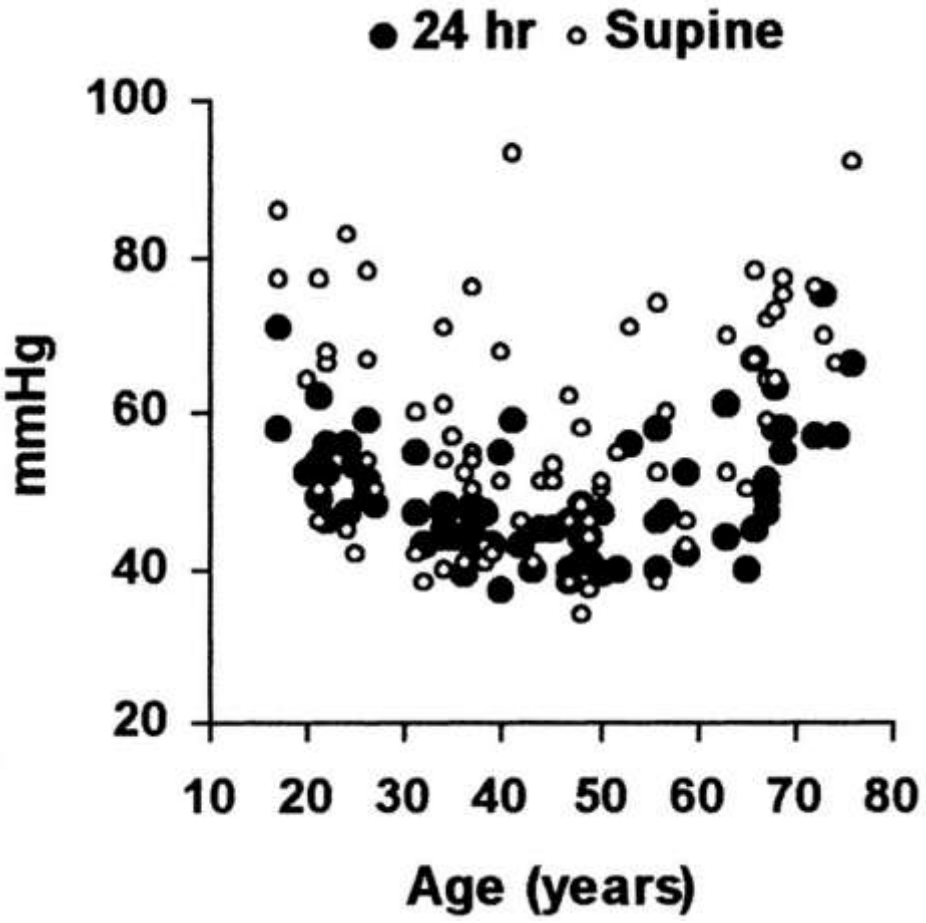
PA et risque CDV

Age	PA	CAD OR (95% CI)
< 50 ans	PAS	1.14 (1.06-1.24)
	PAD	1.34 (1.18-1.51)
	PP	1.02 (0.89-1.17)
50-59 ans	PAS	1.08 (1.02-1.15)
	PAD	1.11 (0.99-1.17)
	PP	1.11 (1.02-1.22)
> 60 ans	PAS	1.17 (1.11-1.24)
	PAD	1.12 (0.99-1.27)
	PP	1.24 (1.16-1.33)

Franklin et al. Circulation 01;103:1245

Déterminants de la pression pulsée

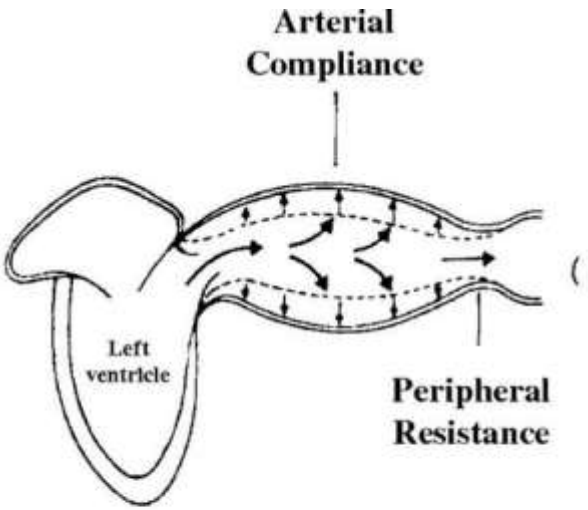
- Sujet jeune:
  - Volume d'éjection
- Sujet âgé:
  - Rigidité artérielle

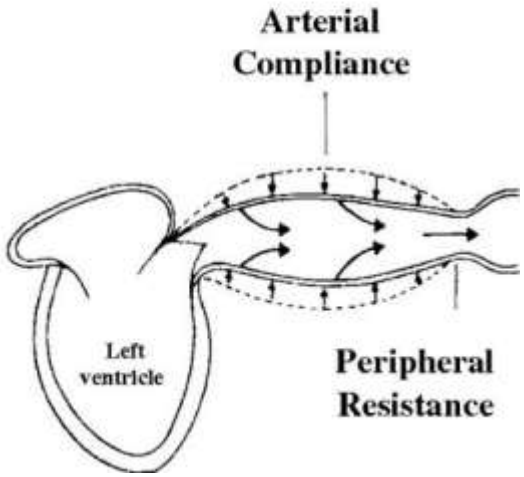


Alfie et al, Hypertension 1999;34:808

Pression artérielle

- Composante stable
  - PAM = RVP x Q
- Composante pulsatile
  - Dépend de la fonction des gros troncs artériels

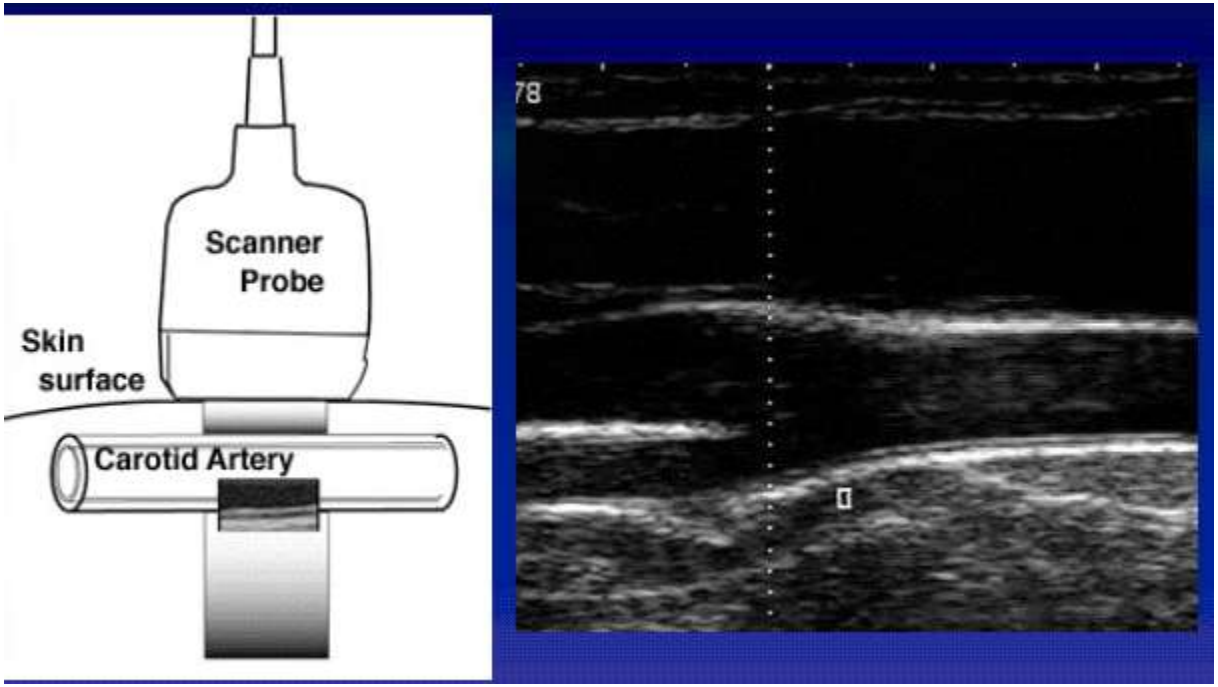


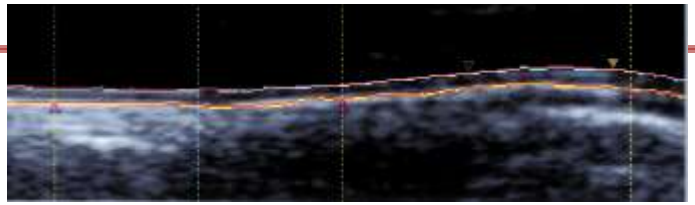


Méthodes d’évaluation non invasive des grosses artères

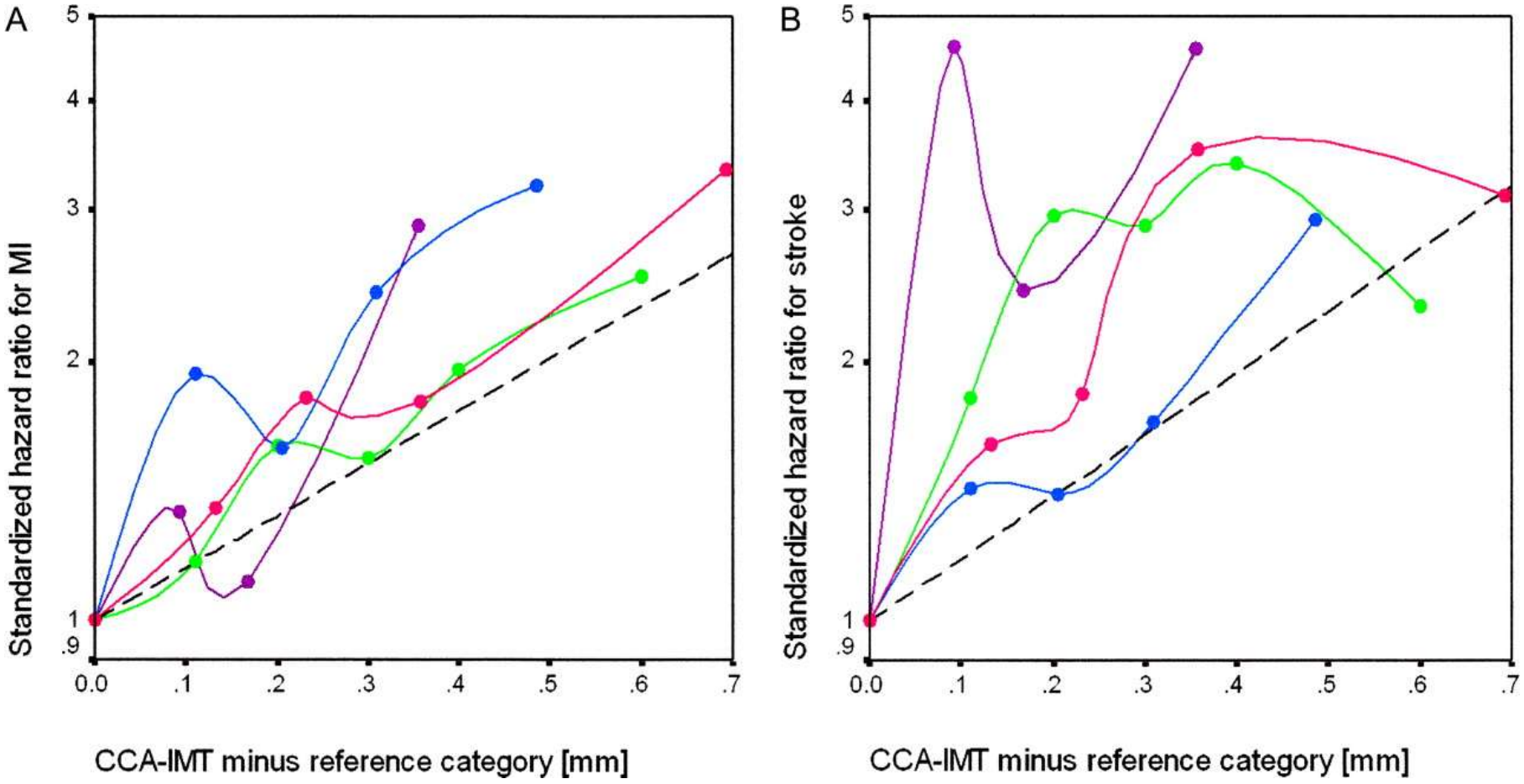
Méthodes d'évaluation non invasive des grosses artères

- Structurelle:
  - Épaisseur intima média (échographie)





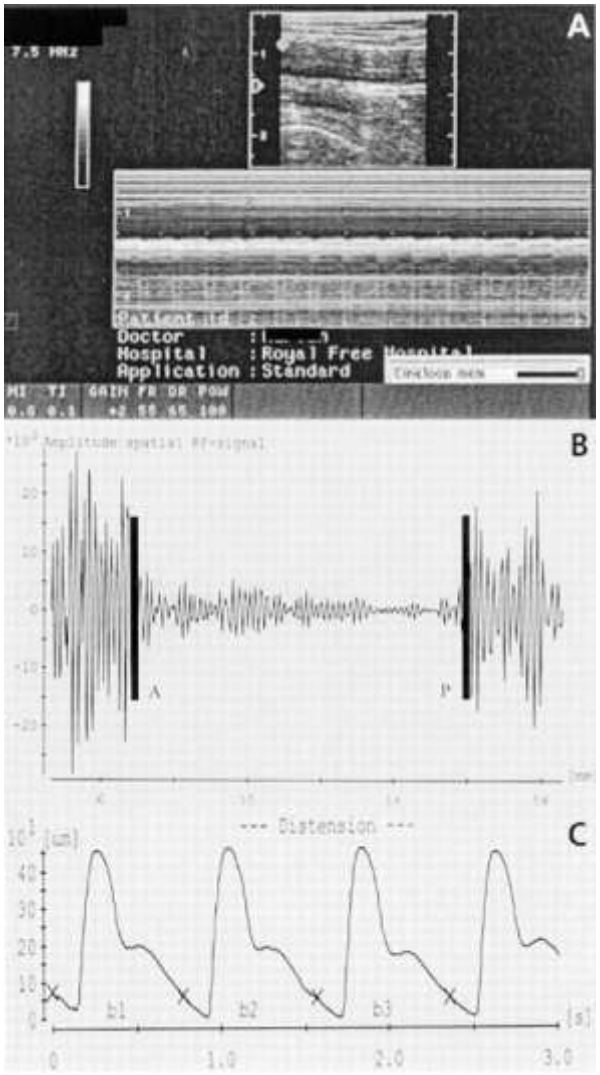
Epaisseur intima média et risque CV
Une relation complexe !



Lorenz MW et al. Circulation 2007;115:459

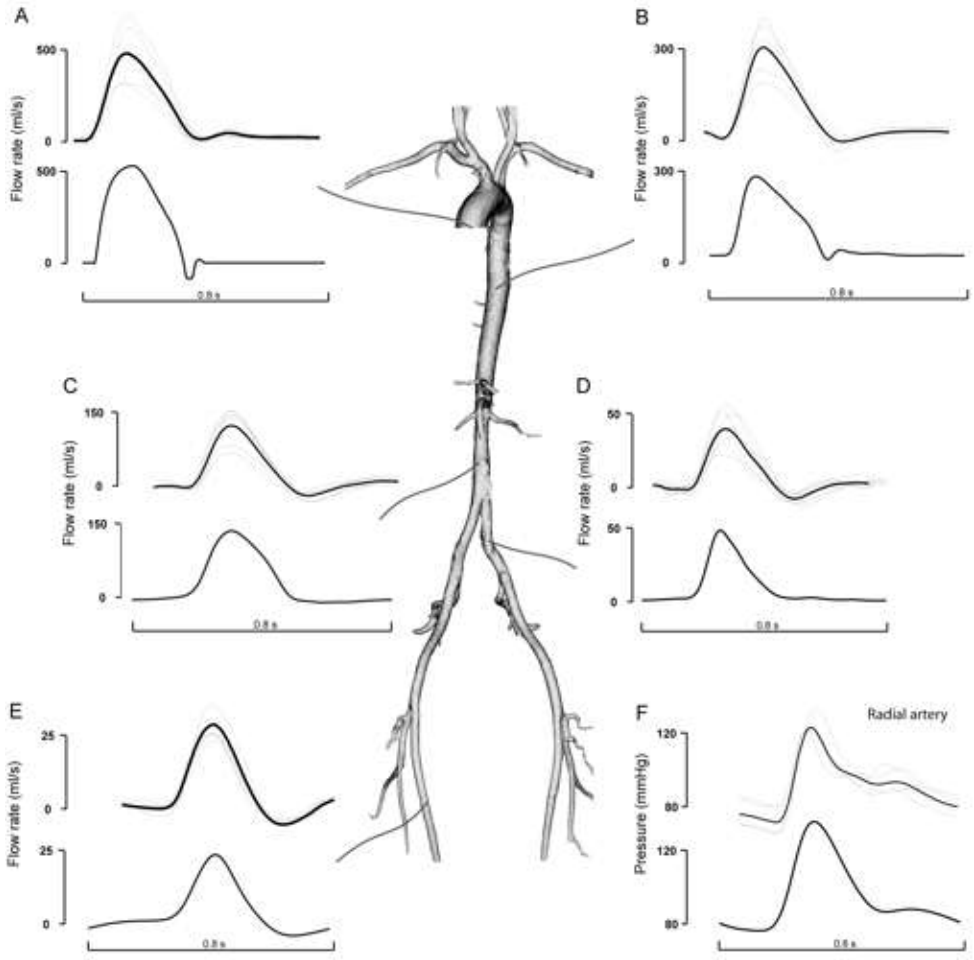
Méthodes d'évaluation non invasive des grosses artères

- Fonctionnelles, locales:
  - Distensibilité carotidienne
    - Diamètre: échographie
    - Pression: tonométrie d'aplanation
    - $DC=(2\Delta D \times D + \Delta D^2)/(PP \times D^2)$
  - Compliance carotidienne
    - $CC = \prod \times (2D \times \Delta D^2)/4PP$
  - Module de Young carotidienne
    - $Einc = D/(IMT \times DC)$



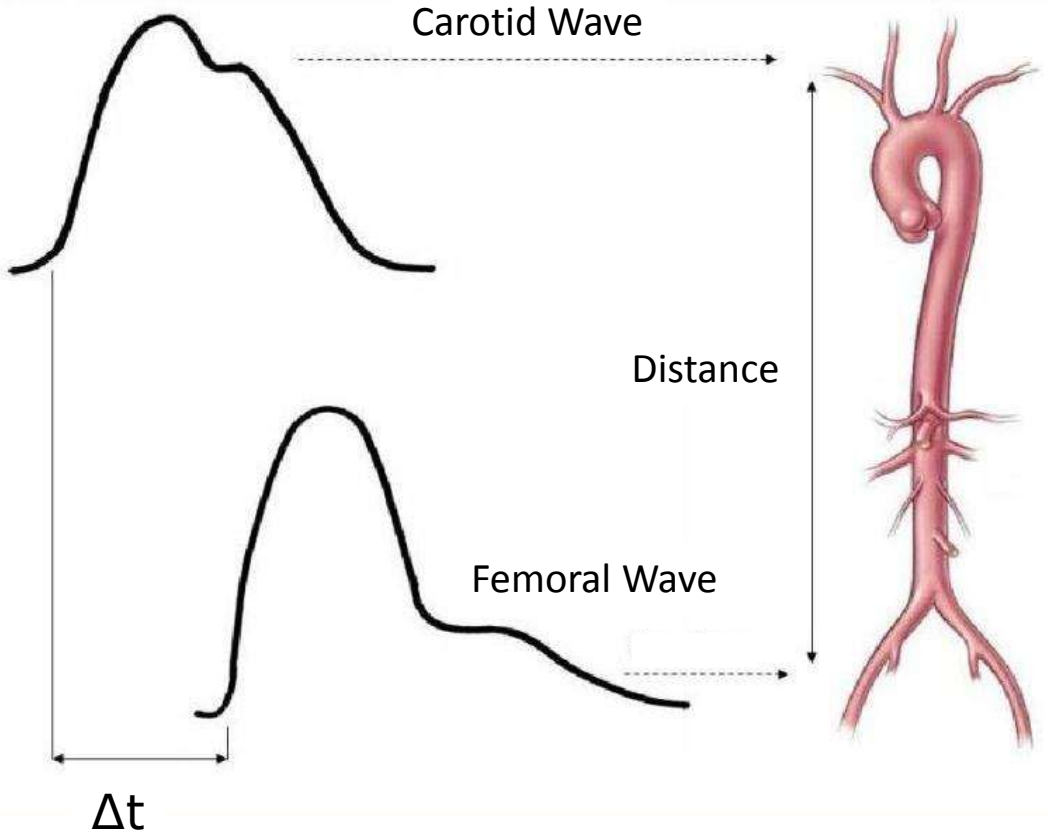
Méthodes d'évaluation non invasive des grosses artères

- Fonctionnelles, générales:
  - Système de propagation d'onde de pression et de débit
  - 2 composantes:
    - Rigidité artérielle : Vitesse de l'onde de pouls
    - Réflexion d'onde: Analyse de l'onde de pouls



Rigidité artérielle

- Vitesse de propagation de l'onde de pouls:
  - VOP = Distance / Δt



Cadre 4: Equation de Moens-Korteweg

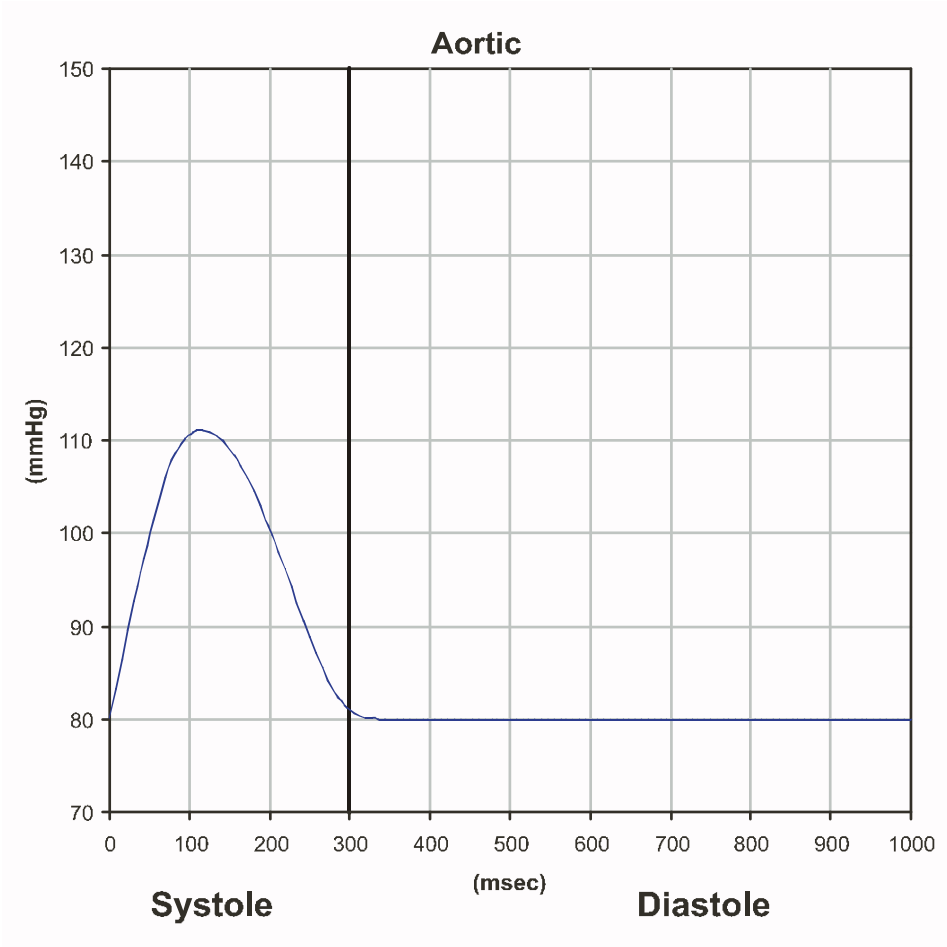
$$c_0 = \sqrt{Eh/2R\rho}$$

c_0: vitesse de propagation; E: module de Young; h: épaisseur pariétale; R: résistance; ρ: densité

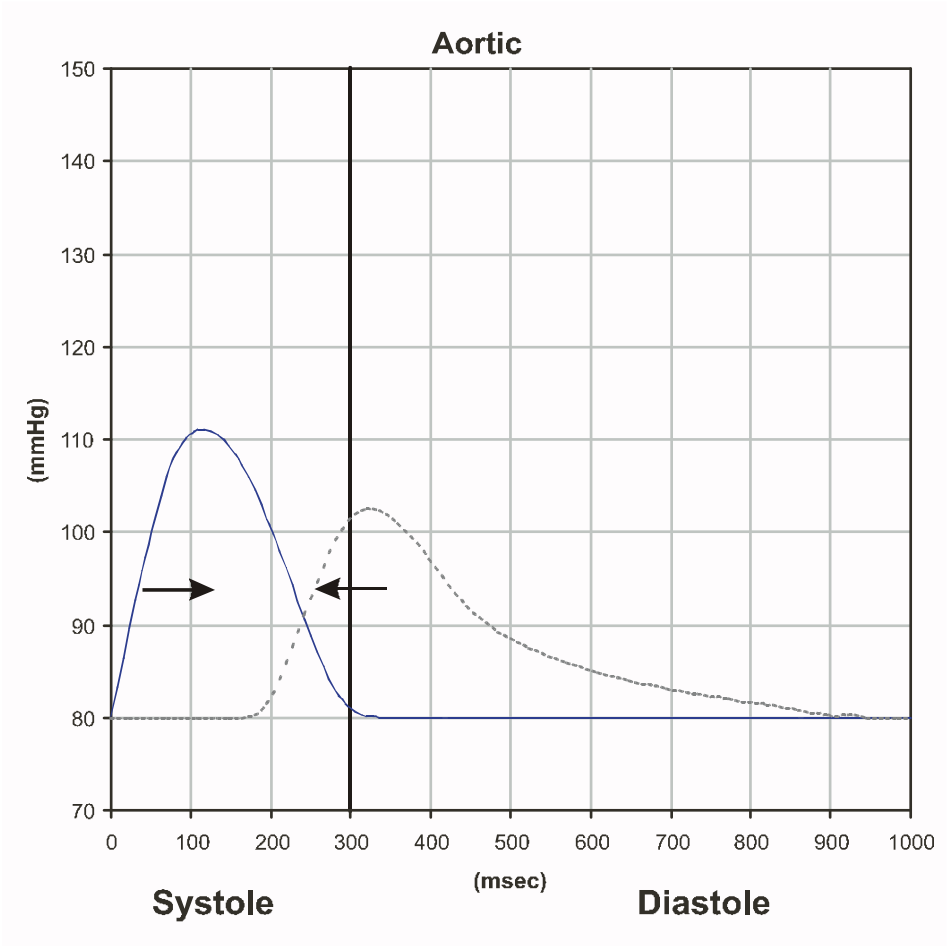
Réflexion d'onde

- Principes de l'analyse de l'onde de pouls
  - Dériver l'onde de pression centrale à partir de l'onde de pression périphérique acquise par tonométrie d'aplanation
  - Extraire de cette onde de pression centrale des informations sur la rigidité artérielle et la réflexion d'onde

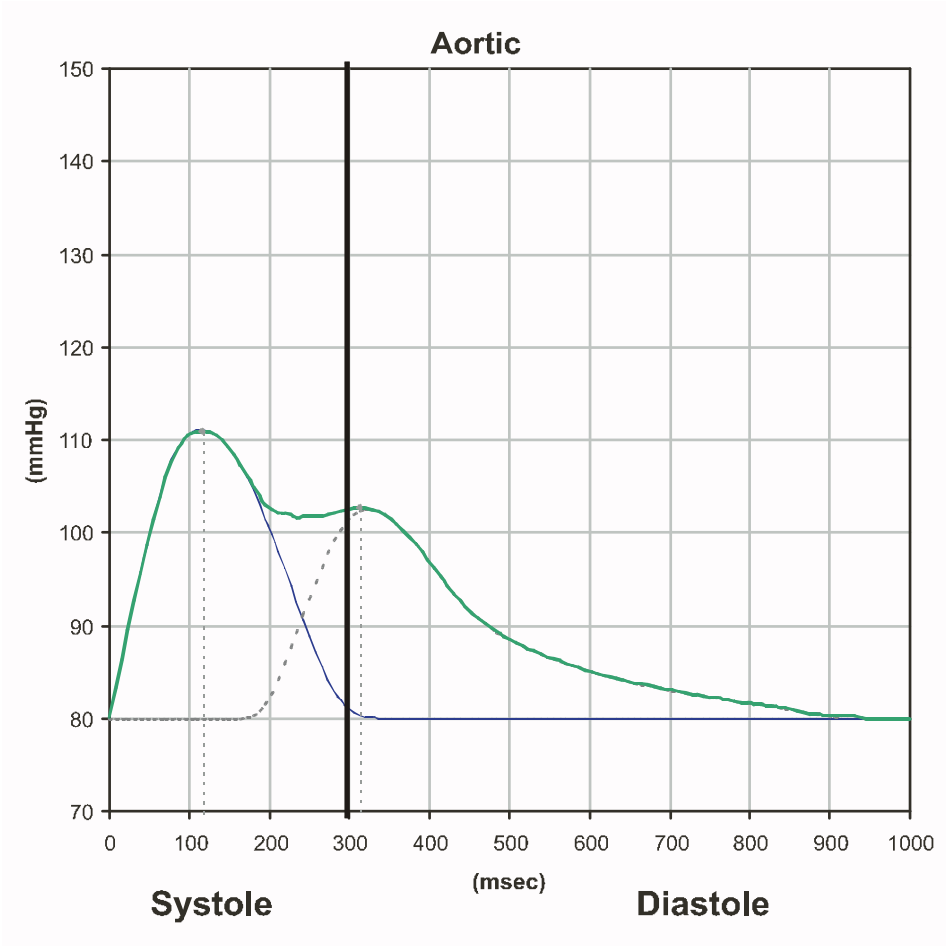
Réflexion d’onde



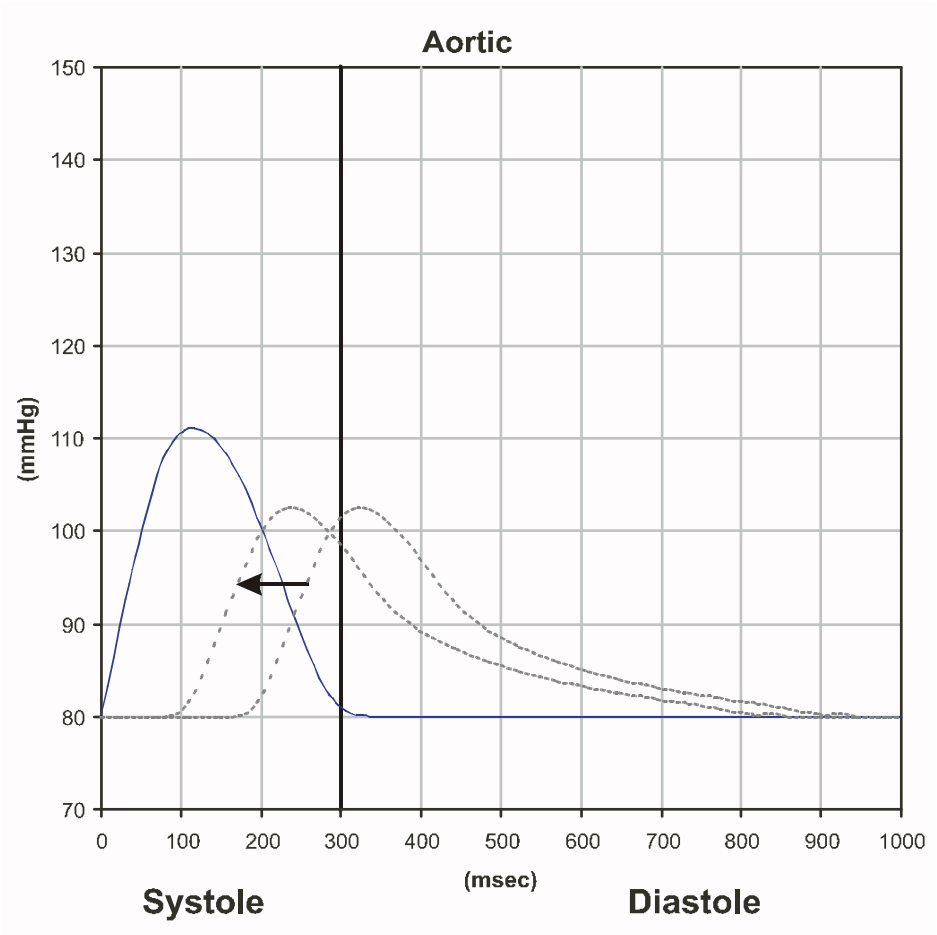
Réflexion d’onde



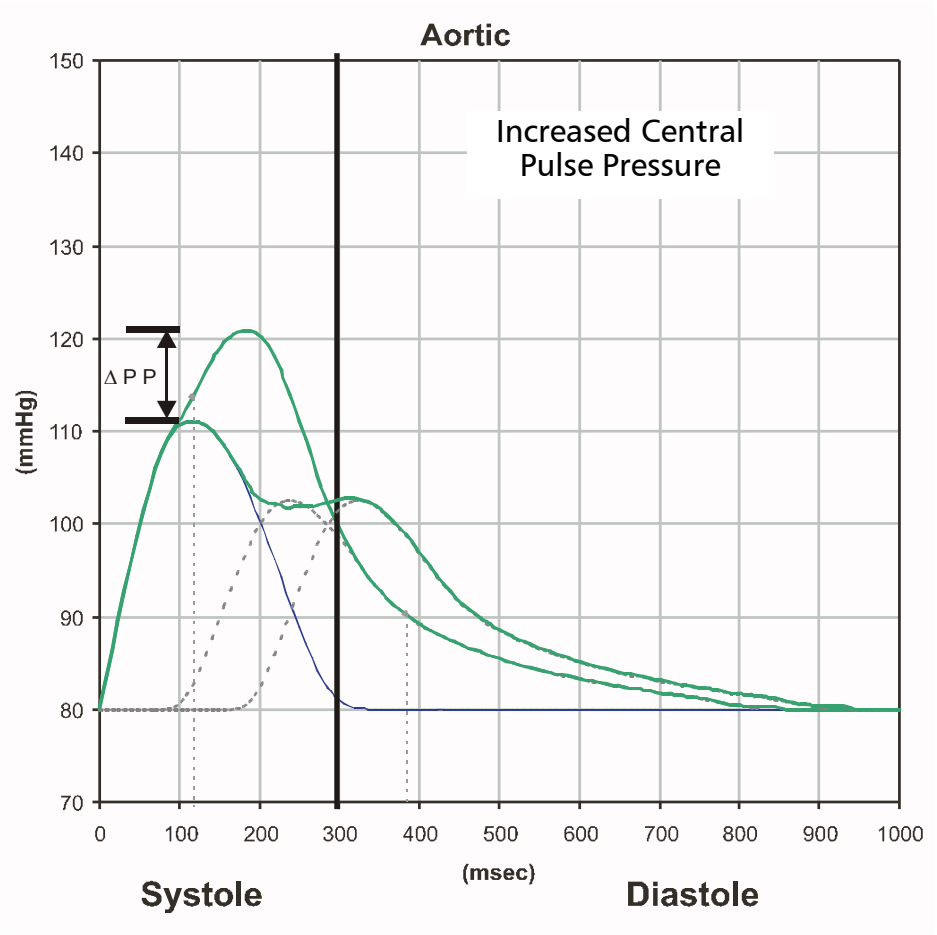
Réflexion d'onde



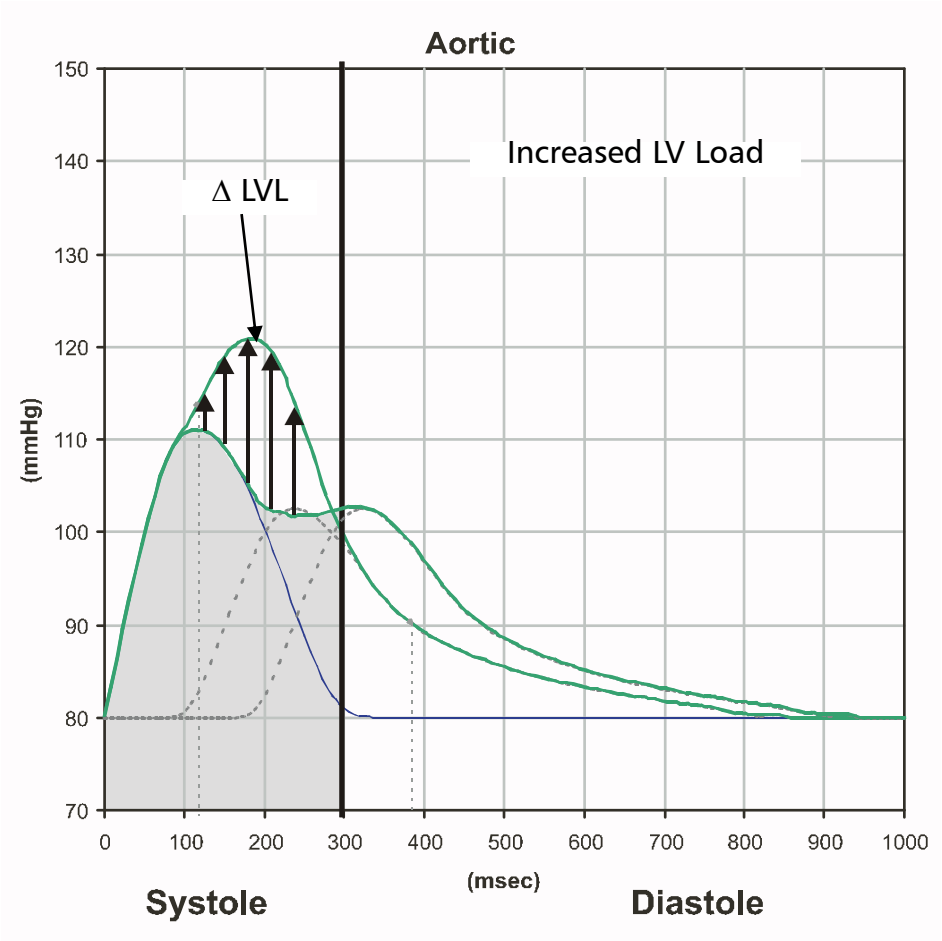
Réflexion d’onde



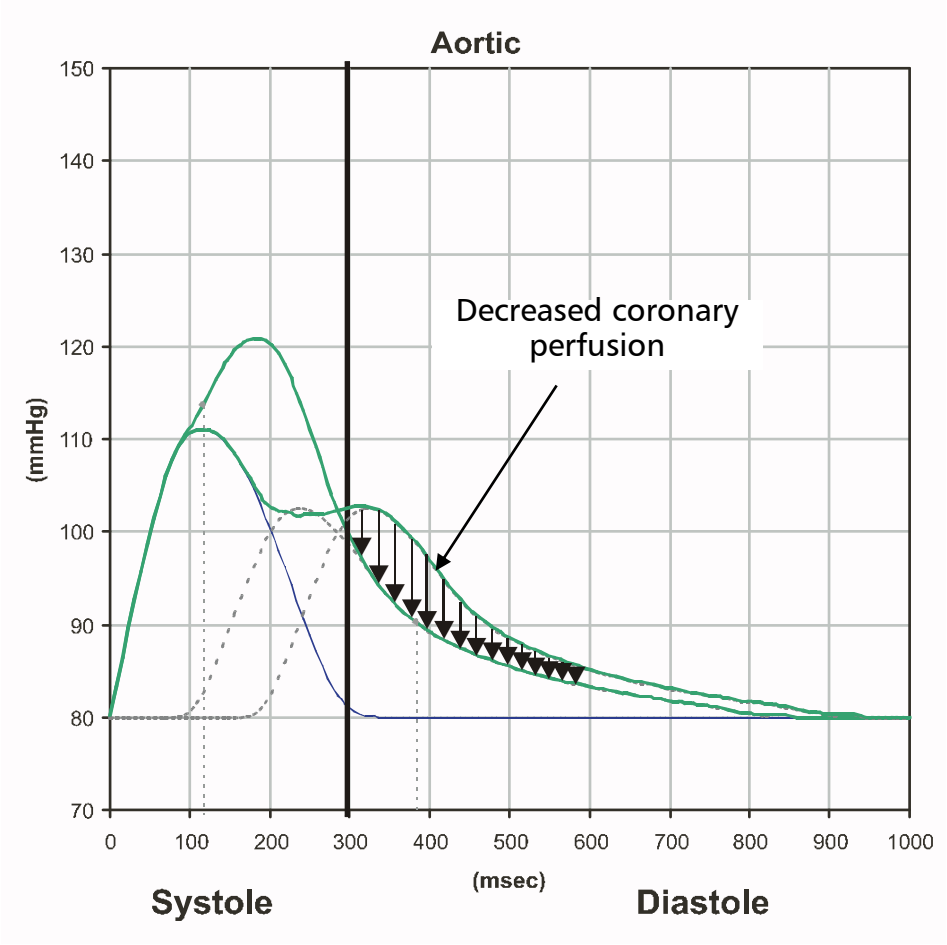
Réflexion d'onde



Réflexion d’onde



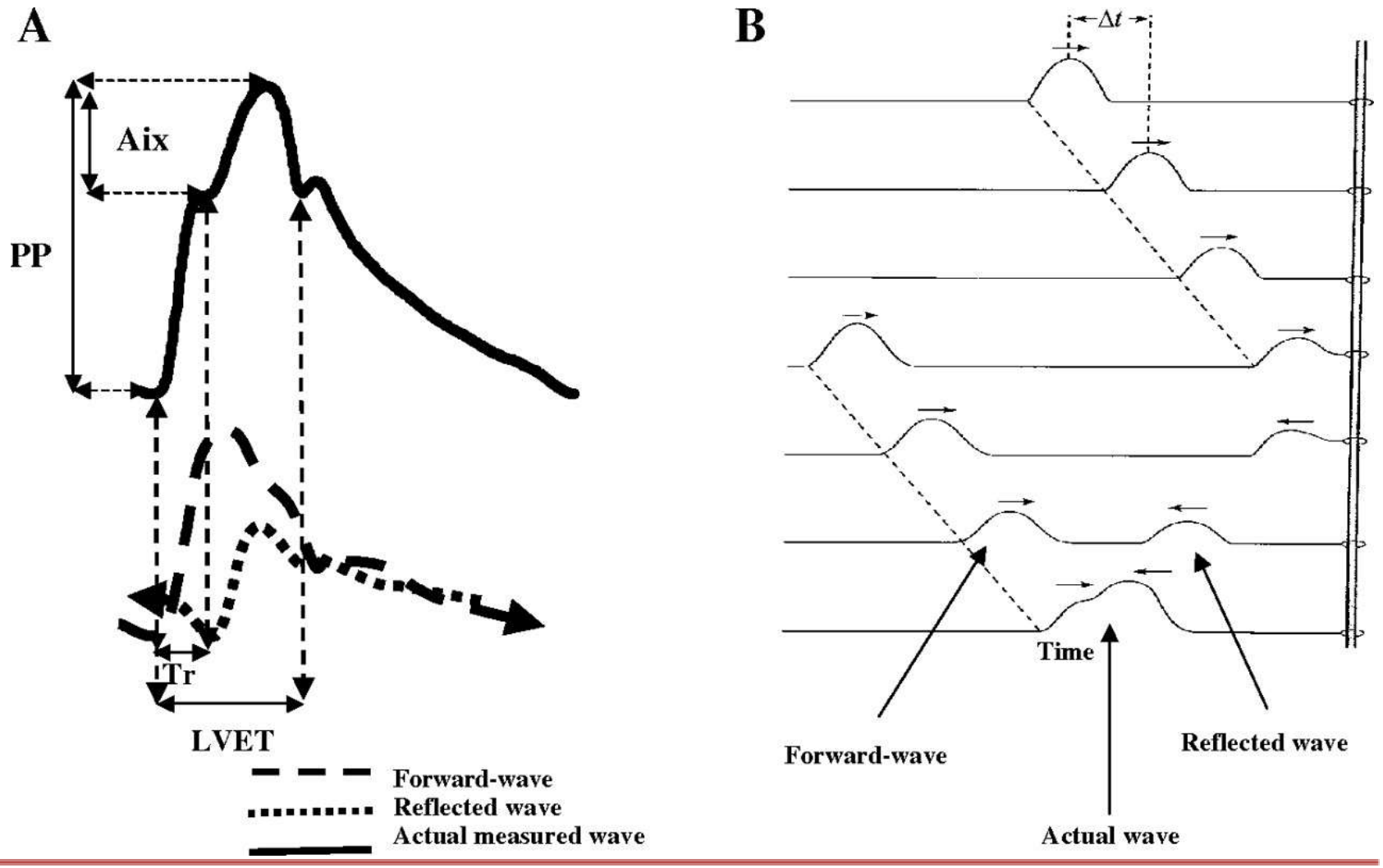
Réflexion d'onde



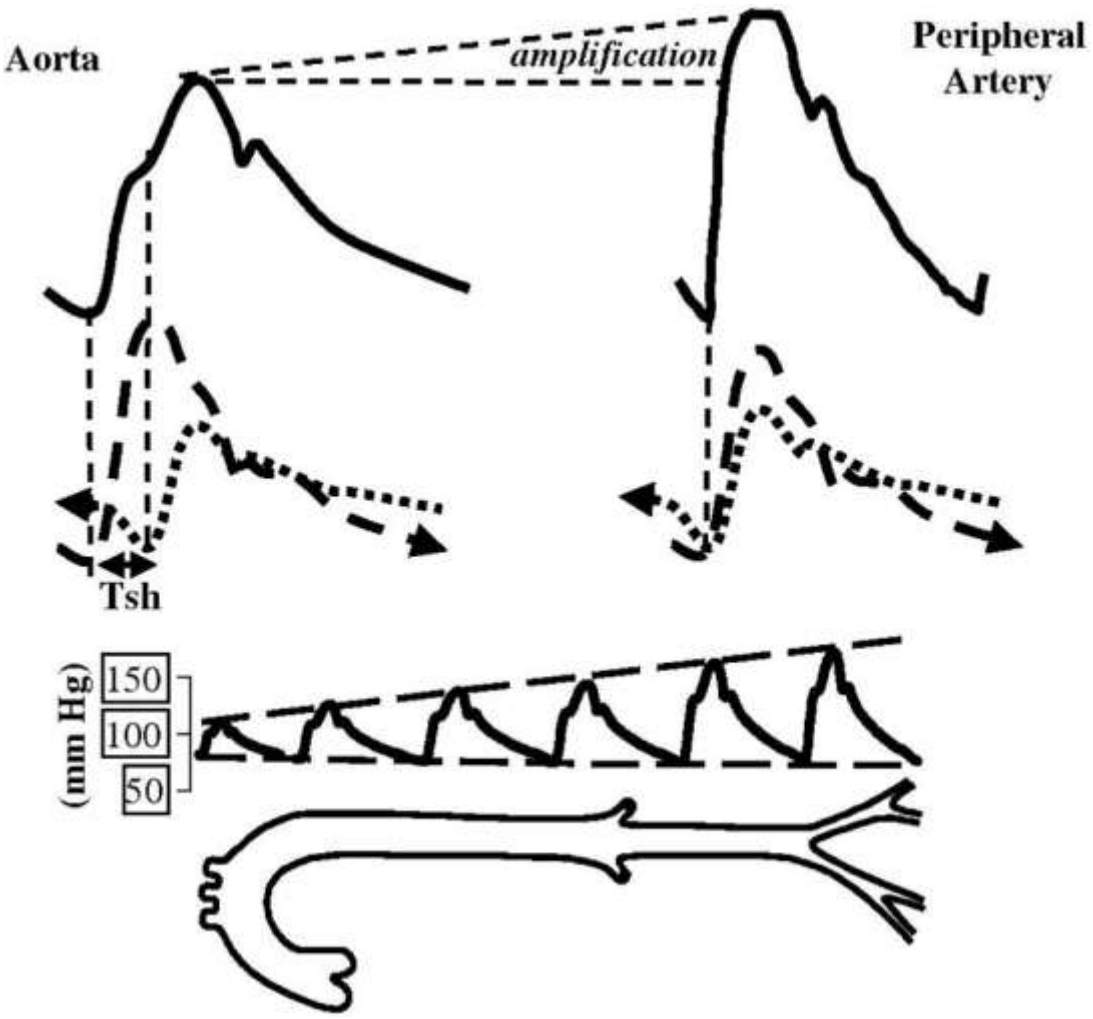
Réflexion d’onde

- 4 déterminants majeurs:
  - La vitesse de propagation de l’onde pouls
  - La durée de la systole (fréquence cardiaque)
  - Les sites de réflexion d’onde
  - Le degré de réflexion d’onde

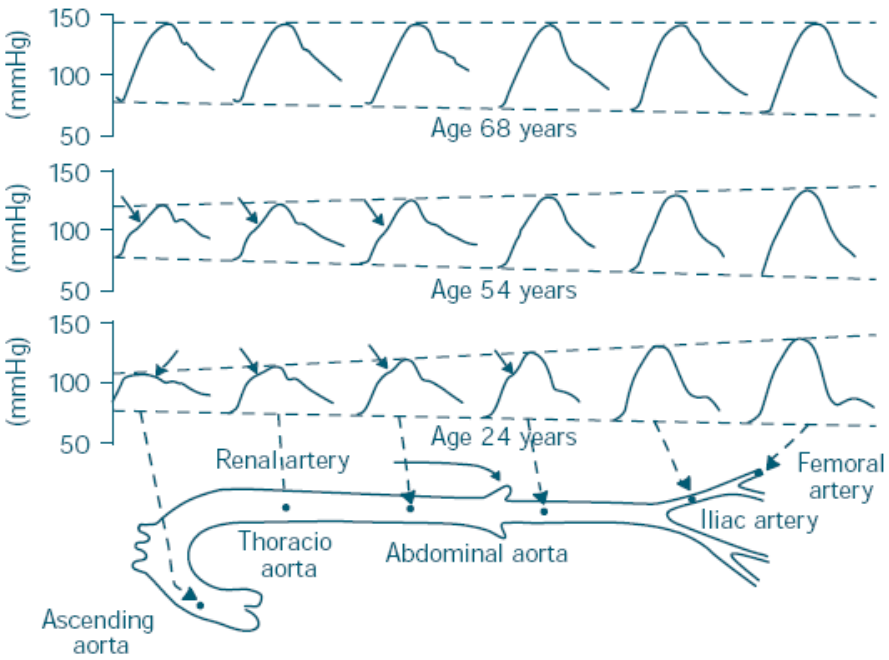
Amplification de l’onde pression



Amplification de l'onde pression

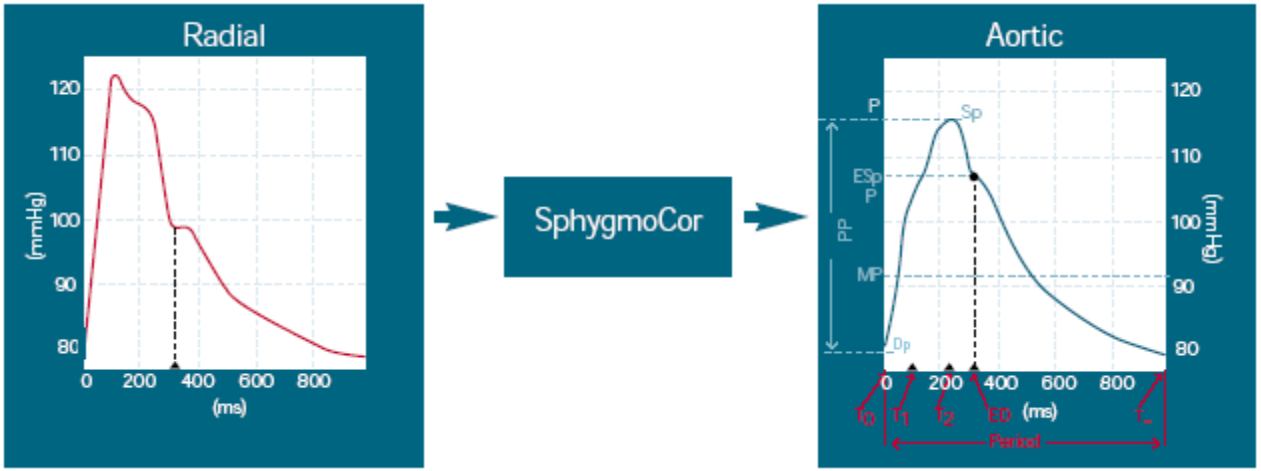


Effect of age on Pulse Wave amplification

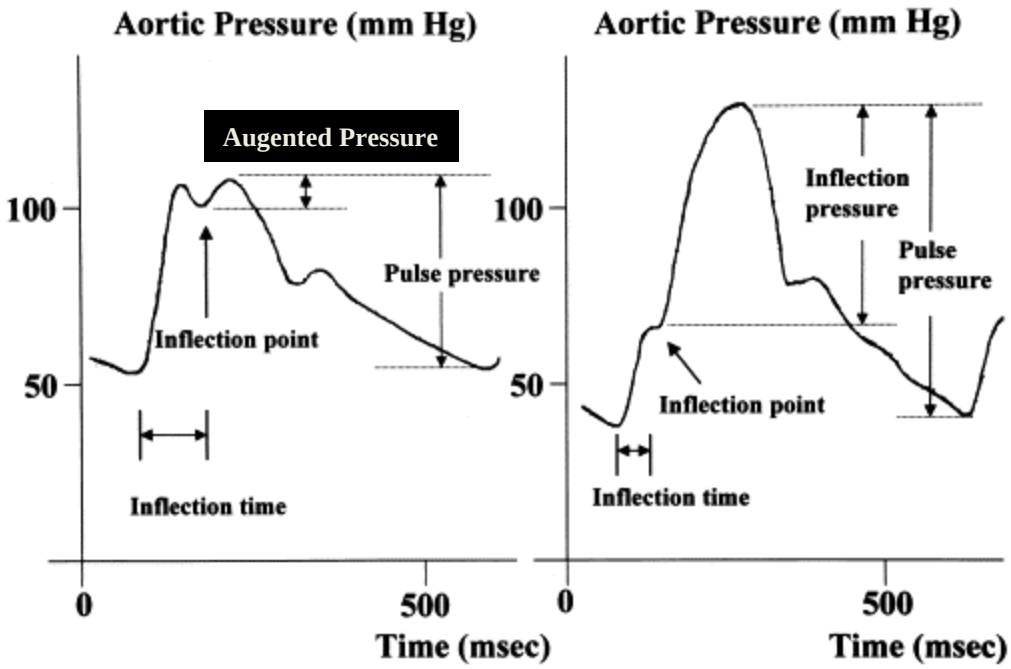


- Pulse wave amplification from central to peripheral arteries decreases with age
- An elevated peripheral pulse pressure is then associated with a higher central pulse pressure in the elderly

Analyse de l’onde de pouls non invasive



Analyse de l'onde de pouls non invasive



Tr, msec: time to return of reflected wave

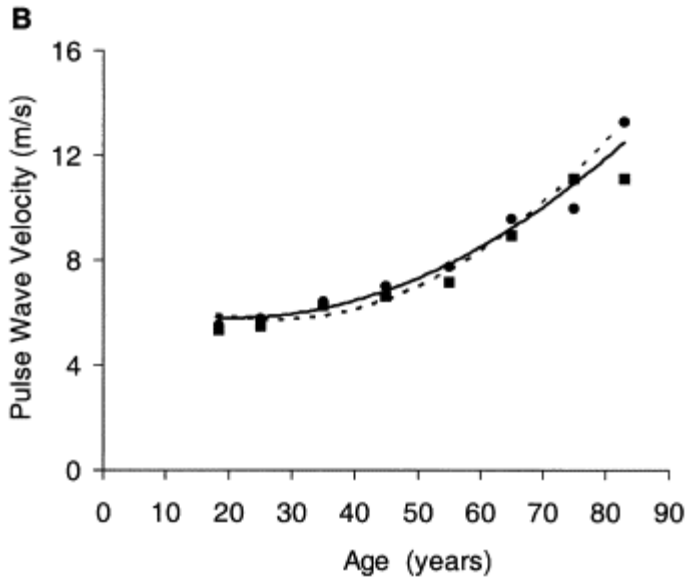
AP,mmHg = Augmented Pressure

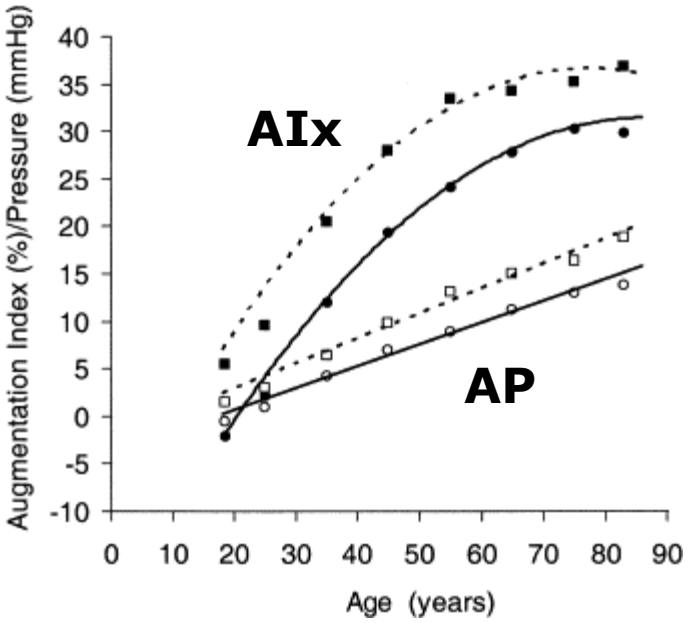
AIx,% = Augmentation Index
= AP/PP

AIx@75 :normalisation for 75 bpm

Déterminants de la fonction artérielle

Vieillissement et fonction artérielle



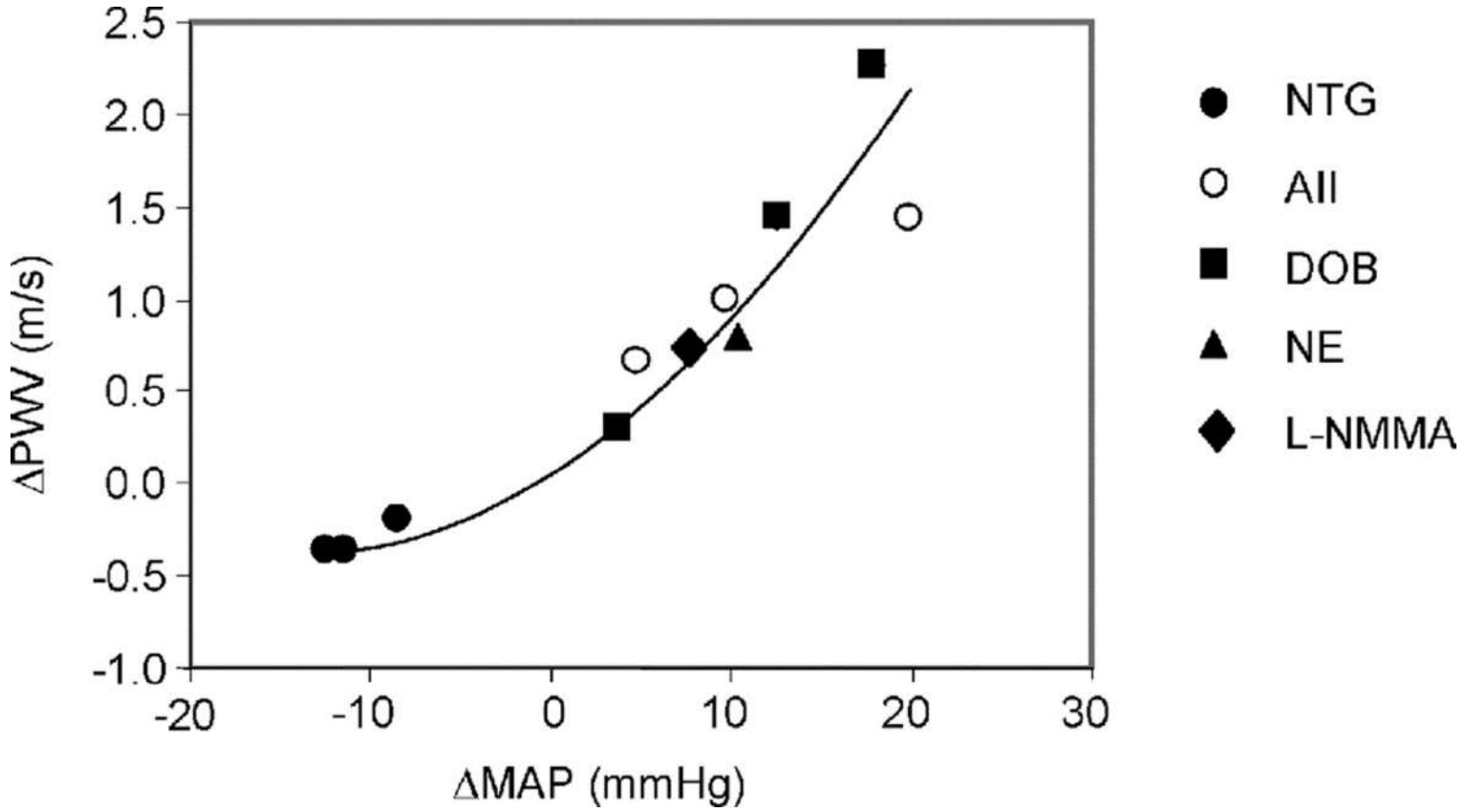


Hommes

Femmes

McEniery. JACC 2005;46:1753

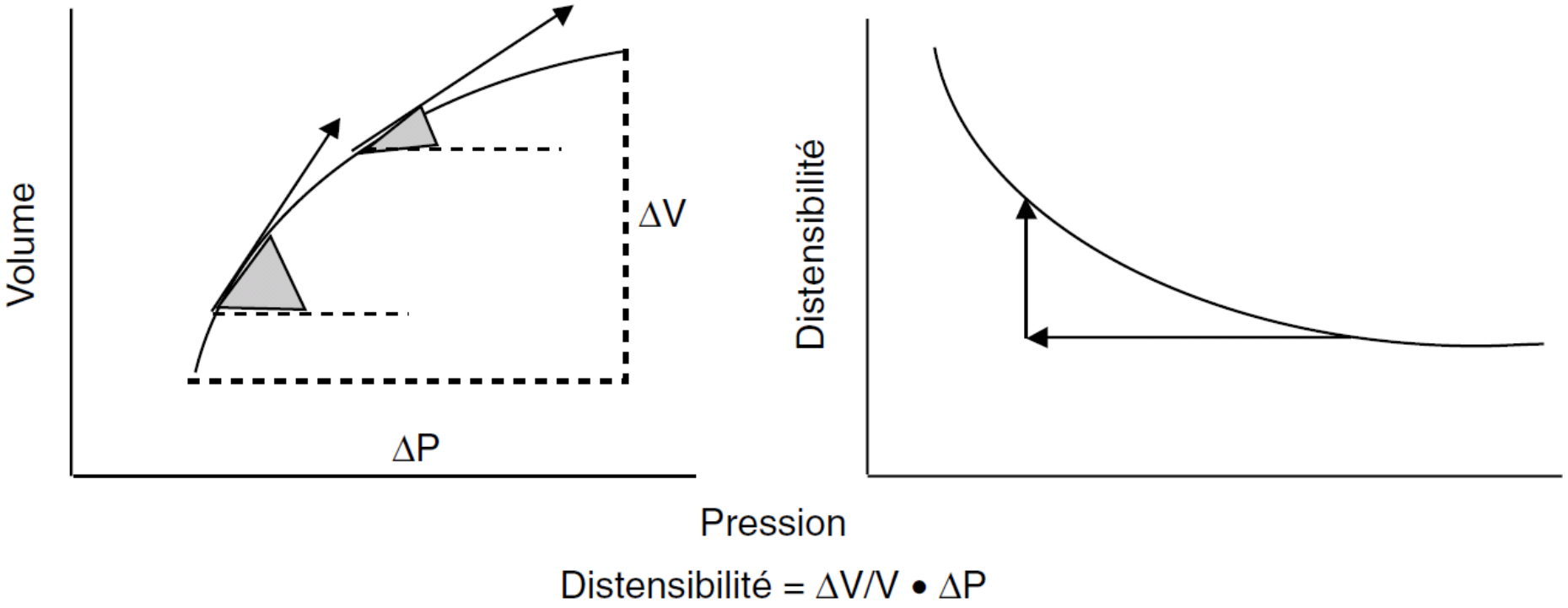
Rigidité artérielle et PA



N = 20 sujets normotendus

Stewart. Hypertension 2006;48:404

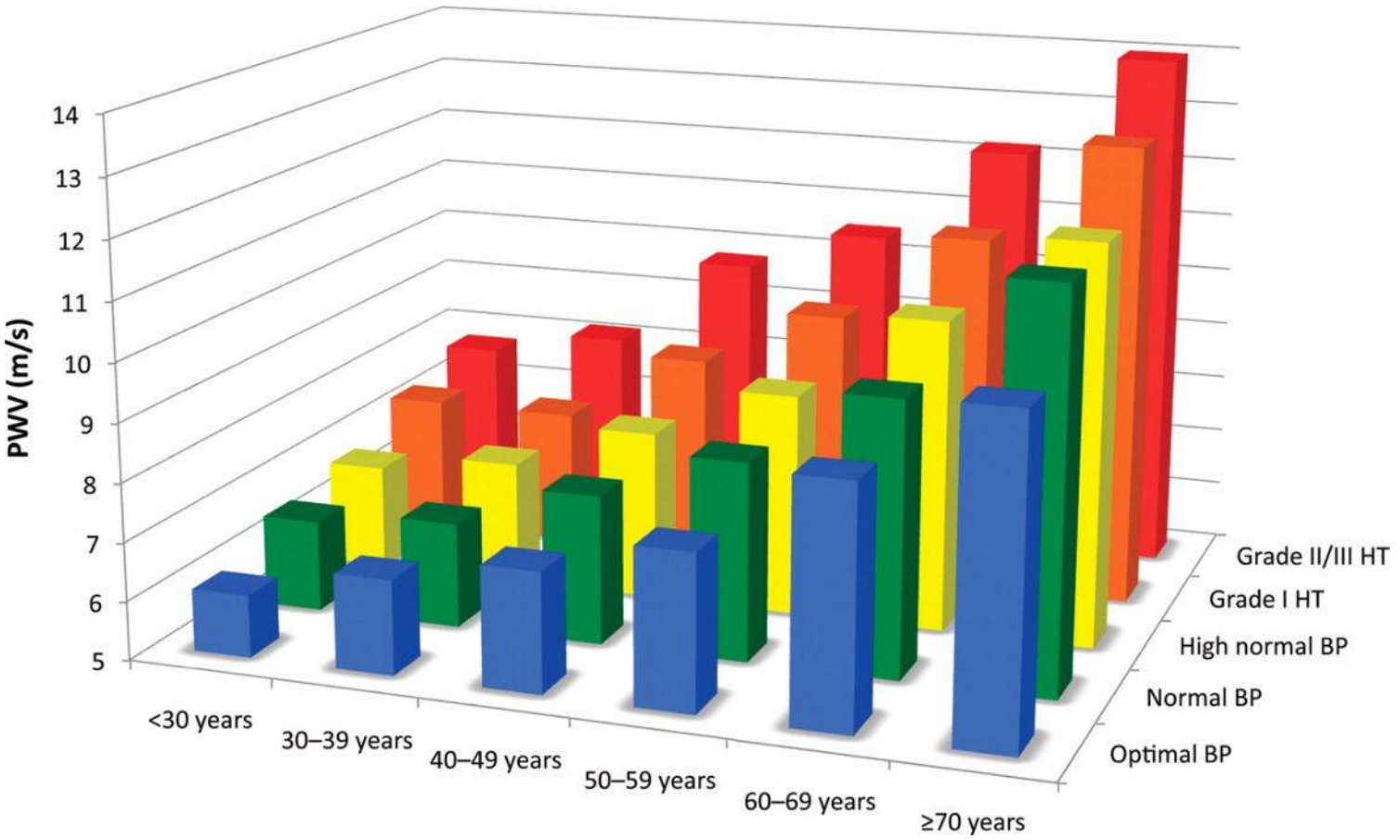
Rigidité – PA: En aigu



Distensibilité = $\Delta V/V \bullet \Delta P$

- La rigidité est corrélée à la PA, de façon non linéaire !

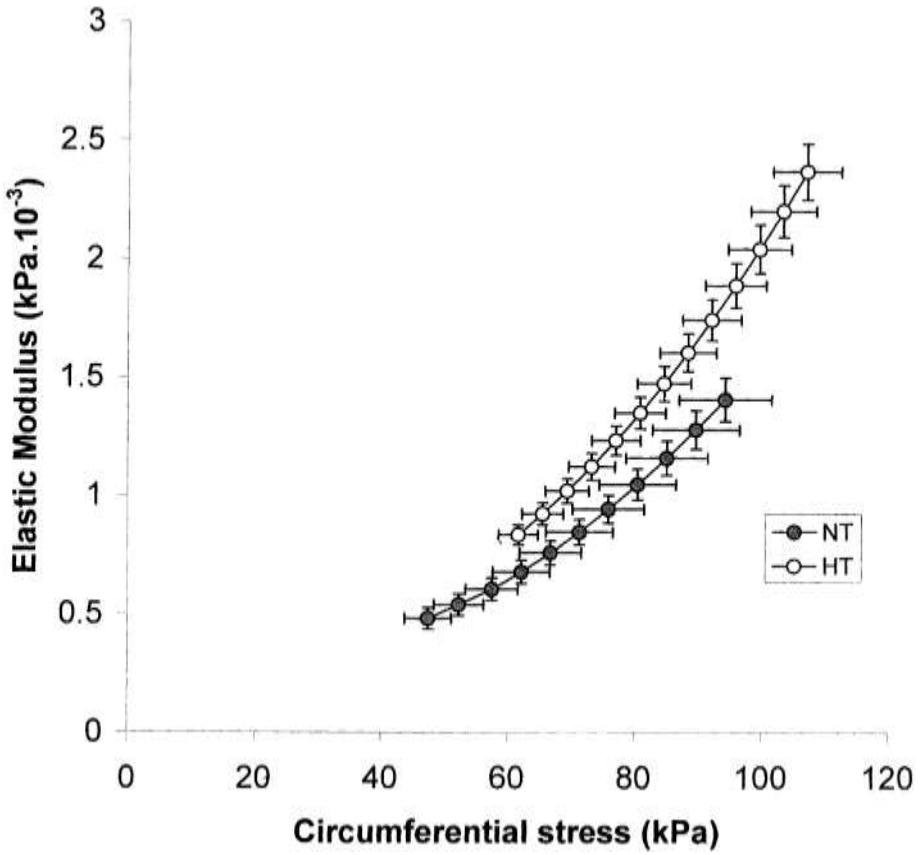
Rigidité artérielle - PA



N=16867

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

Rigidité artérielle dans l'HTA

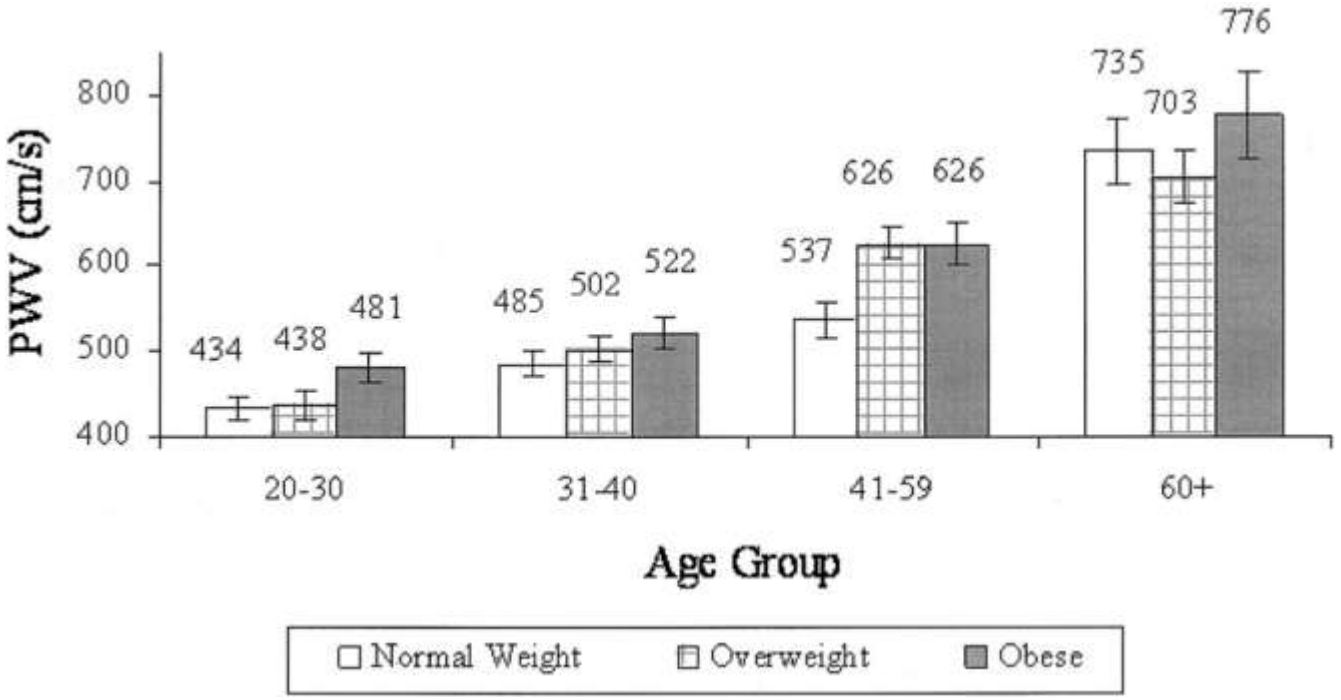


N=40 NT, 102 HT
Carotid

- À même niveau de contrainte (PA), la rigidité augmente dans l'HTA

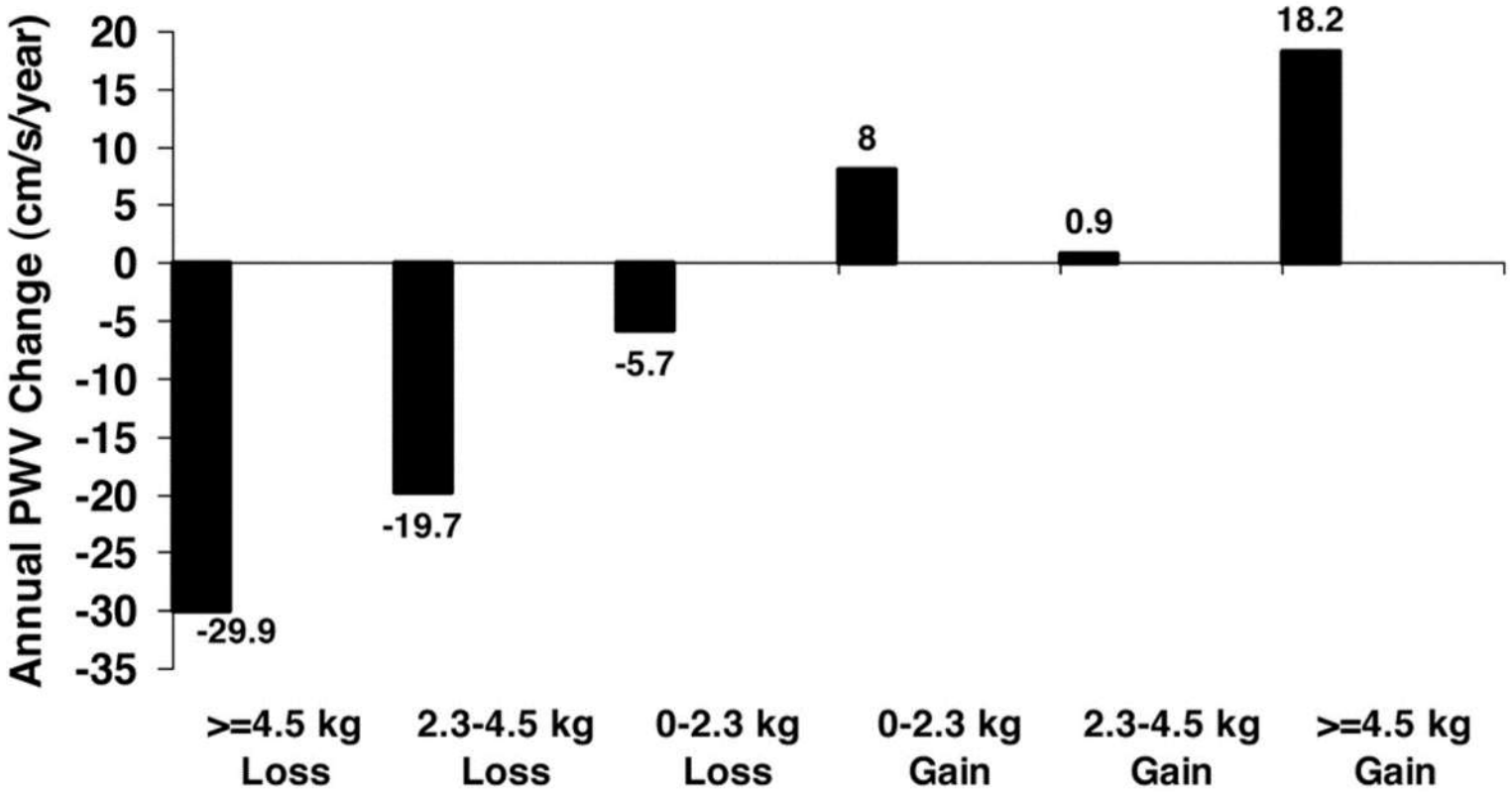
Bussy et al. Hypertension 2000;35:1049

Obésité et rigidité artérielle



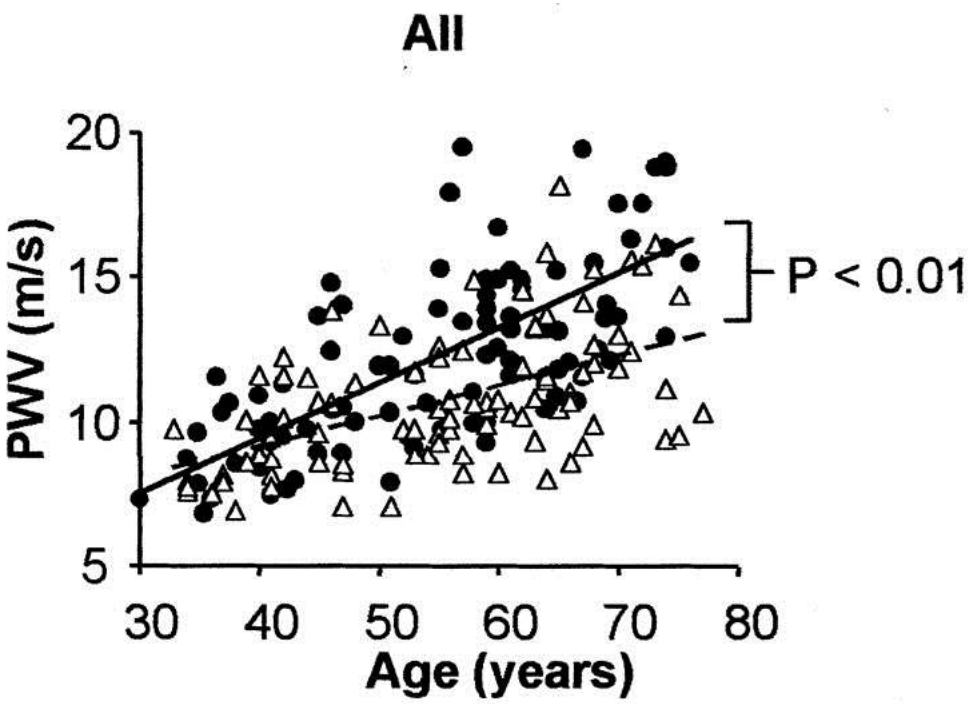
Wildman. Hypertension 2003;42:468

Obésité et rigidité artérielle



Wildman. Hypertension 2005;45:187

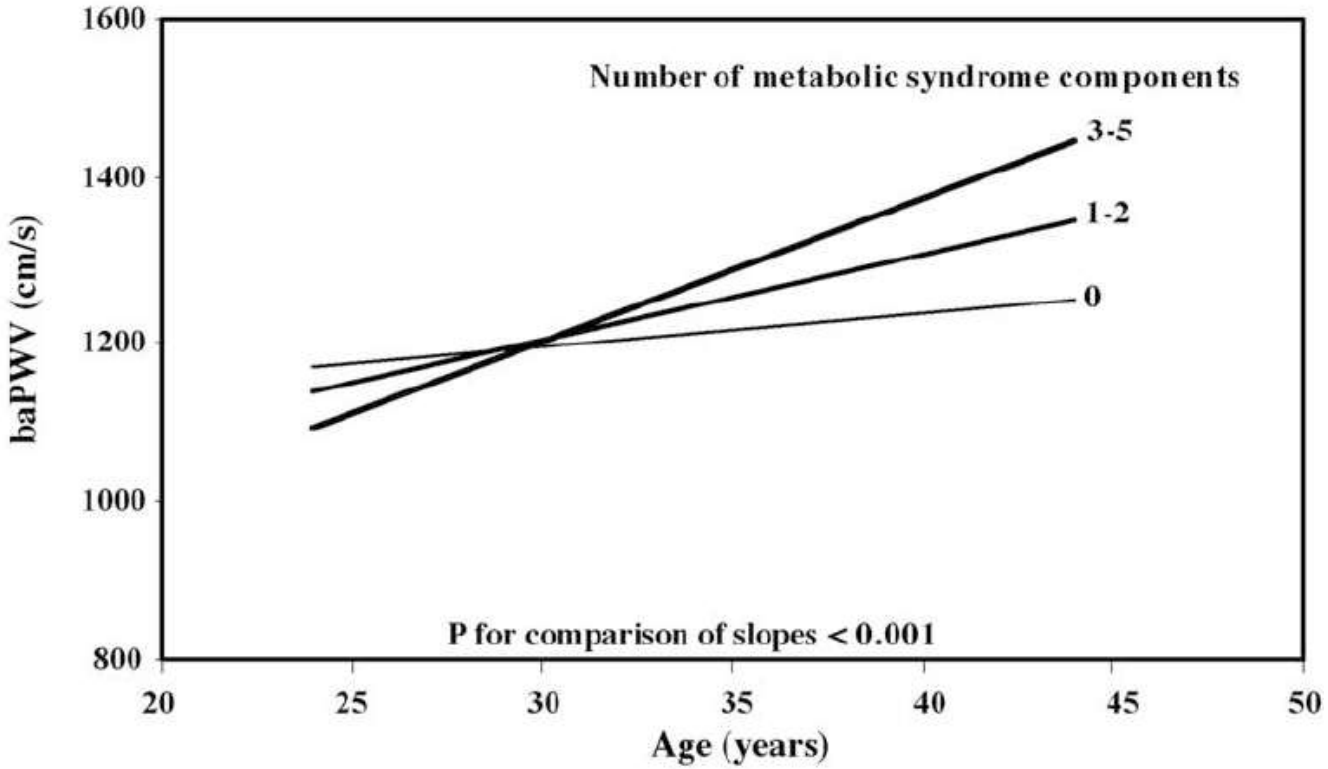
Diabète et rigidité artérielle



Δ: Controls
•: Type 2 diabetes

De Angelis et al. Hypertension 2004;44:67

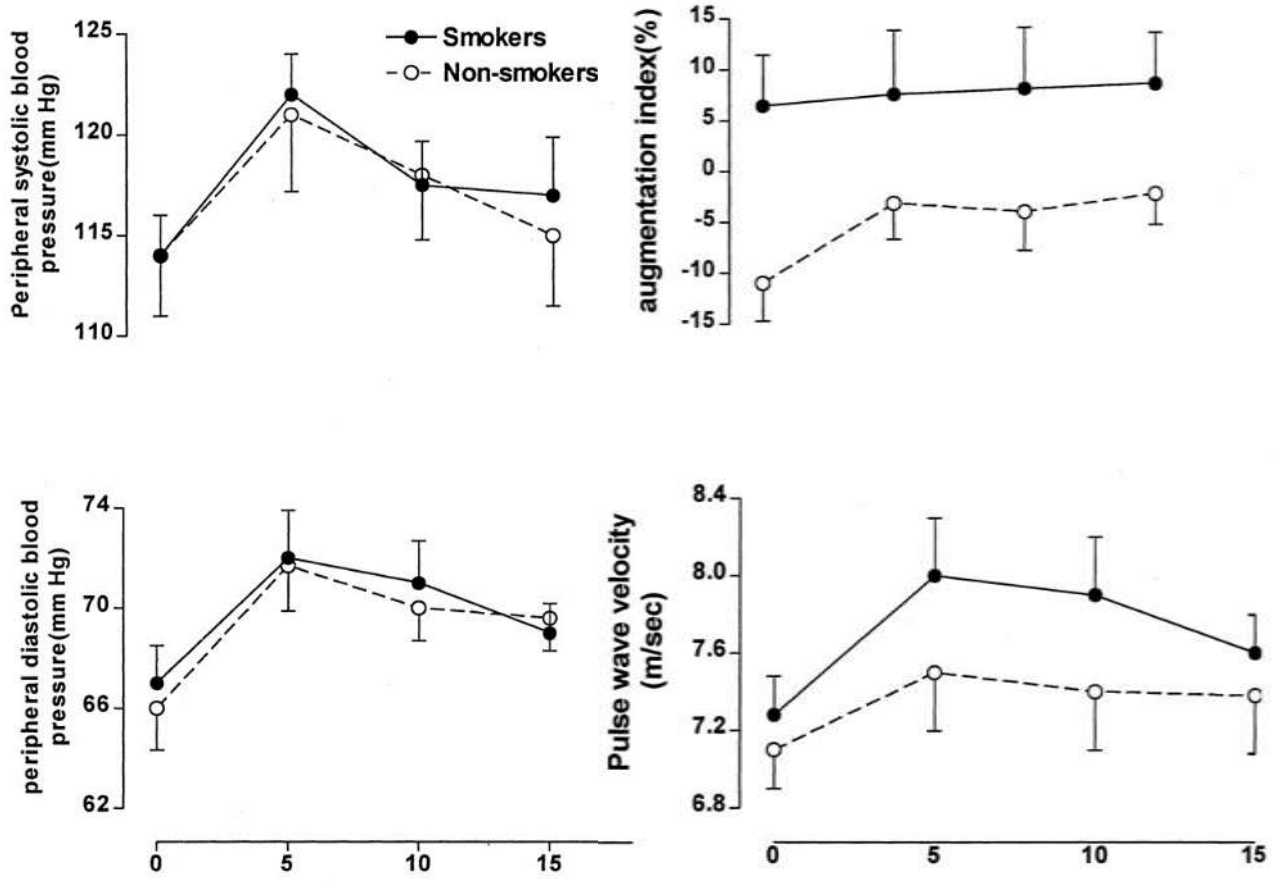
Syndrome métabolique et rigidité artérielle



- La rigidité artérielle augmente avec le nombre de critères du syndrome métabolique

Li. Atherosclerosis 2005;180:349

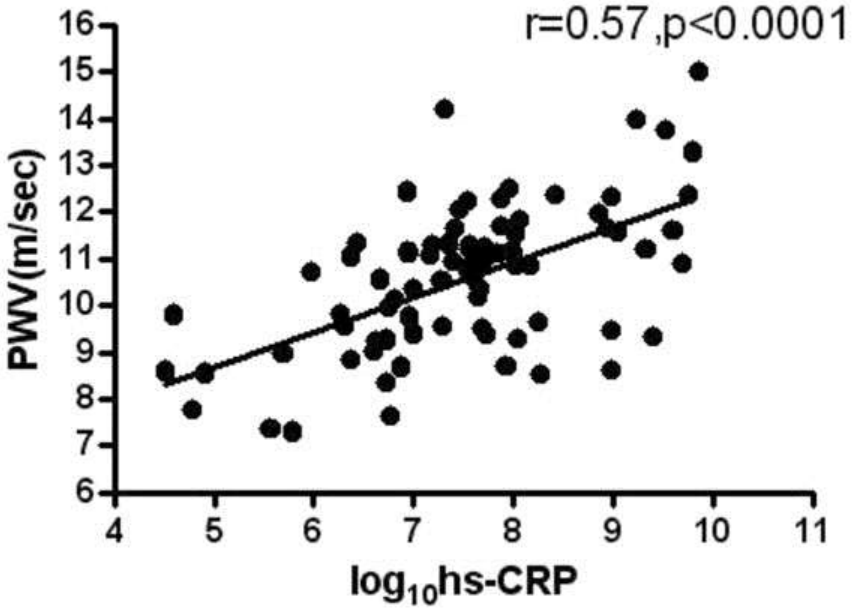
Tabac et rigidité artérielle

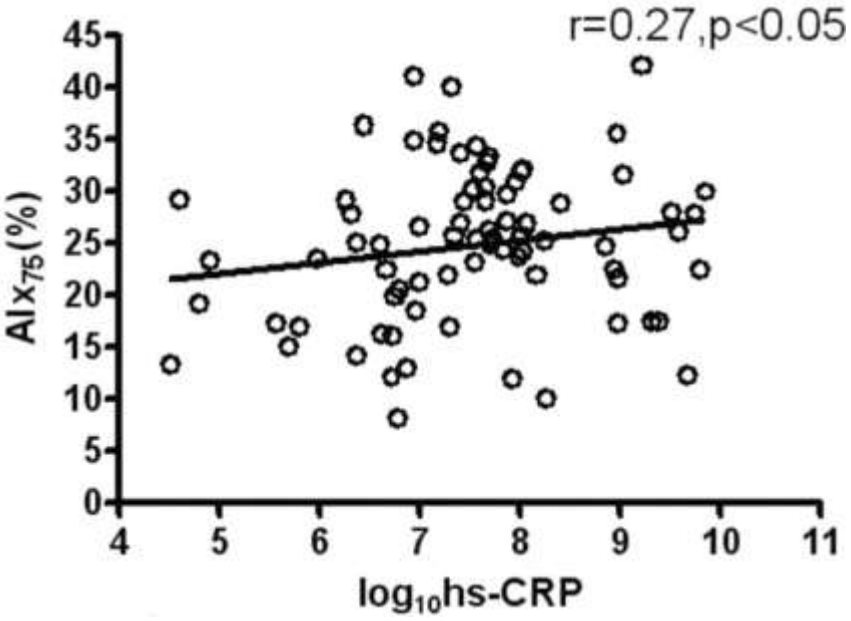


185 non-smokers, 52 smokers, normotensive

Mahmud et al. Hypertension 2003;41:183

Inflammation et rigidité artérielle

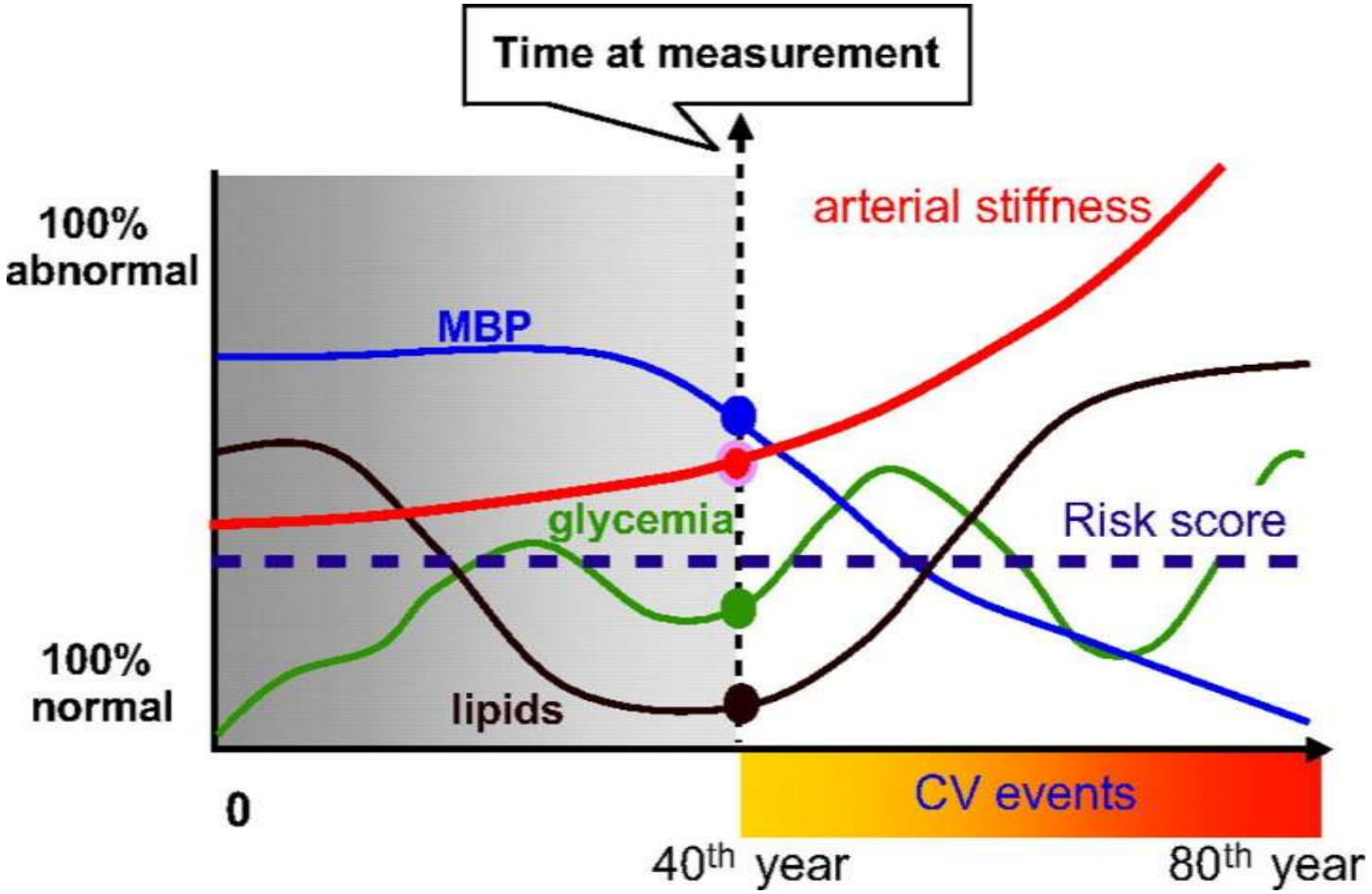




N=78, hypertensive

Mahmud. Hypertension 2005;46:1118

Rigidité artérielle: intégrateur de l'exposition aux FdR CV



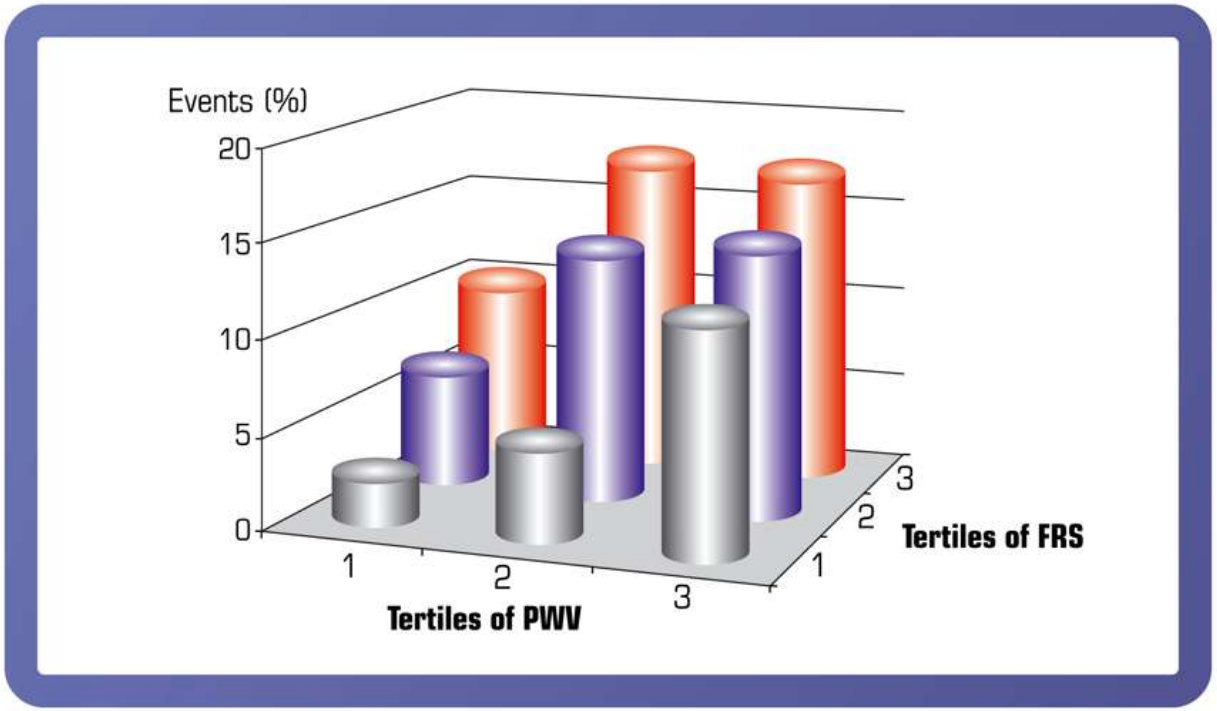
Nilsson PM et al. Hypertension 2009;54:3

Fonction artérielle: associée à de nombreux facteur de risque CV

Question:
Est-ce un critère intermédiaire et indépendant du risque CDV ?

Rigidité artérielle et risque CDV

- Evènements CDV

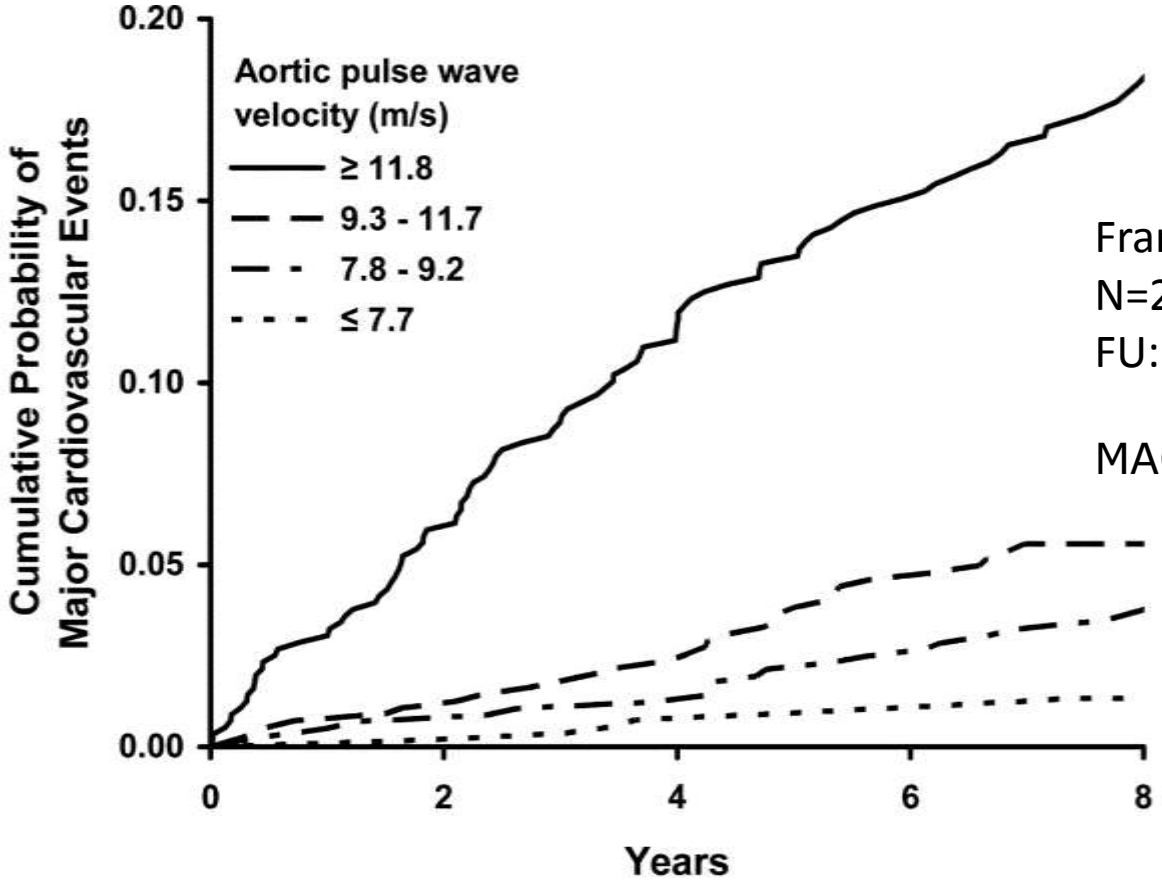


- N=1045
- HTA essentielle
- Suivi 6 ans
- 150 évènements

- Dans l'HTA, la rigidité artérielle est corrélée au risque CDV, indépendamment des autres FdR

Boutouyrie et al. Hypertension 2002;39:10

Rigidité artérielle et risque CV



Framingham
N=2232
FU: 8 yrs

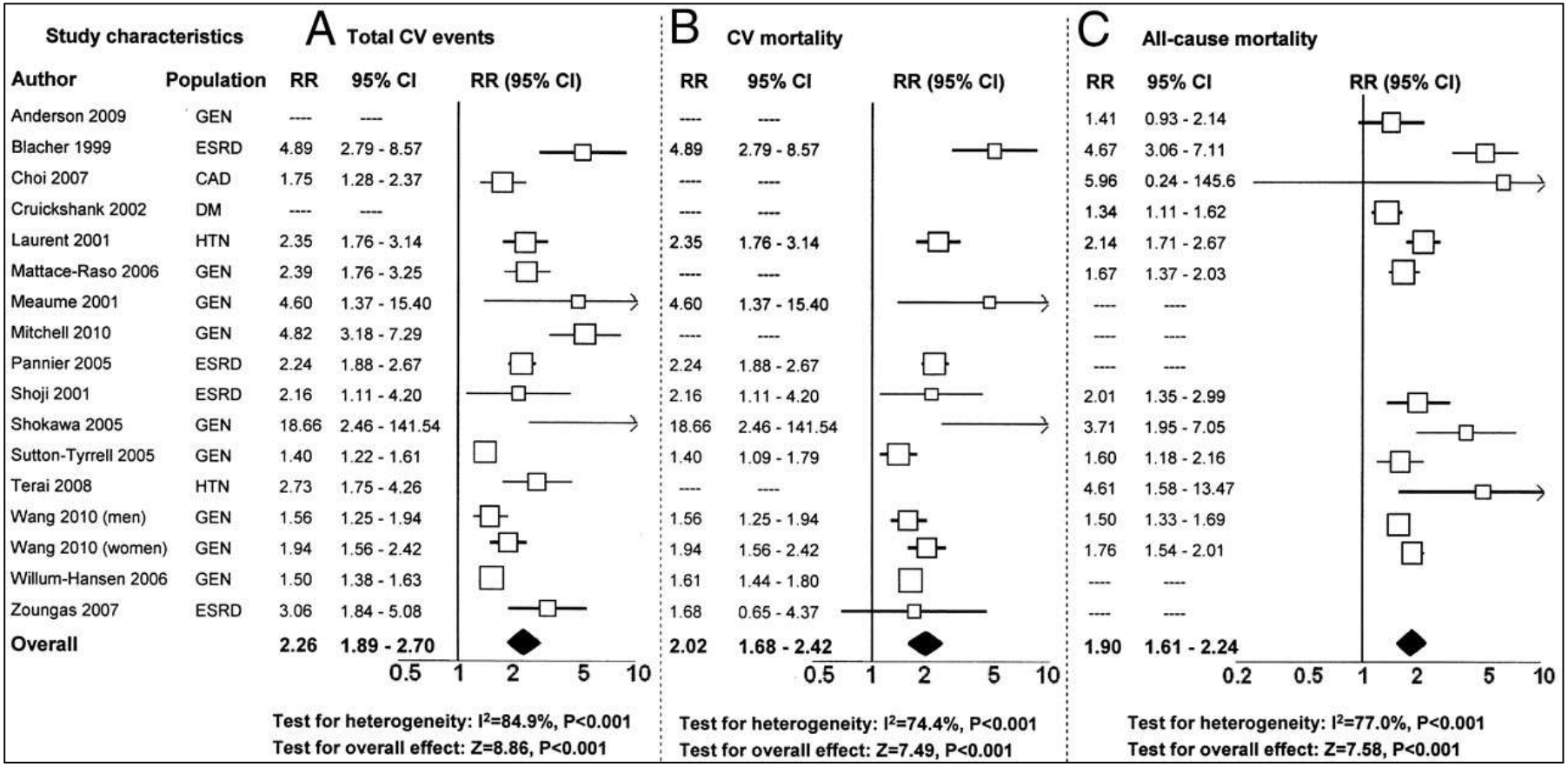
MACE: First Major CV event

- Adjusted HR: 3.4 (95% IC, 1.14-8.3) si PWV ≥ 11.8 vs PWV ≤ 7.7 m/s

Mitchell et al. Circulation 2010;121:505

Rigidité artérielle et risque CDV

- RR and 95% CI for High Aortic PWV and Clinical Events



Vlachopoulos. J Am Coll Cardiol, 2010; 55:1318-1327

European Heart Journal
doi:10.1093/eurheartj/eht151

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)

Authors/Task Force Members: Giuseppe Mancia (Chairperson) (Italy)*, Robert Fagard (Chairperson) (Belgium)*, Krzysztof Narkiewicz (Section co-ordinator) (Poland), Josep Redon (Section co-ordinator) (Spain), Albert (Italy), Michael Böhm (Germany), Thierry Christia (Czech Republic), Guy De Backer (Belgium), Anna Maurizio Galderisi (Italy), Diederick E. Grobbee (N (Sweden), Paulus Kirchhof (Germany/UK), Sverre Stéphane Laurent (France), Athanasios J. Manolis ((Sweden), Luis Miguel Ruilope (Spain), Roland E. S Per Anton Sirnes (Norway), Peter Sleight (UK), M Bernard Waeber (Switzerland), Faiez Zannad (Fra

ESH and ESC Guidelines

J Hypertens 2013

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2013 ESH-ESC Guidelines for the management of Hypertension
Evaluation of global CV risk

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to Moderate risk	Moderate to high risk	High Risk	High risk
Organ Damage OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

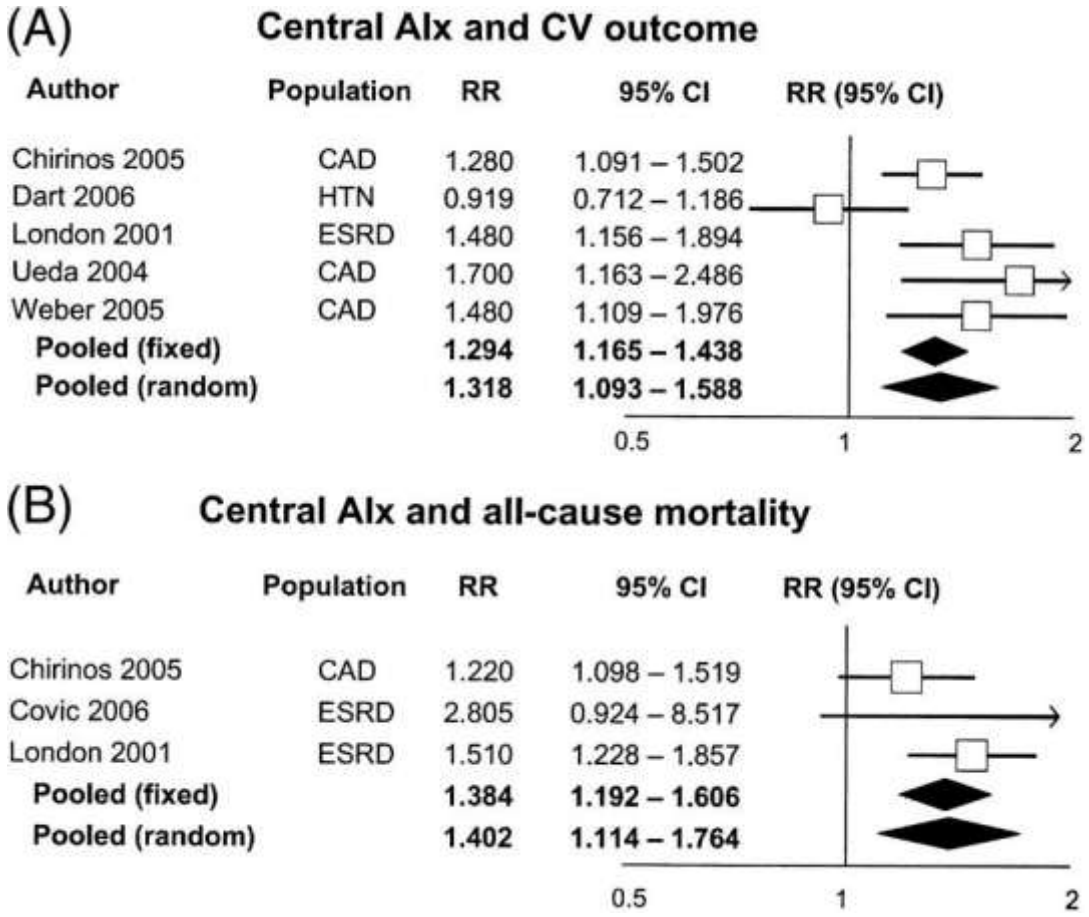
2013 ESH-ESC Guidelines for the management of Hypertension
Markers of subclinical organ damage

Risk factors
Male sex
Age (men ≥55 years; women ≥65 years)
Smoking
Dyslipidaemia
Total cholesterol >4.9 mmol/L (190 mg/dL), and/or
Low-density lipoprotein cholesterol >3.0 mmol/L (115 mg/dL), and/or
High-density lipoprotein cholesterol: men <1.0 mmol/L (40 mg/dL), women <1.2 mmol/L (46 mg/dL), and/or
Triglycerides >1.7 mmol/L (150 mg/dL)
Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dL)
Abnormal glucose tolerance test
Obesity [BMI ≥30 kg/m^2 (height^2)]
Abdominal obesity (waist circumference: men ≥102 cm; women ≥88 cm) (in Caucasians)
Family history of premature CVD (men aged <55 years; women aged <65 years)

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)

Réflexion d'onde et risque CV

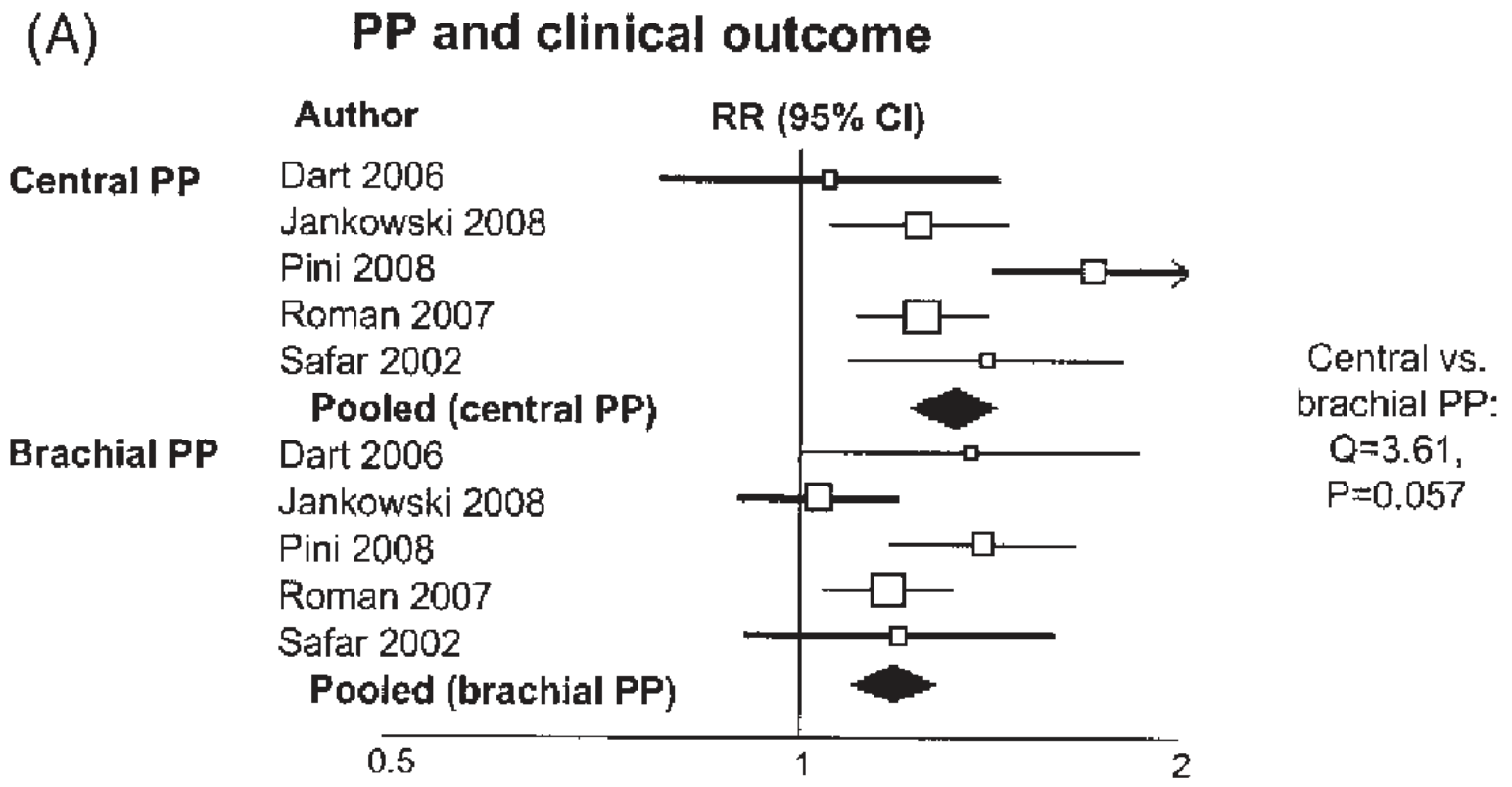
- RR and 95% CI for an absolute 10% increase in central AIx



Vlachopoulos. Eur Heart J 2010;31:1865-1871

Pression centrale et risque CV

- RR and 95% CI for an increase in 1-SD in PP

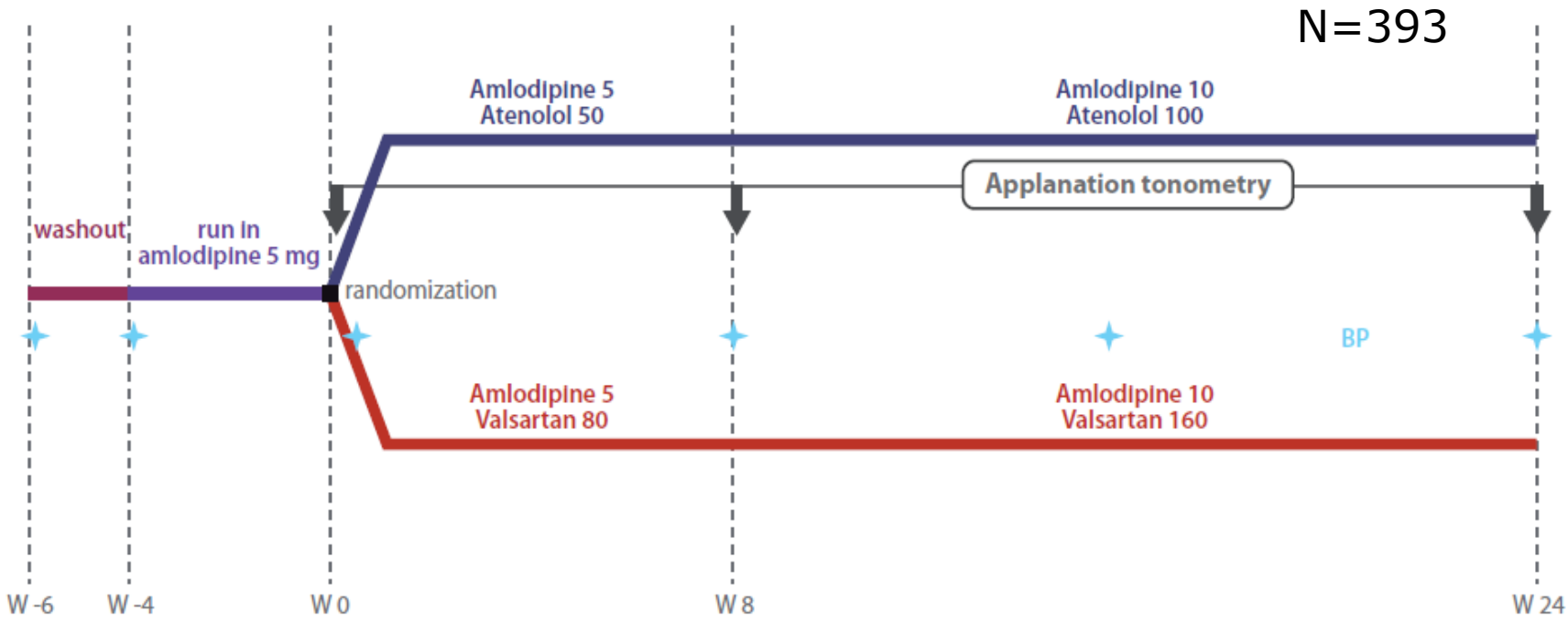


Vlachopoulos. Eur Heart J 2010;31:1865-1871

Fonction artérielle et traitements anti-HTA

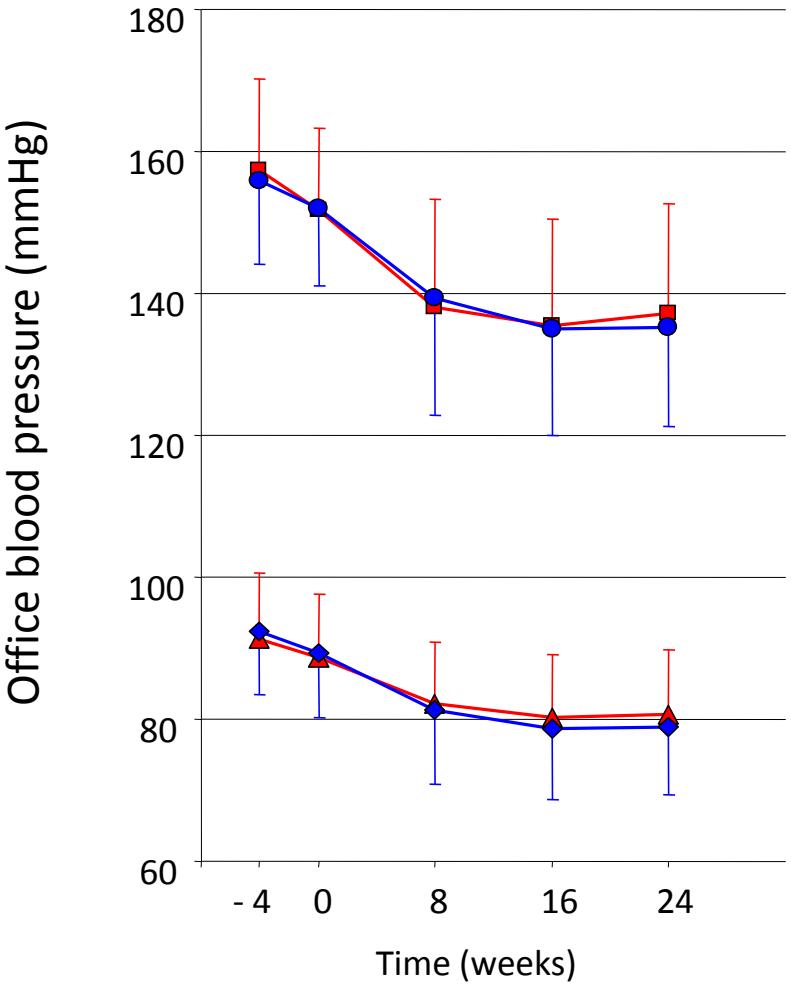
Etude Explor: fonction artérielle

- PROBE (Prospective, Randomized, Blinded Endpoint)
- Parallel groups, Forced titration



EXPLOR Study: Hypertension 2010, 55:1314-1322

Blood pressure response to amlodipine/valsartan and amlodipine/atenolol



Office SBP (mmHg)

Mean difference at W8: -1.14 [-4.28 to 1.99] mmHg

NS

Amlodipine+atenolol

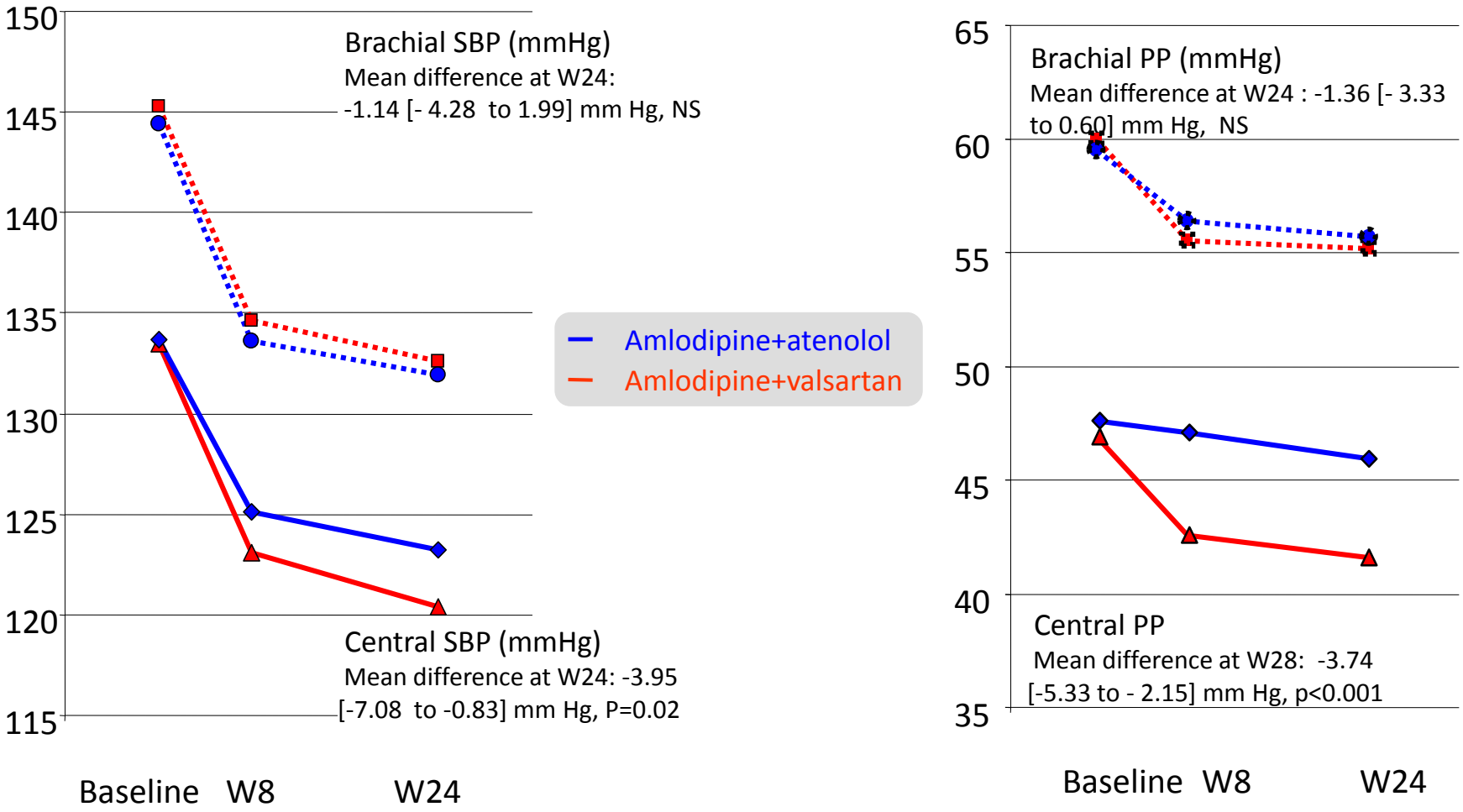
Amlodipine+valsartan

Office DBP (mmHg)

Mean difference at W28: -1.14 [-4.28 to 1.99] mmHg, NS

EXPLOR Study: Hypertension 2010, 55:1314-1322

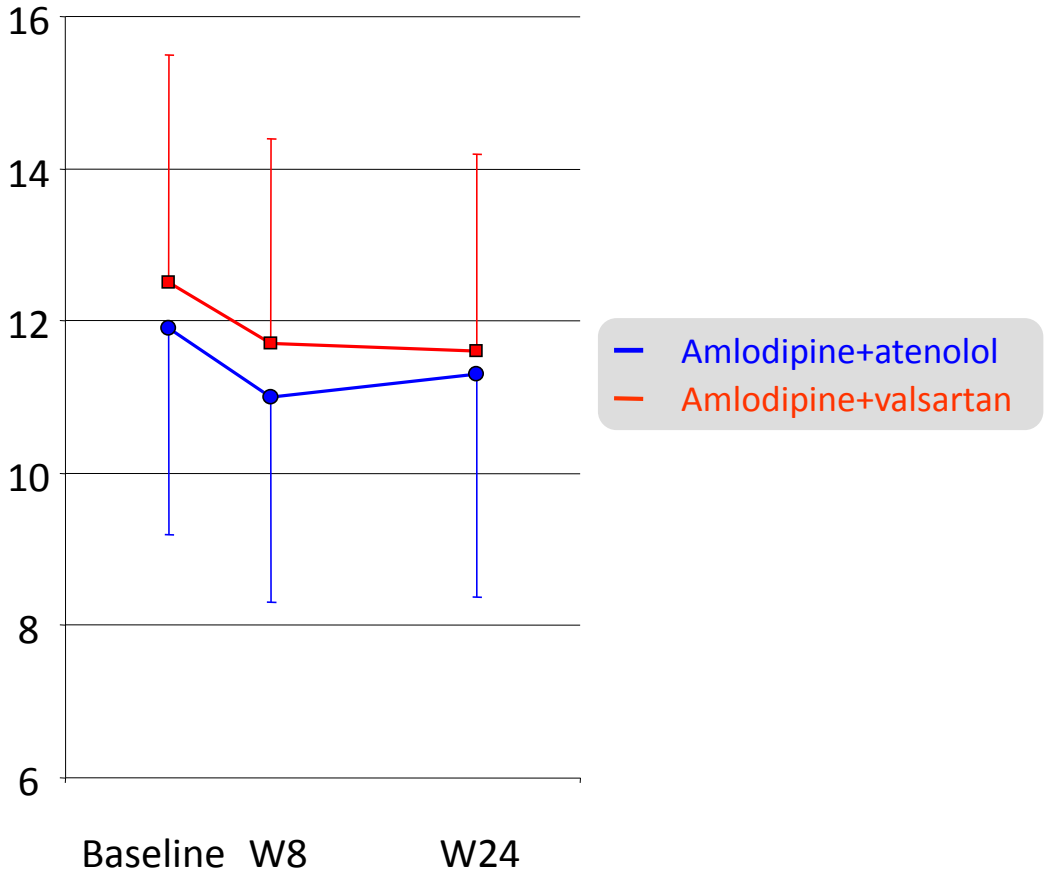
BP response to amlodipine/valsartan and amlodipine/atenolol



EXPLOR Study: Hypertension 2010, 55:1314-1322

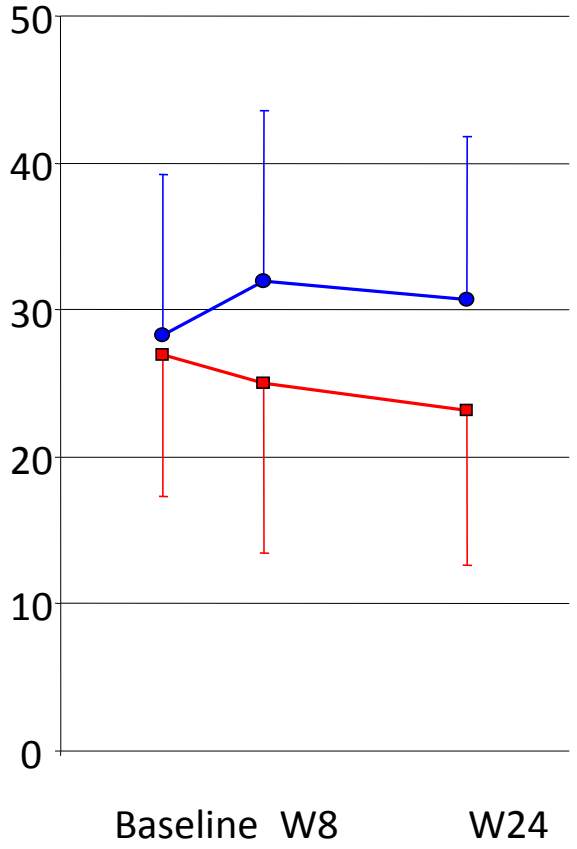
Changes in PWV and AIx after amlodipine/valsartan and amlodipine/atenolol

Carotid to femoral pulse wave velocity (m/sec)



Mean difference at W24 : -0.02 m/s [-0.46 to 0.41], NS

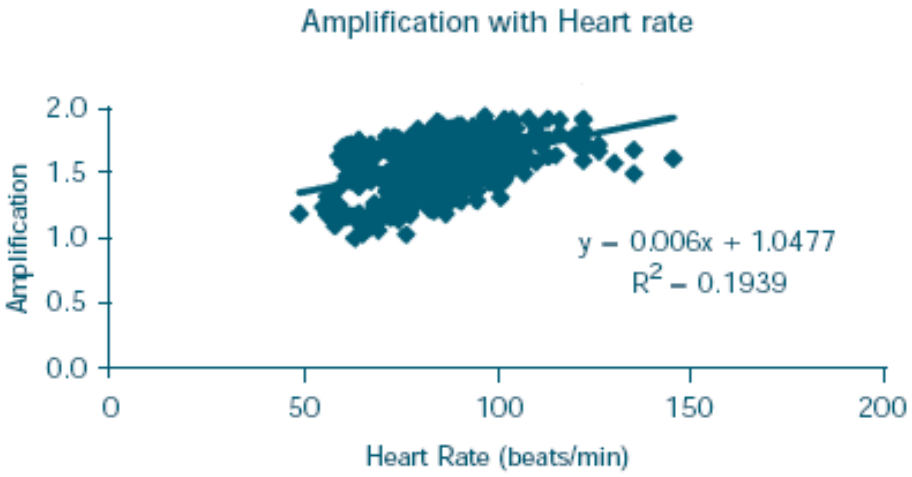
Aortic augmentation index (%)



Mean difference at W24 -6.50% [-8.28 to -4.72] p<0.001

EXPLOR Study: Hypertension 2010, 55:1314-1322

Effect of heart rate on Pulse Wave amplification



- Pulse wave amplification from central to peripheral arteries decreases with heart rate
- Clinical implications of an elevated peripheral pulse pressure will depend on heart rate
- any intervention that causes an increase in heart rate can cause a significant overestimation.

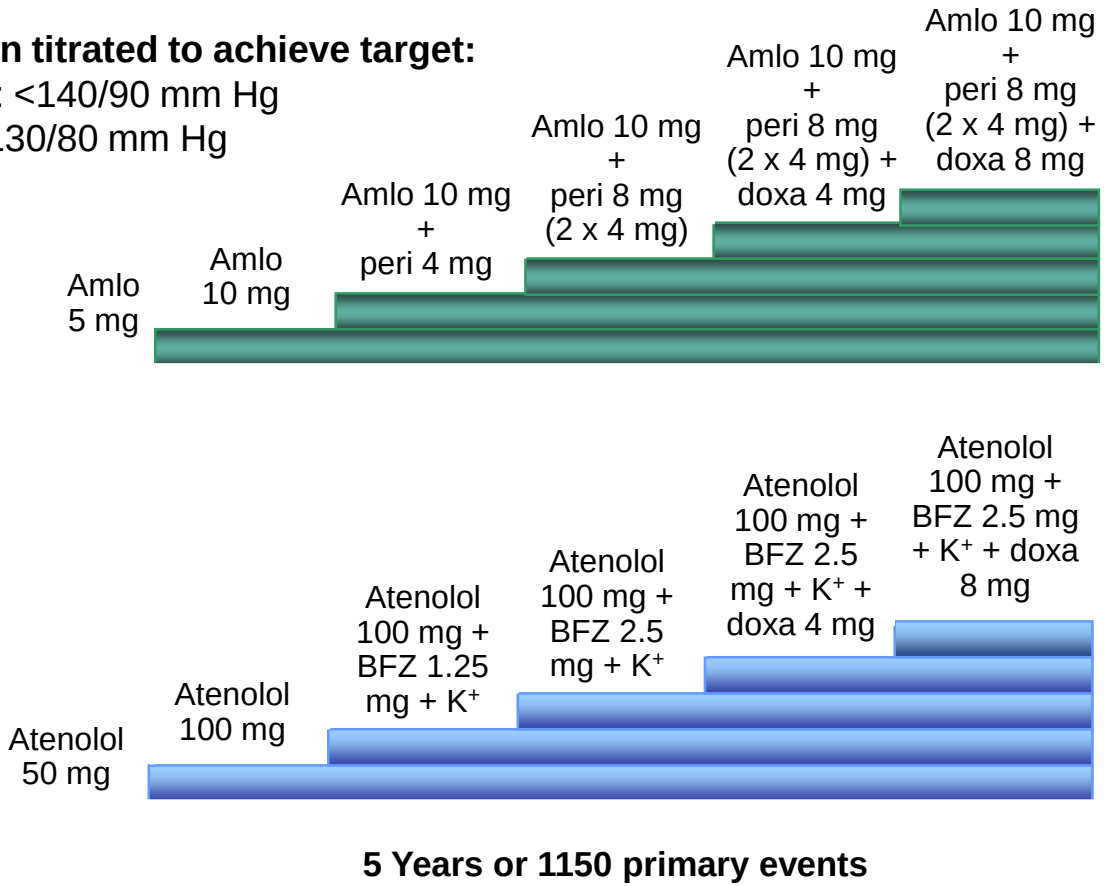
ASCOT-BPLA: Treatment algorithm for BP targets

19,342 patients
40–79 y
with
U N T R E A T E D
SBP ≥160 mmHg
and/or
DBP ≥100 mmHg
OR
T R E A T E D
SBP ≥140 mmHg
and/or
DBP ≥90 mmHg

RANDOMIZATION

In each arm, pts with total cholesterol ≤6.5 mmol/L randomized to atorvastatin (10 mg) or placebo daily (n = 10,297)

BP medication titrated to achieve target:
No diabetes: <140/90 mm Hg
Diabetes: <130/80 mm Hg

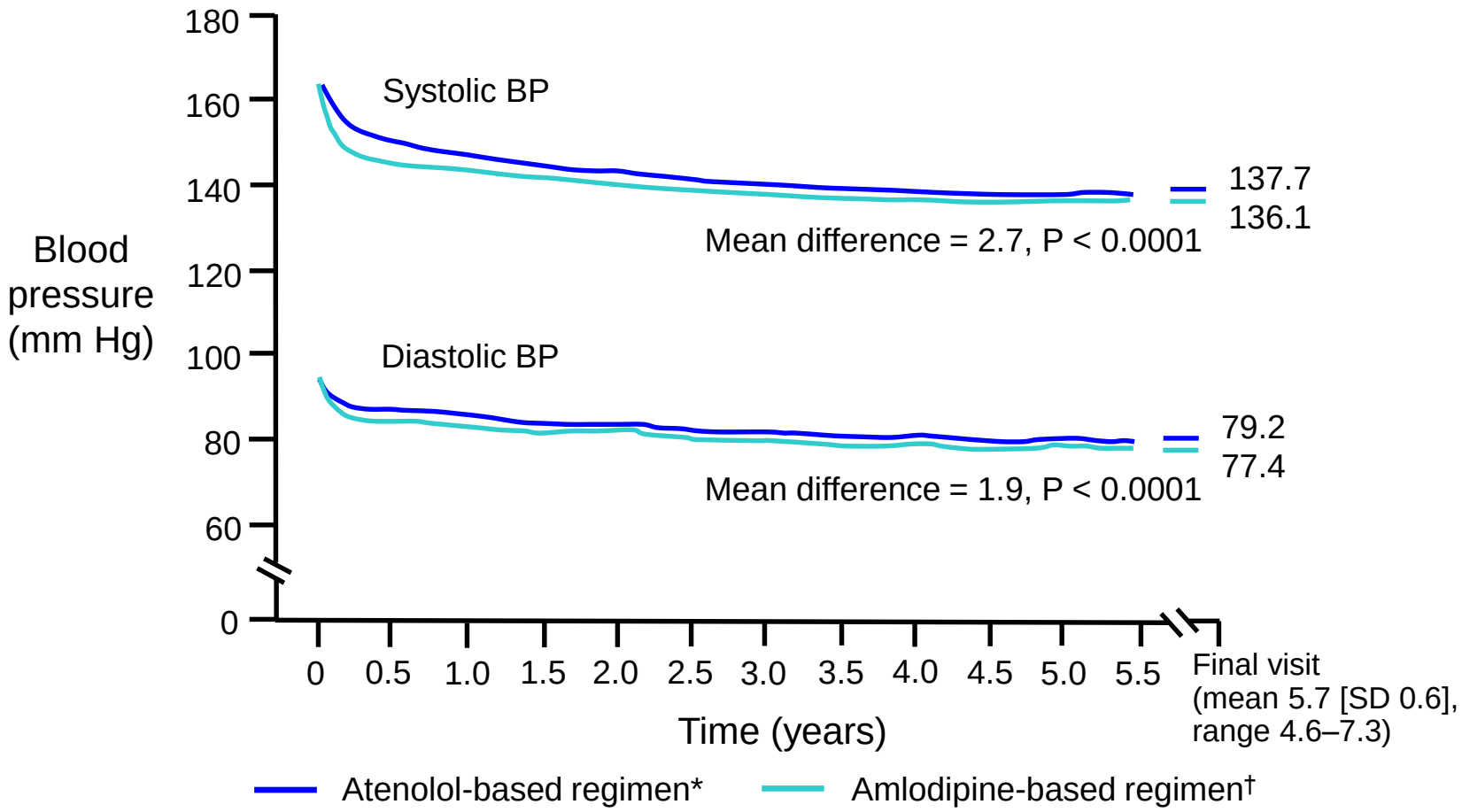


5 Years or 1150 primary events

Amlo = amlodipine; Peri = perindopril;
Doxa = doxazosin; BFZ = bendroflumethiazide

Sever PS et al. J Hypertens. 2001;19:1139-47.

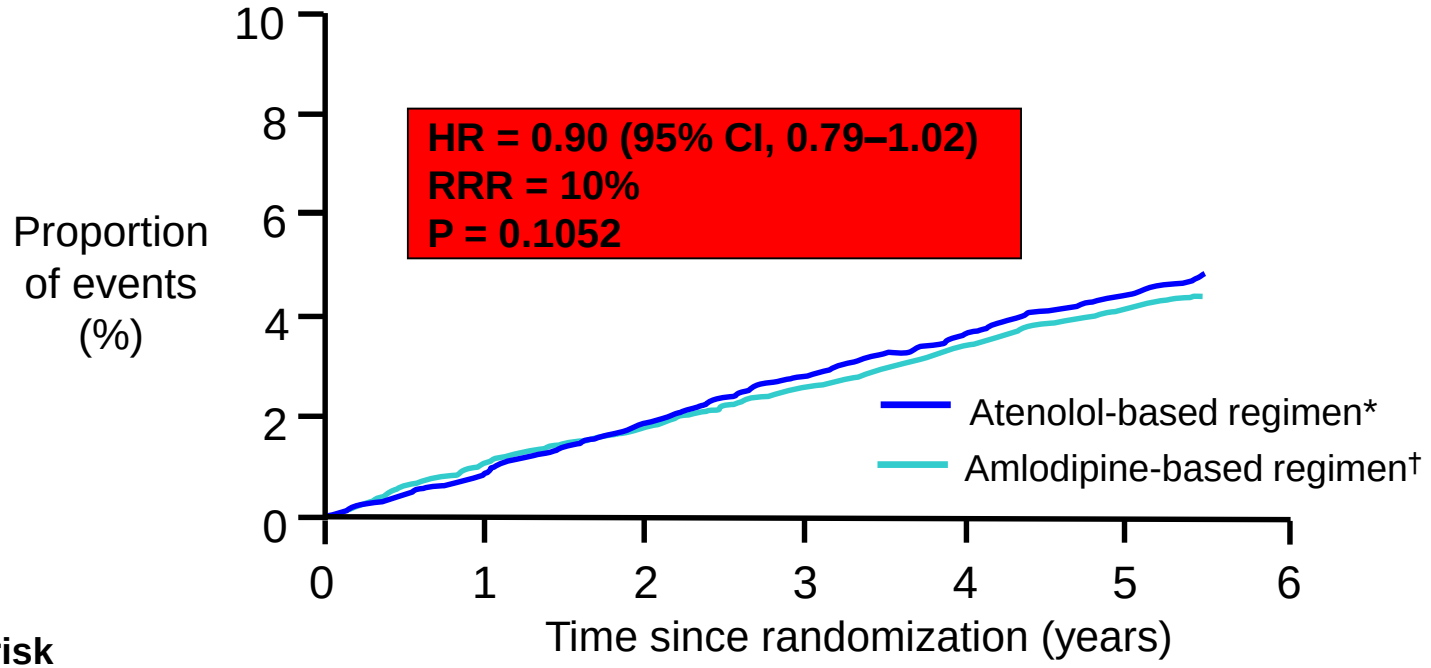
ASCOT-BPLA: Reductions in BP over time



*Atenolol 50–100 mg ± bendroflumethiazide 1.25–2.5 mg/potassium prn
†Amlodipine 5–10 mg ± perindopril 4–8 mg prn

Dahlöf B et al; ASCOT Investigators. *Lancet*. 2005;366:895-906.

ASCOT-BPLA: Reduction in primary outcome (nonfatal MI and fatal CHD)



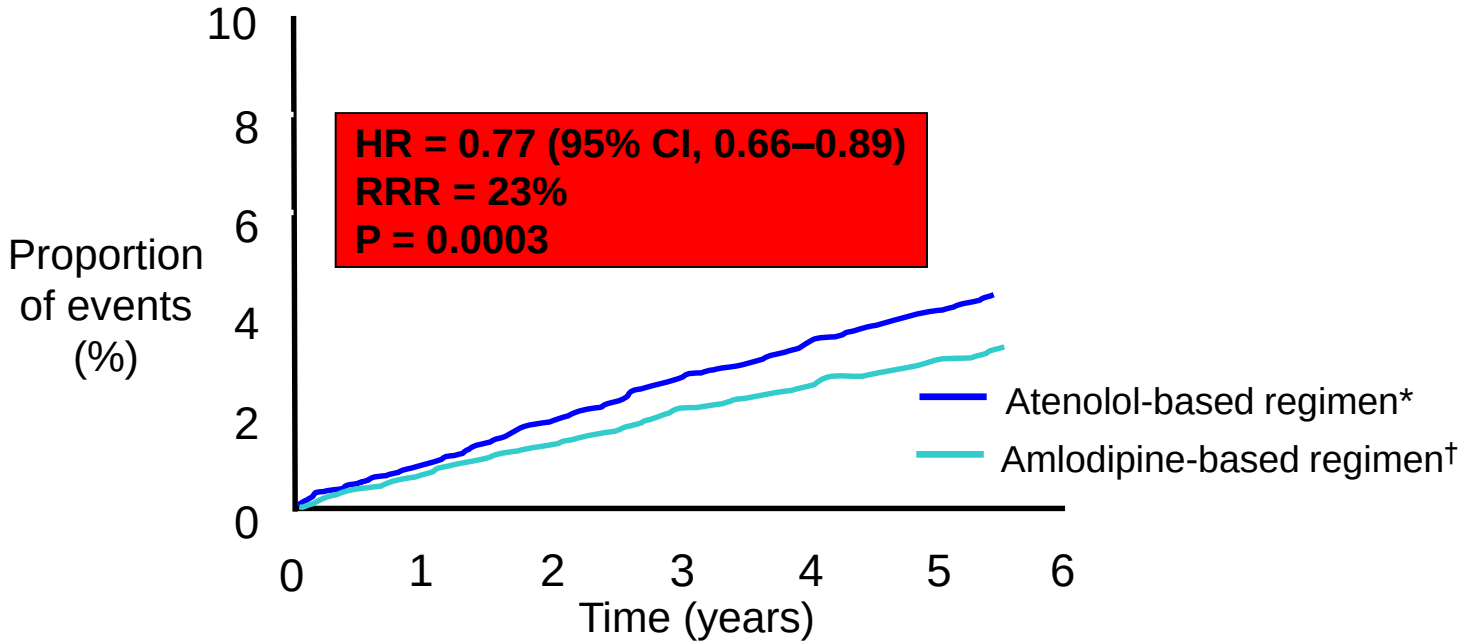
Number at risk

Amlodipine-based regimen (429 events)	9639	9475	9337	9168	8966	7863
Atenolol-based regimen (474 events)	9618	9470	9290	9083	8858	7743

*Atenolol 50–100 mg ± bendroflumethiazide 1.25–2.5 mg/potassium prn
†Amlodipine 5–10 mg ± perindopril 4–8 mg prn

Dahlöf B et al; ASCOT Investigators. *Lancet*. 2005;366:895-906.

ASCOT-BPLA: Reduction in fatal and nonfatal stroke



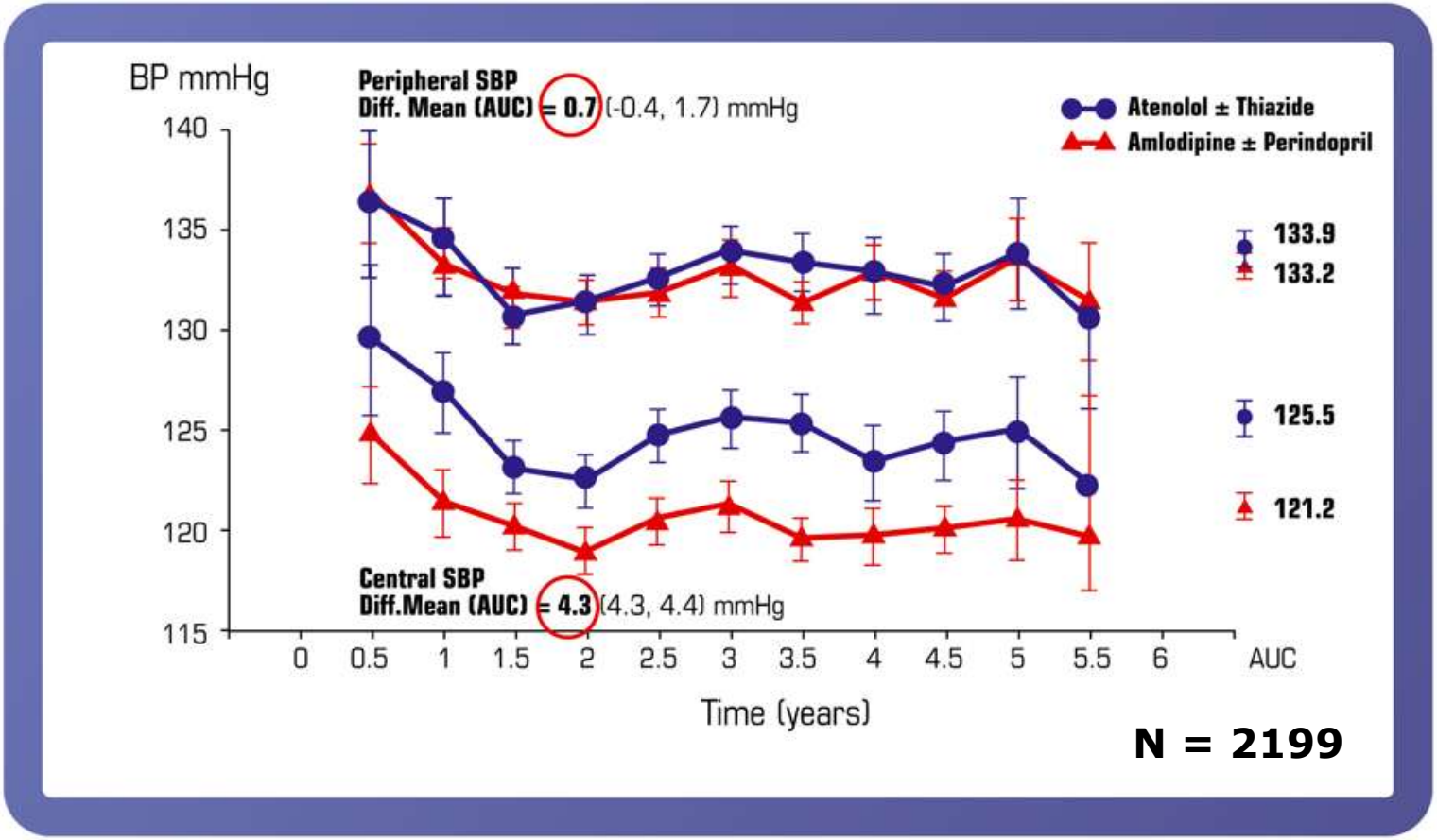
Number at risk

Amlodipine-based regimen (327 events)	9639	9483	9331	9156	8972	7863
Atenolol-based regimen (422 events)	9618	9461	9274	9059	8843	7720

*Atenolol 50–100 mg ± bendroflumethiazide 1.25–2.5 mg/potassium prn
†Amlodipine 5–10 mg ± perindopril 4–8 mg prn

Dahlöf B et al; ASCOT Investigators. *Lancet*. 2005;366:895-906.

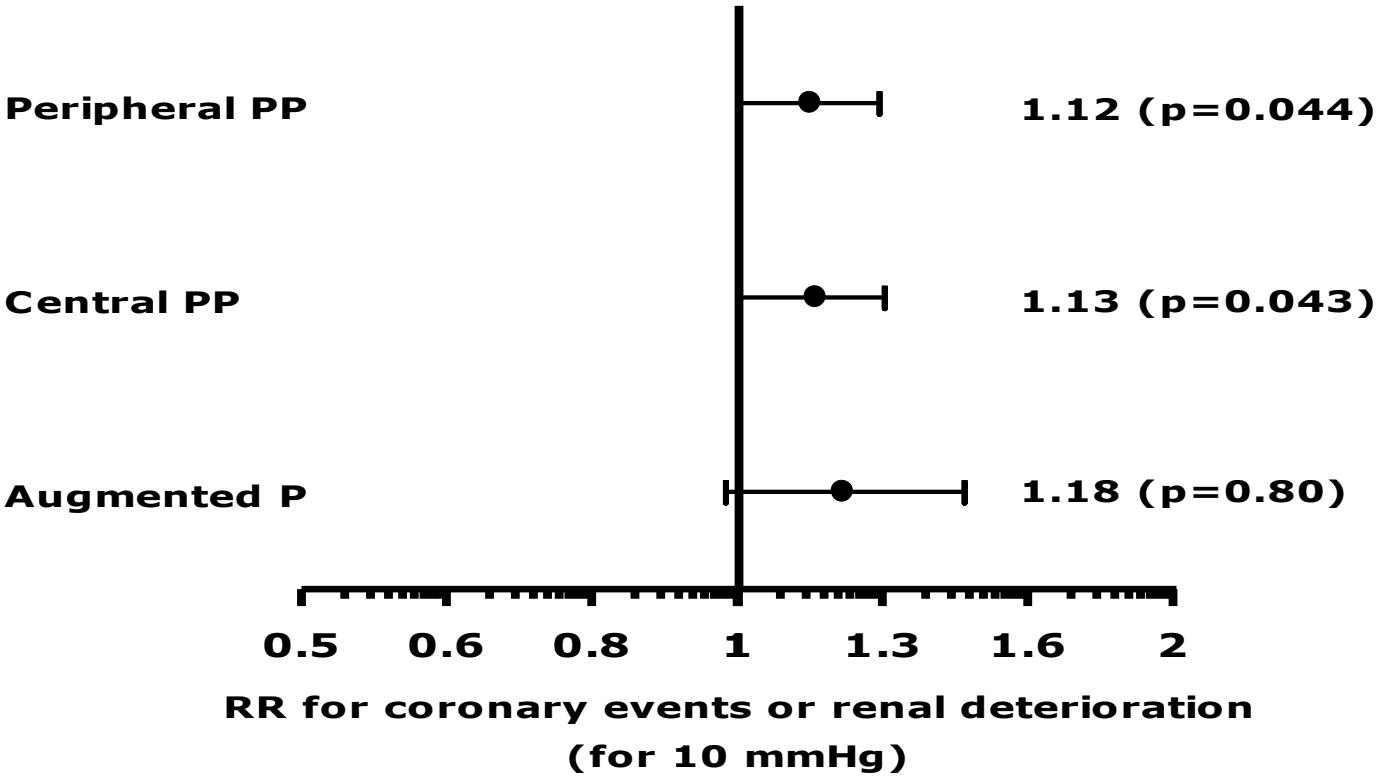
Etude Ascot-Cafe



- NB: pas de différence sur la baisse de PWV

CAFE Investigators. Circulation 2006;113:1213

Etude Ascot-Cafe



- Risque corrélé à la PP centrale (mais aussi périphérique)

CAFE Investigators. Circulation 2006;113:1213

Fonction artérielle: critère intermédiaire et indépendant du risque CV

Question:
Est-ce un critère de substitution du risque CDV ?

Qualités d'un critère de substitution des évènements cardiovasculaires (CV)

- apporter la preuve de concept : qu'il existe une différence de niveau du biomarqueur entre les patients ayant un événement CV et ceux indemnes d'événements
- montrer la valeur prédictive du biomarqueur pour les événements CV
- montrer la valeur additive du biomarqueur aux marqueurs classiques
- en démontrer l'utilité clinique: en d'autres termes, montrer que la prédiction du risque est suffisamment modifiée pour recommander une modification de traitement.

- montrer qu'une stratégie de prise en charge fondée sur l'utilisation du biomarqueur entraîne une moindre occurrence des événements CV

A valider !

Etude SPARTE

- SPARTE: Stratégie de Prévention cardiovasculaire basée sur la rigidité ARTErielle
- Objectif : la normalisation de la rigidité artérielle au-delà la PA est associée à une réduction du risque CV
- N = 3000, randomisation Traitement Conventionnel (normalisation TA) vs Traitement Ajusté (normalisation TA et VOP < 10m/s)

Conclusion

- La rigidité artérielle (VOP) et le degré de réflexion d'onde (Aix) sont des déterminants indépendants du risque CDV
- L'étude de la fonction artérielle peut permettre de mieux évaluer le risque CDV
- La fonction artérielle peut être étudiée de façon non invasive en pratique quotidienne
- Perspective: L'évaluation de la fonction artérielle pourra éventuellement aider au choix du traitement anti-HTA et à son efficacité sur la réduction du risque CV global, au-delà de la baisse de la PA