Central arterial haemodynamics and components of periodontitis in a cross-sectional population-based study

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Inserm U1027

Mona Lisa study

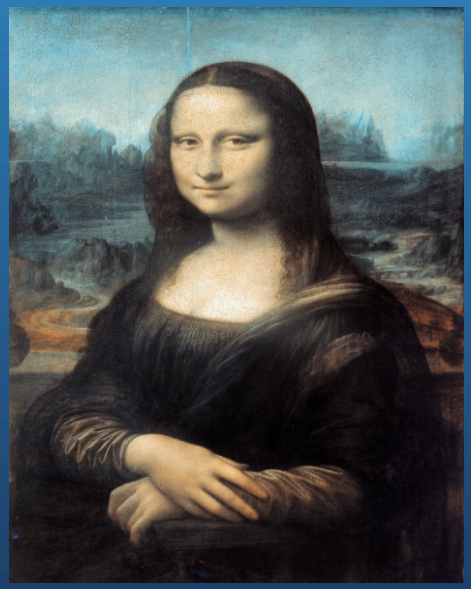
- Monitoring National du Risque Artériel
- Cross-sectional study
- Risk factors prevalence in France
- 4800 patients

MONA LISA
Transversal study : recruitment of 4800 patients aged 35 to 74

Bas-Rhin (northeast)
1600 patients

Haute-Garonne (southwest)
1600 patients

Lille (north)
1600 patients



Bucco-dental study (CPP 2006)
276 eligible patients

21 patients excluded (edentulous or endocarditis-prone)

Study
255 patients

Material & Methods

Inclusion criteria

- Aged 35-74
- Social security
- Consentment signed for bucco-dental study

Exclusion criteria

- Edentulous
- Endocarditis-prone

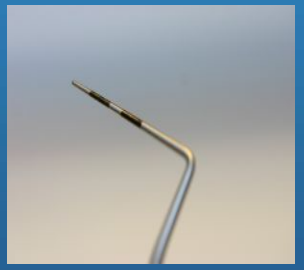
- Questionnaire, Clinical exam, biological exam

Buccodental examination

Single examiner at stomatology unit

Parodontal indices

- Each tooth except wisdom teeth
- Parodontal probe PCP 127 Hu Friedy 3.6.9.12
- On 4 sites (distal, vestibular, mesial, lingual or palatine) for each tooth (17-27; 37-47).
- Repeatability of measures tested on 20 patients
- **Dental Plaque Index (PI) (Silness et Loe, 1964)**
- **Gingival Inflammation (GI) (Loe et Silness, 1963)**
- **Pocket Depth (PD) (mm)**
- **Clinical Attachment Loss (CAL) (mm)**



Parodontal probe

Periodontitis

Inflammatory disease of dental support tissue due to pathogenic bacteria

CAL: Clinical Attachment Loss
From sulcus bottom to enamel-cement junction ↕

PD: Deep Pockets ↕
From sulcus bottom to gum free margin

One periodontitis definition

Page and Eke criteria, 2007

➢ **Periodontitis**

- **No periodontal disease or mild**
- **Moderate periodontitis :** at least 2 sites with CAL ≥ 4 mm, **or** at least 2 sites with PD ≥ 5 mm.
- **Severe periodontitis** : at least 2 sites with CAL ≥ 6 mm, **and** at least 1 site with PD ≥ 5 mm.

Only mesial and distal sites are evaluated

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Periodontal Disease and Atherosclerotic Vascular Disease: Does the Evidence Support an Independent Association? : A Scientific Statement From the American Heart Association

Peter B. Lockhart, Ann F. Bolger, Panos N. Papapanou, Olusegun Osinbowale, Maurizio Trevisan, Matthew E. Levison, Kathryn A. Taubert, Jane W. Newburger, Heather L. Gornik, Michael H. Gewitz, Walter R. Wilson, Sidney C. Smith, Jr and Larry M. Baddour

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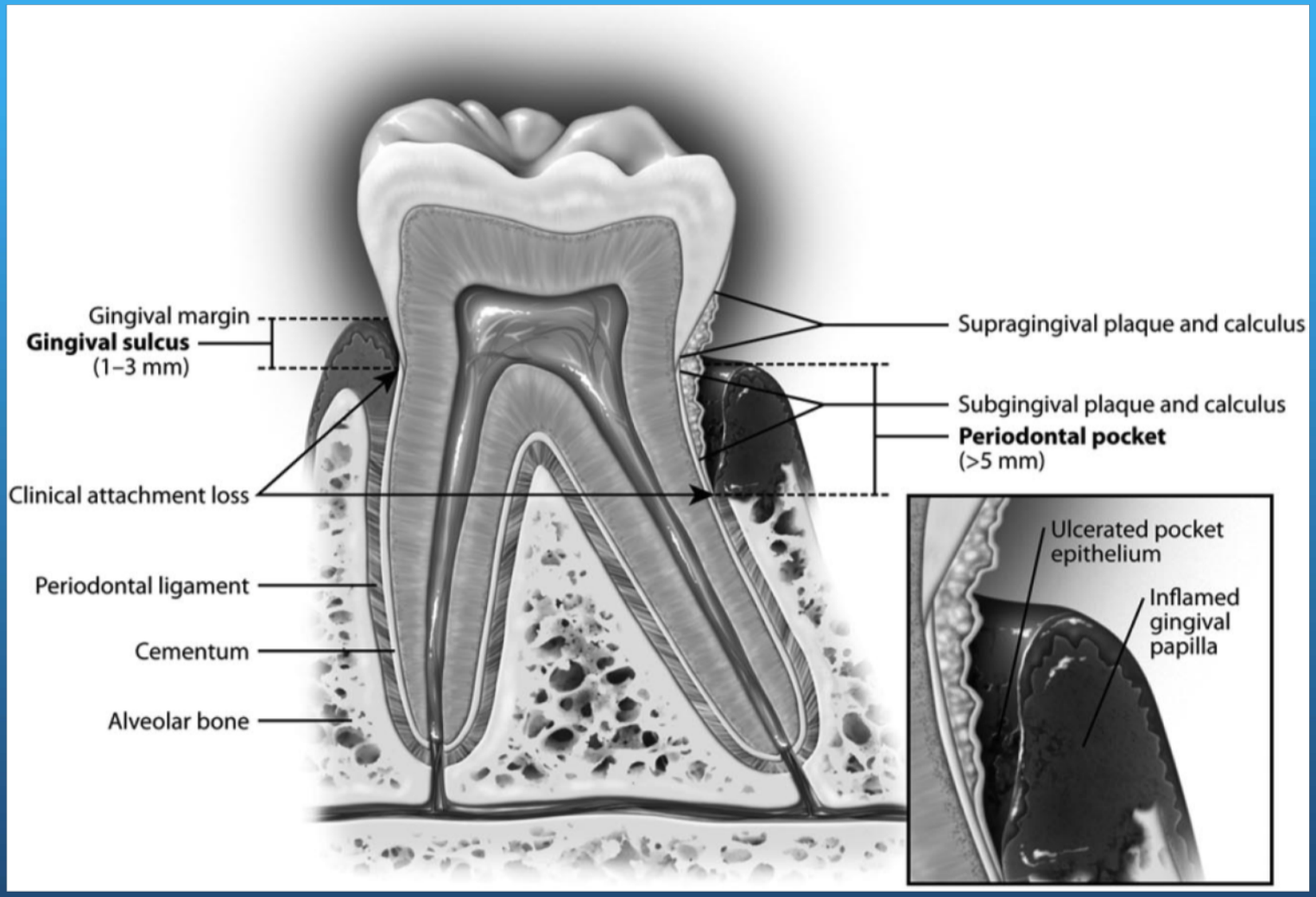

Gingival margin
Gingival sulcus
(1–3 mm)
Clinical attachment loss
Periodontal ligament
Cementum
Alveolar bone
Supragingival plaque and calculus
Subgingival plaque and calculus
Periodontal pocket
(>5 mm)
Ulcerated pocket epithelium
Inflamed gingival papilla

Table 2. Bacteriology of Dental Plaque

	Facultative	Anaerobic
Gram-positive cocci	*Streptococcus sanguis* *Streptococcus oralis* *Streptococcus mutans*	
Gram-positive bacilli		*Actinomyces naeslundii* *Actinomyces odontolyticus* *Actinomyces viscosus*
Gram-negative cocci	*Neisseria* species	*Veillonella* species
Gram-negative bacilli	*Aggregatibacter* (formerly *Actinobacillus*) *actinomycetemcomitans* *Capnocytophaga* species *Eikenella corrodens* *Helicobacter pylori* *Chlamydophila pneumoniae*	*Porphyromonas gingivalis* *Fusobacterium nucleatum* *Prevotella intermedia* *Tannerella forsythia* *Selenomonas noxia* *Campylobacter rectus*
Spirochetes		*Treponema denticola* Other *Treponema* species
Methanogenic archaea		*Methanobrevibacter oralis*-like
Sulfate-reducing bacteria and archaea		*Desulfomicrobium orale* *Desulfovibrio*

Indirect Mechanisms: Systemic Inflammation

Atherosclerosis may begin during childhood, with initial infiltration of the endothelium with fatty substances, and progresses over many decades. Chronic, quiescent atheroma-

Indirect Mechanisms: Mimicry

Molecular mimicry has been raised as a possible mechanism linking periodontal infection with atherosclerosis. Molecular mimicry is thought to occur when sequence similarities between foreign and self-peptides produce cross-activation of auto-reactive T or B cells that can lead to tissue pathology or autoimmunity.[103] Cross-reactive autoantibodies to periodontal bacterial lipopolysaccharides and heat shock proteins have been identified[96–99] and invoked as a potential explanation for the putative relationship between PD and ASVD.[104] Expression of host protective heat shock proteins (HSPs) such as HSP60 on

Direct Mechanisms: Bacteremia and Vascular Infection by Periodontal Pathogens

Adults harbor more than a billion bacteria in their mouths. Although the flora varies in different oral regions, the area of greatest potential relevance to atherosclerosis is the periodontal pocket. The total surface area of the pockets in patients with periodontitis is estimated to be between 8 and 20 cm^2, and regions of ulceration in the pocket place the bacterial biofilm in close proximity to the circulation.[112]

AHA scientific statement 2012

- Link between periodontitis and atherosclerosis
- Common CV risk factors : tobacco use, age, diabetes
- Against the former means against the latter?
- No causal link
- Diminution of inflammation and endothelial dysfunction

Periodontitis and MetS
Benguigui 2010

- Glucose metabolism impairment
  - Grossi 1998
- Dyslipidemia
  - Lösche 2000
- Diabetes
  - Madianos 2002
- Inflammation
  - Loos 2005
- Endothelial dysfunction
  - Higashi 2008
  - Tonetti 2007
  - Amar 2003

		Number of sites with CAL ⩾ 4 mm		Number of sites with PD ⩾ 4 mm		Number of sites with CAL ⩾ 5 mm	
		RR	95% CI	RR	95% CI	RR	95% CI
HOMA index for insulin resistance							
Total population							
I	Quartile	1.00		1.00		1.00	
II	Quartile	1.07	0.74–1.54	1.14	0.73–1.76	1.20	0.74–1.95
III	Quartile	1.41	0.97–2.06	1.37	0.87–2.16	1.48	0.89–2.46
IV	Quartile	1.48	1.02–2.15	1.74	1.11–2.73	1.73	1.05–2.84
			$p = 0.018$*		$p = 0.007$*		$p = 0.022$*
Non-diabetics subjects ($n = 238$)							
I	Quartile	1.00		1.00		1.0	
II	Quartile	1.05	0.72–1.54	1.05	0.67–1.66	1.17	0.71–1.92
III	Quartile	1.31	0.88–1.94	1.27	0.79–2.04	1.26	0.74–2.13
IV	Quartile	1.52	1.02–2.27	1.61	1.00–2.61	1.82	1.08–3.07
			$p = 0.021$*		$p = 0.027$*		$p = 0.023$*
Non-smoker subjects ($n = 204$)							
I	Quartile	1.00		1.00		1.0	
II	Quartile	1.11	0.72–1.71	1.07	0.64–1.78	1.25	0.71–2.21
III	Quartile	1.15	0.72–1.82	1.09	0.62–1.92	1.19	0.64–2.23
IV	Quartile	1.26	0.82–1.96	1.46	0.86–2.48	1.44	0.81–2.57
			$p = 0.309$*		$p = 0.131$*		$p = 0.240$*

Model was adjusted for age, gender, educational level, smoking habits, alcohol consumption, CRP, and dental plaque.

*p-value for trend.

CAL, clinical attachment loss; PD, probing pocket depth; RR, relative risks; 95% CI, 95% confidence interval; CRP, C-reactive protein.

Dental status and obesity
Benguigui 2012

- Sheiham 2002; Marcenes 2003; Hilgert 2009; Ostberg 2009
- Benguigui 2012
  - Pocket depth (PD) and plaque index (PI) linked with obesity
  - Missing teeth without association with BMI
  - Clinical Attachment Loss (CAL) not linked with BMI
- Oral bacteria (*Selenomonas noxia? Goodson 2009)*
- Insulinoresistance through TNFa elevation or adiponectin diminution

- Plaque index (PI) : quantitative marker of supragingval bacteria
- Pocket depth (PD) : associated to bacteria in periodontitis
- Clinical attachment loss (CAL) : bone resorption

Gingival microcirculation

- Kervongbundit et al. (Odontology 2002-2003)
- Blood flow greater in maxillar anterior > mandibular anterior teeth
- Blood flow greater in alveolar mucosa > attached ginigiva > interdental gingiva > free gingiva
- Blood flow greater in moderate gingivitis > healthy gingiva
- Ginigivitis : disruption of vascular networks

Central Blood Pressure Measurements and Antihypertensive Therapy

A Consensus Document

(*Hypertension*. 2007;50:154-160.)

Enrico Agabiti-Rosei, Giuseppe Mancia, Michael F. O'Rourke, Mary J. Roman, Michel E. Safar, Harold Smulyan, Ji-Guang Wang, Ian B. Wilkinson, Bryan Williams, Charalambos Vlachopoulos

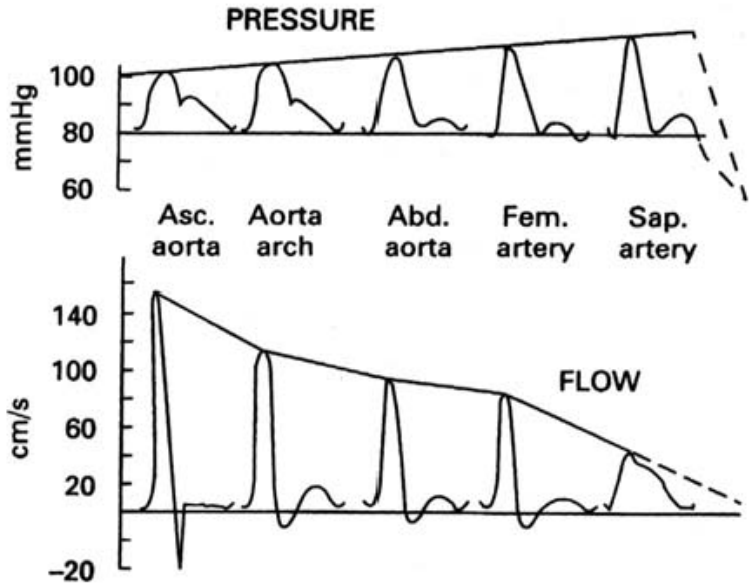


Figure 1. Change in contours in pressure wave (top) and flow wave (bottom) between the ascending aorta and the saphenous artery (reprinted from Reference 3).

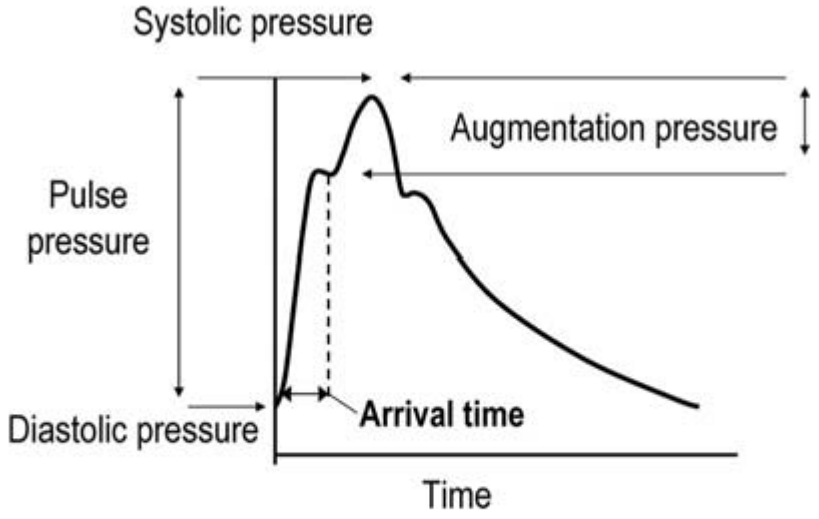
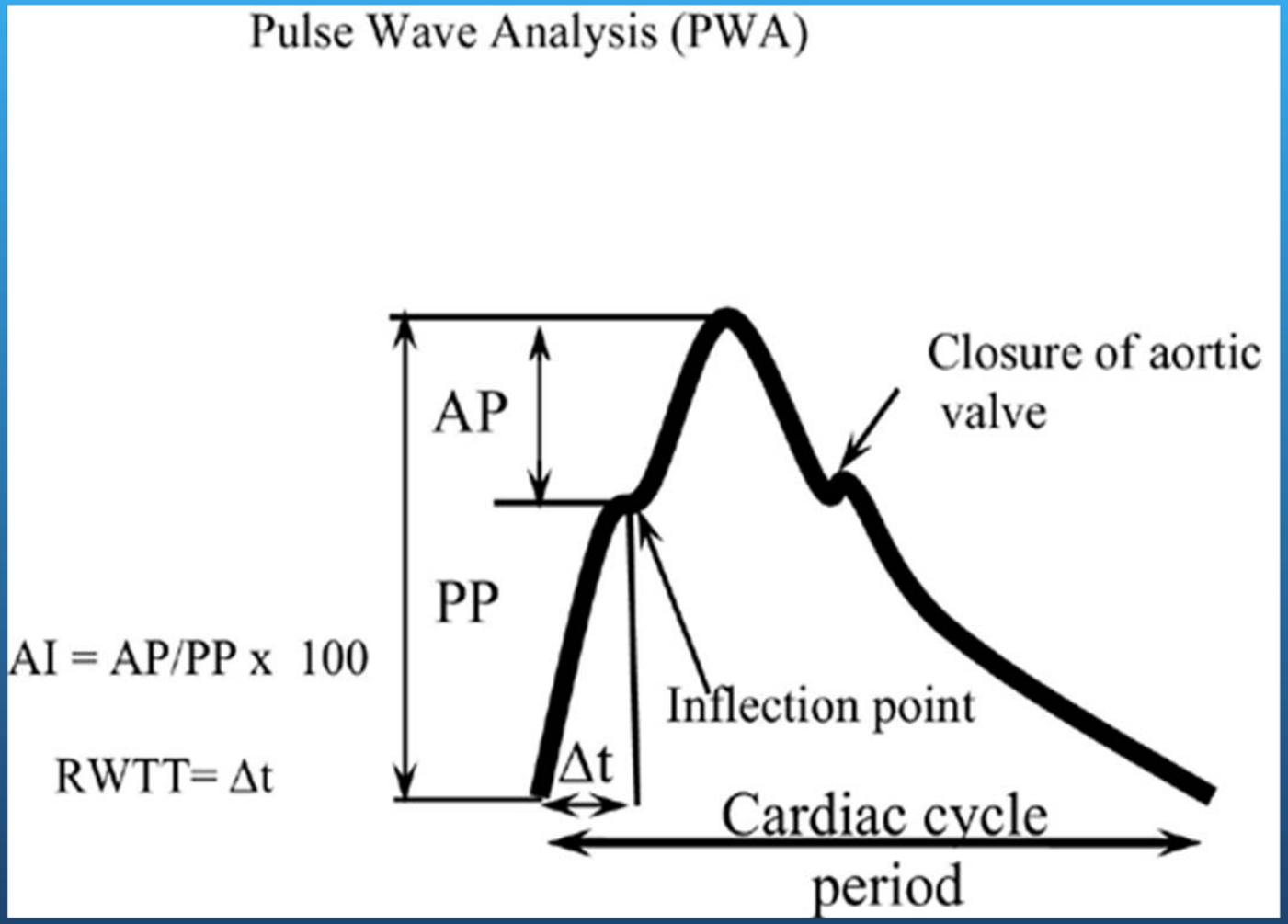
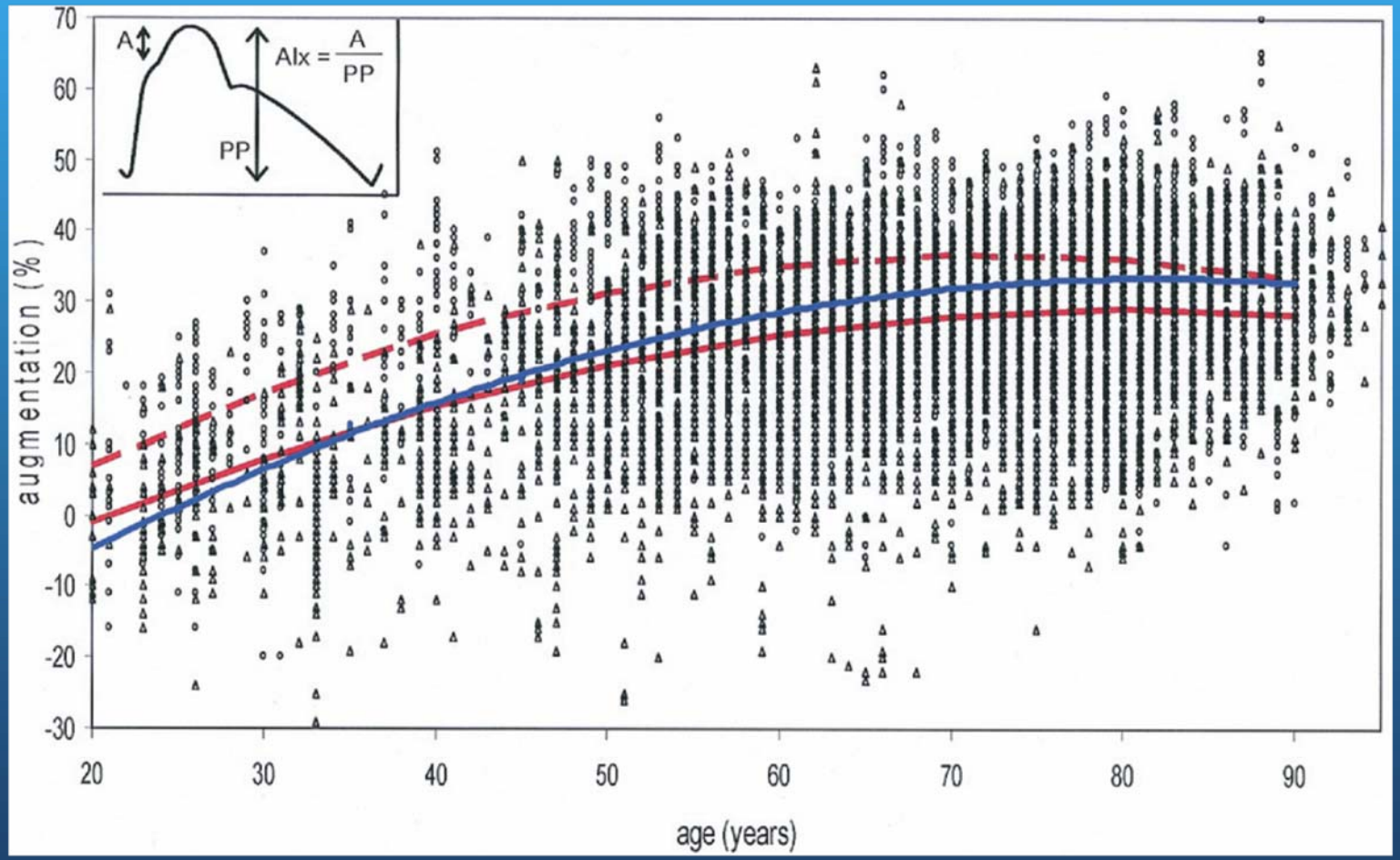


Figure 2. Central pressure waveform. The height of the late systolic peak above the inflection defines the augmented pressure, and the ratio of augmented pressure to PP defines the augmentation index (in percentage; modified from Reference 6).

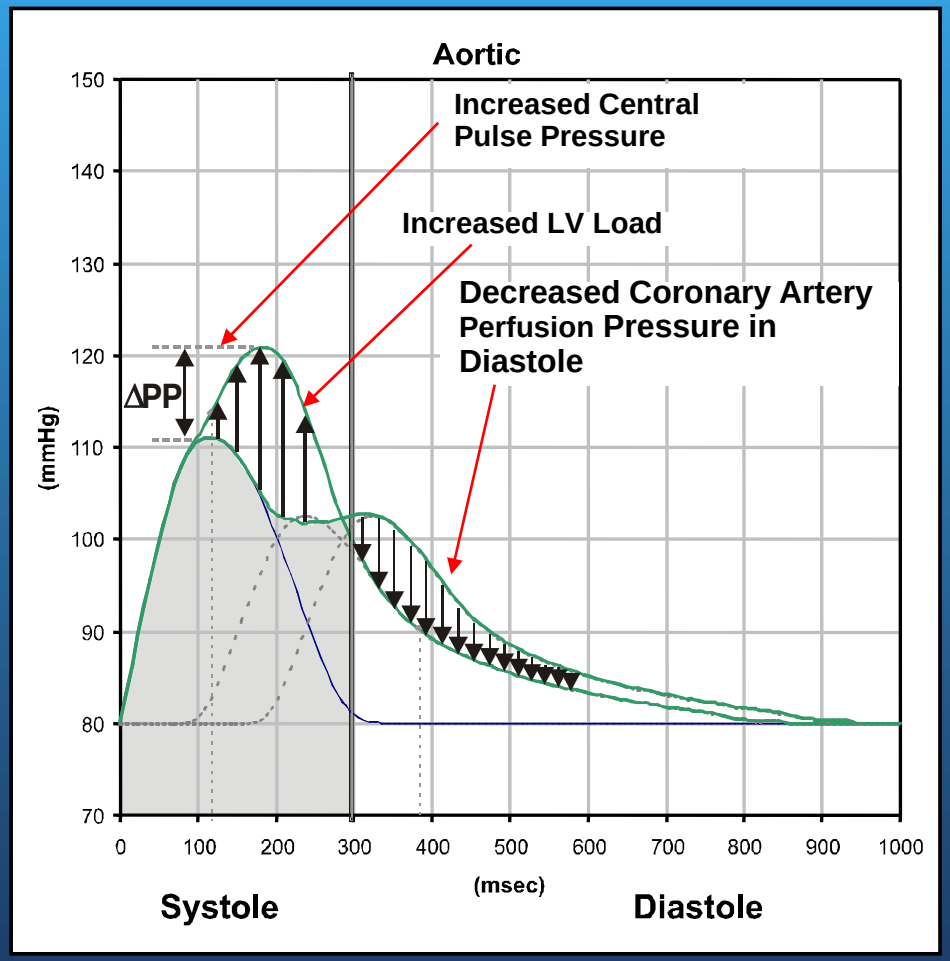

Pulse Wave Analysis (PWA)
AP
PP
Closure of aortic valve
Inflection point
Δt
Cardiac cycle period
AI = AP/PP x 100
RWTT= Δt


A
AIx = A/PP
PP
augmentation (%)
age (years)
70
60
50
40
30
20
10
0
-10
-20
-30
20
30
40
50
60
70
80
90

Central haemodynamics

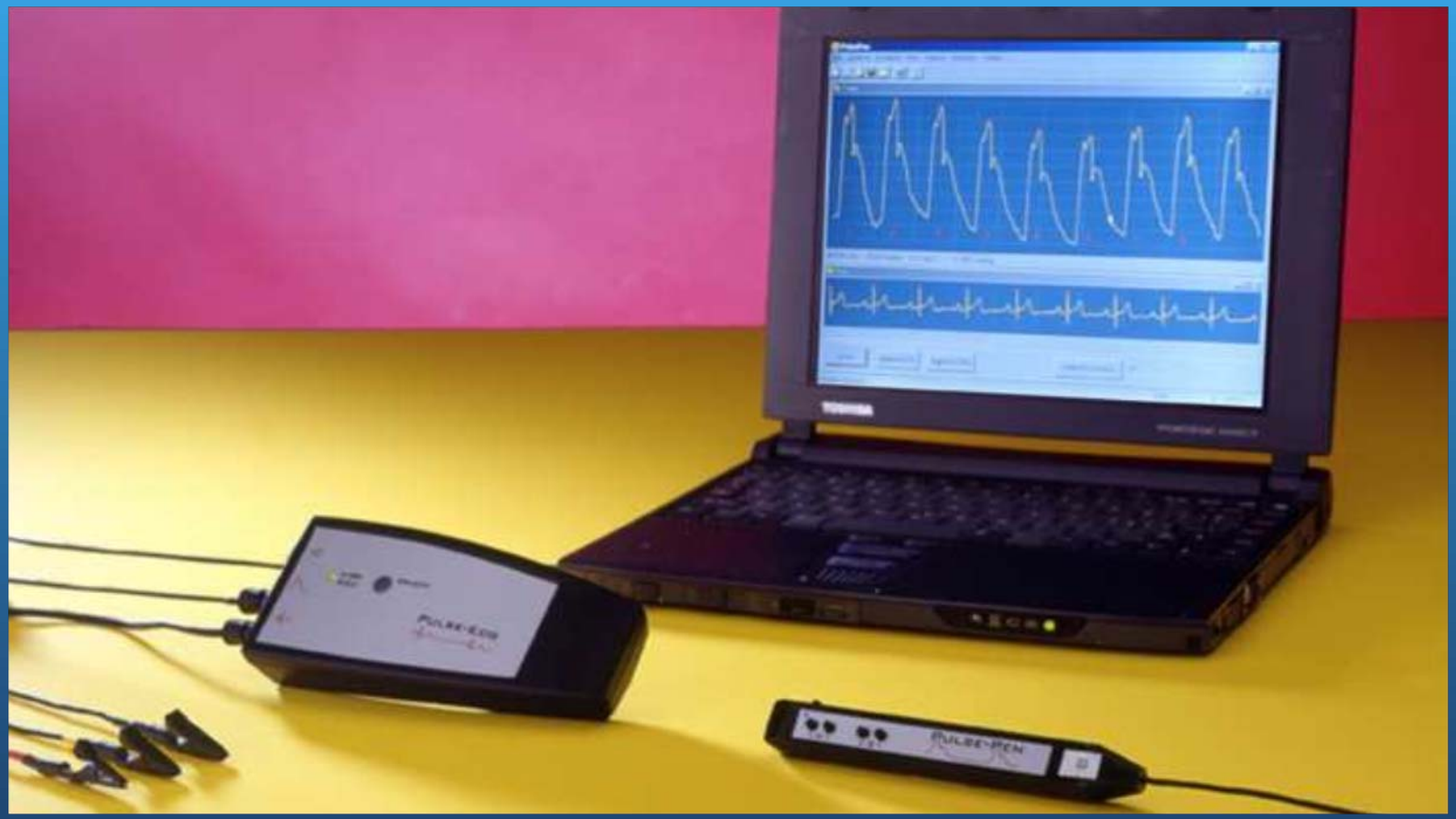
- CBP increases with age
- Before 50 : CBP increases due to greater wave reflection amplitude
- After 50 : CBP increases due to PWV increase
- AIx=AP/PP%

The Impact of the Early Wave Reflection



- This earlier return to the heart of the reflected pressure wave (due to stiffening of the arteries) changes the aortic root pressure waveform, … with 3 key clinical implications
- Central pulse pressure increases … increasing risk of stroke and renal failure
- LV Load increases…. increasing LV mass, and accelerating progress towards LV hypertrophy and heart failure
- Coronary artery perfusion pressure in diastole reduces…. increasing risk of myocardial ischemia

PulsePen



Statistical analysis

- Logiciel STATA 9
- To test univariate associations between augmentation index and each explanatory variable using:

  Chi square tests if the explanatory variable was qualitative

  Student tests if the explanatory variable was quantitative
- To test multivariate associations between augmentation index and explanatory variable into binomial logistic regression models using a step by step regression procedure.

Results

- 255 patients
- 140 men/85 women
- Age: mean 58+/-9 years
- 158 with periodontitis (62%)

Univariate association between augmentation index and dental variables.

	IA <=13%	IA >13%	P value*
Number of missing teeth, mean ± sd	3.19 ± 4.59	3.60 ± 4.38	0.477
Periodontitis, n(%)			**0.068**
No periodontitis	**33 (26.0%)**	**18 (14.4%)**	
Moderate	**50 (39.4%)**	**54 (43.2%)**	
Severe	**44 (34.6%)**	**53 (42.4 %)**	

*P value for chi2 (qualitative variables) or Student test (quantitative variables)

*** Exlanatory variables for which the p value was smaller than 0.2 were introduced in multivariate logistic regression models**

Univariate association between augmentation index and dental variables.

	IA <=13%	IA>13%	P value
Number of dental sites with, n(%):			
Gingival Index (GI)>=2			
[0-33[	66 (52.0 %)	61(48.8 %)	
[33-112]	61 (48.0 %)	64 (51.2 %)	0.615
Plaque Index (PI) >=2			
[0-7[	65 (51.2 %)	58 (46.4 %)	
[7-69]	62 (48.8 %)	67 (53.6 %)	0.448
Clinical attachment loss (CAL) >=4mm			
[0-16[	**70 (55.1%)**	**57 (44.9%)**	
[16-87]	**56 (44.8%)**	**69 (53.6%)**	**0.101**
Pocket depth (PD) >=4mm			
[0-4[	**72 (56.7%)**	**56 (44.3%)**	
[4-65]	**55 (43.3%)**	**69 (55.2%)**	**0.059**

Multivariate associations between augmentation index and explanatory variables after using a step by step binomial logistic regression procedure

	IA >=13%		
	OR	95% [IC]	P value
Women	4.92	[2.65-9.12]	<0.0001
Heart rate (bpm)	0.96	[0.93-0.99]	0.010
Hypertension*	1.92	[1.04-3.52]	0.035
BMI ≥ 25 kg/m^2	1.78	[1.01-3.16]	0.048
Periodontitis			
No or mild	1		
Moderate	2.23	[1.05-4.74]	0.036
Severe	2.64	[1.21-5.78]	0.015

Or and 95% IC measured associations between the outcome variable « the augmentation index » and each explanatory variables staying in binomial logistic regression models after using a step by step regression procedure.

Explanatory variables for initial models were: age, gender, educational level, smoking habits, alcohol consumption, hypertension, heart rate, BMI (>= 25 kg/m^2) and HDL-cholesterol and one after one each dental variables.

* Hypertension defined as SBP ≥ 140 or DBP ≥ 90 mmHg or antihypertensive drug treatment

Multivariate associations between augmentation index and explanatory variables after using a step by step binomial logistic regression procedure

	IA>=13%		
	OR	95% [IC]	P value
Women	4.55	[2.49-8.32]	<0.0001
Heart rate (bpm)	0.96	[0.93-0.99]	0.006
Hypertension*	1.92	[1.05-3.53]	0.034
BMI ≥ 25 kg/m^2	1.85	[1.04-3.27]	0.034
Number of sites with CAL>=4mm			
[0-16]	1		
[16-87]	1.75	[1.01-3.02]	0.044

Or and 95% IC measured associations between the outcome variable « the augmentation index » and each explanatory variables staying in binomial logistic regression models after using a step by step regression procedure.

Explanatory variables for initial models were: age, gender, educational level, smoking habits, alcohol consumption, hypertension, heart rate, BMI (>= 25 kg/m^2) and HDL-cholesterol and one after one each dental variable.

* Hypertension defined as SBP ≥ 140 or DBP ≥ 90 mmHg or antihypertensive drug treatment

Multivariate associations between augmentation index and explanatory variables after using a step by step binomial logistic regression procedure

	IA>=13%		
	OR	95% [IC]	P value
Women	4.60	[2.51-8.34]	<0.0001
Heart rate (puls/mn)	0.96	[0.93-0.99]	0.005
Hypertension*	1.96	[1.07-3.58]	0.029
BMI ≥ 25 kg/m^2	1.77	[1.00-3.14]	0.050
Number of sites with PD> 4mm			
[0-4]	1		
[4-65]	1.76	[1.01-3.05]	0.044

Or and 95% IC measured associations between the outcome variable « the augmentation index » and each explanatory variables staying in binomial logistic regression models after using a step by step regression procedure.

Explanatory variables for initial models were: age, gender, educational level, smoking habits, alcohol consumption, hypertension, heart rate, BMI (>= 25 kg/m^2) and HDL-cholesterol and one after one each dental variable.

* Hypertension defined as SBP ≥ 140 or DBP ≥ 90 mmHg or antihypertensive drug treatment

Results

- Periodontitis
- Clinical attachment loss (CAL)
- Pocket depth (PD)
- are associated with augmentation index (Aix)
  - In the multiple regression model
- No association with
  - Gingival inflammation (GI),
  - Dental plaque index (PI),
  - Number of missing teeth

Perspectives

- Elevation of Augmentation Index
- Early reflected wave
- Global microcirculation impairment

- CAL=bone resorption
  - Local microcirculation impairement?
  - Leading to general microcirculation impairment?