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Arterial stiffness.

Oral exam questions

- Arterial elasticity – significance
- Arterial pulse, pulse wave

- Mr. Folkow - 19th century – added physical characteristics to individual sections of the vascular system (aorta – compliance;
- arterioles – resistance; veins – capacity)

- Basic relationship: blood pressure is a function of SV and PO
- Compliance: $\Delta V / \Delta P$

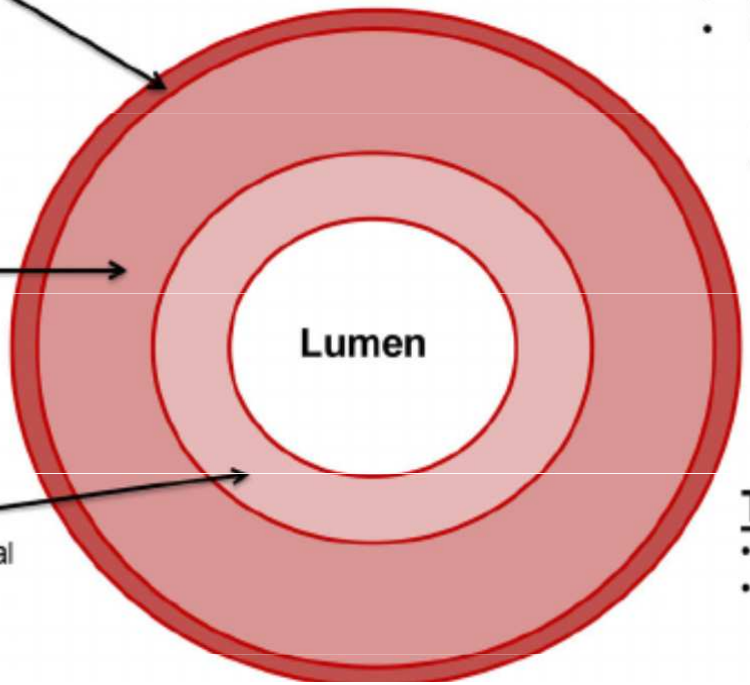
Factors of arterial stiffness changes

A. Vascular Structure

Tunica adventitia
- Fibroblasts
- Collagen-containing matrix
- External elastic lamina

Tunica media
- Smooth muscle cells
- Elastic fibers

Tunica intima
- Monolayer of endothelial cells
- Internal elastic lamina



B. Stiffness Pathology

Tunica adventitia
- Collagen deposition
- Increase in fibroblasts

Tunica media
- Collagen deposition
- Elastin degradation
- RAAS Signaling
  - AT1R & MR
- VSMC stiffness
  - Increase in α-SMA & β1-integrin

Tunica intima
- Endothelial dysfunction
- Oxidative stress

!
- Elastin degradation
- Collagen deposition
- Endothelial dysfunction

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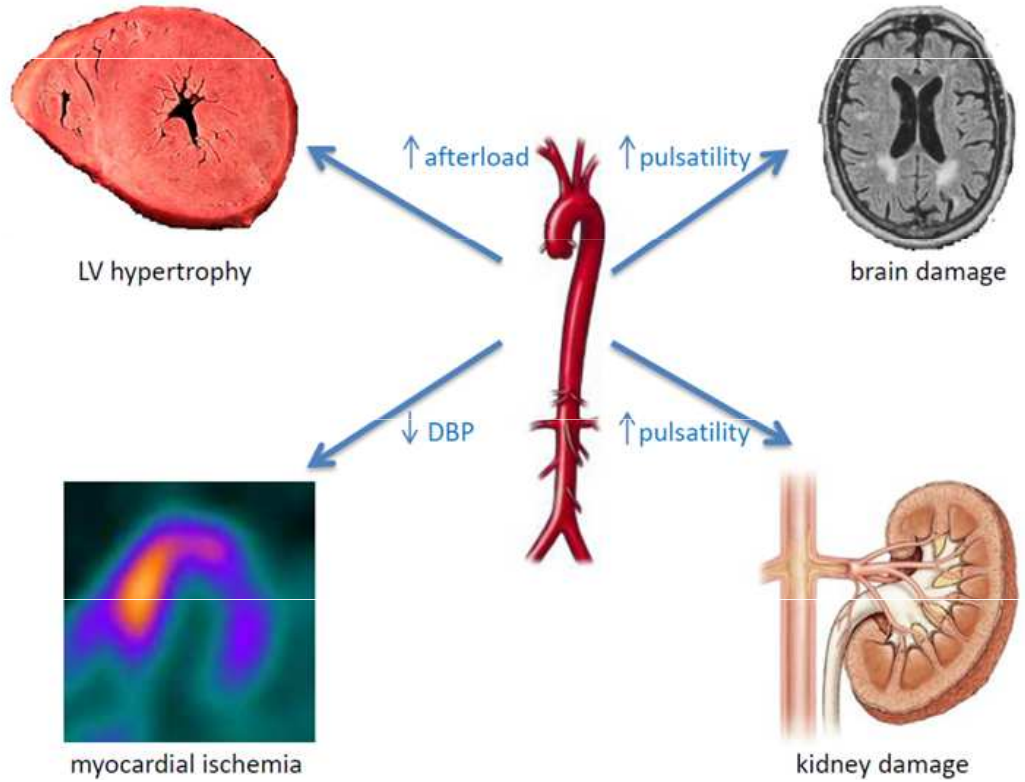
Complications of the higher arterial stiffness



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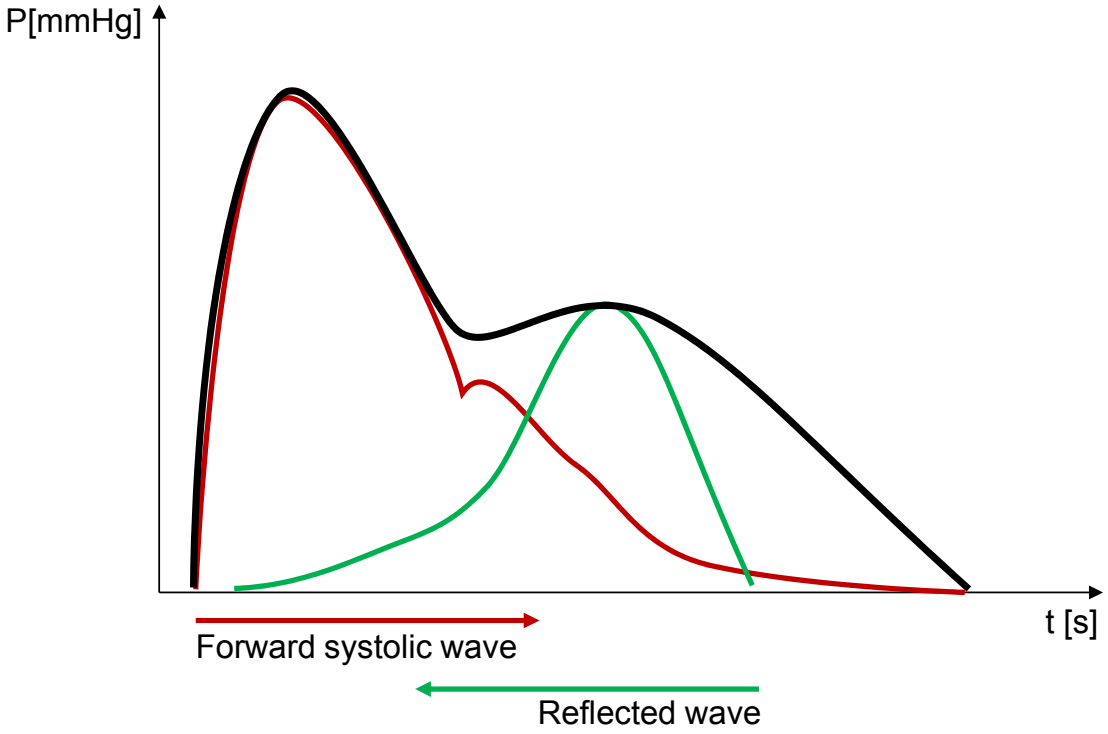
Pulse wave



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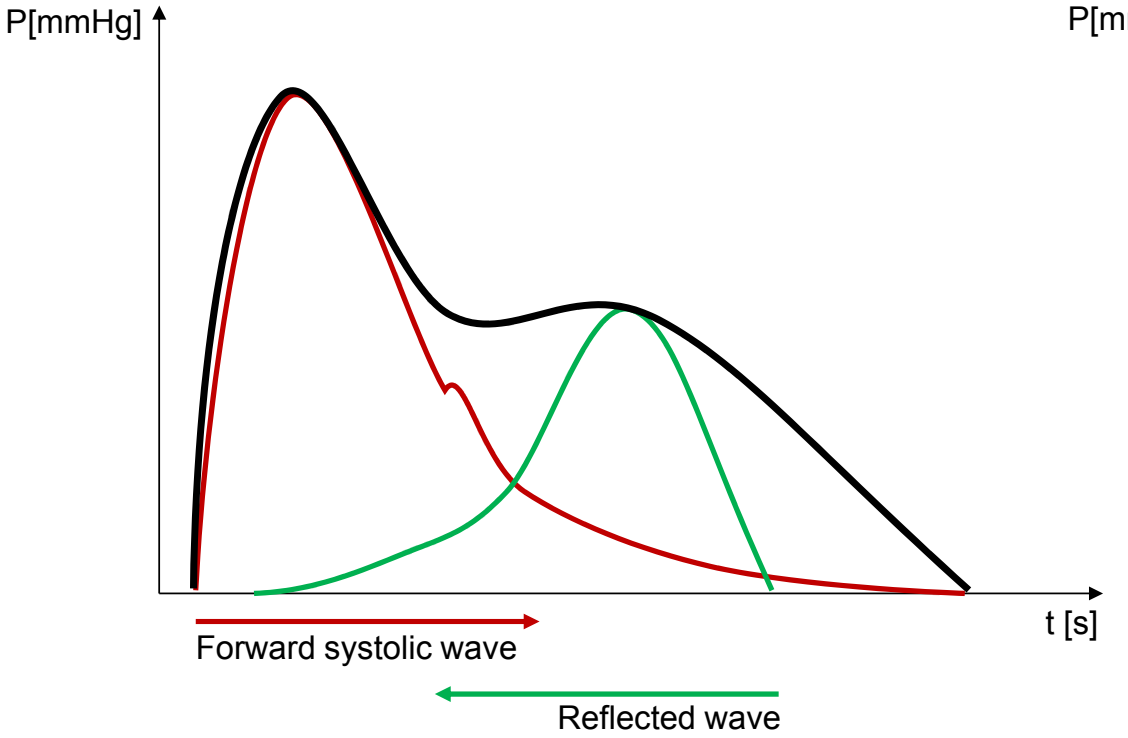
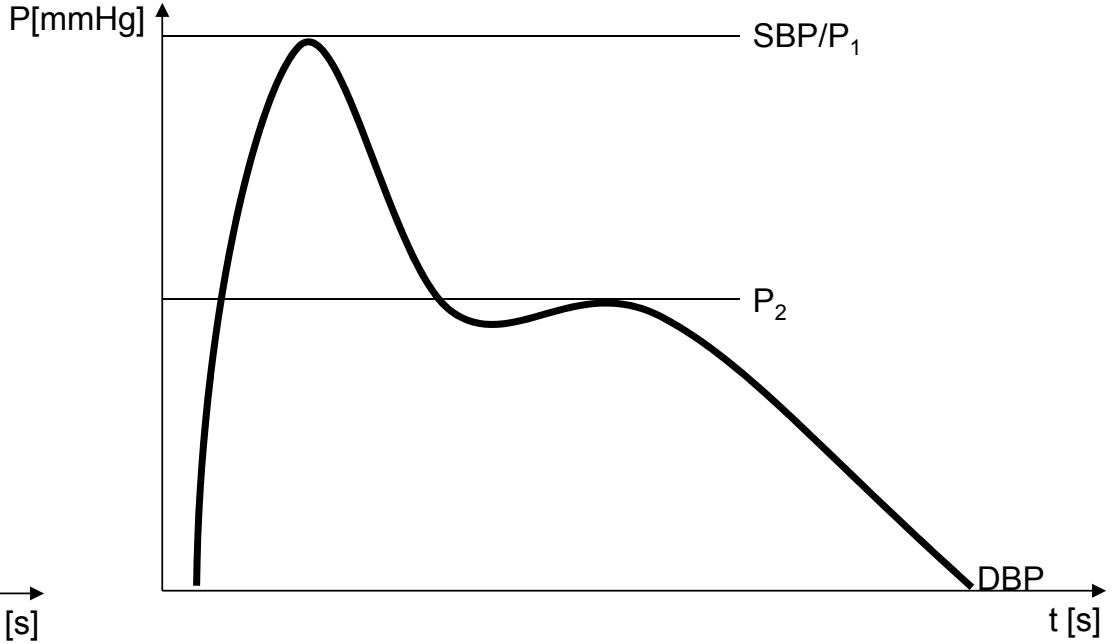
- Reflected wave increases = augments blood pressure in the aorta
- Physiologically: in young people, the reflected wave mainly affects the diastolic pressure, which increases – and thus contributes to better filling of the coronary circulation and better nutrition of the endocardium

Pulse wave





PP=SBP – DBP

mBP=DBP+1/3PP

AP=P_2 – P_1

SBP – systolic blood pressure, DBP – diastolic blood pressure, P_1 – pressure at peak of systolic flow, P_2 – pressure of the reflected wave, PP – pulse pressure, mBP – mean blood pressure, ***AP – augmented pressure***

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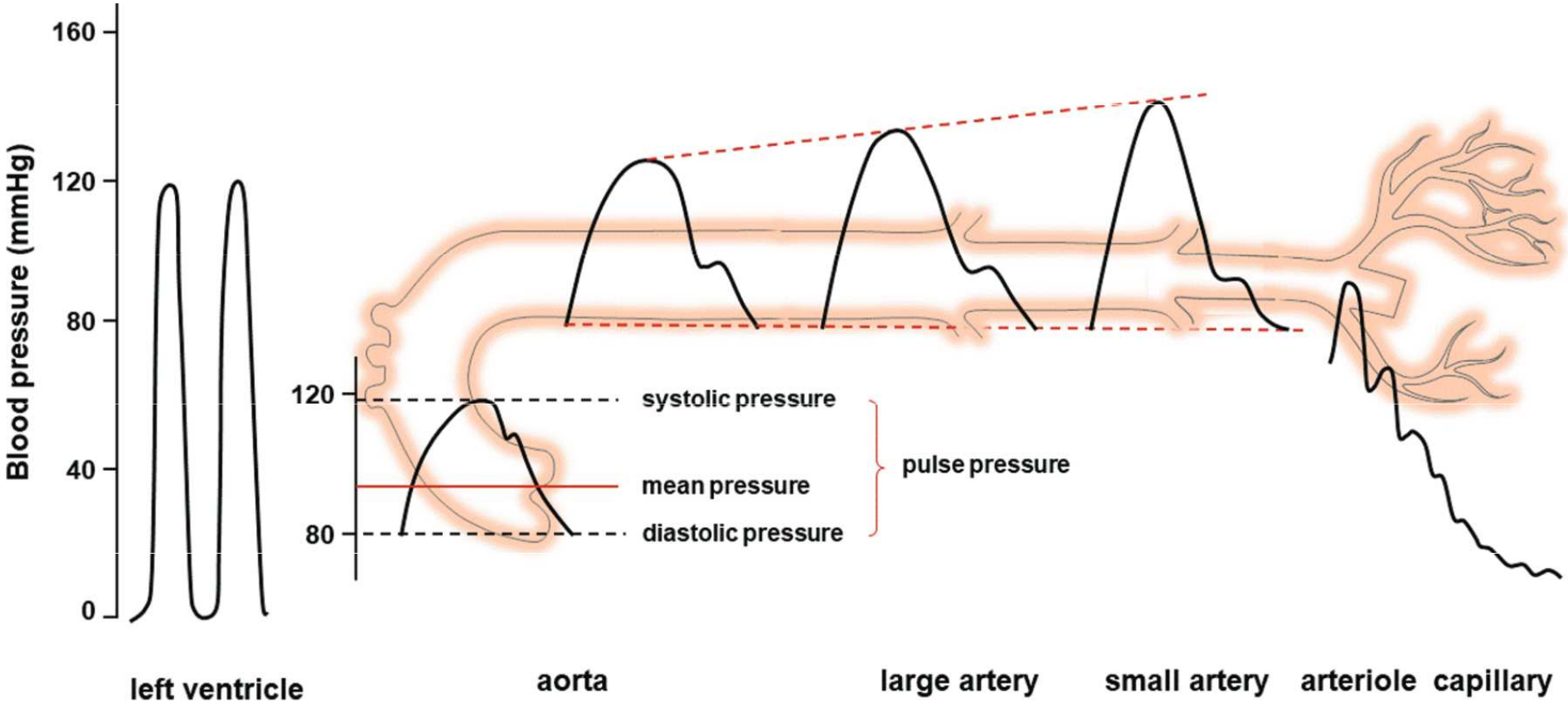
Pulse wave at different vascular segments



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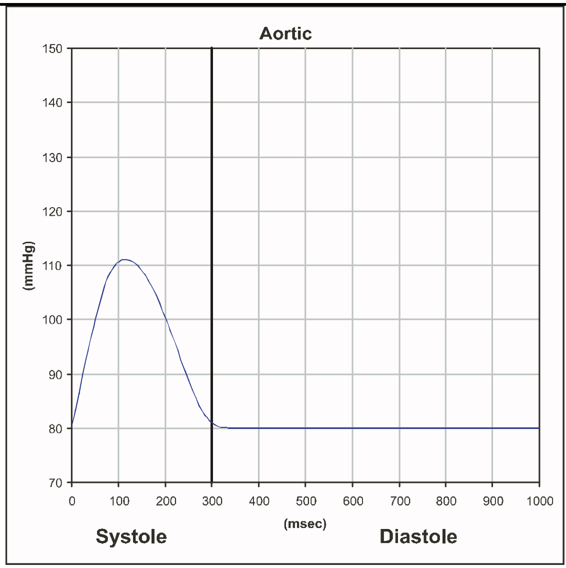
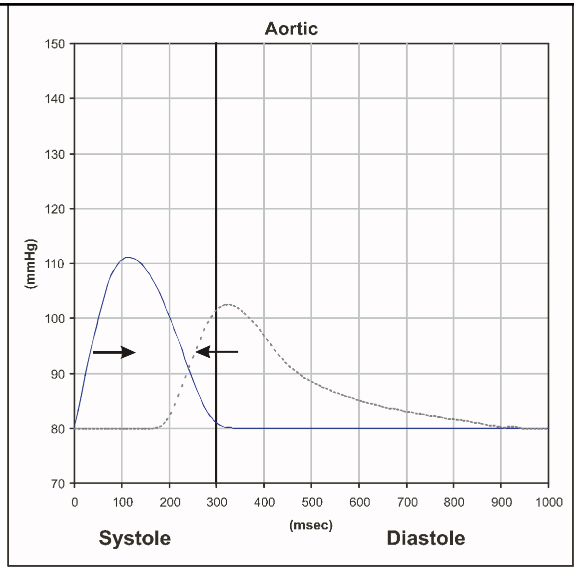


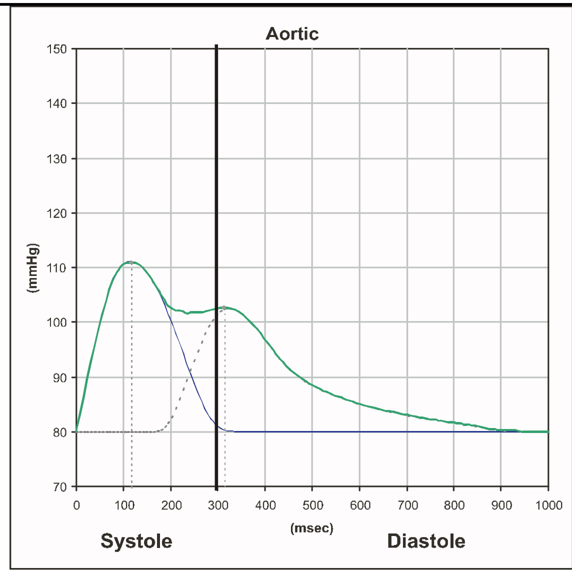
- If the aorta was an long open-ended tube providing a simple resistance to flow (i.e., there was no wave reflection), then:
- The pressure wave in the aortic root would show a single peak for each contraction.



If we connect the network of arteries with all its bifurcations and vascular beds, then

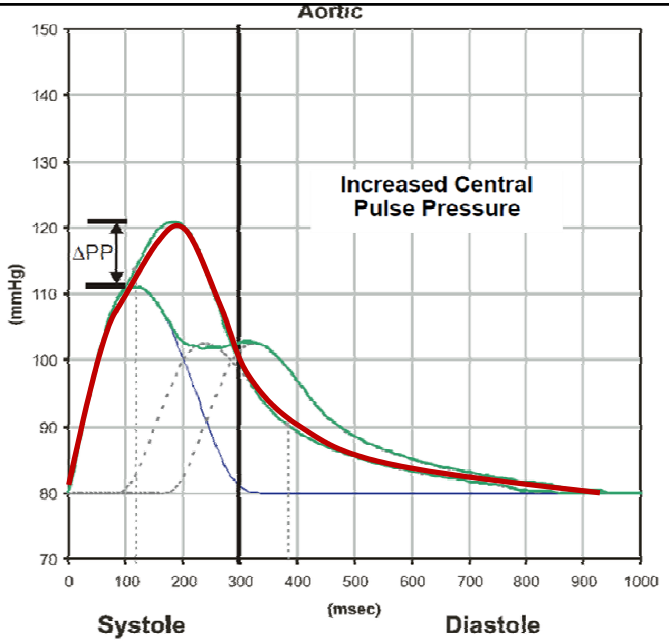
... as this primary wave travels along the arteries it will generate **reflected waves from each bifurcation and from the peripheral vascular beds.**

... all these small reflected waves return to the heart, **summing to create a reflected wave as shown**, starting even before the end of systole

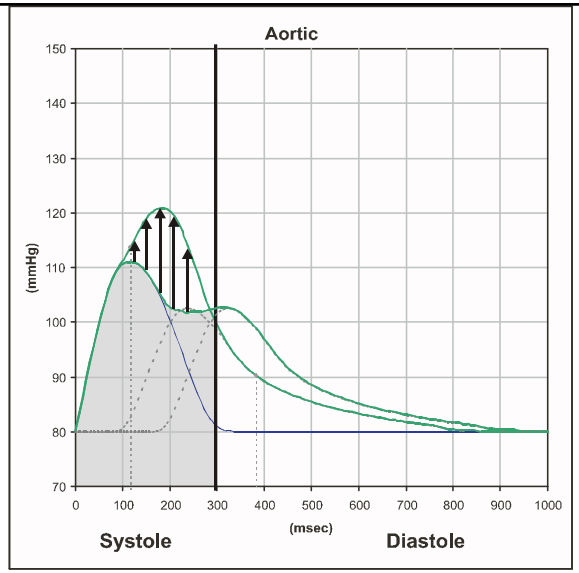


- **Pressure in the aortic root is the sum of the outgoing and reflected wave (the green wave)**
- Note: importantly how the reflected wave boosts the coronary artery perfusion pressure - the aortic root pressure - during diastole when over 95% of perfusion of the sub-endocardium takes place

– In older people, the arteries are stiffer and peripheral resistance is higher, the reflected wave reaches the aorta earlier, still at the time of systole and is absent in diastole – therefore they have high systolic pressure and low diastolic pressure – **isolated systolic hypertension**

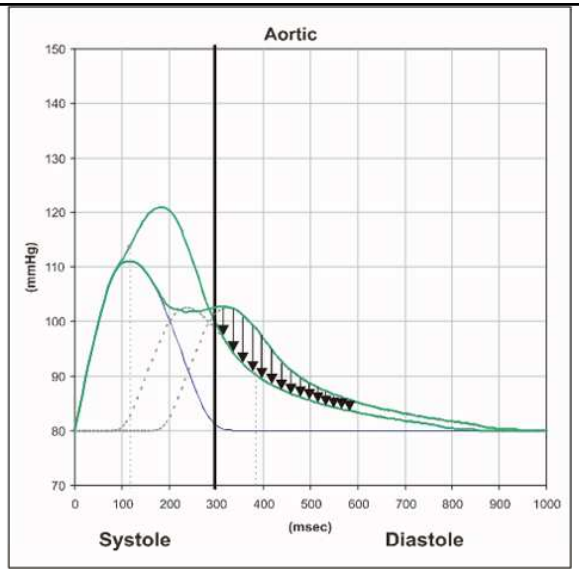


- **If the patient arteries get stiffer….**
- **then pulse wave velocity increases, and reflected wave arrives back at the heart sooner.**
- Now there is a very different aortic root pressure waveform (green wave).
- As a result of this, there are **three important clinical implications**.



- First, the **central systolic pressure** and **central pulse pressure** is **increased**.
- An increase in the central pulse pressure that stresses cerebral blood vessels **increases stroke risk**
- NOTE: this change in central systolic pressure can occur without any changes occurring in peripheral systolic pressure.

- Second, there is an **increase in left ventricular load (LV load).**
- Increase in LV load accelerates increase in LV mass and **increases LV hypertrophy**
- The area under the pressure-time curve during systole is by definition LV load.
- This increase in LV Load (late systolic "afterload") is shown by the black arrowed region



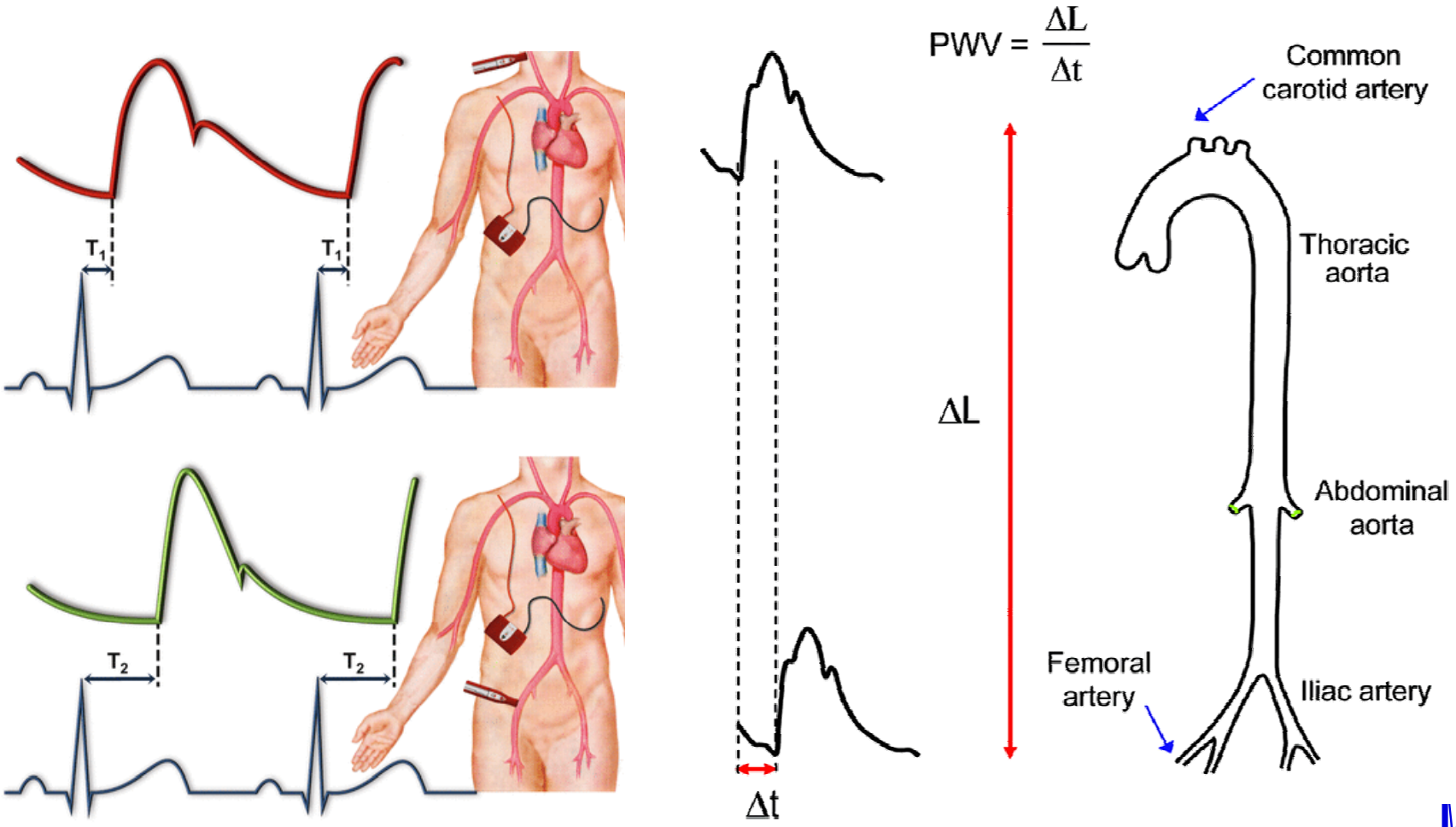
- Third, the pressure that is perfusing the coronary arteries during the critical diastole period is reduced, **increasing the risk of myocardial ischemias**.
- **CONCLUSION: Increasing arterial stiffness independ-ently** increases the risk of **all three** major cardiovascular outcomes**.**

Sex differences in mechanisms of arterial stiffness

	Males	Females
Mechanism	**Relevant pathways**	
ECM alterations	↑ Collagen ↓ Elastin	↑ Collagen
VSMC stiffening	↑ β1-integrin Rho kinase	Unknown
Oxidative stress	↑ Superoxide Mitochondrial-derived ROS NADPH-oxidase	↑ Superoxide eNOS uncoupling via BH(4) reductions
Inflammation	↑ NF-κB T-cell activation	↑ NF-κB
RAAS signalling	↑ SMC-MR AT1R activation	↑ EC-MR ENaC

ECM - extracellular matrix; VSMC - vascular smooth muscle cell; eNOS - endothelial NOS; NADPH - NAD phosphate oxidase; BH(4) - tetrahydrobiopterin; SMC-MR - smooth muscle cell mineralocorticoid receptor; AT1R - angiotensin II type 1 receptor; EC-MR - endothelial cell mineralocorticoid receptor; ENaC - epithelial sodium channel.

PWV measurement – Sphygmography in practicals



A highly compliant aorta has a relatively low PWV (< 6 m/s)

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Use in clinical practice

- Non-invasive investigation of arterial stiffness is gradually moving from the position of experiments to clinical practice
- Started thanks to new recommendations of the European Hypertensive Society in Milan in 2007 – pulse wave velocity testing was included among the main diagnostic methods and in the process of determining the risk of cardiovascular disease + evaluation of the effect of treatment of essential hypertension

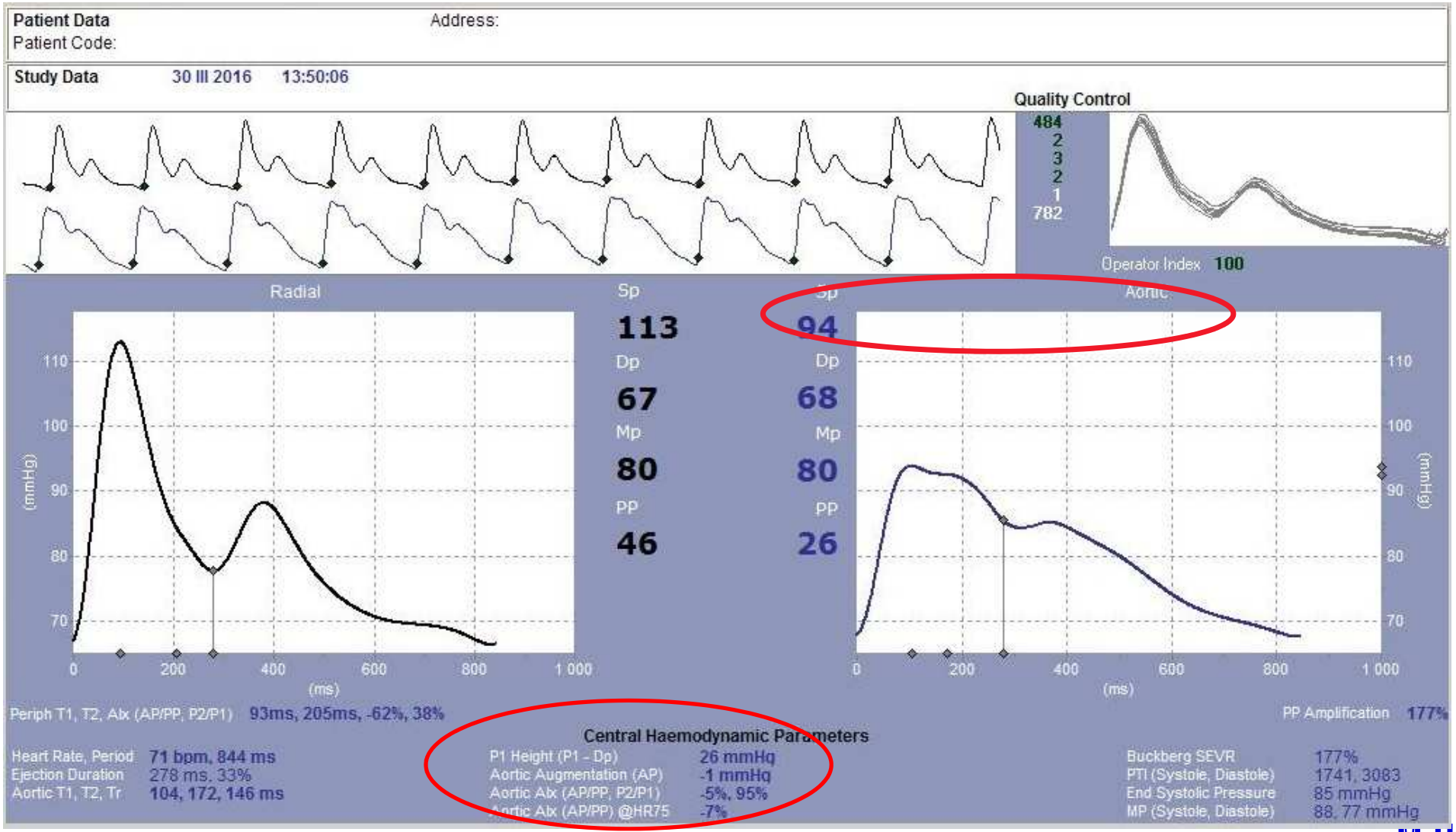
- Arterial stiffness expresses damage to their walls by risk factors over a long period of time (years), while blood pressure values fluctuate physiologically and may not reflect the degree of damage to the vascular wall

- Using techniques for measuring the pulse wave velocity, it is possible to calculate **the central aortic pressure**, which is a stronger prognostic parameter than the pressure measured on the brachial artery and more accurately expresses **the load on the heart**

- Changes in arterial stiffness are clinically imperceptible

- Methods are a modern trend for determining the risk of cardiovascular disease –
  - risk of developing hypertension
  - risk of sudden cardiac death

– Device Sphygmocor – company: AtCor Medical, Australia


Patient Data
Address:
Patient Code:
Study Data 30 III 2016 13:50:06
Quality Control
484
2
3
2
1
782
Operator Index 100
Radial
Aortic
Sp
113
Dp
67
Mp
80
PP
46
Sp
94
Dp
68
Mp
80
PP
26
110
100
90
80
70
(mmHg)
0
200
400
600
800
1 000
(ms)
Periph T1, T2, Alx (AP/PP, P2/P1) 93ms, 205ms, -62%, 38%
PP Amplification 177%
Central Haemodynamic Parameters
P1 Height (P1 - Dp) 26 mmHg
Aortic Augmentation (AP) -1 mmHg
Aortic Alx (AP/PP, P2/P1) -5%, 95%
Aortic Alx (AP/PP) @HR75 -7%
Heart Rate, Period 71 bpm, 844 ms
Ejection Duration 278 ms, 33%
Aortic T1, T2, Tr 104, 172, 146 ms
Buckberg SEVR 177%
PTI (Systole, Diastole) 1741, 3083
End Systolic Pressure 85 mmHg
MP (Systole, Diastole) 88, 77 mmHg

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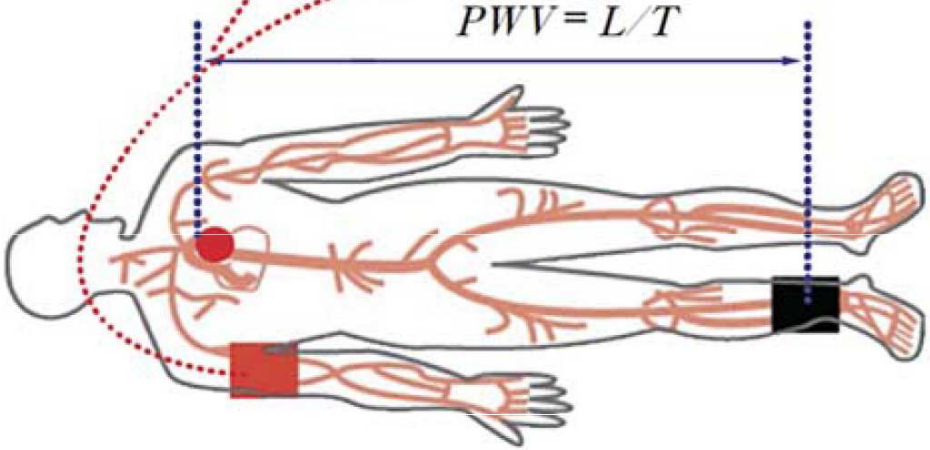
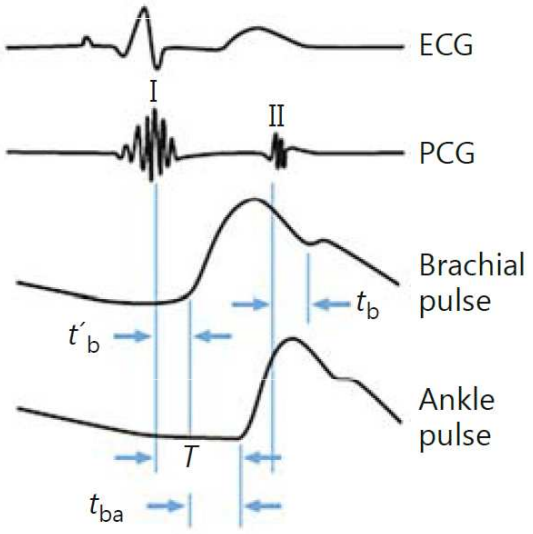
– Device VaSera, company: Fukuda Denshi, Japan

Cardio-ankle vascular index – CAVI - measurement

$$CAVI = a\left[\frac{2\rho}{\Delta P}\left[\ln\frac{Ps}{Pd}\right]PWV^2\right]+b$$

$$PWV = L/T$$





● Reference value of CAVI

CAVI<8.0	Normal range
8.0≦CAVI<9.0	Borderline
9.0≦CAVI	Arteriosclerosis suspected

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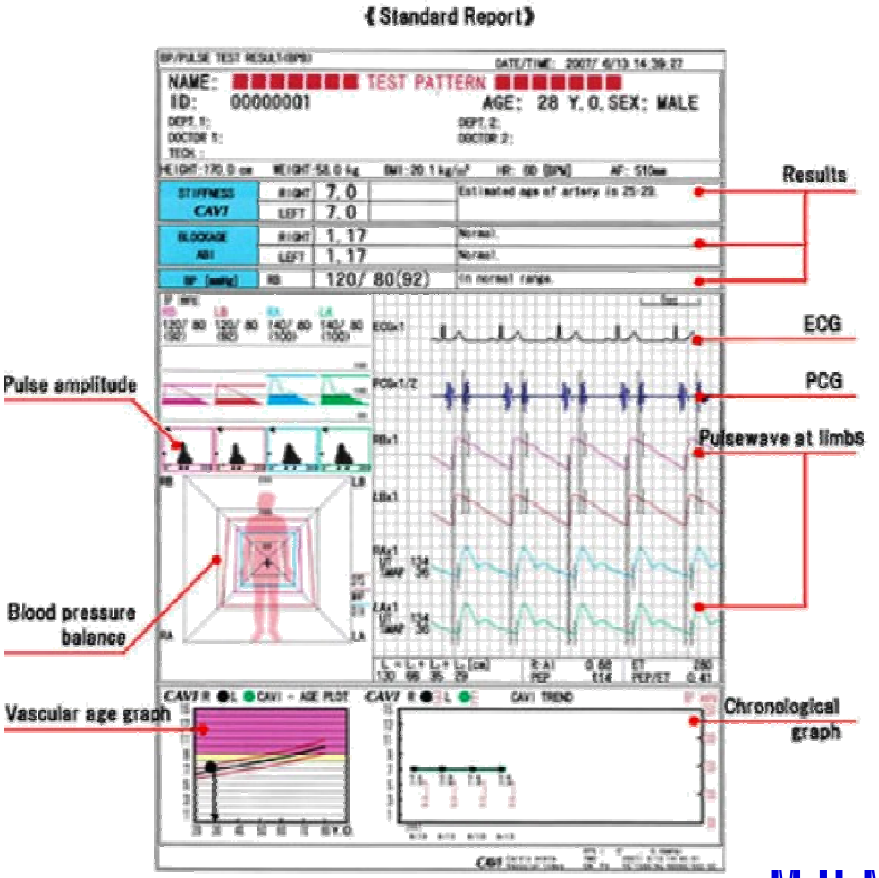
CAVI measurement



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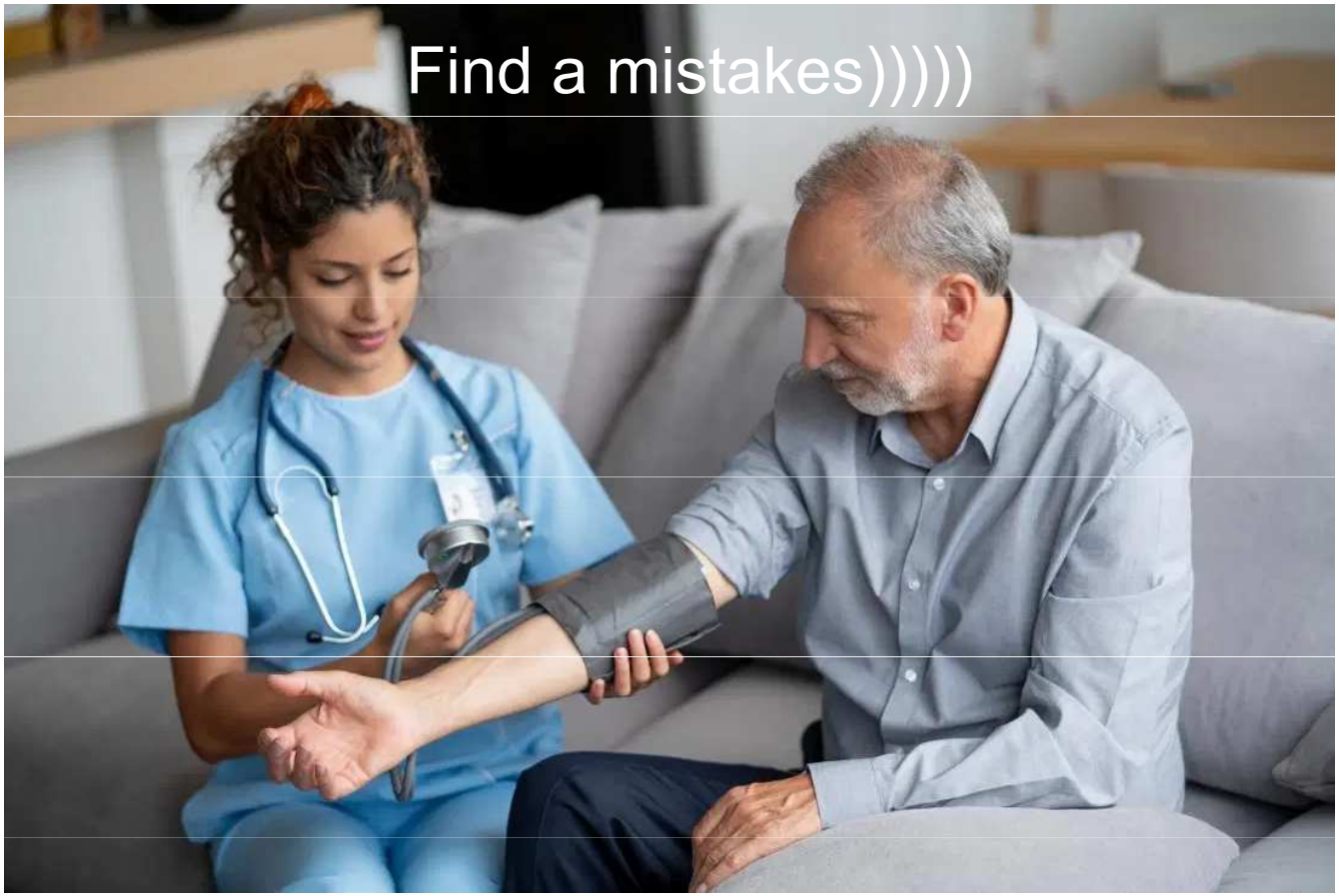
Thank you for your attention



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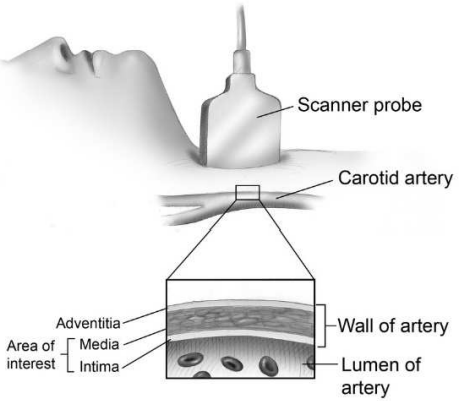
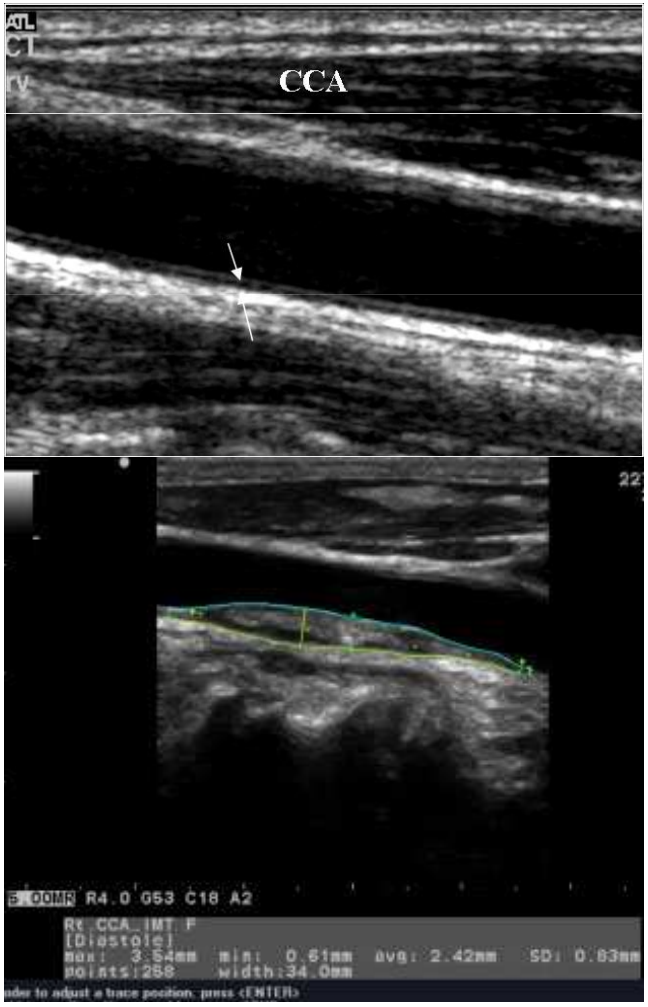
Ultrasound measurement





age		IMT_R (mm)	IMT_L (mm)
25-35	Mean	0.39±0.07	0.40±0.07
	V%	18.26	17.37
	CI	0.36<x<0.42	0.38<x<0.42
35-45	Mean	0.43±0.07	0.46±0.09
	V%	15.15	18.59
	CI	0.41<x<0.45	0.43<x<0.49
45-55	Mean	0.47±0.08	0.50±0.11
	V%	17.49	21.18
	CI	0.44<x<0.50	0.47<x<0.54
55-65	Mean	0.52±0.11	0.54±0.11
	V%	21.01	20.89
	CI	0.48<x<0.56	0.50<x<0.58
65-75	Mean	0.55±0.09	0.57±0.09
	V%	16.65	14.60
	CI	0.53<x<0.59	0.55<x<0.61

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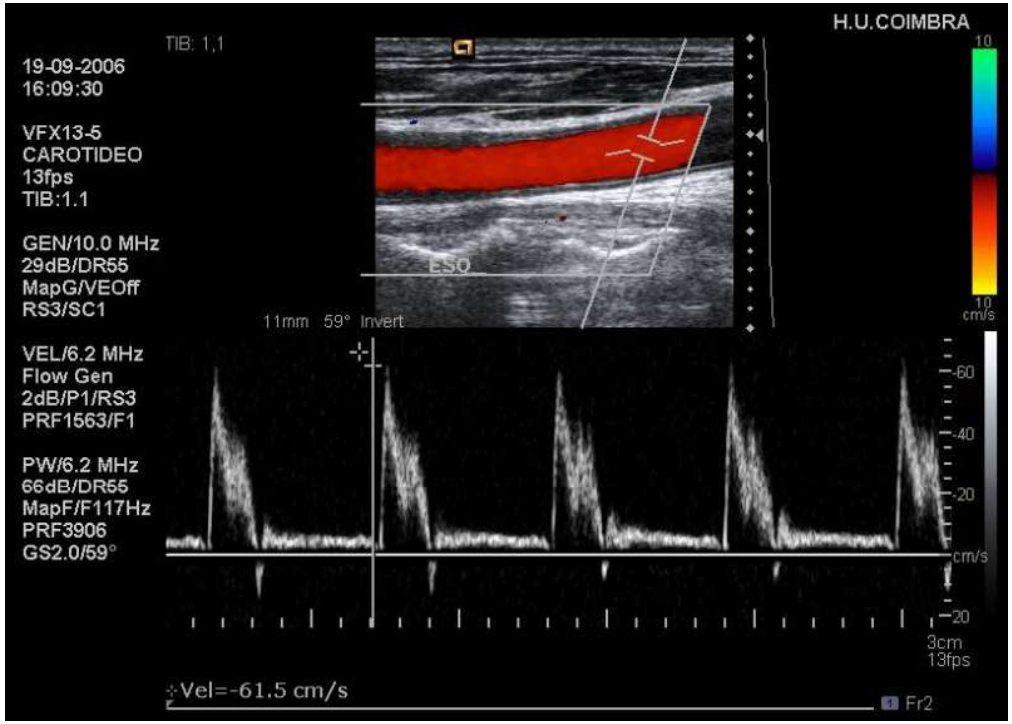
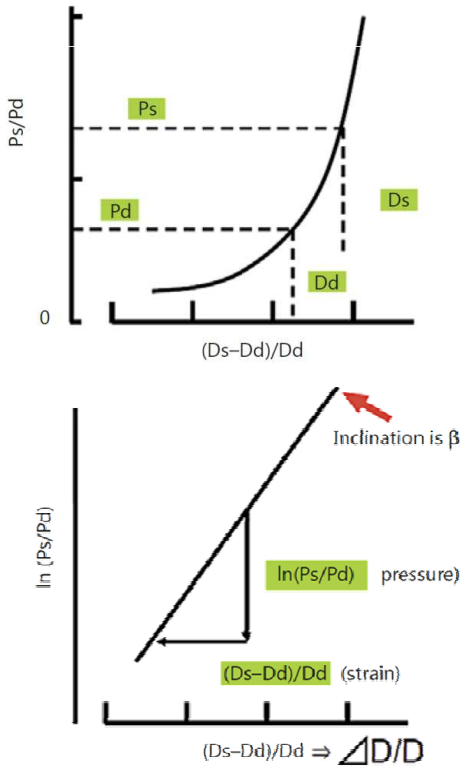
Ultrasound measurement (β – index).

$$\beta = \left(\ln \frac{P_s}{P_d}\right)\left(\frac{D}{\Delta D}\right)$$





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