Control of Myocardial Blood Flow

"Blood goes where it is needed"

John Hunter, 1794 Cited by Dunker DJ and Bache RJ Physiol Rev , 2008

Bernard De Bruyne, MD, PhD
Cardiovascular Center Aalst
OLV-Clinic Aalst, Belgium

www.cardio-aalst.be

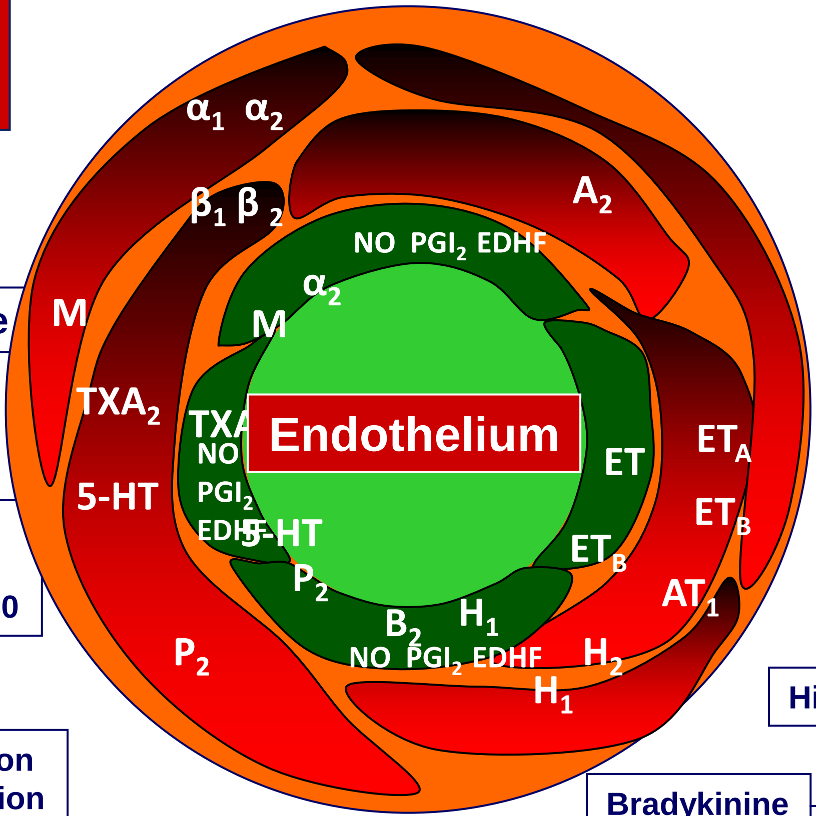
The Control of Resting Myocardial Blood Flow

Neuro-humoral factors

- Noradrenaline
  Adrenaline
- Acethylcholine

Metabolic factors

- Adenosine
- PO_2
- PCO_2, H^+, K^+



Physical factors

- Arterial Pressure
  Coronary pressure
  RAP, LVDP and Pf=0
- Systolic compression
  Diastolic compression

Endo- and paracrine factors

- Angiotensine II
- Histamine
- Bradykinine

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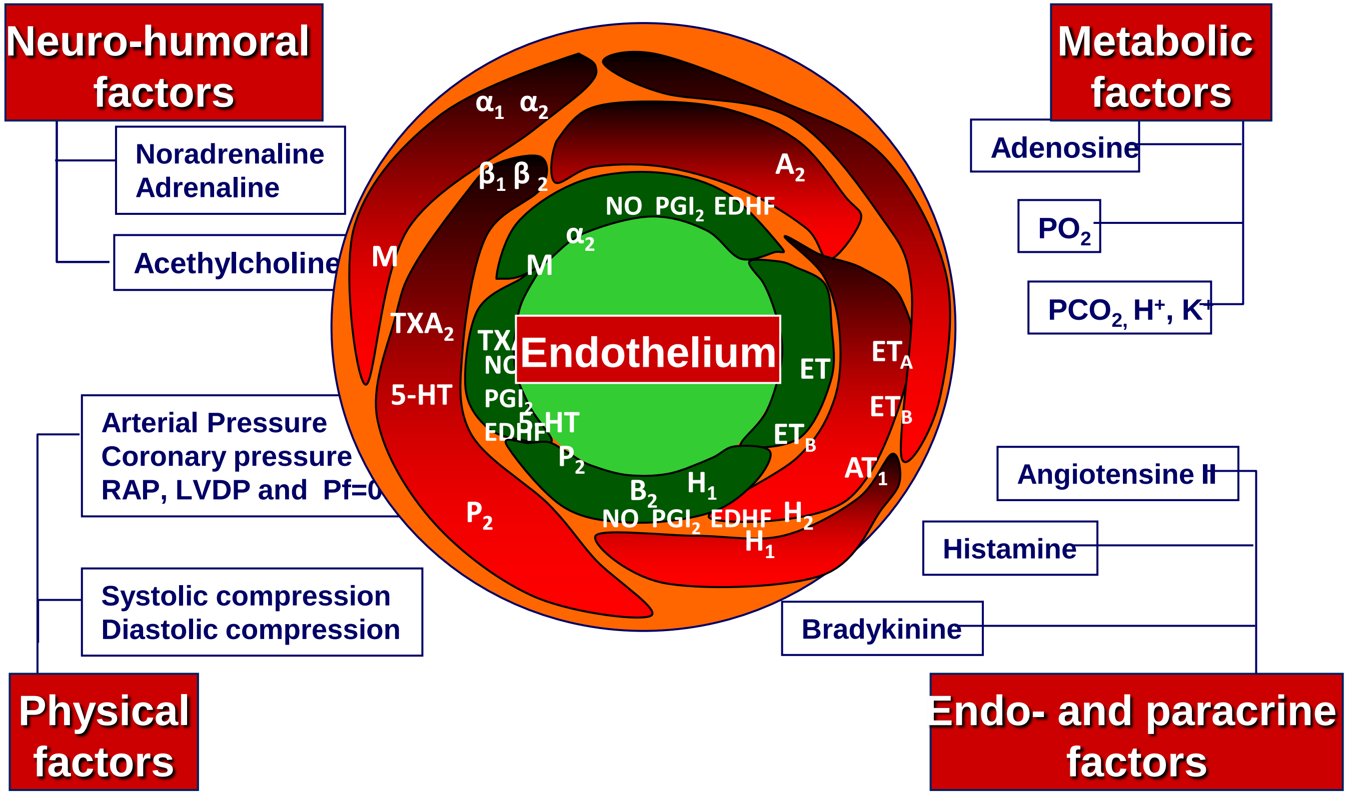
Adapted from D.J.G.M. Duncker

The Control of Resting Myocardial Blood Flow



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The balance between supply and demand depends on mechanisms which are multiple, interacting, cumulative, nonlinear

ETP, Sofia Antipolis, April 2013

Adapted from D.J.G.M. Duncker

Physiol Rev 88: 1009–1086, 2008;
doi:10.1152/physrev.00045.2006.

Regulation of Coronary Blood Flow During Exercise

DIRK J. DUNCKER AND ROBERT J. BACHE

Division of Experimental Cardiology, Department of Cardiology, Thoraxcenter, Cardiovascular Research Institute COEUR, Erasmus University Medical Center, Rotterdam, The Netherlands; and Division of Cardiology, Department of Medicine, Minnesota Medical School, Minneapolis, Minnesota

...Myocardial blood flow during resting conditions ... in normal human subjects is generally reported in the range of 0.5–1.5 ml/min/g of myocardium. The wide range of resting values of left ventricular blood flow in awake animals appears to be related to the state of alertness. Animals conditioned to rest quietly in the laboratory have the lowest reported values, whereas animals standing on a treadmill ready to run have higher heart rates and higher coronary flow rates...

(Dunker DJ and Bache RJ Physiol Review 2008)

ABC of Coronary Physiology
For the Interventionalist

1. About Pressure, flow, mass, resistance, etc, ...
2. Epicardial vs microvascular compartments
3. Flow-function relationship
4. Coronary autoregulation

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- Adenosine
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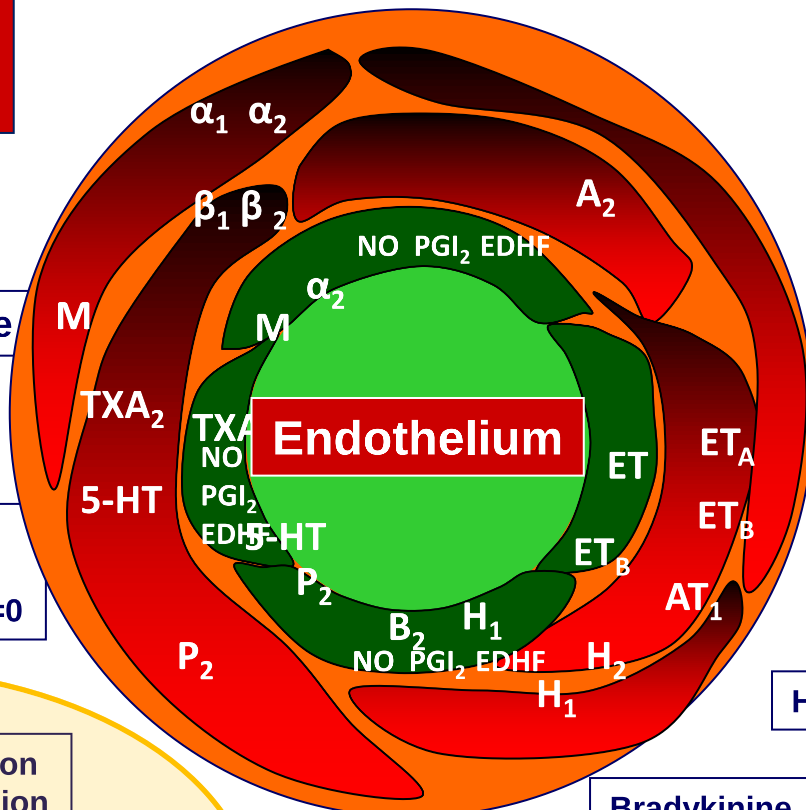

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Endo- and paracrine factors

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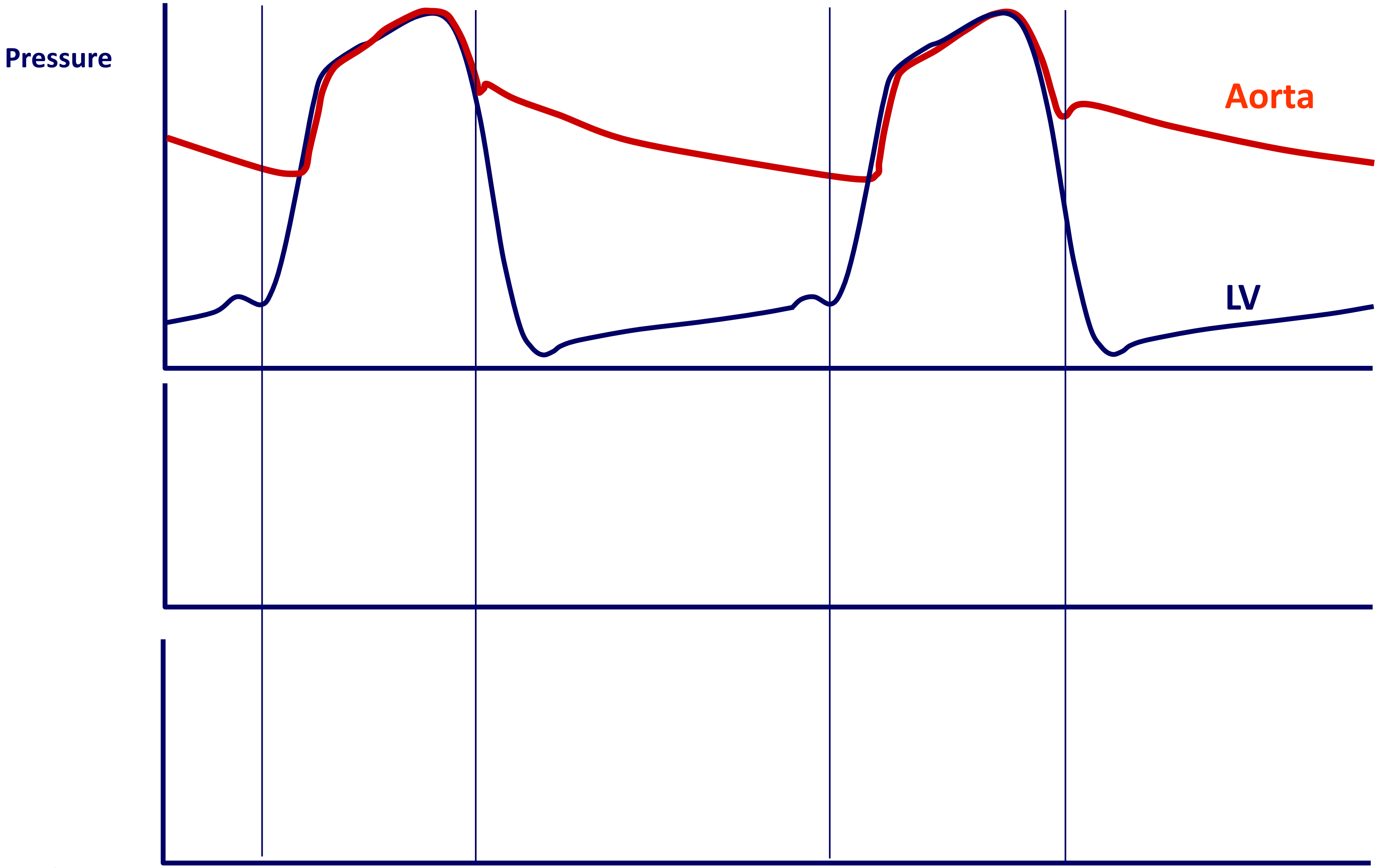
ETP, Sofia Antipolis, April 2013

Adapted from D.J.G.M. Duncker

Extravascular Compressive Forces



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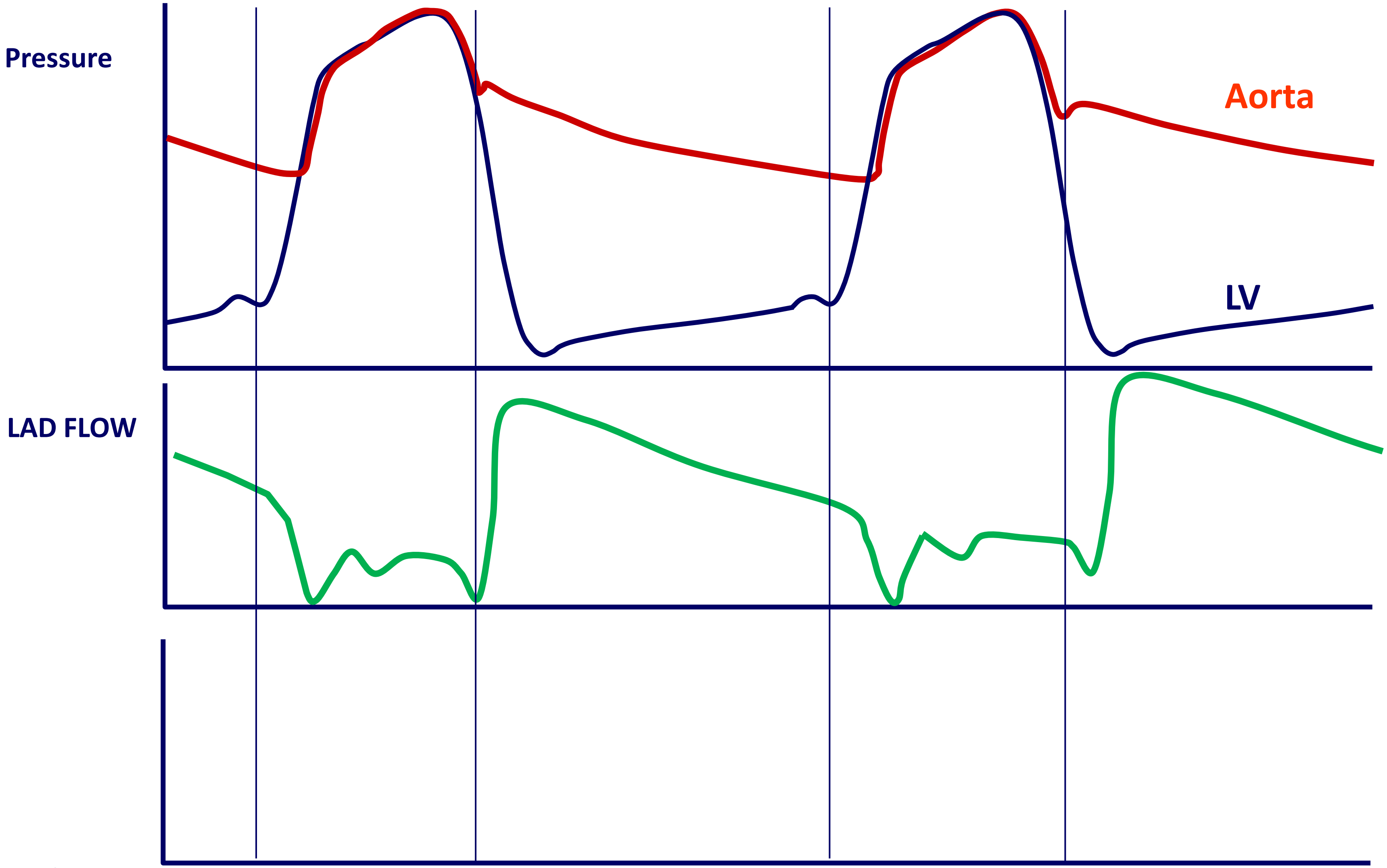

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ETP, Sofia Antipolis, April 2013

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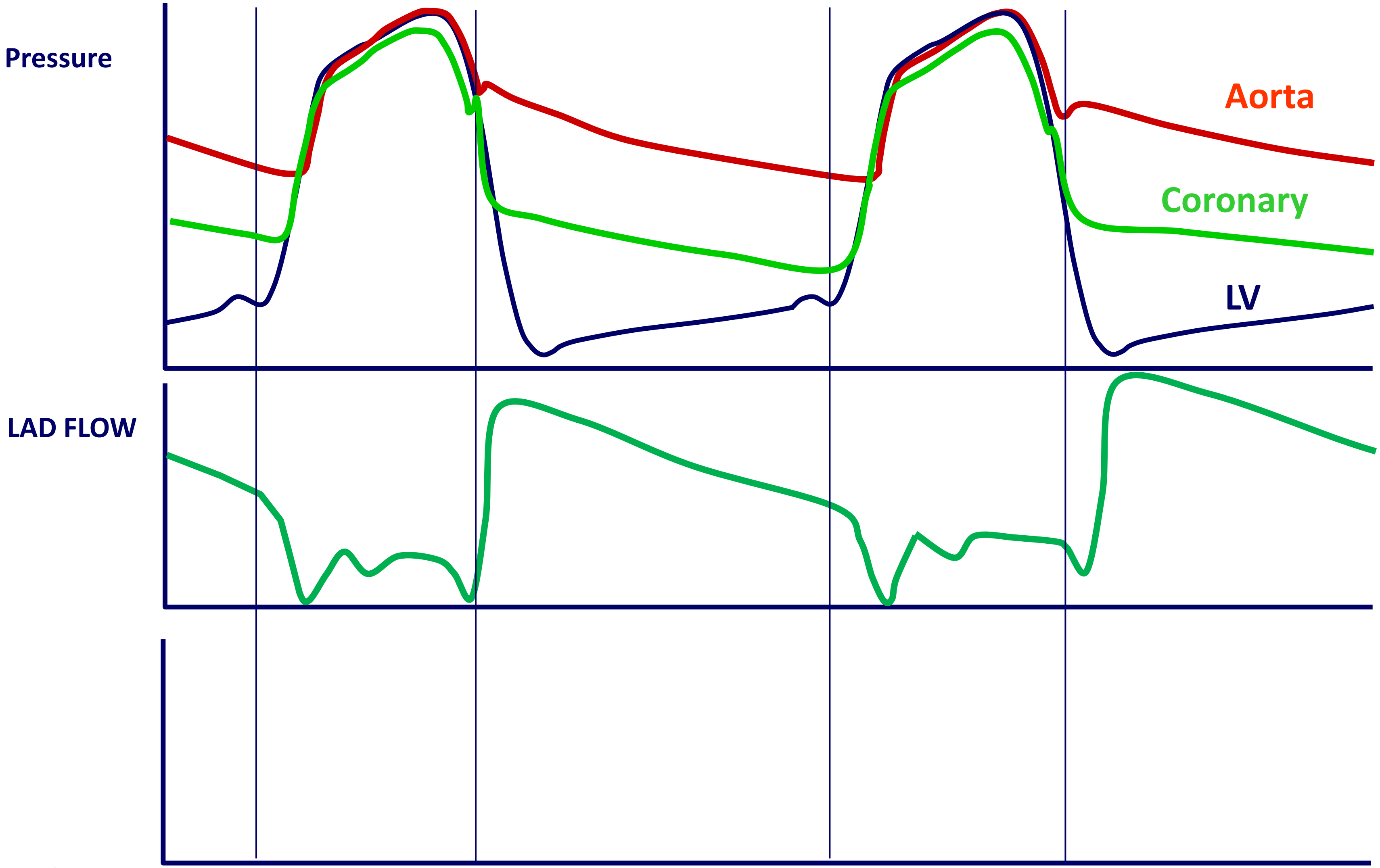

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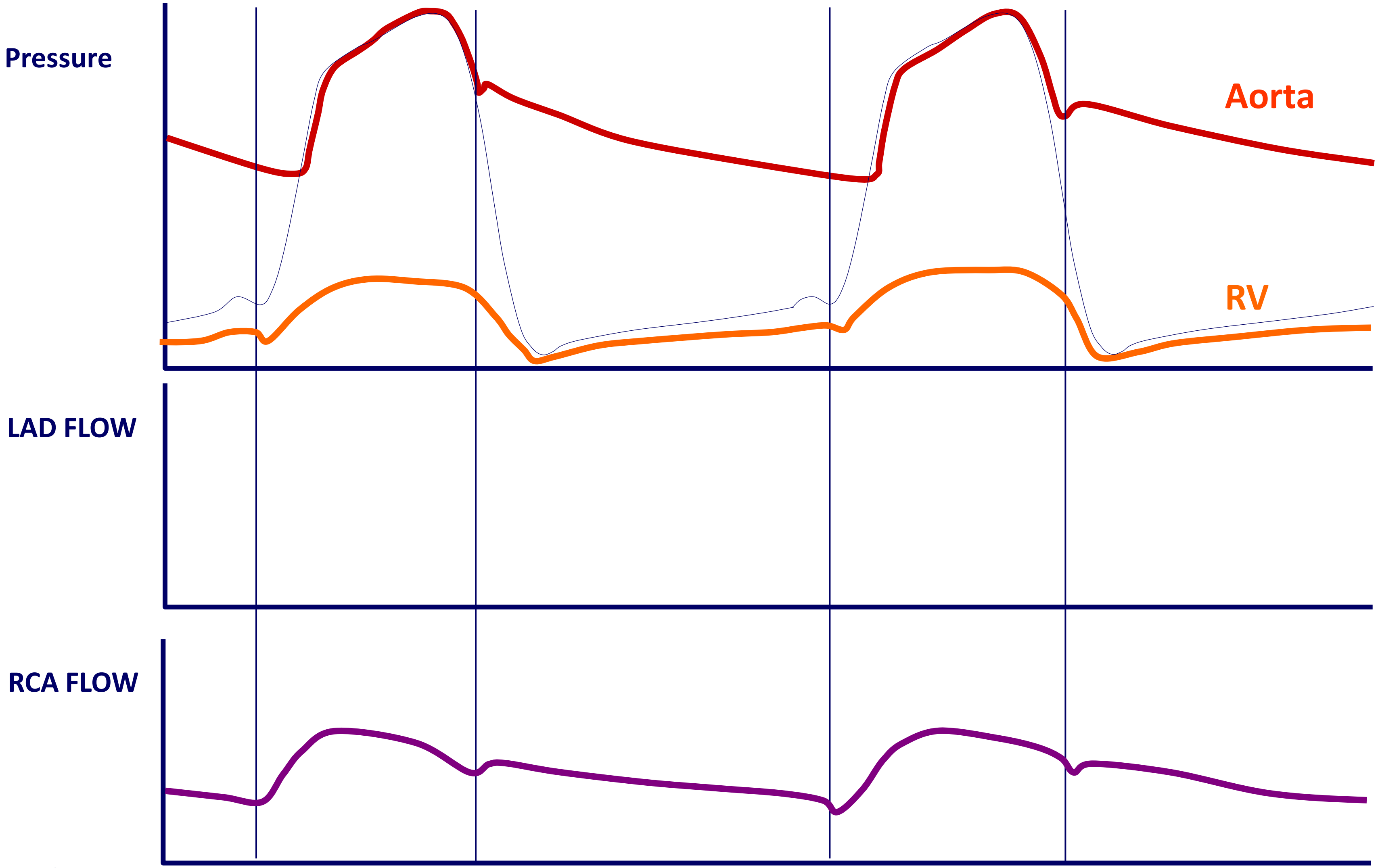

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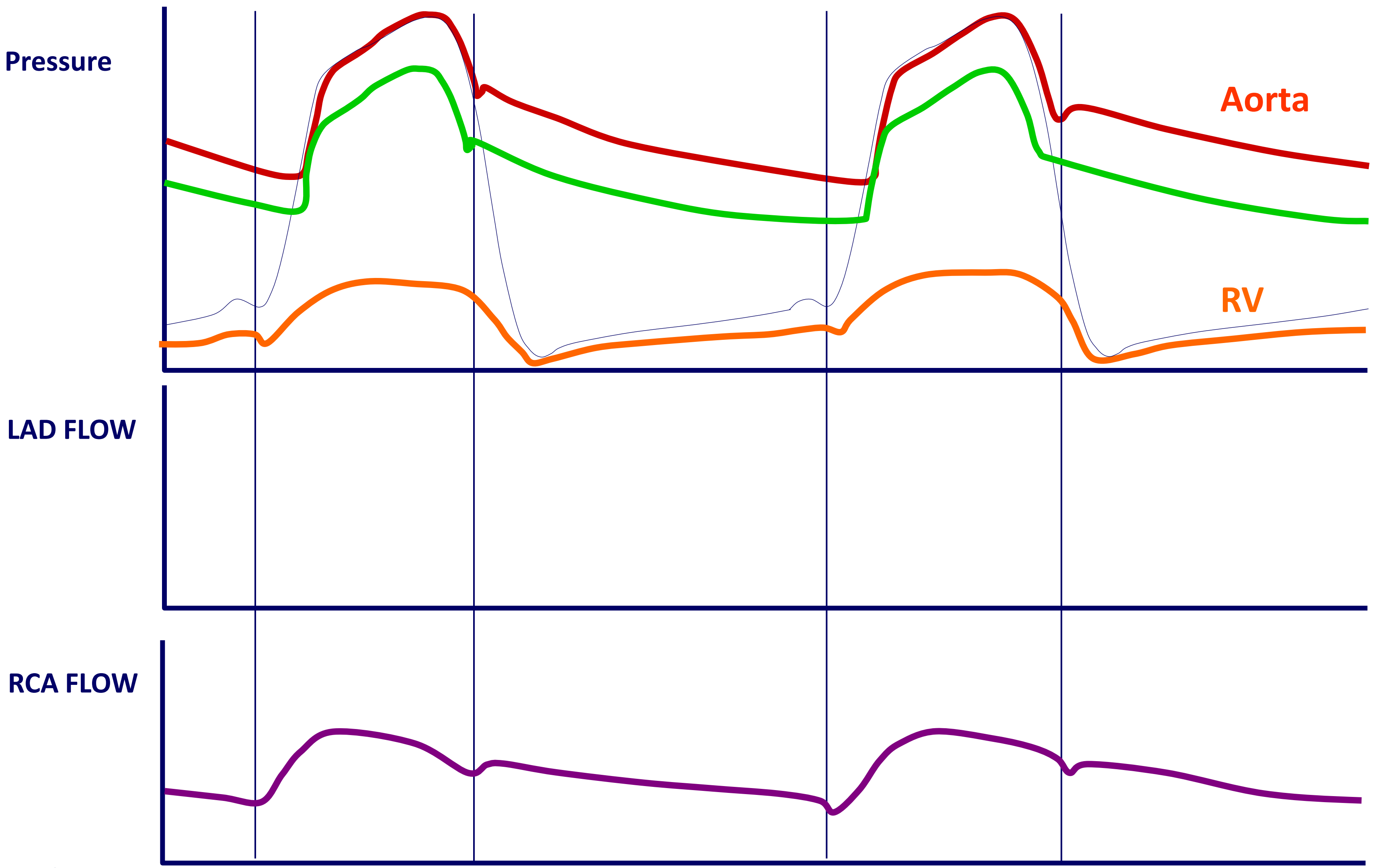

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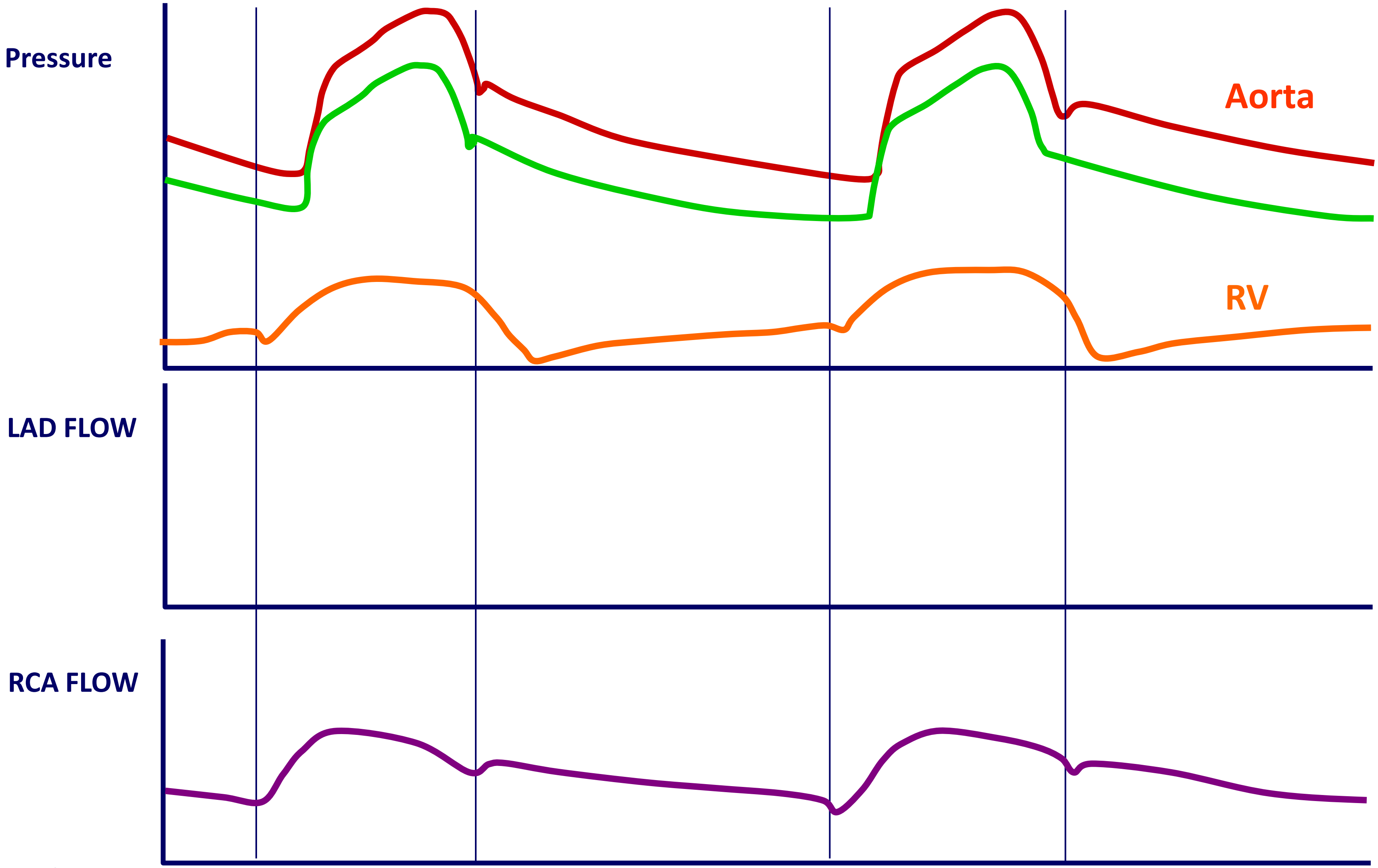

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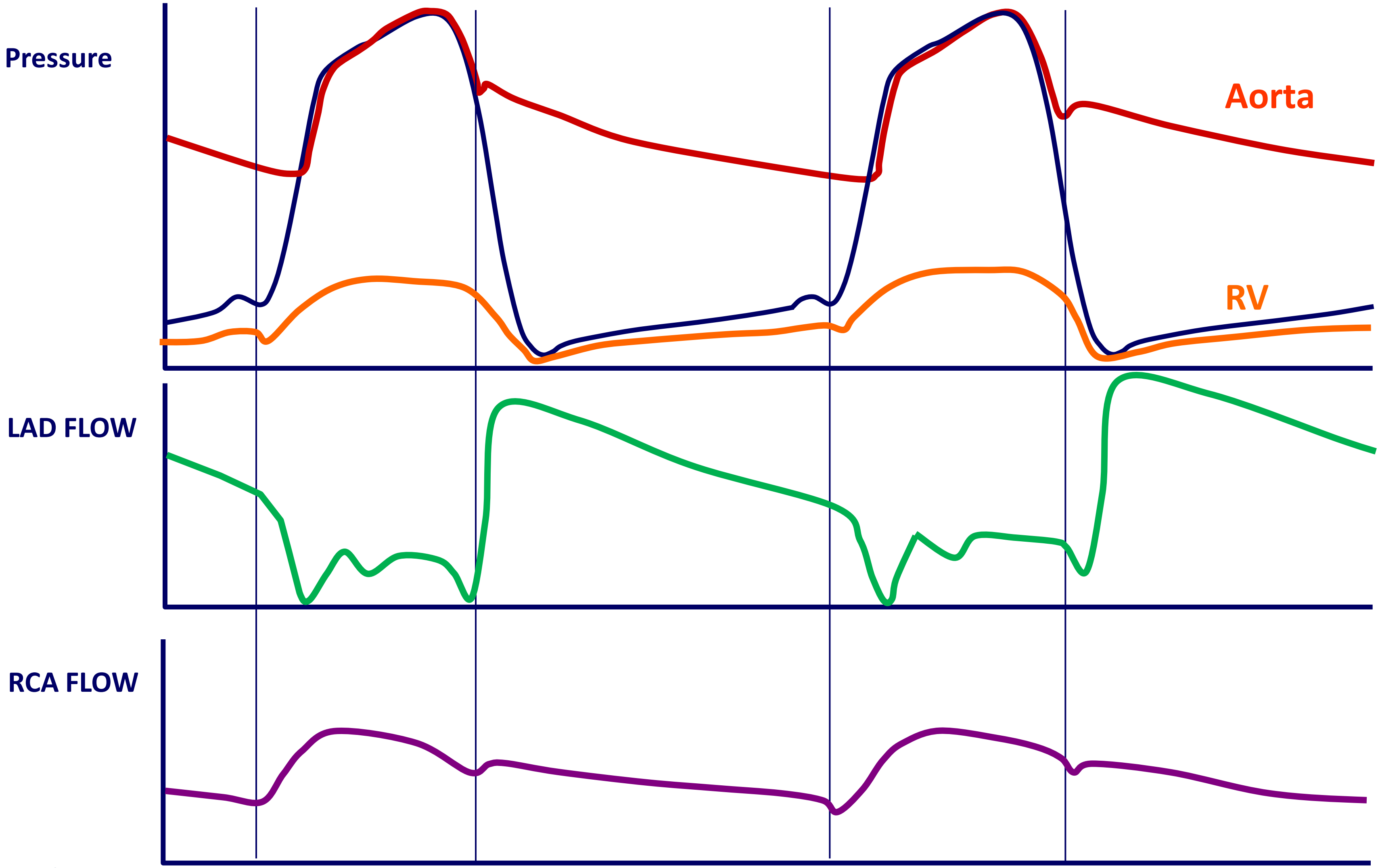

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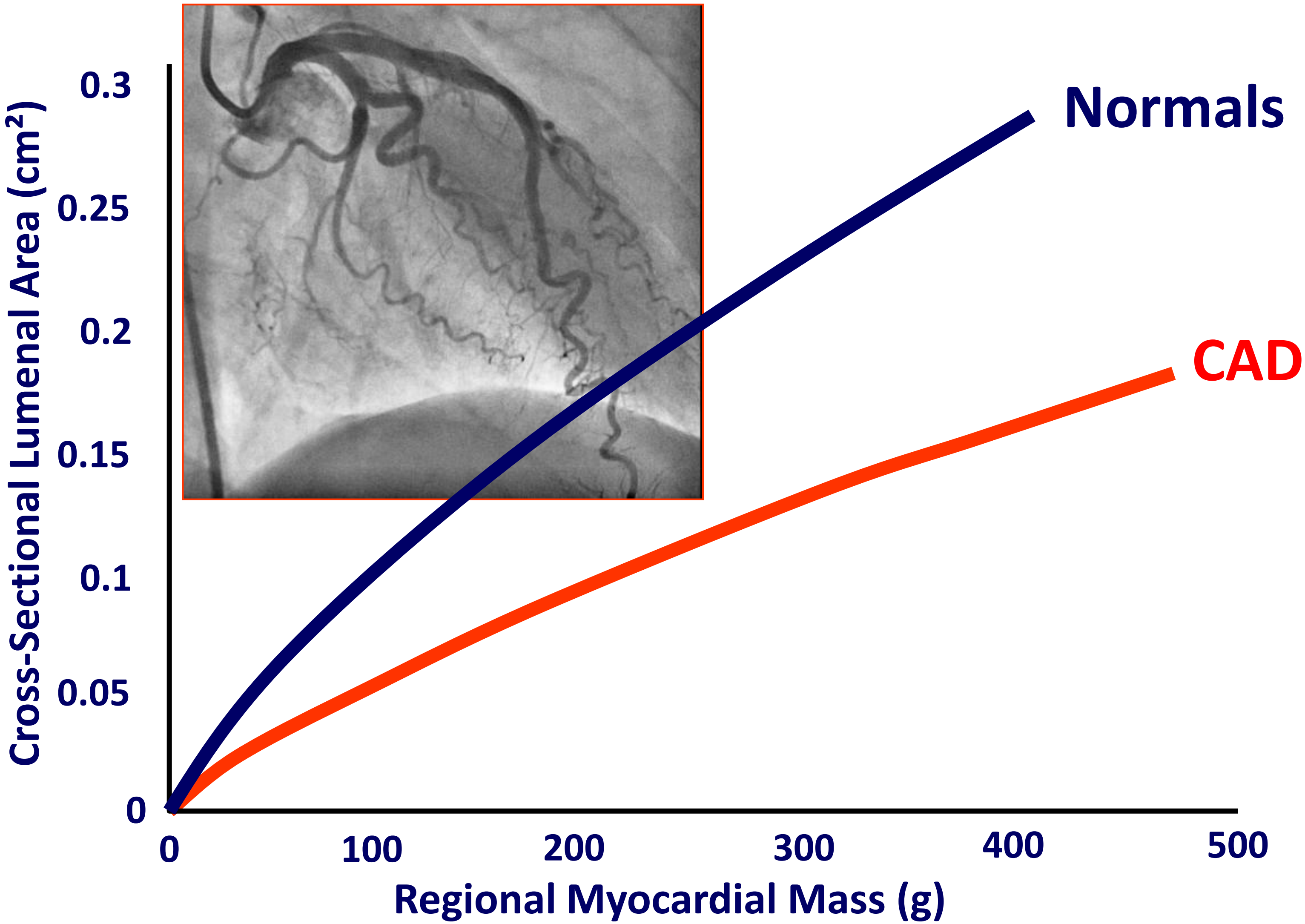
Relation between Vessel Size and Myocardial Mass



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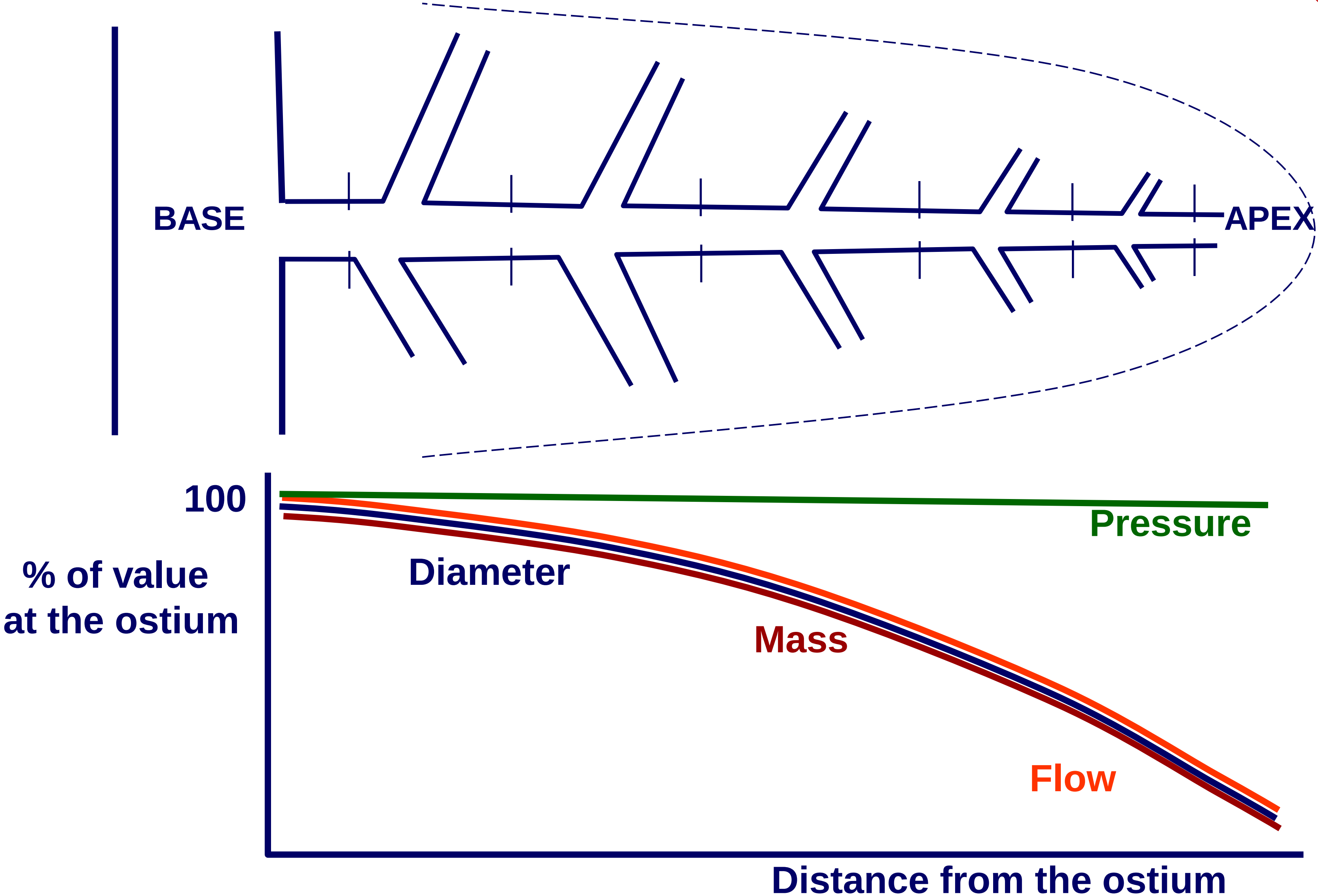
C. Seiler et al Circulation 1992

Pressure, Flow, Resistance, and Vessel Size



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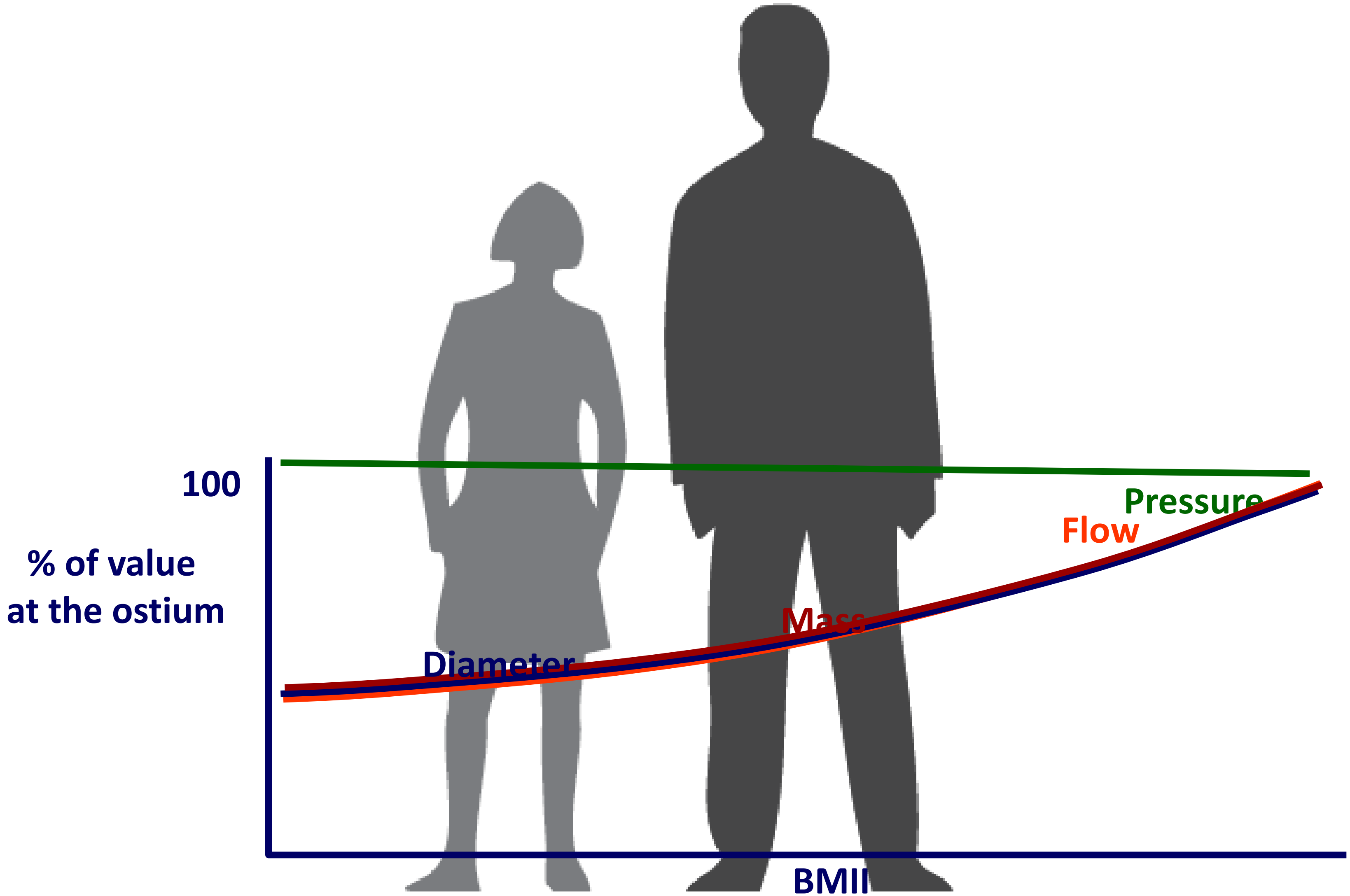

Pressure, Flow, Resistance, and Vessel Size

	Tree Shrew	Human	Blue Whale
Body Mass [kg]	0.005	70	100,000
Heart Weight [kg] $(\sim M^1)$	$3.3x10^{-5}$	0.46	660
Stroke Volume [ml] $(\sim M^1)$	0.0033	46	66,000
Heart Rate[s^{-1}] $(\sim M^{-1/4})$	11 (>600 bpm)	1	0.16 (<10 bpm)
Cardiac Output [L/min] $(\sim M^{3/4})$	0.003	5	1000
Radius of Aorta [cm] $(\sim M^{3/8})$	0.02	1	15
Mean Aortic Velocity [cm/sec] $(\sim M^0)$	10	10	10
Mean Aortic Pressure [mmHg] $(\sim M^0)$	100	100	100
Mean Aortic Reynold's No. $(\sim M^{3/8})$	15	530	8080 (turbulent!)
Mean Aortic Shear Stress [dynes/cm^2] $(\sim M^{-3/8})$	180	5	0.3

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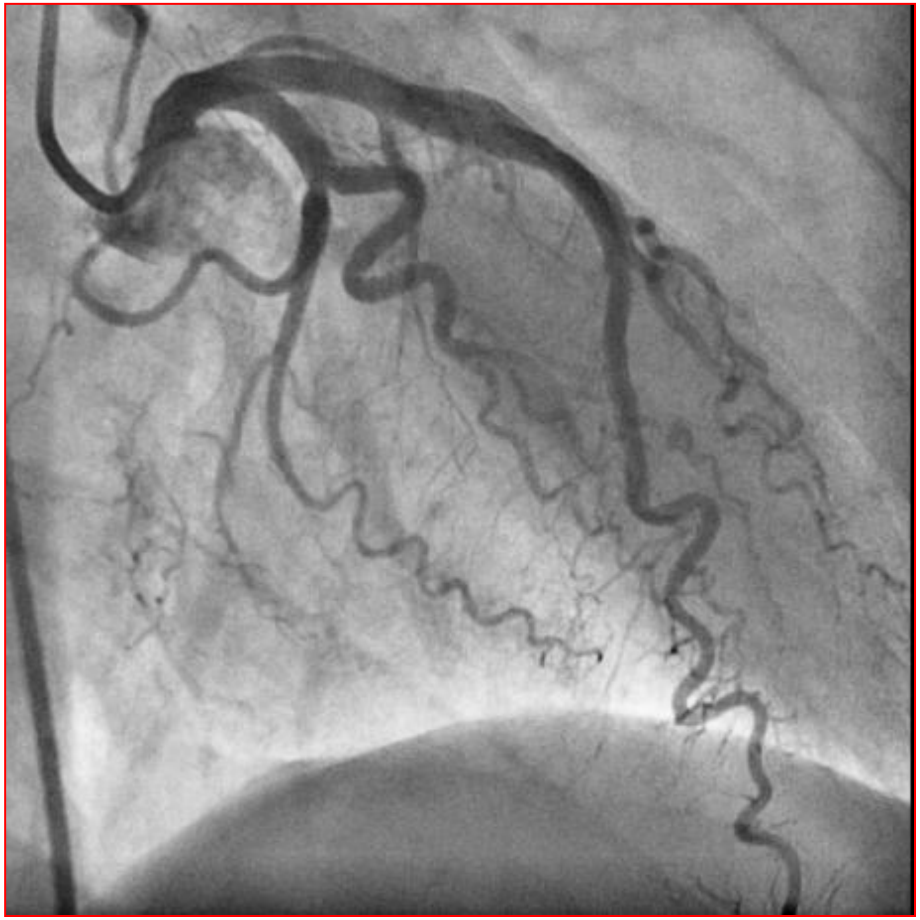
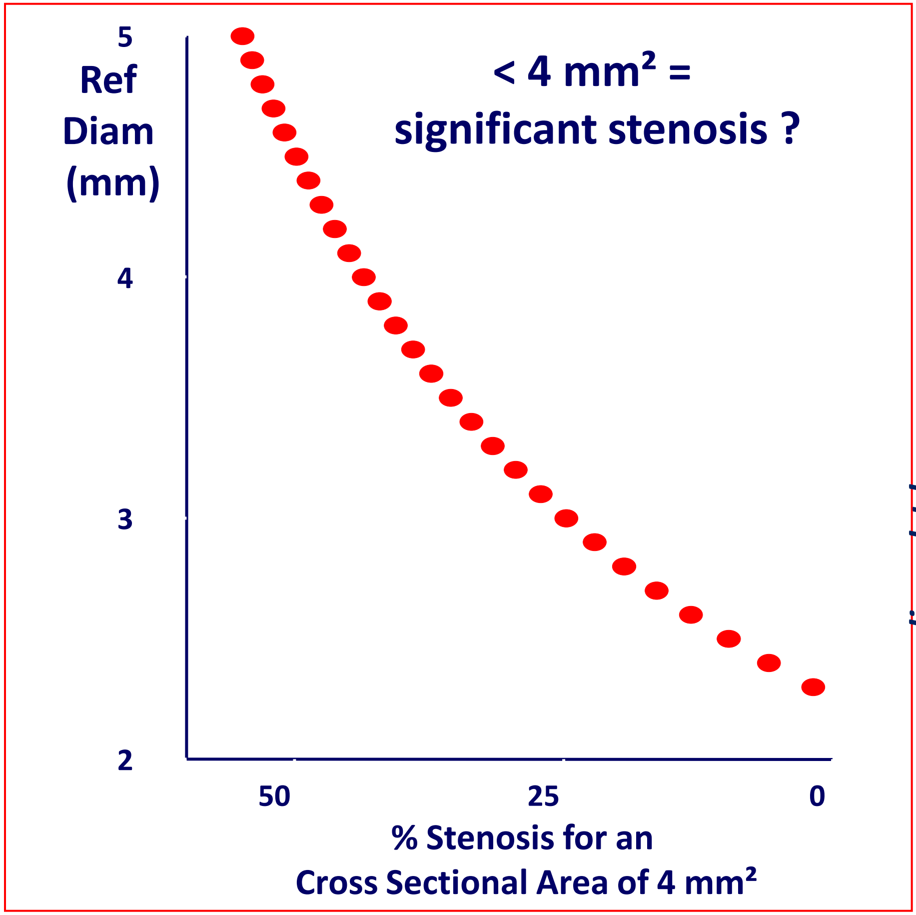
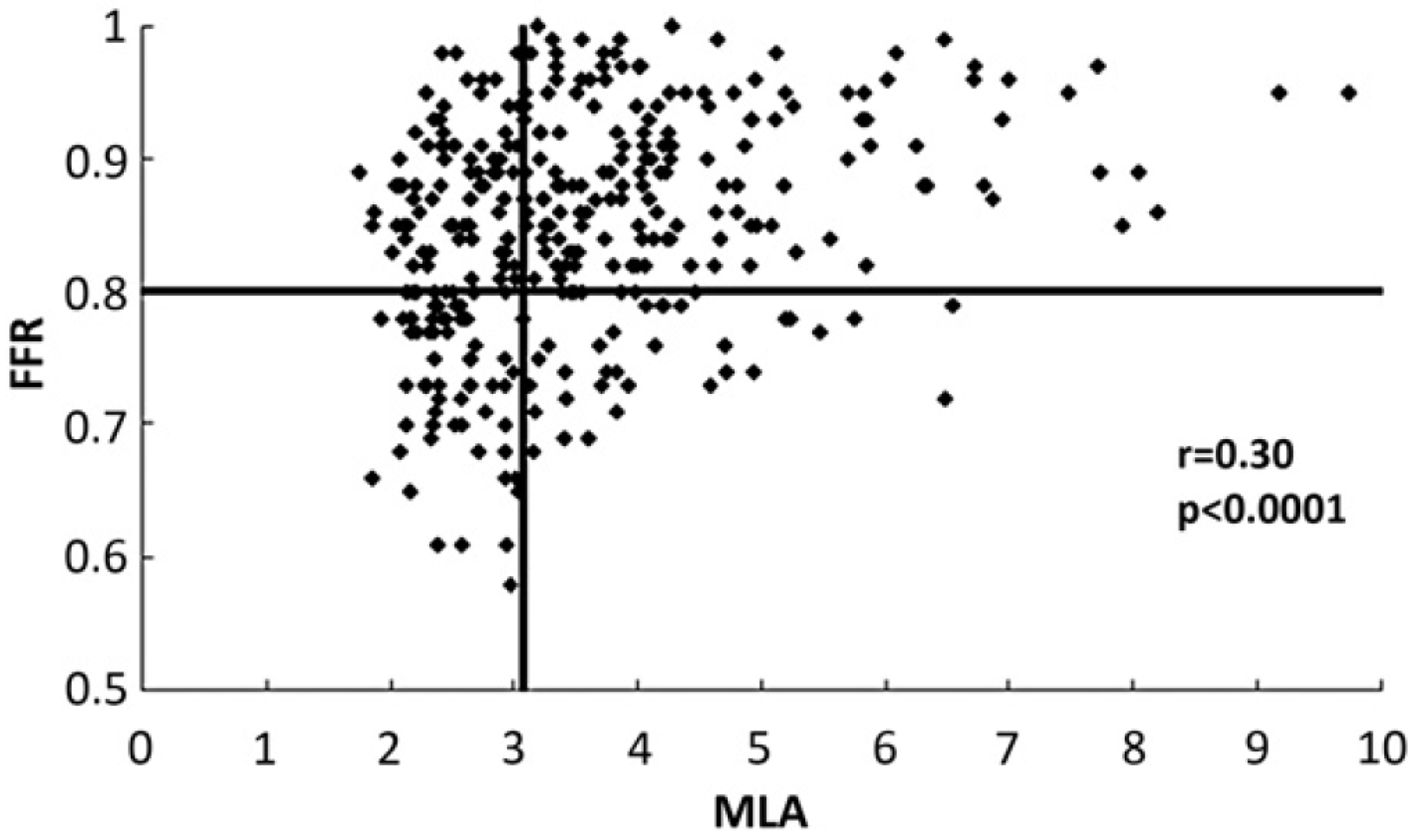
Pressure, Flow, Resistance, and Vessel Size





Pressure, Flow, Resistance, and Vessel Size

Relationship between CSA by IVUS and FFR



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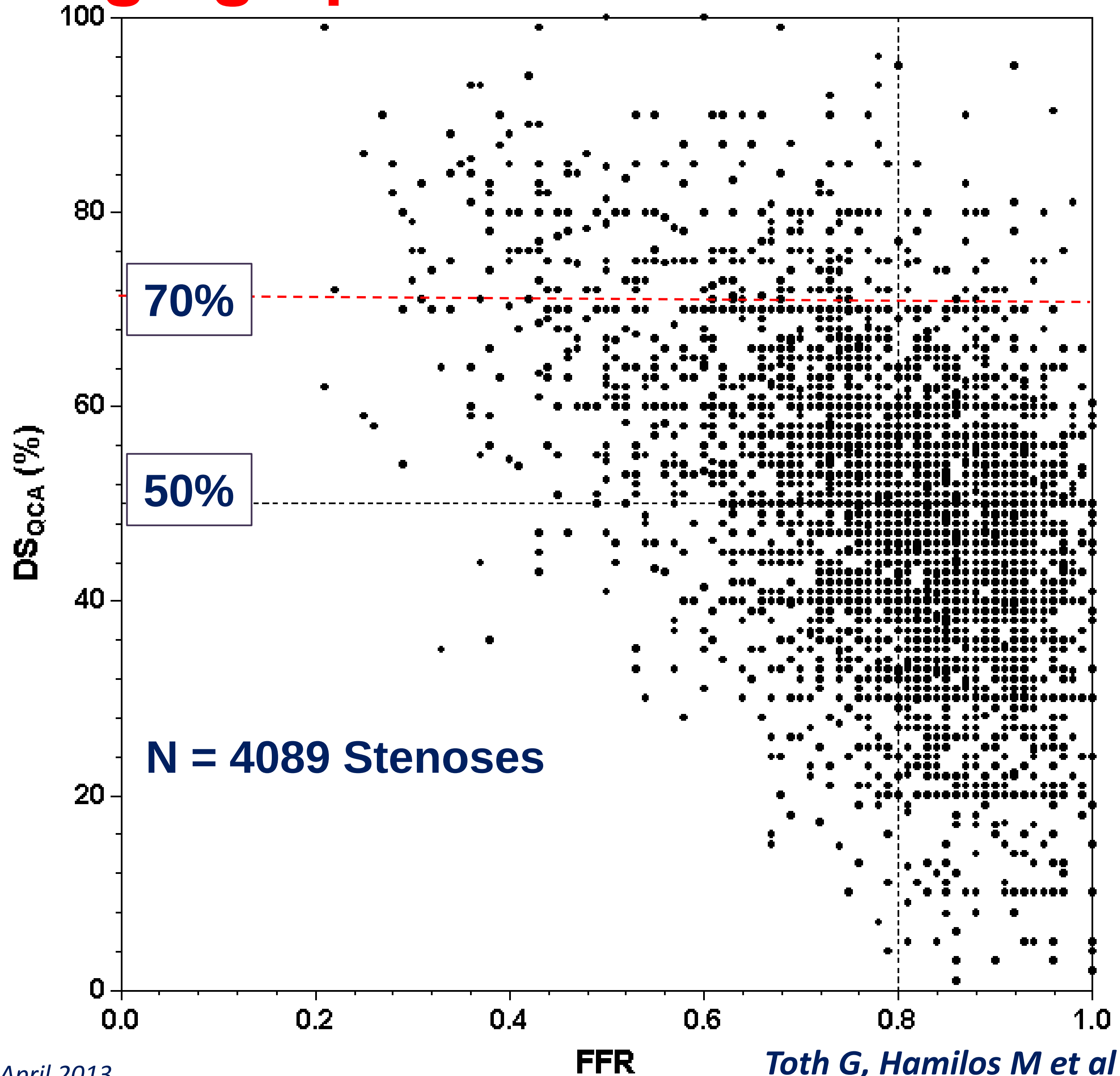
Waksman R et al JACC 2013

Angiographic Definition of "CAD"



Diagnostic Accuracy

60%

66%

Toth G, Hamilos M et al Submitted 2013

Function trumps anatomy

ABC of Coronary Physiology
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1. **About Pressure, flow, resistance, etc, ...**
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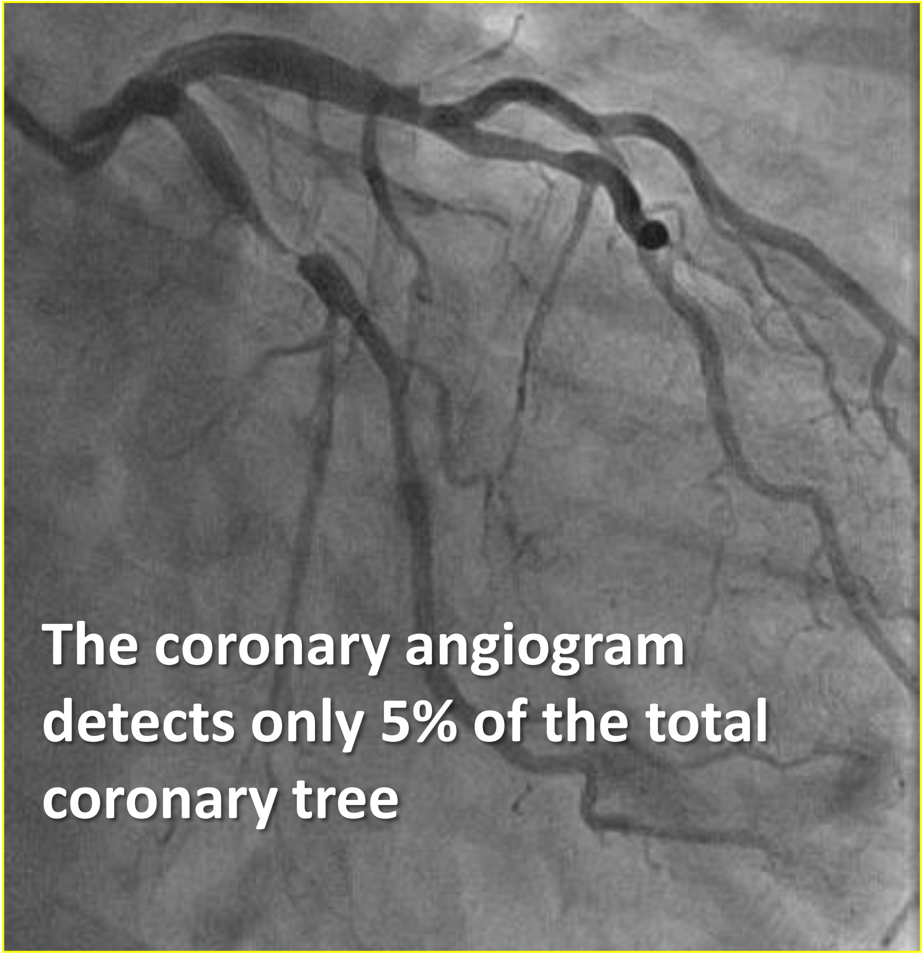
3. **Flow-function relationship**
4. **Coronary autoregulation**

Two-Compartment Model of the Coronary Circulation



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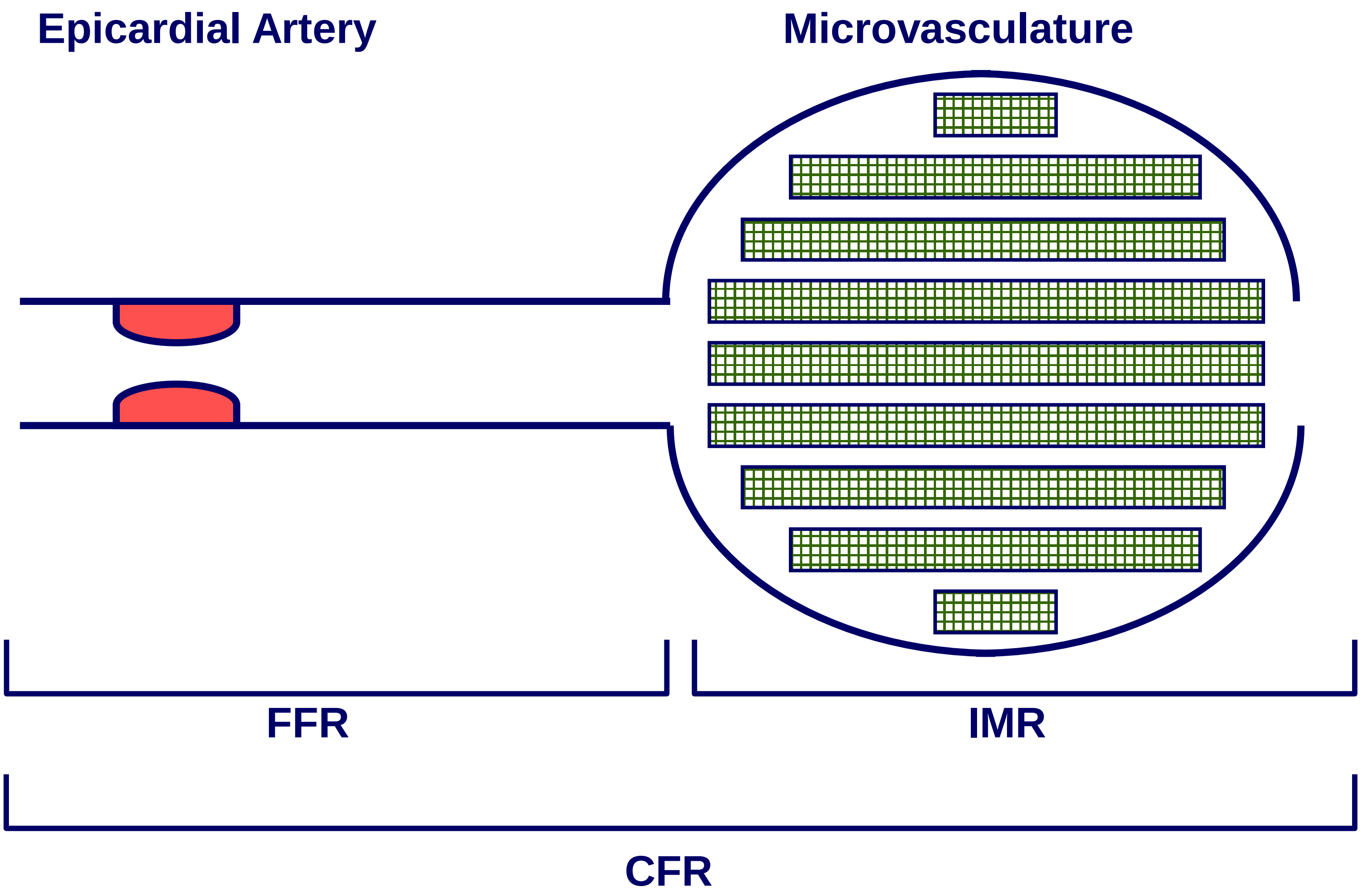

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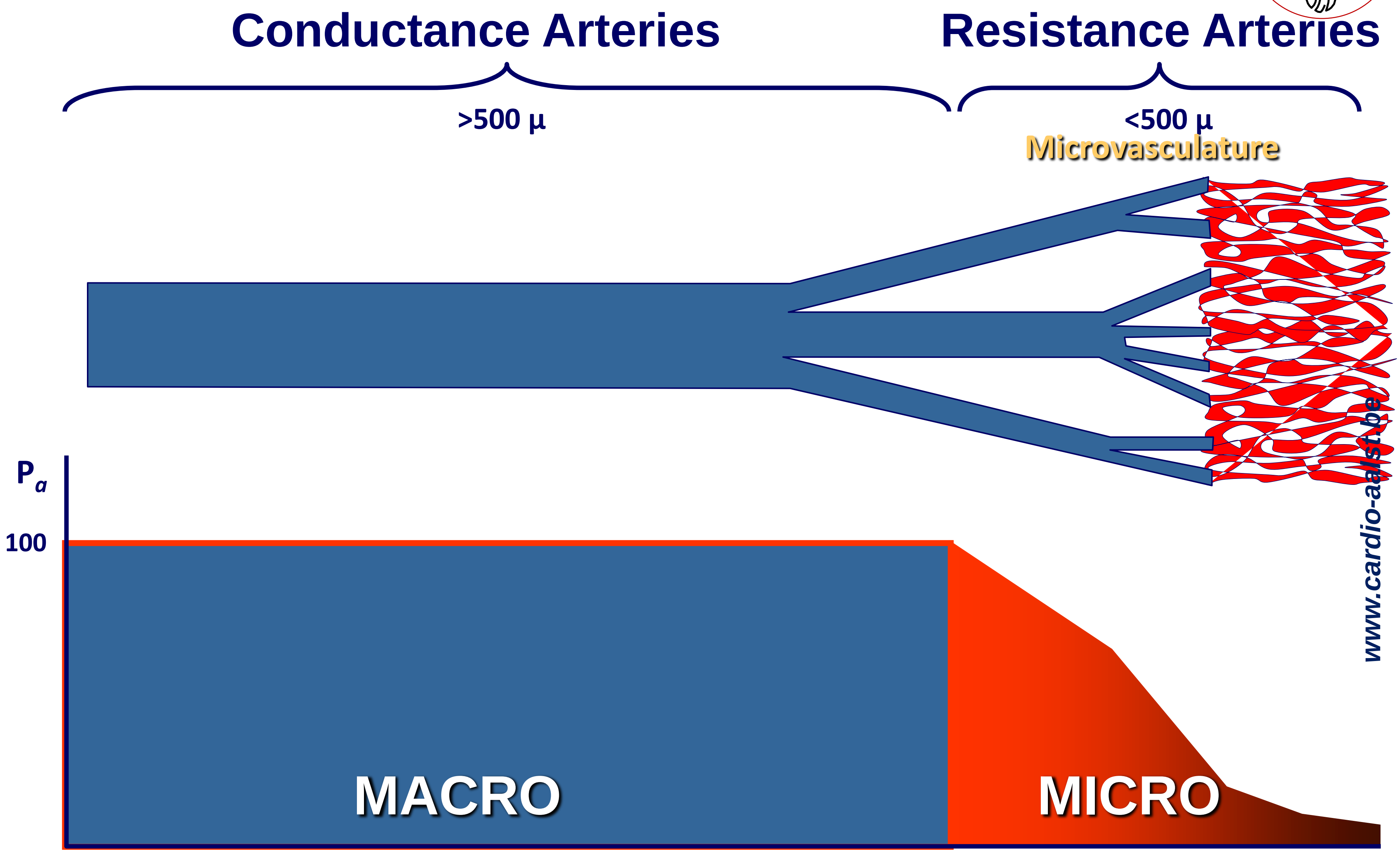

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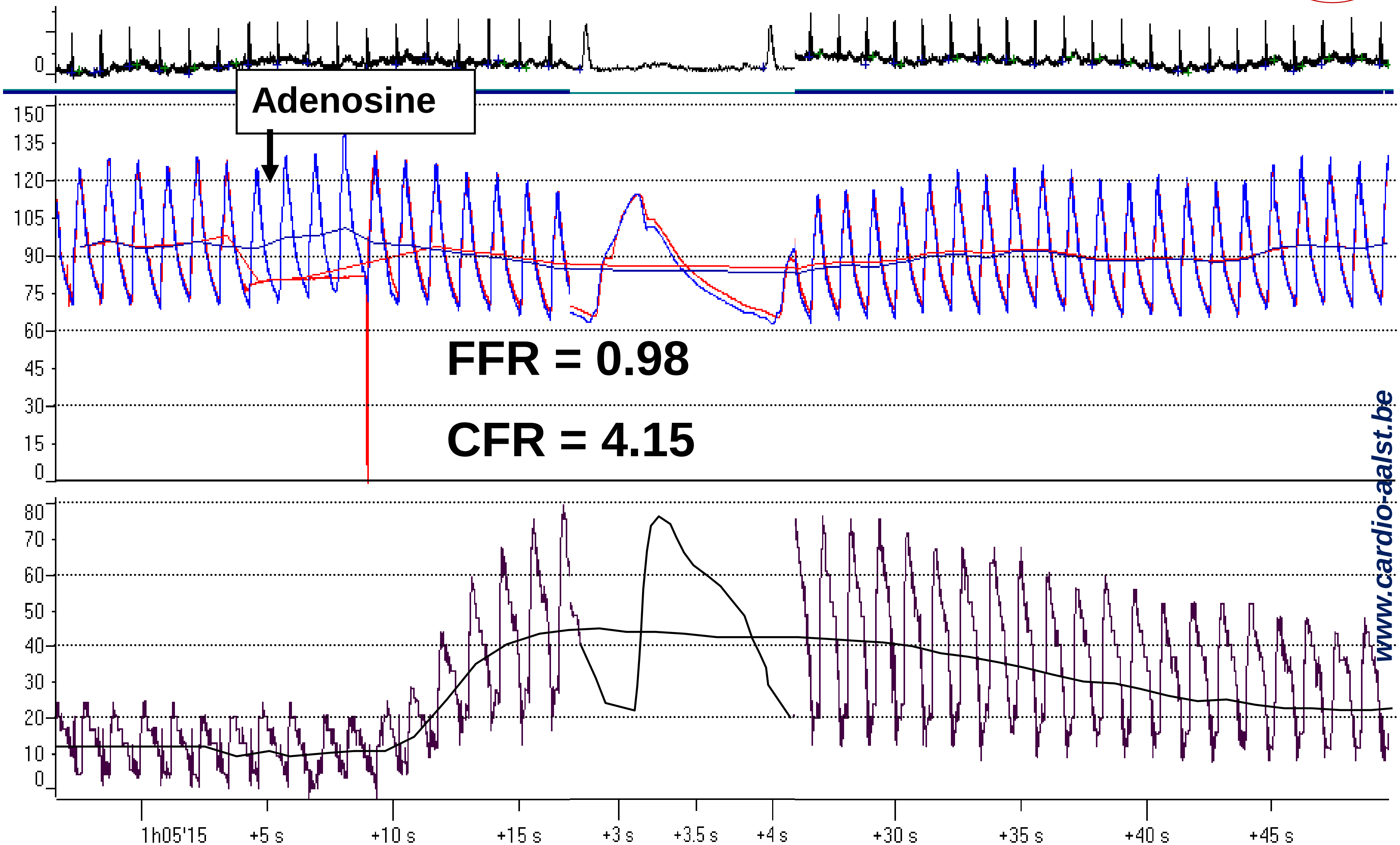
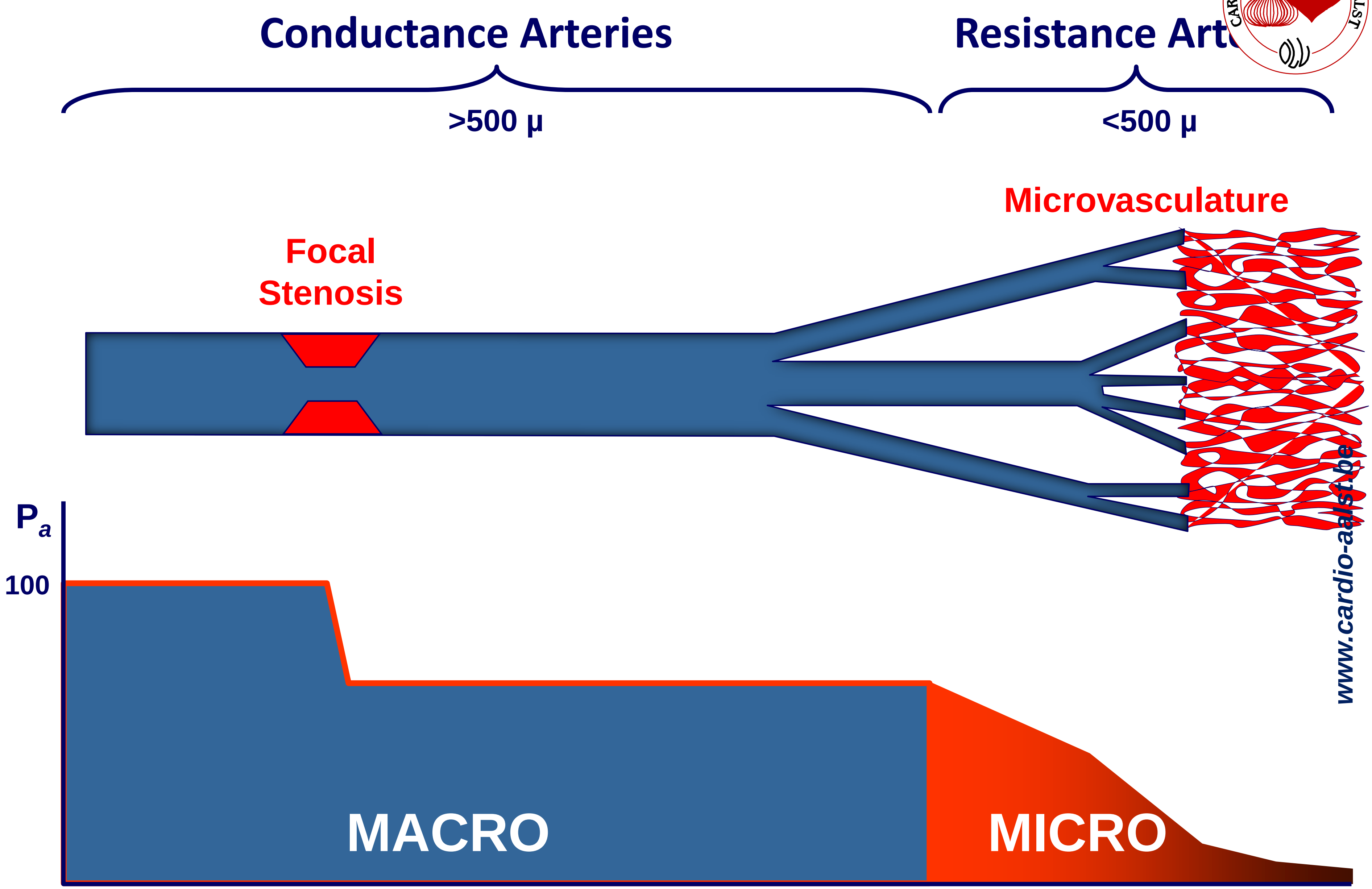
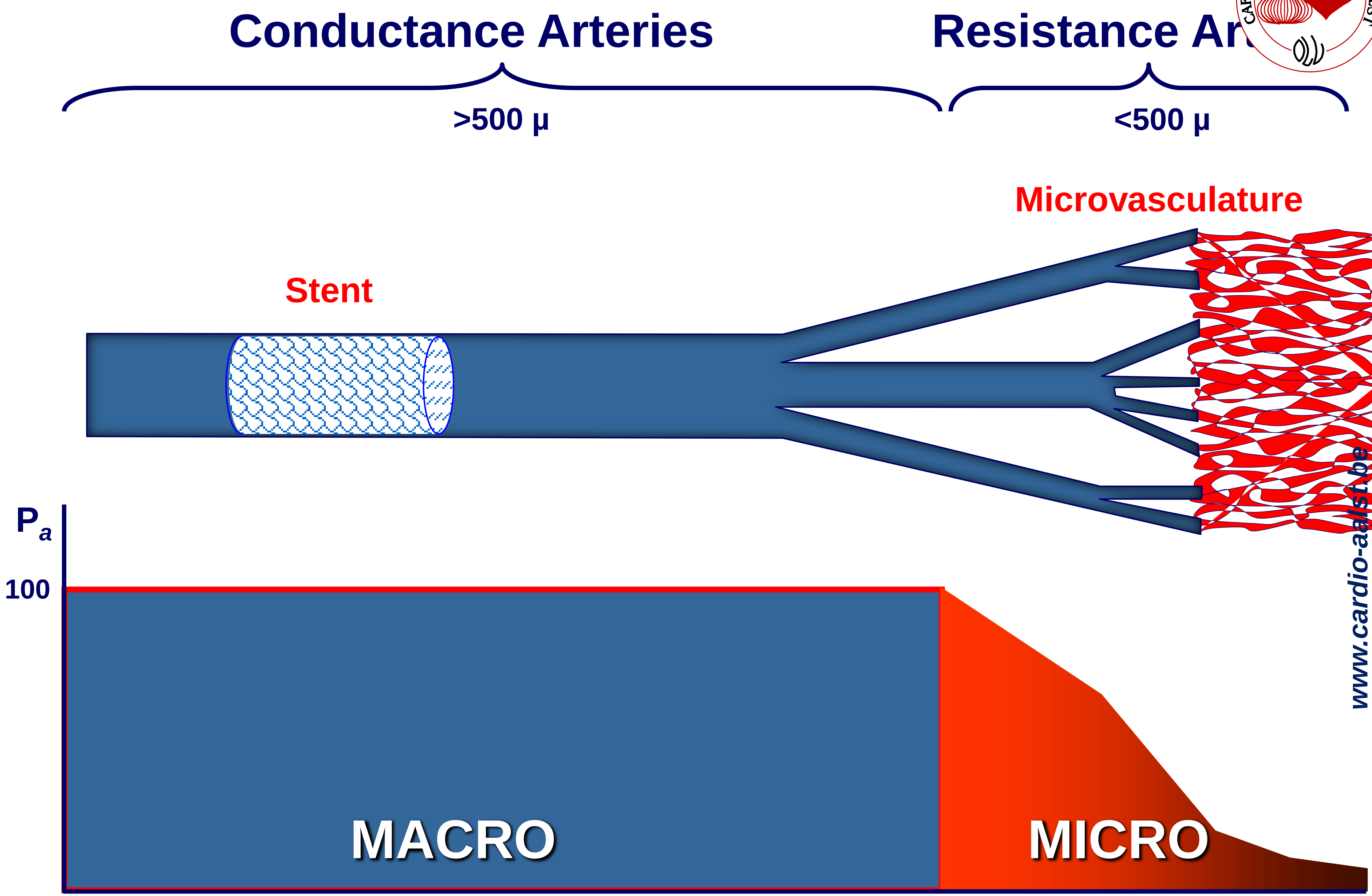
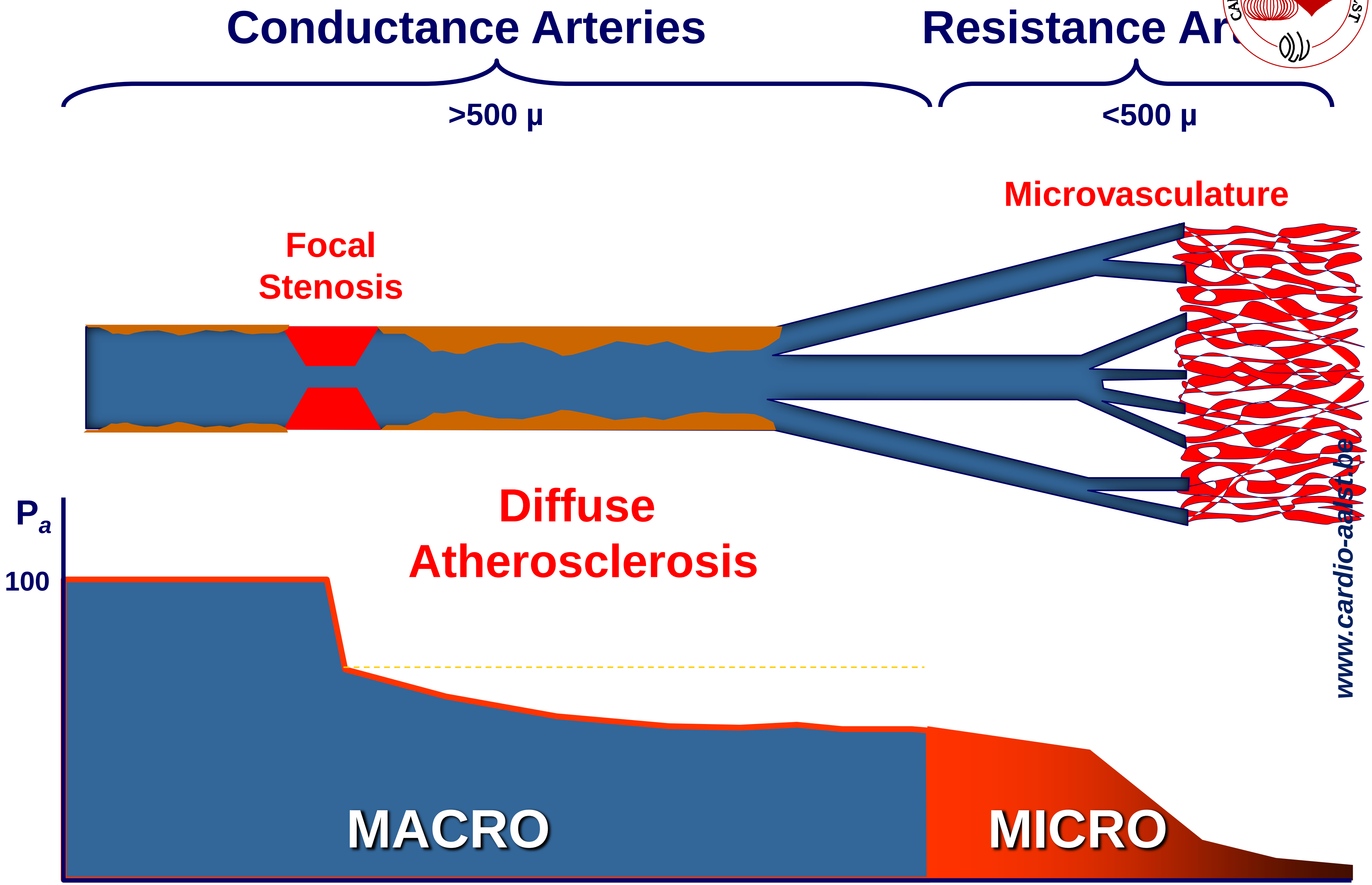



Conductance Arteries
Resistance Art
>500 µ
<500 µ
Microvasculature
Focal
Stenosis
P a
100
MACRO
MICRO
www.cardio-aalst.be

Control of MBF




Conductance Arteries
Resistance Ar
>500 µ
<500 µ
Microvasculature
Focal
Stenosis
Diffuse
Atherosclerosis
Pa
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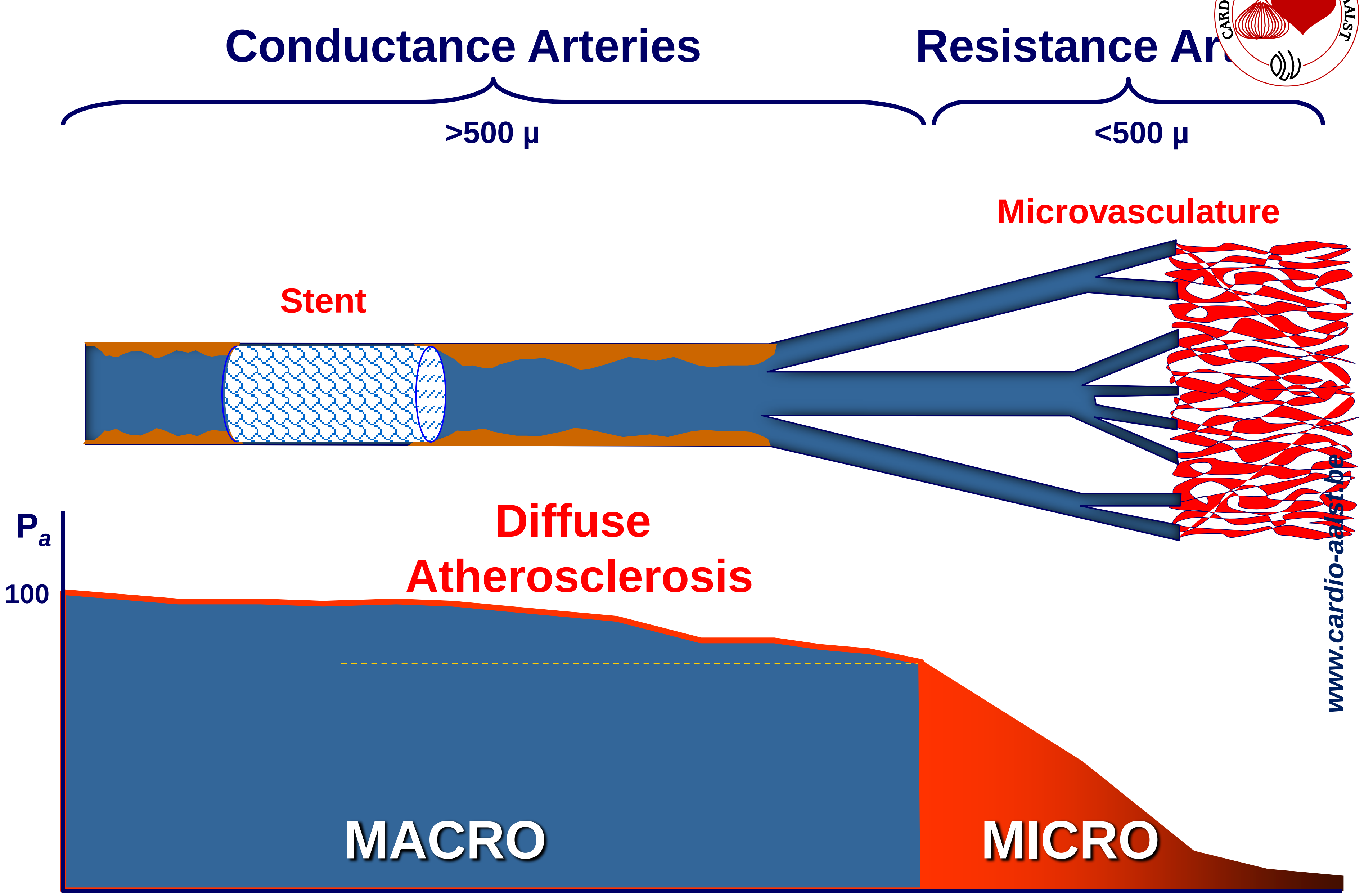
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Diffuse
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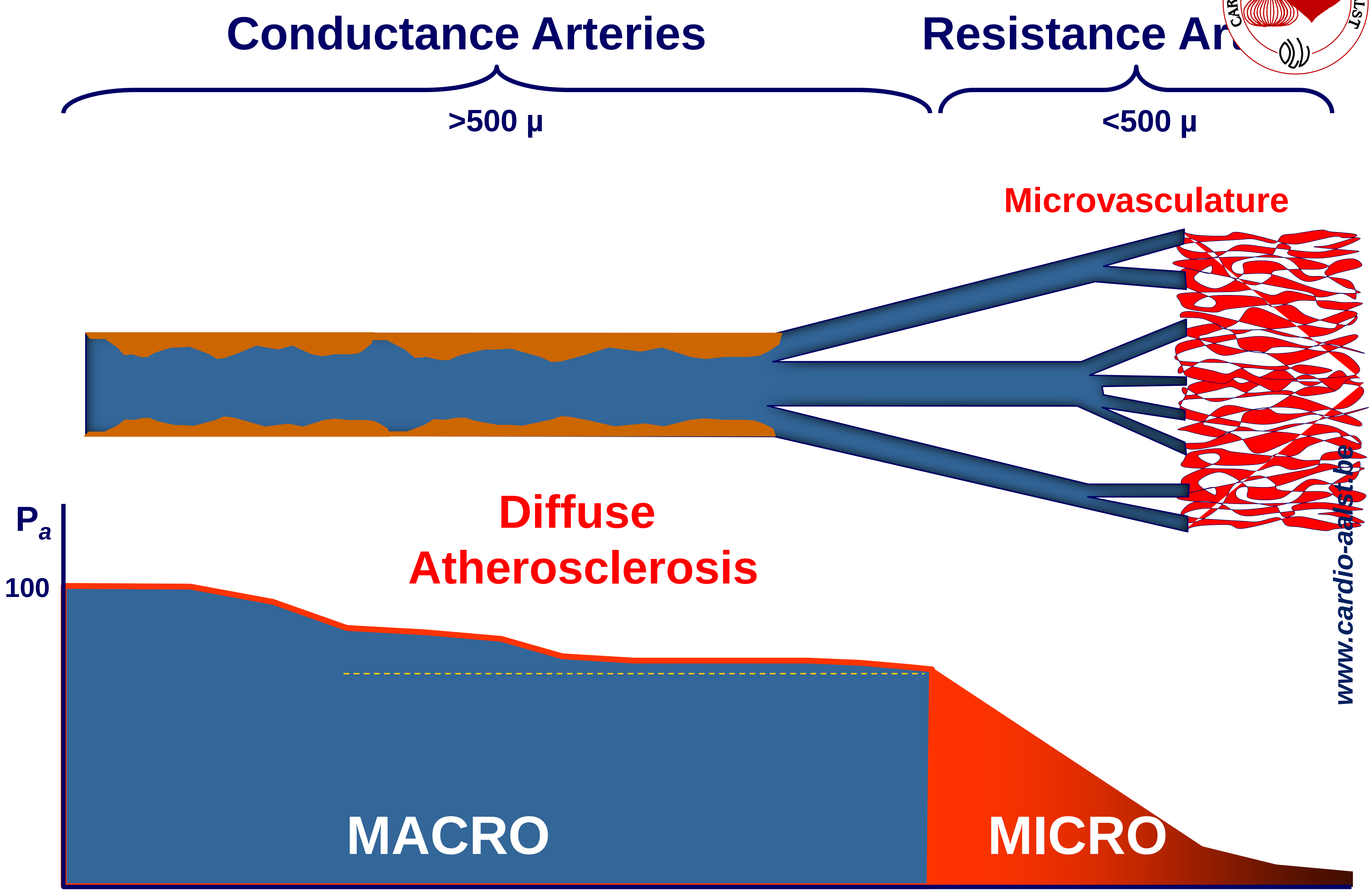
www.cardio-aalst.be
CARDIOVASCULAR CENTER AALST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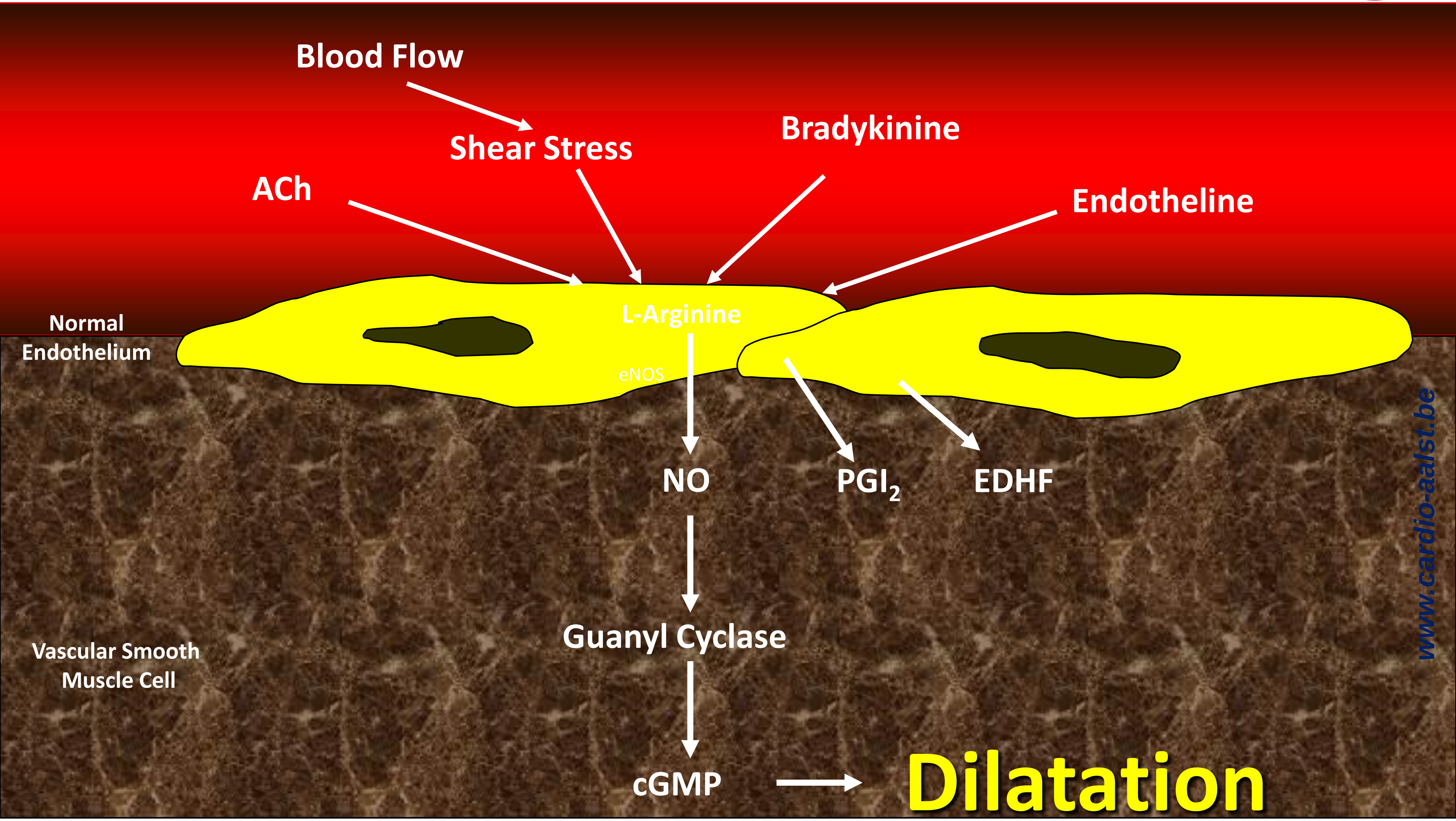
Endothelial Control of Coronary Blood Flow



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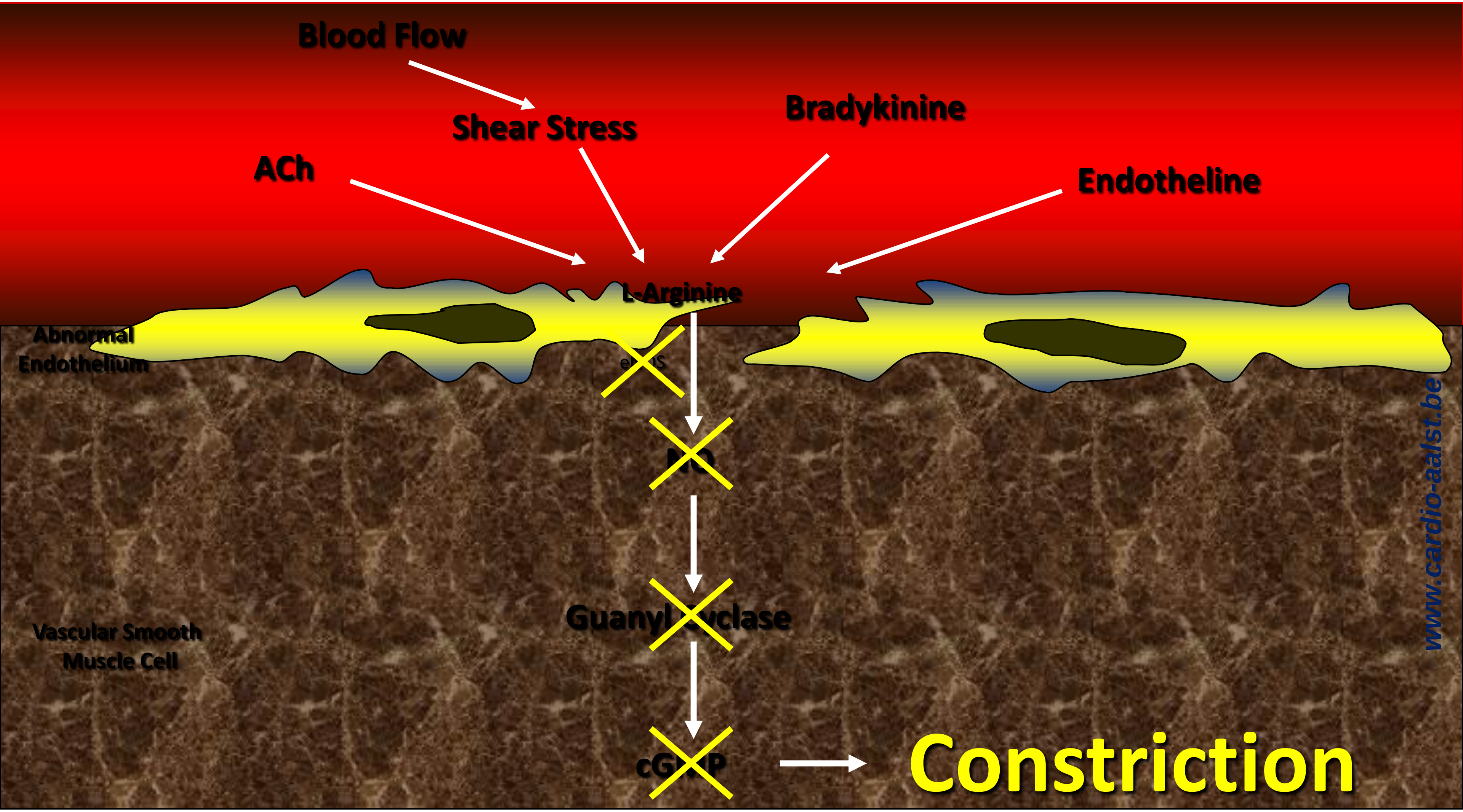
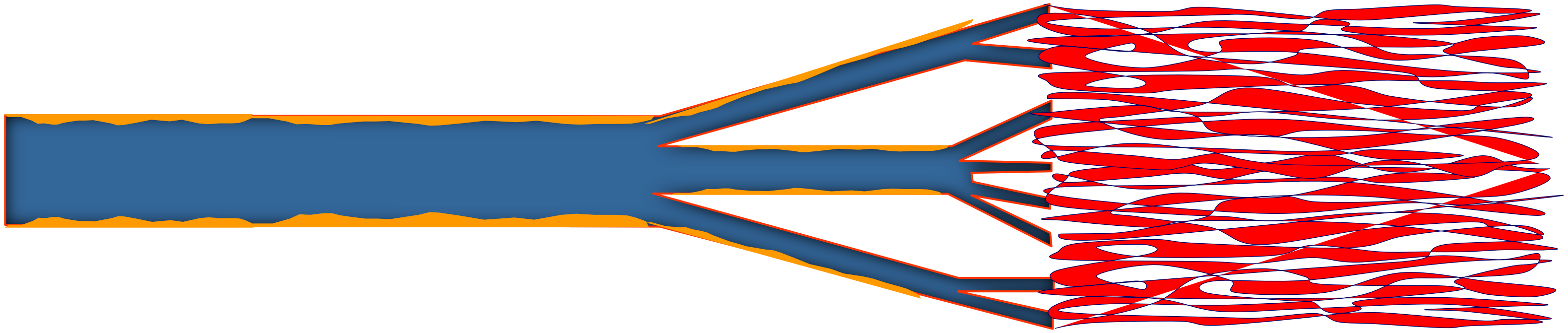


Importance of Maximal Vasodilation

Epicardial
= Conductance
Arteries > 550 µ

Microvasculature
= Resistance
Arteries < 550 µ



Nitrates → ~~Vasospasm~~

Adenosine → ~~Autoregulation~~

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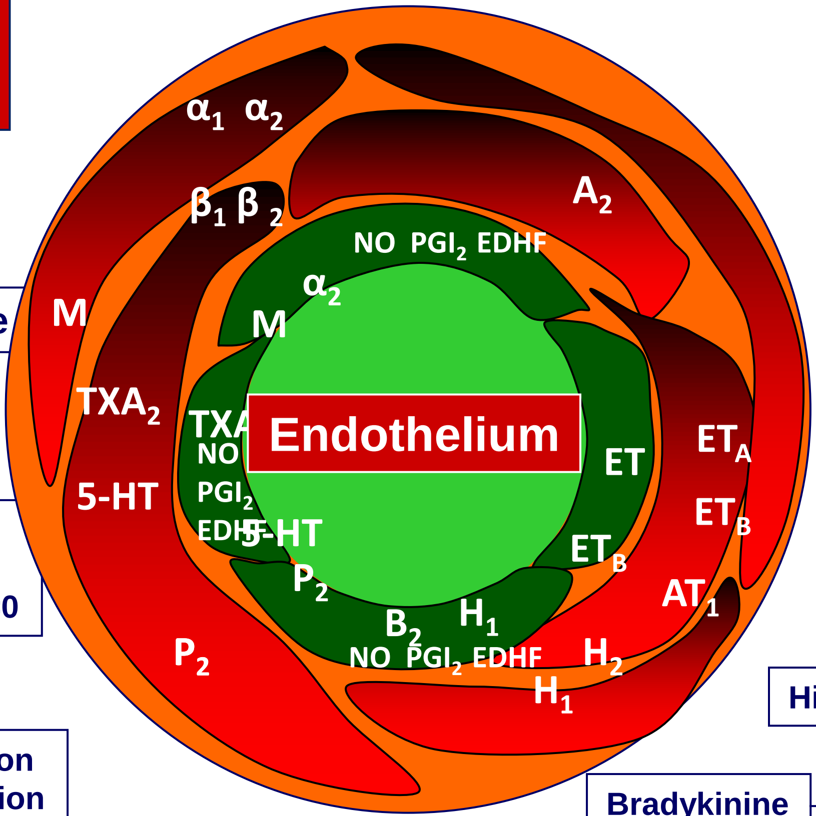

Metabolic factors

- Adenosine
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Adapted from D.J.G.M. Duncker

The Control of Myocardial Blood Flow

Endothelium

Metabolic factors

Physical factors

Neuro-humoral factors

Endo- and paracrine factors

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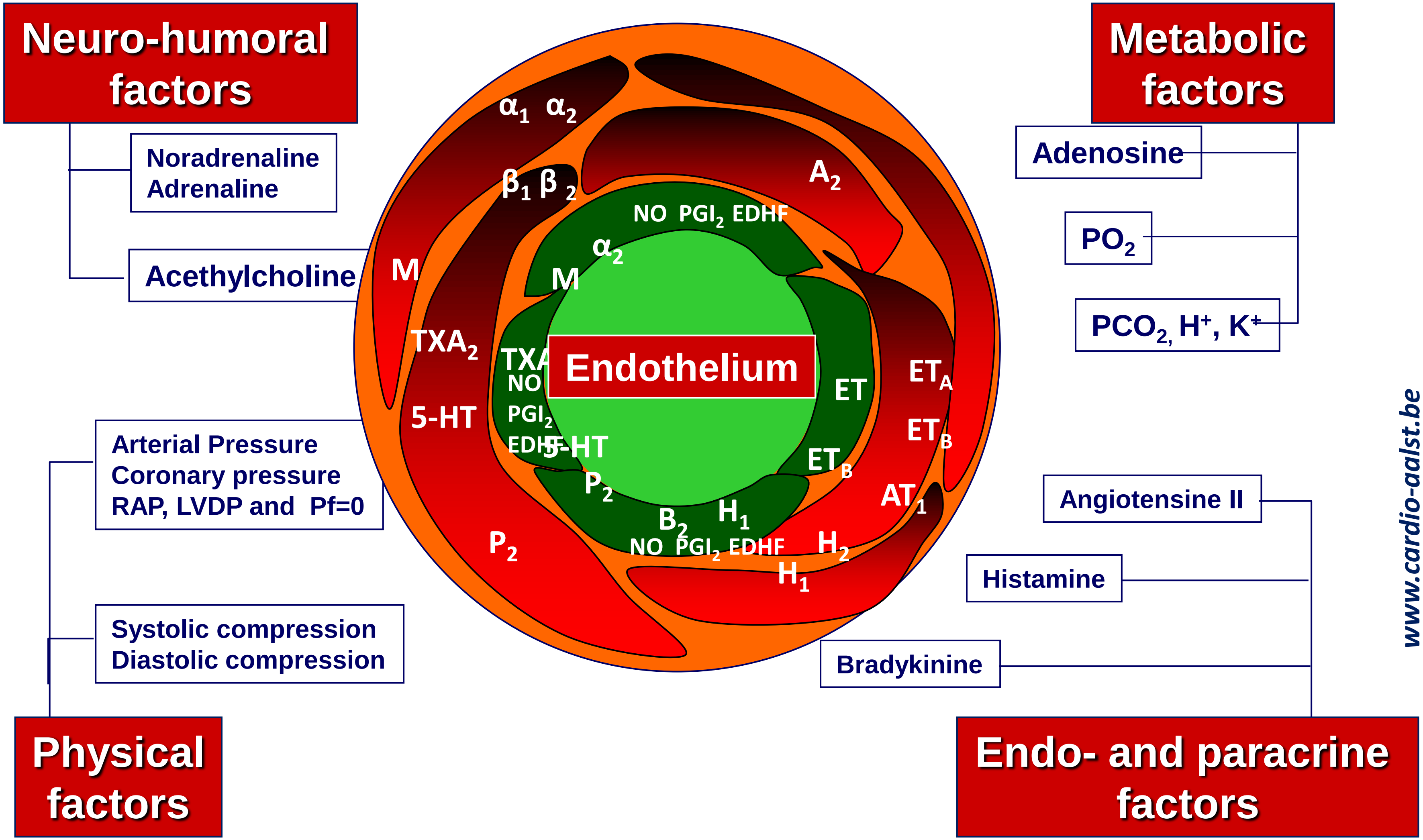
Multiple, interacting, cumulative, nonlinear mechanisms

Coronary Autoregulation

Adapted from D.J.G.M. Duncker

The Control of Resting Myocardial Blood Flow



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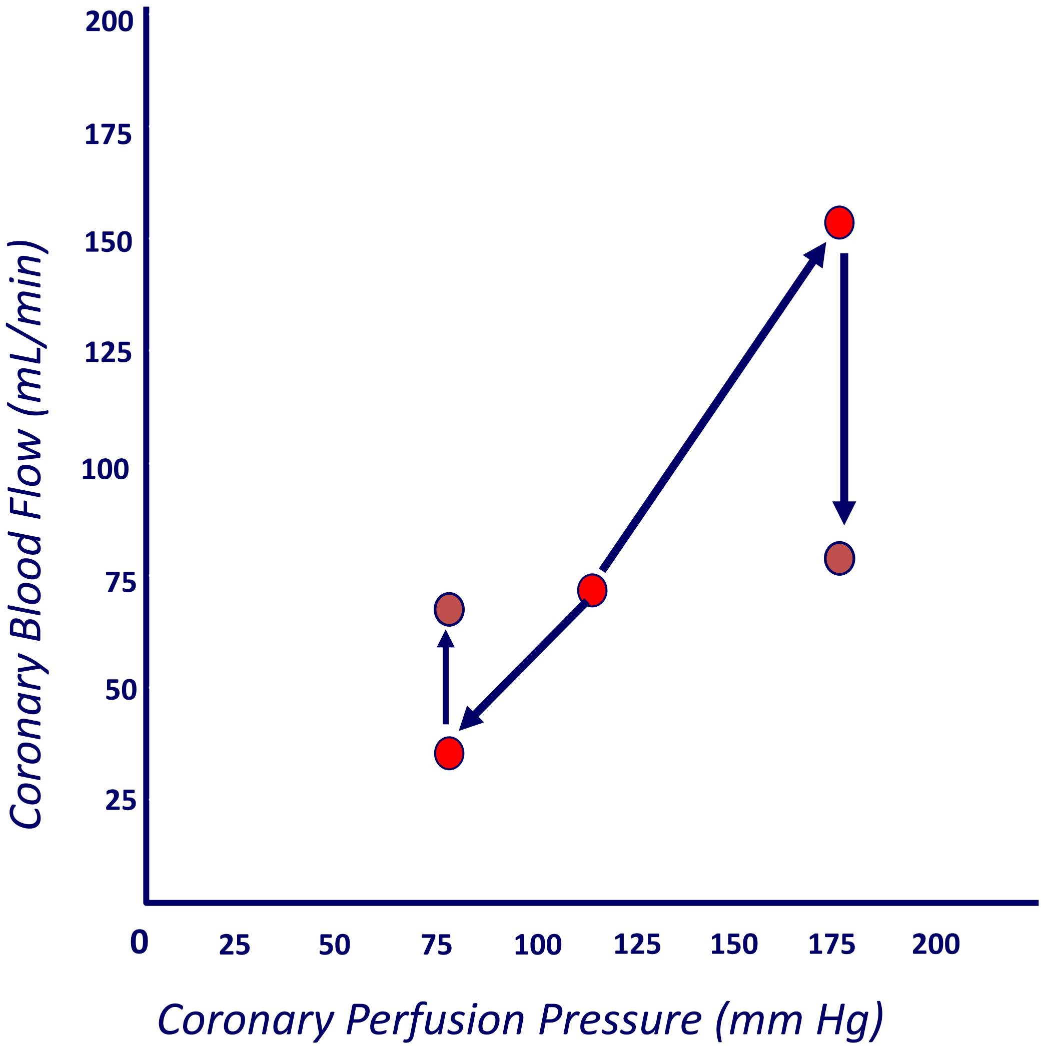
Adapted from D.J.G.M. Duncker

Maximal hyperemia is easier to get than true resting conditions

Autoregulation

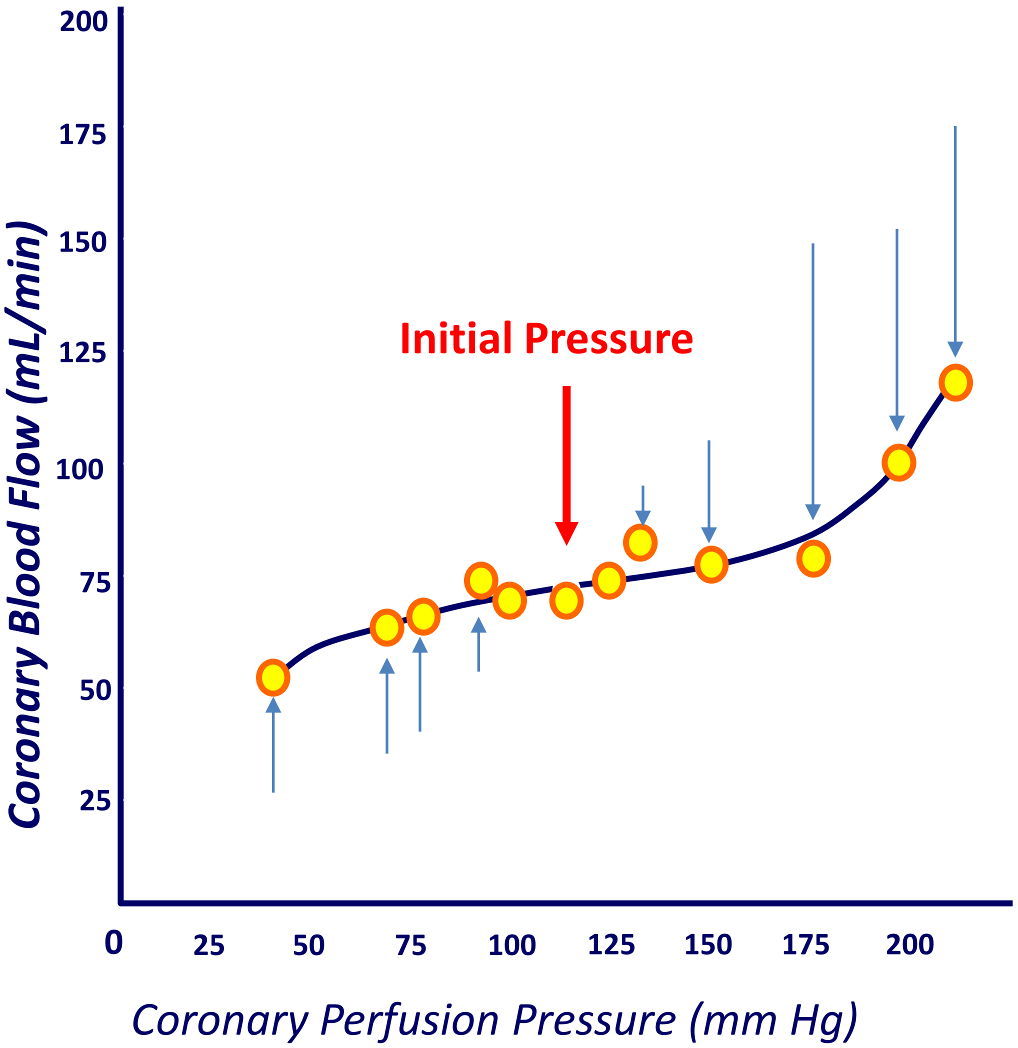
The ability of the heart of maintaining flow constant in case of change of perfusion pressure without the intervention of any other external mechanism

Coronary Autoregulation



Rubio and Berne, Prog CV Disease 1975

Autoregulatory Range



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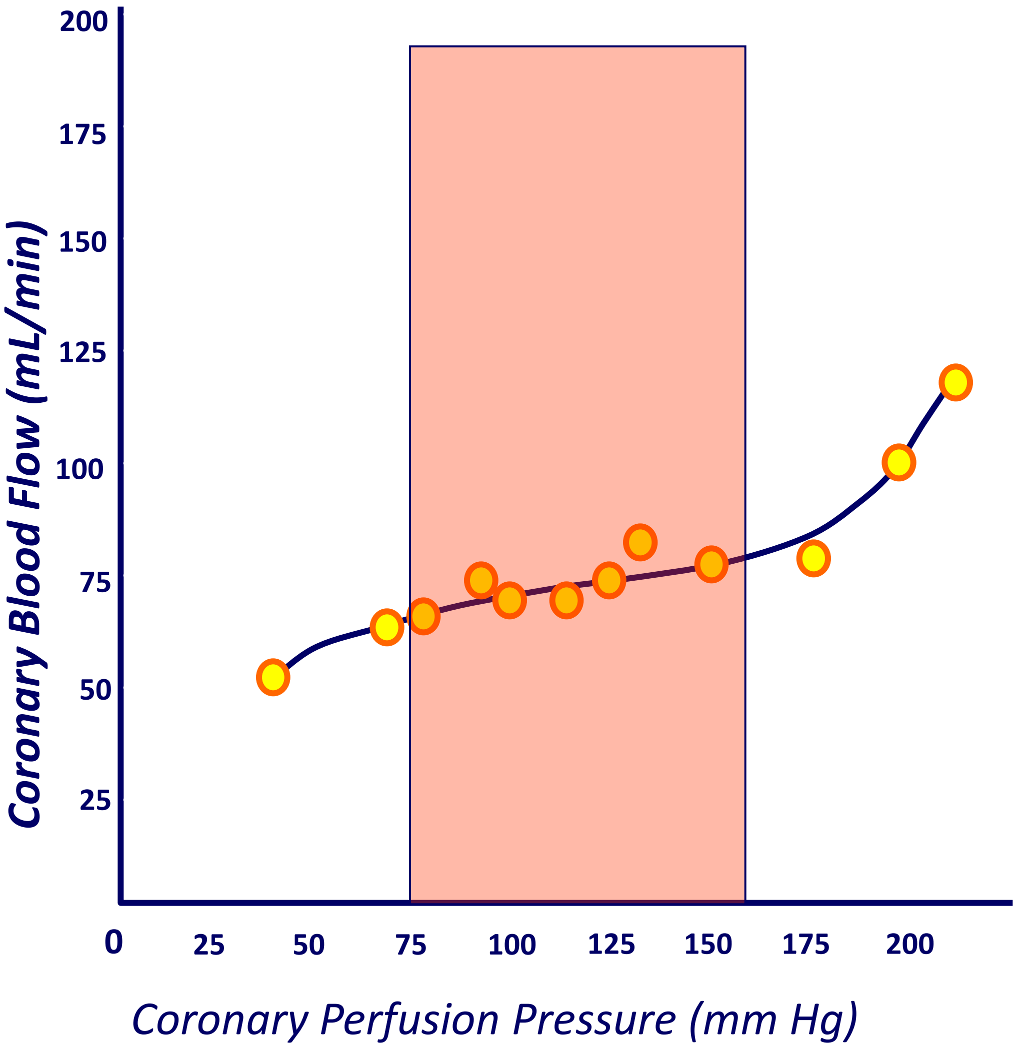
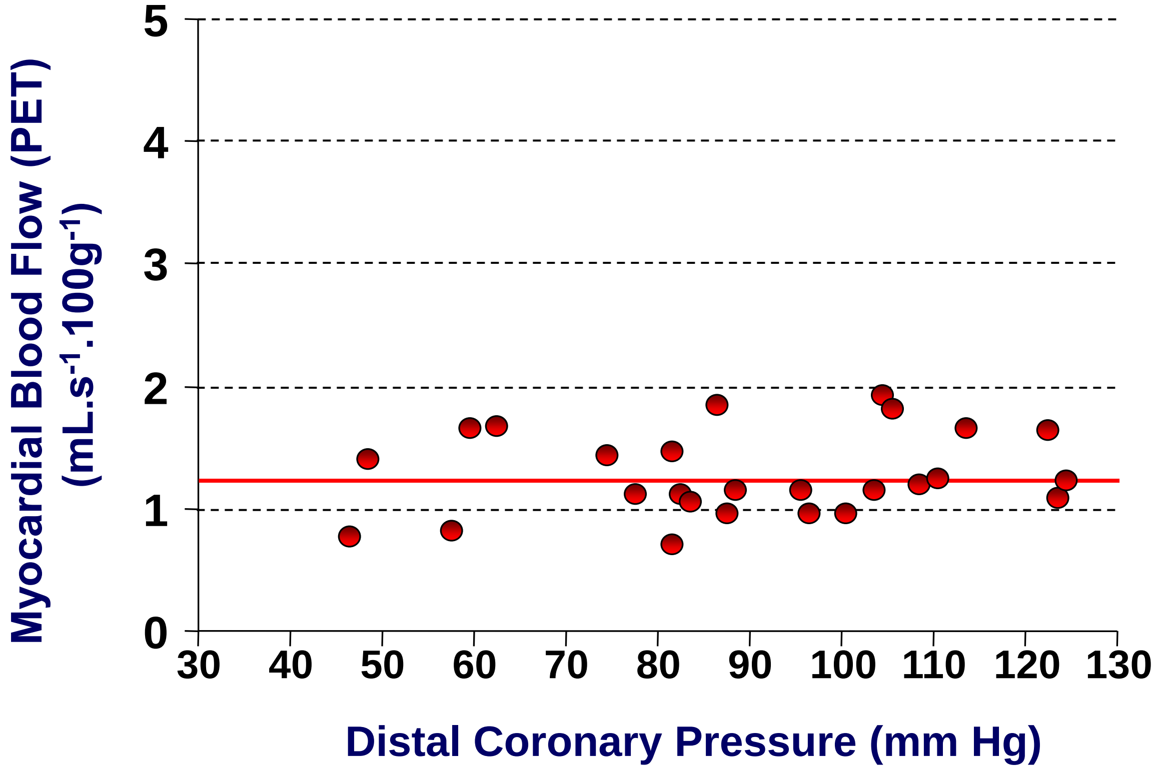


Rubio and Berne, Prog CV Disease 1975

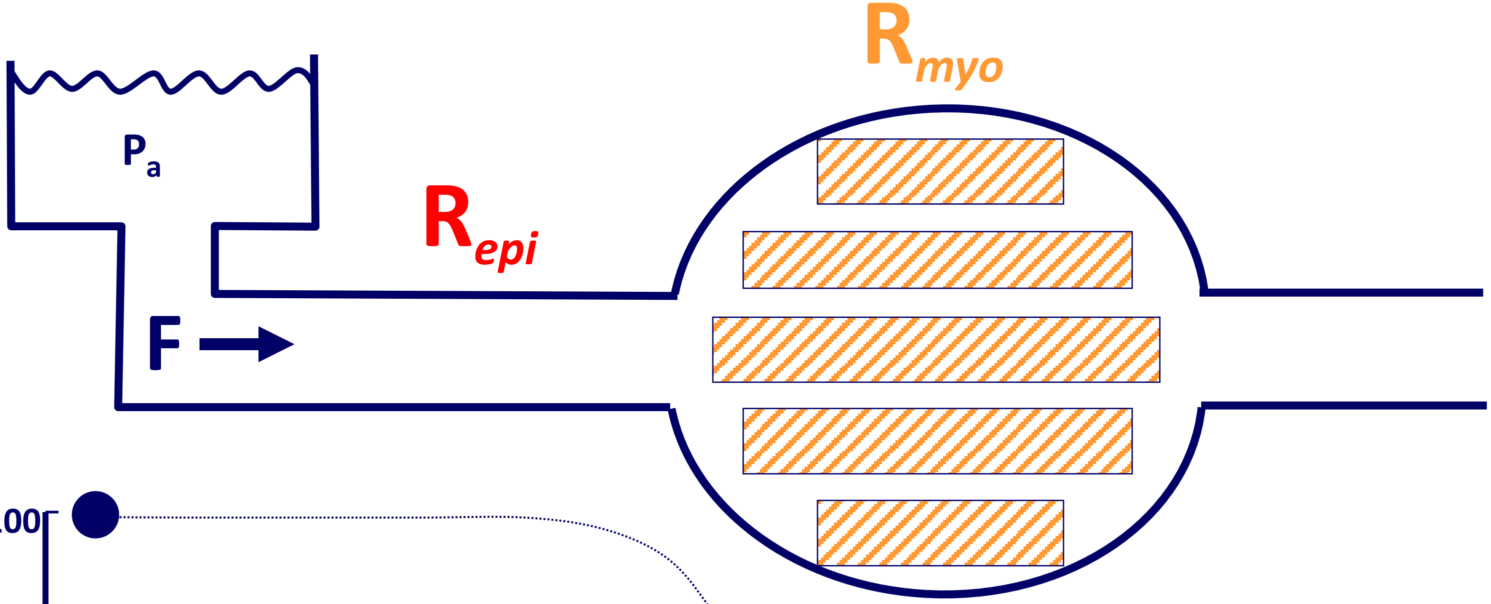
Autoregulation

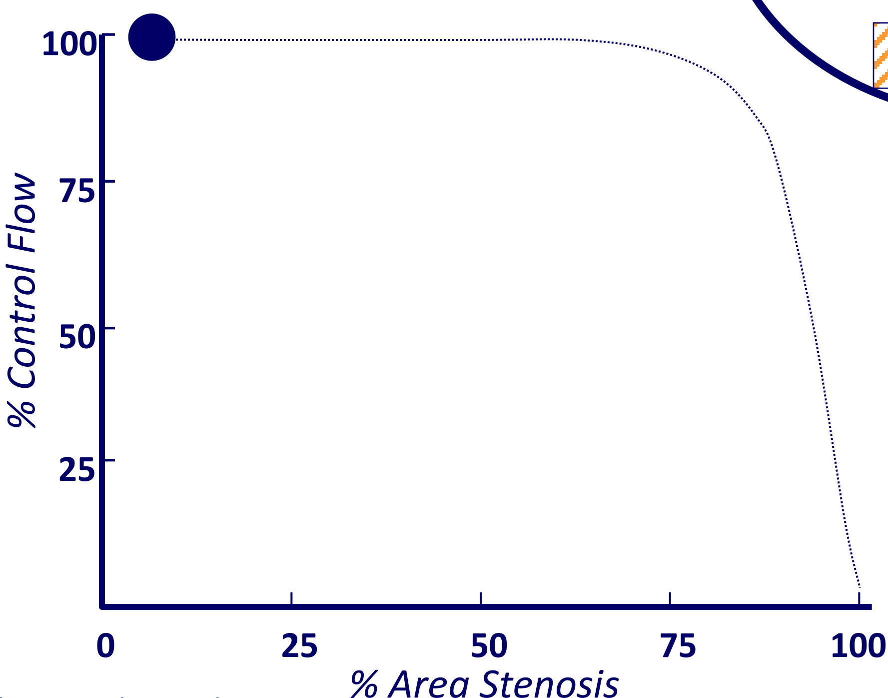
- Proximal LAD stenosis (n = 26)
- Normal LV systolic function
- PET fow measurements (^{15}O-labeled water) at rest



De Bruyne et al, 1996 unpublished data

Flow, Pressure, and Resistance





$$F = \frac{\Delta P}{R_{epi} + R_{myo}}$$

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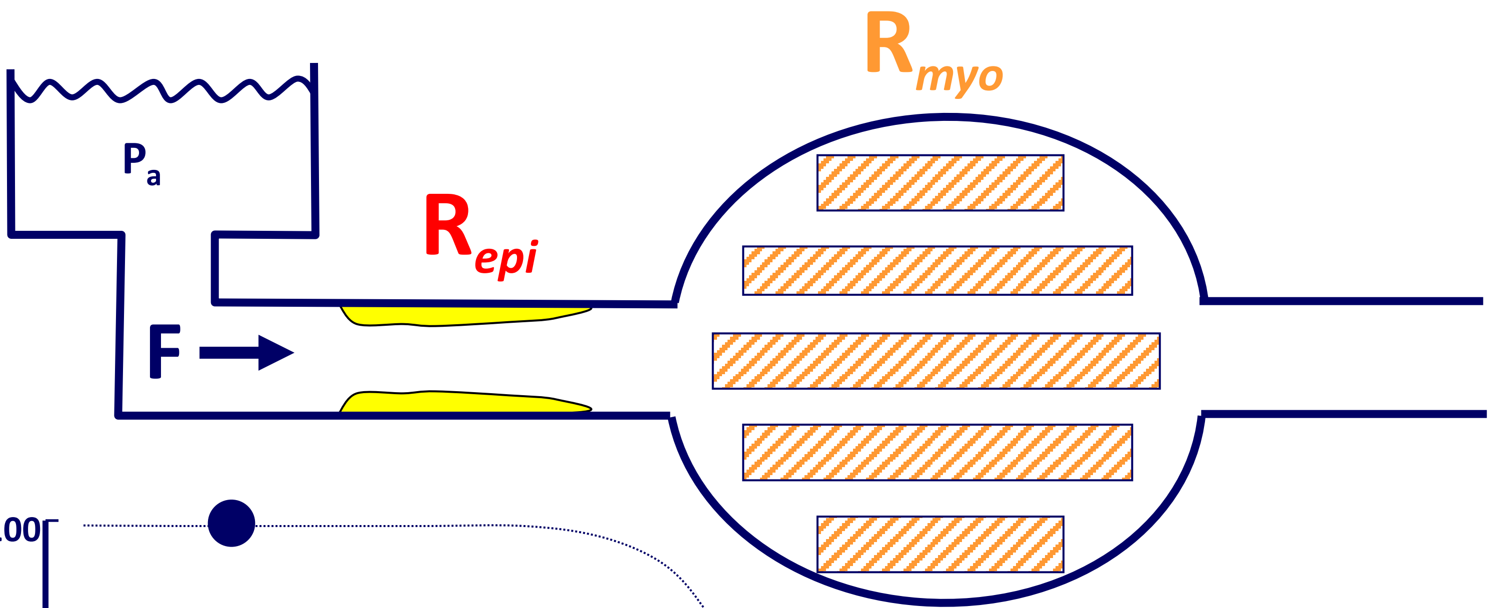
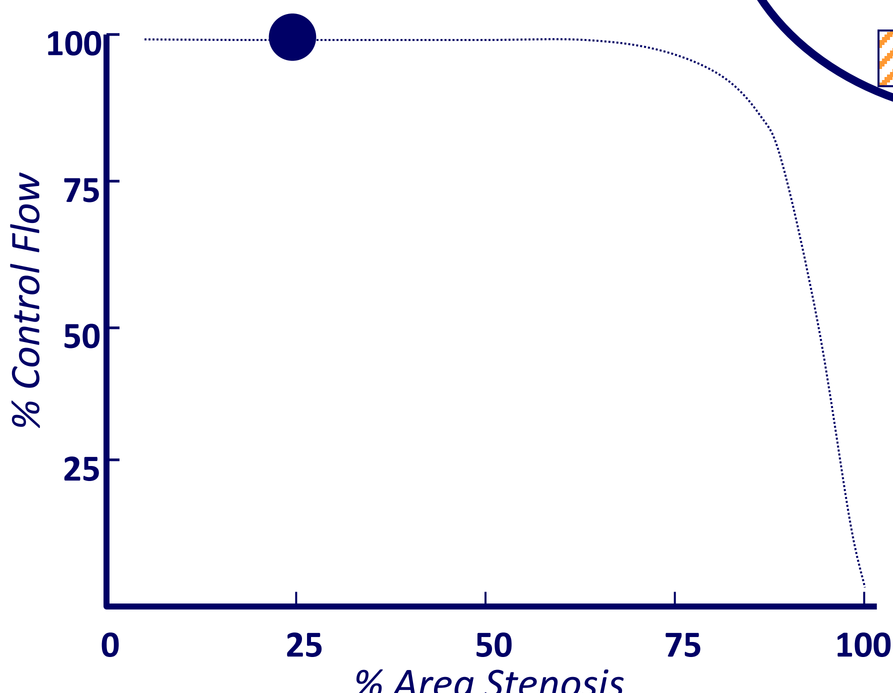
K. Lance Gould, 1974

Flow, Pressure, and Resistance





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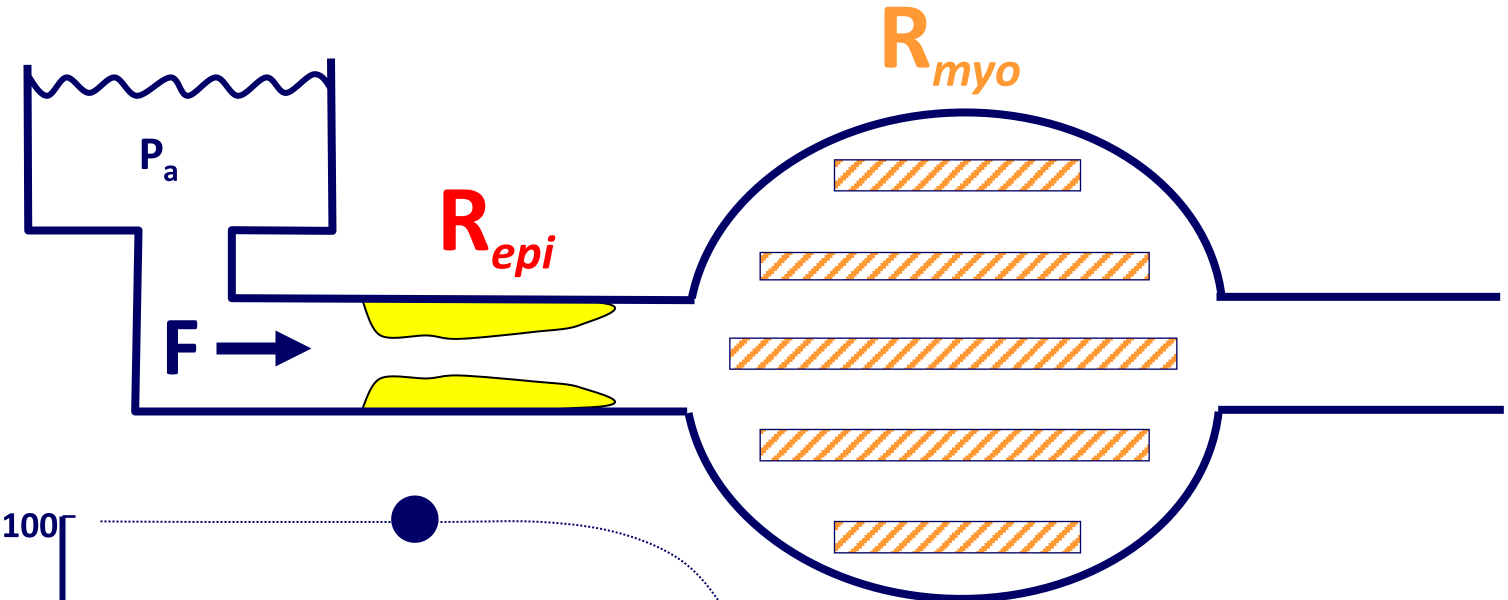

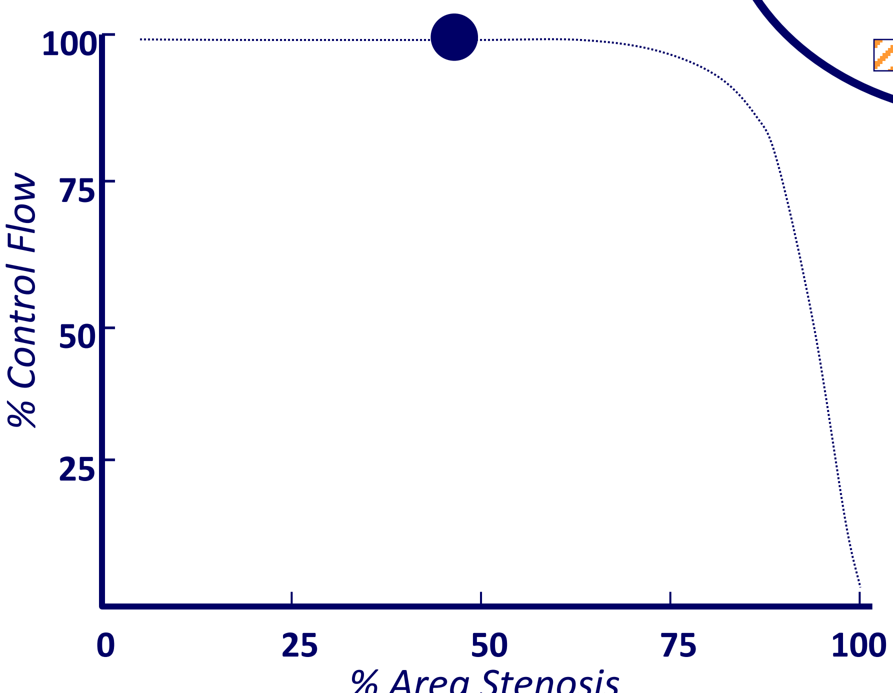

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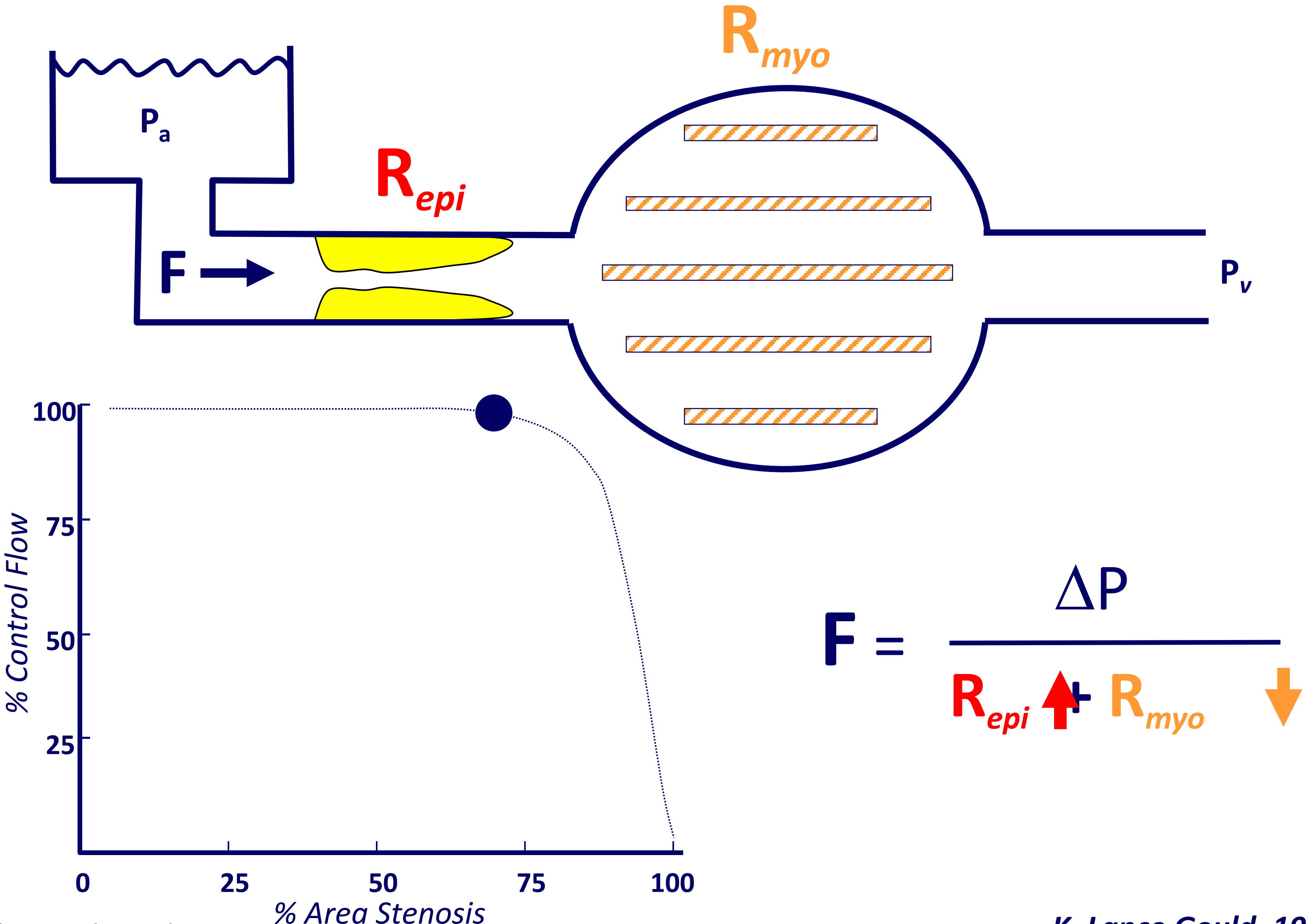

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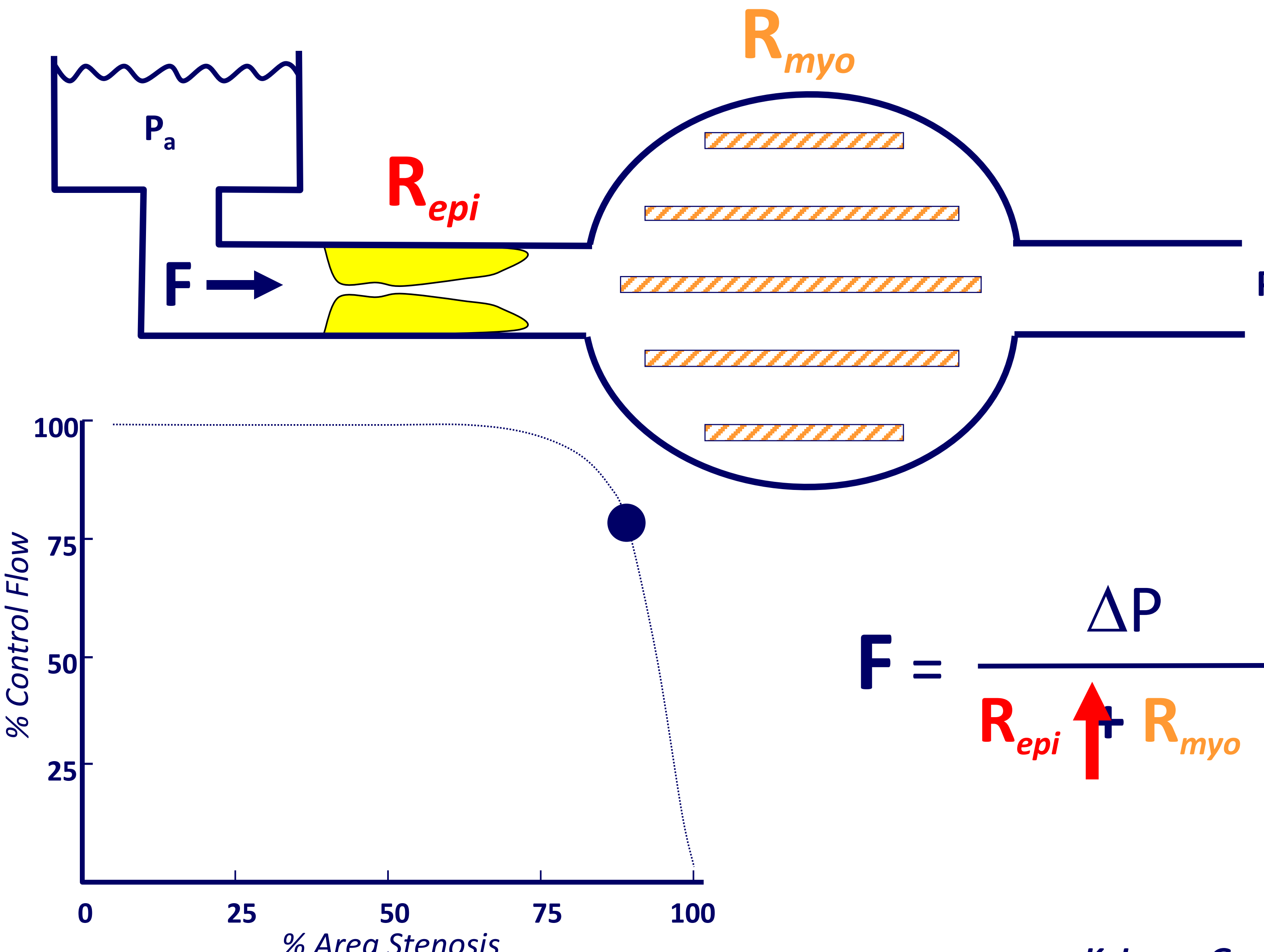

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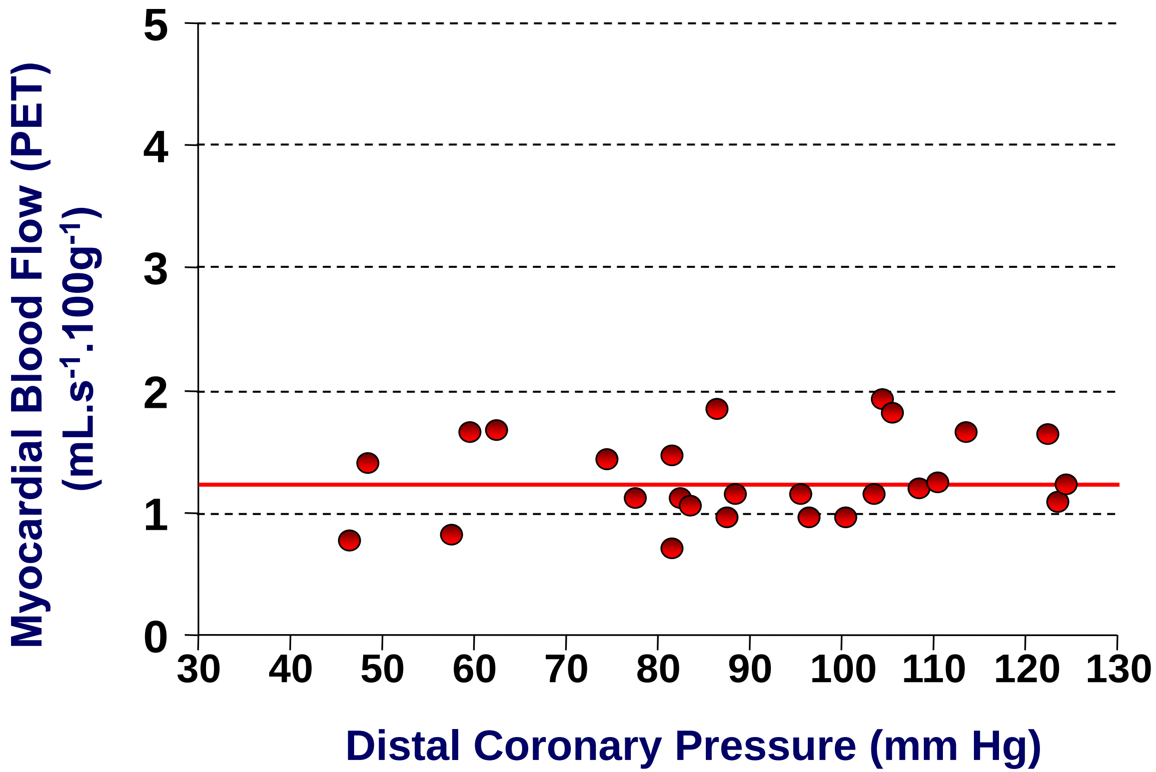
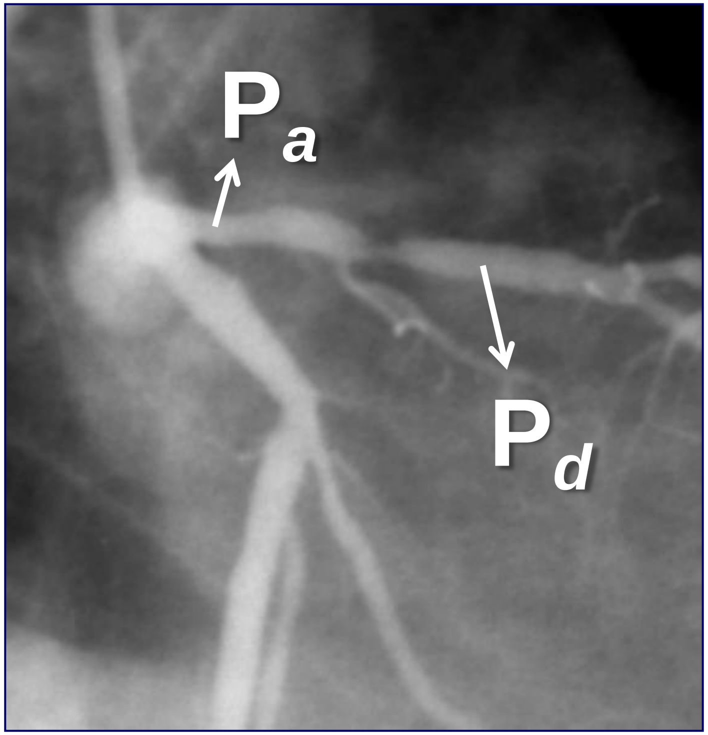


De Bruyne et al, 1996 unpublished data

Fractional Flow Reserve

FFR = ratio of hypermic flow in the stenotic vessel to hyperemic flow in the same vessel but in the absence of the stenosis

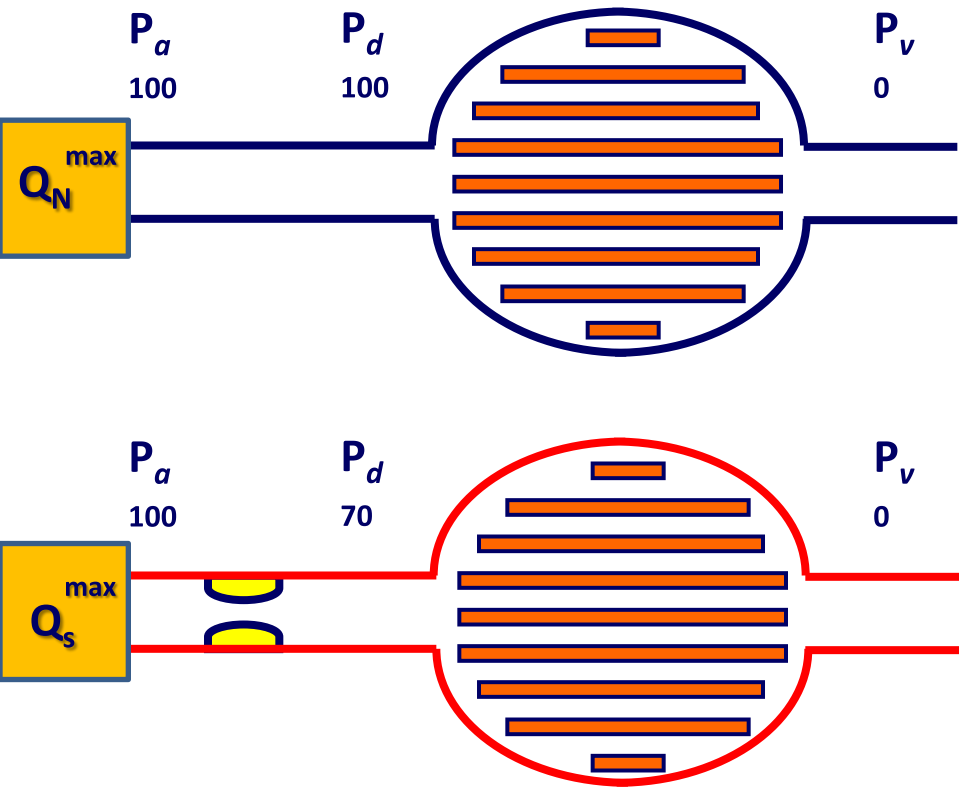
FFR = extent to which (%) maximal myocardial flow is limited by the epicardial stenosis

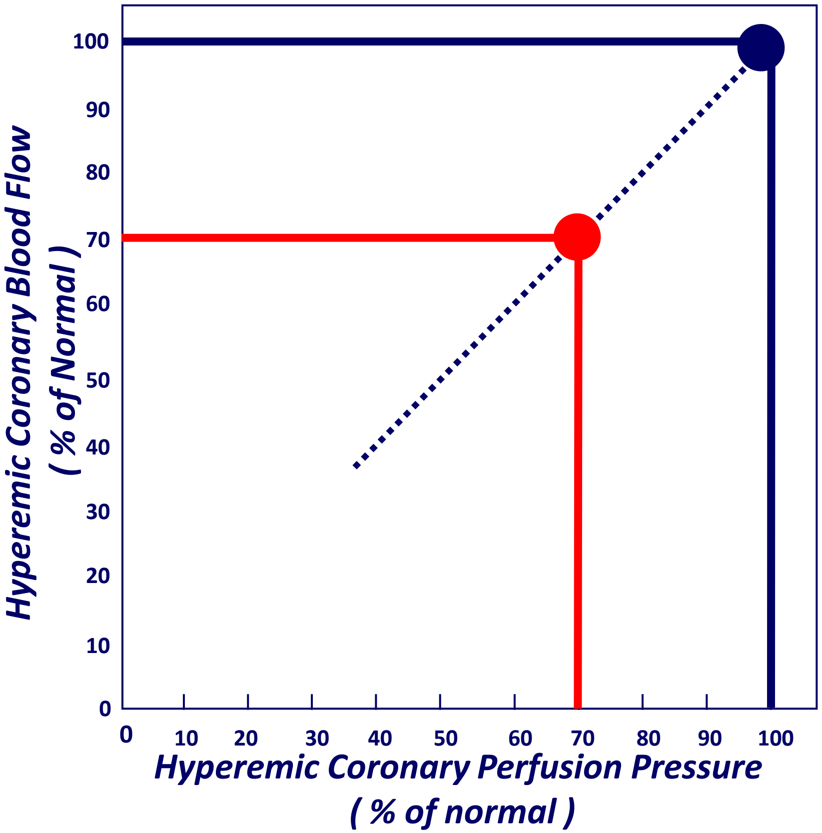


$$FFR = \frac{Q^S_{max}}{Q^N_{max}} = \frac{P_d}{P_a}$$

During maximal hyperemia
(i.e. during maximal transstenotic flow, when the relationship between pressure flow is linear)

Pressure-Flow Relationship During Maximal Vasodilation





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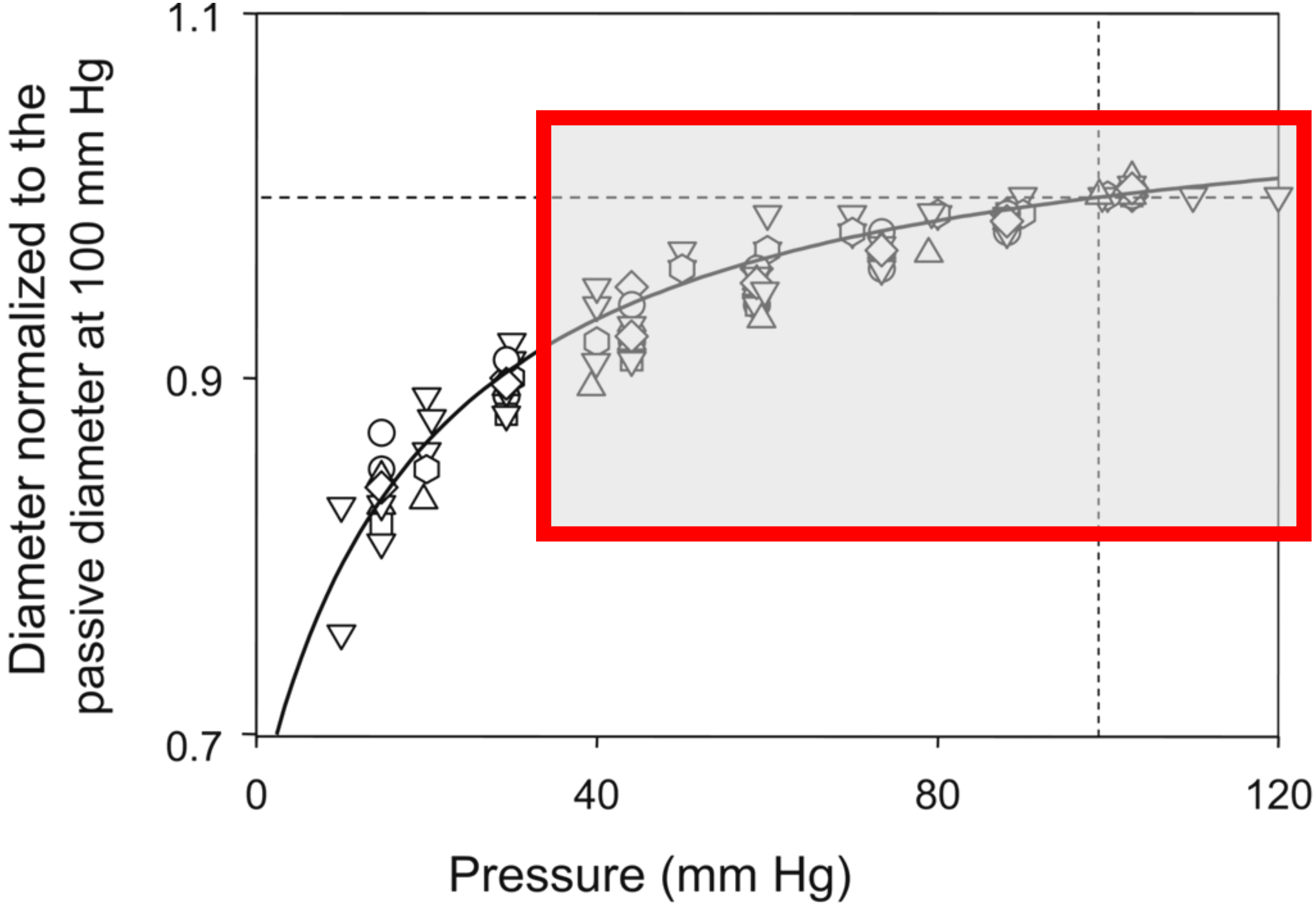
Non-Linearity of the Pressure-Resistance Relationship ?



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Spaan, J. A.E. et al. Circulation 2006

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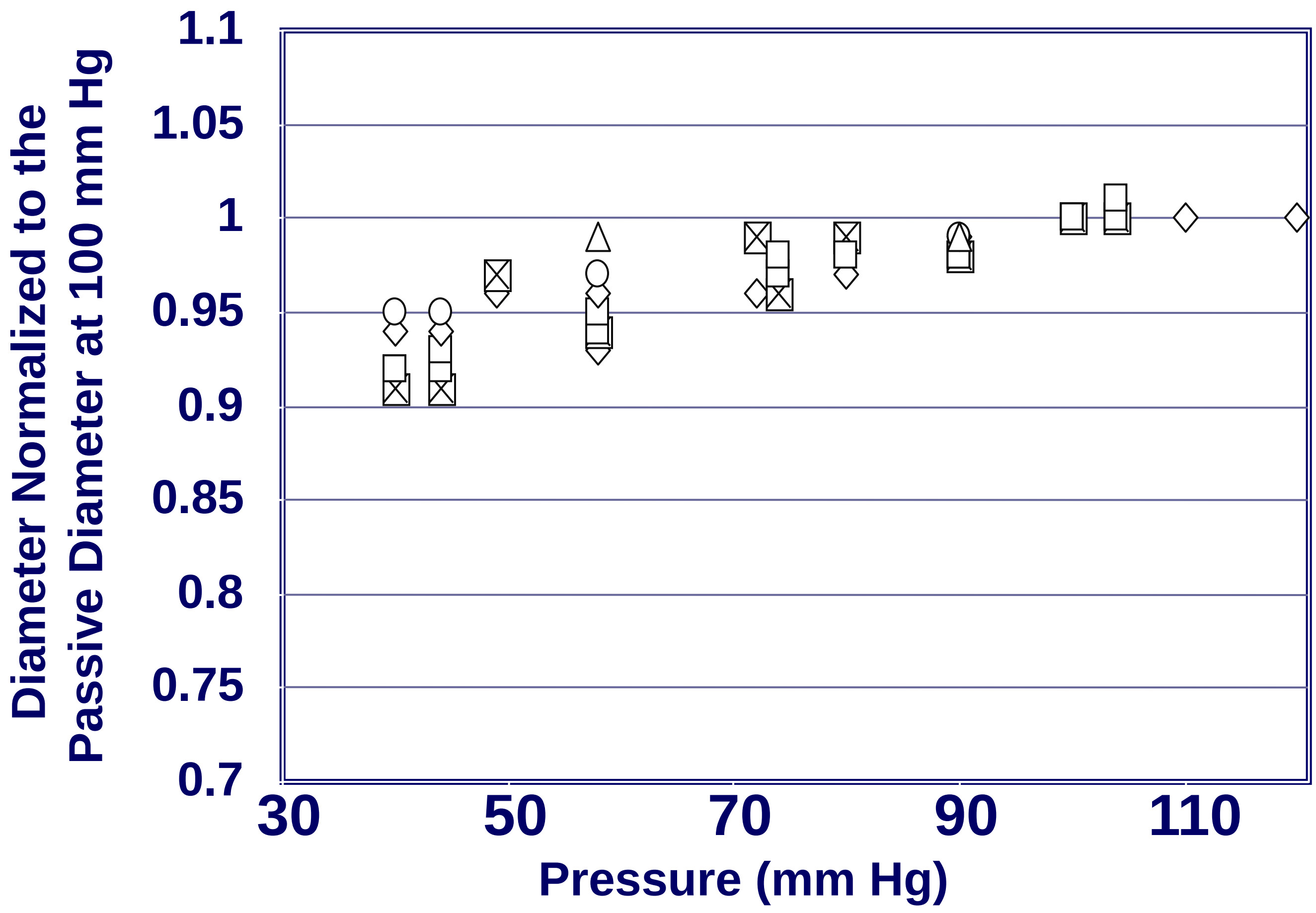

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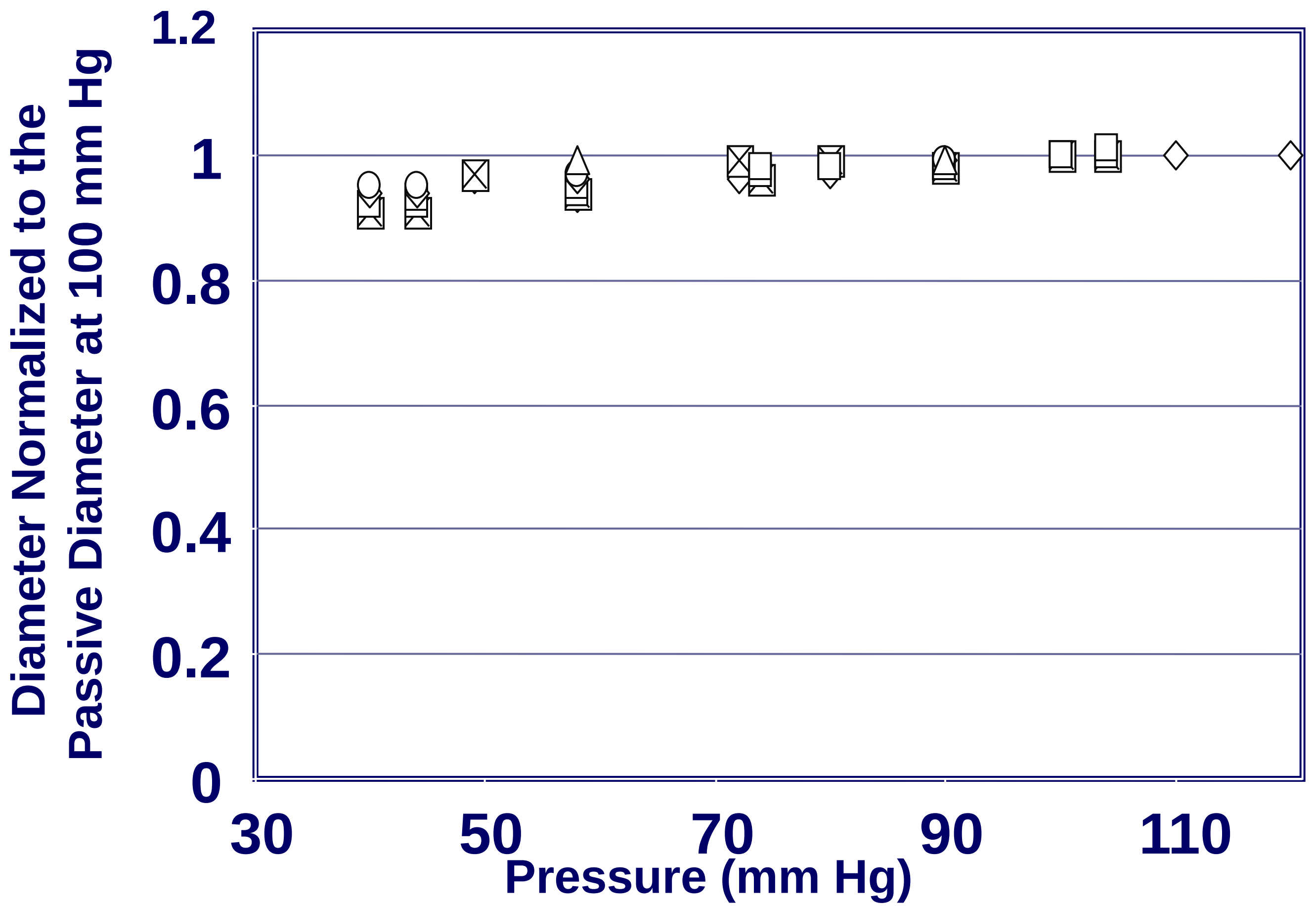
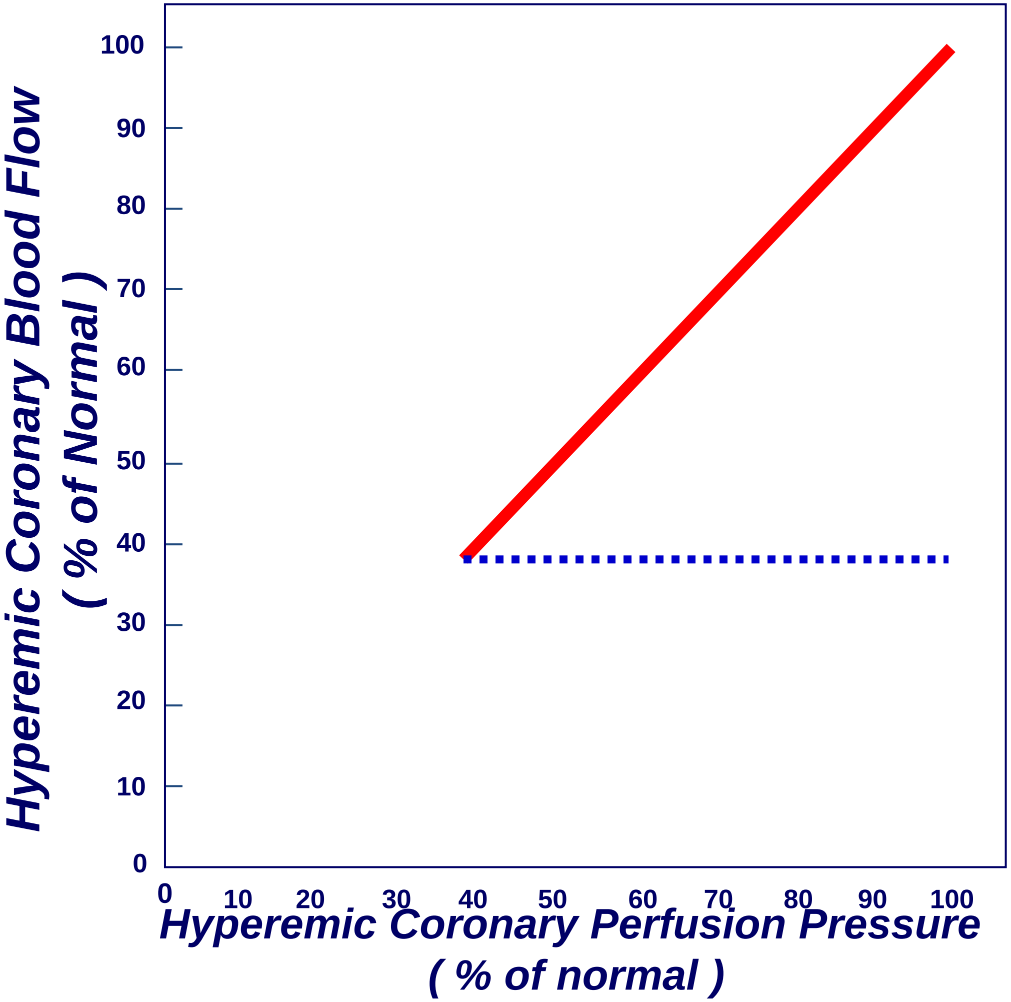


Adapted from Spaan, J. A.E. et al. Circulation 2006

Pressure-Flow Relationship During Maximal Vasodilation



Conclusions

The control of myocardial blood flow is amazingly complicated

This complexity is 'due' to the importance of constantly matching oxygen demand

When performing 'coronary physiology' in the cath lab a thorough understanding of the basic mechanisms is mandatory

Conclusions