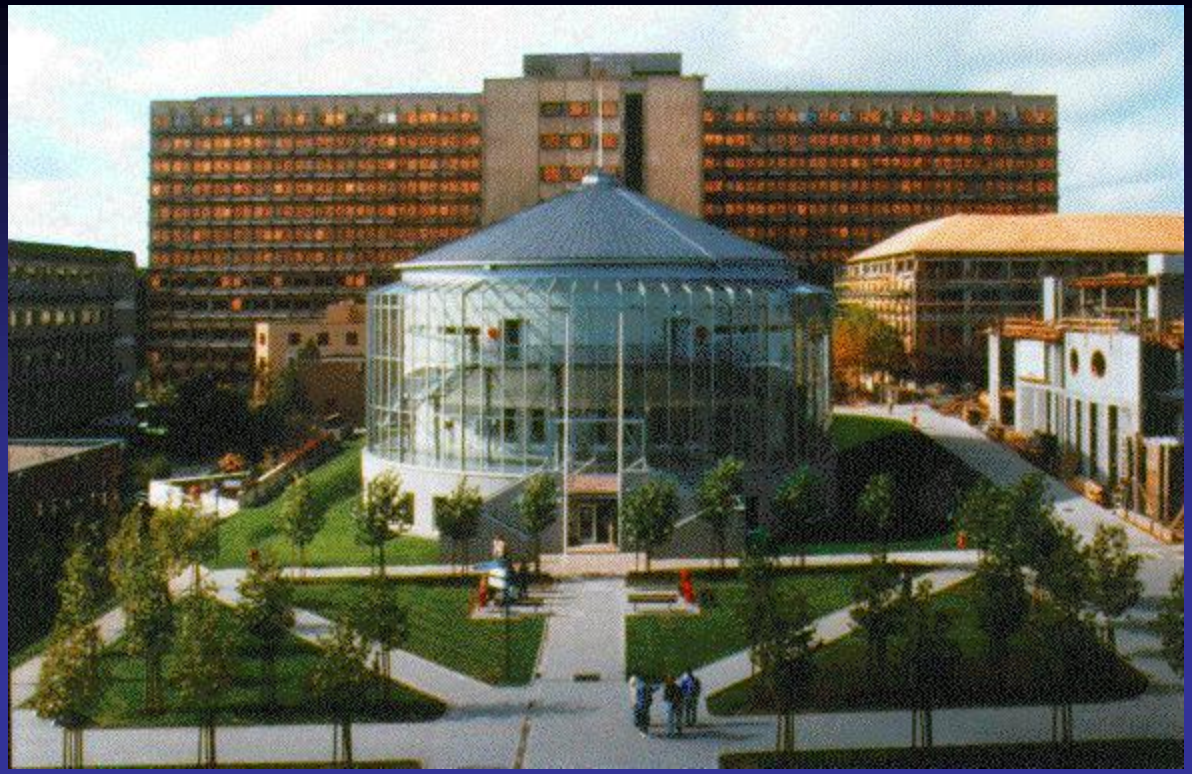


Microcirculation et sepsis

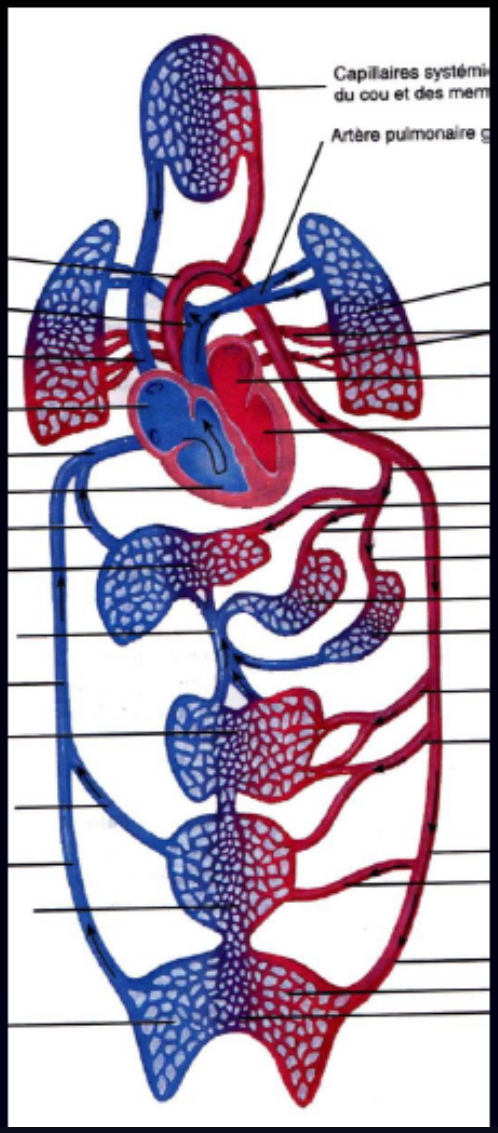
Pr Creteur J.
Service de Réanimation médico-chirurgicale
Hôpital universitaire Erasme - Université Libre de Bruxelles
Bruxelles Belgique

WHY COULD THE STUDY OF THE MICROCIRCULATION BE SO IMPORTANT?

WHY COULD THE STUDY OF THE MICROCIRCULATION BE SO IMPORTANT?

- **Primary site of gas and nutrient exchange**

Determinants of oxygen transport



- Heart to tissues: convection
  - Cardiac output
  - Arterial pressure
    (distribution of regional perfusion)
  - Arterial O2 content
- Within tissues: diffusion
  - Perfused microvascular density
  - Perfusion heterogeneity
  - Capillary 02 content

Goals of resuscitation

Goals of resuscitation

Restore adequate flow and pressure

Goals of resuscitation

Restore adequate flow and pressure

Restore and/or improve tissue perfusion

Goals of resuscitation

Restore adequate flow and pressure

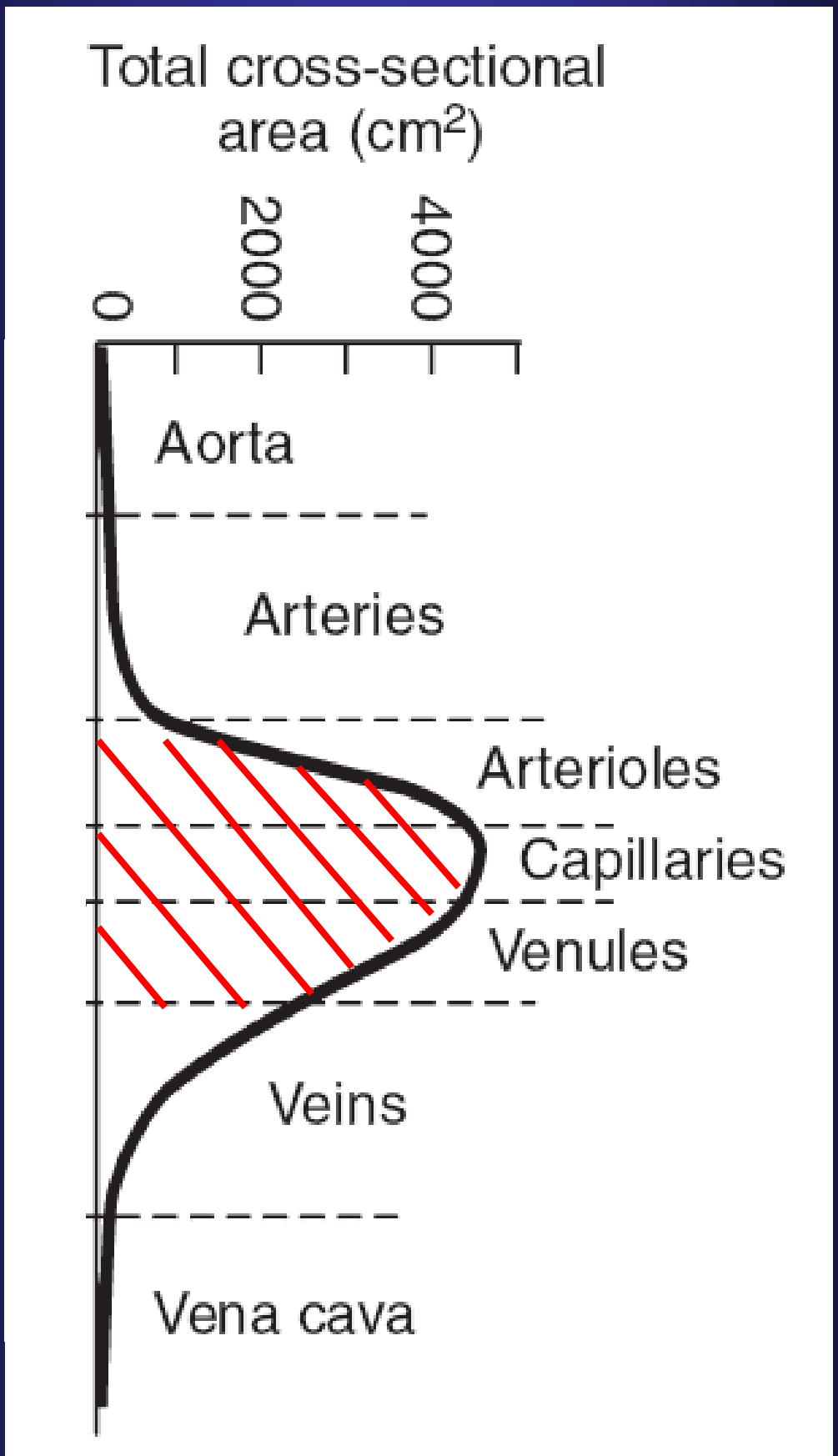
Restore and/or improve tissue perfusion

Make cells happy

WHY COULD THE STUDY OF THE MICROCIRCULATION BE SO IMPORTANT?

- Primary site of gas and nutrient exchange

- Largest endothelial surface of the body
  - Inflammation
  - Activation of coagulation

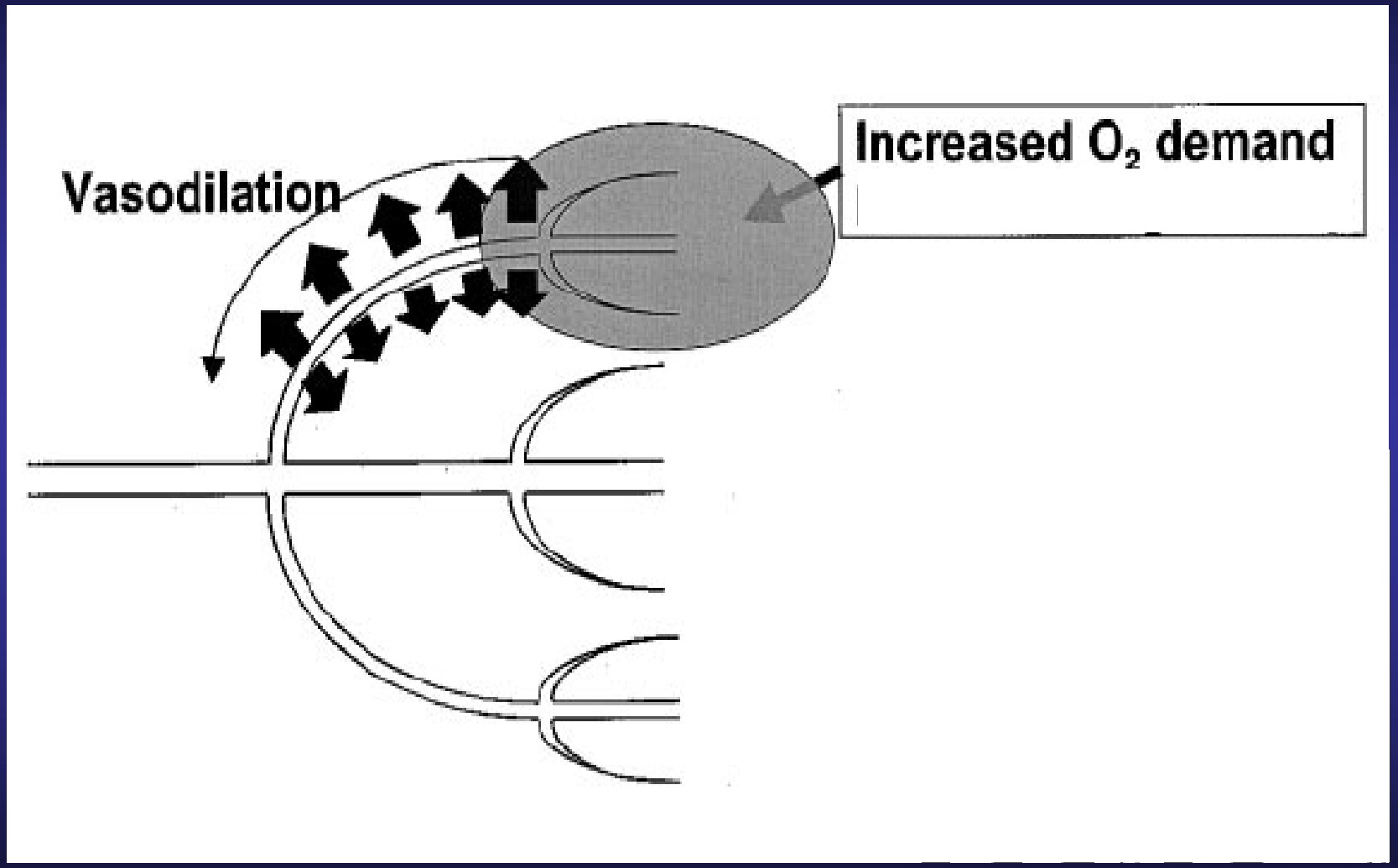

Total cross-sectional area (cm^2)
0
2000
4000
Aorta
Arteries
Arterioles
Capillaries
Venules
Veins
Vena cava

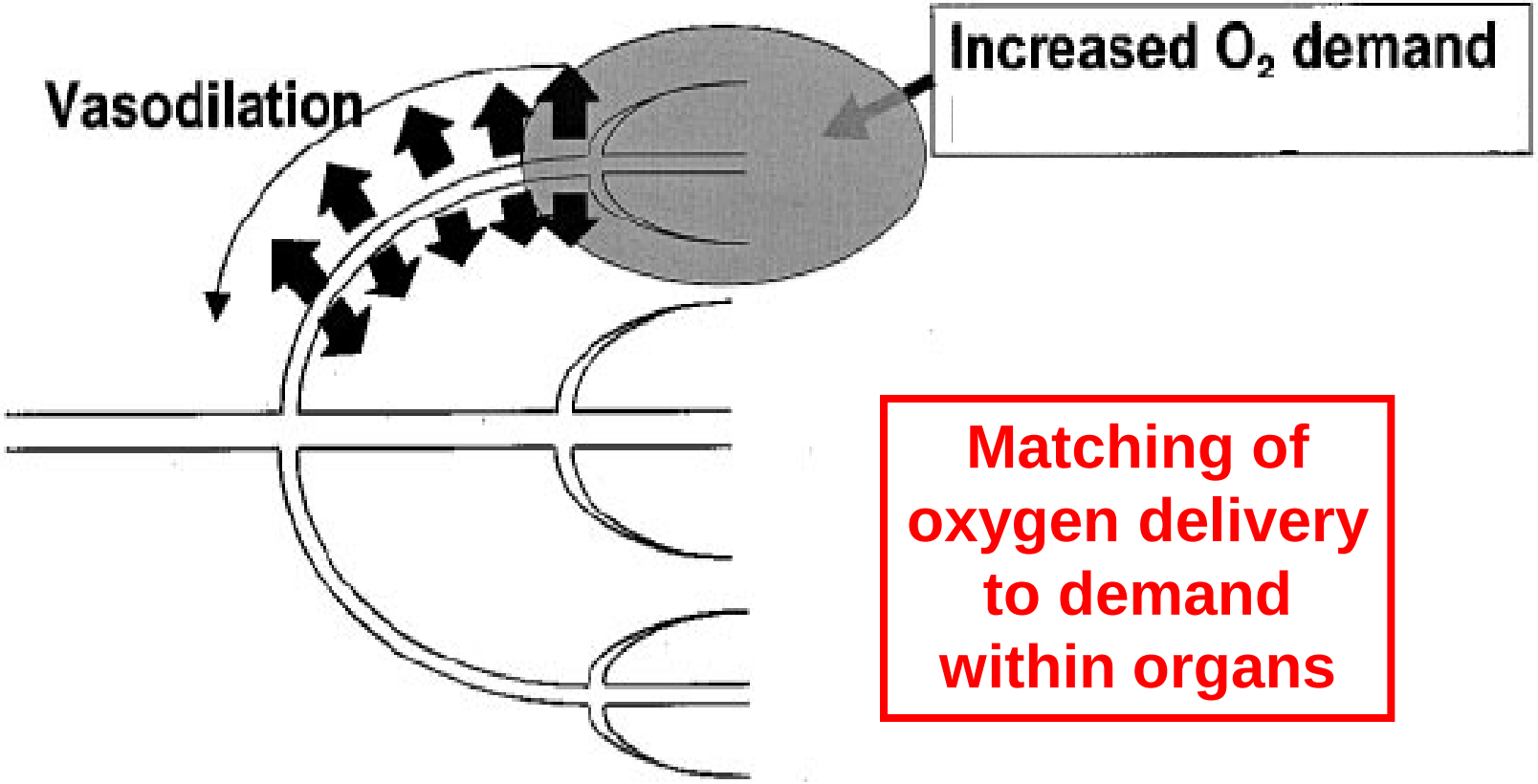
WHY COULD THE STUDY OF THE MICROCIRCULATION BE SO IMPORTANT?

- Primary site of gas and nutrient exchange

- Largest endothelial surface of the body
  - Inflammation
  - Activation of coagulation

- Independent functional system for distributing blood flow
  - Active regulation
  - Passive regulation

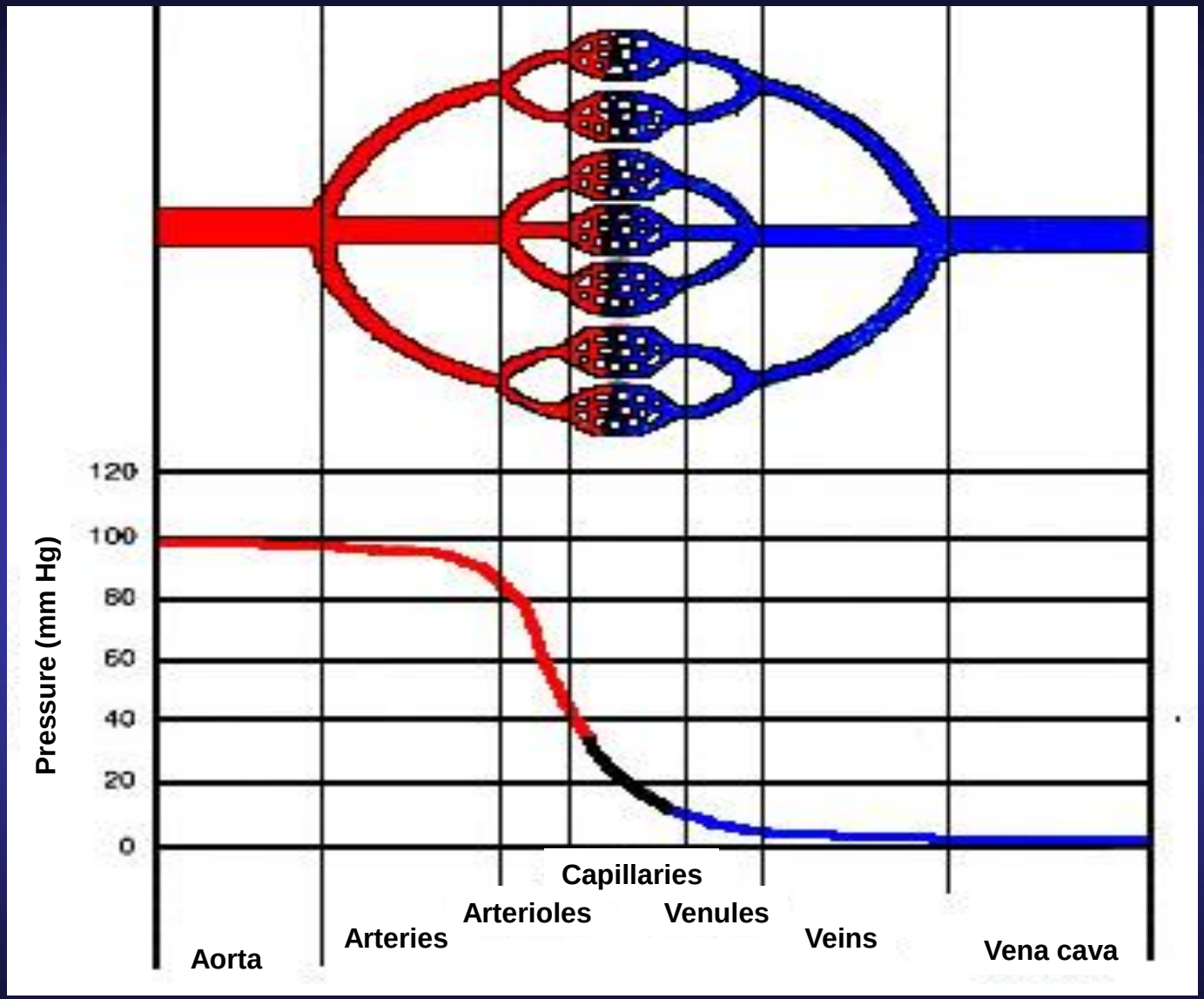

Vasodilation
Increased O_2 demand



Matching of oxygen delivery to demand within organs

- Independent functional system for distributing blood flow
  - Active regulation

- **Independent functional system for distributing blood flow**
  - **Active regulation**
    - **vascular tone of the resistance vessels (arteriolar network)**


Pressure (mm Hg)
120
100
80
60
40
20
0
Capillaries
Arterioles
Venules
Aorta
Arteries
Veins
Vena cava

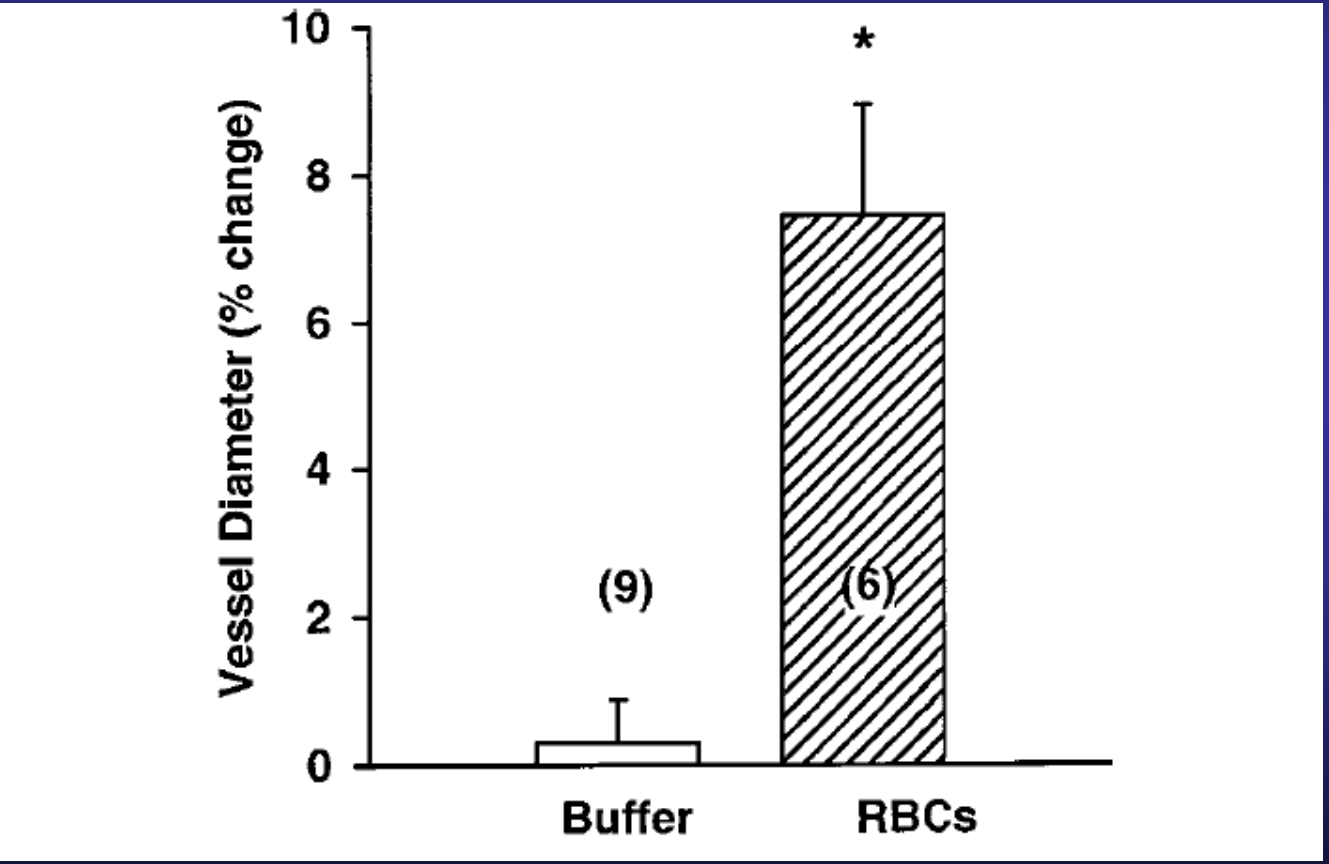
- **Independent functional system for distributing blood flow**
  - **Active regulation**
    - **vascular tone of the resistance vessels (arteriolar network)**
    - **integrated myoendothelial regulatory unit**

- **Independent functional system for distributing blood flow**
  - **Active regulation**
    - **vascular tone of the resistance vessels (arteriolar network)**
    - **integrated myoendothelial regulatory unit**
      - **oxygen sensors**

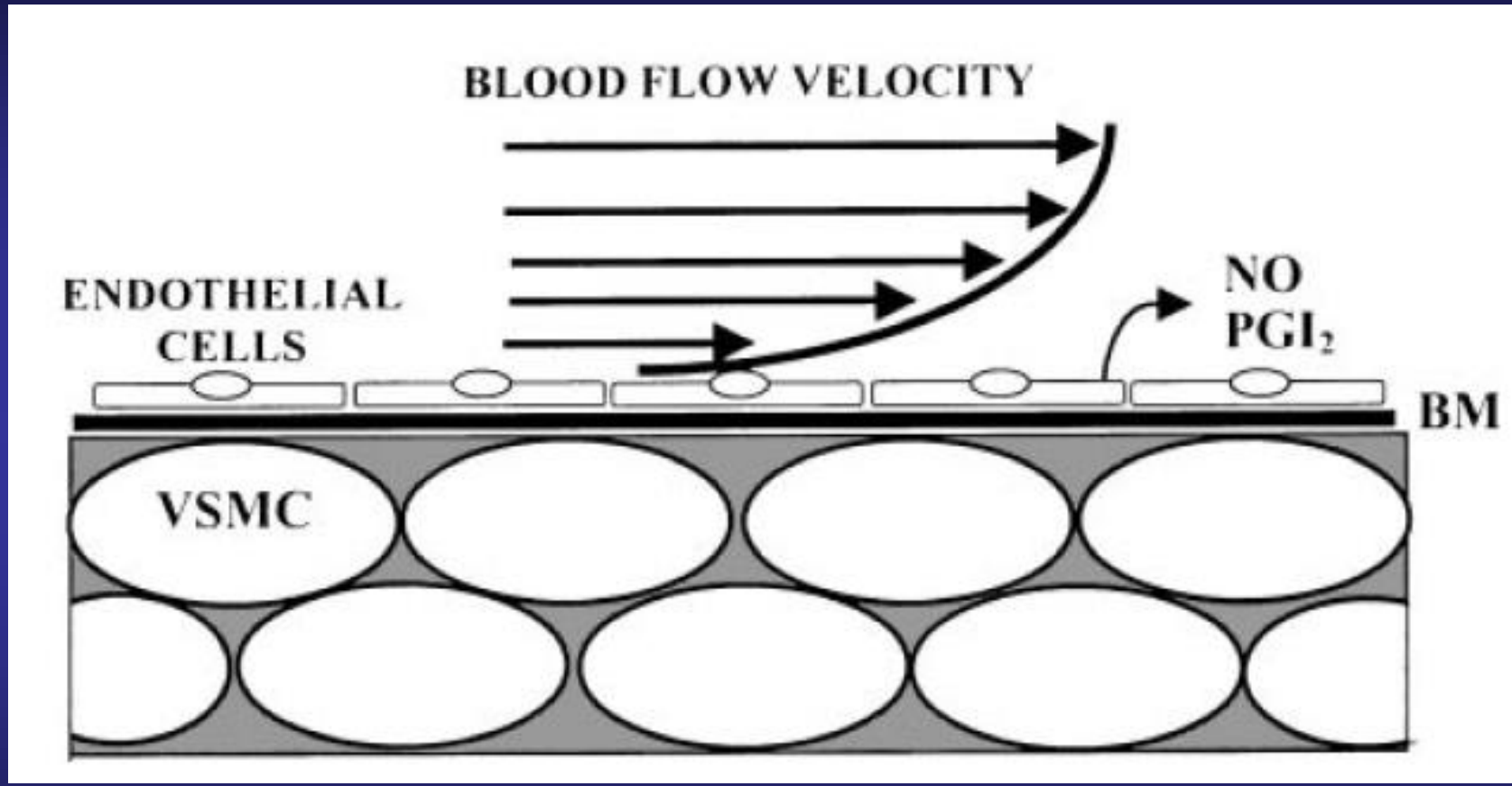
Hypoxic ATP release from RBCs and vessel dilation

Dietrich et al. Am J Physiol 2000 ; 278 : H1294

Isolated perfused cerebral arterioles of rats exposed to low extraluminal pO2

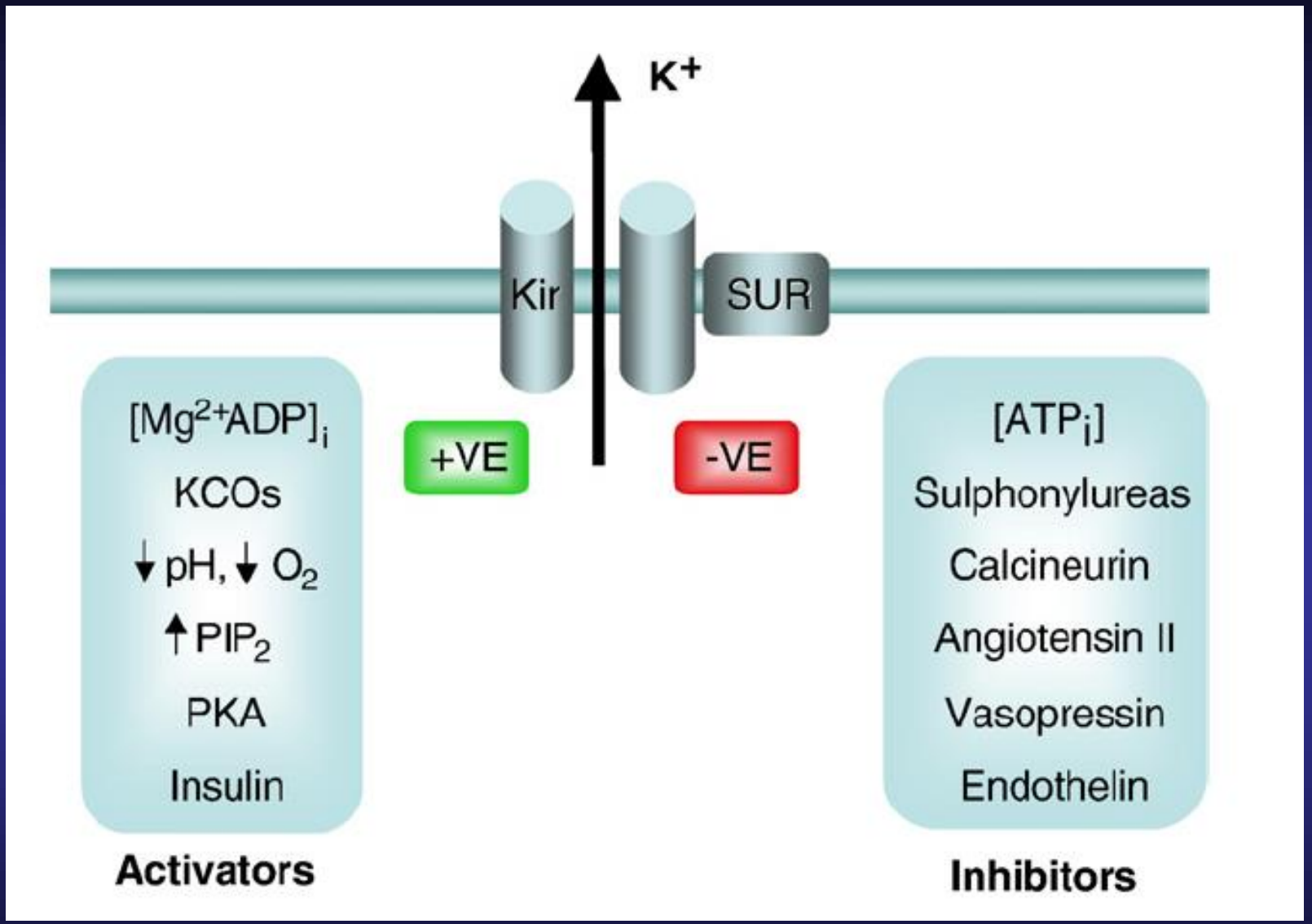


- **Independent functional system for distributing blood flow**
  - **Active regulation**
    - **vascular tone of the resistance vessels (arteriolar network)**
    - **integrated myoendothelial regulatory unit**
      - **oxygen sensors - shear stress**


BLOOD FLOW VELOCITY
ENDOTHELIAL CELLS
NO
PGI2
BM
VSMC

- **Independent functional system for distributing blood flow**
  - **Active regulation**
    - **vascular tone of the resistance vessels (arteriolar network)**
    - **integrated myoendothelial regulatory unit**
      - **oxygen sensors - shear stress**
      - **production of endothelium-derived vasoactive agents**

- **Independent functional system for distributing blood flow**
  - **Active regulation**
    - **vascular tone of the resistance vessels (arteriolar network)**
    - **integrated myoendothelial regulatory unit**
      - **oxygen sensors - shear stress**
      - **production of endothelium-derived vasoactive agents**
      - **K_{ATP} channels**


K+
Kir
SUR
+VE
-VE
[Mg2+ADP]i
KCOs
↓pH, ↓O2
↑PIP2
PKA
Insulin
Activators
[ATPi]
Sulphonylureas
Calcineurin
Angiotensin II
Vasopressin
Endothelin
Inhibitors

- **Independent functional system for distributing blood flow**

  - **Active regulation**

    - vascular tone of the resistance vessels (arteriolar network)

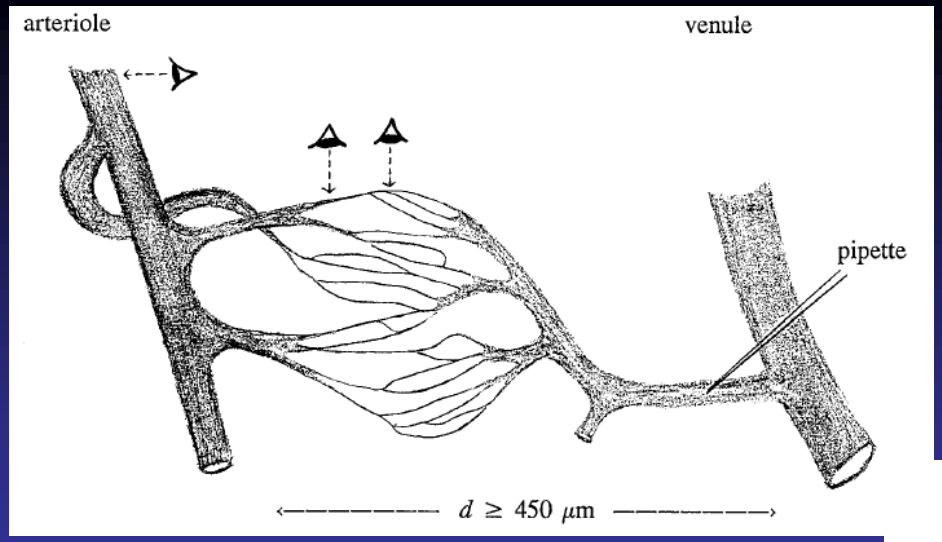
    - <u>integrated myoendothelial regulatory unit</u>

      - oxygen sensors - shear stress

      - production of endothelium-derived vasoactive agents

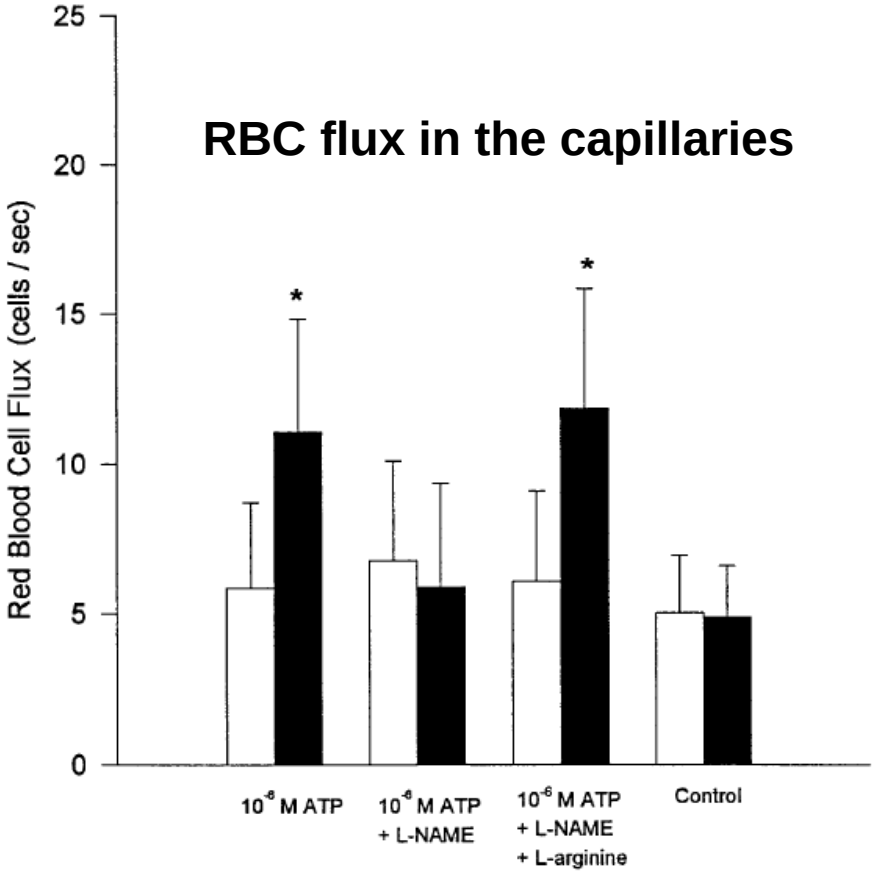
      - K_{ATP} channels

      - propagation of the information from the capillary endothelium onto the terminal arteriole (endothelial or smooth muscle gap junctions)



Conducted vascular response: Communication across the capillary bed

Collins et al. Microvascular Research 1999 ; 56 : 43



- **Independent functional system for distributing blood flow**
  - **Active regulation**
    - **vascular tone of the resistance vessels (arteriolar network)**
    - **integrated myoendothelial regulatory unit**
      - **oxygen sensors - shear stress**
      - **production of endothelium-derived vasoactive agents**
      - **K_{ATP} channels**
      - **propagation of the information from the capillary endothelium onto the terminal arteriole (endothelial or smooth muscle gap junctions)**
  - **Passive regulation**

- **Independent functional system for distributing blood flow**

  - **Active regulation**

    - vascular tone of the resistance vessels (arteriolar network)

    - integrated myoendothelial regulatory unit
      - oxygen sensors - shear stress
      - production of endothelium-derived vasoactive agents
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      - propagation of the information from the capillary endothelium onto the terminal arteriole (endothelial or smooth muscle gap junctions)

  - **Passive regulation**

    - local vessel resistance (diameter and length)

Poiseuille's law:

Flow in a capillary is

- proportional to

the driving pressure (ΔP)
the fourth power of the capillary radius (r)

- inversely proportional to

capillary length (L)
blood viscosity (η)

$$\text{Capillary flow} = \pi r^4 \Delta P / 8 L \eta$$

- **Independent functional system for distributing blood flow**

  - **Active regulation**

    - vascular tone of the resistance vessels (arteriolar network)

    - integrated myoendothelial regulatory unit
      - oxygen sensors - shear stress
      - production of endothelium-derived vasoactive agents
      - K_{ATP} channels
      - propagation of the information from the capillary endothelium onto the terminal arteriole (endothelial or smooth muscle gap junctions)

  - **Passive regulation**

    - local vessel resistance (diameter and length)

    - hemorheologic factors (blood viscosity, RBC deformability)

- **Independent functional system for distributing blood flow**

  - **Active regulation**

    - vascular tone of the resistance vessels (arteriolar network)

    - integrated myoendothelial regulatory unit
      - oxygen sensors - shear stress
      - production of endothelium-derived vasoactive agents
      - K_{ATP} channels
      - propagation of the information from the capillary endothelium onto the terminal arteriole (endothelial or smooth muscle gap junctions)

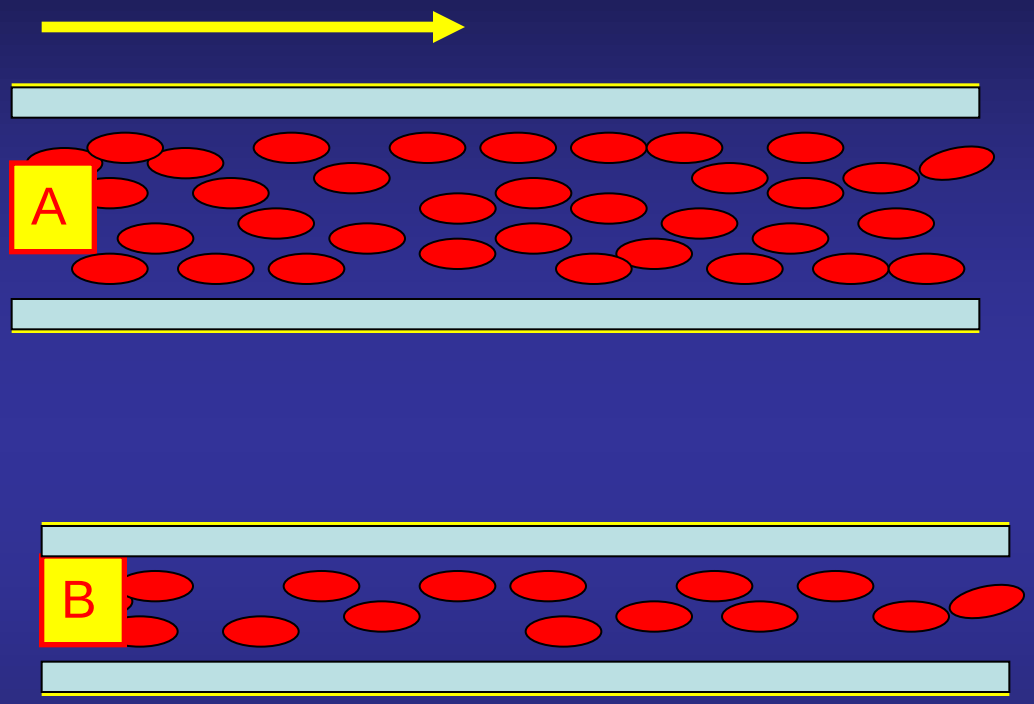
  - **Passive regulation**

    - local vessel resistance (diameter and length)

    - hemorheologic factors (blood viscosity, RBC deformability)

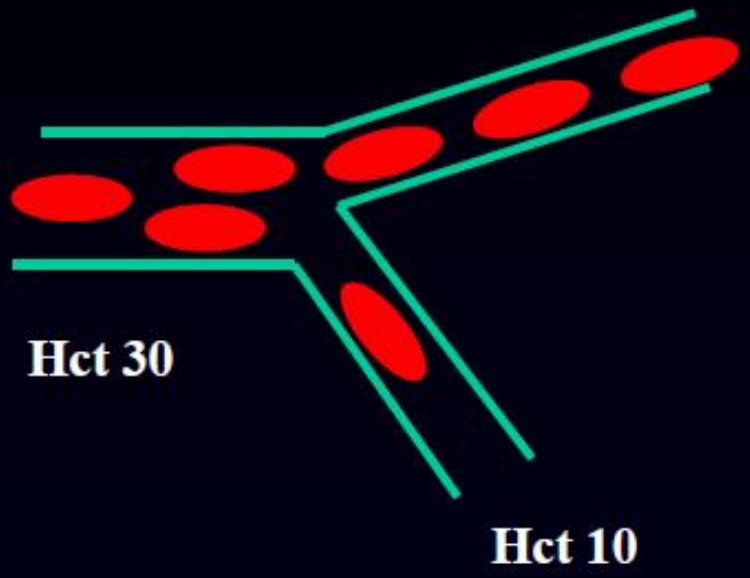
    - Farhaeus effect (i.e. the drop in vessel hematocrit along the arteriolar tree to the capillary bed)

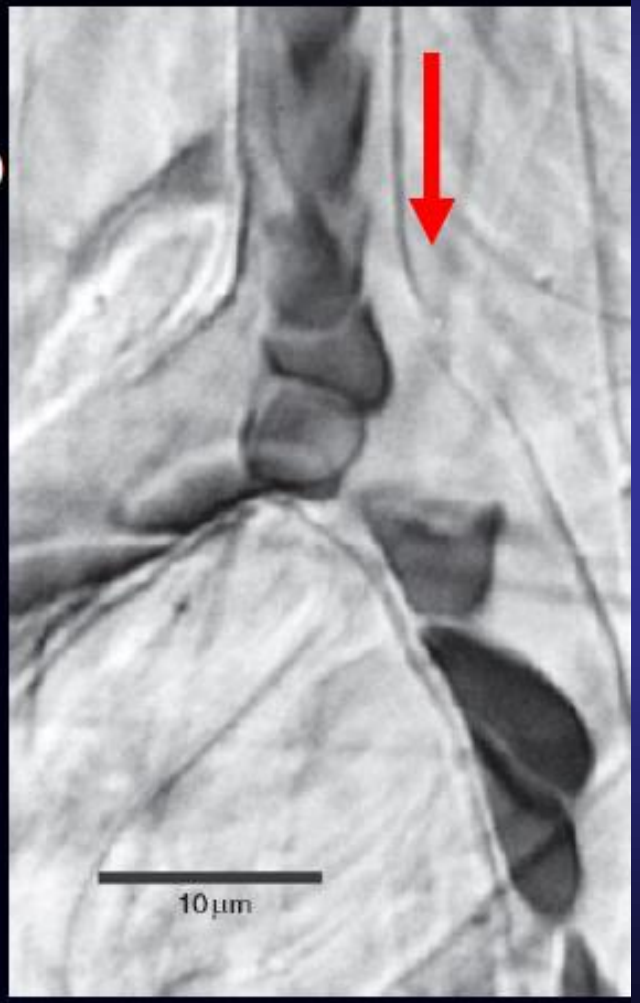
Flow



Hct A > Hct B

Due to kinetic inertia, red blood cells will preferentially go straightforward, accordingly the hematocrit will be lower in vessels with a large angle at origin.

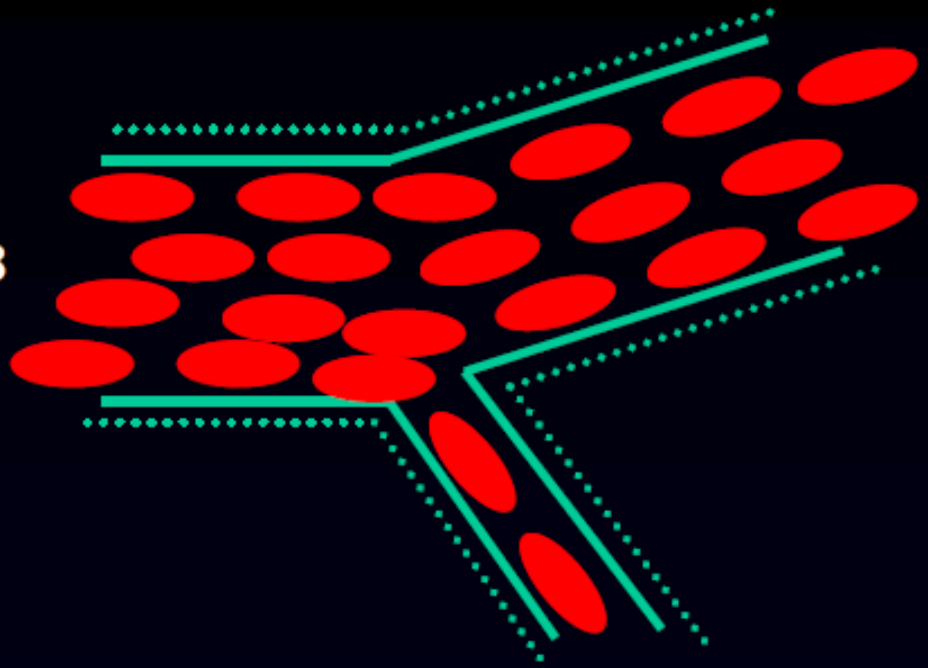




Cockelet et al
Microcirculation 2:1-18;1982

Heterogeneity of Hct at branchpoints

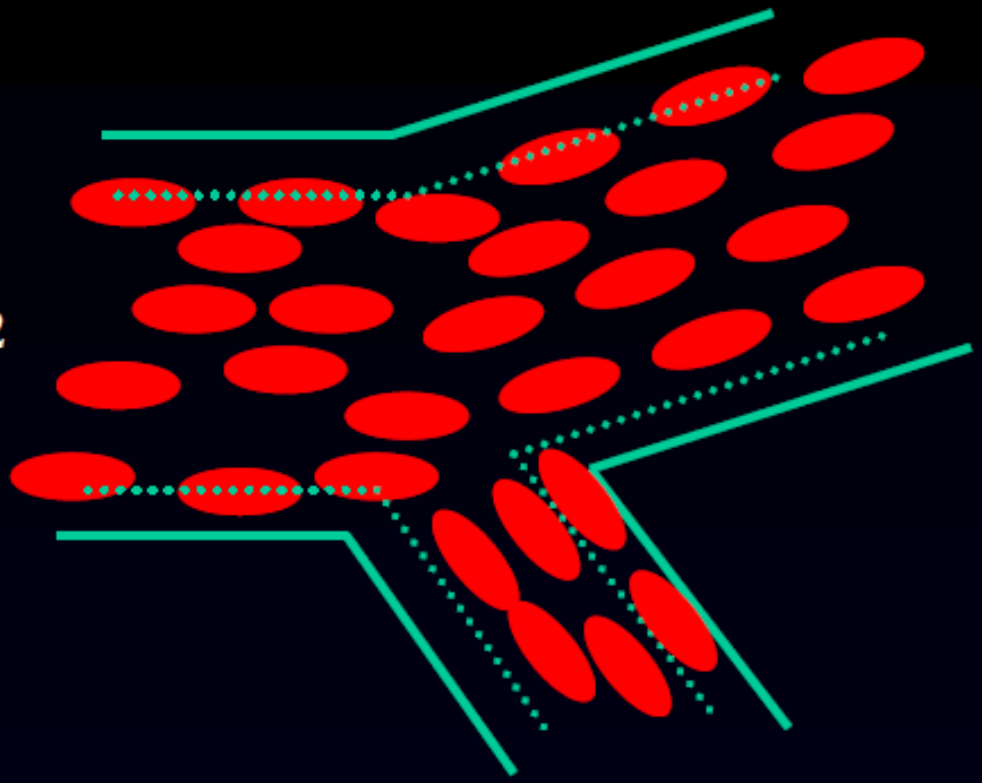
Impact of vasoconstriction



Decrease in Hct with vasoconstriction (especially in small vessels)

Heterogeneity of Hct at branchpoints

Impact of vasodilation



Increase in Hct with vasodilation (especially in small vessels)

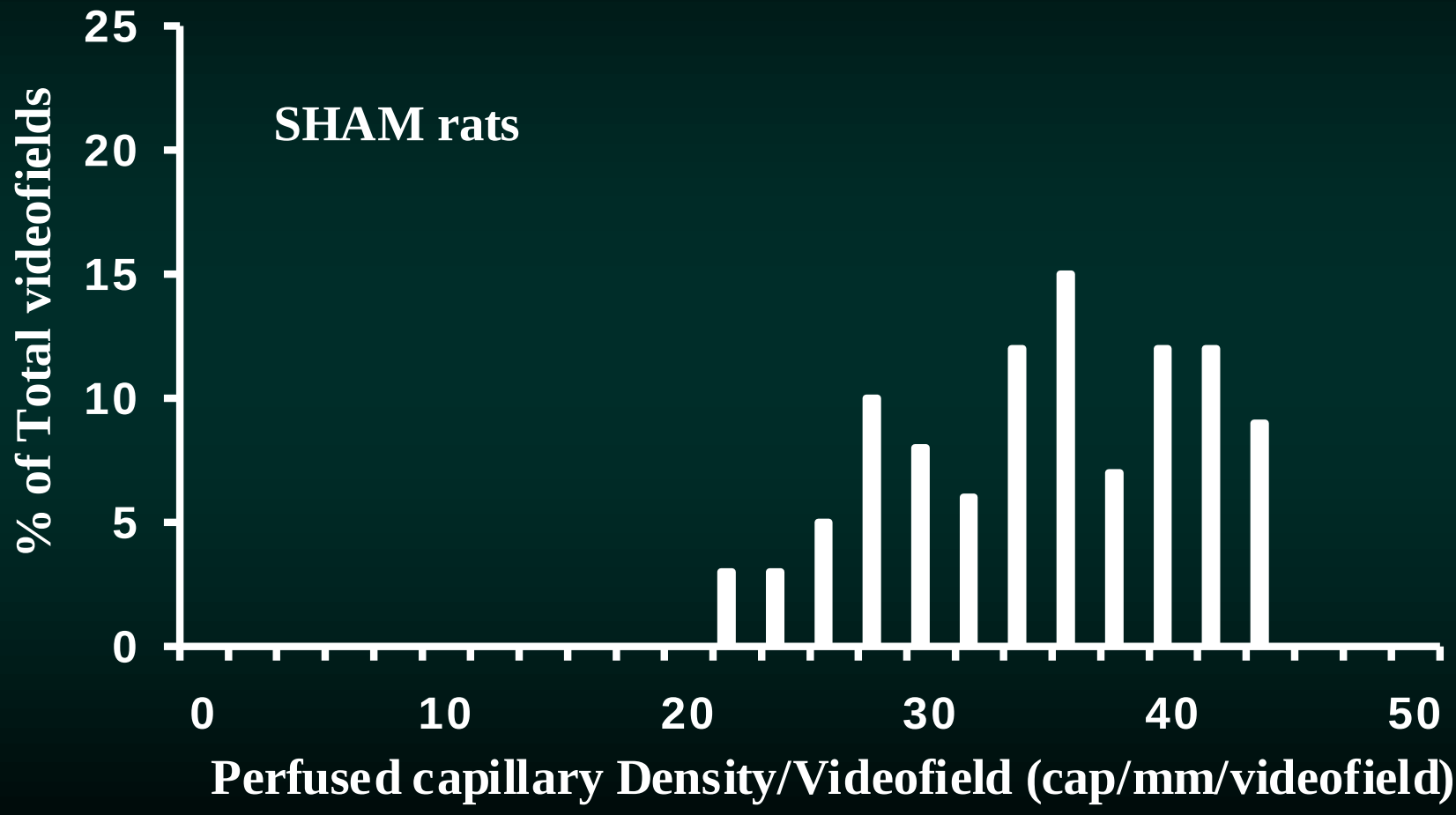
MICROCIRCULATORY ALTERATIONS IN SEPSIS

[redacted]

[redacted]

Alteration of microvascular perfusion in normotensive sepsis.

(Lam C, et al. J Clin Invest. 1996)



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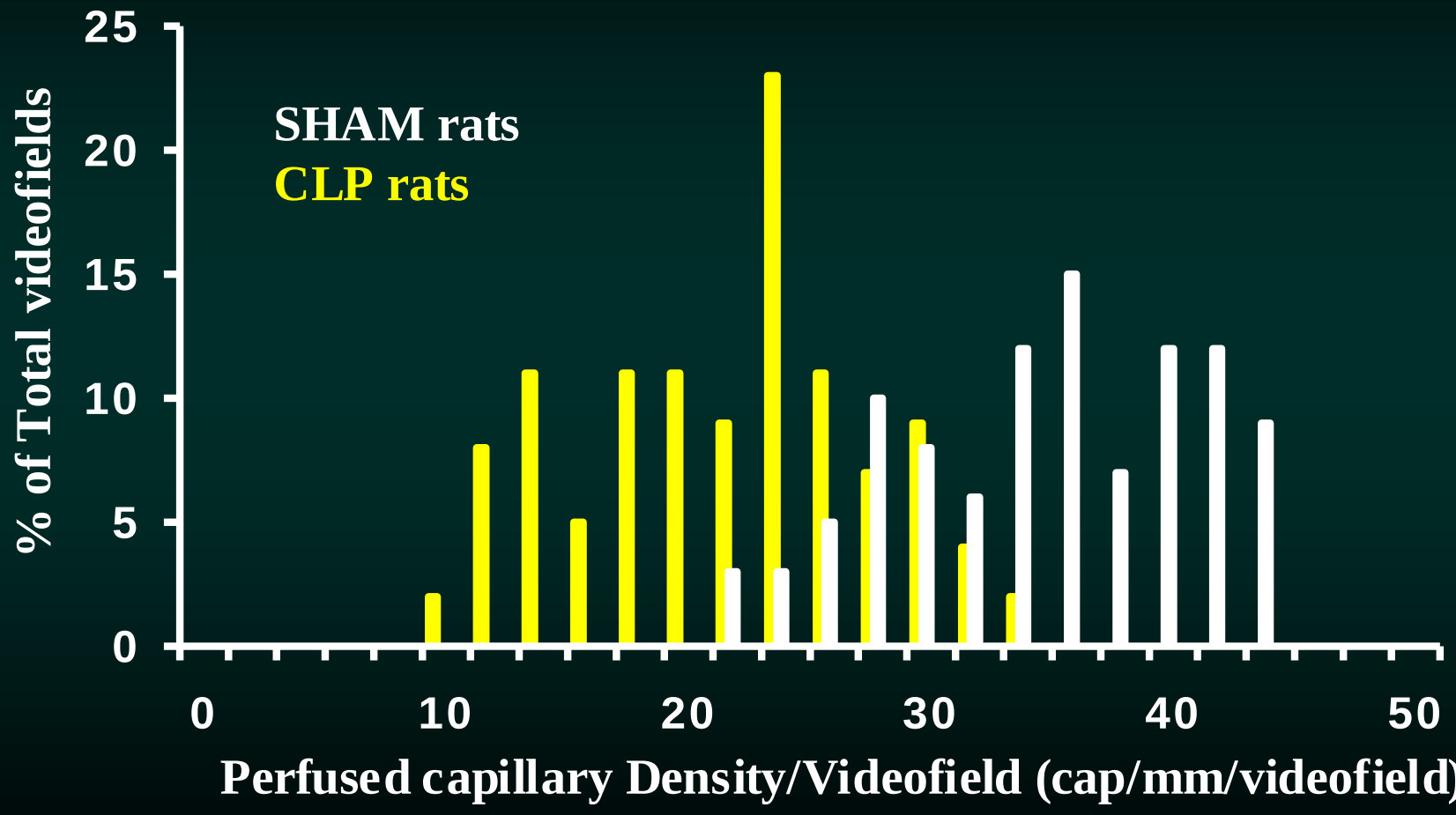
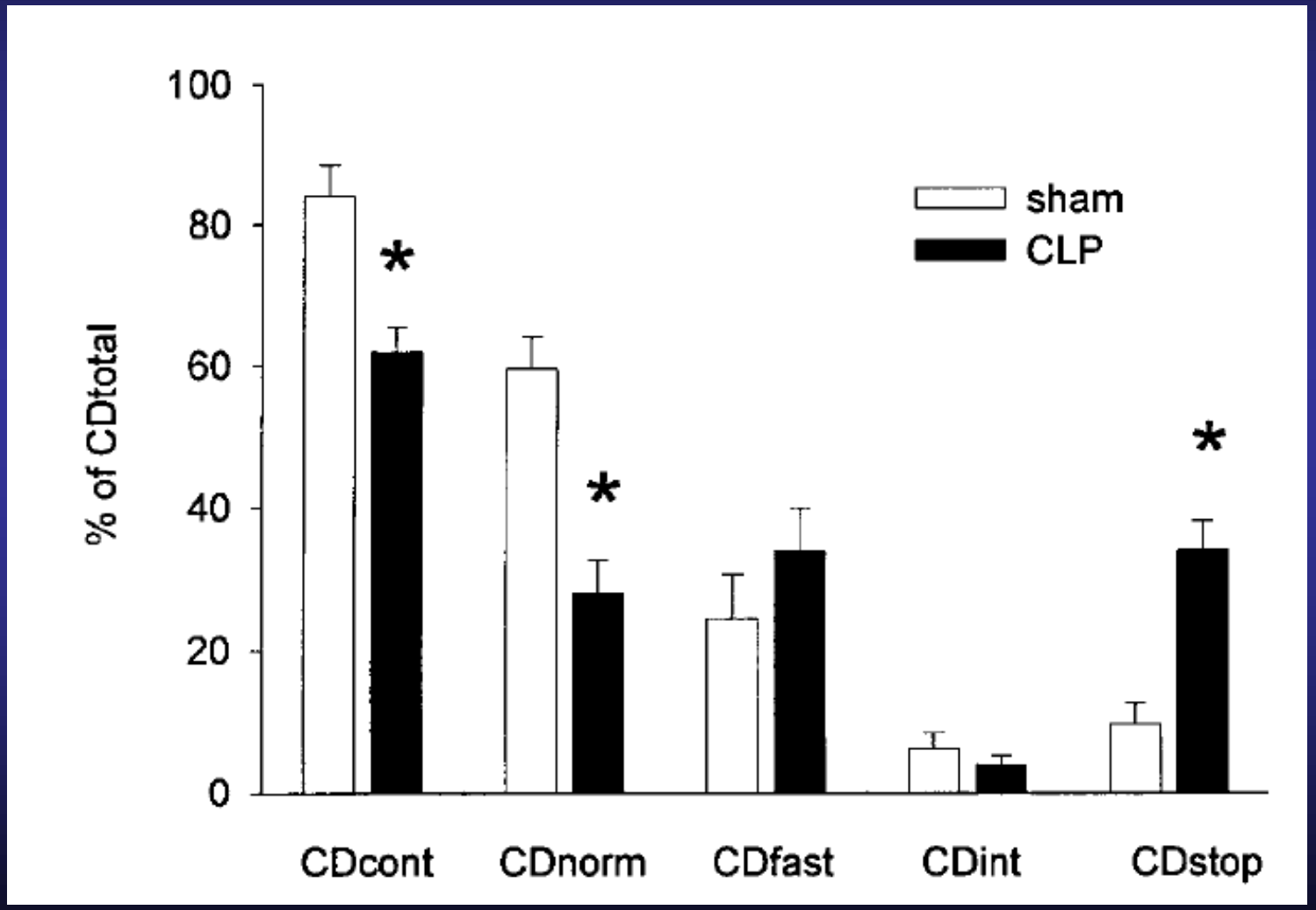


Rat – CLP – skeletal muscle

Ellis et al. Am J Physiol 2002 ; 282 : H156



Mechanisms that may be involved in the development of microcirculatory alterations in sepsis

Mechanisms that may be involved in the development of microcirculatory alterations in sepsis

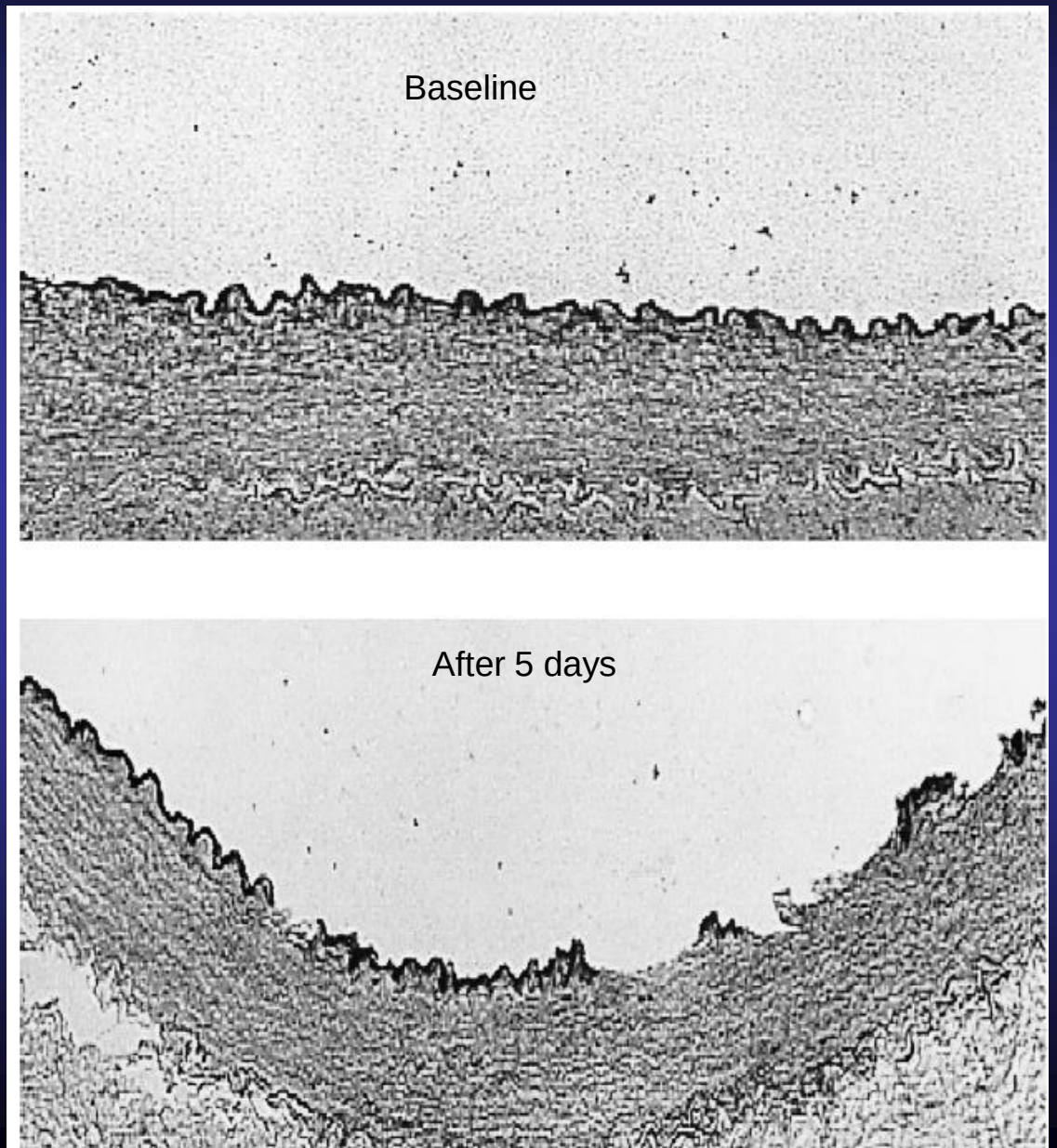
Endothelial dysfuntion

- decreased sensitivity to vasoconstricting and vasodilating substances
- alteration in communication between endothelial cells

Effect of a single EDTX dose on blood vessel function

Leclerc et al. Crit Care Med 2000 ; 28 : 3672

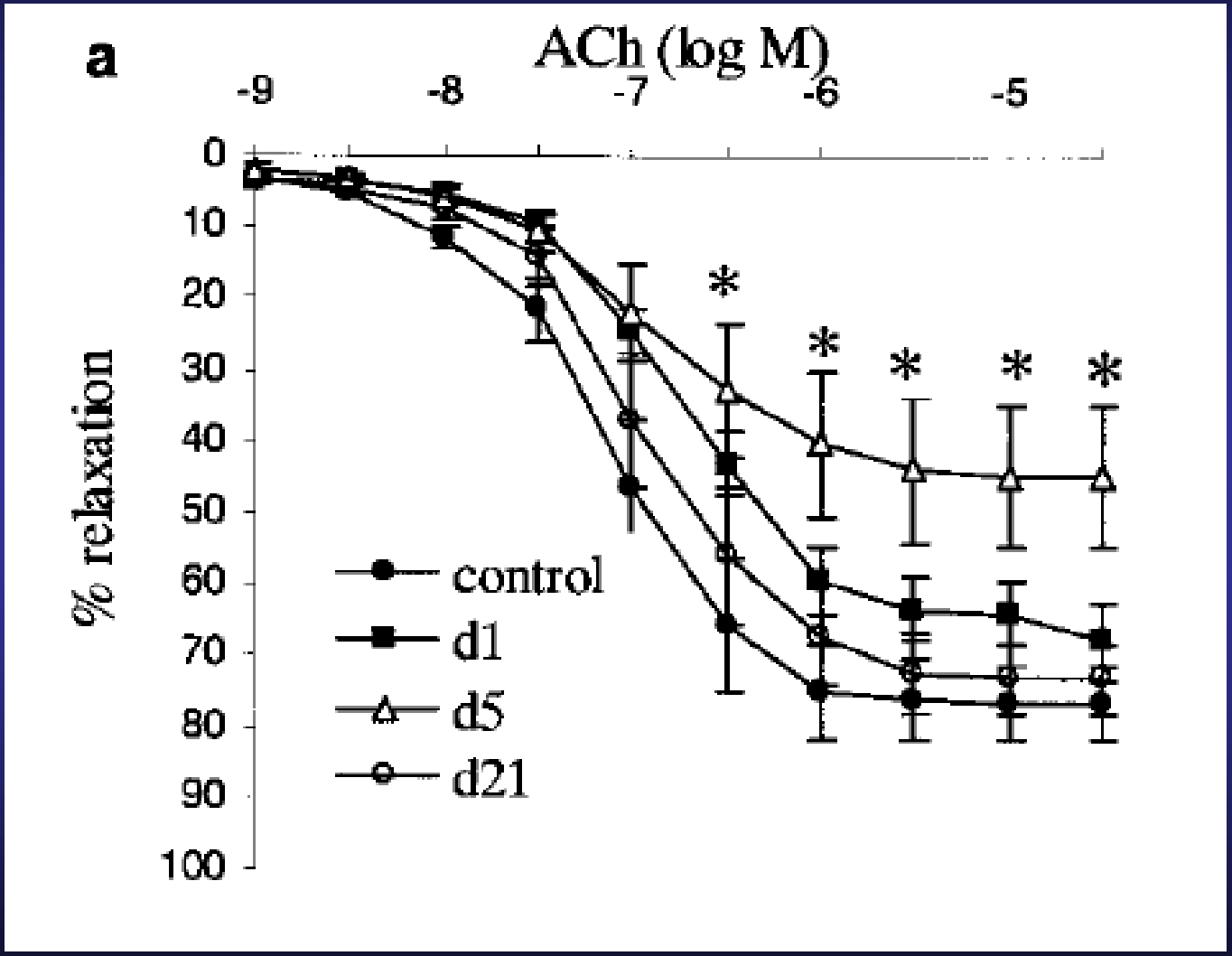
Rabbit
PECAM-1 antibodies



Effect of a single EDTX dose on blood vessel function

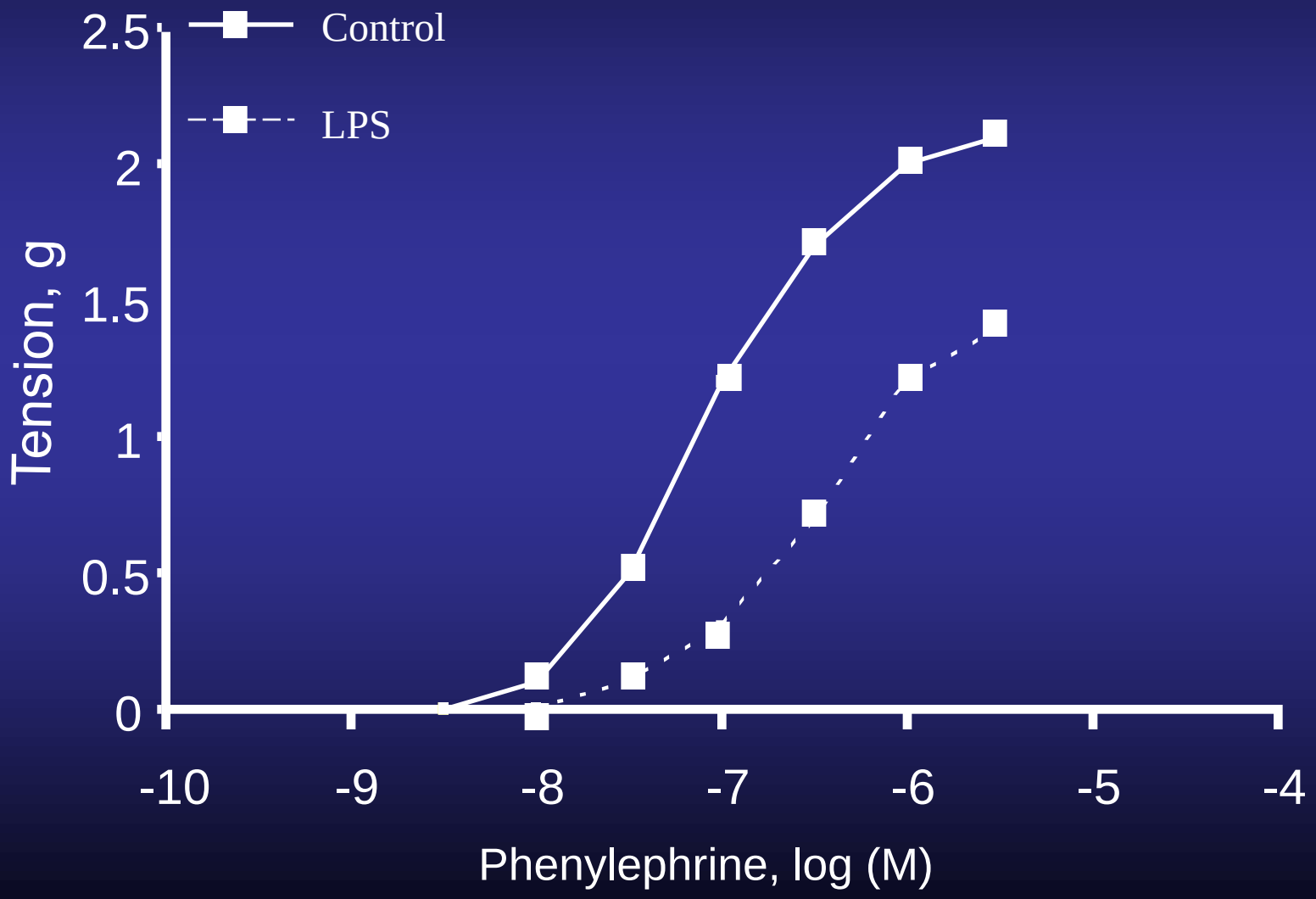
Leclerc et al. Crit Care Med 2000 ; 28 : 3672

Rabbit



Vascular reactivity of rat aorta incubated with endotoxin.

(Kilbourn RG, et al. Biochem Biophys Research Comm. 1994)

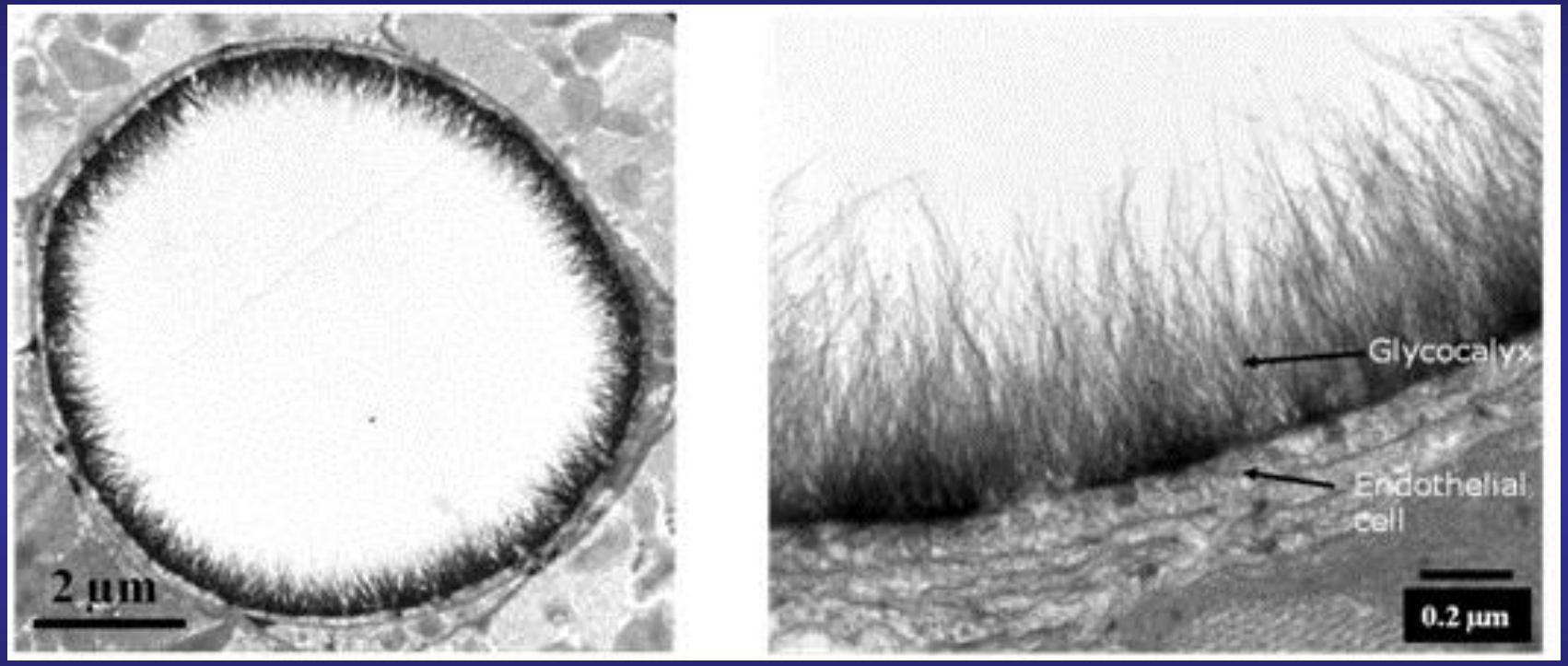


Mechanisms that may be involved in the development of microcirculatory alterations in sepsis

Endothelial dysfuntion

- decreased sensitivity to vasoconstricting and vasodilating substances
- alteration in communication between endothelial cells

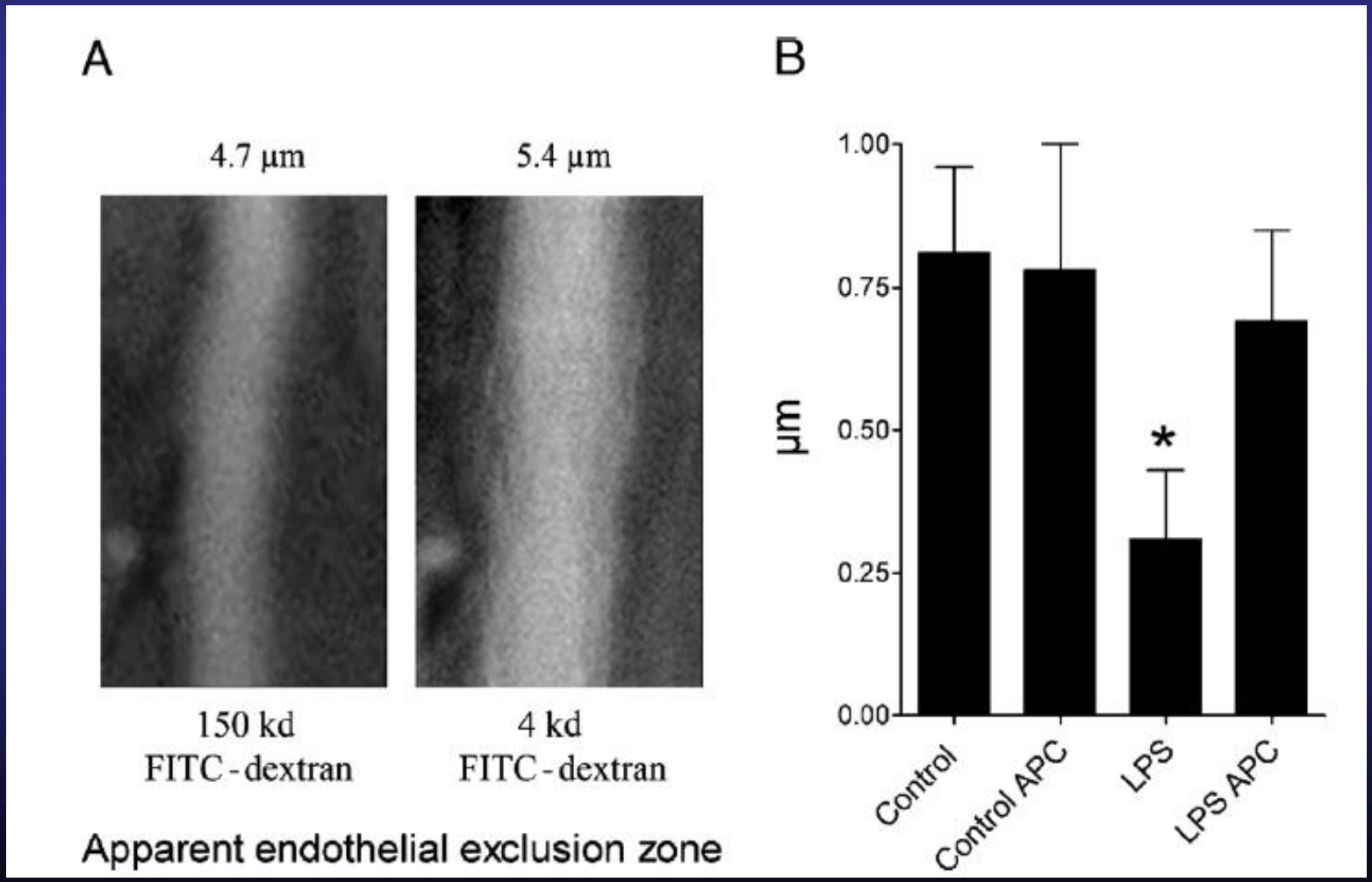
Glycocalyx alterations


2 µm
Glycocalyx
Endothelial cell
0.2 µm

Vascular oxidative stress and endothelial glycocalyx damage

Marechal et al. Shock 2008 ; 29 : 572-576

Rats - EDTX
Small intestine muscularis layer



Mechanisms that may be involved in the development of Microcirculatory alterations in sepsis

Endothelial dysfuntion

- decreased sensitivity to vasoconstricting and vasodilating substances
- alteration in communication between endothelial cells

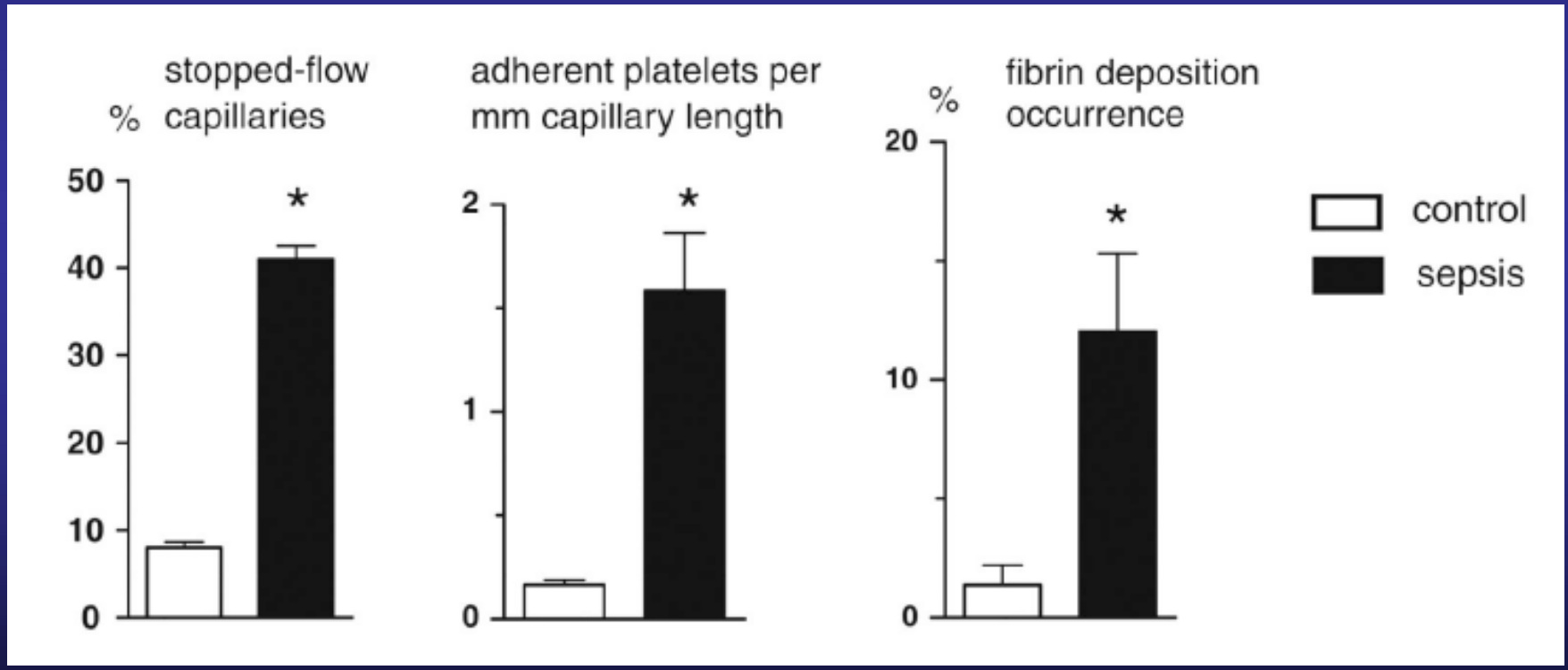
Glycocalyx alterations

Activation of coagulation

Impaired microvascular perfusion in sepsis requires activated coagulation and P-selectin-mediated platelet adhesion in capillaries

Secor et al. Intensive Care Med 2010, 36:1928-1934

Mice - injection of feces into the peritoneum.



Mechanisms that may be involved in the development of Microcirculatory alterations in sepsis

Endothelial dysfuntion

- decreased sensitivity to vasoconstricting and vasodilating substances
- alteration in communication between endothelial cells

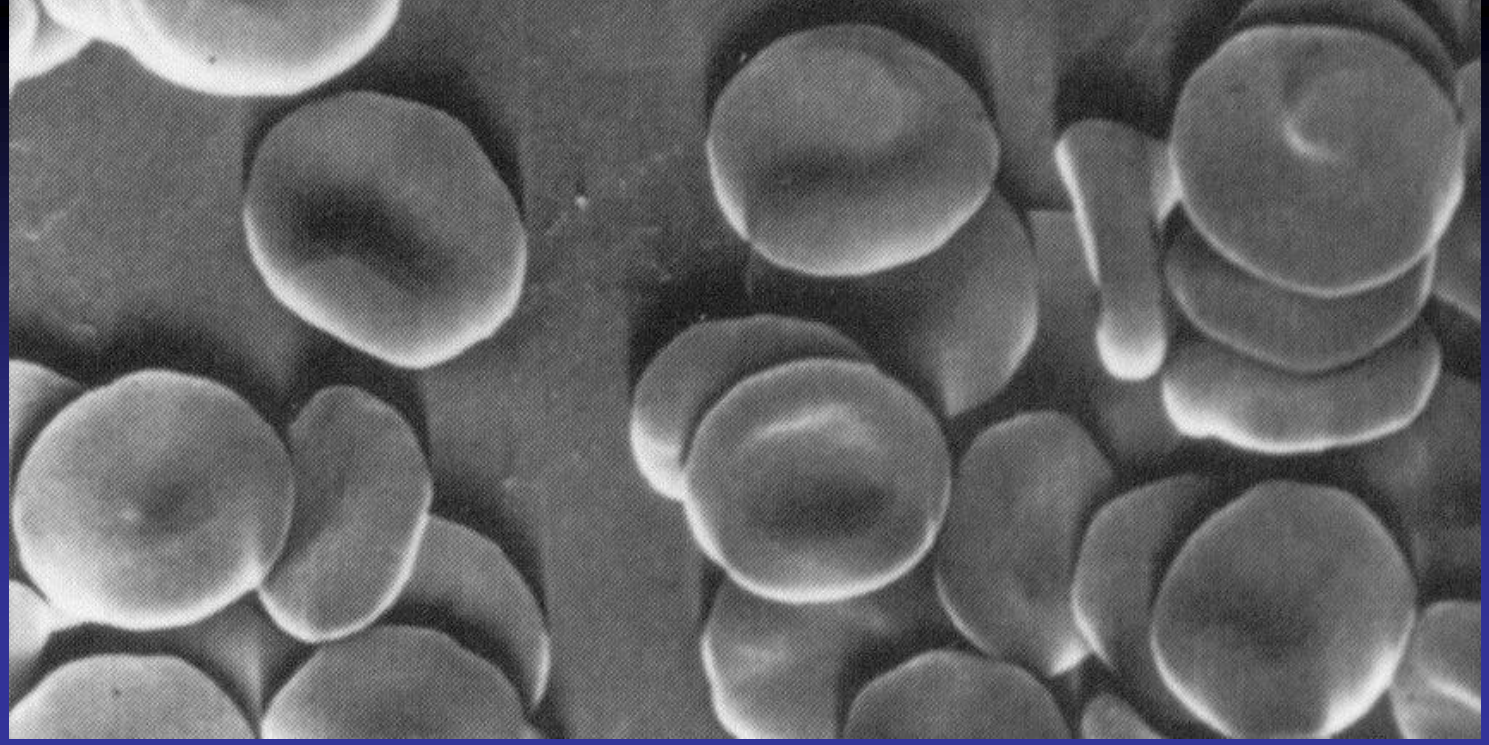
Glycocalyx alterations

Activation of coagulation

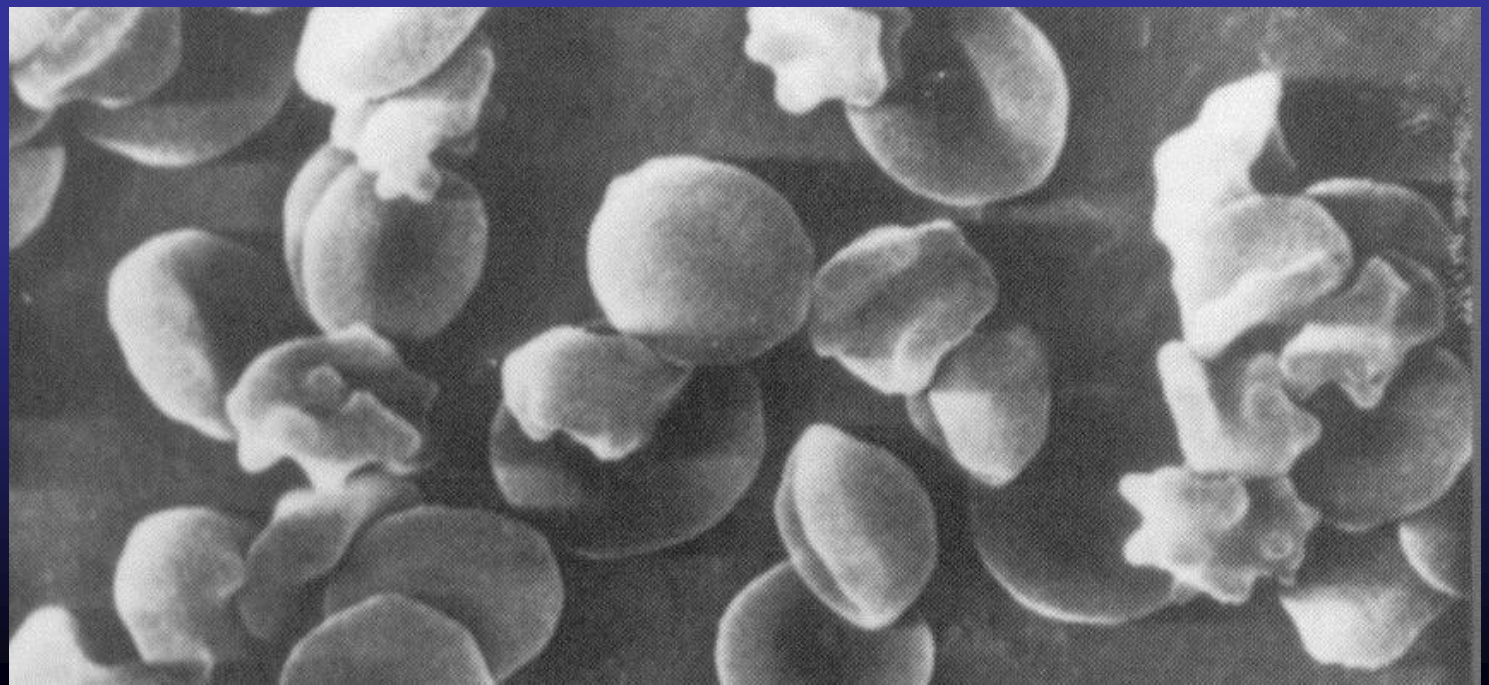
Interactions with circulating cells

- Leukocyte rolling and adhesion
- Platelets rolling and adhesion
- Alterations of RBC deformability

CONTROLE



SEPSIS



[illegible]

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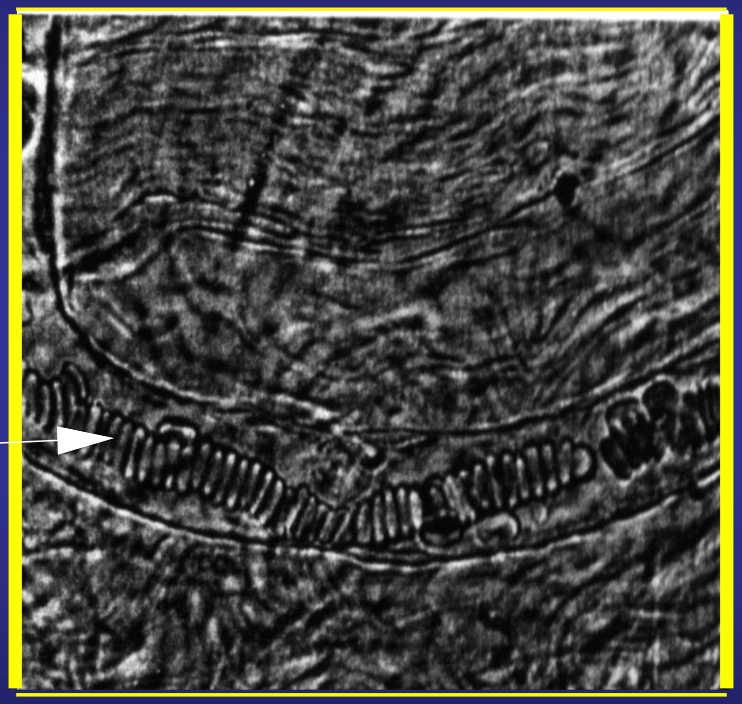


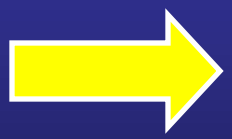
[illegible]

[illegible]

[illegible]

STUDIES ON HUMAN SUBLINGUAL MICROCIRCULATION IN SEPSIS

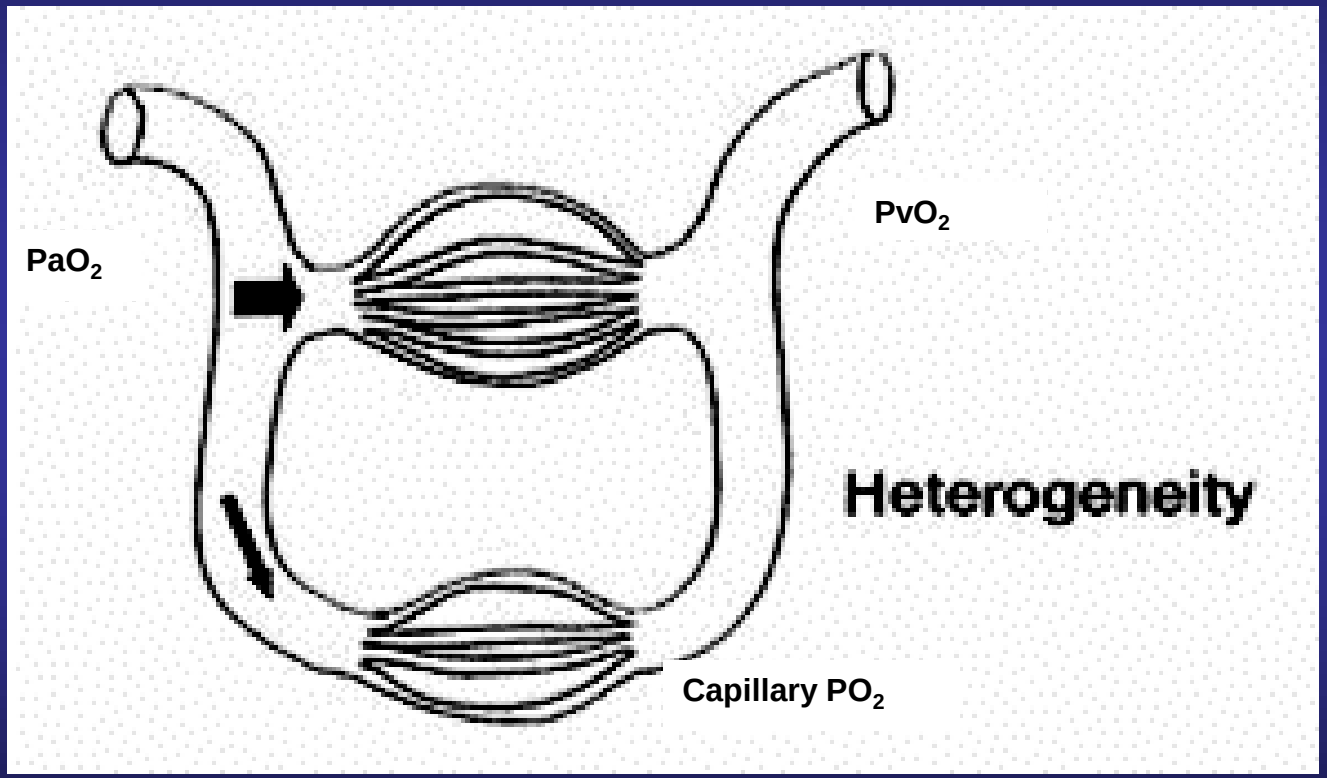
- Decrease in microvascular density
- Decrease in the proportion of perfused capillaries
- Increase in heterogeneity between areas



TISSUE HYPOXIA

Microcirculatory oxygenation and shunting in sepsis and septic shock

After Ince et al. Crit Care Med 1999; 27:1369-1377



Microcirculatory oxygenation and shunting in sepsis and septic shock

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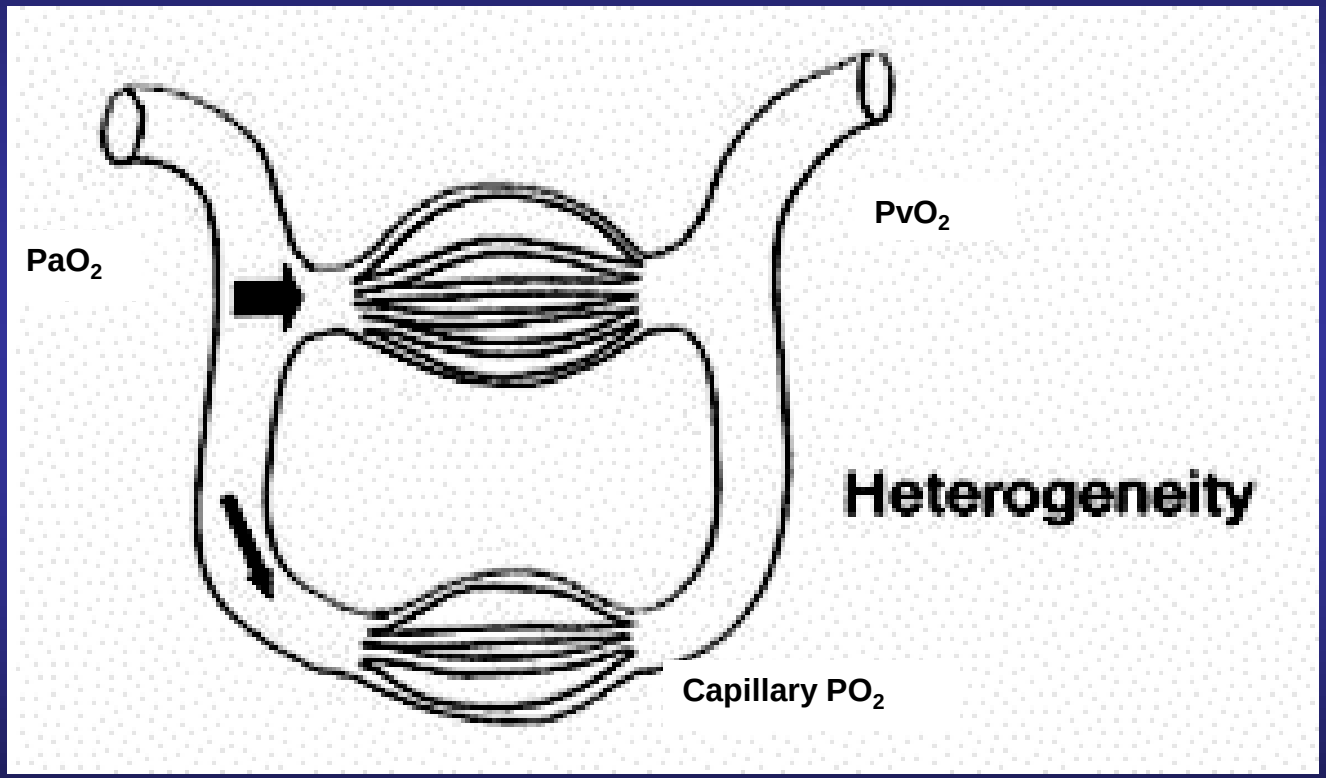


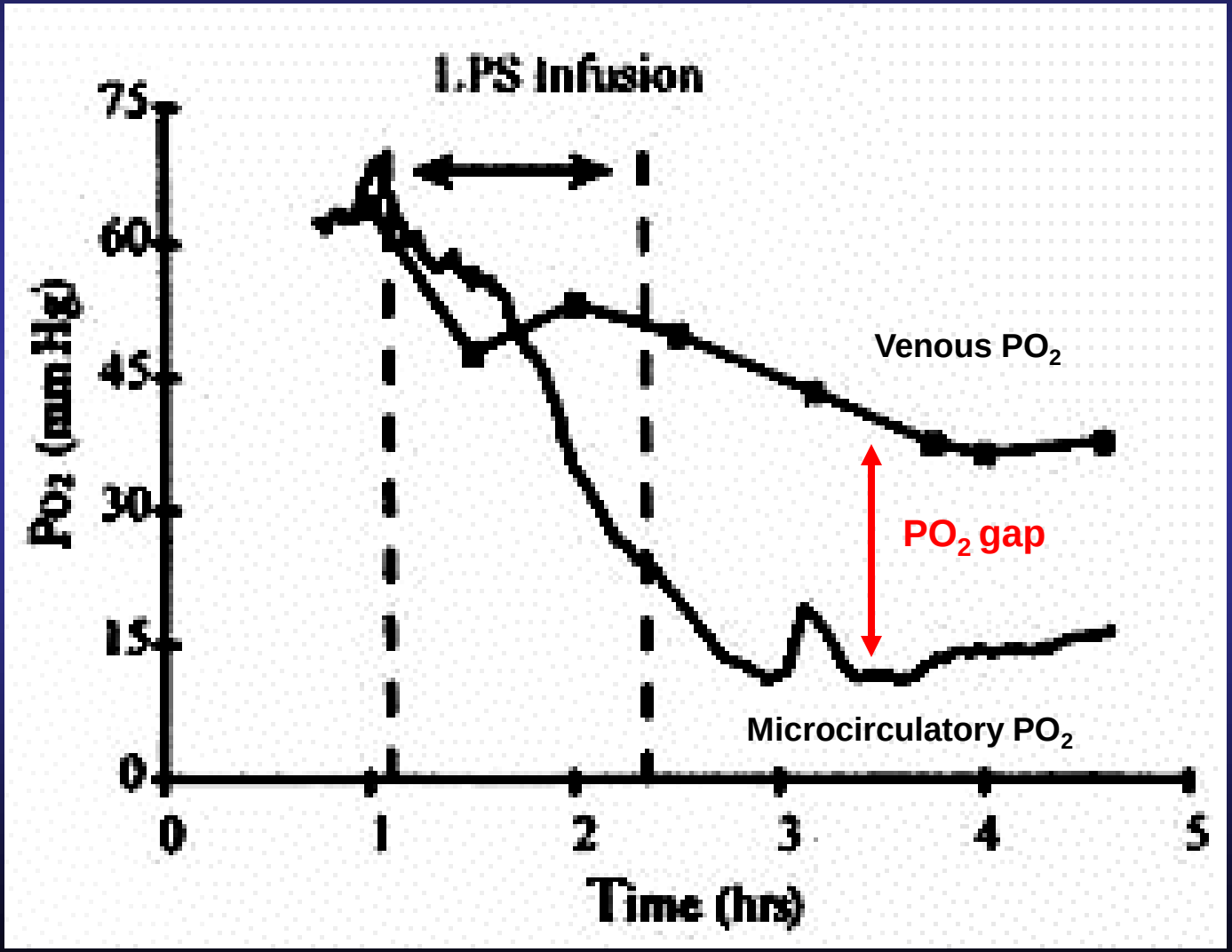
PvO_2 > Capillary PO_2

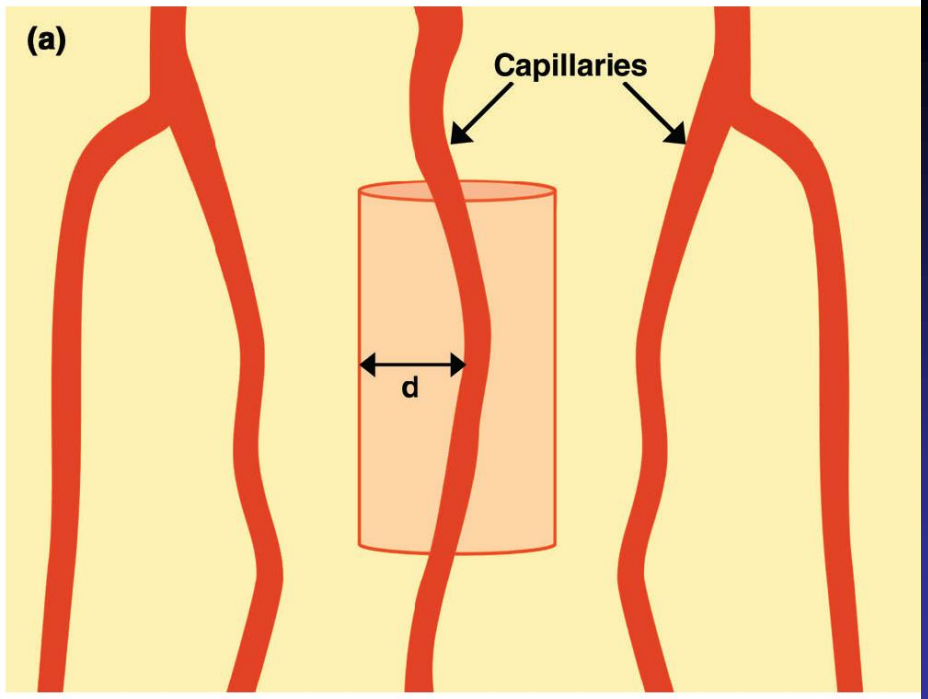
Microcirculatory oxygenation and shunting in sepsis and septic shock

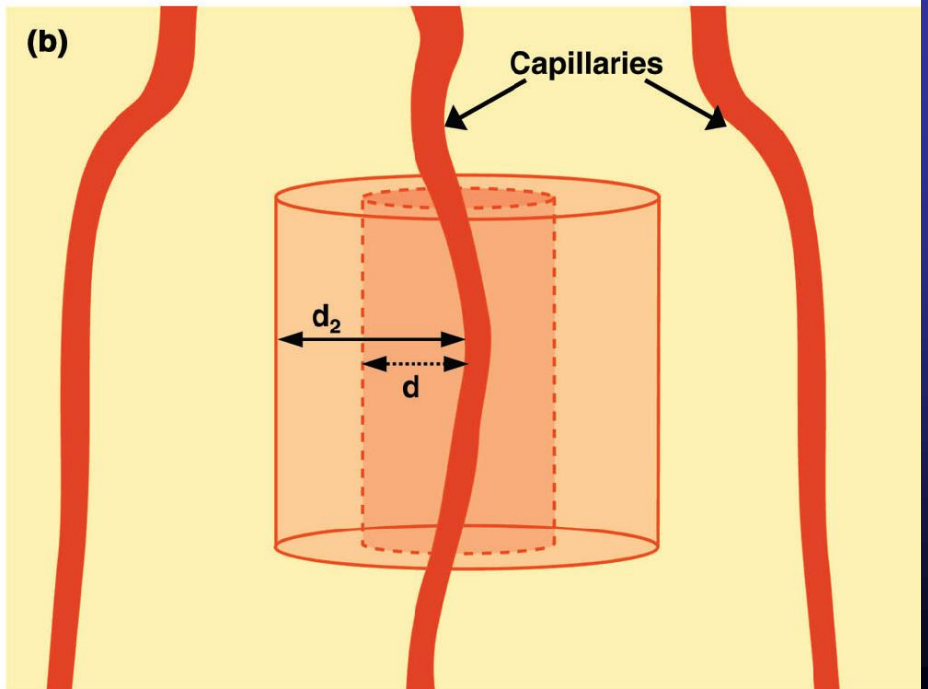
Ince et al. Crit Care Med 1999; 27:1369-1377

Pig ileum

Pd-porphyrin phosphorescence

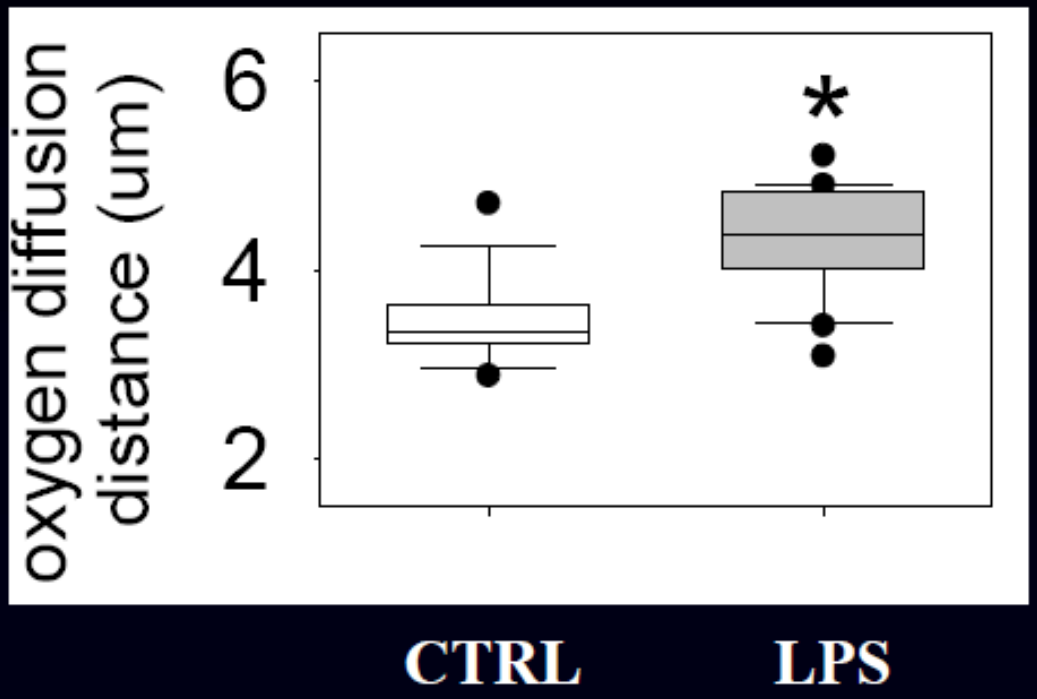



(a)
Capillaries
d


(b)
Capillaries
d_2
d

Consequences…

Bateman et al
AJP 293/H448;2007

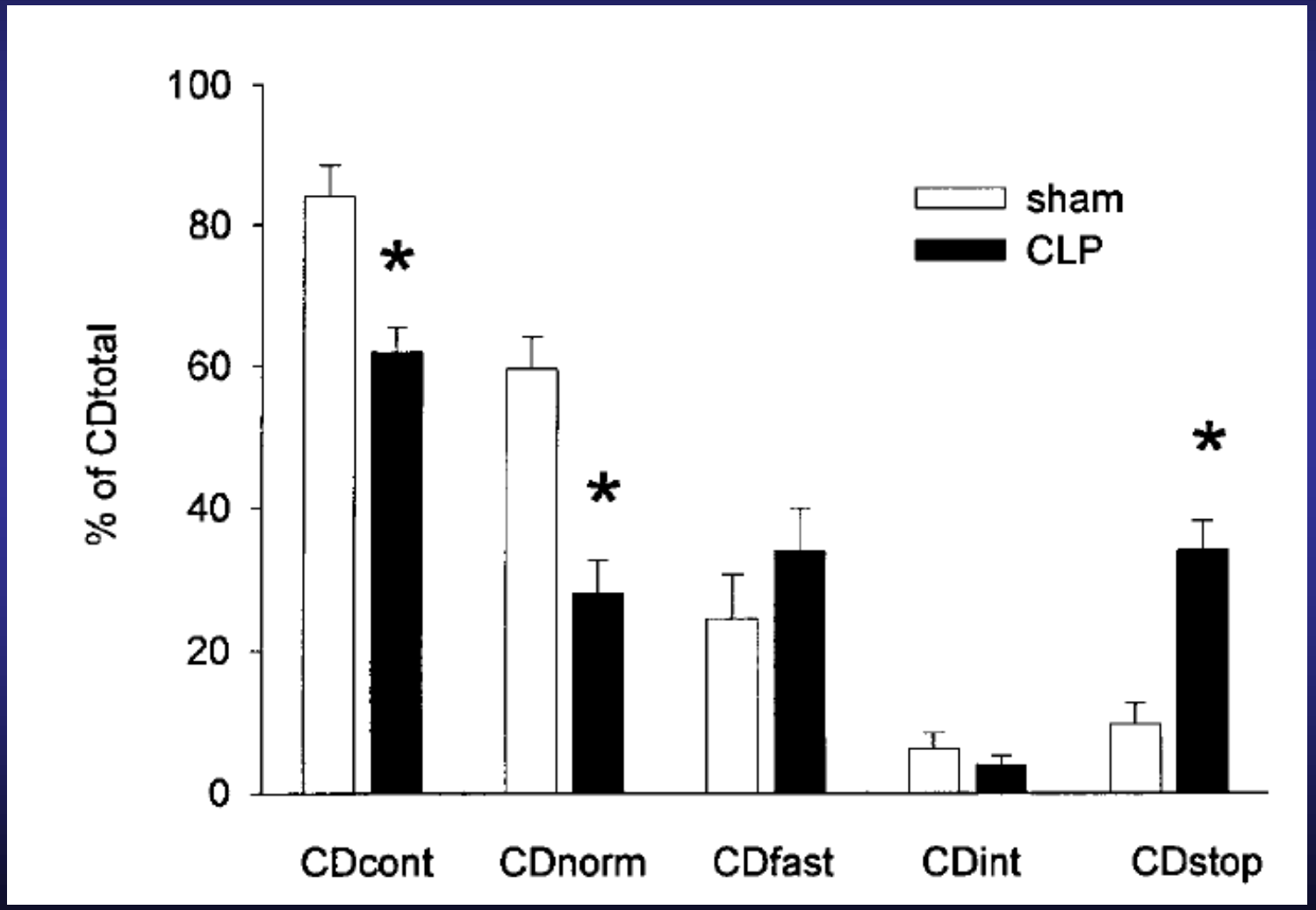


Cardiomyocytes rats

Capillary O2 extraction in sepsis

Ellis et al. Am J Physiol 2002 ; 282 : H156

Rat – CLP – skeletal muscle



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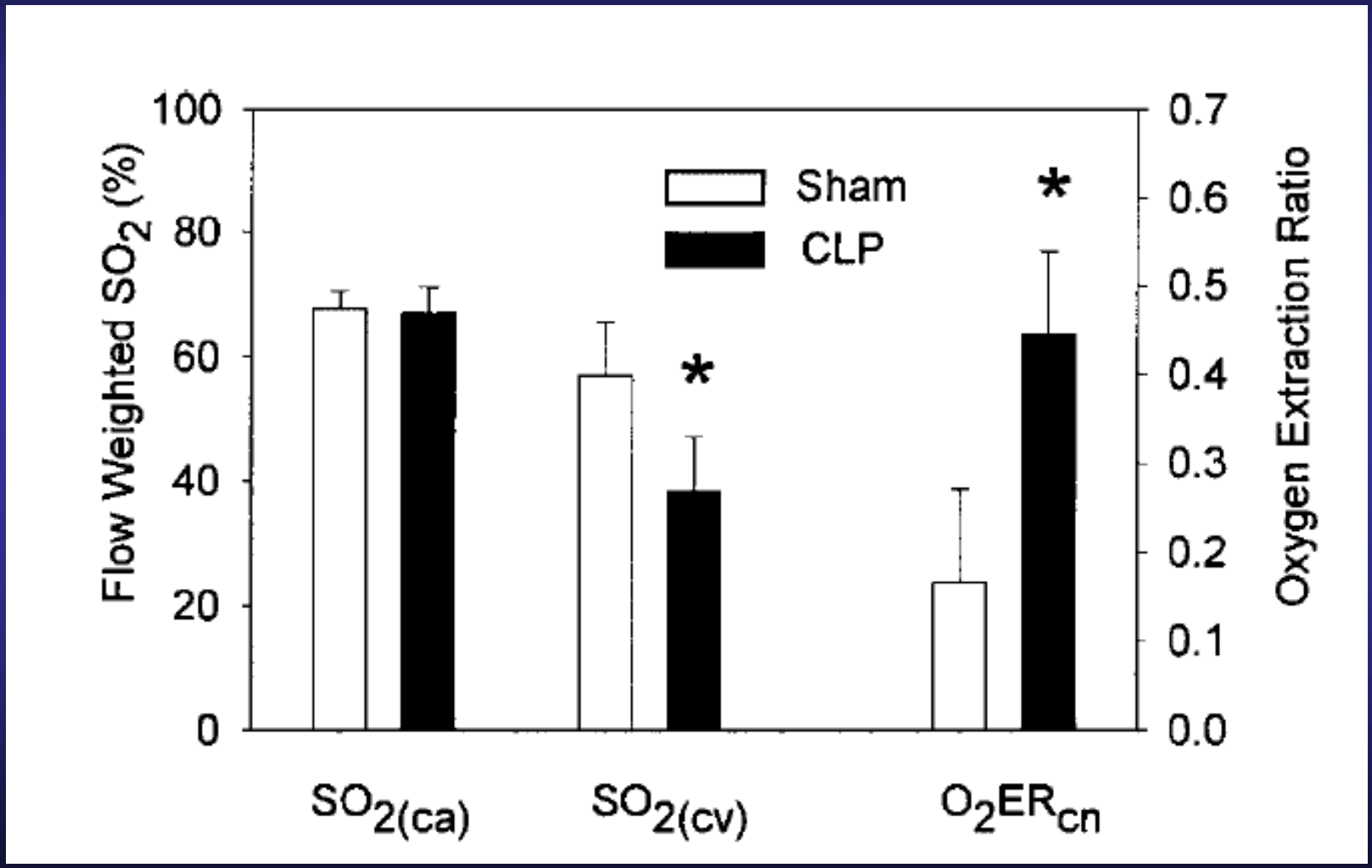
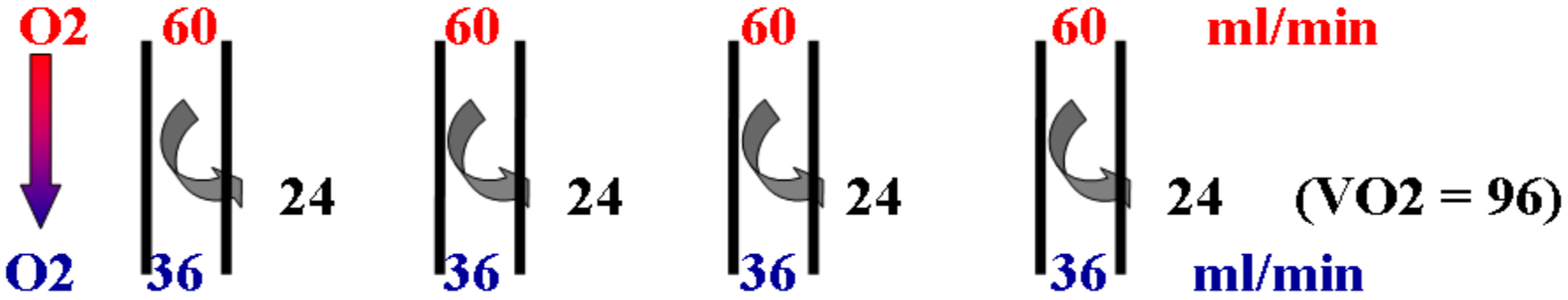
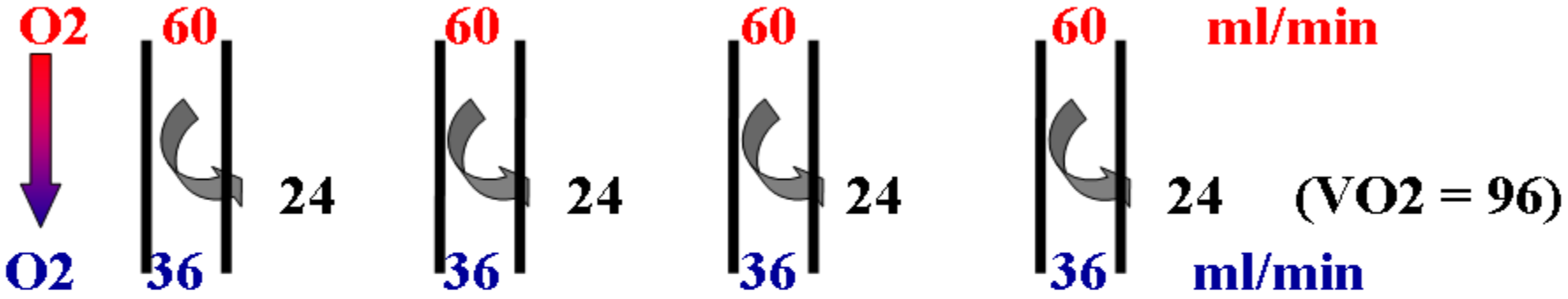


Normal flow



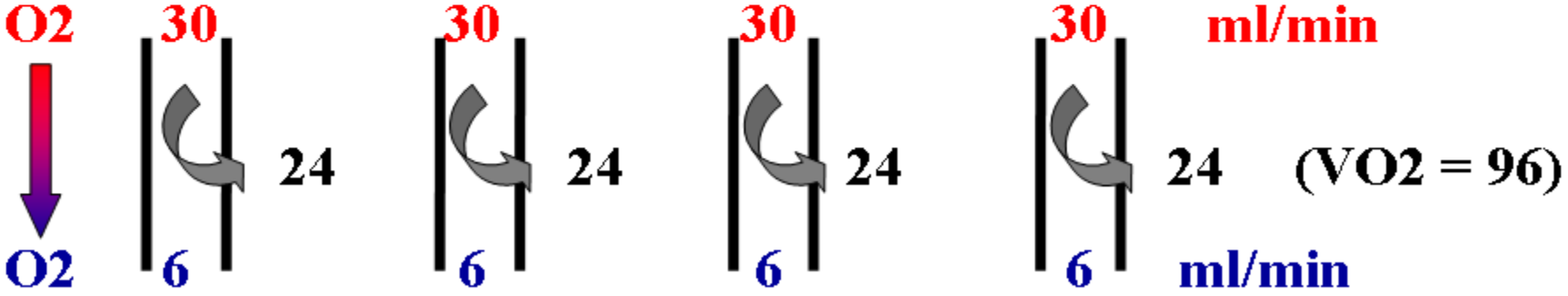
SvO2 60%

Normal flow



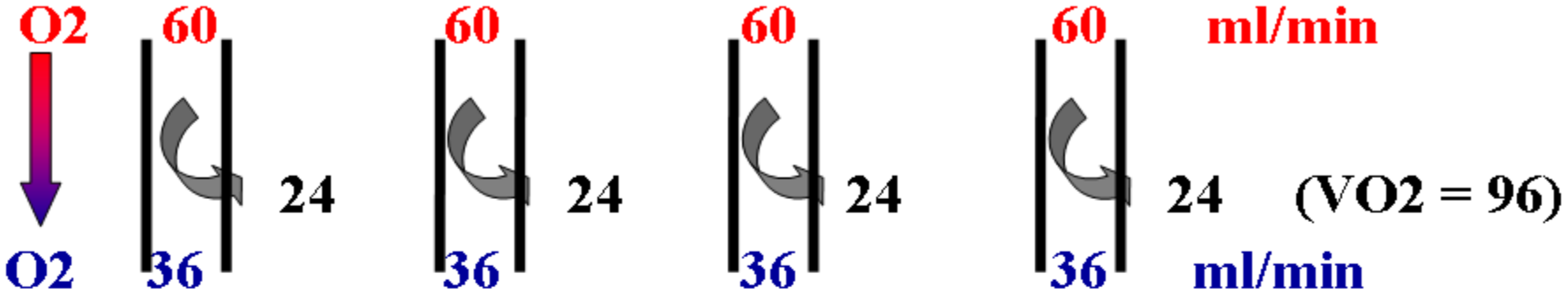
SvO2 60%

Low but homogenous flow



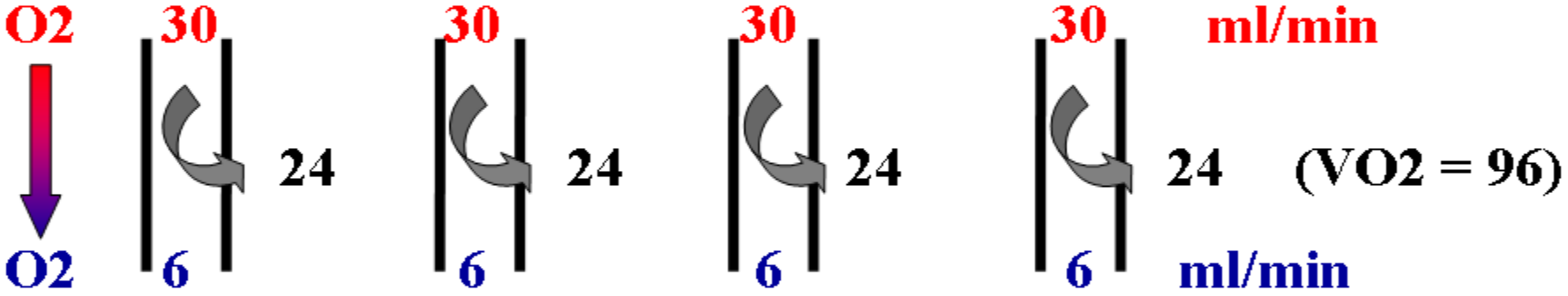
SvO2 20%

Normal flow



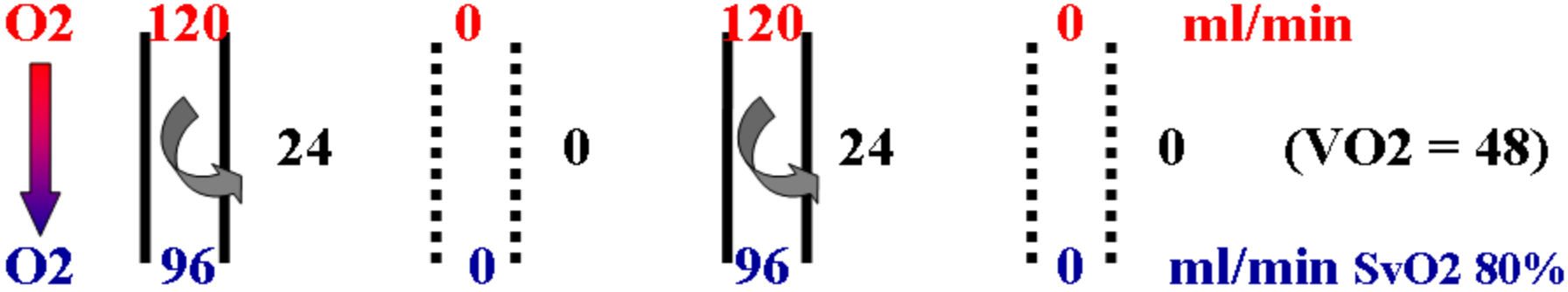
SvO2 60%

Low but homogenous flow



SvO2 20%

Heterogenous flow



Monitoring the microcirculation

Direct measurements

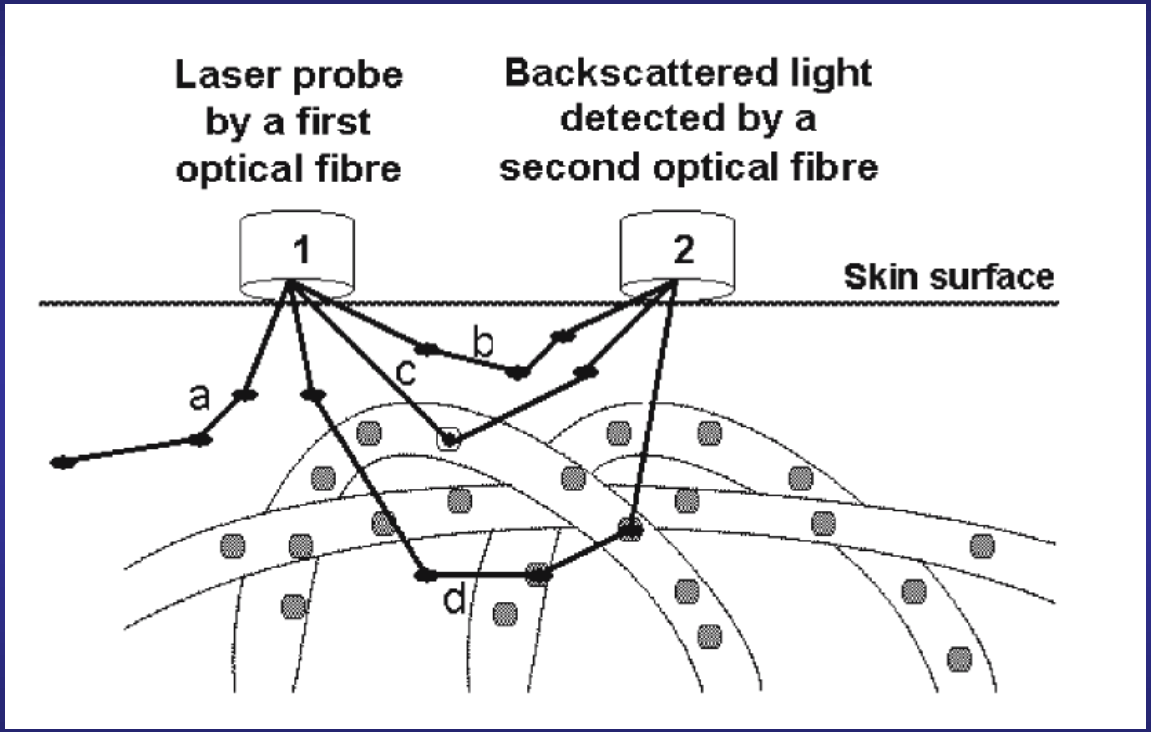
- Laser-Doppler flowmetry
- OPS - SDF imaging techniques

Indirect measurements

- NIRS
- CO2 tissue monitoring

Monitoring the microcirculation

Laser-Doppler flowmetry

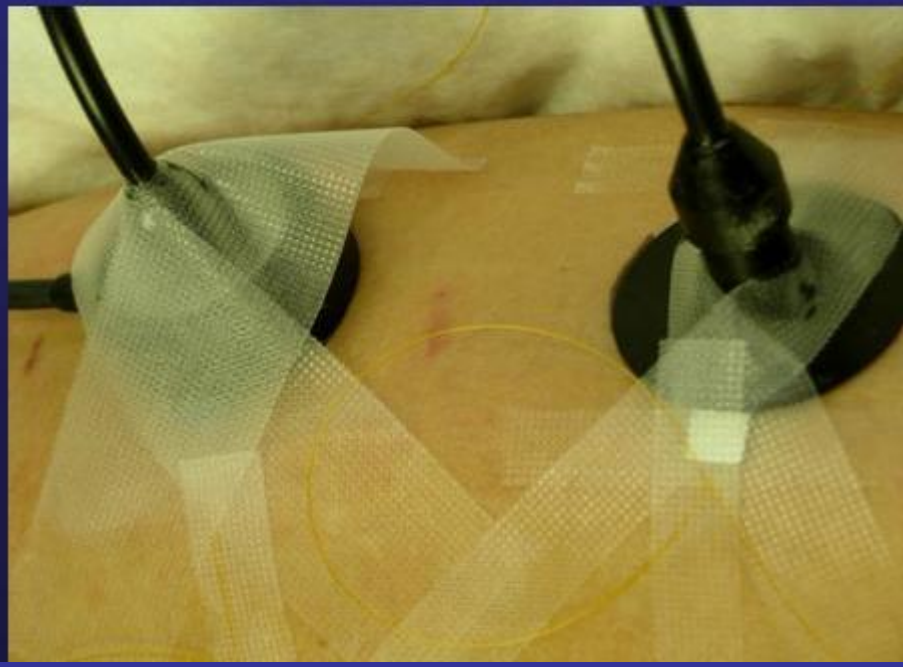


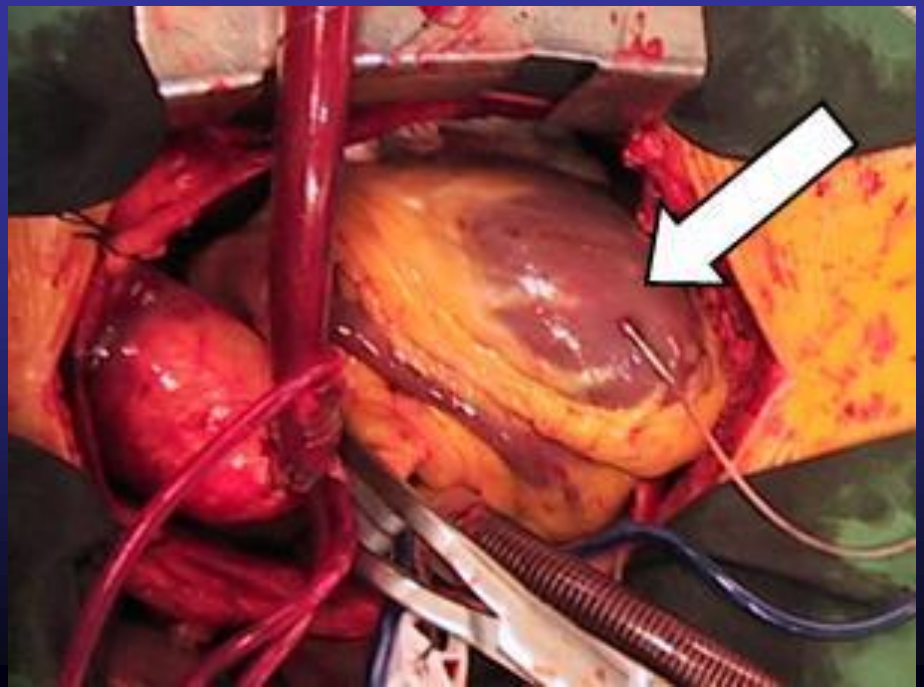
Microvascular Perfusion (Red Blood Cell Flux)	=	Number of blood cells moving in the tissue sampling volume	x	Mean velocity of these cells

Monitoring the microcirculation

Laser-Doppler flowmetry

- Cheap – non-invasive
- Can be applied on various tissues





Monitoring the microcirculation

Laser-Doppler flowmetry

- Cheap – non-invasive
- Can be applied on various tissues
- Provides measurement of blood flow in relative units (mV or BPU)
  (only relative changes to baseline can be assessed)
- Does not take into account the heterogeneity of blood flow,
  the measured parameter representing the average
  of the velocities in all the vessels included in the
  investigated volume (1 mm^3)

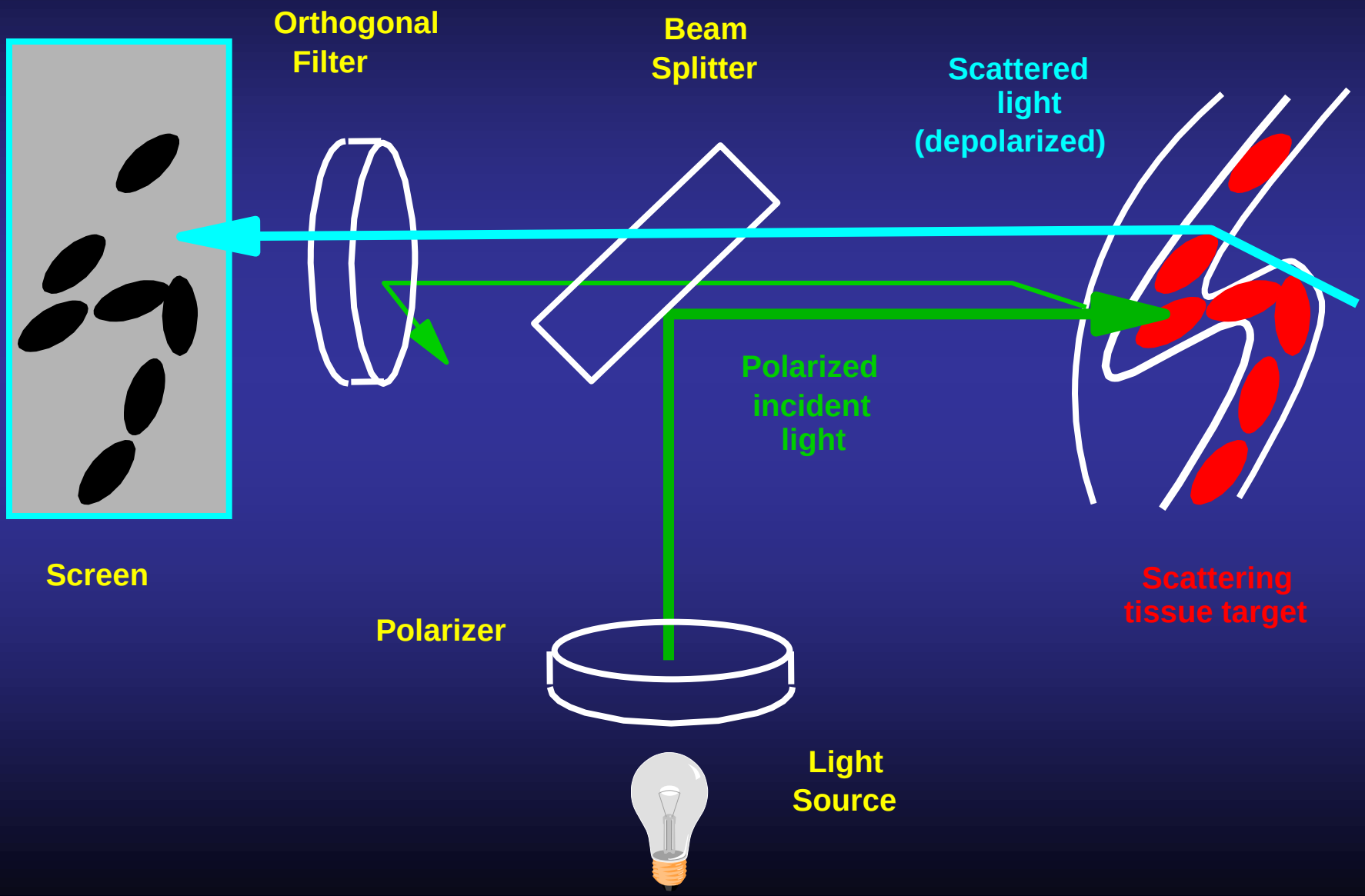
Monitoring the microcirculation

OPS – SDF imaging techniques

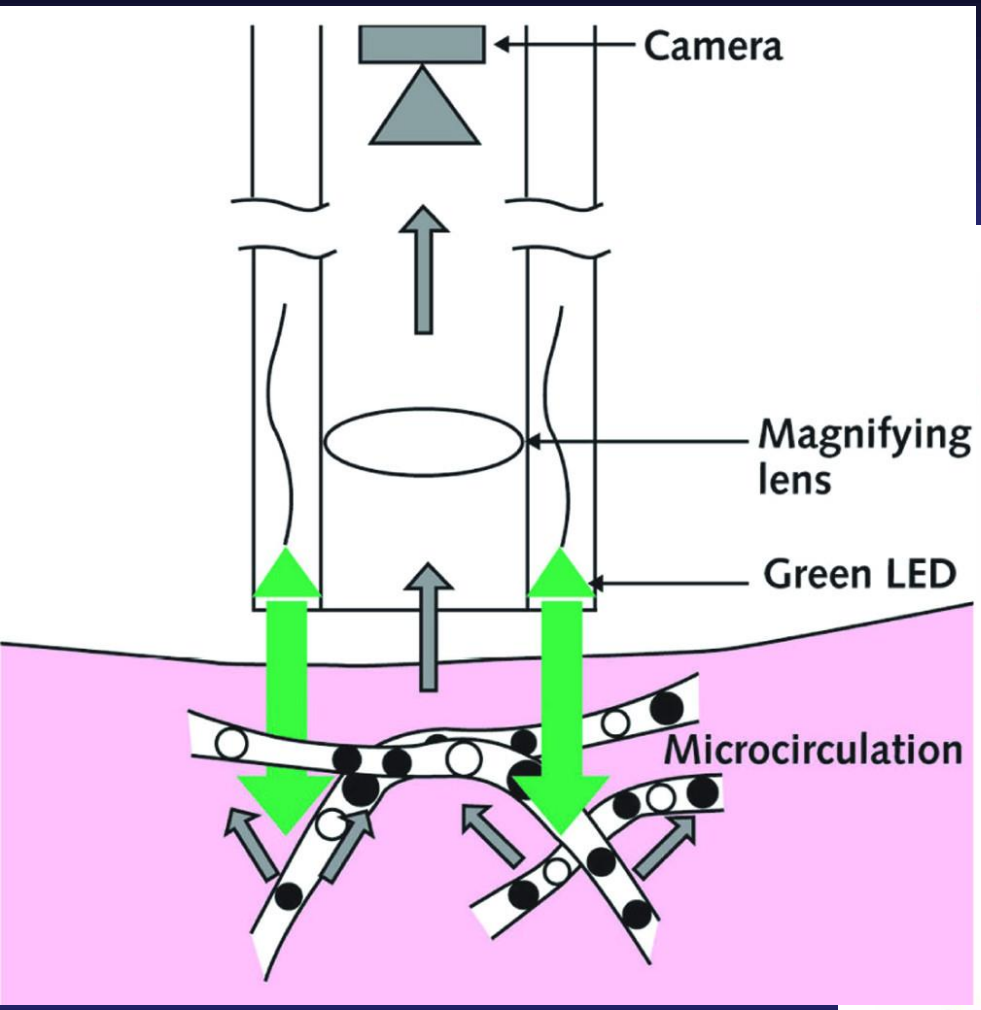
- Orthogonal Polarisation Spectral imaging technique
- Sidestream Dark Field imaging technique

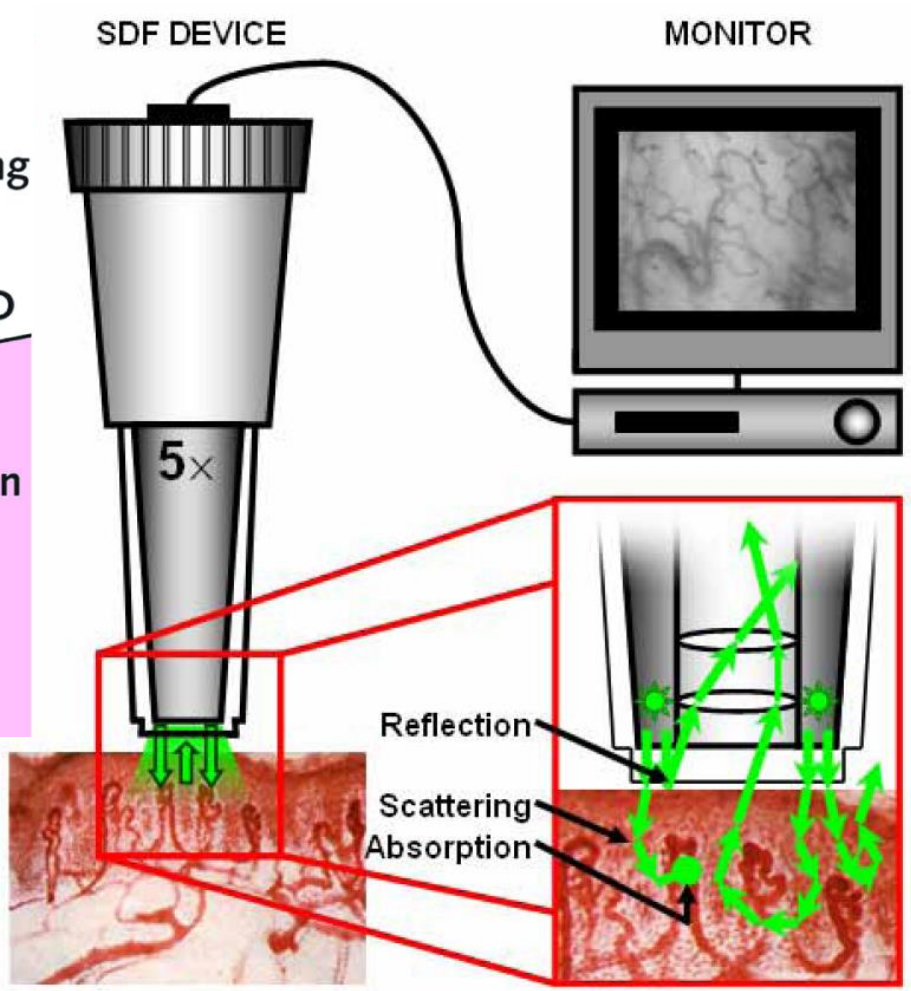
OPS imaging technique

ORTHOGONAL POLARIZATION SPECTRAL IMAGING



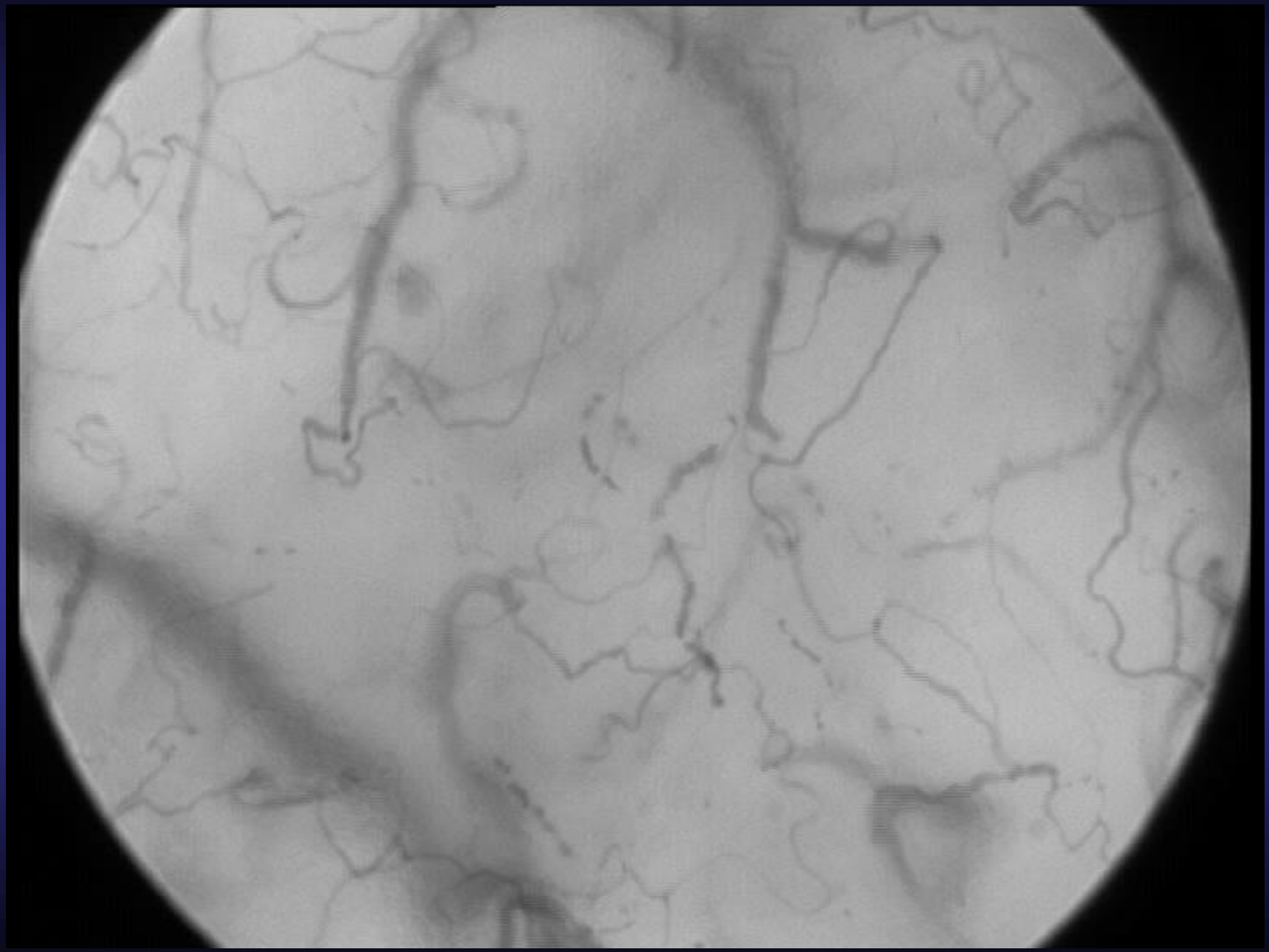
SIDESTREAM DARK FIELD IMAGING

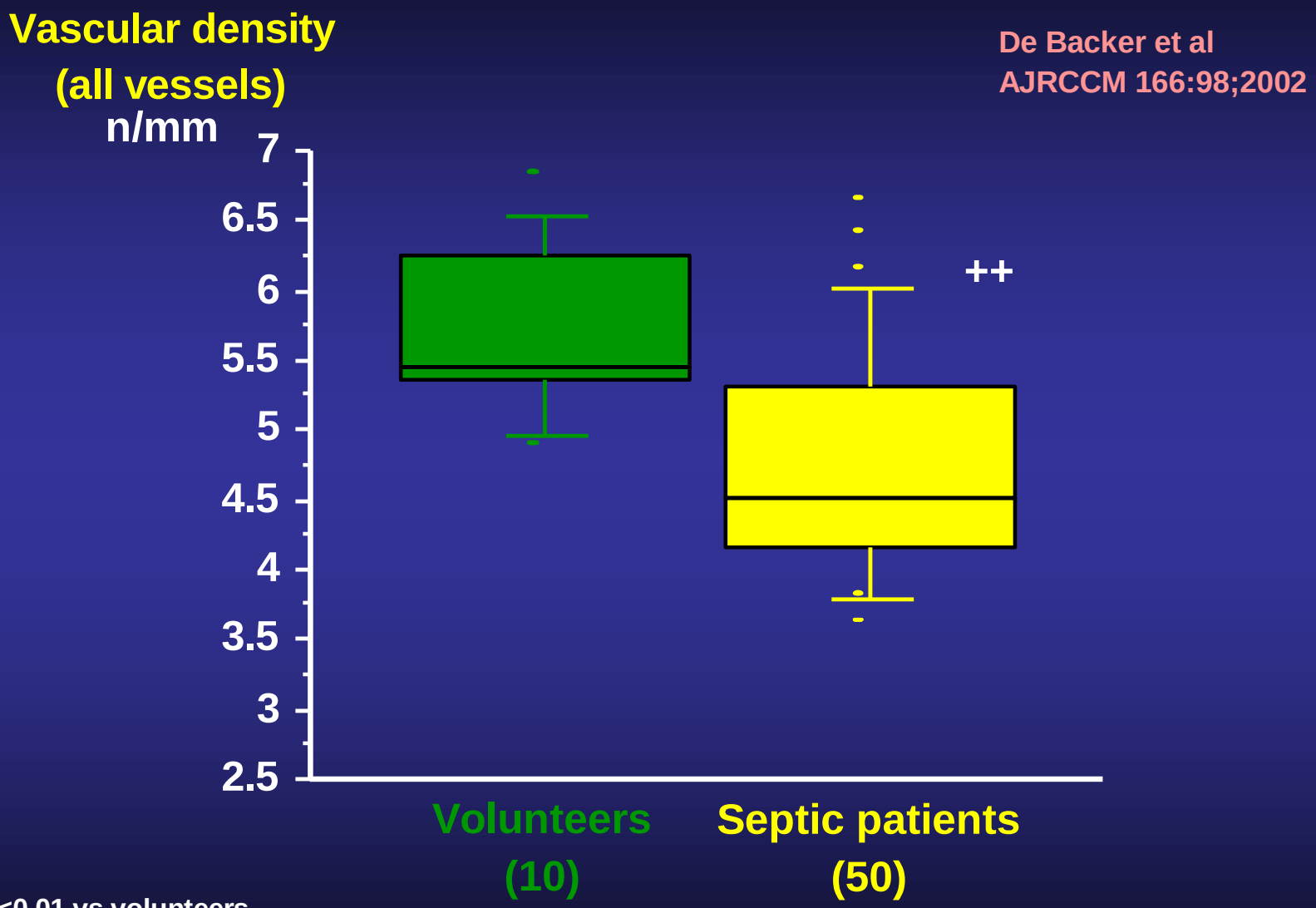




Healthy volunteer

Severe sepsis

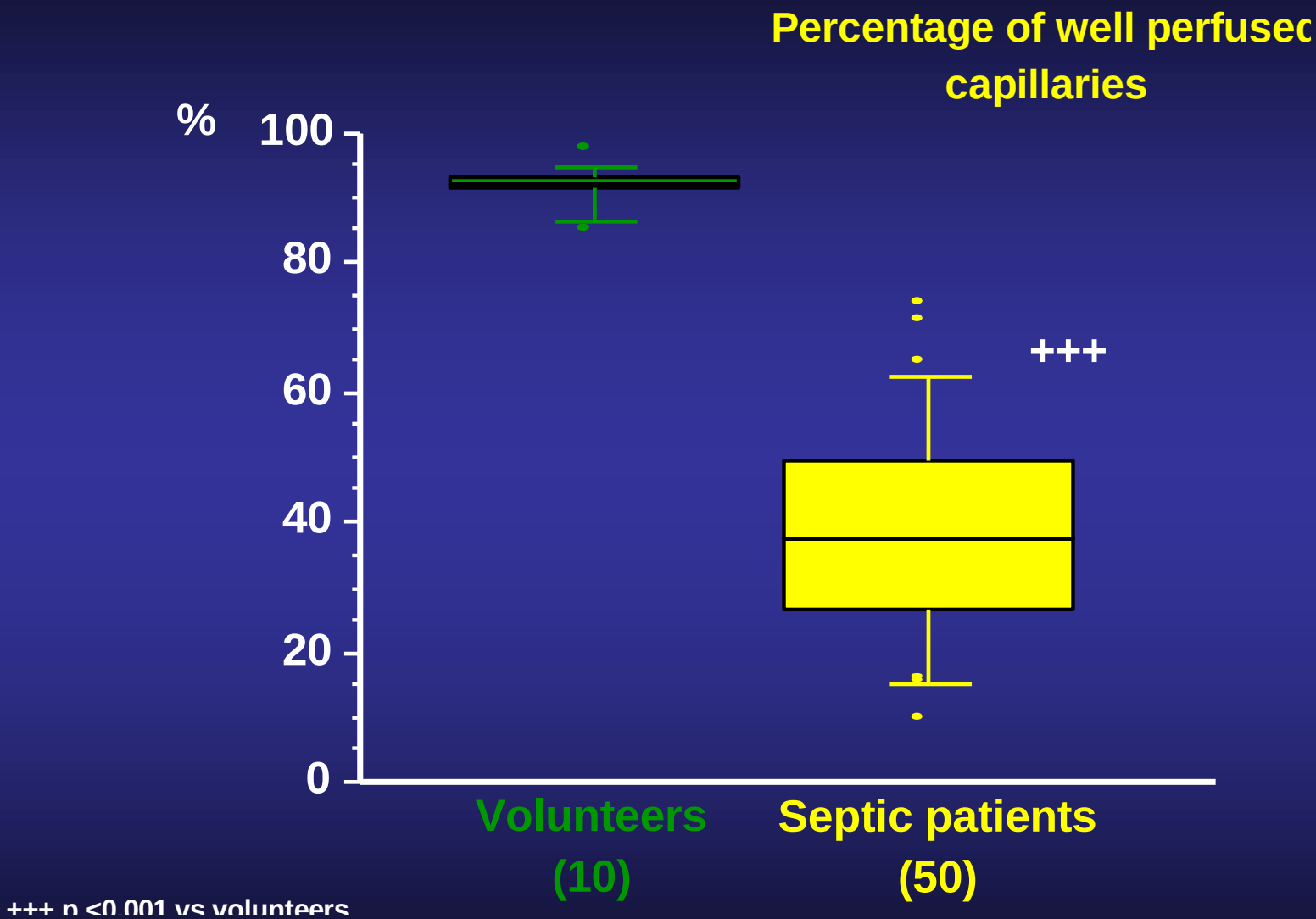




De Backer et al
AJRCCM 166:98;2002

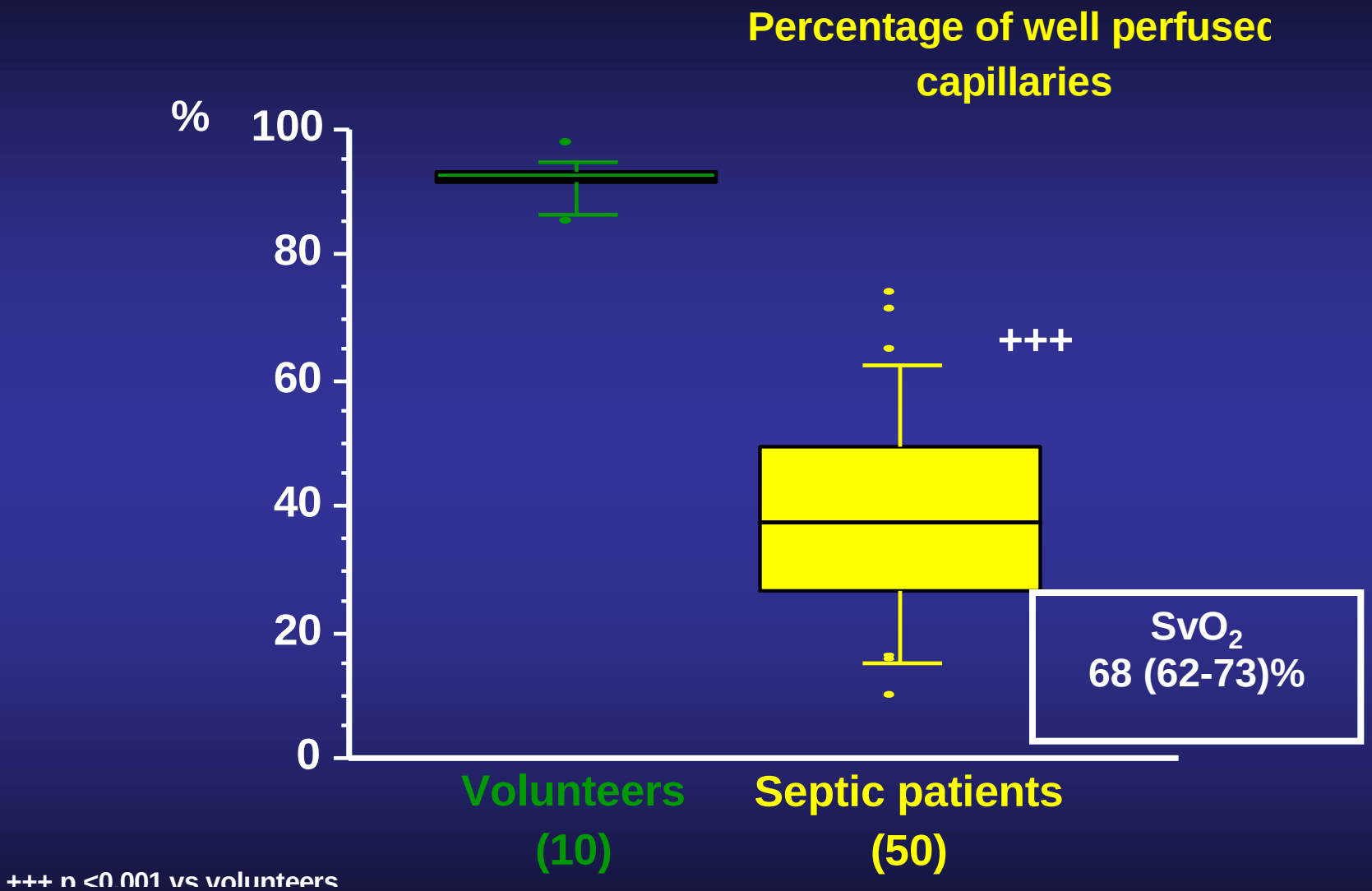
++ p <0.01 vs volunteers

MICROCIRCULATORY ALTERATIONS IN SEPTIC PATIENTS



De Backer et al. 2002. Am J Respir Crit Care Med. 166: 98

MICROCIRCULATORY ALTERATIONS IN SEPTIC PATIENTS



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Near Infrared Spectroscopy

- Non-invasive technique that uses differential absorption properties of HbO_2 and Hb to evaluate tissue oxygen saturation.

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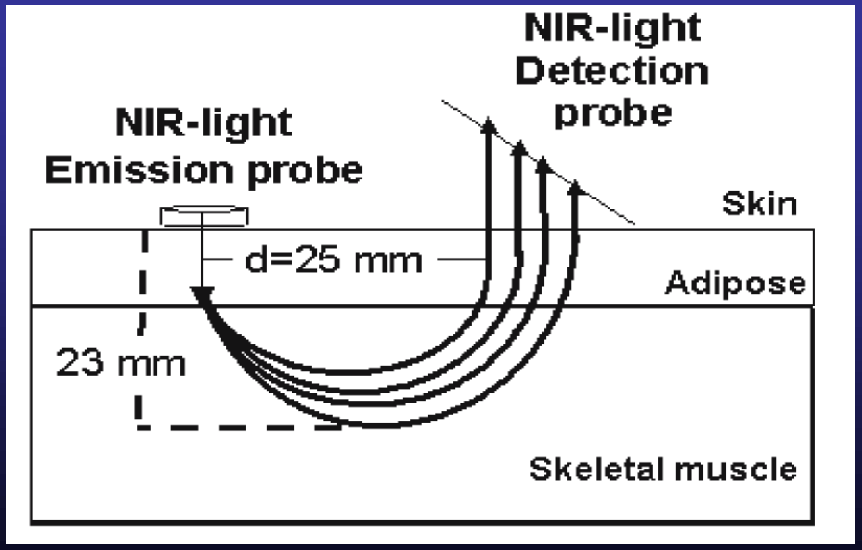
- The near infrared light (650-900 nm) easily crosses biological tissues, which have a low absorption power, and is absorbed only by hemoglobin, myoglobin and oxidized cytochrome.



→

Proportion of HbO2/Hb

StO2

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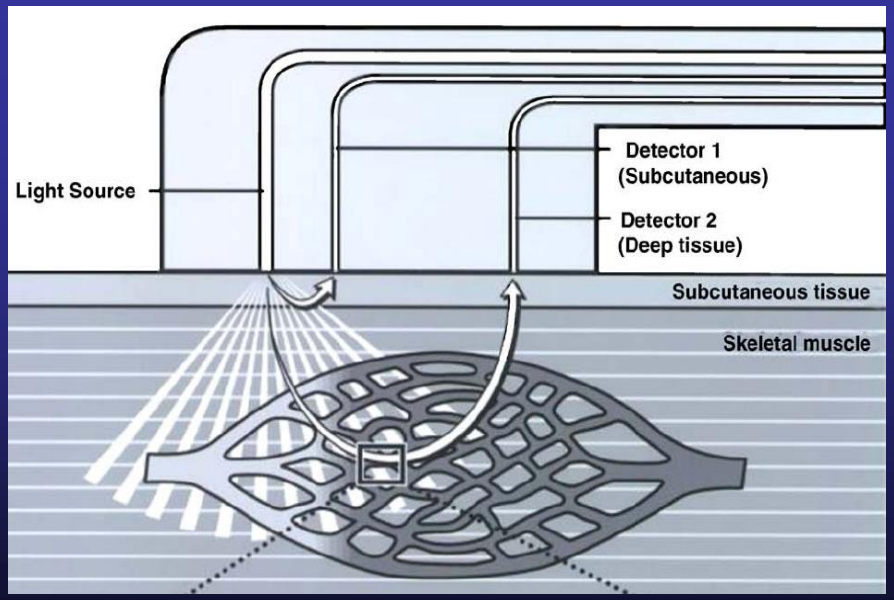

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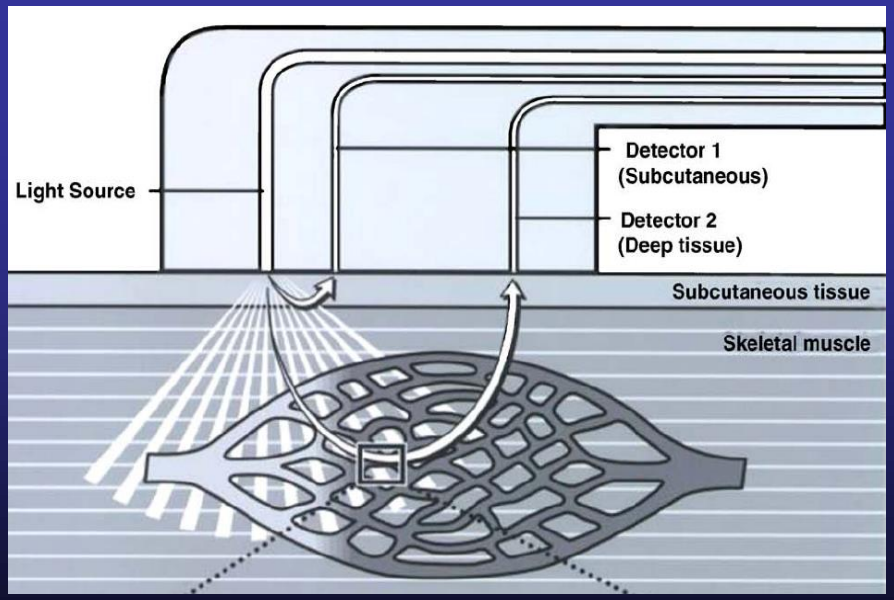
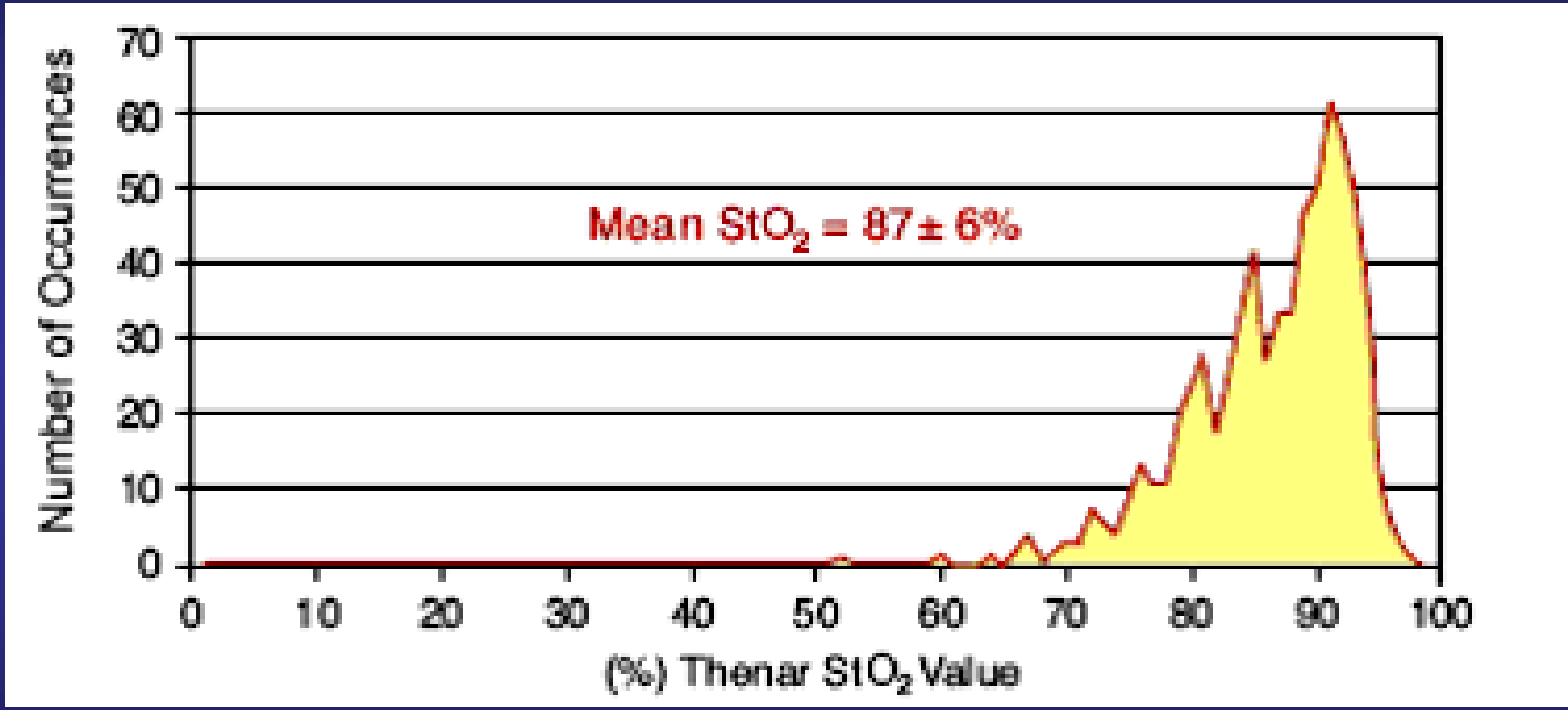


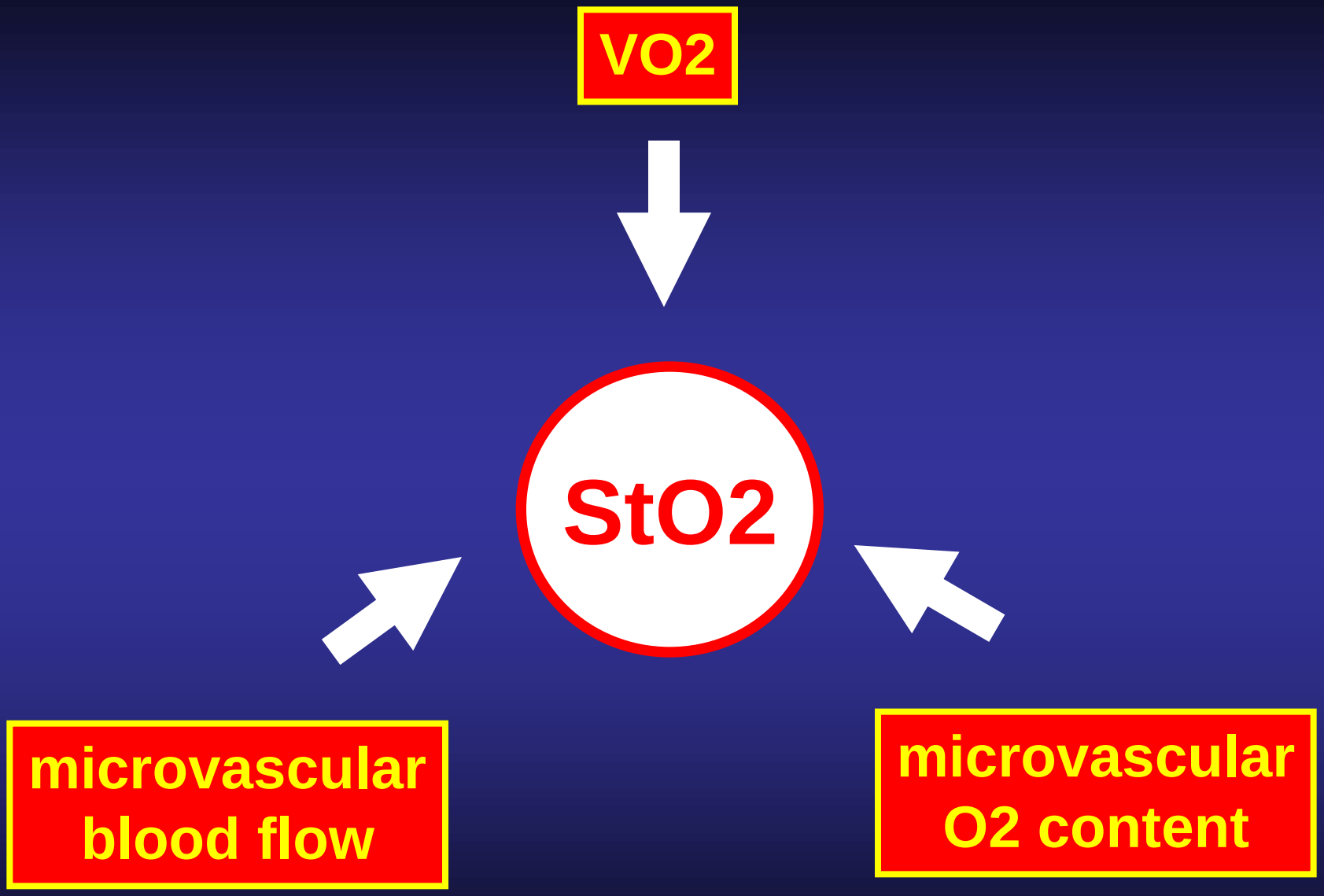
Proportion of HbO2/Hb

SmicrovO2

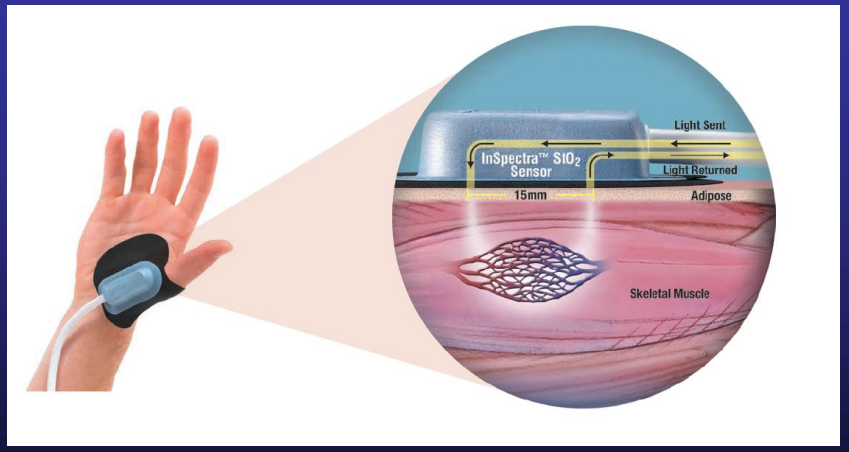
StO2 measurements on the thenar eminence of 707 healthy volunteers



Crookes et al *J Trauma* 2005; 58:806-813


VO2
StO2
microvascular blood flow
microvascular O2 content

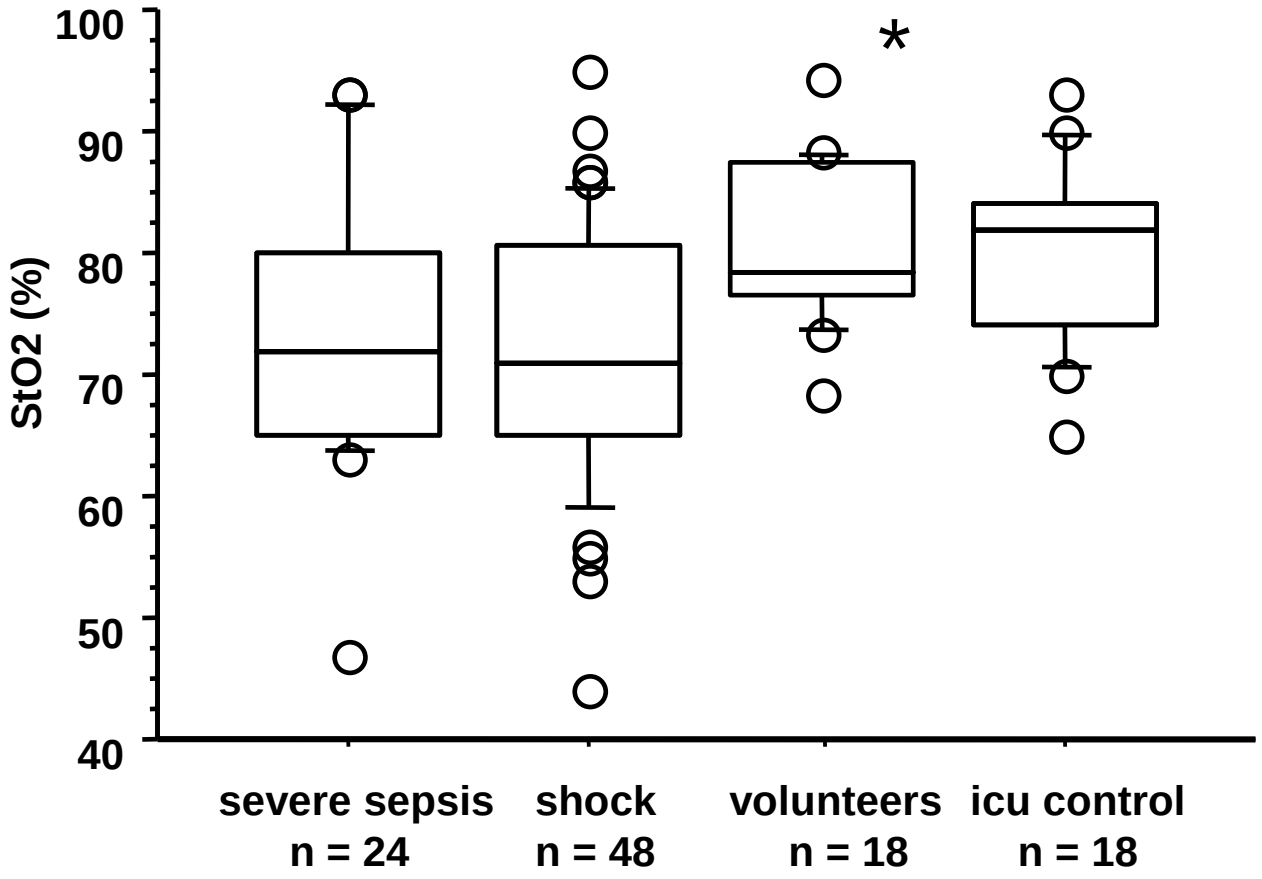
Muscle tissue oxygen saturation = StO_2



StO_2 can be used to quantify:

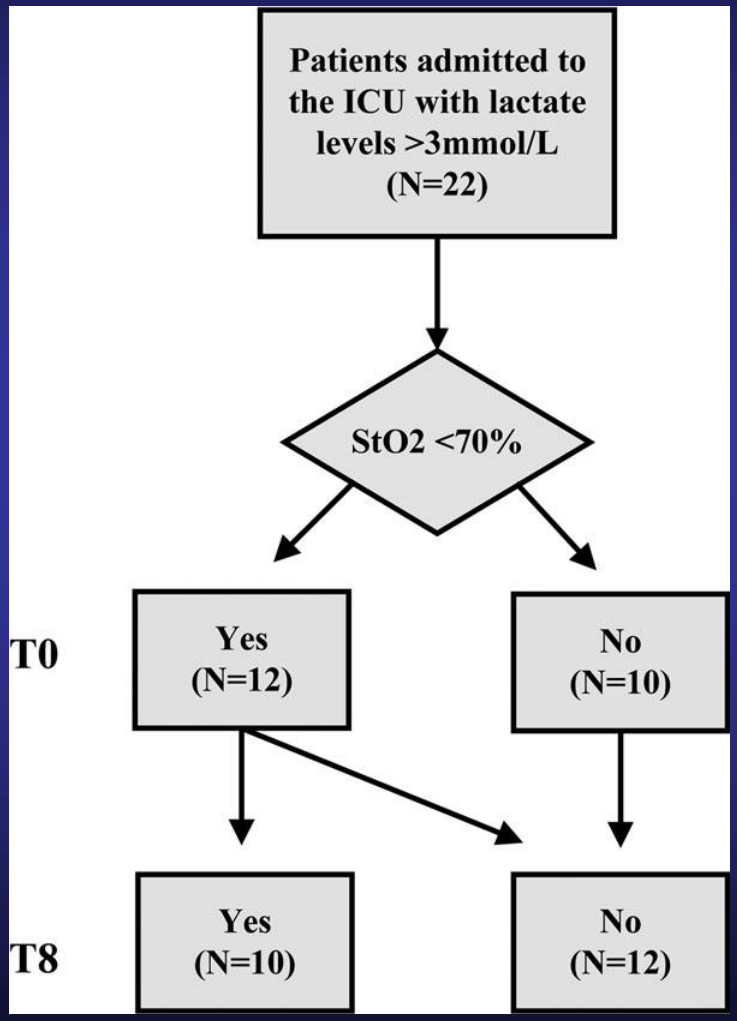
- **tissue oxygenation**
- **microvascular function**

Creteur et al. Intensive Care Med 2007 ; 33 : 1549-1556



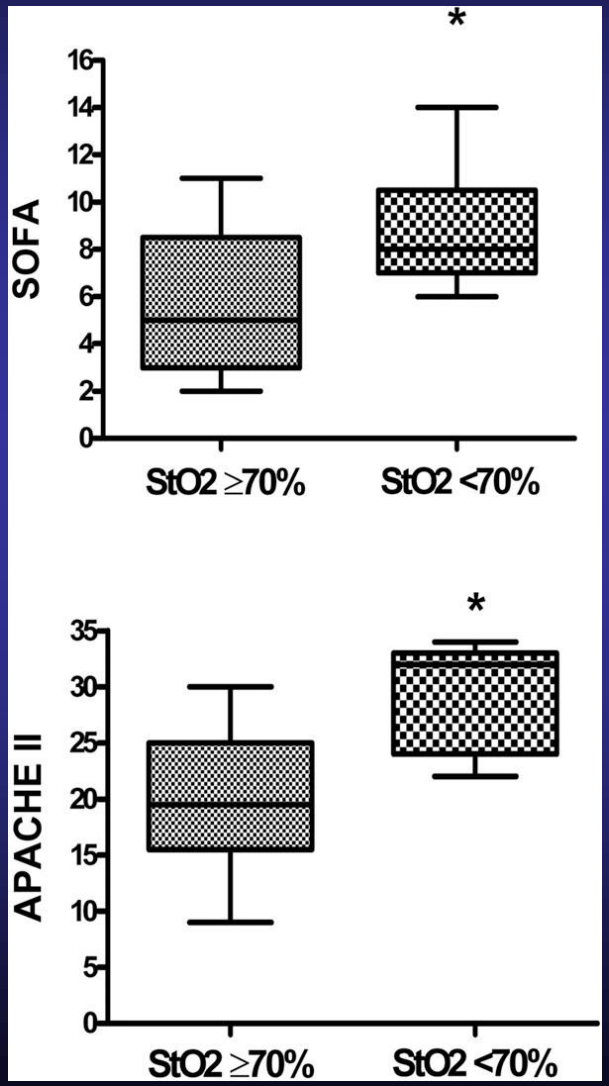
Low StO2 at the end of EGDT is associated with worse outcome in critically ill patients

Lima *et al. Critical Care* 2009 13(Suppl 5):S13



4 deaths

1 death



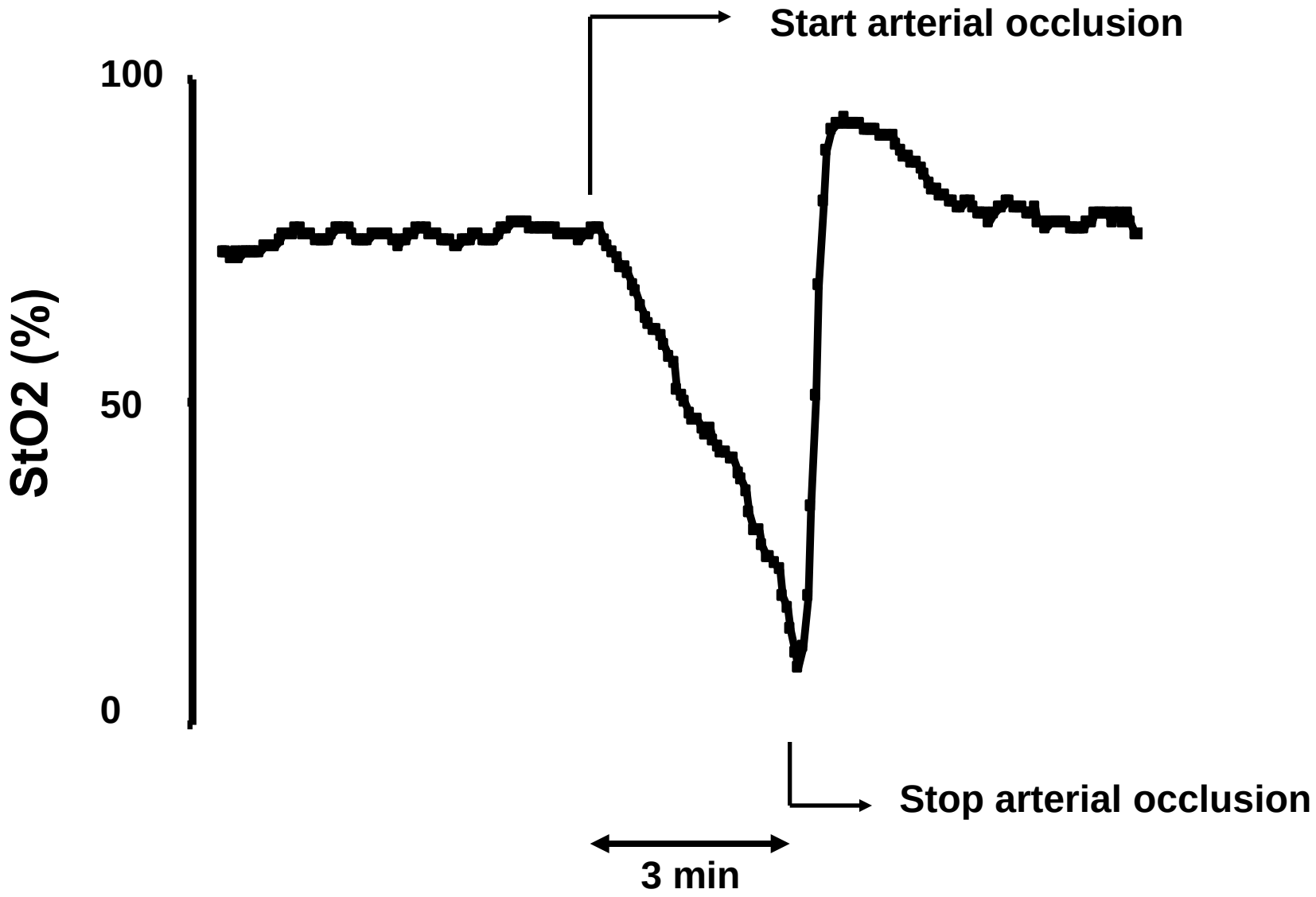
Creteur et al. Intensive Care Med 2007 ; 33 : 1549-1556

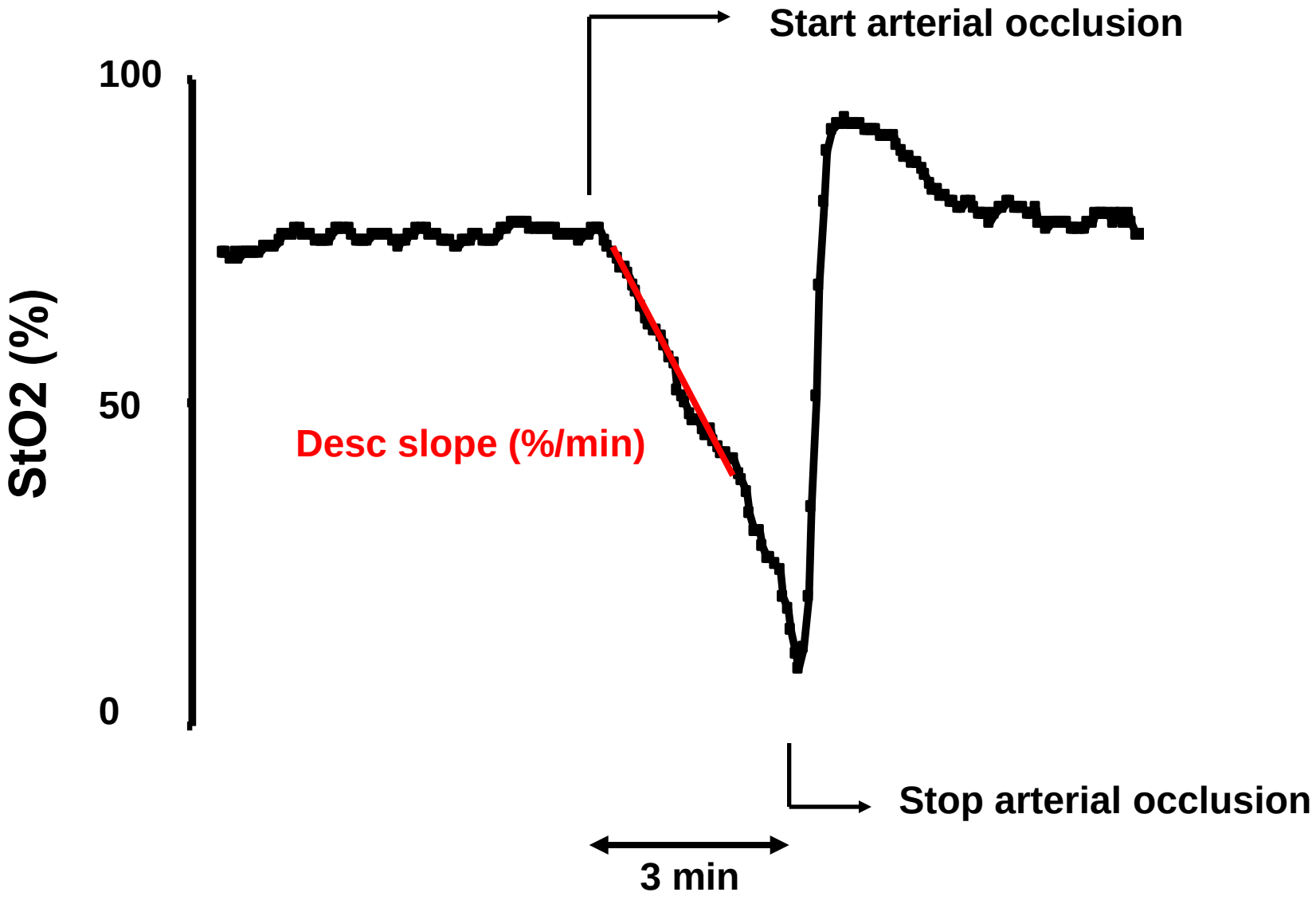
DYNAMIC NIRS-DERIVED VARIABLES

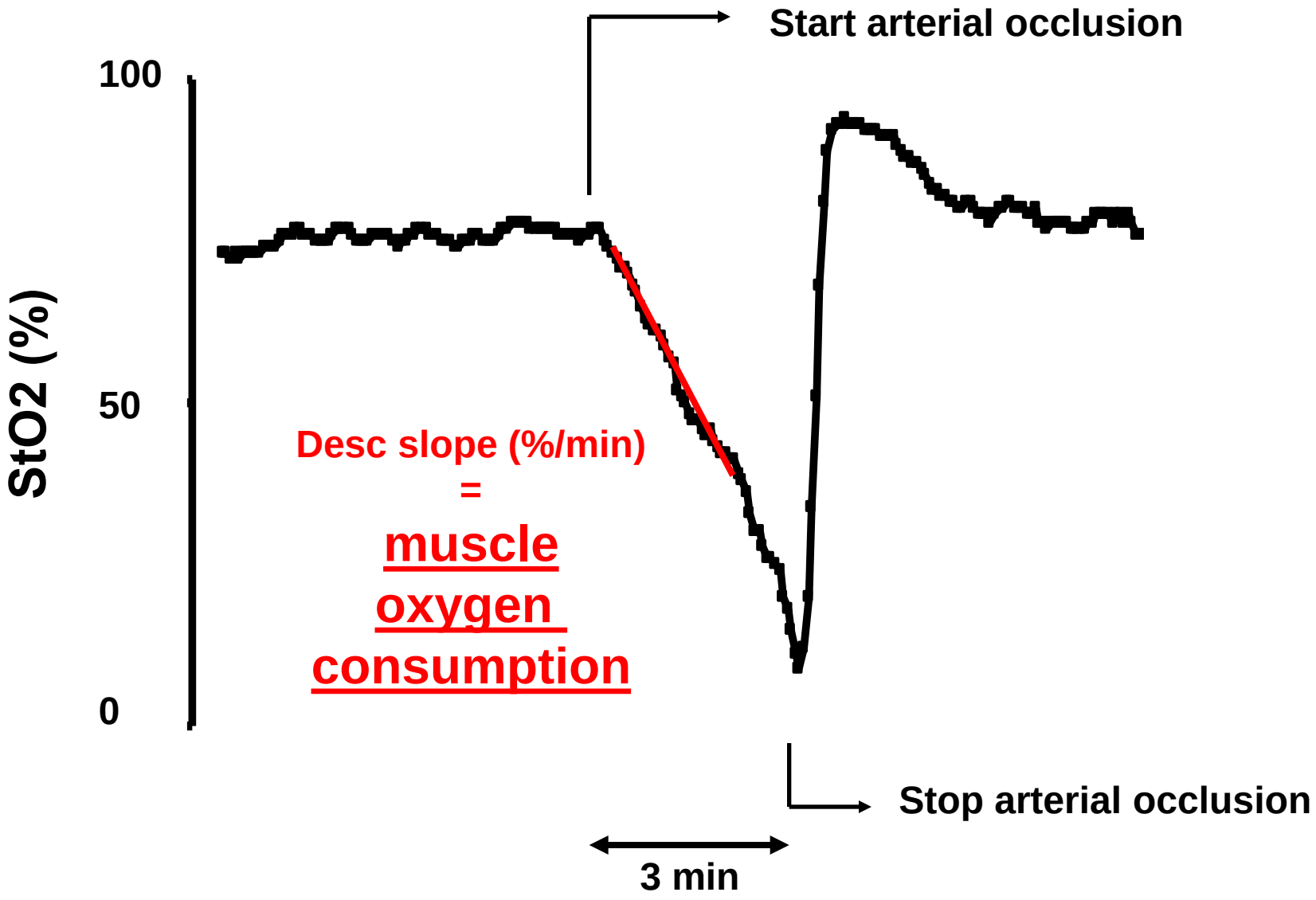
- Thenar muscle oxygen saturation (StO_2) measured continuously by NIRS

- A vaso-occlusive test (VOT) (arterial occlusion) :

  - upper limb ischemia induced by the inflation of a pneumatic cuff around the upper arm to 50 mmHg above SAP (3 min)

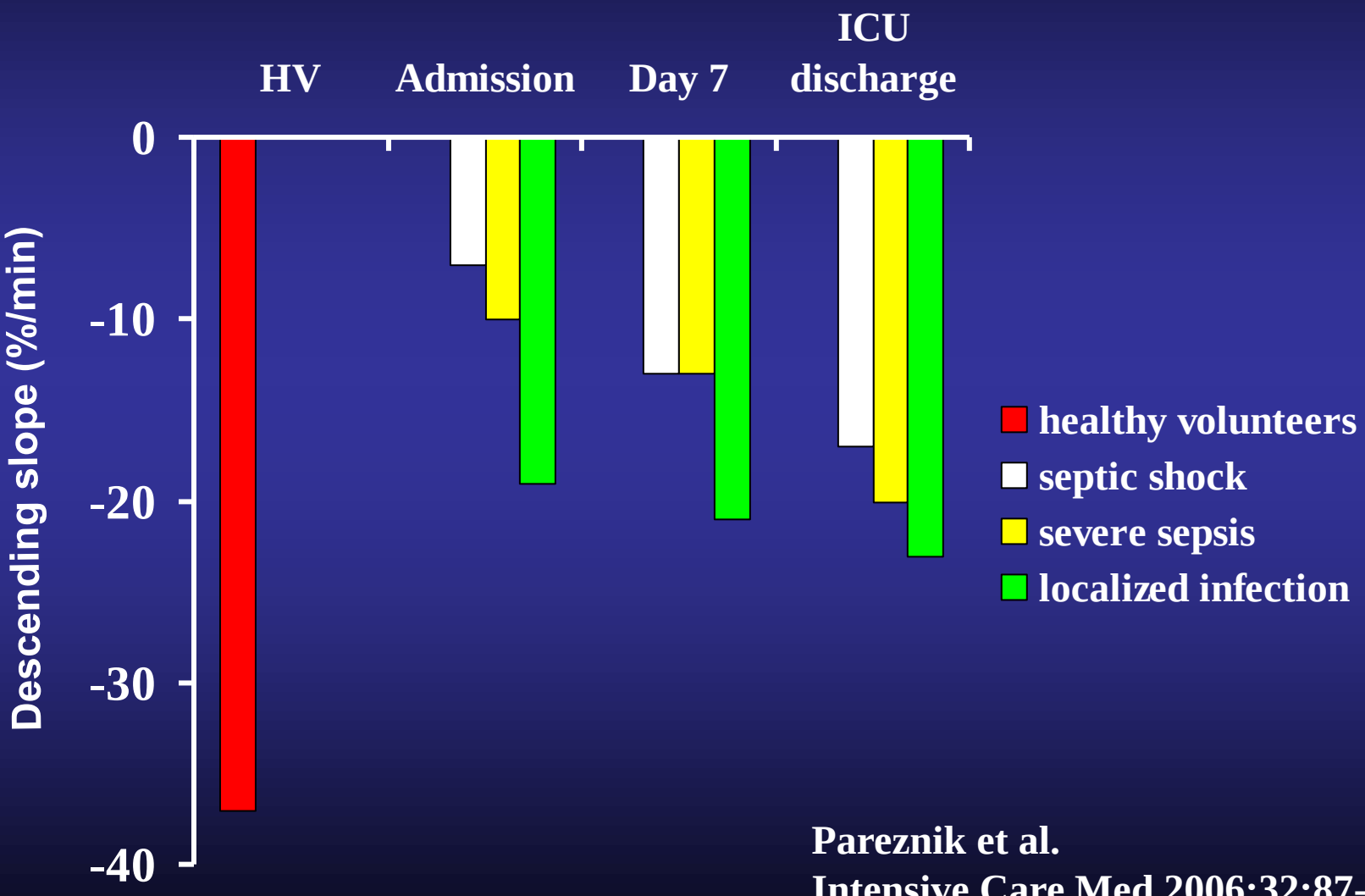

Start arterial occlusion
100
50
0
StO2 (%)
Stop arterial occlusion
3 min


Start arterial occlusion
100
50
0
StO2 (%)
Desc slope (%/min)
Stop arterial occlusion
3 min

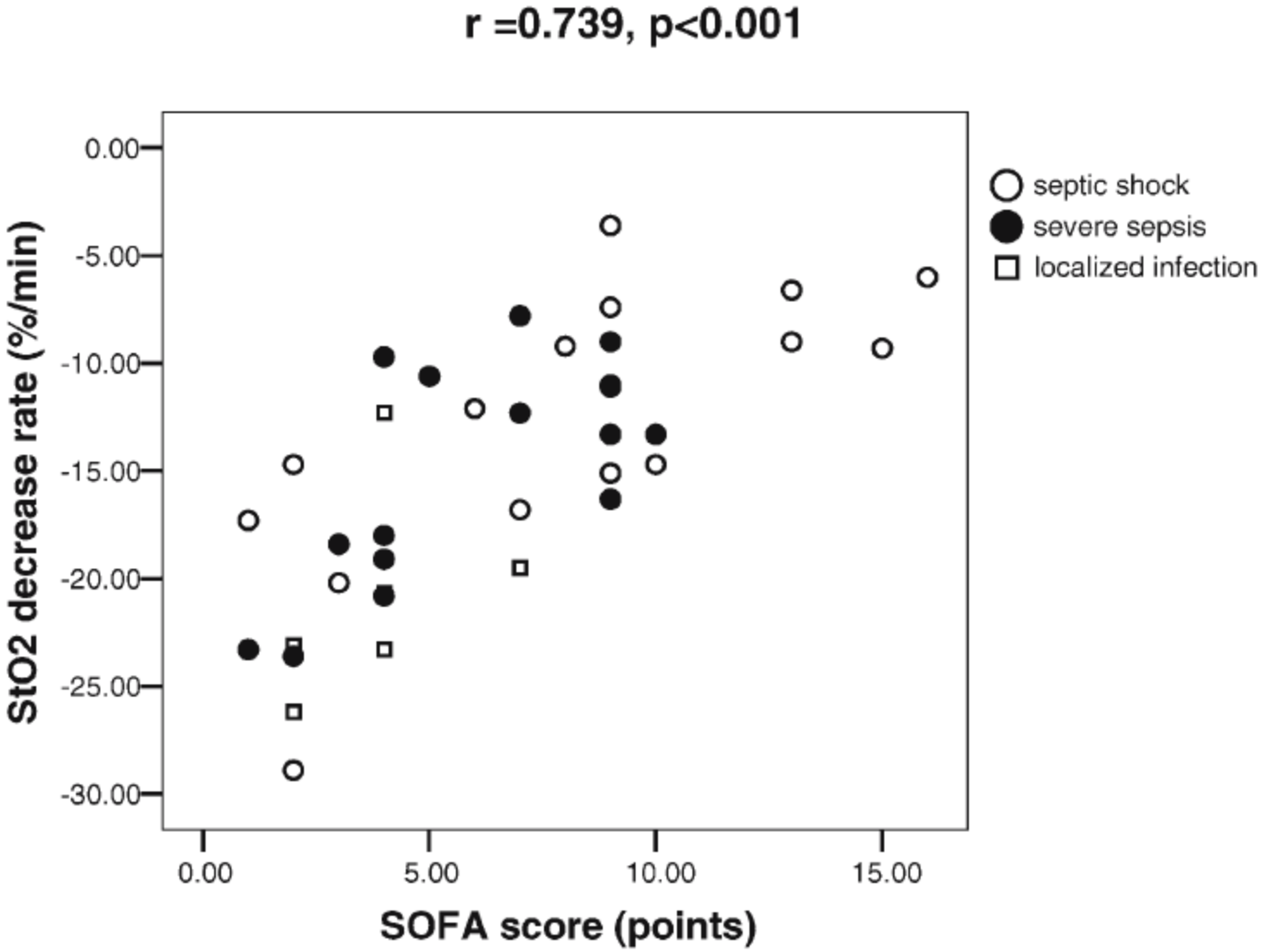

Start arterial occlusion
100
StO2 (%)
50
0
Desc slope (%/min)
=
muscle
oxygen
consumption
Stop arterial occlusion
3 min

Changes in muscle tissue oxygenation during stagnant ischemia

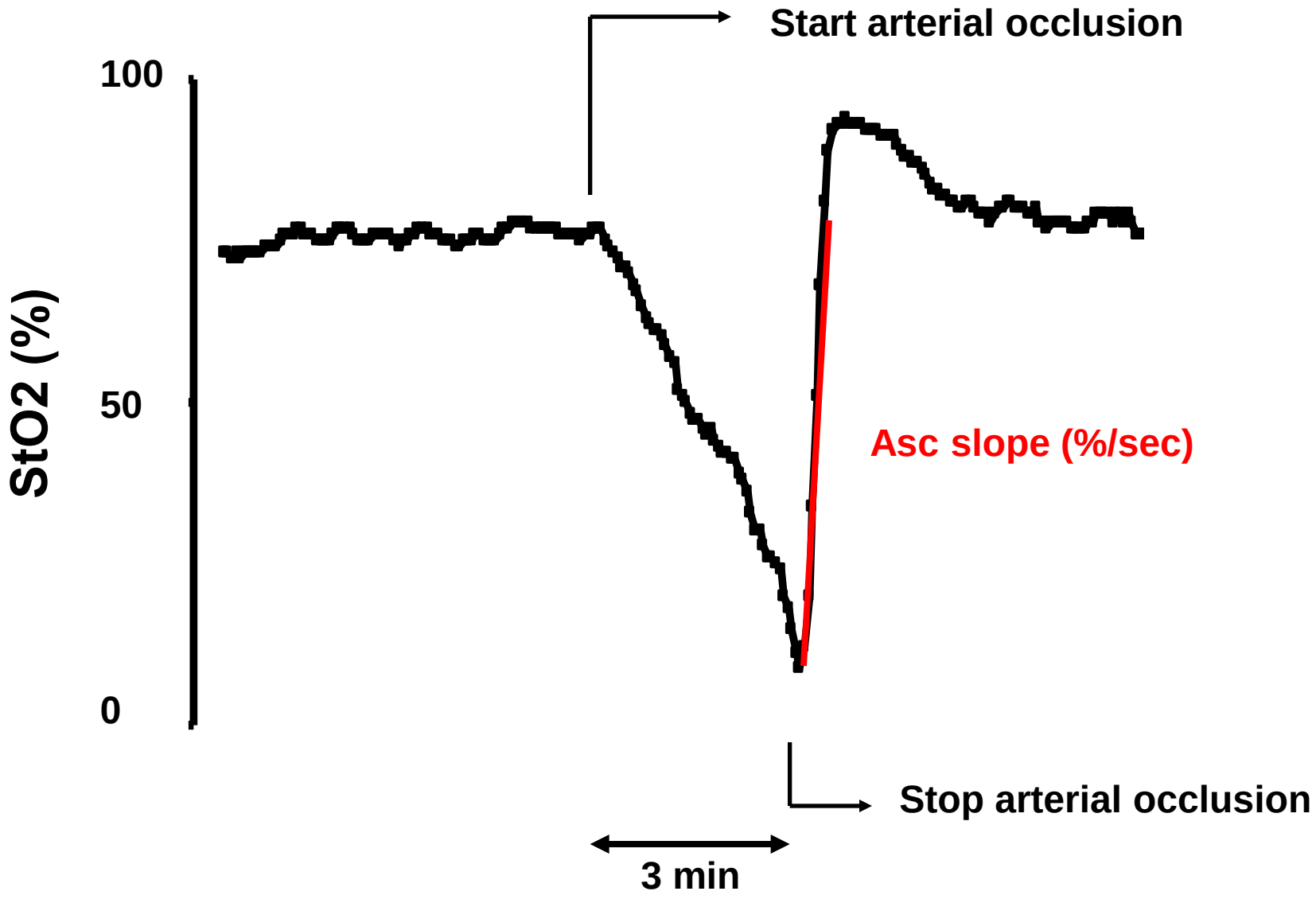
thenar muscle - ischemia induced by rapid pneumatic cuff inflation

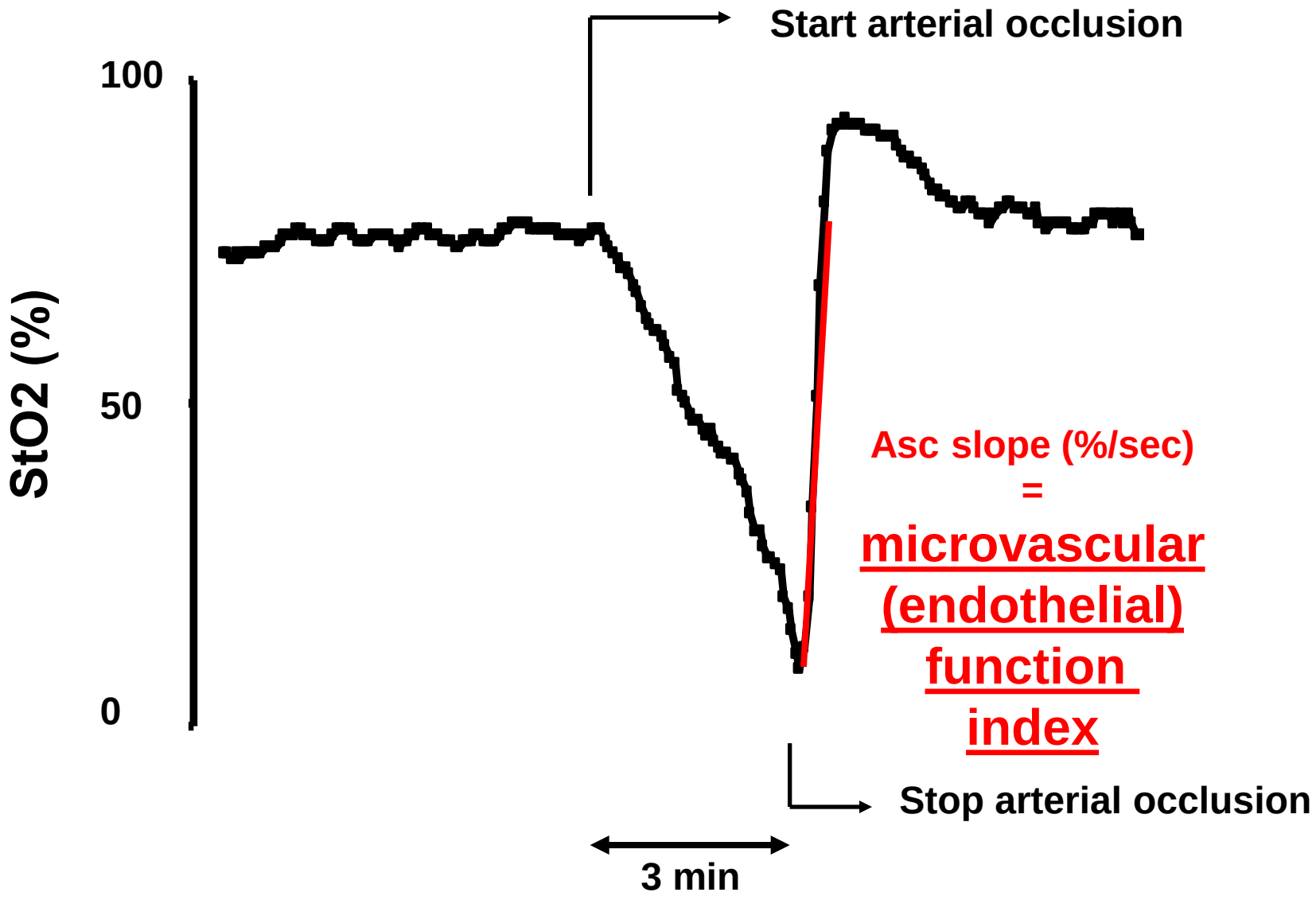


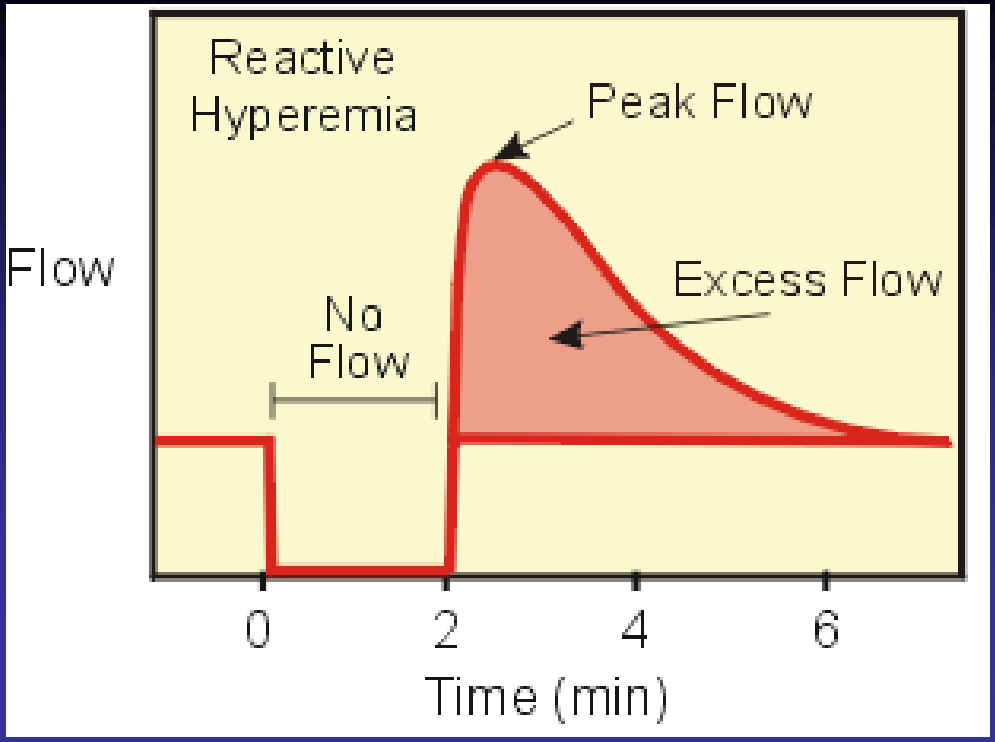
Pareznik et al.
Intensive Care Med 2006:32:87-92



Pareznik et al.
Intensive Care Med 2006:32:87-92


Start arterial occlusion
100
50
0
StO2 (%)
Asc slope (%/sec)
Stop arterial occlusion
3 min


Start arterial occlusion
100
50
0
StO2 (%)
Asc slope (%/sec)
=
microvascular
(endothelial)
function
index
Stop arterial occlusion
3 min



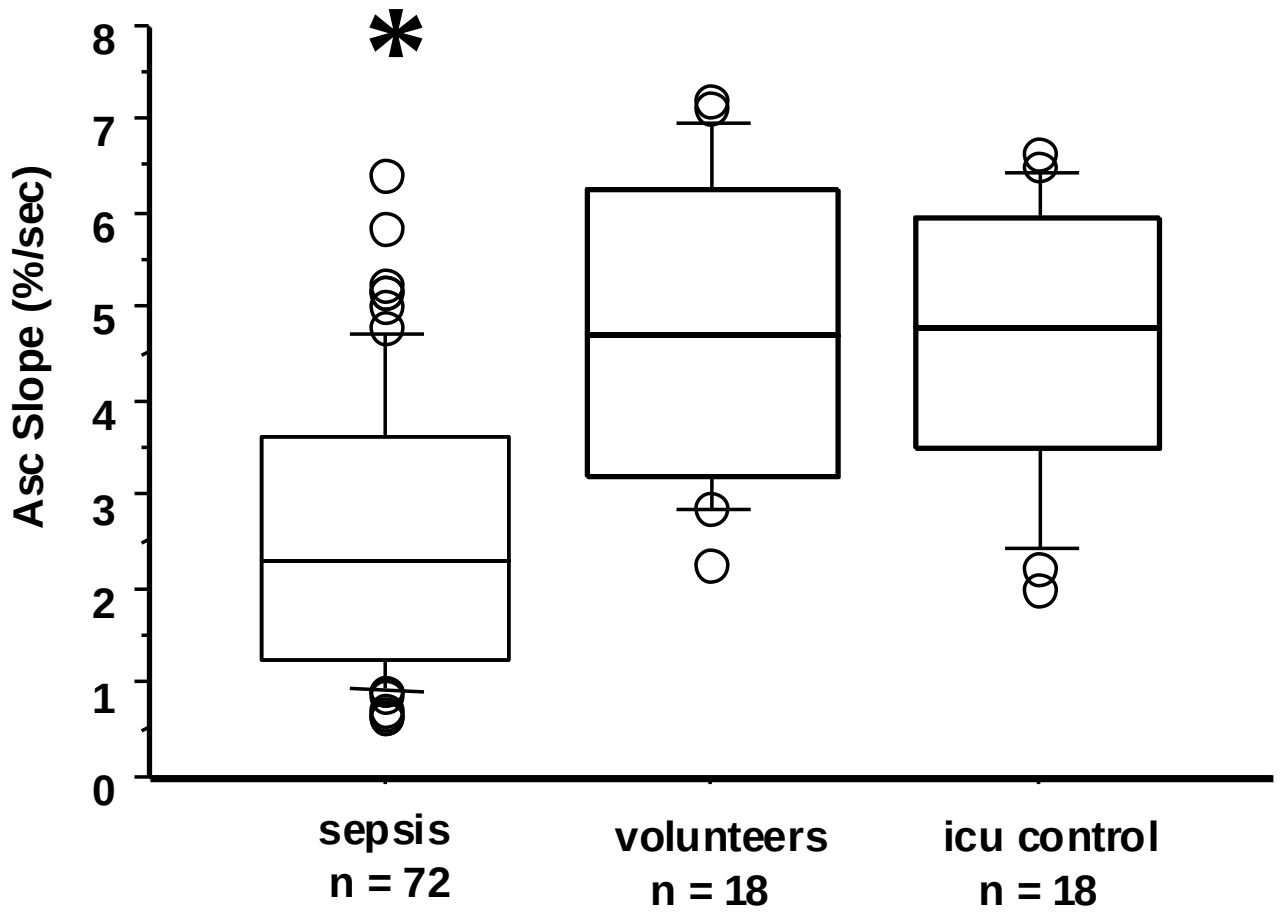
Reactive hyperemia is the transient increase in organ blood flow that occurs following a brief period of ischemia.

In general, the ability of an organ to display reactive hyperemia is similar to its ability to display **autoregulation (vasoreactivity)**

- Increasing flow in previously patent capillaries
- Recruiting additional capillaries

Creteur et al. Intensive Care Med 2007 ; 33 : 1549-1556

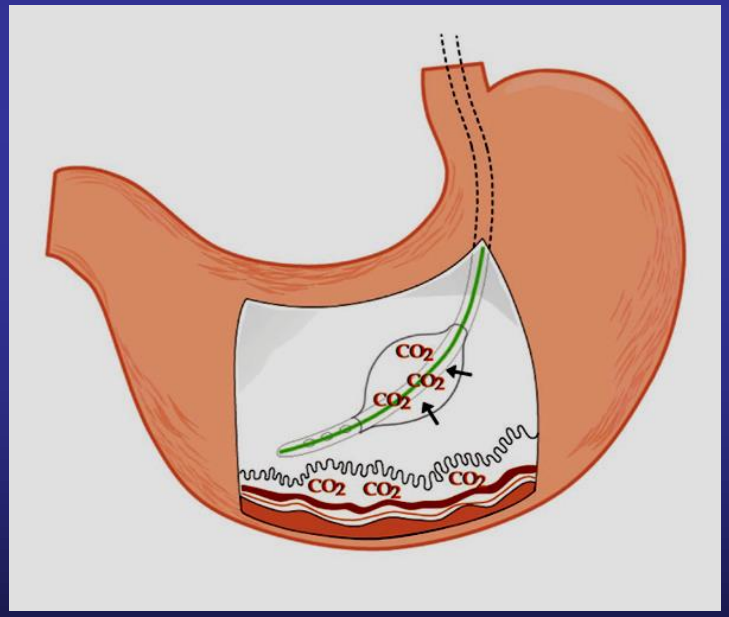
* p < 0.001 vs volunteers and ICU control



Monitoring tissue perfusion

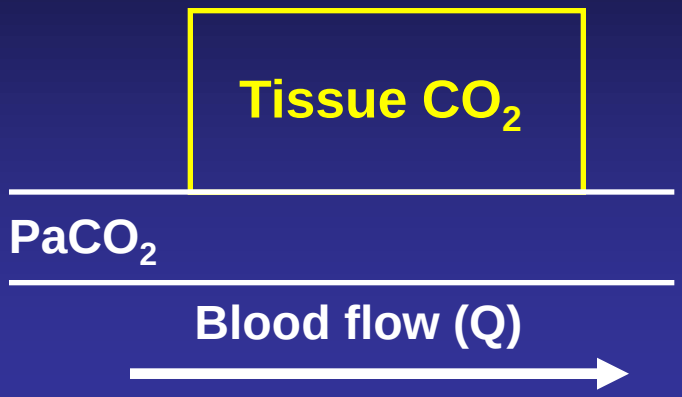
Tissue CO_2 monitoring

Gastric tonometry

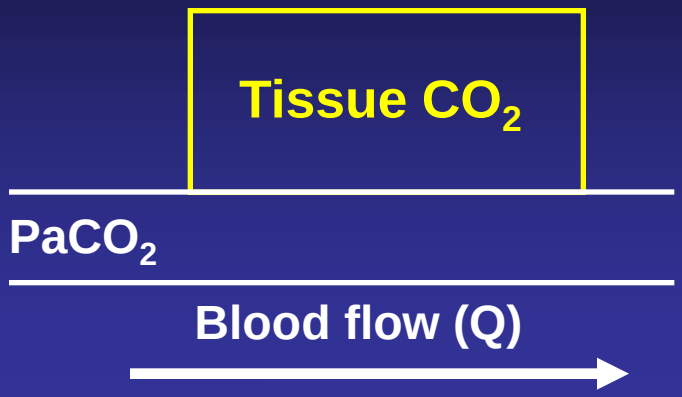


Sublingual capnometry

Determinants of tissue CO_2

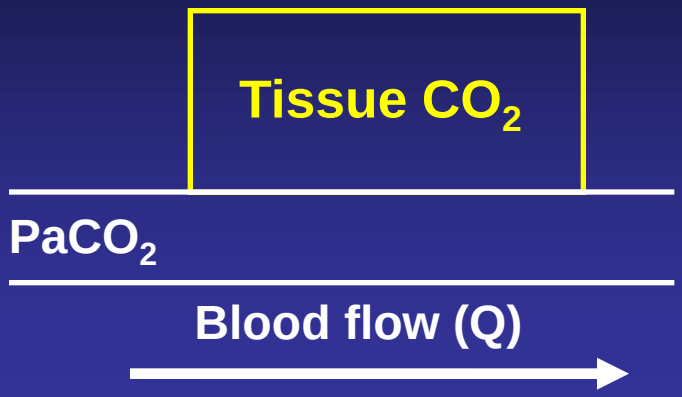


Determinants of tissue CO_2



Tissue CO_2 = PaCO2 + K (VCO_2/Q)

Determinants of tissue CO_2



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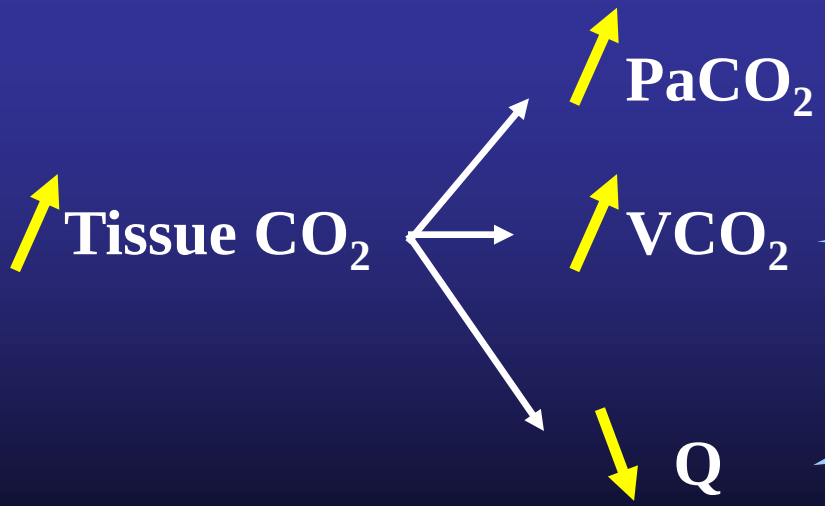
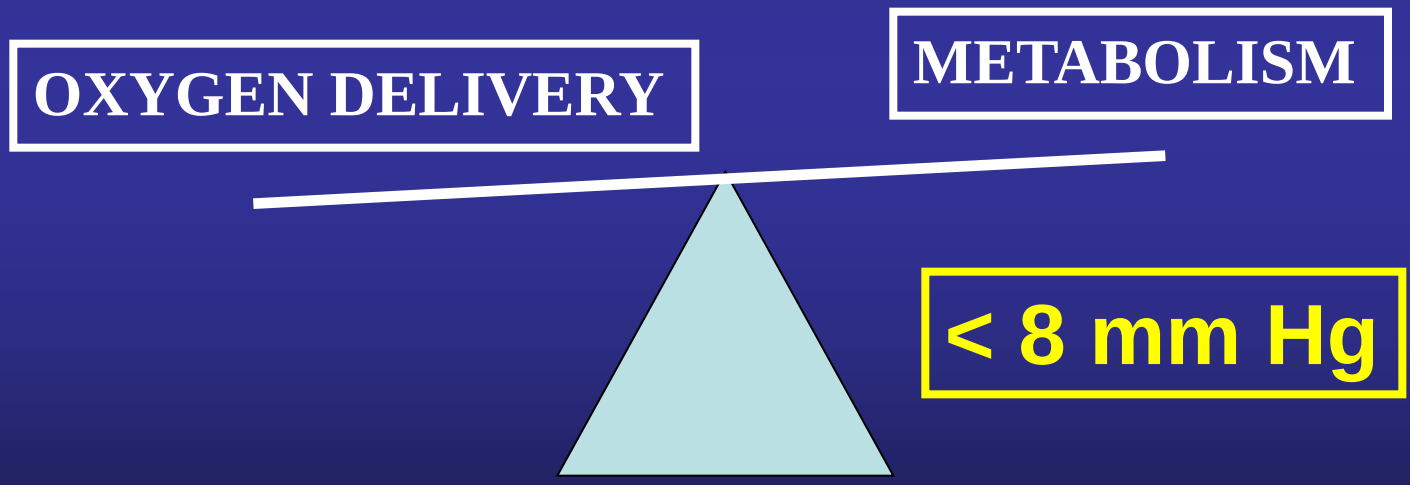


Increase in tissue metabolism

- **Decrease in systemic and/or regional blood flow (decrease in CO_2 clearance)**

Determinants of tissue CO_2

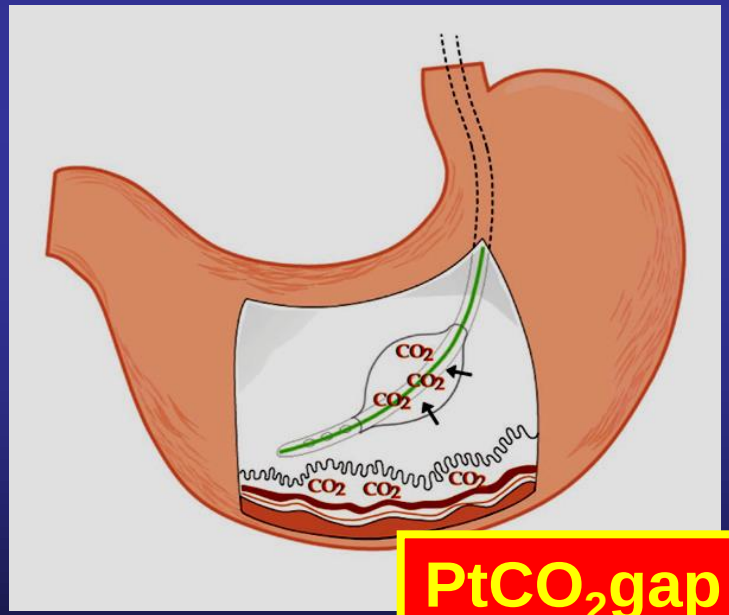
Tissue CO_2 gradient = Tissue CO_2 - $PaCO_2$



Monitoring tissue perfusion

Tissue CO_2 monitoring

Gastric tonometry



Sublingual capnometry

$PtCO_2gap = PtCO_2 - PaCO_2$

Normal value < 8 mm Hg

Increased tissue CO_2

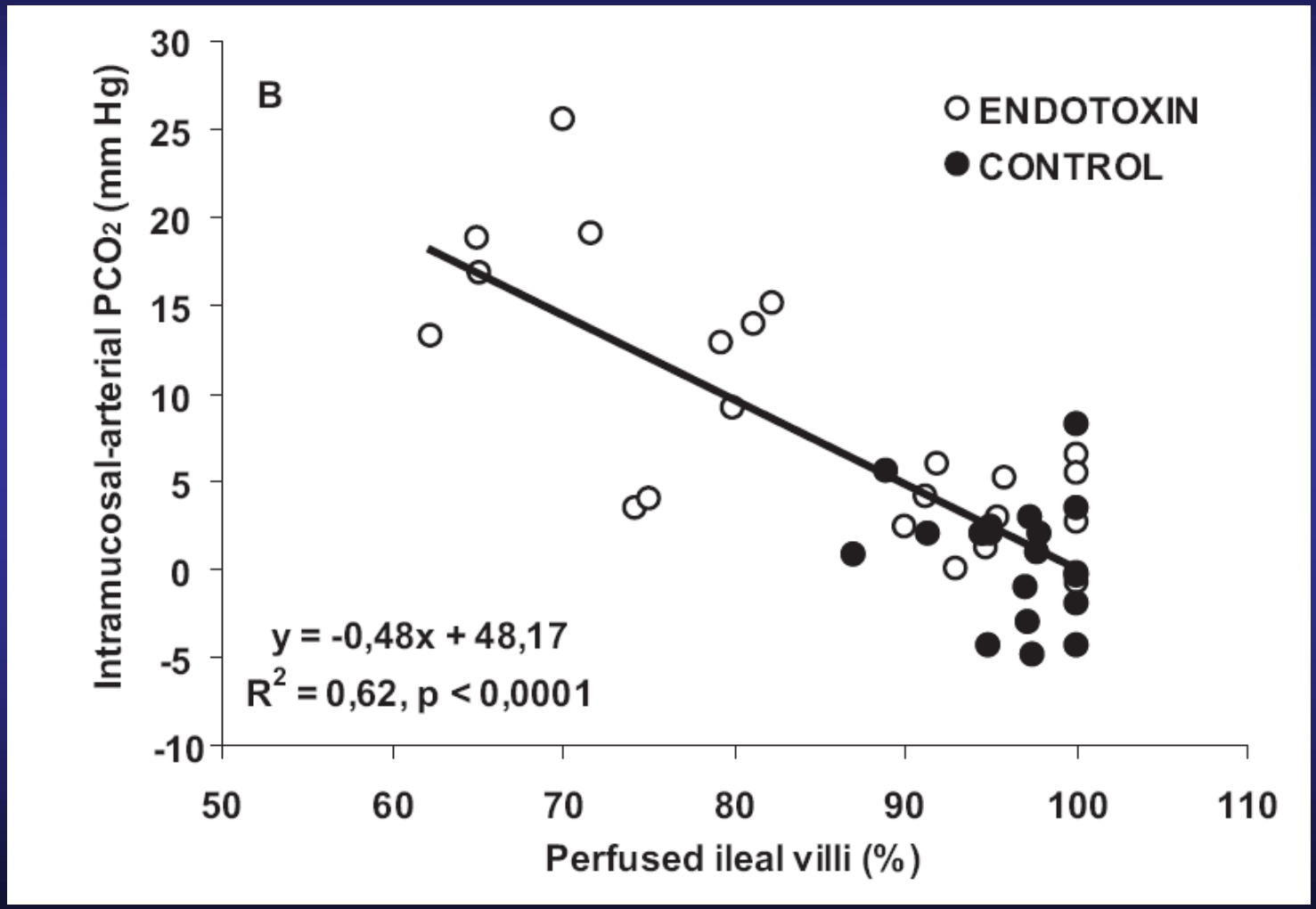
=

Inadequate tissue perfusion

Villi hypoperfusion and intramucosal acidosis in endotoxemia

Dubin et al. Crit Care Med. 2008; 36:535-542

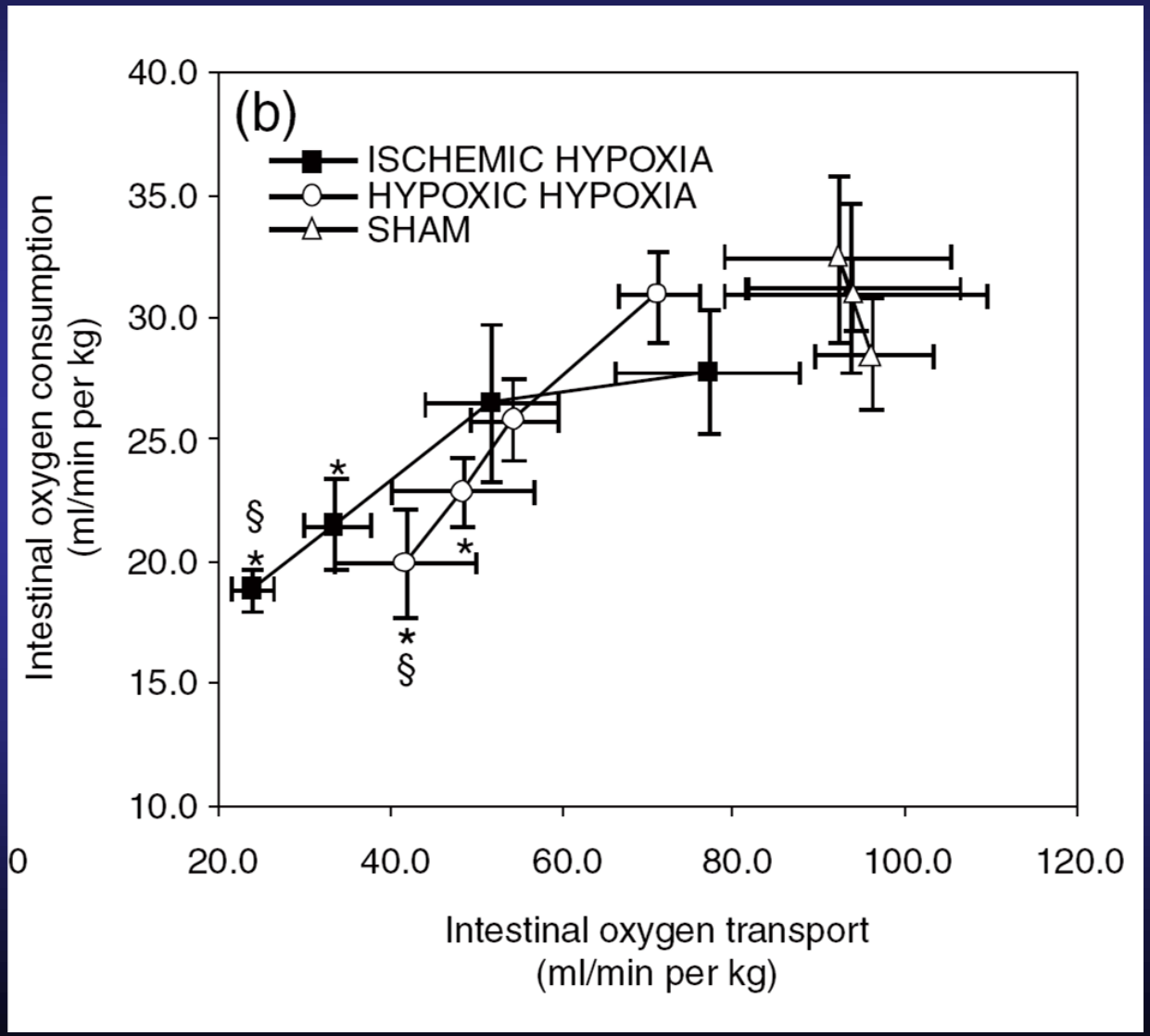
Sheep - endotoxemia



Ischemic vs hypoxic hypoxia and intramucosal acidosis in endotoxemia

Dubin et al. Crit Care. 2002; 6:514-520

Sheep



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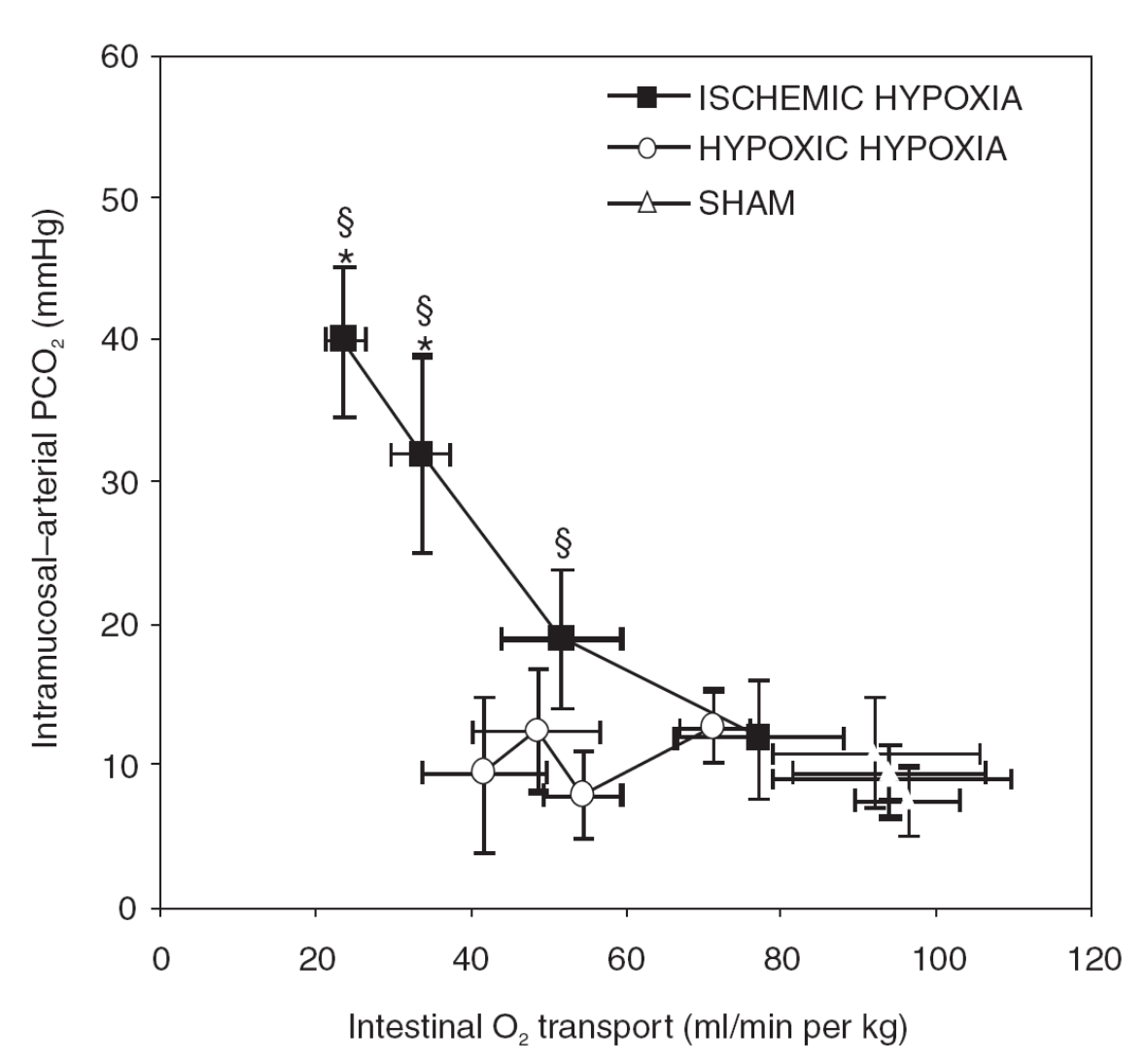
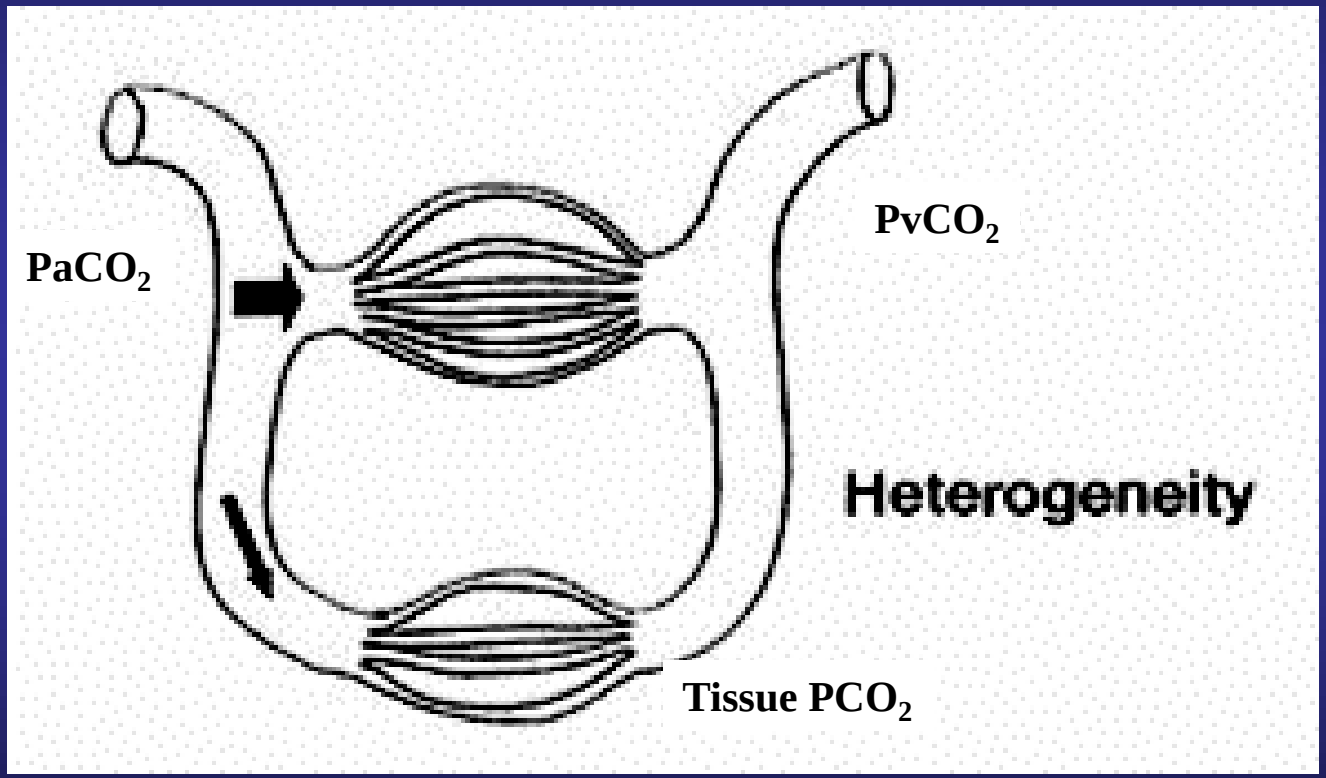


Microcirculatory oxygenation and shunting in sepsis and septic shock

After Ince et al. Crit Care Med 1999; 27:1369-1377



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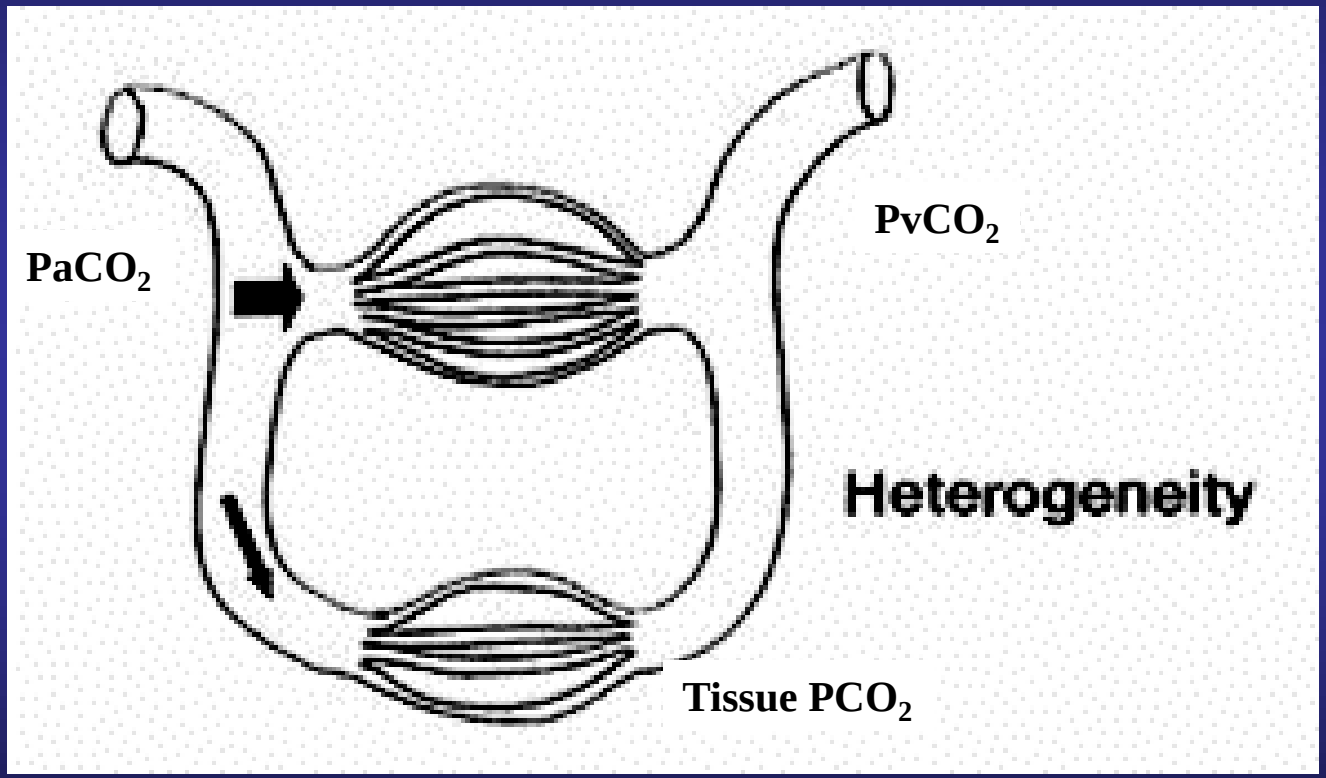
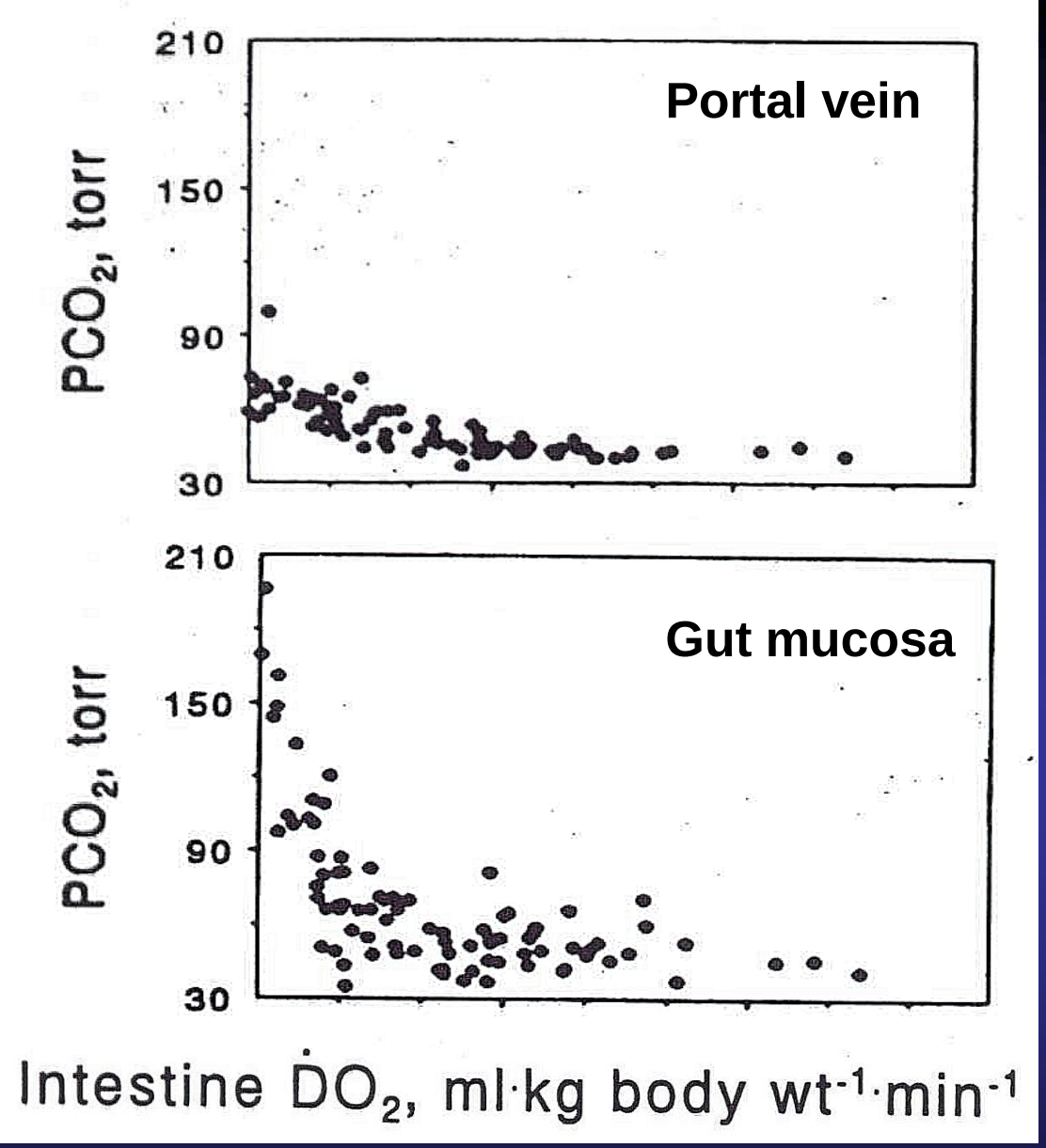
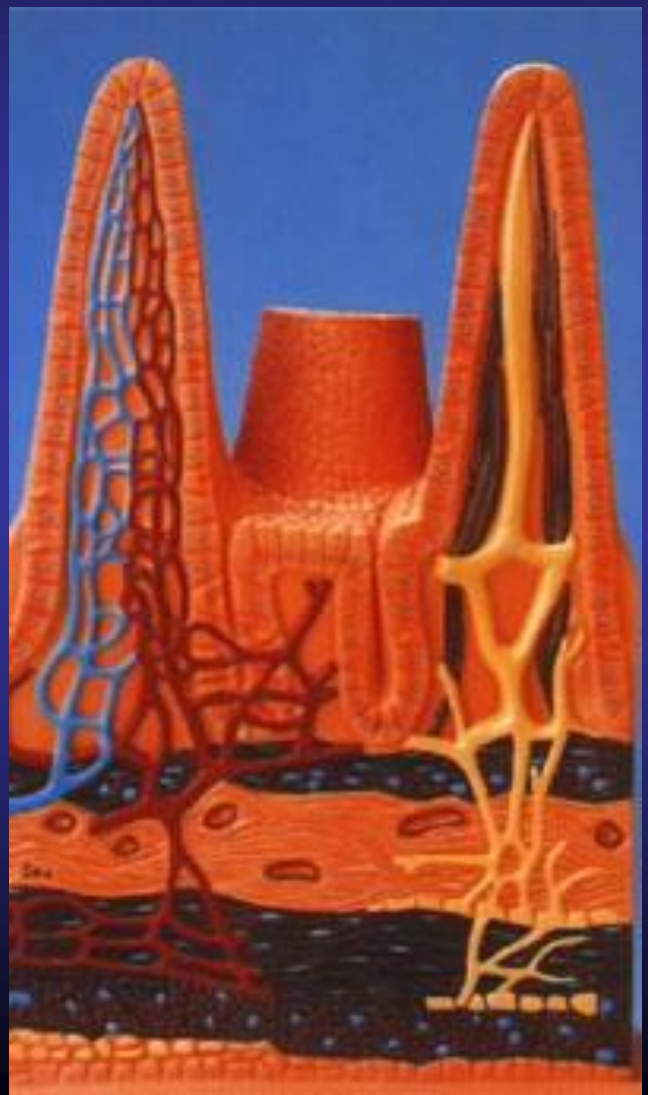


Tissue PCO_2 > $PvCO_2$

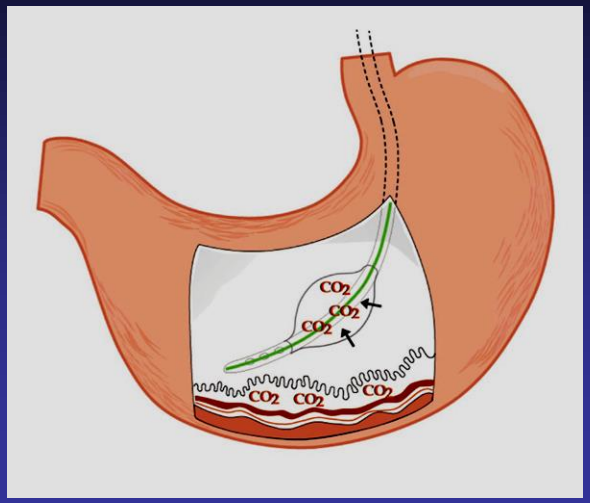


Progressive lethal cardiac tamponade in anesthetized dogs

From Schlichtig et al. JAP. 1994: 76; 2443.

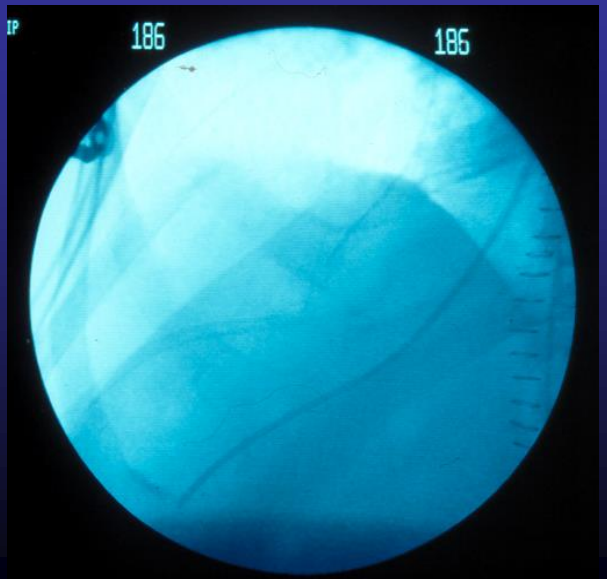


gastric tonometry



Gastric mucosa PCO_2

Hepatic vein catheterization

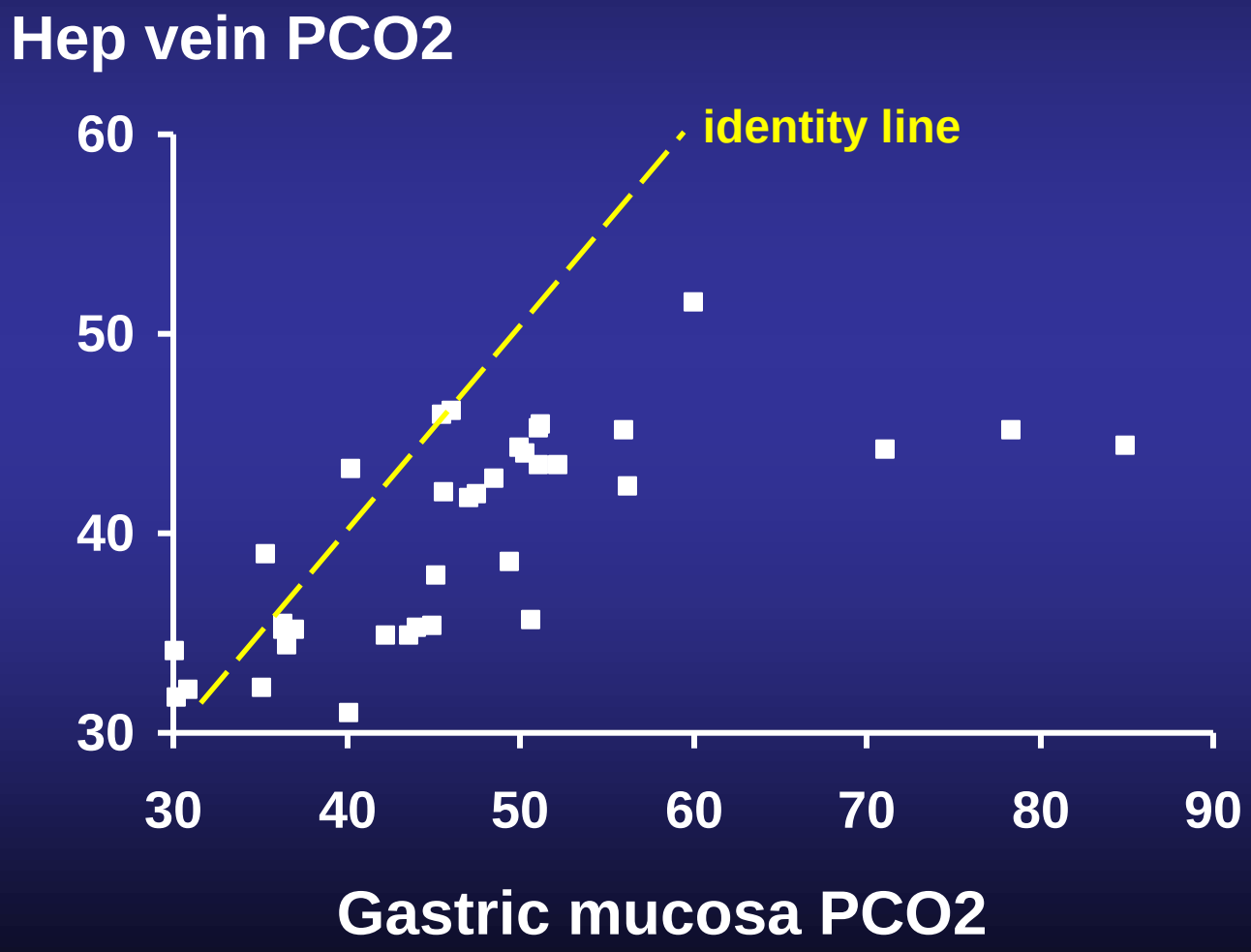


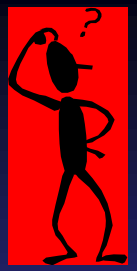
Sus hep vein PCO_2

PCO_2gap values in patients with septic shock

Creteur et al. Crit Care Med 1999: 27;2480-2484

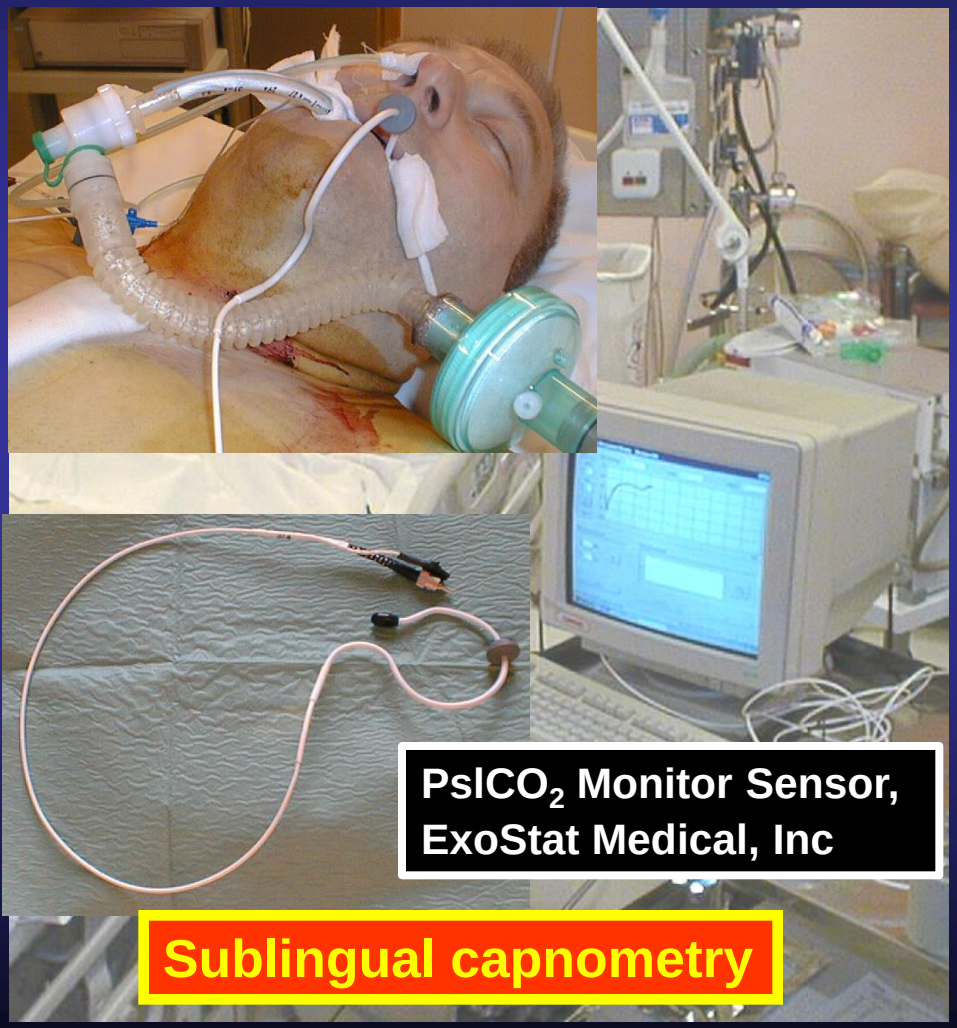
N = 36 hemodynamically stabilized septic patients



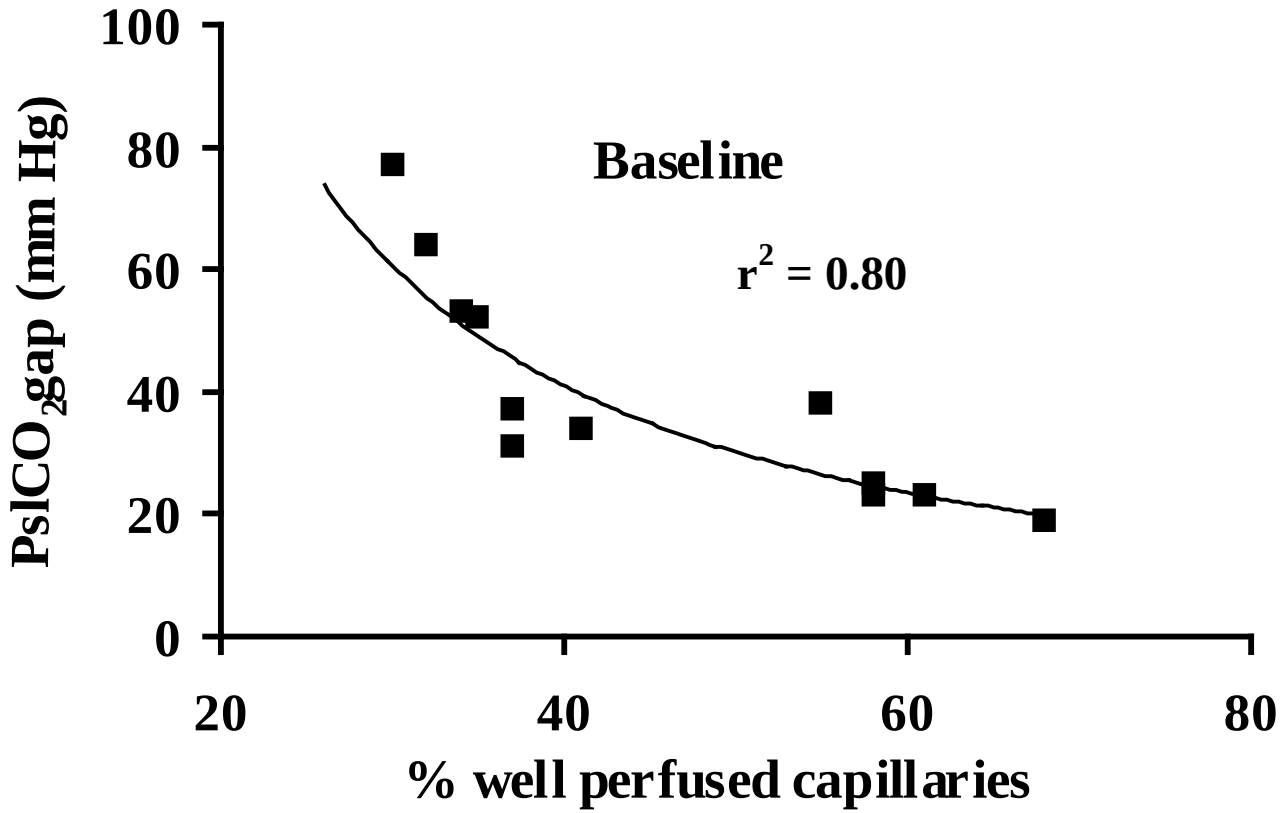


In patients with severe sepsis:

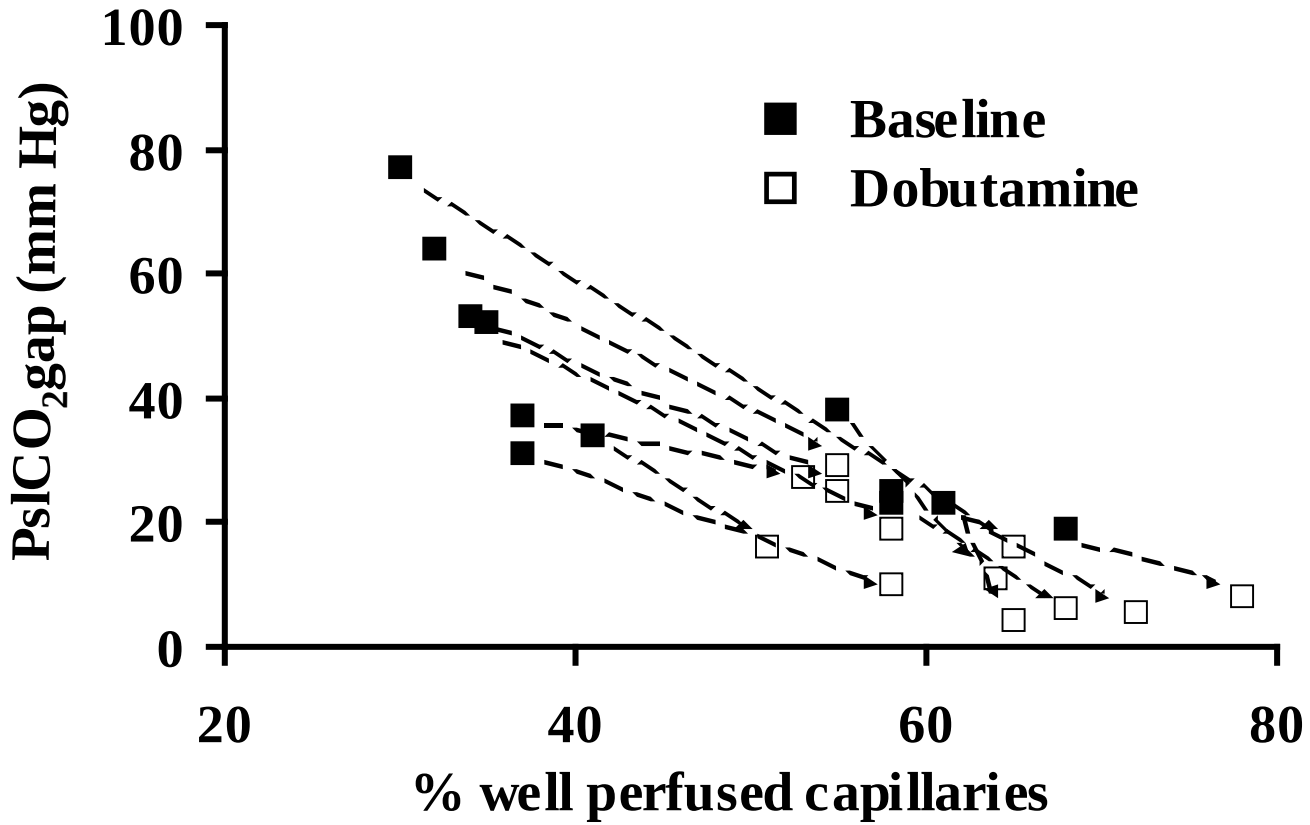
- **Is there a link between the increase in tissue CO_2 and the microcirculatory alterations?**



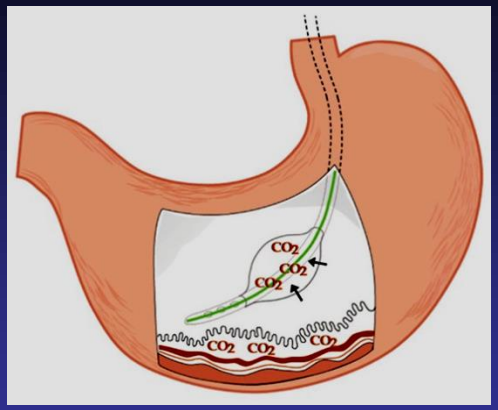
Creteur et al. Intensive Care Med 2006; 32:516 - 523



Creteur et al. Intensive Care Med 2006; 32:516 - 523



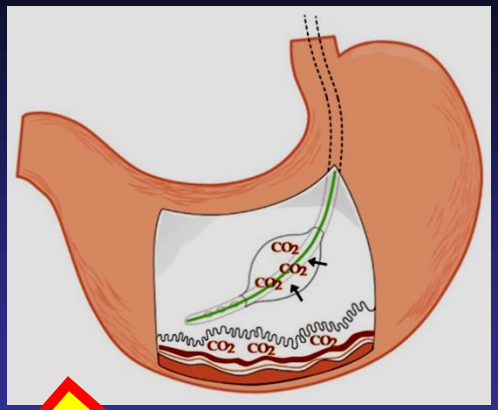
Gastric capnometry



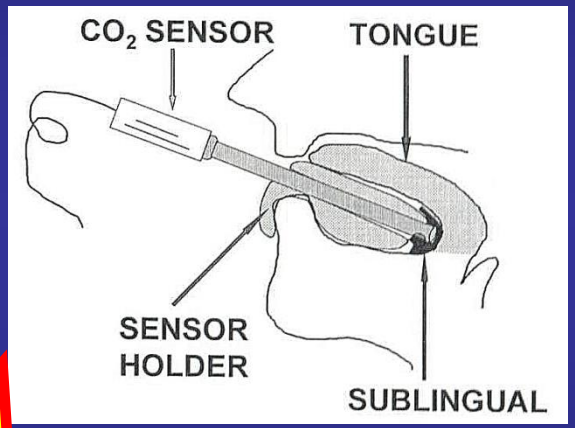
CO2 monitoring

Gastric capnometry

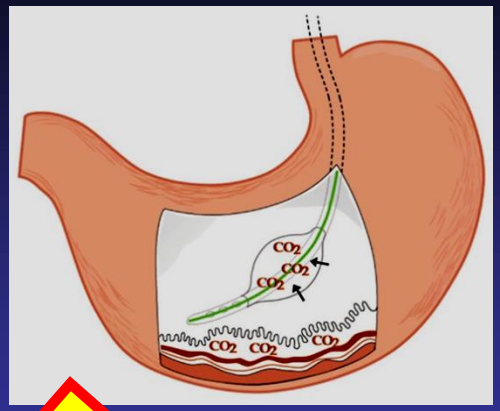
CO2 monitoring



Sublingual capnometry

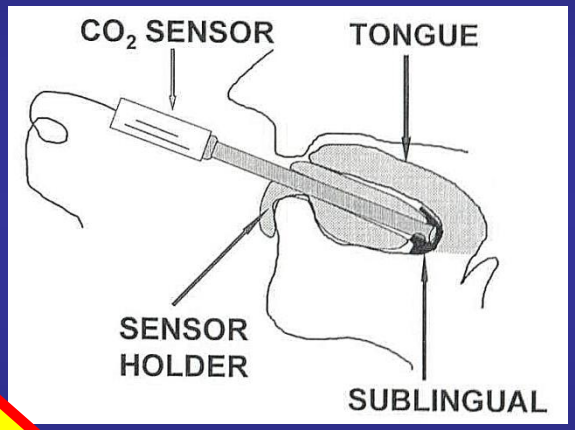


Gastric capnometry

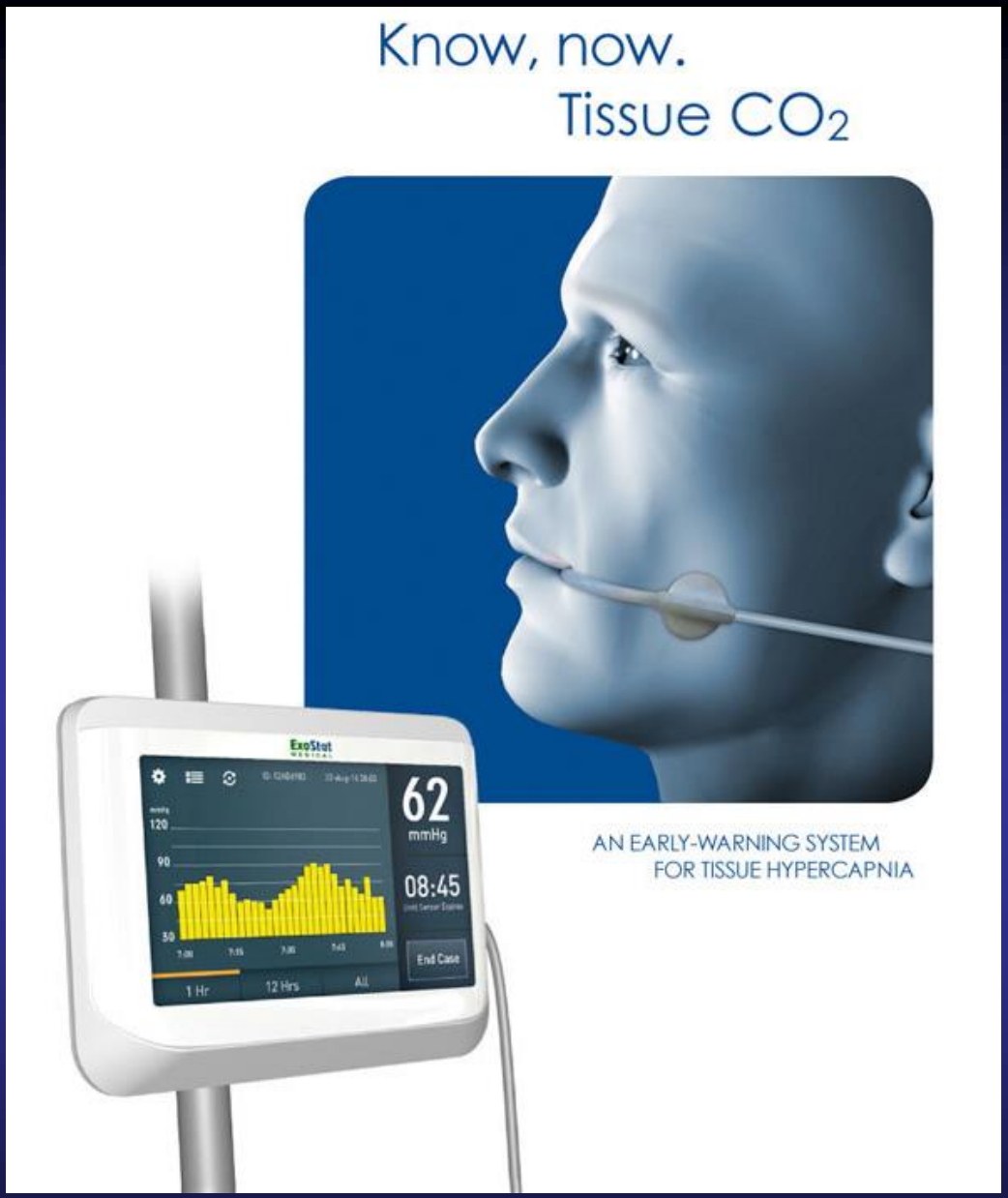


CO2 monitoring

Sublingual capnometry



Buccal capnometry



$P_{om}CO_2$

oral mucosal CO_2

ExoStat MEDICAL

MicroStat™ System

Tissue perfusion monitoring

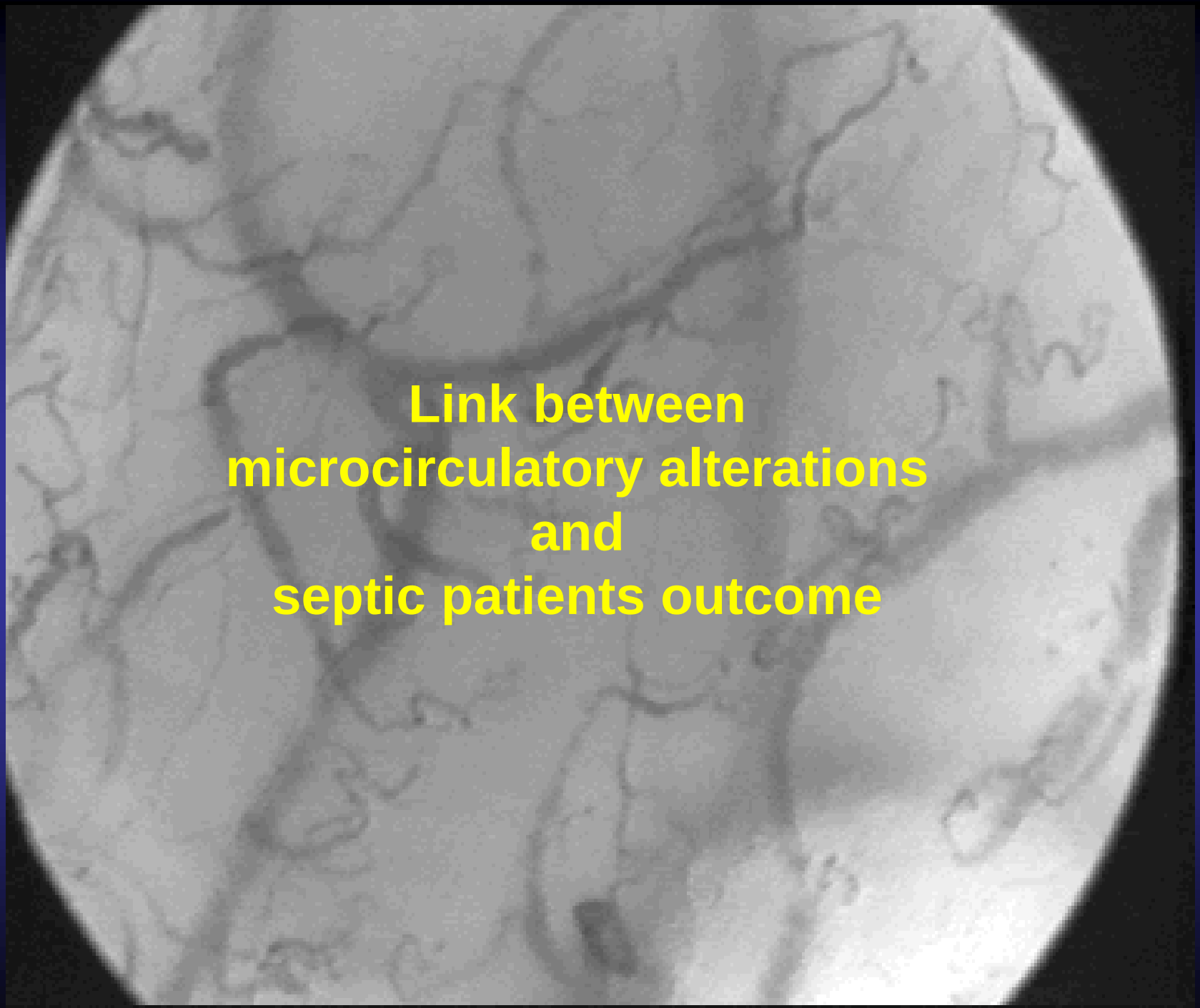
- **Direct measurements**

  - LDF
  - OPS
  - SDF

  } - microvascular blood flow

- **Indirect measurements**

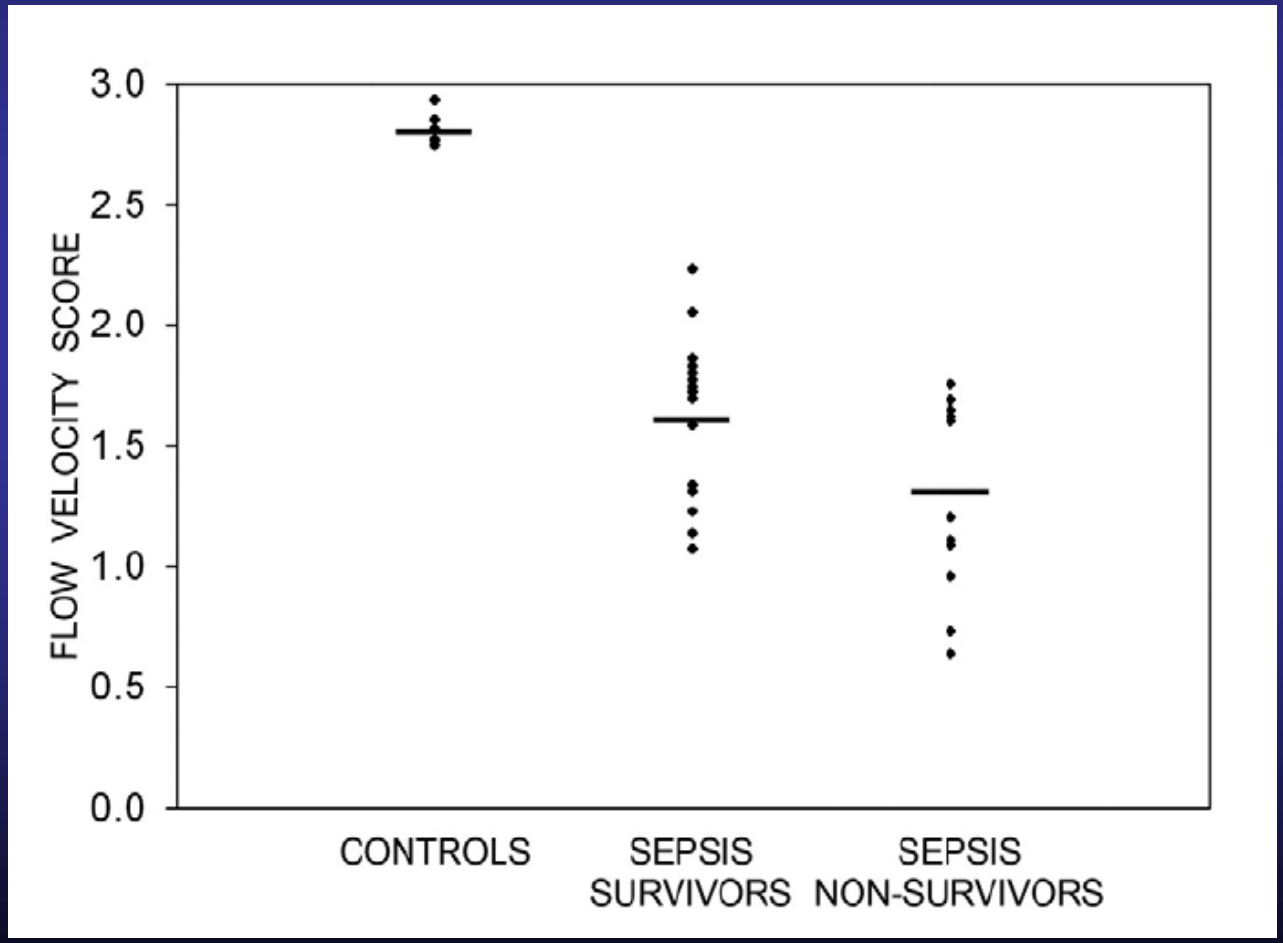
  - NIRS (StO2 - VOT) - « tissue » oxygenation
    - vasoreactivity (endothelial function)
    - VO2
  - Tissue CO2 - flow vs metabolism


Link between
microcirculatory alterations
and
septic patients outcome

Early microcirculatory alterations in severe sepsis

Trzeciak et al Ann Emerg Med 2007; 49:88-98

N = 26 severe sepsis patients
OPS – sublingual site



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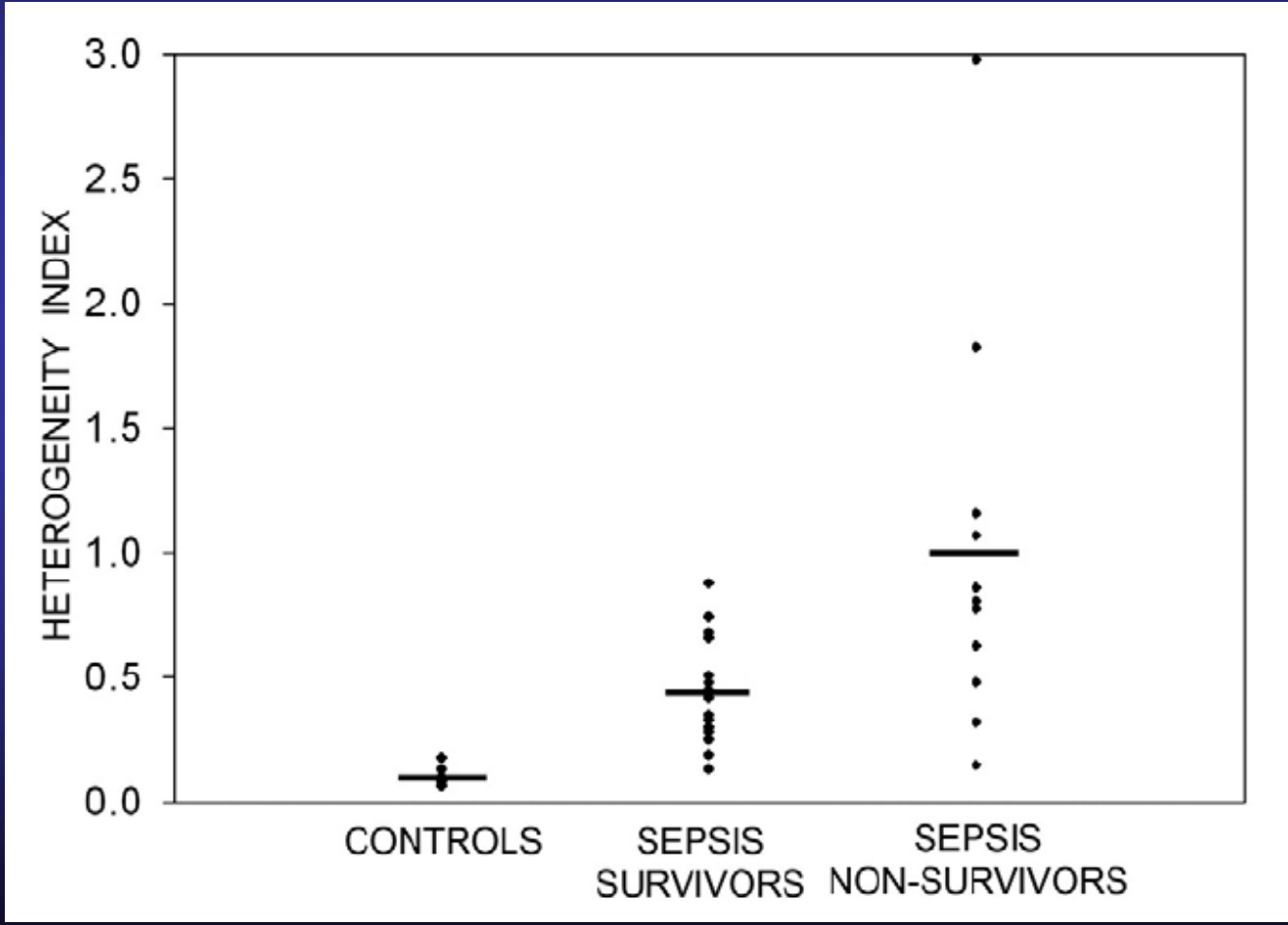
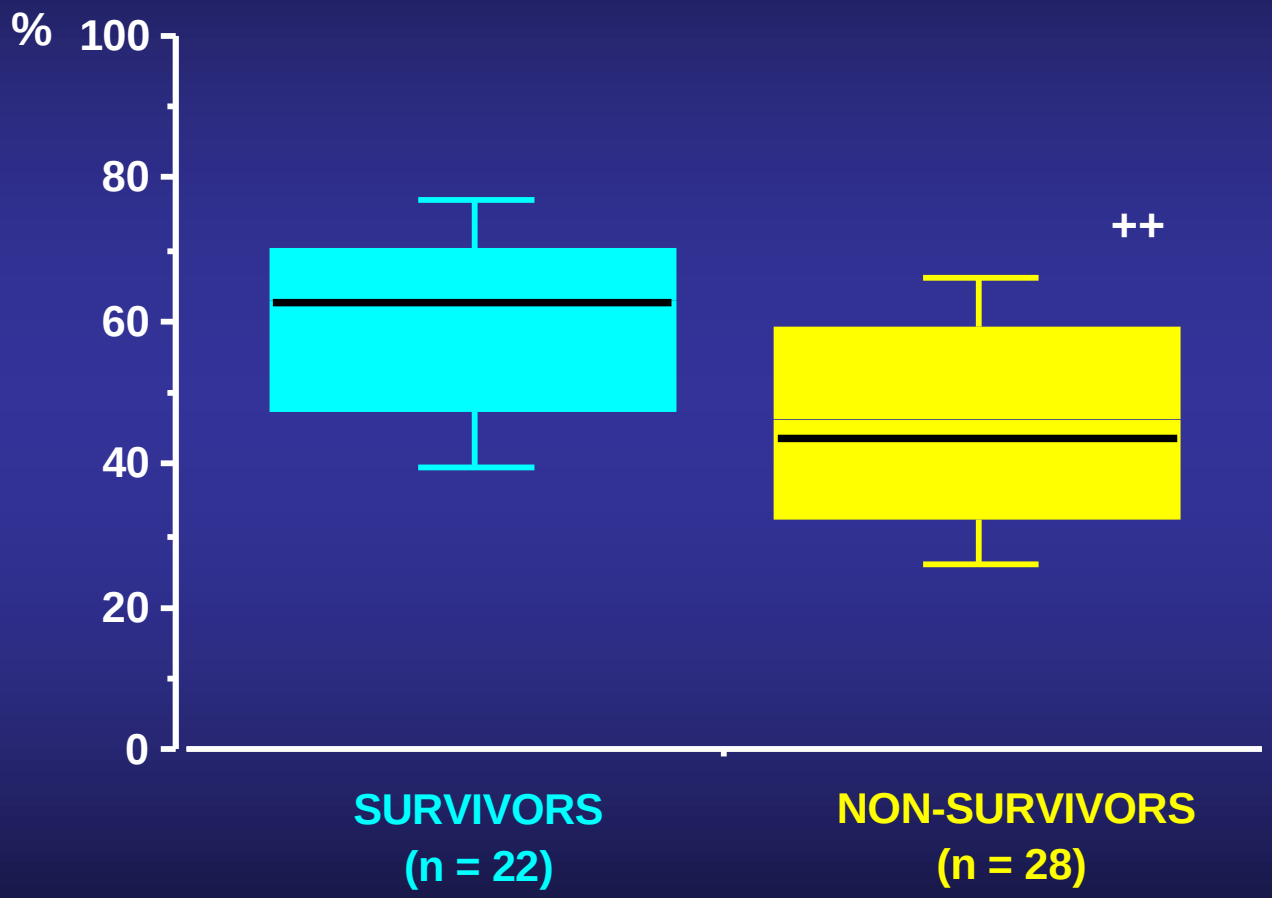


MICROCIRCULATORY ALTERATIONS IN SEPTIC PATIENTS

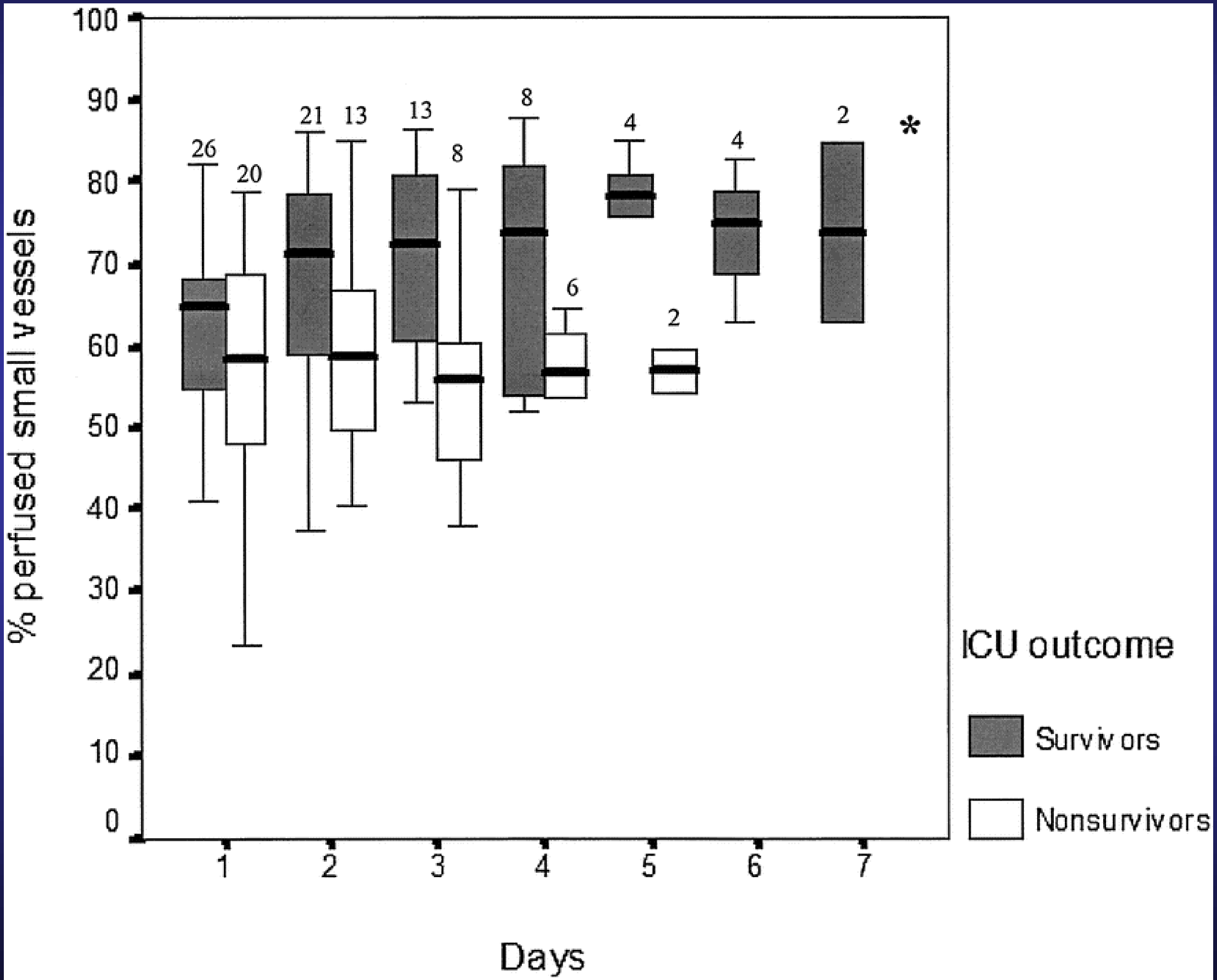
SEPSIS

Proportion of well perfused capillaries

De Backer et al
AJRCCM 166:98;200



++ p <0.01 vs survivors



% perfused small vessels
100
90
80
70
60
50
40
30
20
10
0
26
20
21
13
13
8
8
6
4
2
4
2
*
1
2
3
4
5
6
7
Days
ICU outcome
Survivors
Nonsurvivors

Sakr et al
CCM 32:1825;2004

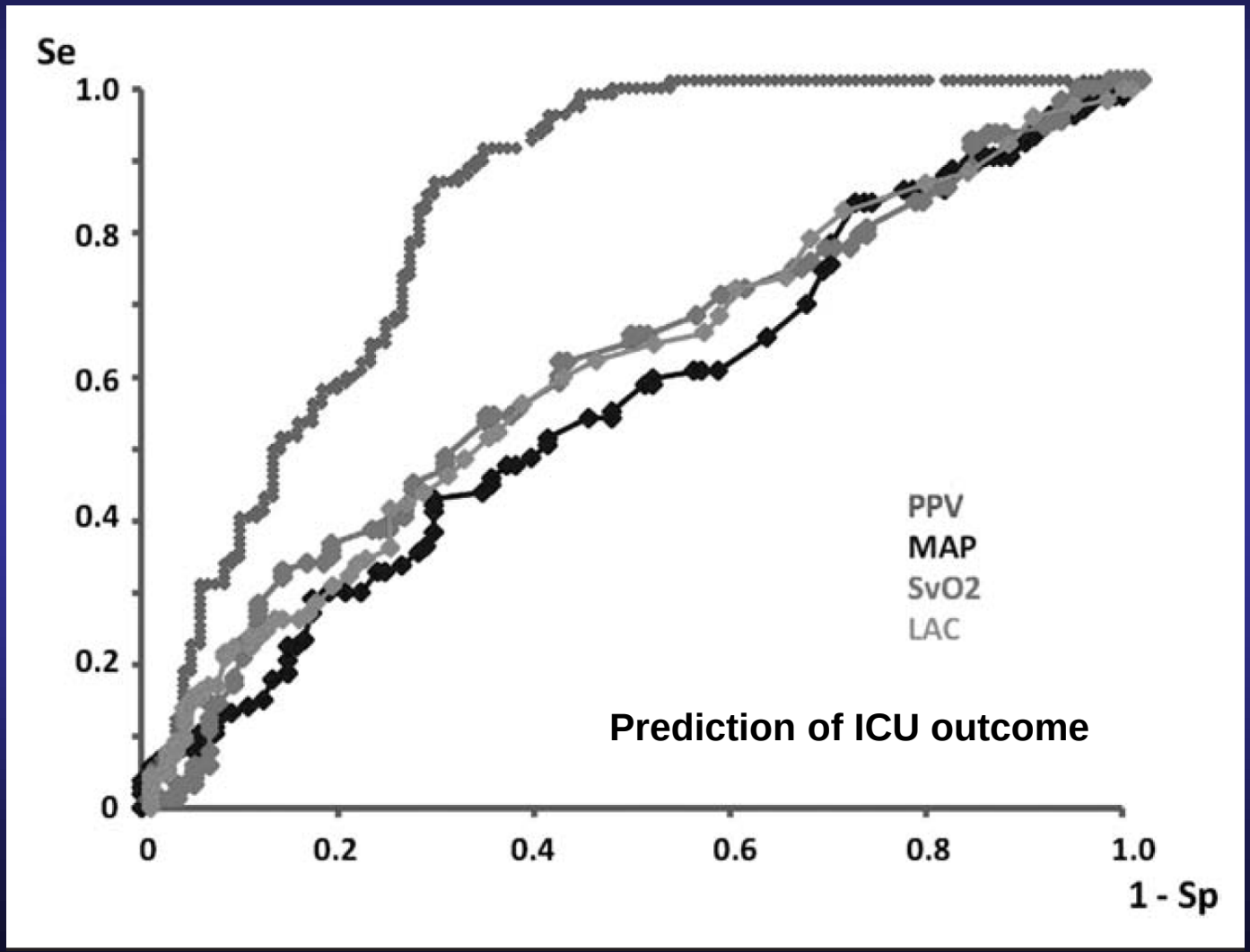
ROC curve area:

- **Changes between day 1 and day 2:**
  - heart rate 0.57
  - mean arterial pressure 0.53
  - CVP 0.51
  - PAOP 0.64
  - cardiac index 0.51
  - SvO_2 0.52
  - DO_2 0.52
  - VO_2 0.50
  - Lactate 0.63
  - **Microvascular perfusion 0.77**
  - SOFA score 0.61

Microcirculatory Alterations in Patients With Severe Sepsis: Relationship With Outcome

De Backer et al. Crit Care Med 2013

n = 252 patients with severe sepsis



Microcirculatory Alterations in Patients With Severe Sepsis: Relationship With Outcome

De Backer et al. Crit Care Med 2013

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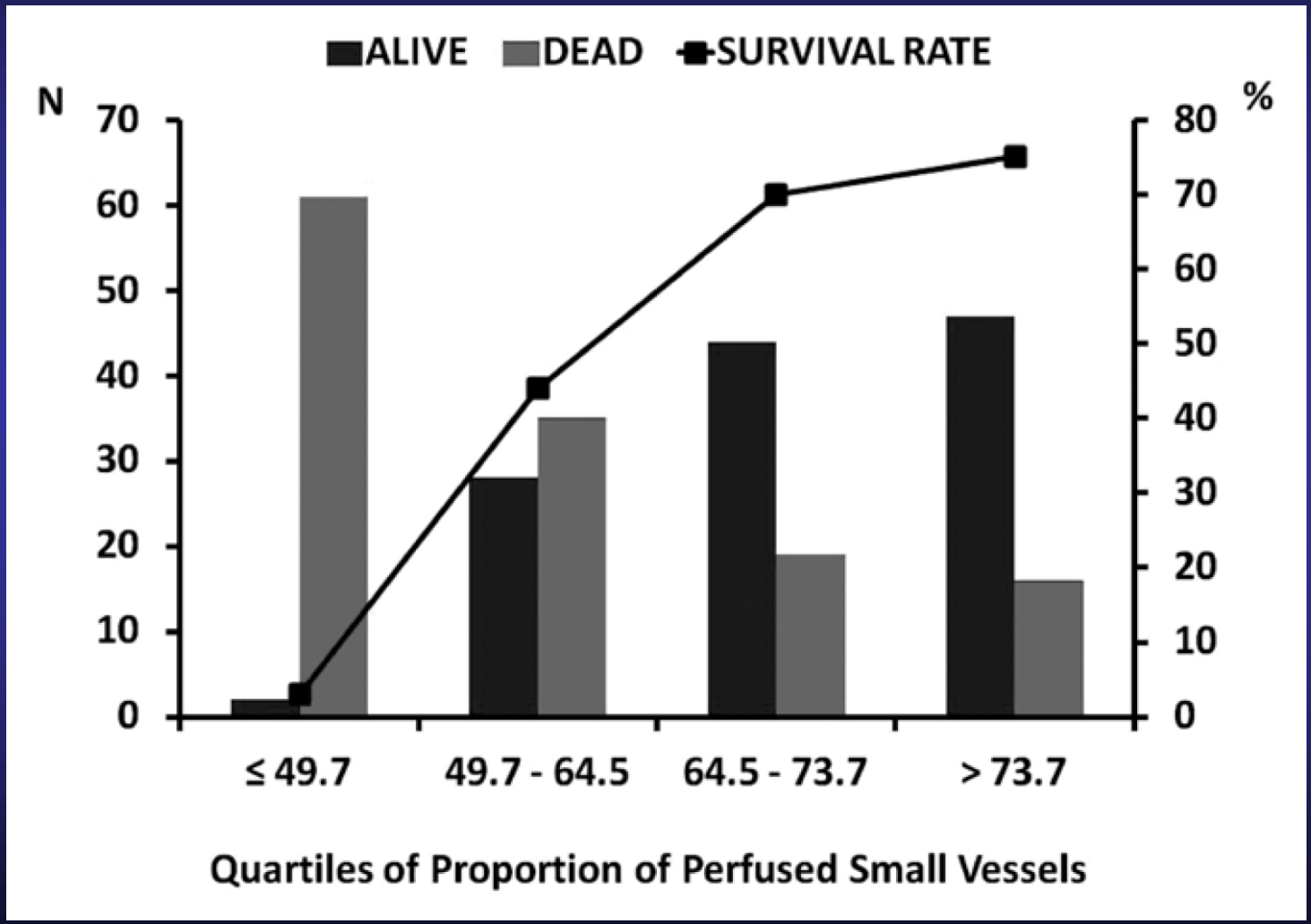
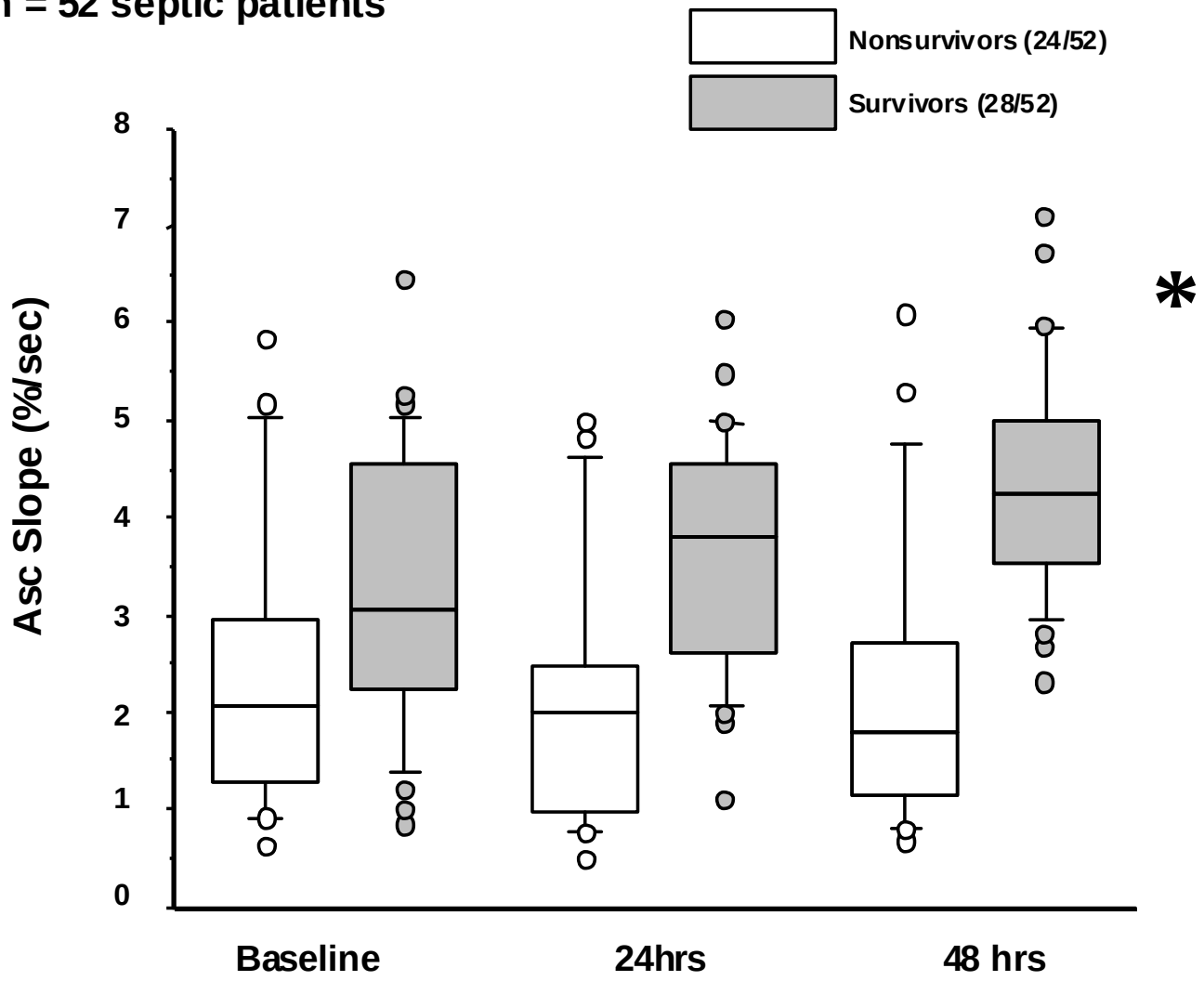


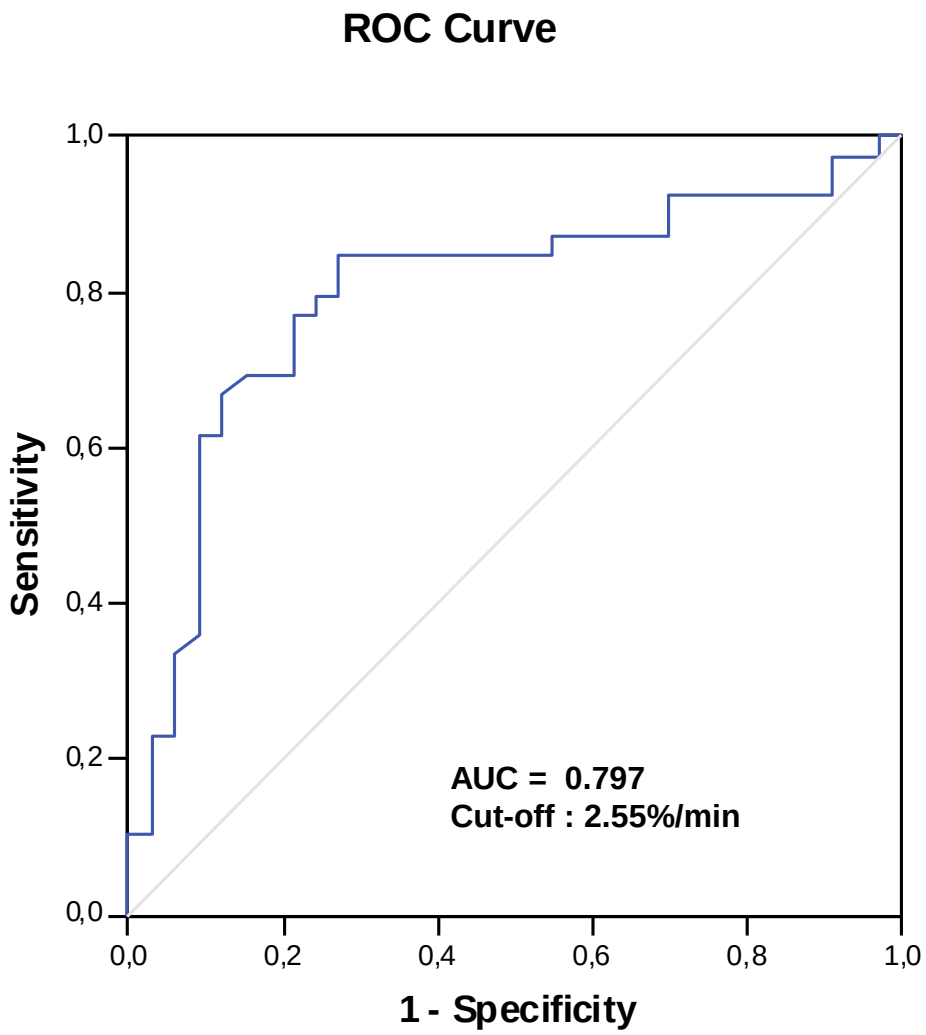
Creteur et al. Intensive Care Med 2007 ; 33 : 1549-1556

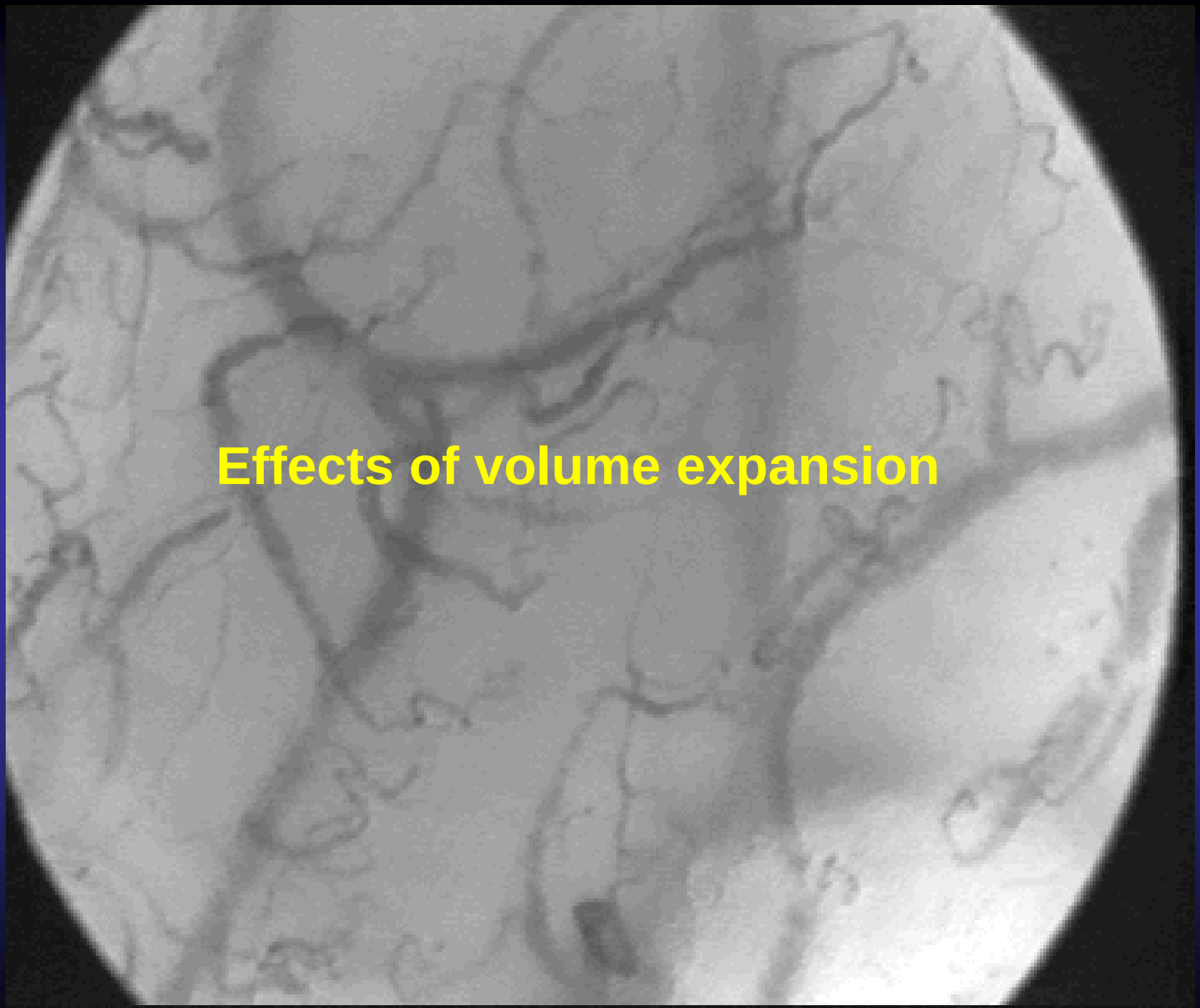
n = 52 septic patients



*analysis of variance: p < 0.01

Admission Asc slope and the prediction of death




Effects of volume expansion

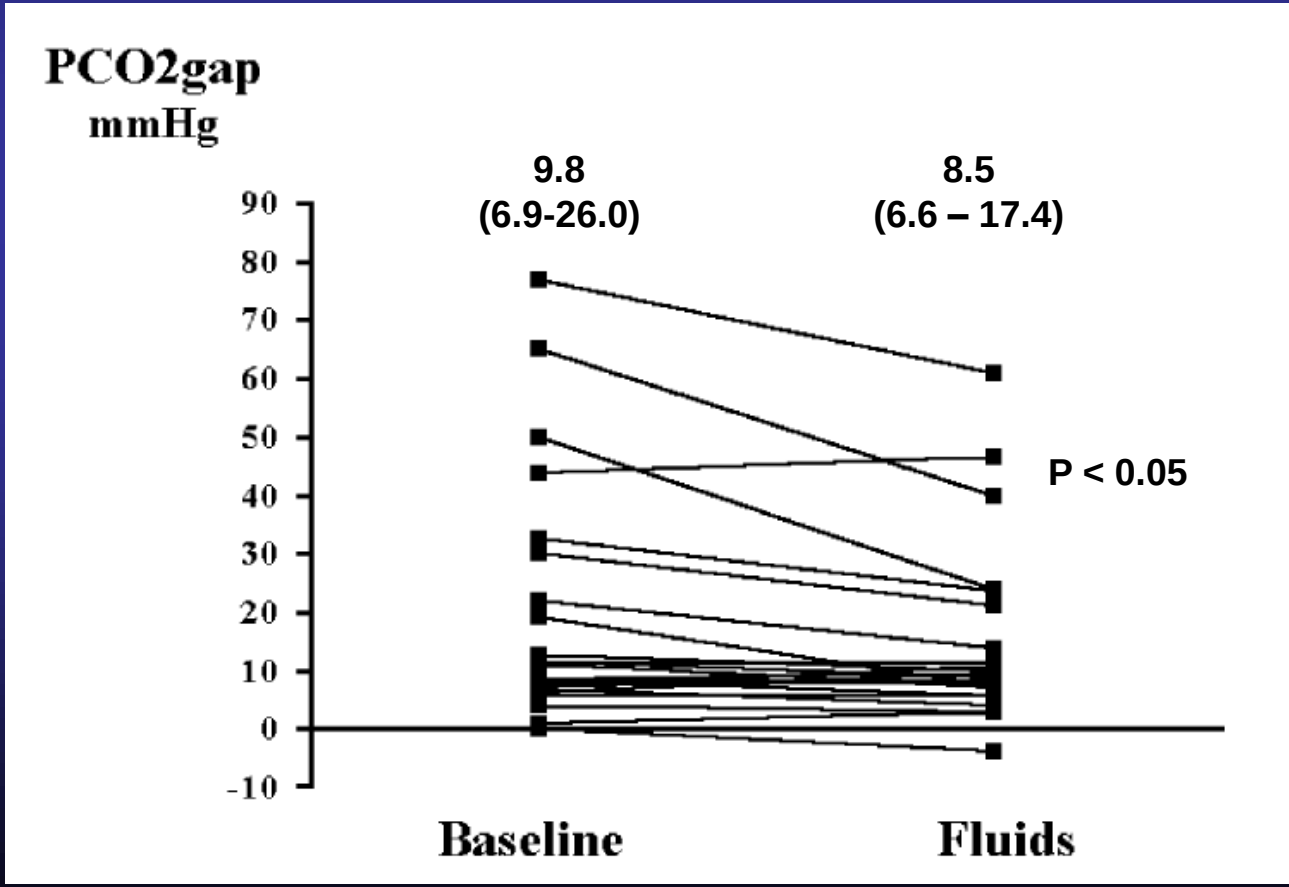
Intensive Care Med (2004) 30:423–429
DOI 10.1007/s00134-003-2115-2

ORIGINAL

Eliézer Silva
Daniel De Backer
Jacques Creteur
Jean-Louis Vincent

Effects of fluid challenge on gastric mucosal PCO_2 in septic patients

24 septic patients - 500 ml HES



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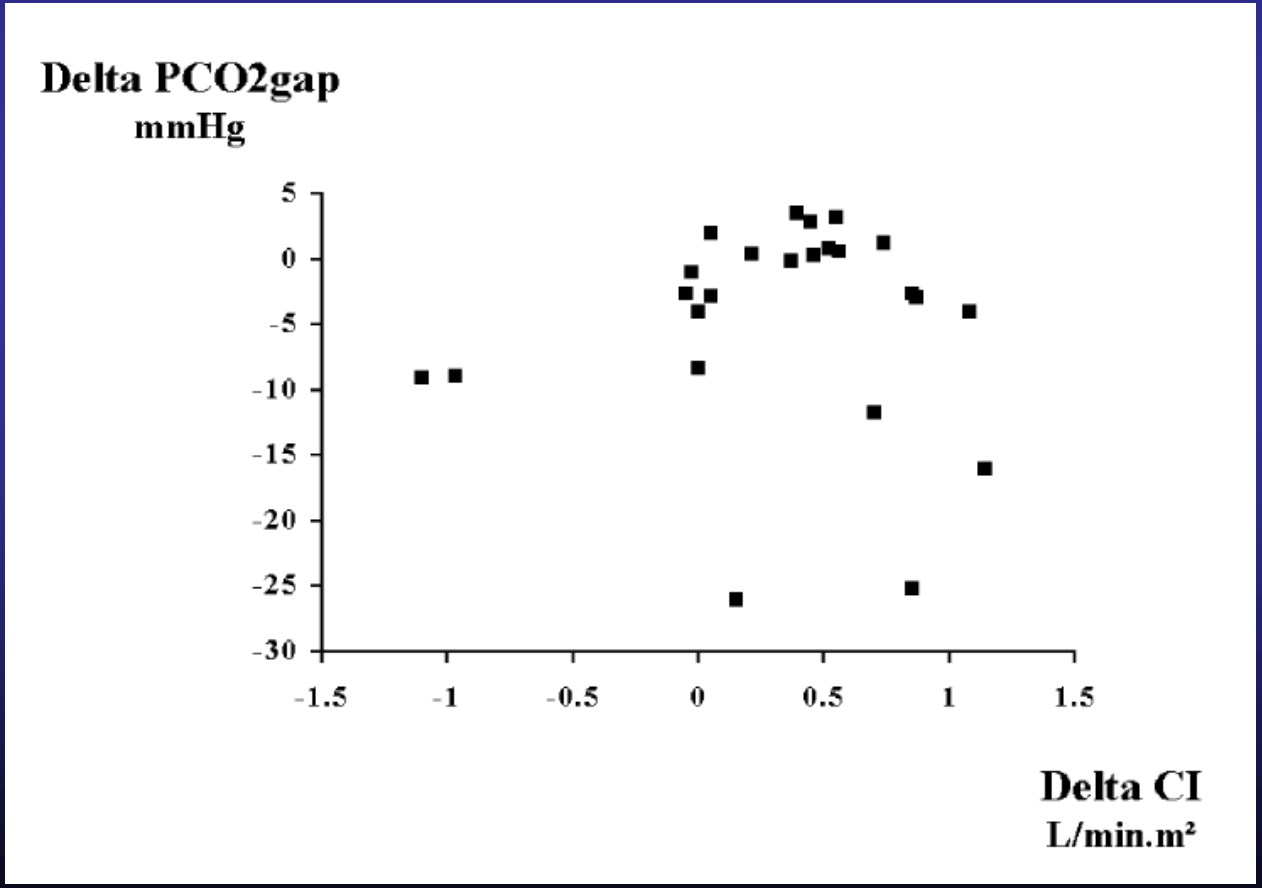

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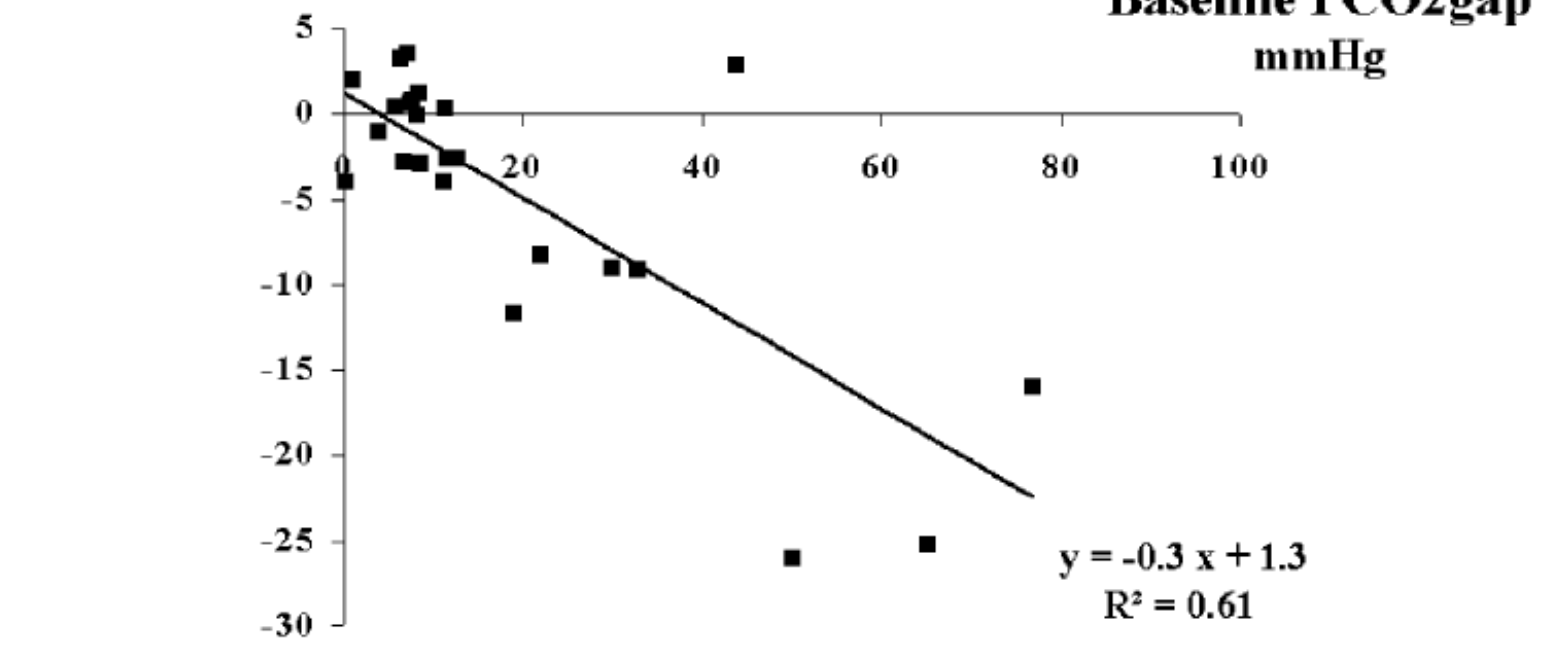
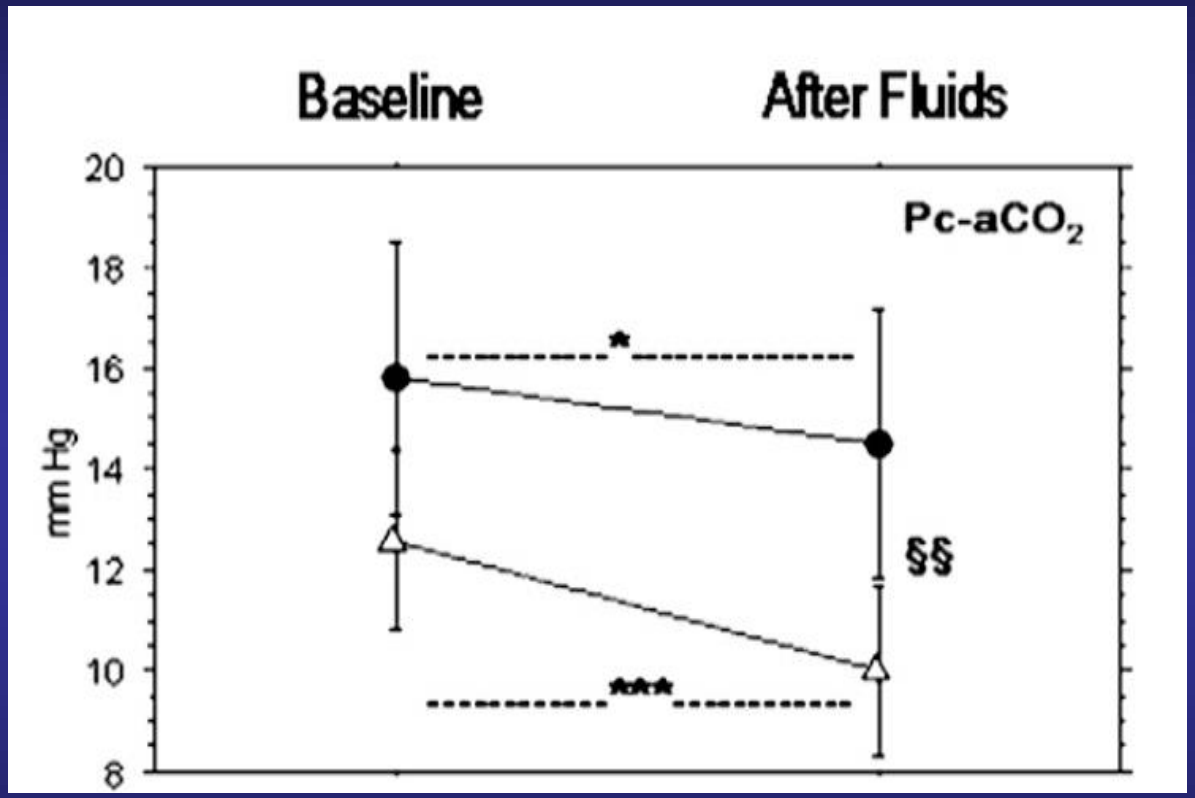
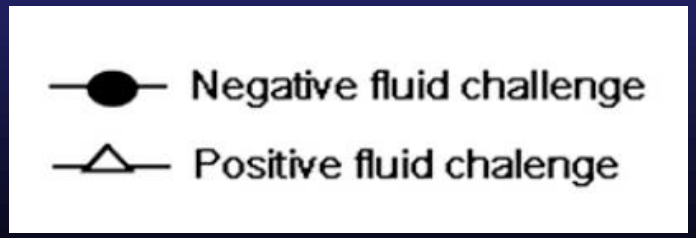


Cutaneous ear lobe PCO2 in patients with septic shock

Vallée et al. Chest 2010;138:1062-1070

n= 16 patients in septic shock- Fluid challenge

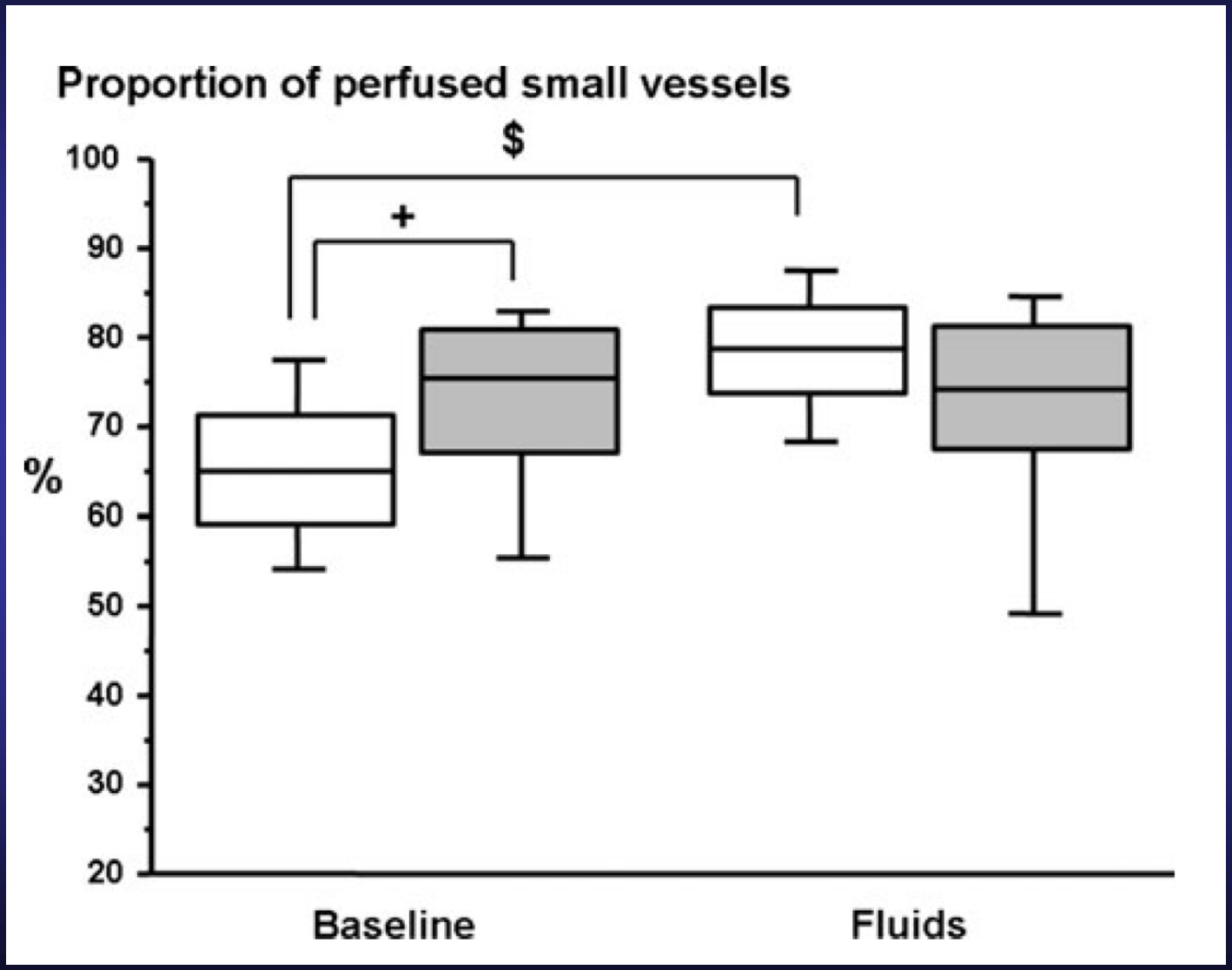


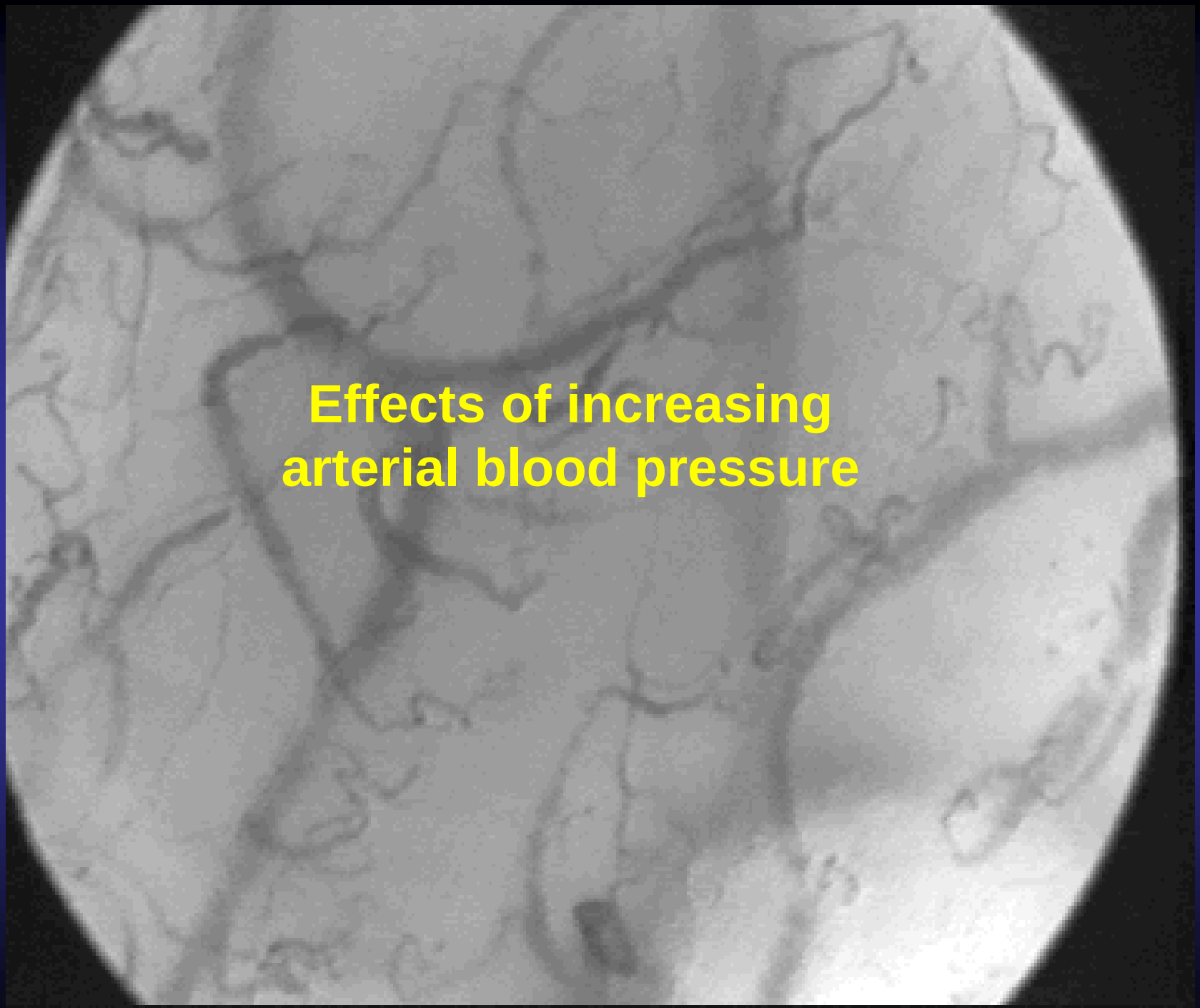


Positive fluid challenge: Delta CO > 15%

Effects of fluids on microvascular perfusion in patients with sepsis

Ospina-Tascon et al. Intensive Care Med 2010;36:949-955

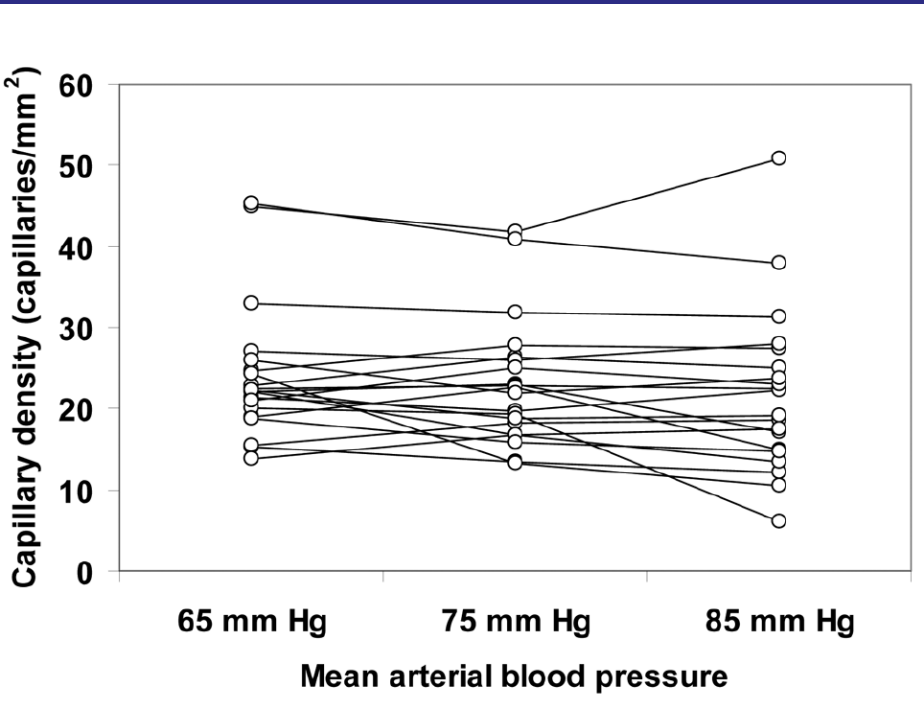


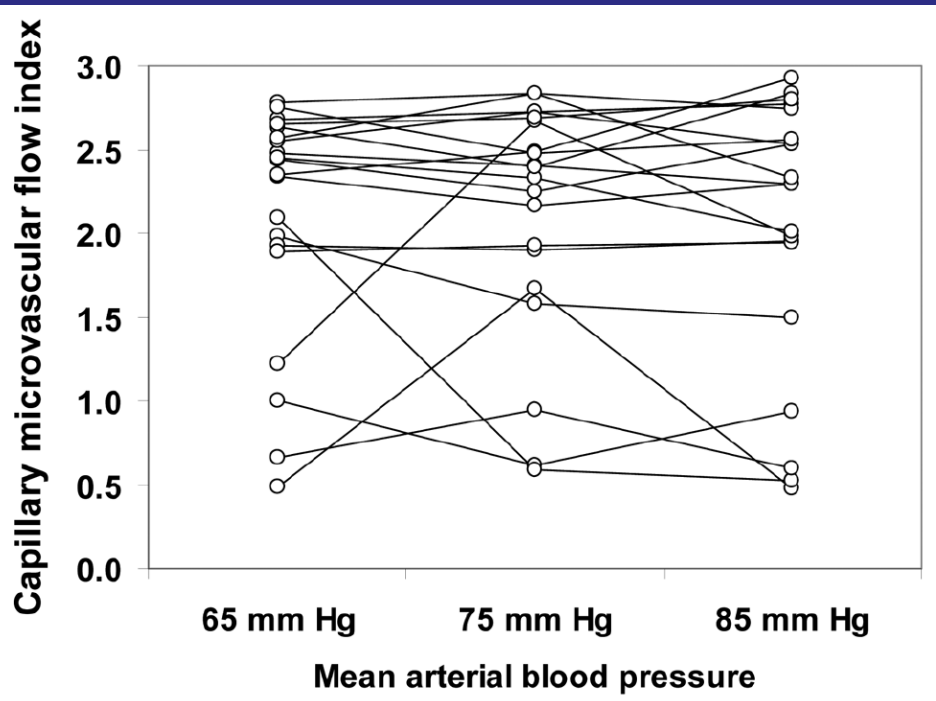

Effects of increasing
arterial blood pressure

Effects of increasing MAP on microcirculatory blood flow

Dubin et al. Crit Care 2009 : 13 ; R92

n = 20 patients in septic shock





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Dubin et al. Crit Care 2009 : 13 ; R92

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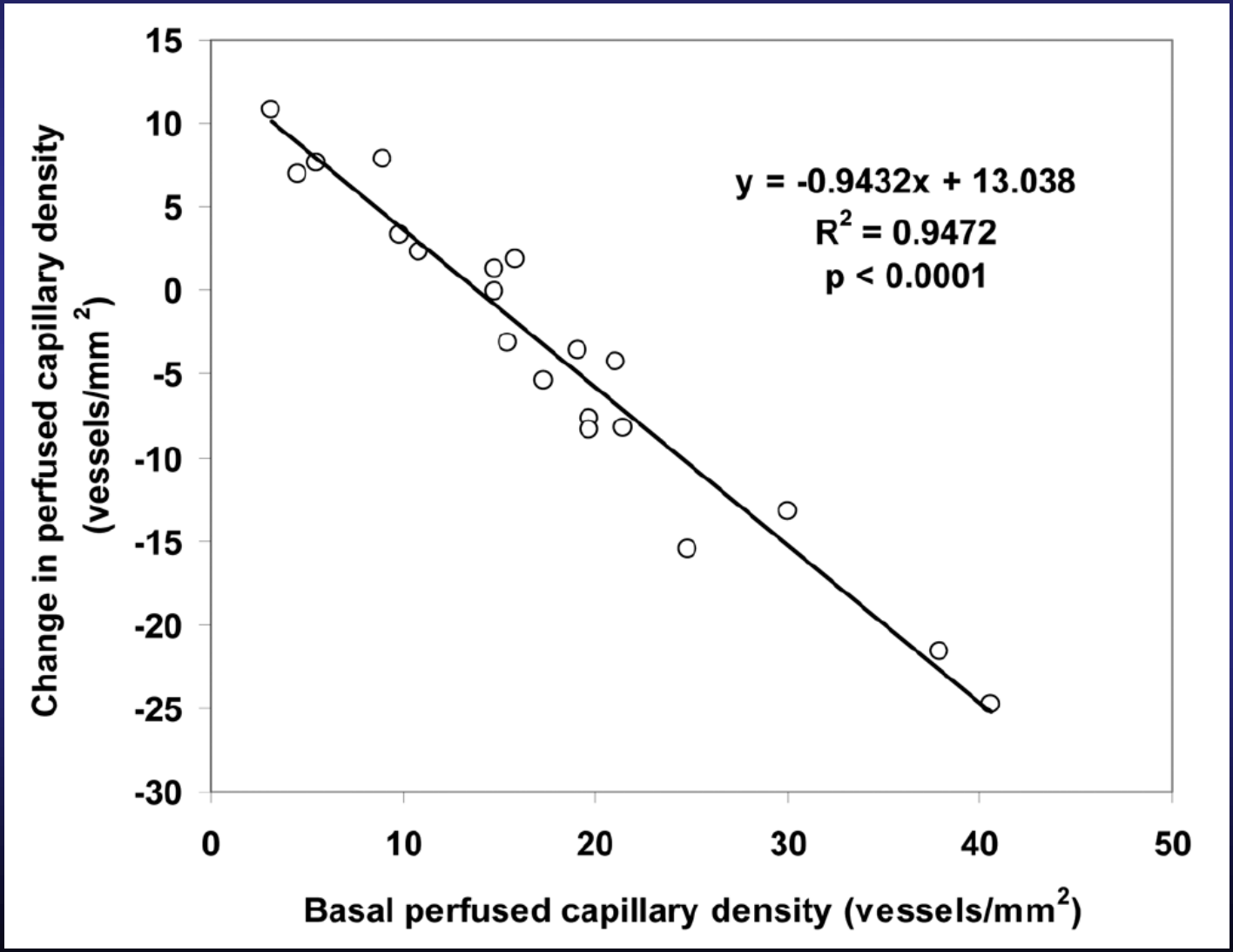

Restoring arterial pressure with norepinephrine improves muscle StO2 in severely hypotensive septic patients

Georger JF et al. Intensive Care Med 2010; 36:1882–1889

n = 28 septic shock patients

	Before norepinephrine (introduction/increase)	After norepinephrine (introduction/increase)
StO_2 (%)	75 ± 9	78 ± 9*
Occlusion time (s)	263 ± 104	274 ± 170
StO_2 desaturation slope (%/min)	9.5 ± 4.4	10.1 ± 4.6
StO_2 recovery slope (%/s)	1.0 ± 0.6	1.5 ± 0.7*
StO_2 max (%)	81 ± 10	86 ± 8*
ΔStO_2 (%)	8 ± 4	10 ± 5*

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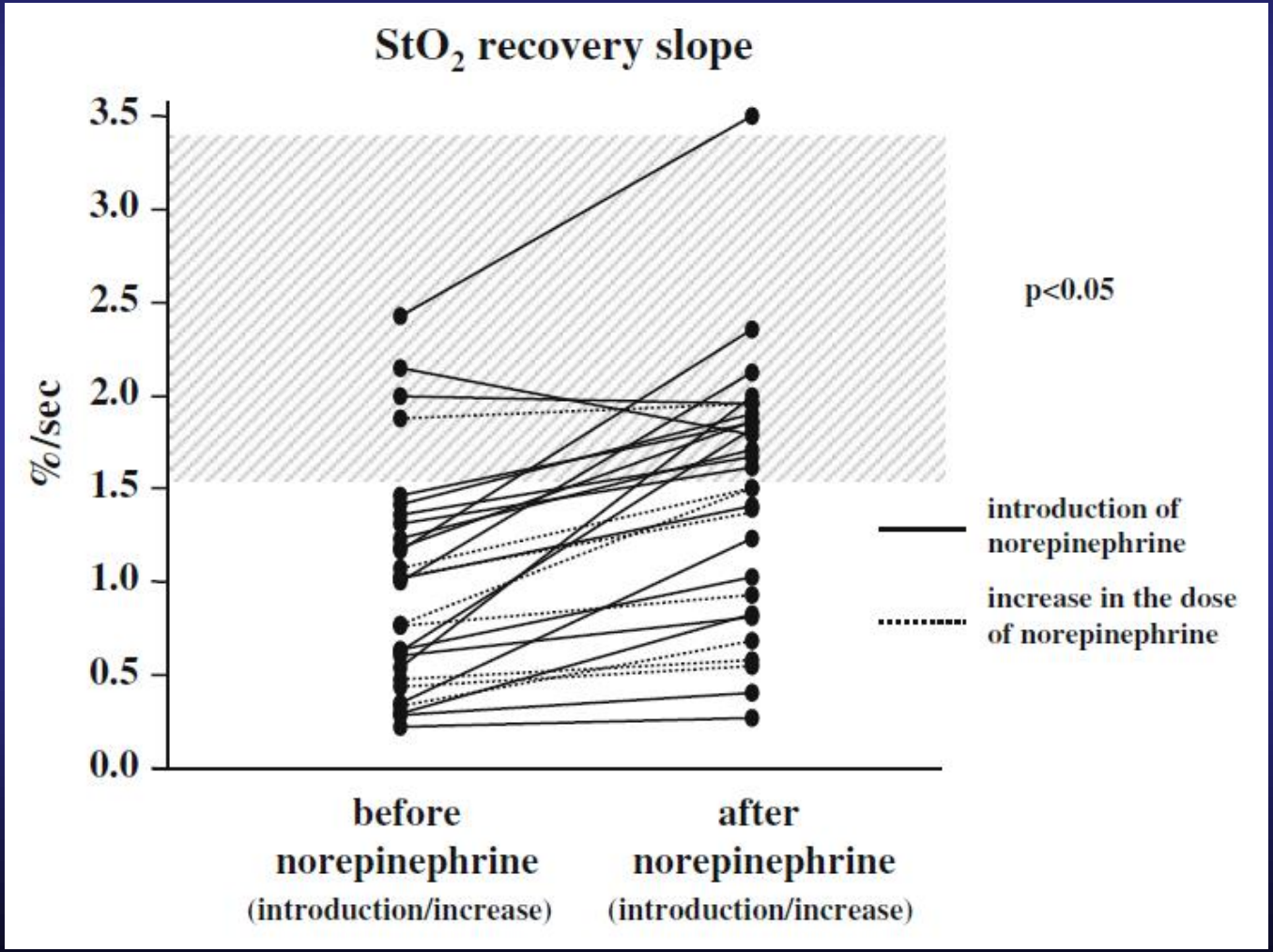
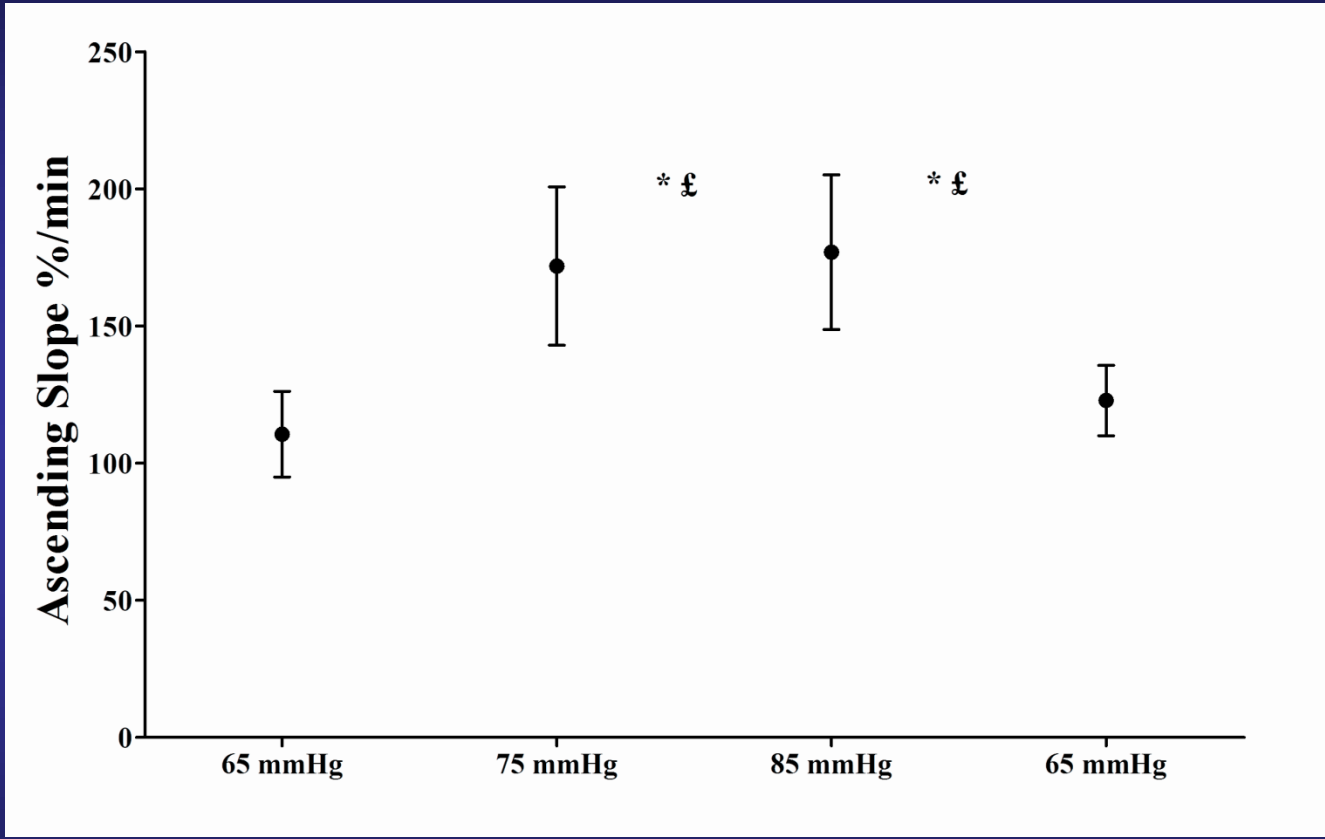


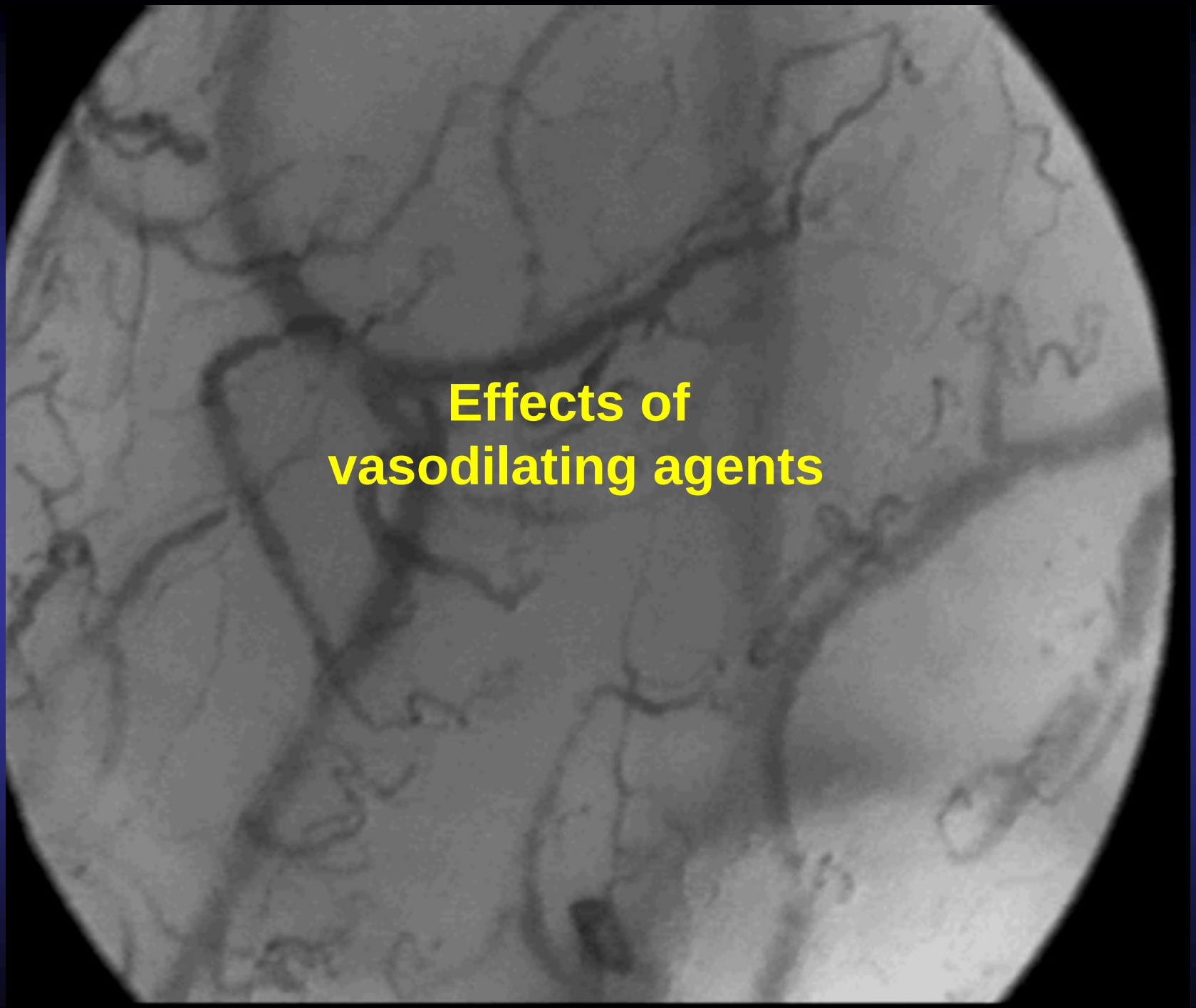
Effects of changes in arterial pressure on organ perfusion during septic shock

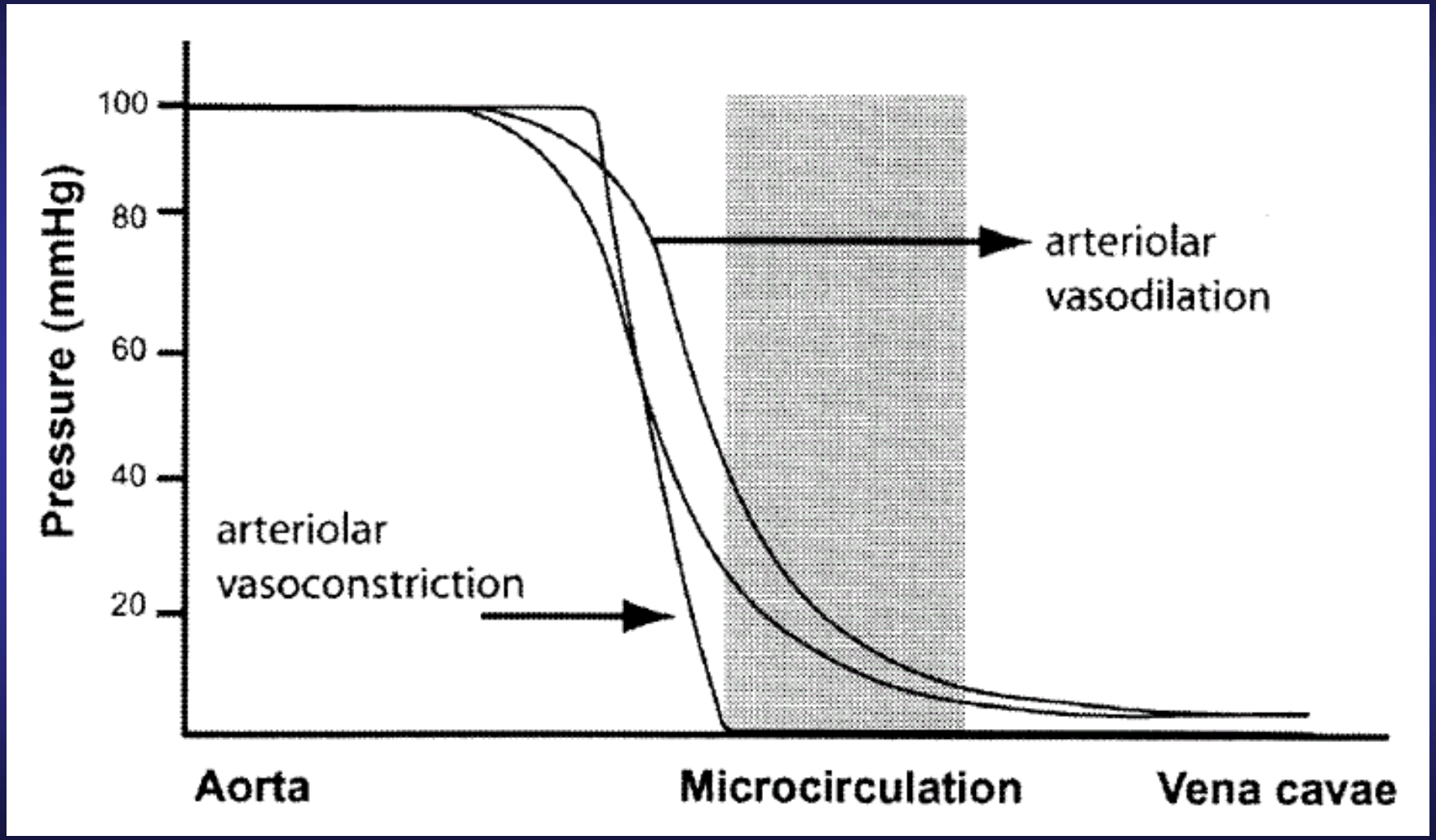
Thooft A et al. Crit Care 2010

Norepinephrine



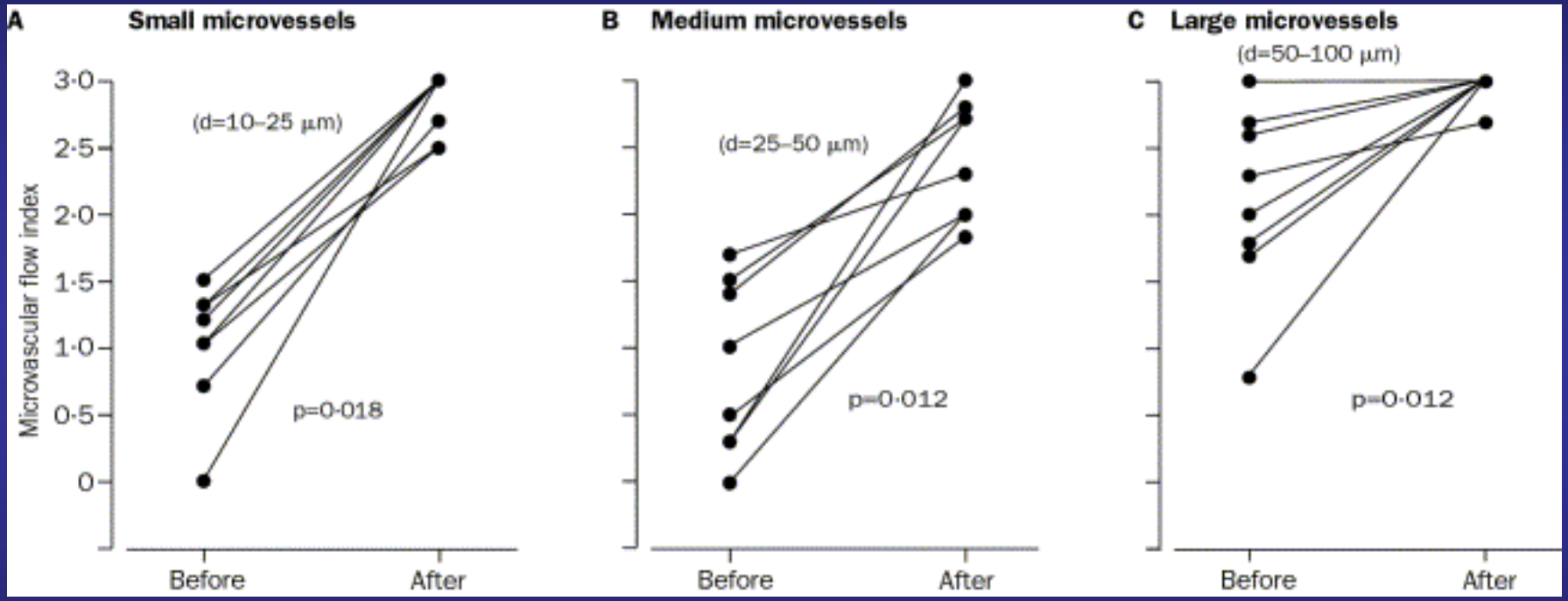
	65 mmHg	75 mmHg	85 mmHg	65 mmHg
PVD (n/mm)	11 (8.6-13.3)	12 (9.4-14.5)	13.2 (11.9-14.5)*	12.1 (9.2-14.9)


Effects of
vasodilating agents


Pressure (mmHg)
100
80
60
40
20
arteriolar
vasodilation
arteriolar
vasoconstriction
Aorta
Microcirculation
Vena cavae

Effects of nitroglycerin

Spronk et al
Lancet 360:1395;2002

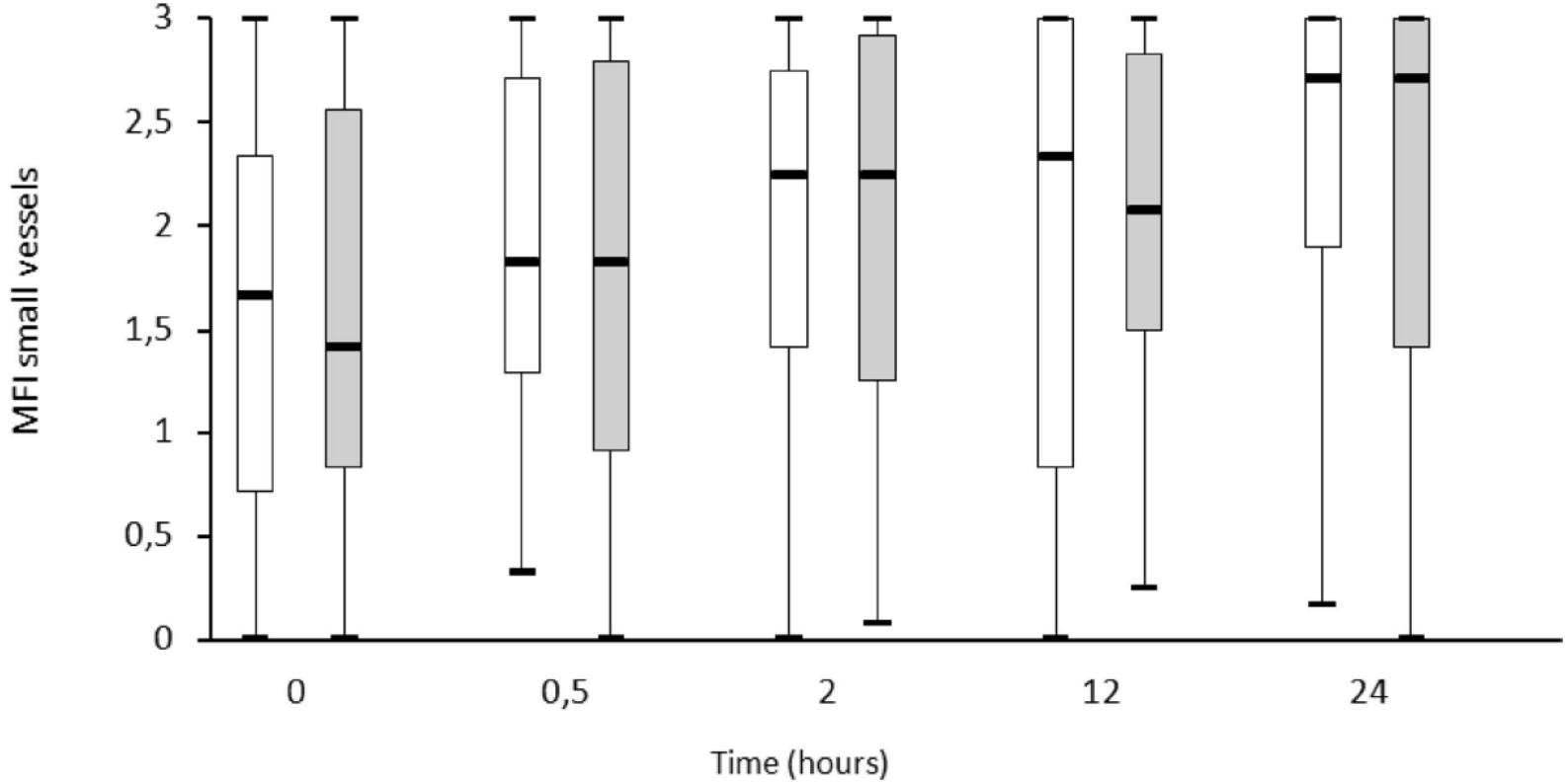


8 pts with septic shock

Effects of nitroglycerin on microcirculatory blood flow

Boerma et al. Crit Care Med 2010 : 38 ; 93-100

n = 70 patients in septic shock



NTG Control

Effects of nitroglycerin on microcirculatory blood flow

Boerma et al. Crit Care Med 2010 : 38 ; 93-100

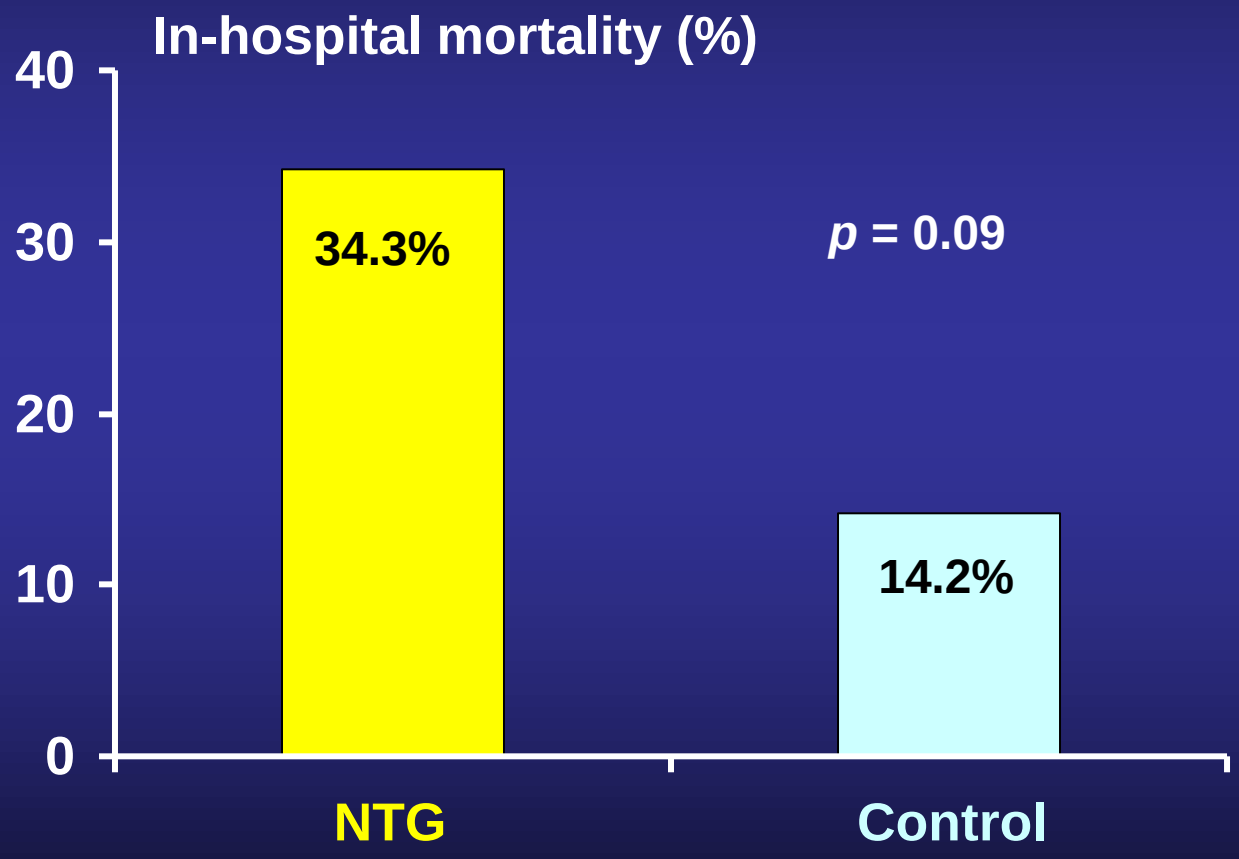
n = 70 patients in septic shock

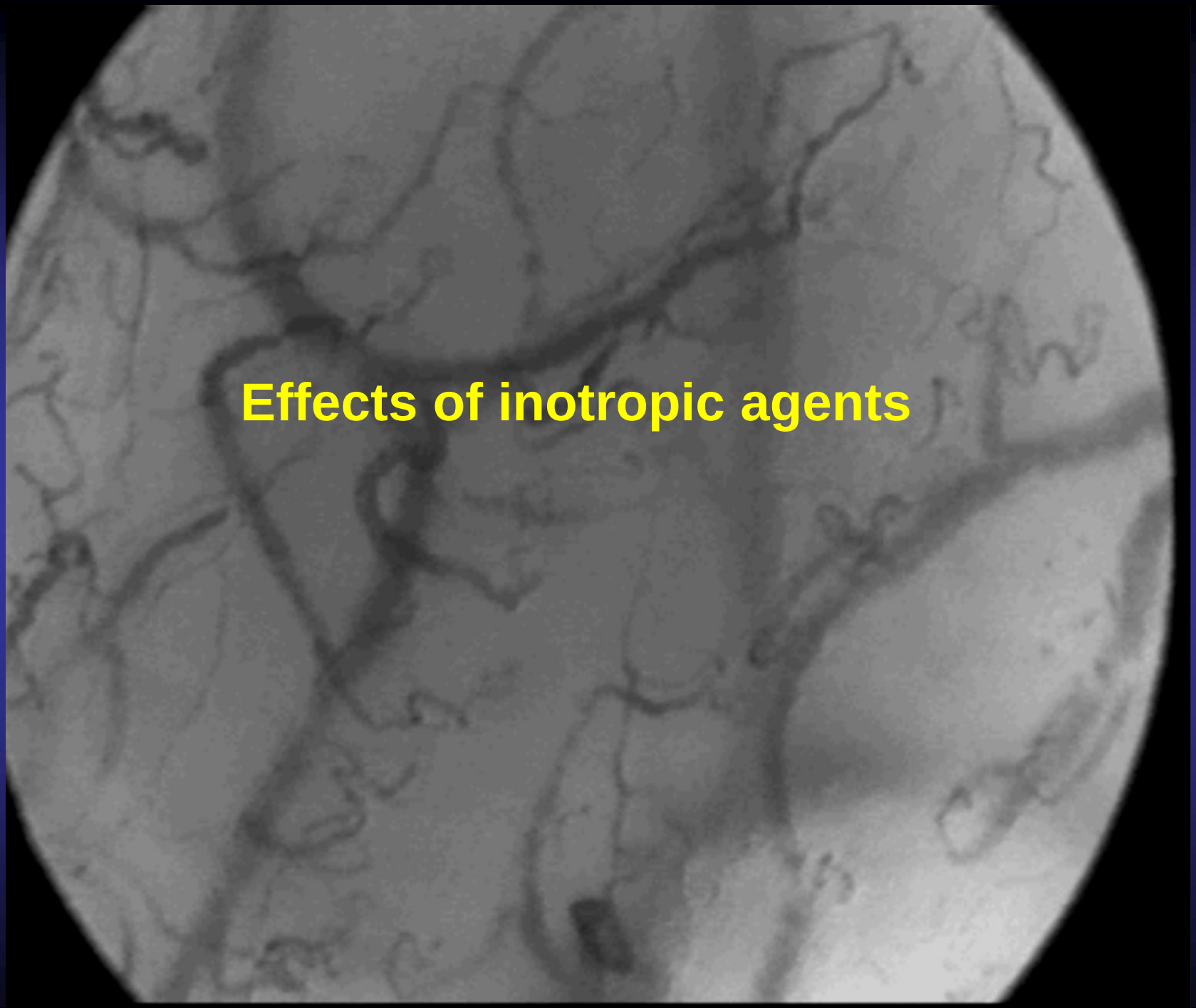
Variables	Baseline NTG (n = 35)	Placebo (n = 35)	24 hrs NTG (n = 32)	Placebo (n = 34)
MFI small vessels	1.67 (0.67–2.42)	1.42 (0.83–2.63)	2.71 (1.85–3)[b]	2.71 (1.27–3)[a]
MFI medium vessels	2.33 (1.83–2.83)	2.33 (2–2.83)	3 (2.75–3)[b]	2.86 (2.19–3)
MFI large vessels	2.92 (2.75–3)	2.92 (2.75–3)	3 (3–3)[a]	2.89 (3–3)
TVD, mm/mm^2	14 (12.8–15.6)	15 (12.3–16.1)	13.9 (12.5–15.7)	14.7 (13.1–16.1)
PPV, %	98 (93–100)	97 (89–100)	100 (98–100)	98 (86–100)[c]
PVD, 1/mm	9.1 (8.3–10.5)	9.8 (8.4–10.8)	10.2 (8.7–11.2)	10.1 (8.5–10.7)
Heterogeneity index	1.76 (0.88–2.84)	1.96 (0.66–3)	0.74 (0–1.62)[b]	0.54 (0–1.76)[a]

Effects of nitroglycerin on microcirculatory blood flow

Boerma et al. Crit Care Med 2010 : 38 ; 93-100

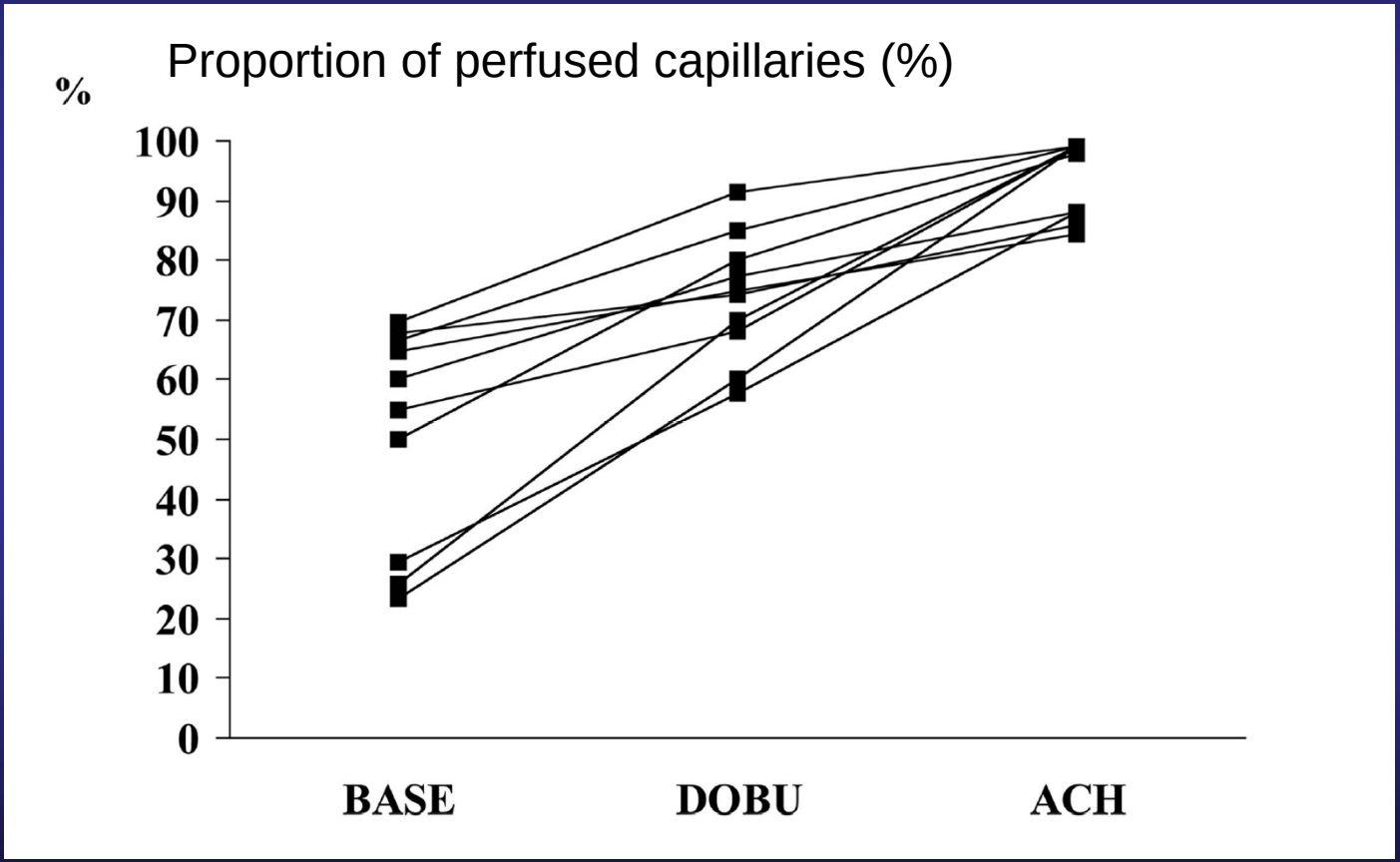
n = 70 patients in septic shock




Effects of inotropic agents

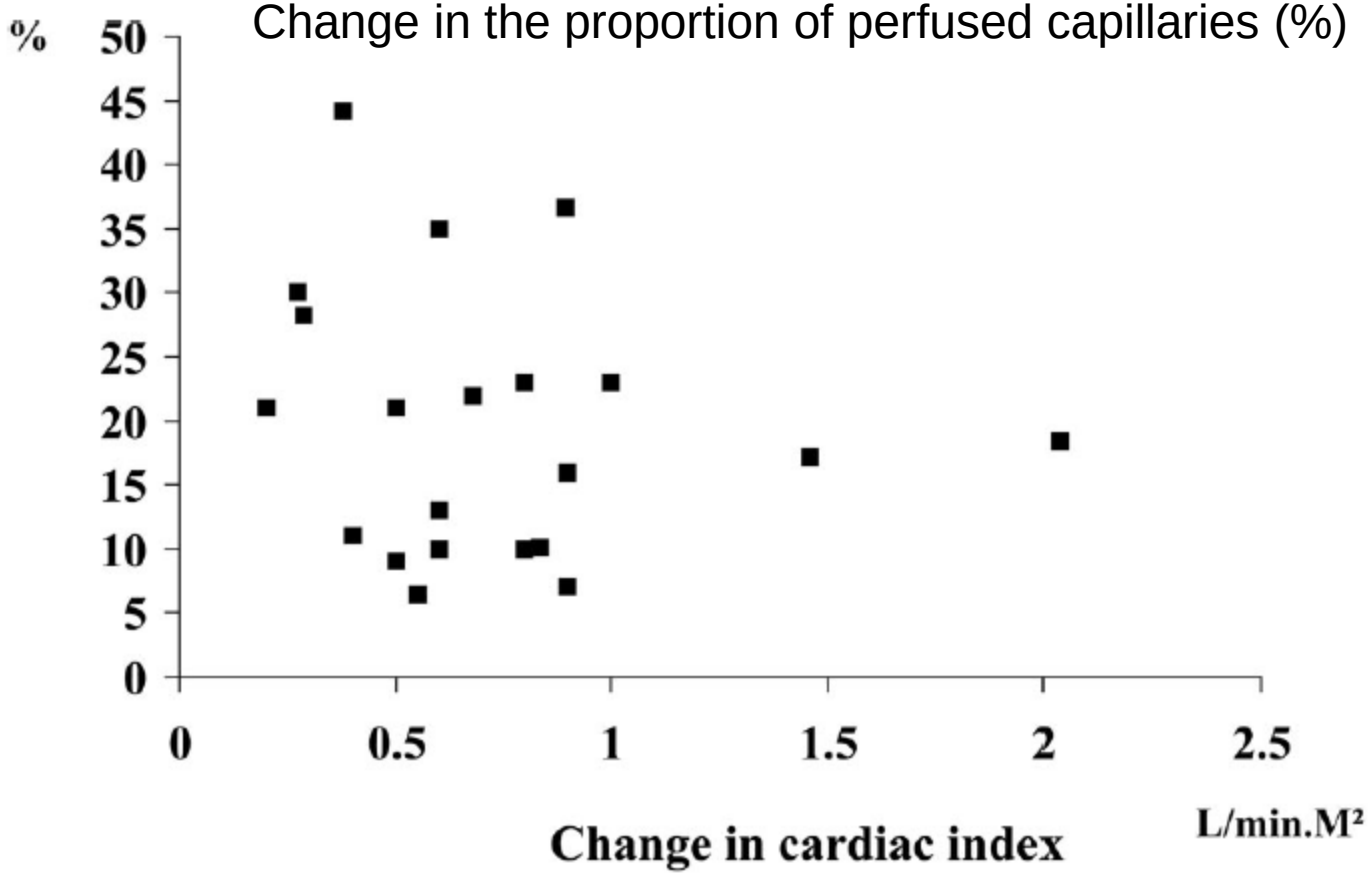
Effects of dobutamine on microcirculatory alterations in patients with septic shock

De Backer et al. Crit Care Med 2006 ; 34 : 403-408



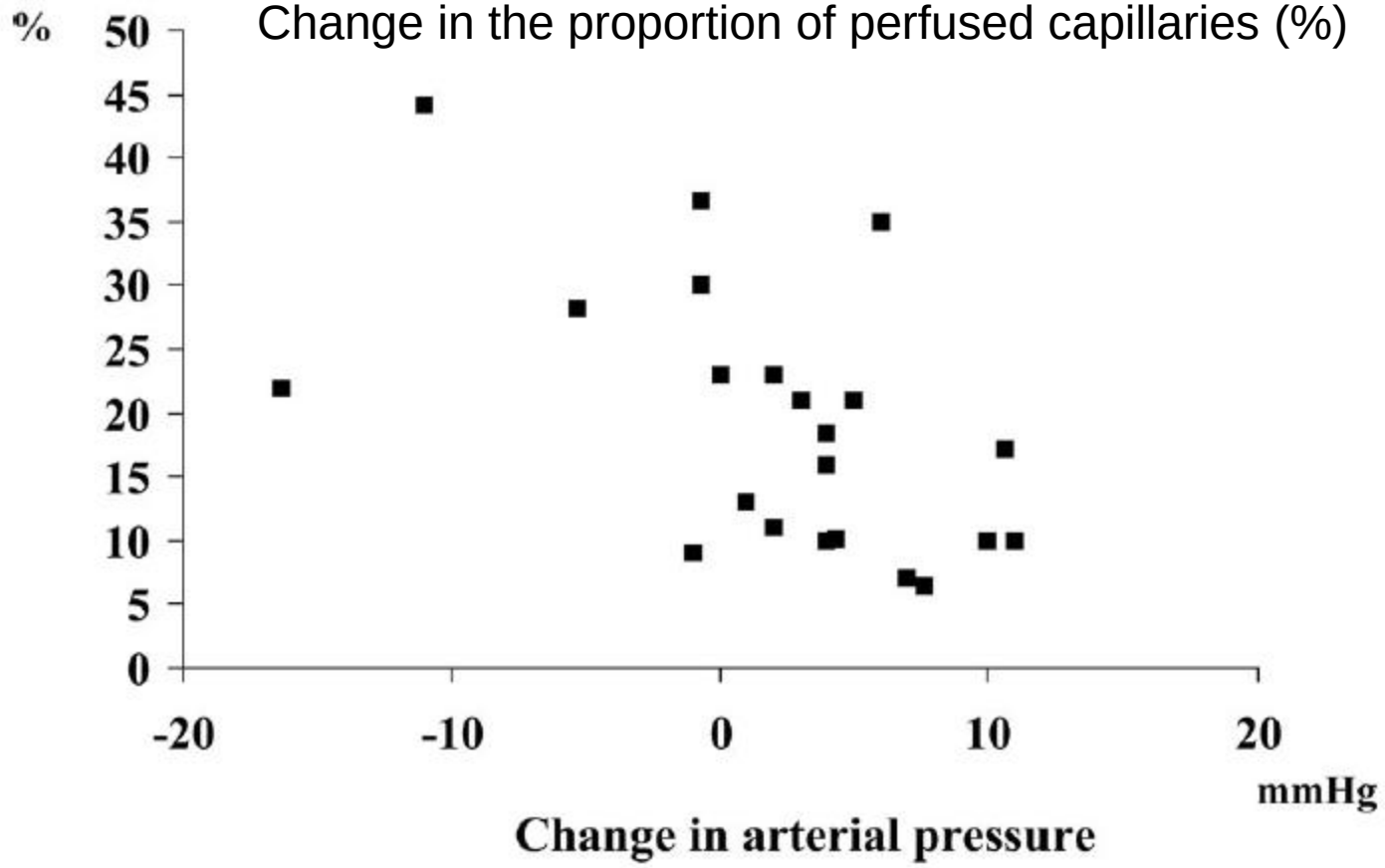
Effects of dobutamine on microcirculatory alterations in patients with septic shock

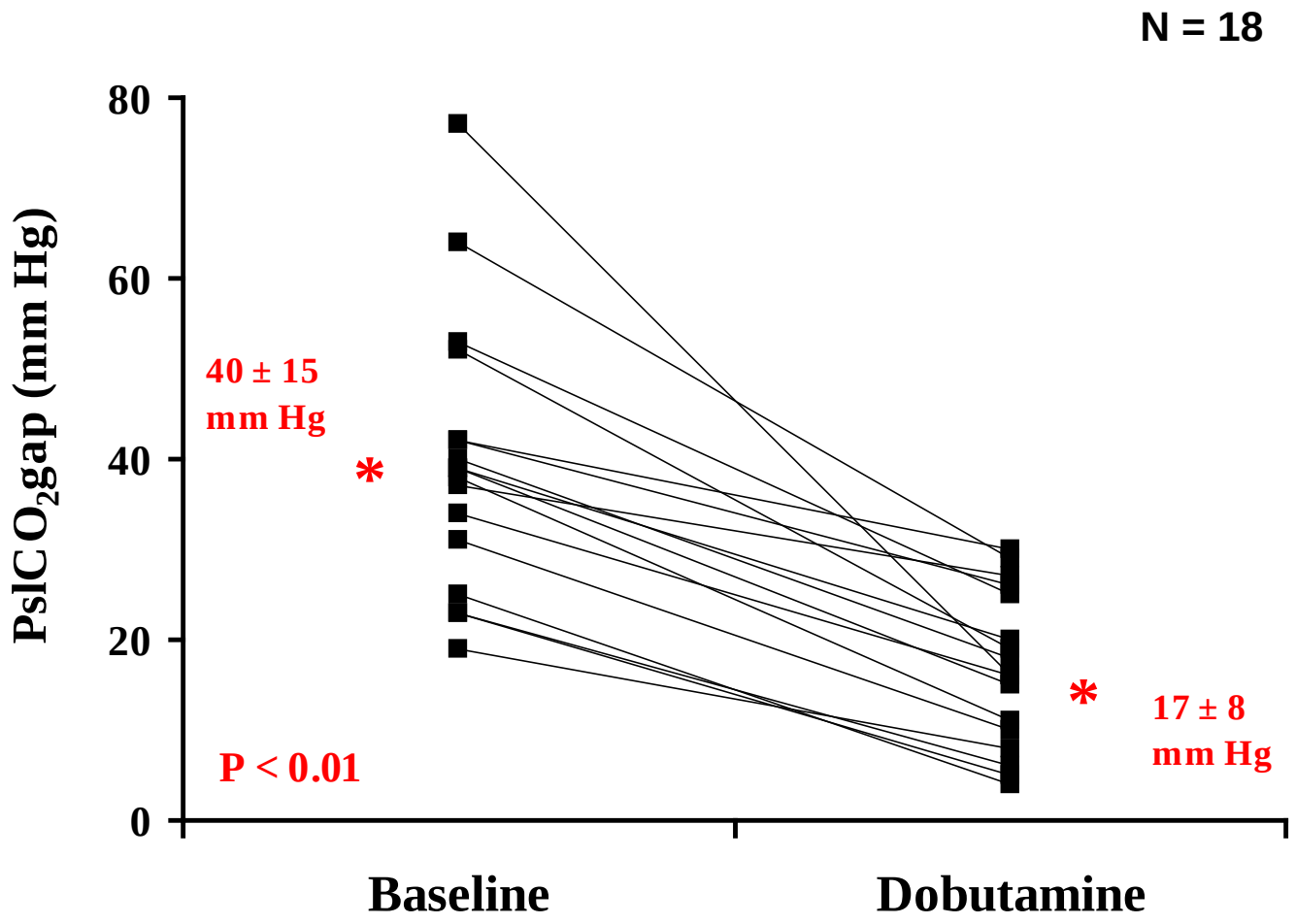
De Backer et al. Crit Care Med 2006 ; 34 : 403-408



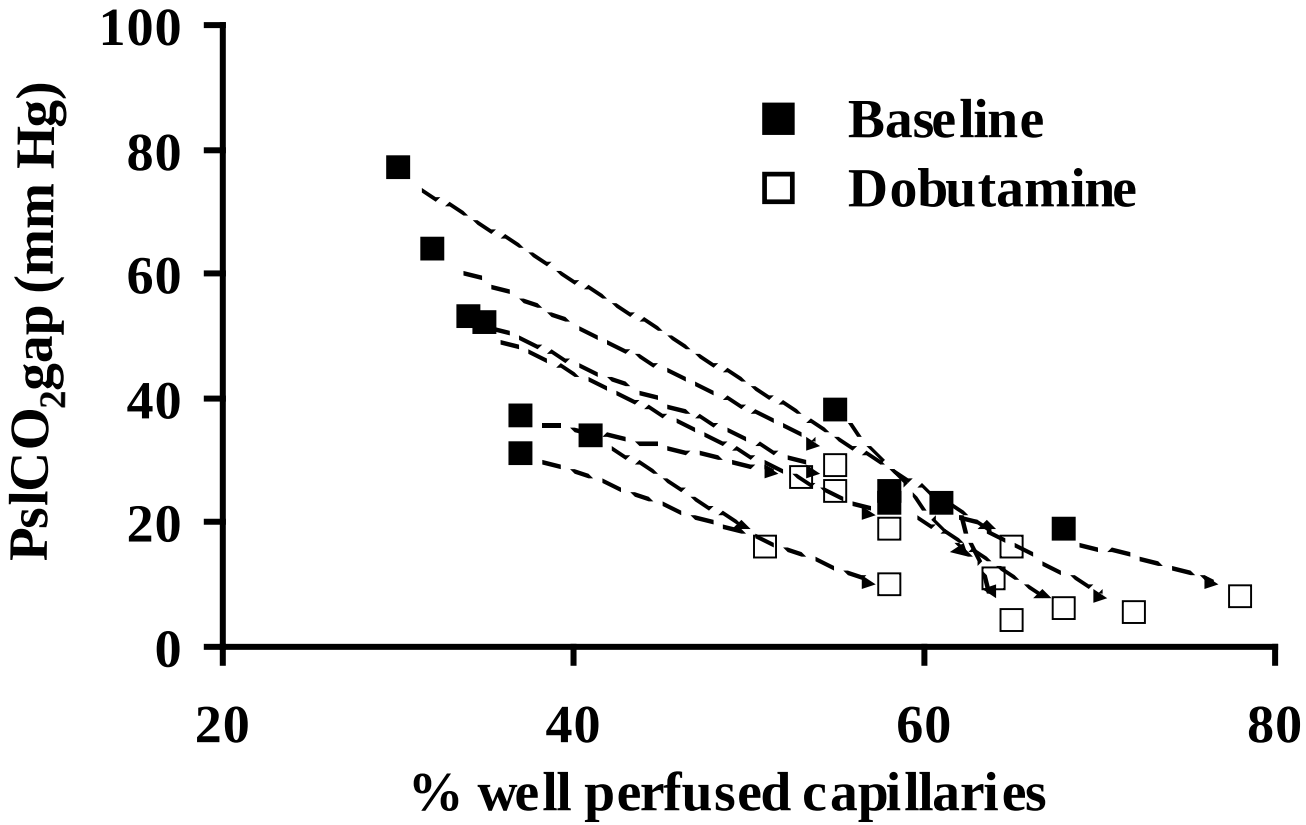
Effects of dobutamine on microcirculatory alterations in patients with septic shock

De Backer et al. Crit Care Med 2006 ; 34 : 403-408





Creteur et al. Intensive Care Med 2006; 32: 516 -523



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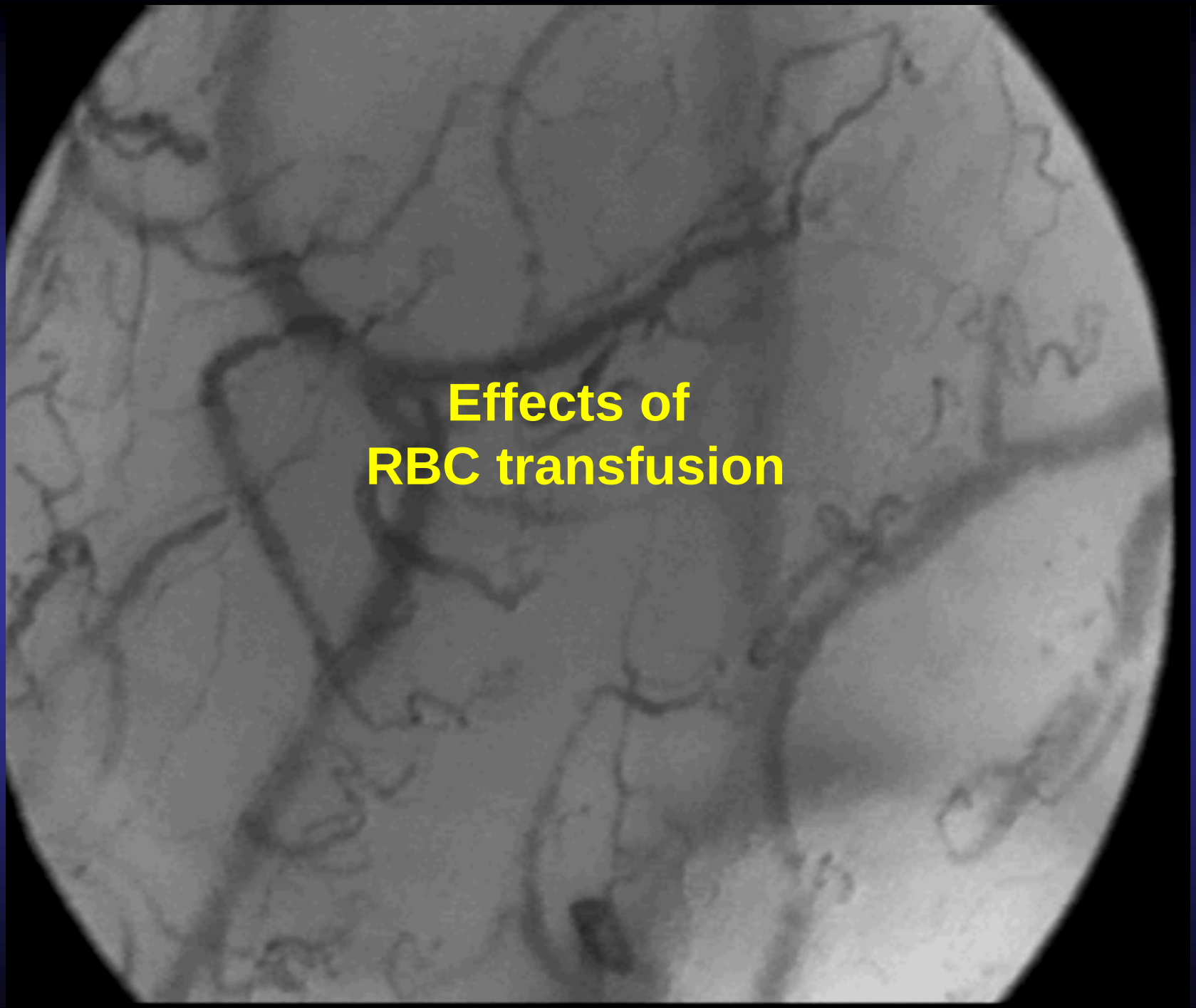
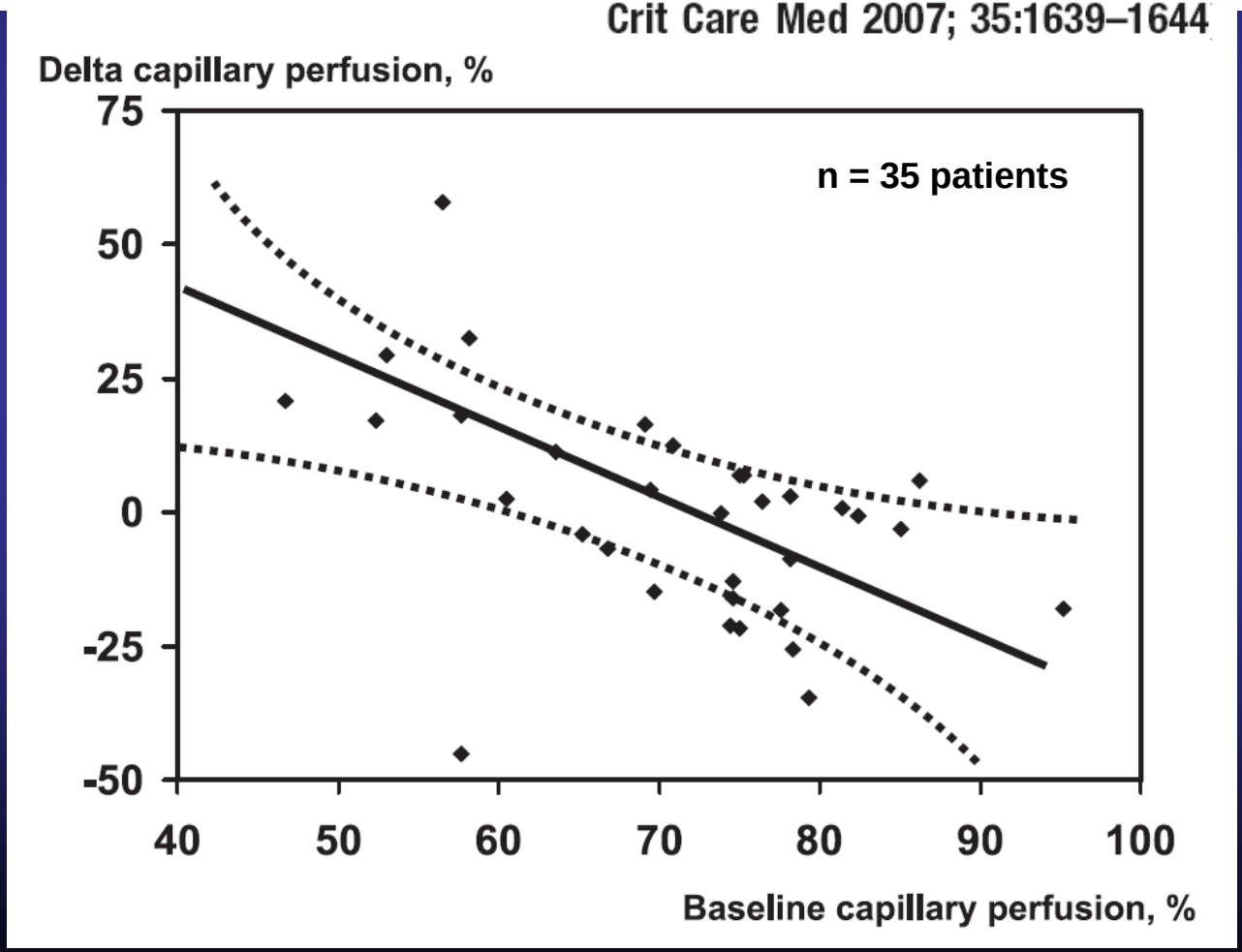

Effects of
RBC transfusion

Microvascular response to red blood cell transfusion in patients with severe sepsis*

Yasser Sakr, MD, PhD; Marialuisa Chierego, MD; Michaël Piagnerelli, MD; Colin Verdant, MD; Marc-Jacques Dubois, MD; Marc Koch, MD; Jacques Creteur, MD, PhD; Antonino Gullo, MD; Jean-Louis Vincent, MD, PhD, FCCM; Daniel De Backer, MD, PhD

Crit Care Med 2007; 35:1639–1644



NIRS TECHNIQUE TO EVALUATE THE EFFECTS OF RED BLOOD CELL TRANFUSION ON TISSUE OXYGENATION

Creteur et al. Critical Care 2009;13 Suppl 5:S11.

n = 44 critically ill patients

	Before	After
Hemoglobin concentration, g/dl	7.1 (6.7 - 7.7)	8.4 (7.1 - 9)*
StO_2, %	90 (81 - 94)	90 (80 - 94)
THI, U	14 (13 - 17)	13 (11 - 18)
StO_2 desc slope*-1 , %/min	22 (17 - 35)	21 (16 - 32)
StO_2 asc slope, %/sec	4.1 (2.1 - 5.4)	3.8 (2.9 - 5.1)
NIR VO_2, U	363 (240 - 536)	373 (215 - 500)

*p < 0.001

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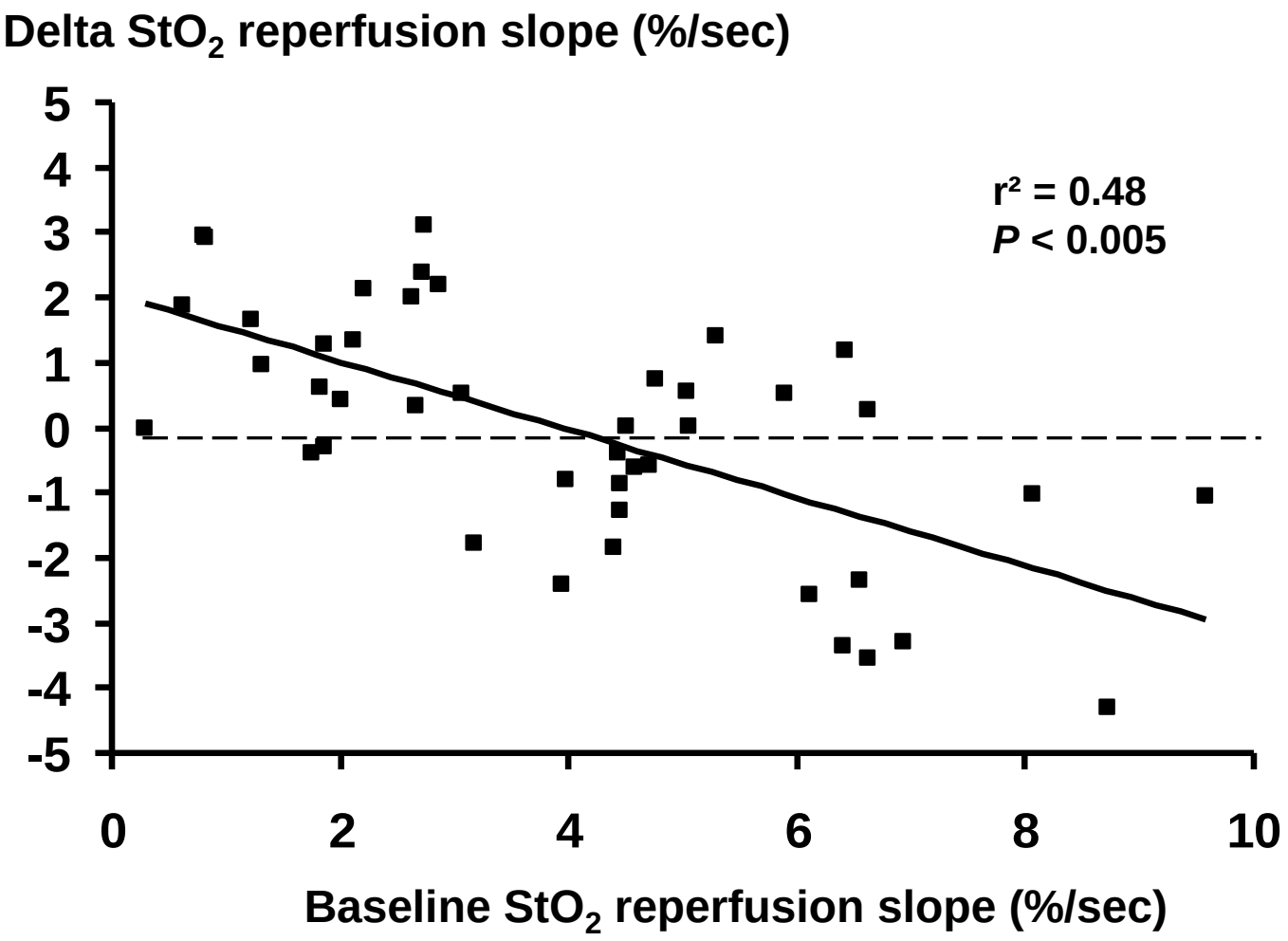

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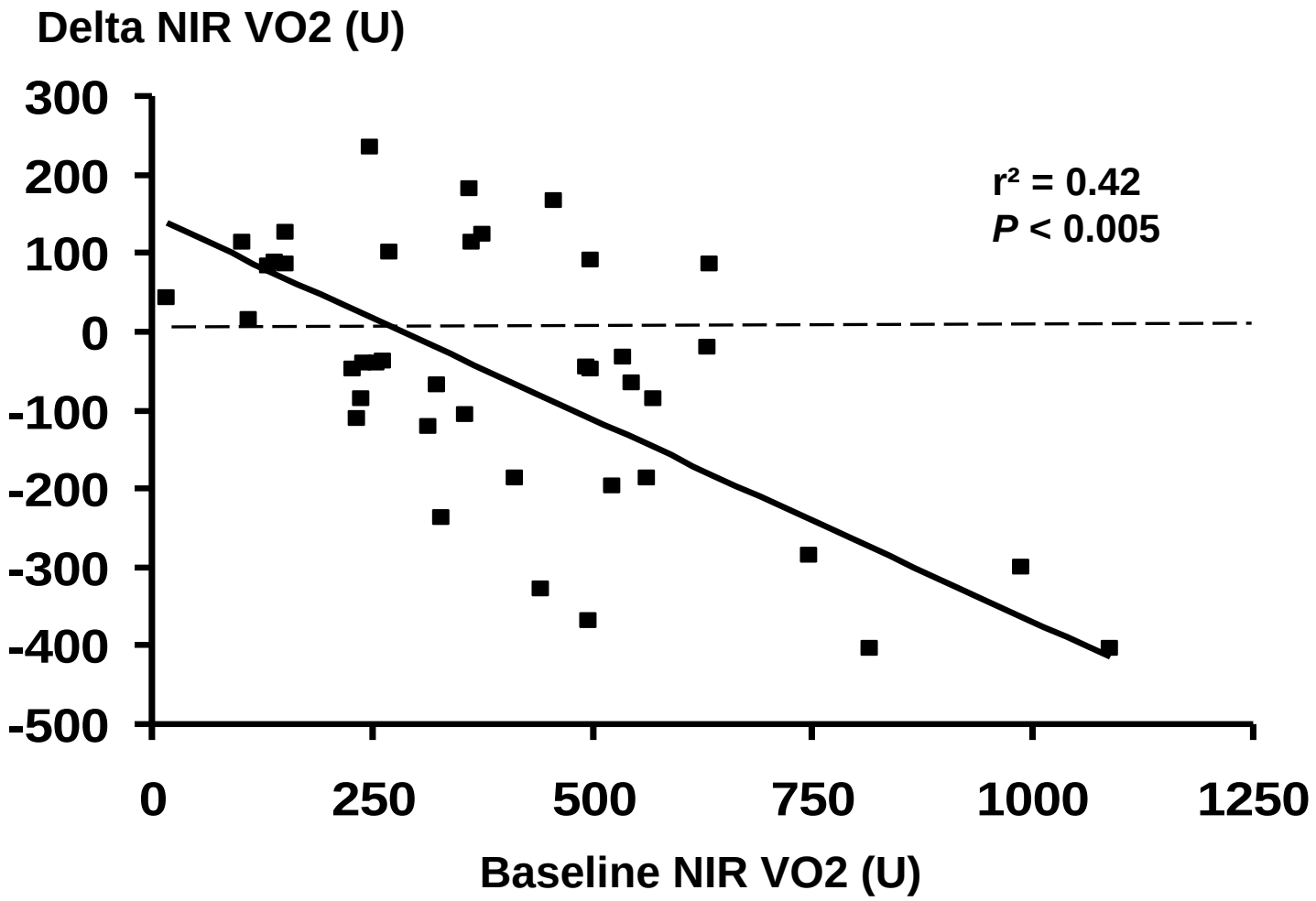

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- **Comprehensive monitoring of the microcirculation is now (almost) feasible in the clinical arena.**
- **Microvascular resuscitation can be achieved by different therapeutic modalities. Nevertheless, the impact on mortality of such therapeutic strategies need to be determined.**