Hypoxie und Mikrozirkulationsstörungen bei Dialysepatienten

29.Berliner Dialyse Seminar
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Oxygen in Maintenance Hemodialysis Patients – is it relevant at all?

What I’ll talk about today

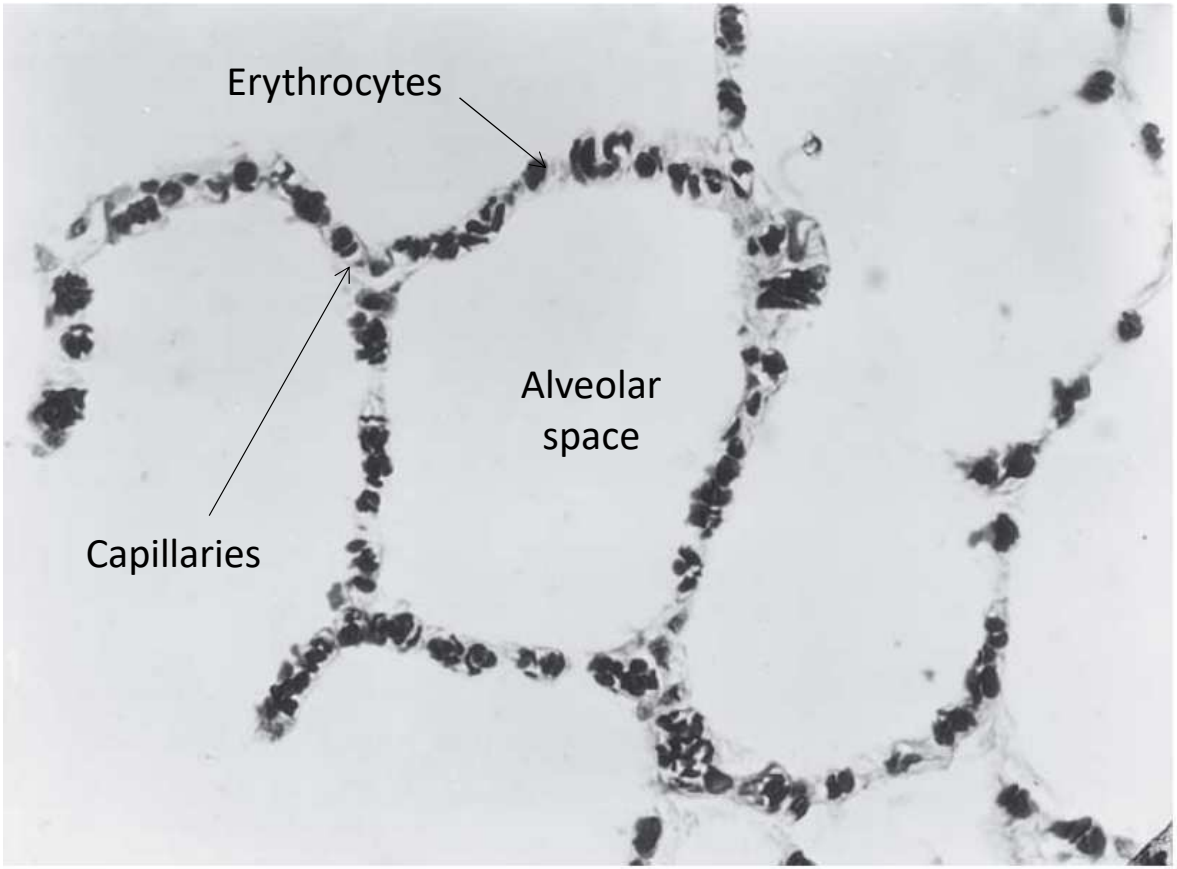
- Physiology of oxygen supply to tissues and organs
- Specific consideration in dialysis patients
- Treatment options

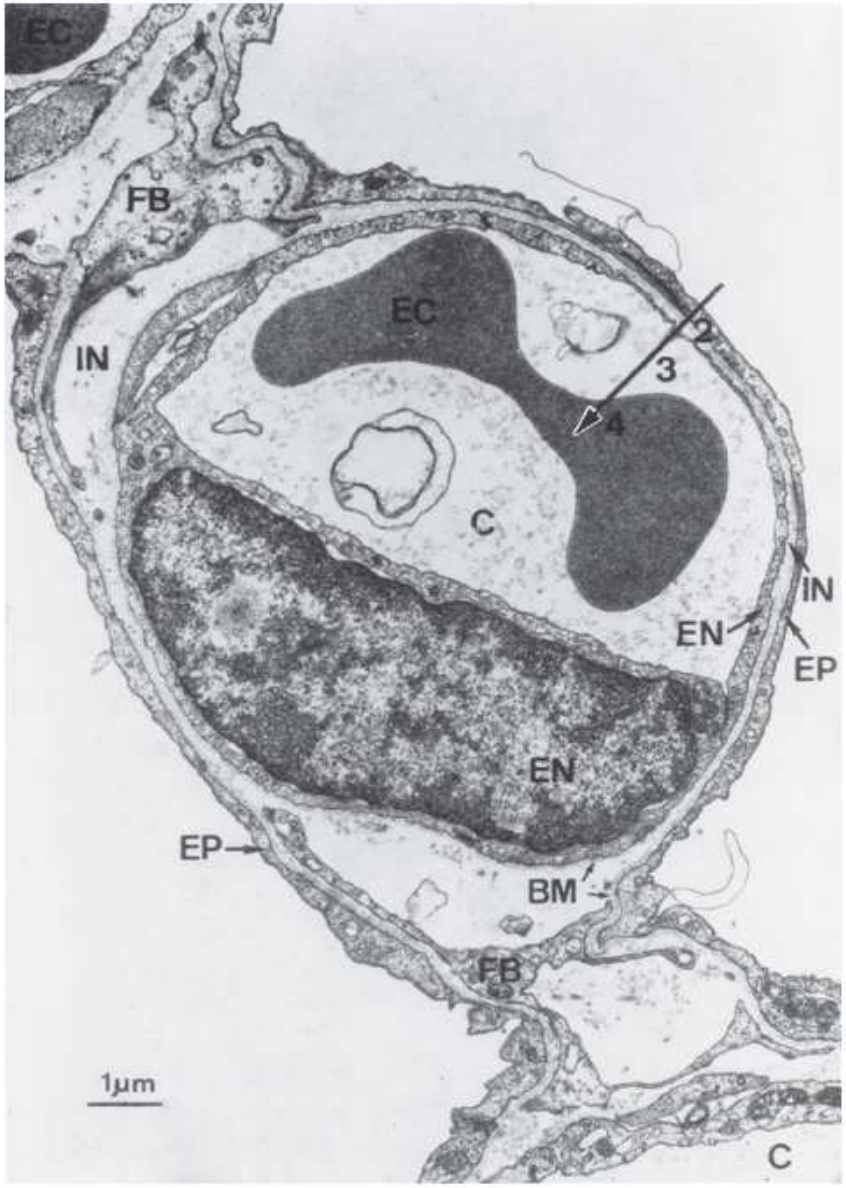
A key function of the circulatory system is the transport of oxygen to the tissues/organs

What are the determinants of oxygen supply?

1. Diffusive transport of oxygen from the alveolar space to red blood cells / hemoglobin
2. Convective transport of oxygen to the capillary bed by means of cardiac output
3. Diffusive transport from the red blood cells to the tissue / organ cells

Alveolar oxygen uptake





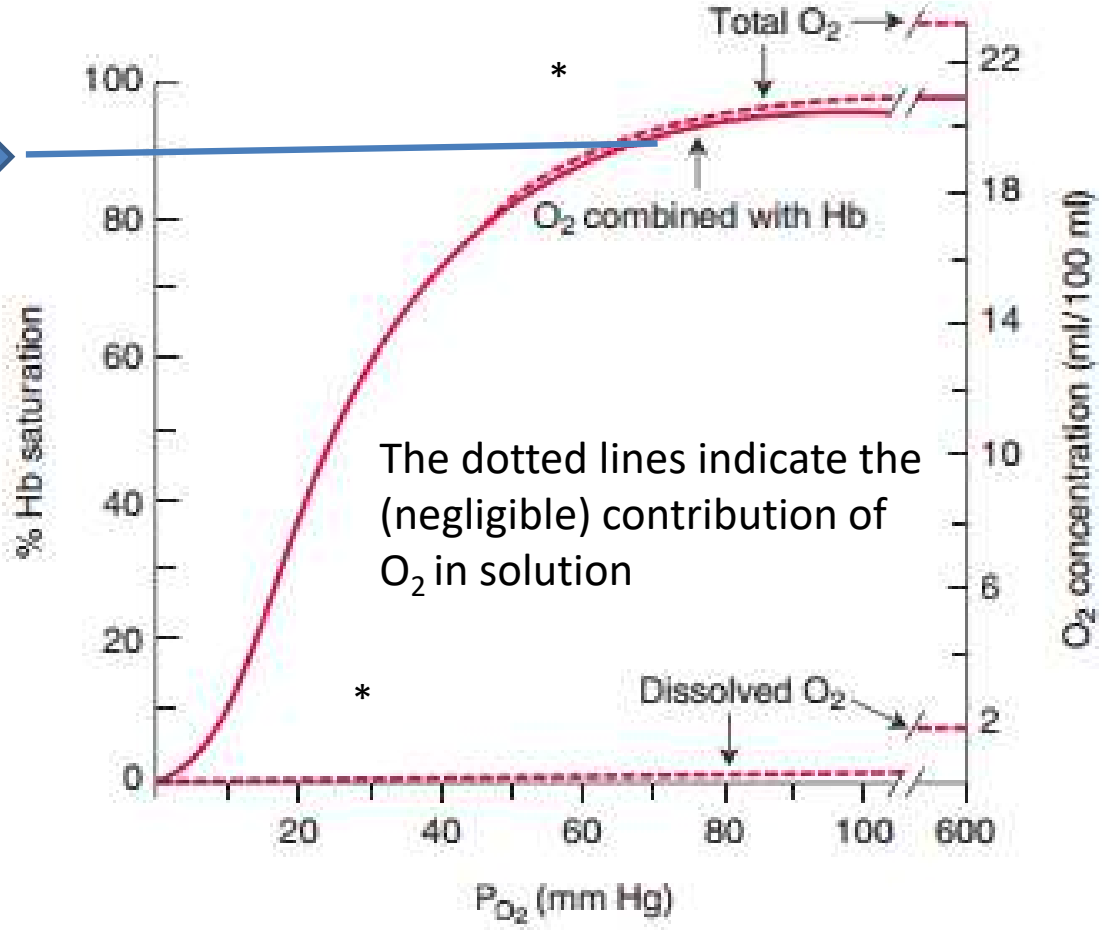
Hemoglobin as oxygen carrier: relationship between the partial pressure of oxygen in the blood (x-axis; normally around 100 mmHg) and

(a) % saturation of hemoglobin (Hb) molecules (left y-axis);

(b) Blood O_2 content at a hemoglobin level of 15 g/dL (right y-axis)

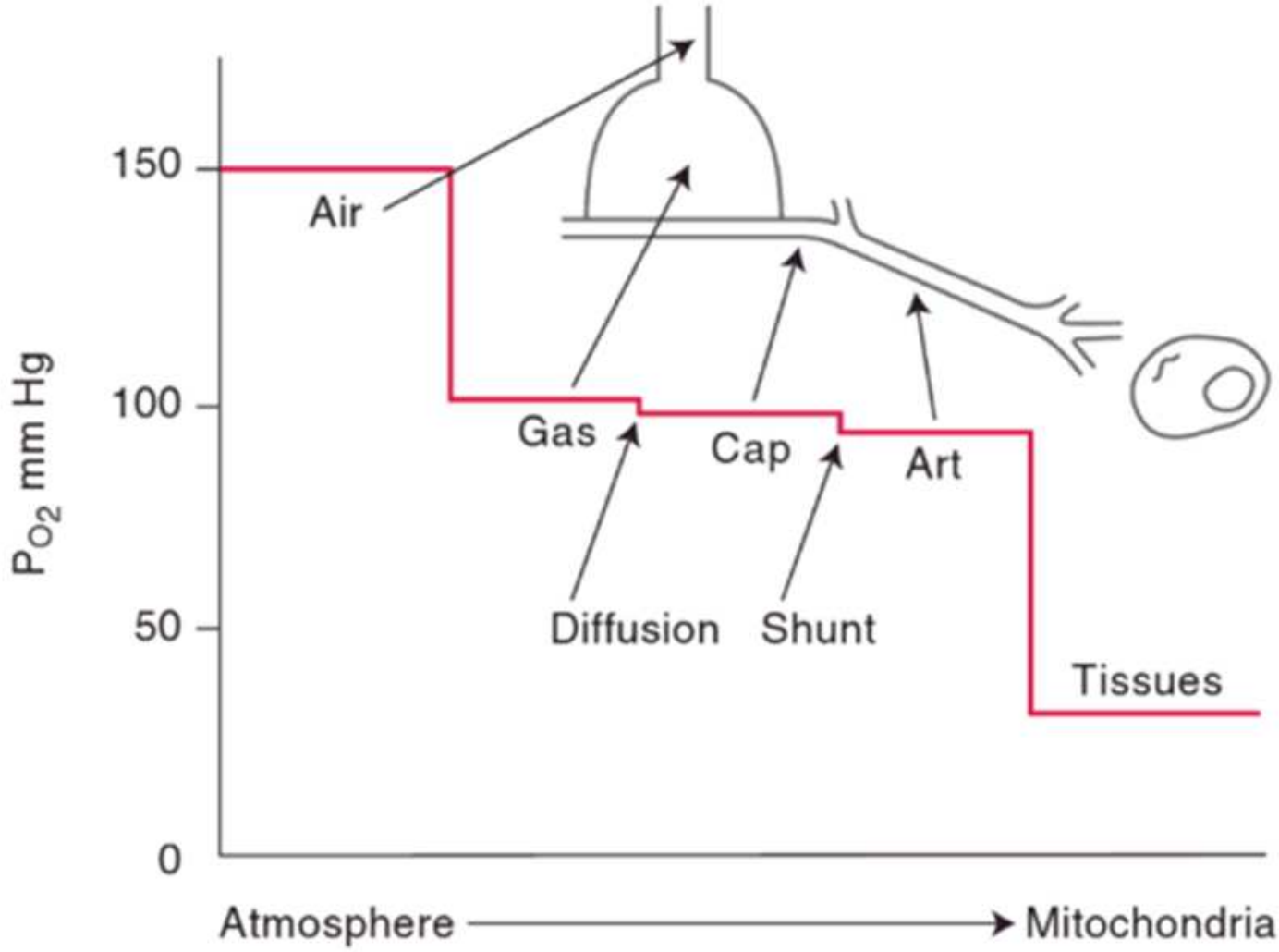
Hypoxemia definition

Hypoxemia is most frequently defined as arterial O_2 saturation < 90%



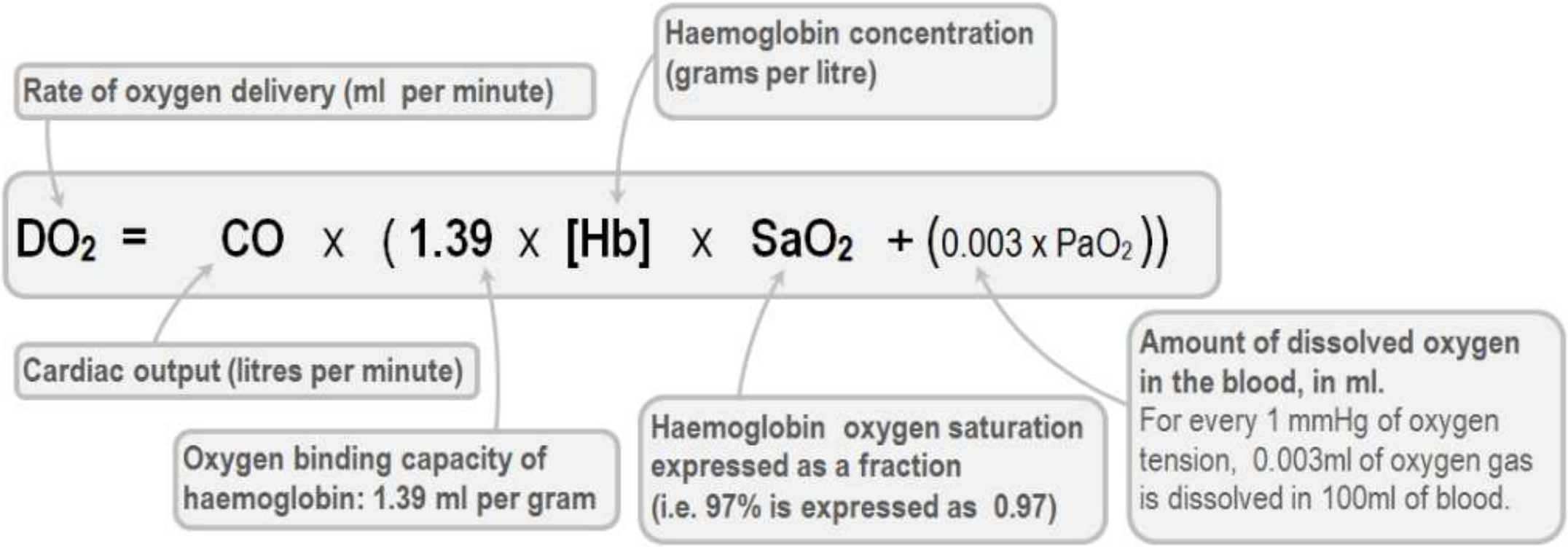
West JB, Respiratory Physiology, 2012

Oxygen partial pressure drops from air to mitochondria

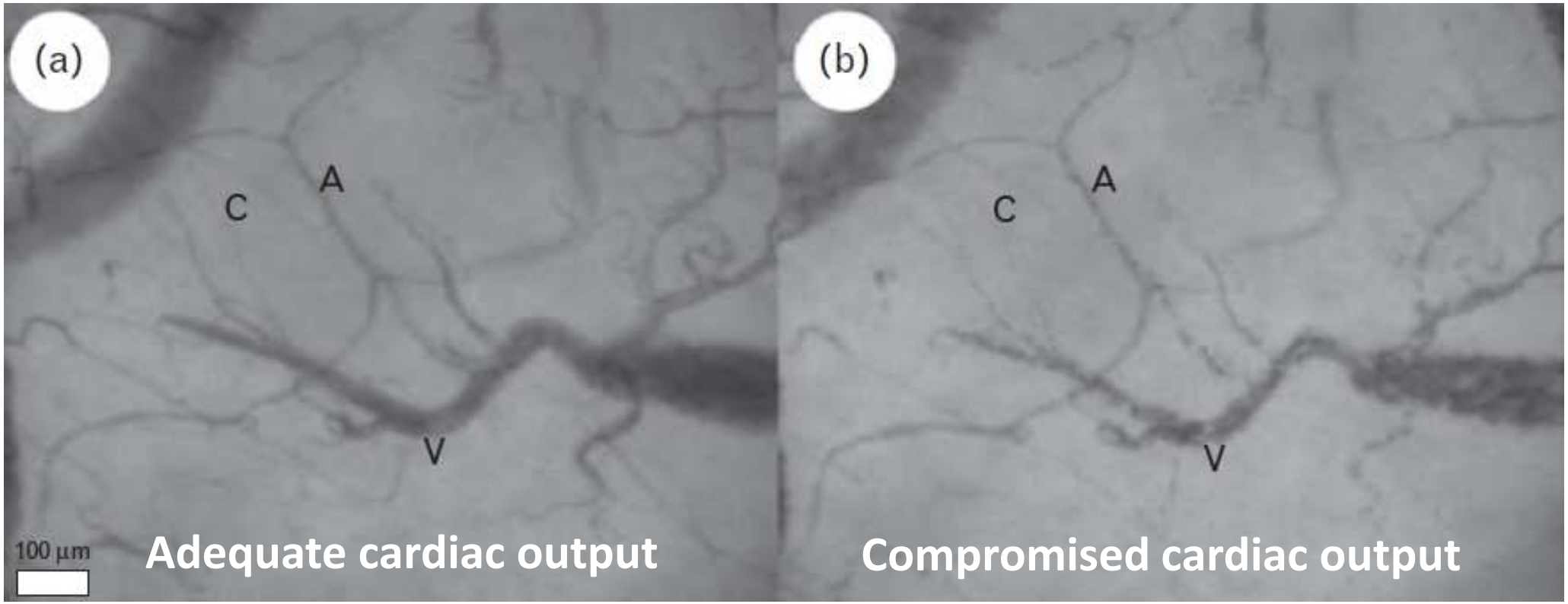


West JB, Respiratory Physiology, 2012

Determinants of convective oxygen supply to the tissues/organs

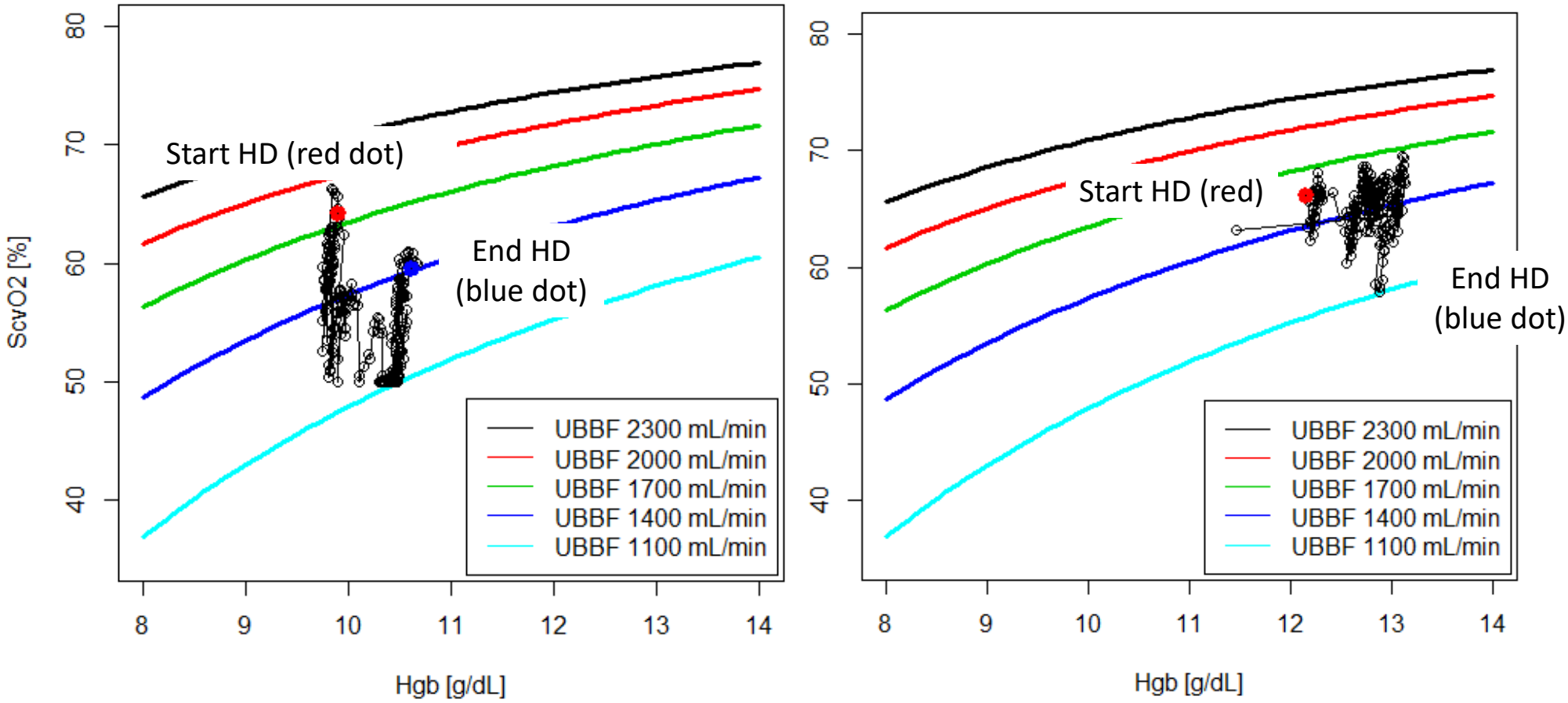


Compromised cardiac output results in reduced capillary flow



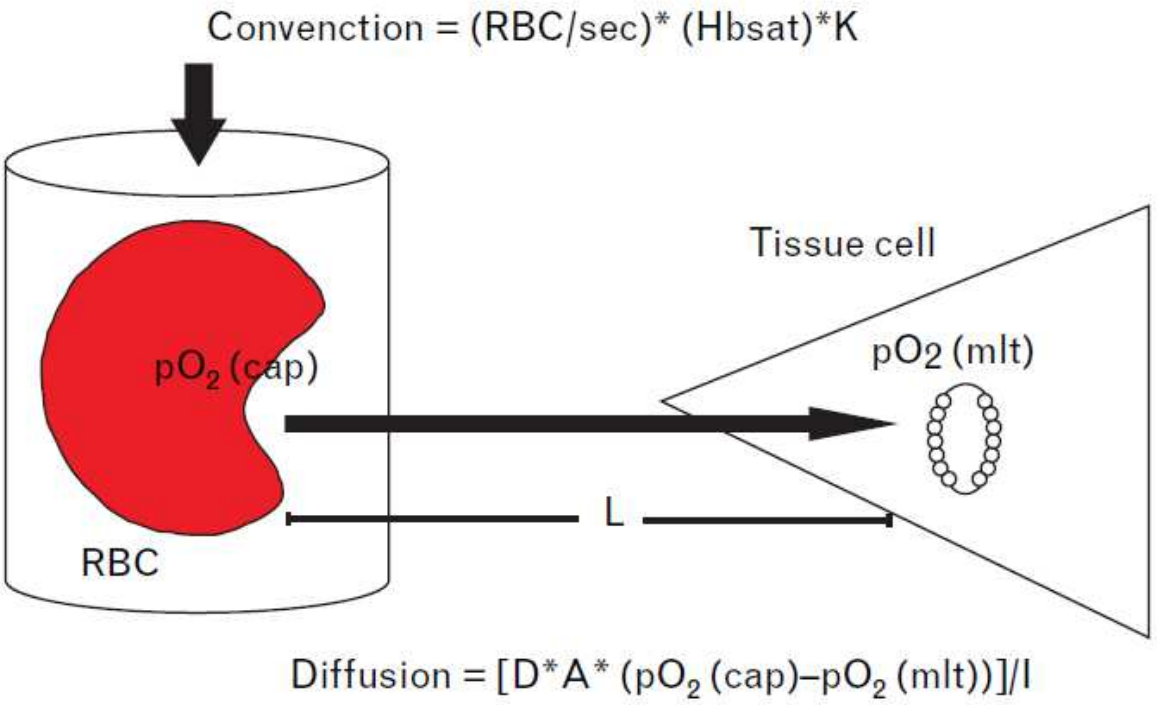
Atasever, J Cardiothorac Vasc Anesth (2011)

Upper body blood flow (UBBF) in 2 patients during hemodialysis



Assumptions: SaO_2 92%, upper body O_2 utilization 65 mL/min

Convective and diffusive determinants of oxygen transport from the microcirculation to the tissue cell



Main convective components: perfusion, hematocrit, oxygen saturation, hemoglobin molecules per RBC

Main diffusive components: oxygen gradient, diffusion distance, surface area, RBC shape

Kara, Curr Opin Anesthesiol 2016, 29:85–93

Oxygen diffusion from the capillaries to the cells – the Krogh cylinder concept

Schack August Steenberg Krogh
1874 - 1949

Drawings by Krogh presented at his Nobel lecture, December 1920

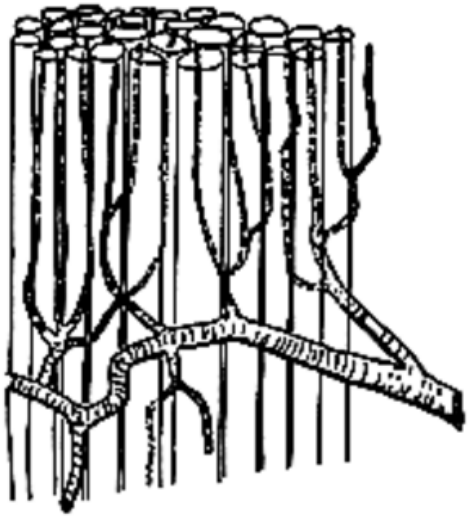


Fig. 1. A small portion of muscle with arterial branches and capillaries. (Schematic.)

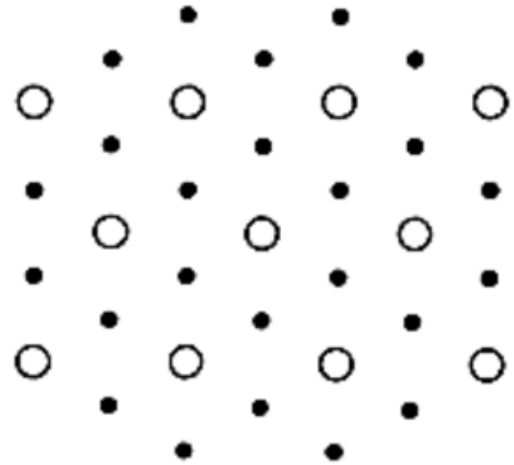
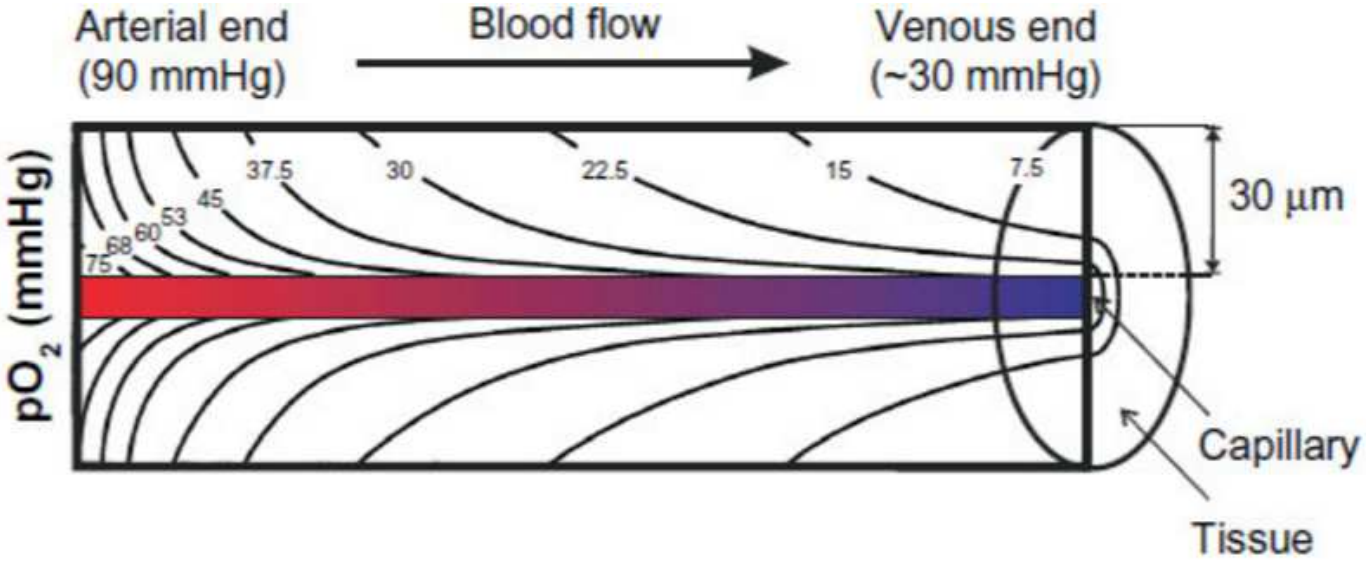
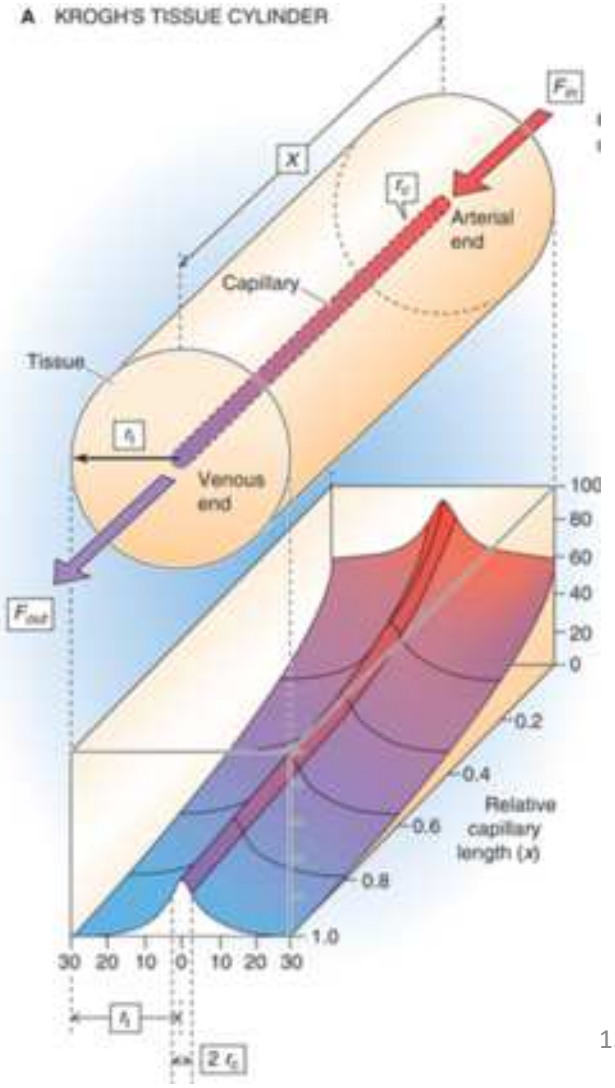


Fig. 2. Cross-section of muscle showing open O and closed • capillaries.

https://www.nobelprize.org/nobel_prizes/medicine/laureates/1920/krogh-lecture.html

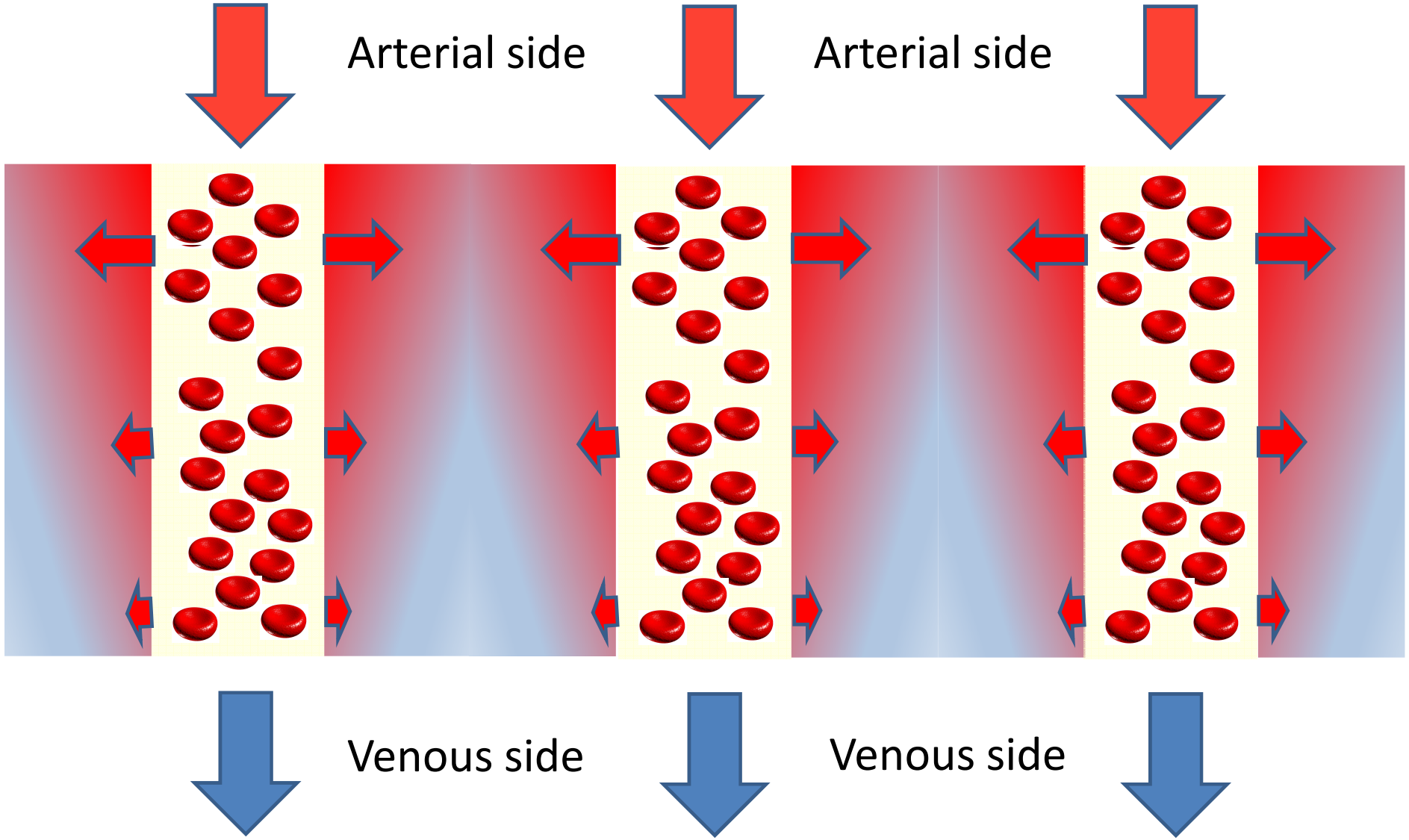
Krogh' cylinder – simulation results





Wenger RH, 2015

Physiological situation: normal perfusion, hematocrit, SaO_2, euvolemia



Specific consideration in dialysis patients

Specific consideration in dialysis patients

- Impaired pulmonary oxygen uptake
  - Increased lung water; ventilation/perfusion mismatch; sleep apnea
- Reduced convective oxygen transport
  - Cardiac insufficiency
  - Anemia
  - Lower arterial oxygen saturation
- Impaired tissue oxygen diffusion
  - Interstitial fluid overload
  - Capillary rarefication

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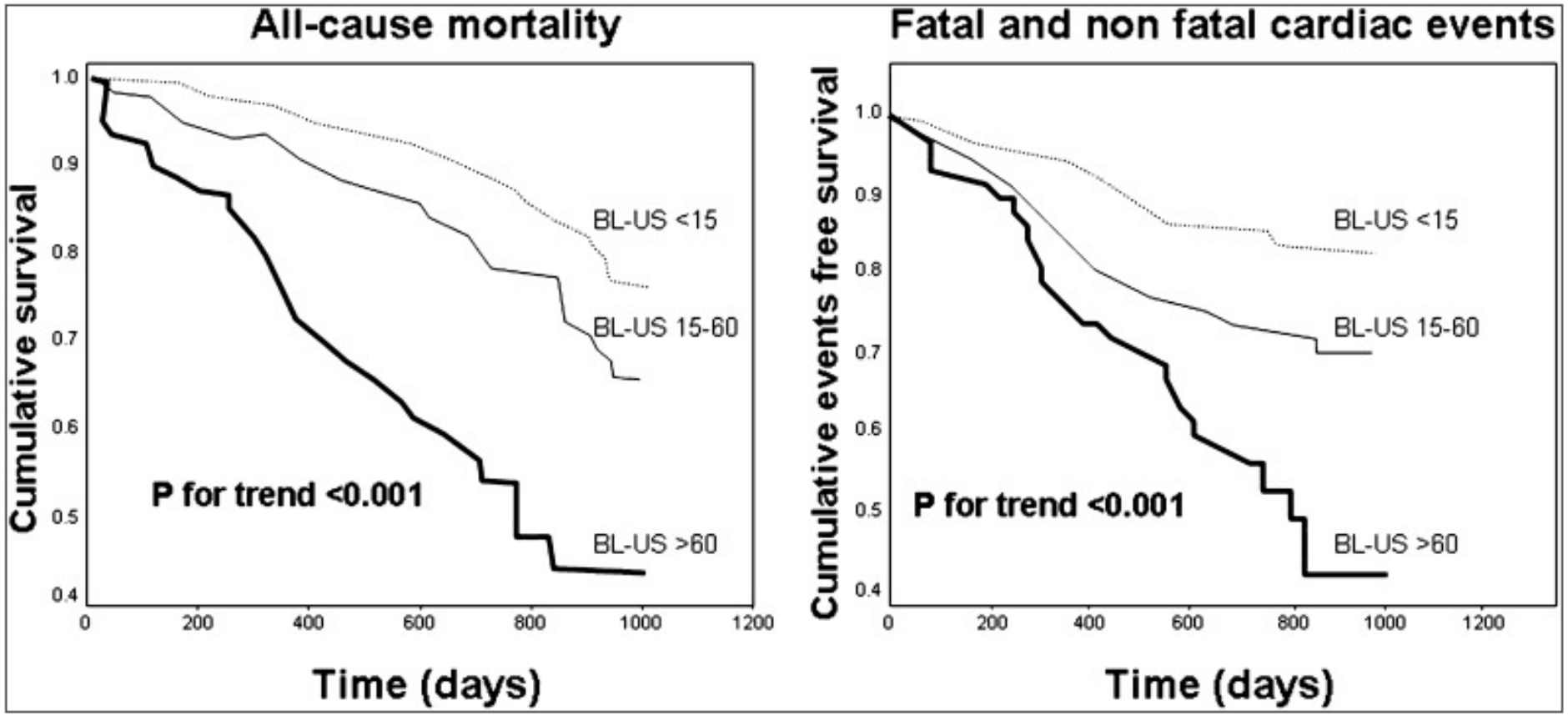
Pulmonary congestion - as determined by pulmonary ultrasound - is associated with poor outcomes



Zoccali, JASN 2013

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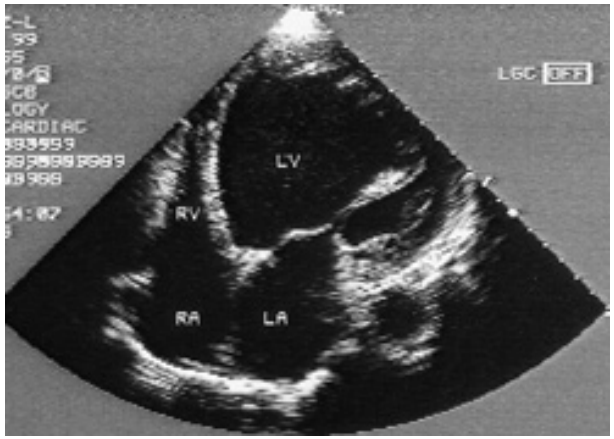
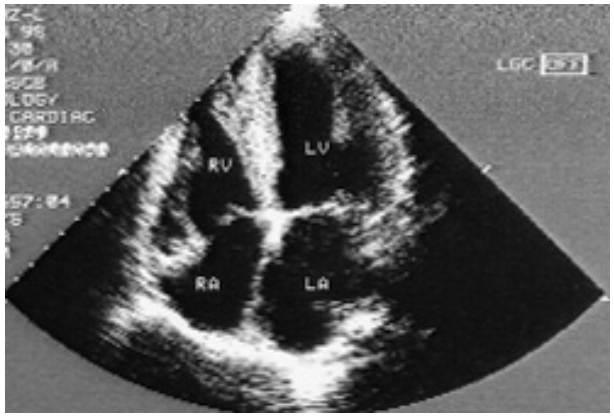
Congestive heart failure in HD



Systolic dysfunction



Diastolic dysfunction

Depending on the population studied and the criteria applied around 20 to 30% of HD patients suffer from some form of heart failure

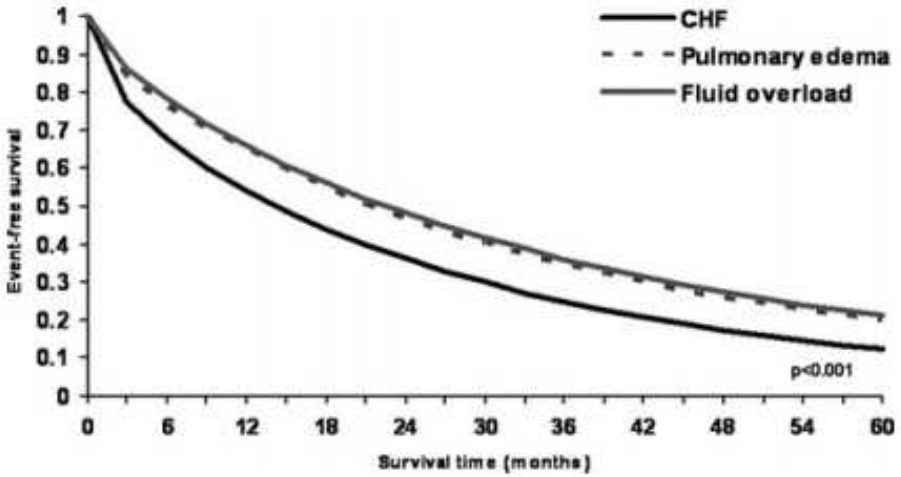
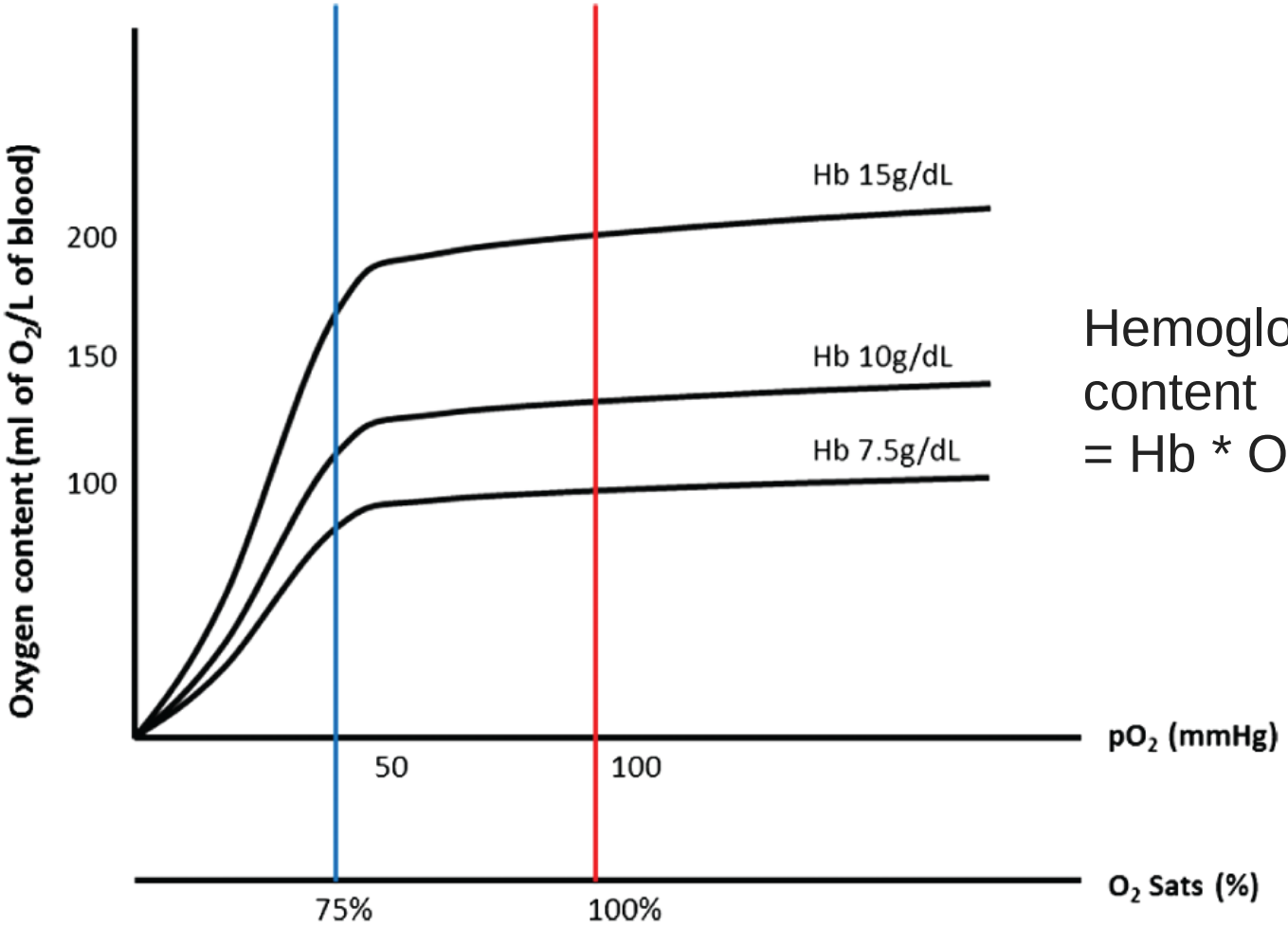


Figure 1. All-cause survival (composite groups). Event-free survival of patients who were on maintenance hemodialysis from first hospitalization after initiation of renal replacement therapy with congestive heart failure (CHF), pulmonary edema, and fluid overload.

Banerjee, CASN 2007

Blood Oxygen Content depends on Hemoglobin Concentration and Oxygen Saturation

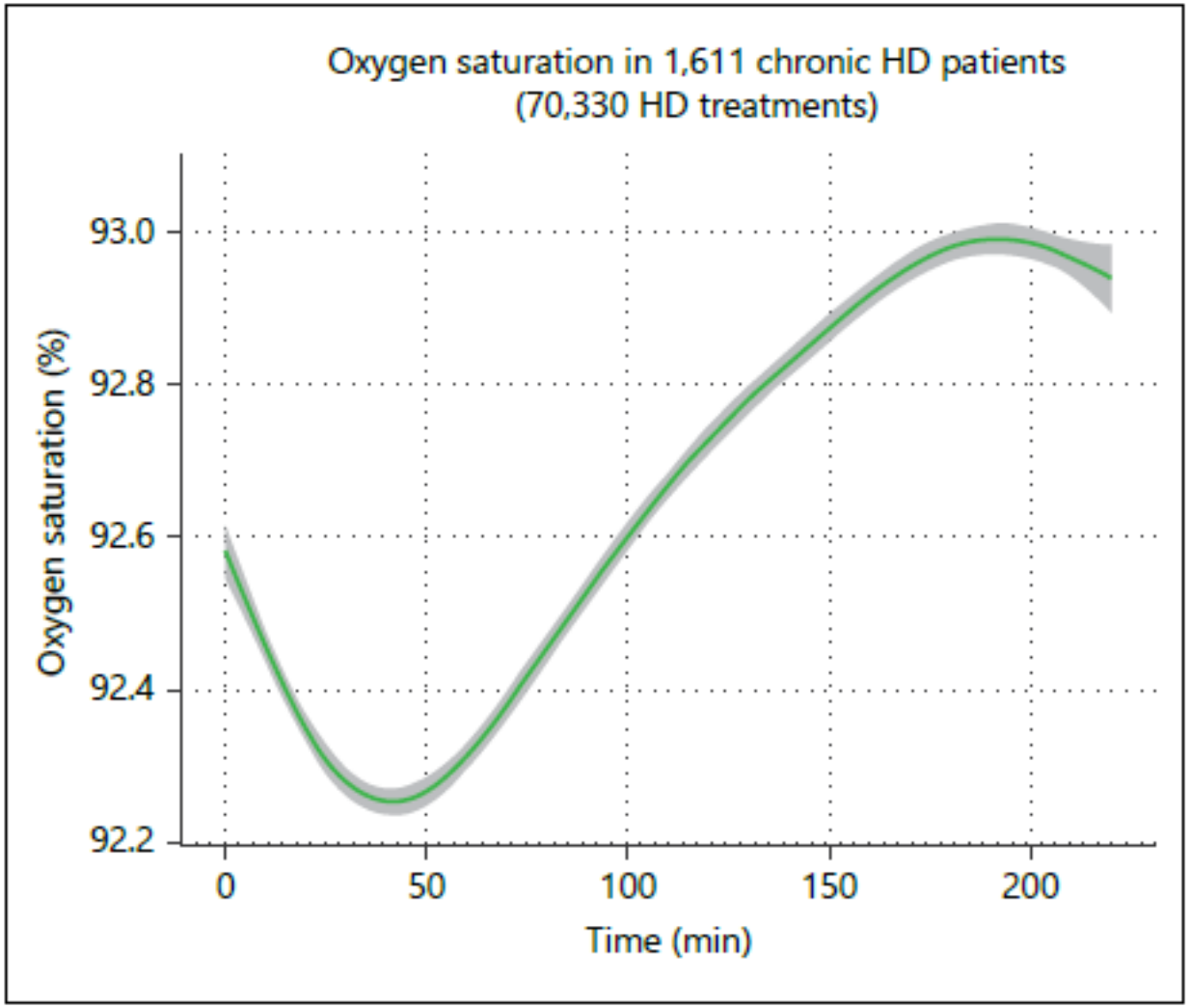


Hemoglobin-bound oxygen content
= Hb * O_2Saturation * 1.39

Clin. Cardiol. 2016, pp 477-483

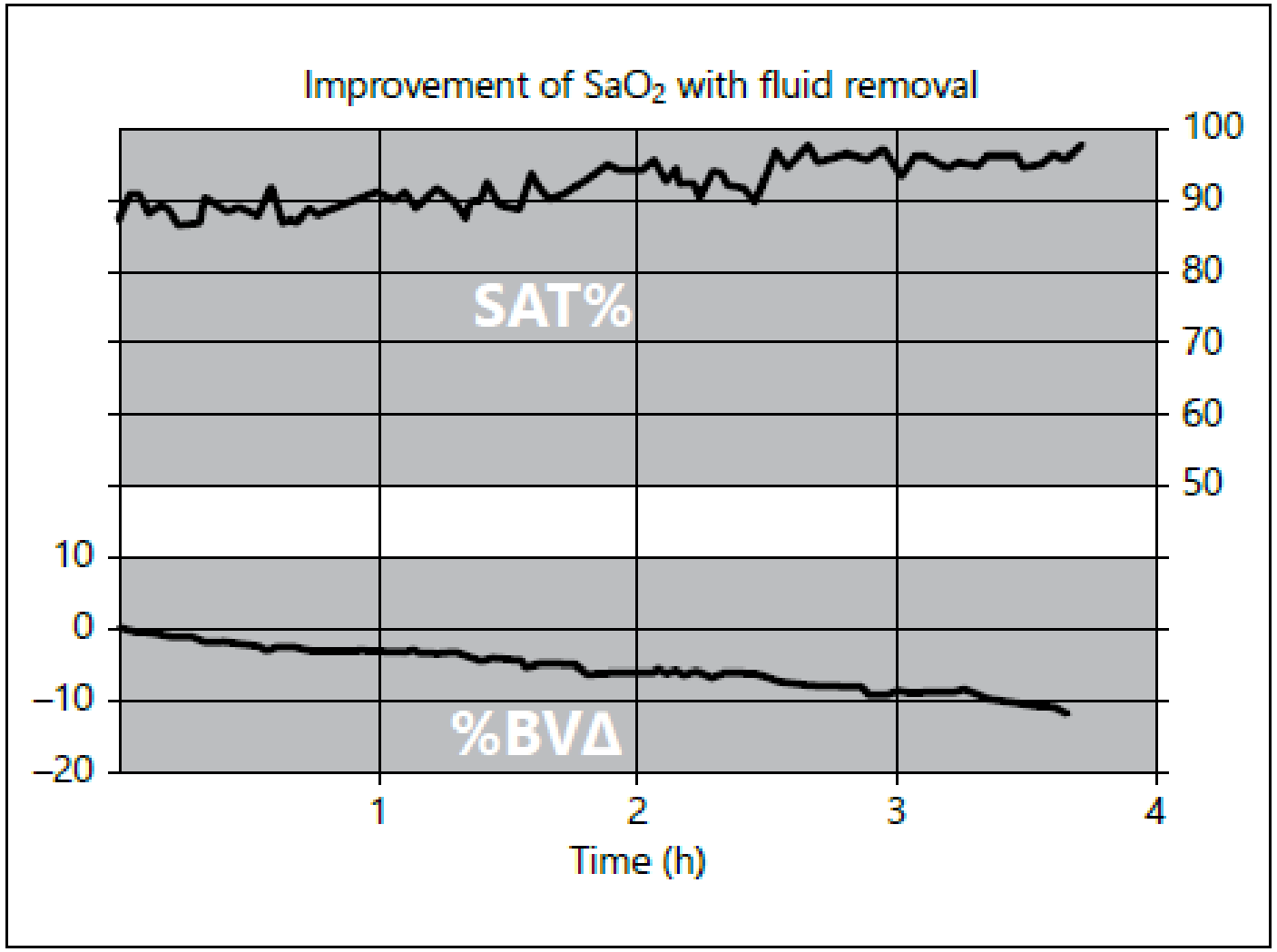
Arterial Oxygen Saturation during Hemodialysis

Time course of intradialytic arterial oxygen saturation



Campos, *Blood Purif* 2016;41:177–187

Association between fluid removal and SaO_2

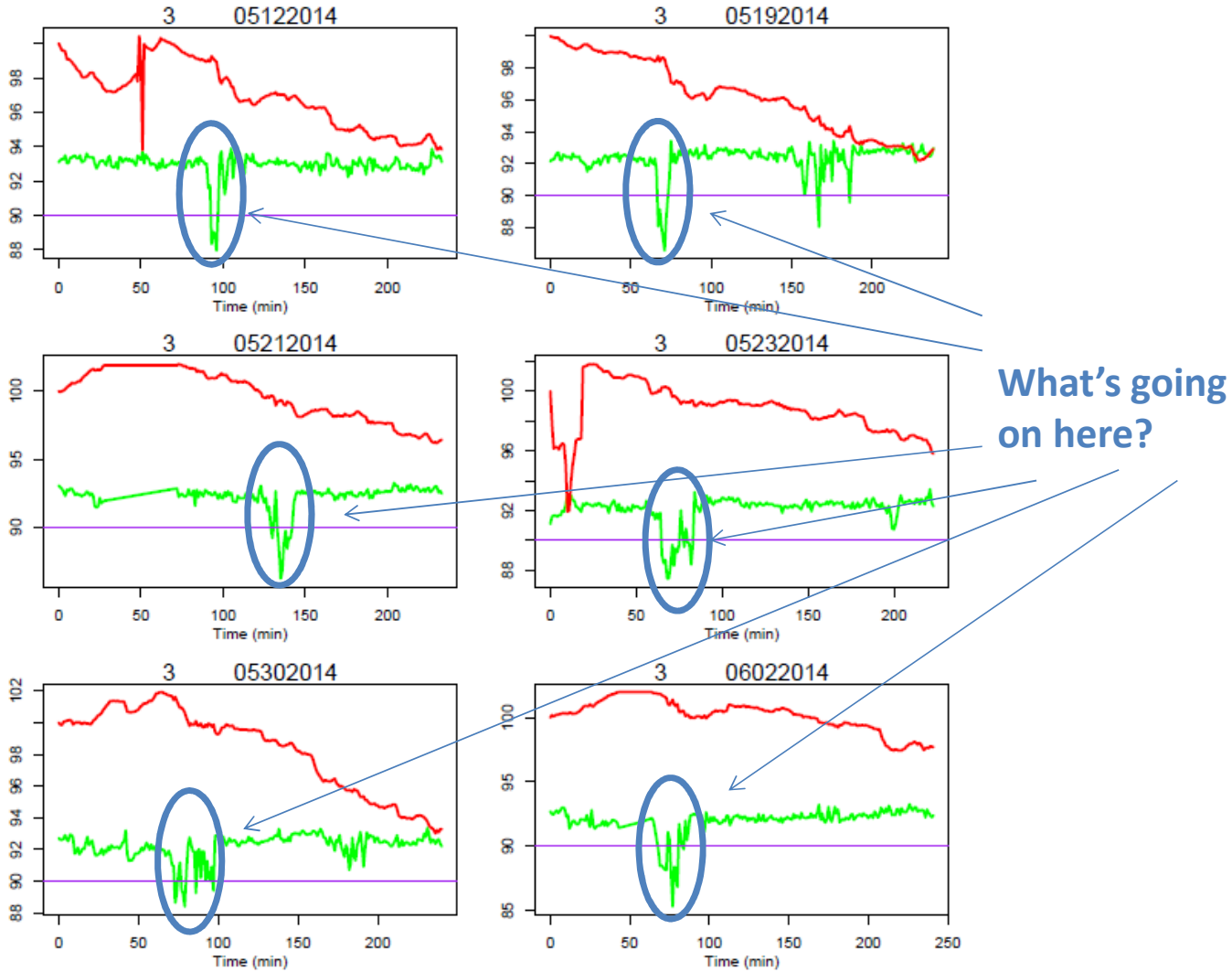


Improved arterial oxygen saturation

Decline in blood volume as a consequence of fluid removal

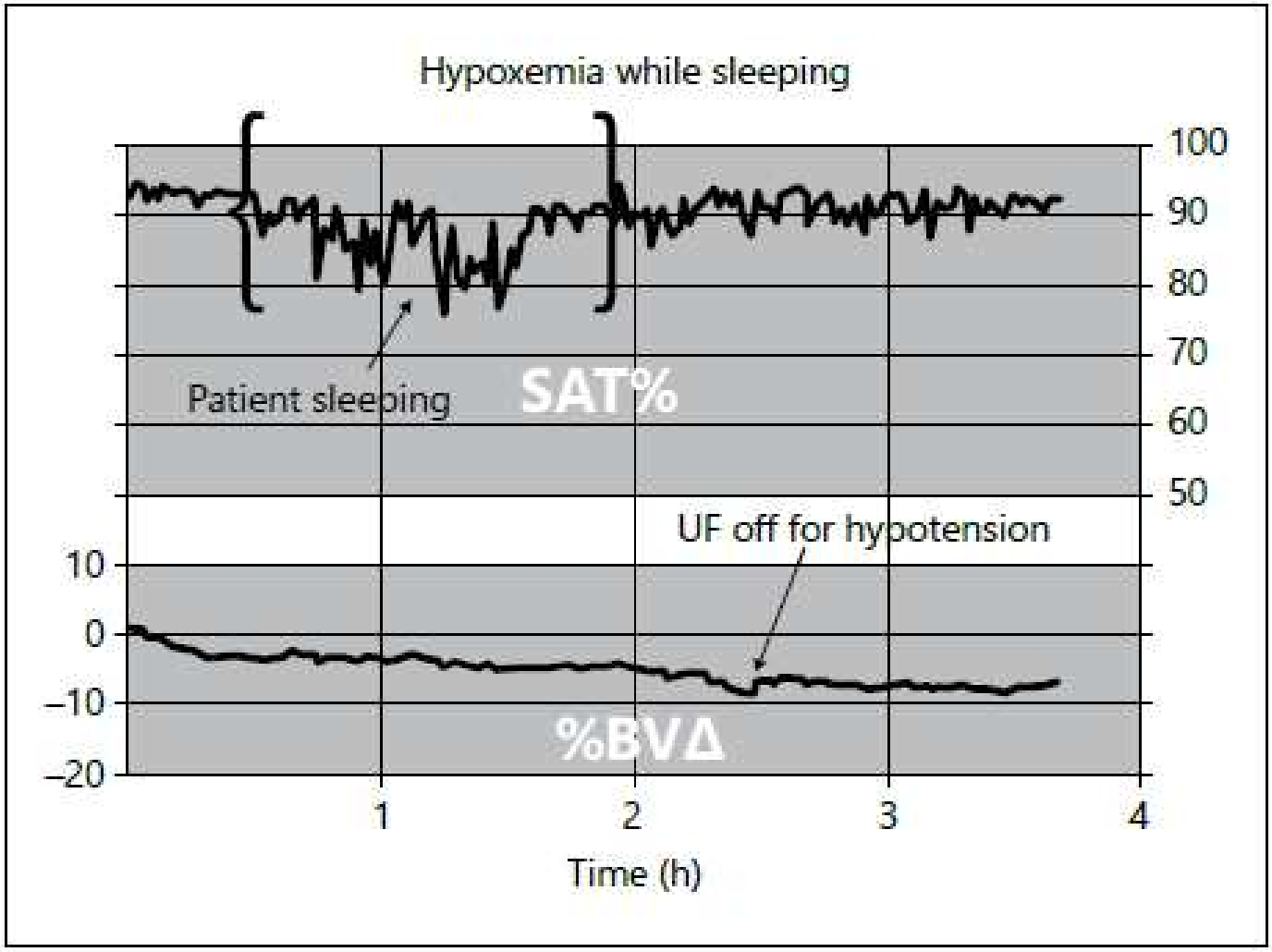
Campos, *Blood Purif* 2016;41:177–187

Arterial O_2 saturation in the same HD patient during six treatments



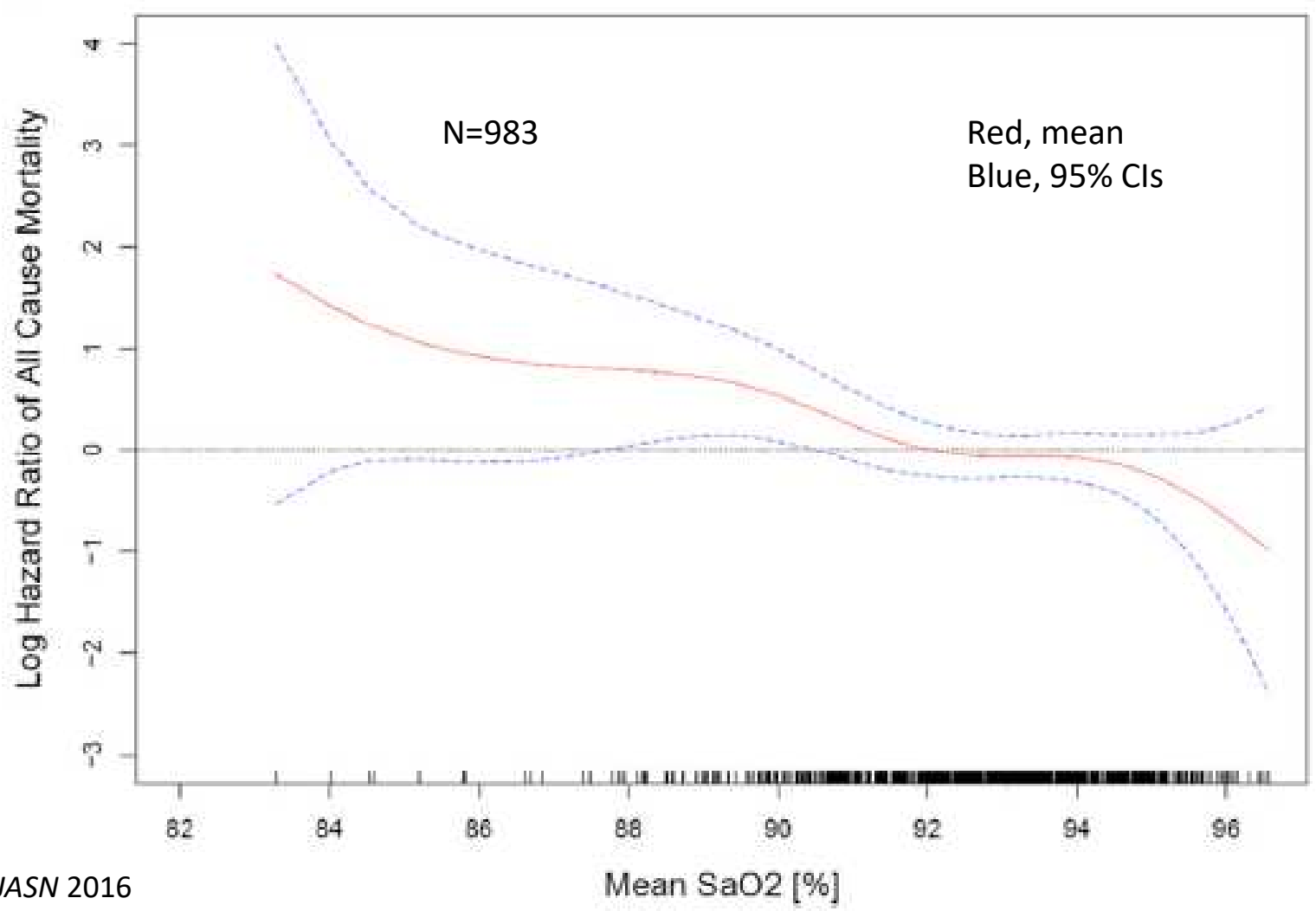
Green line, O_2 saturation
Red line, relative blood volume

Intradialytic hypoxemia may occur while sleeping



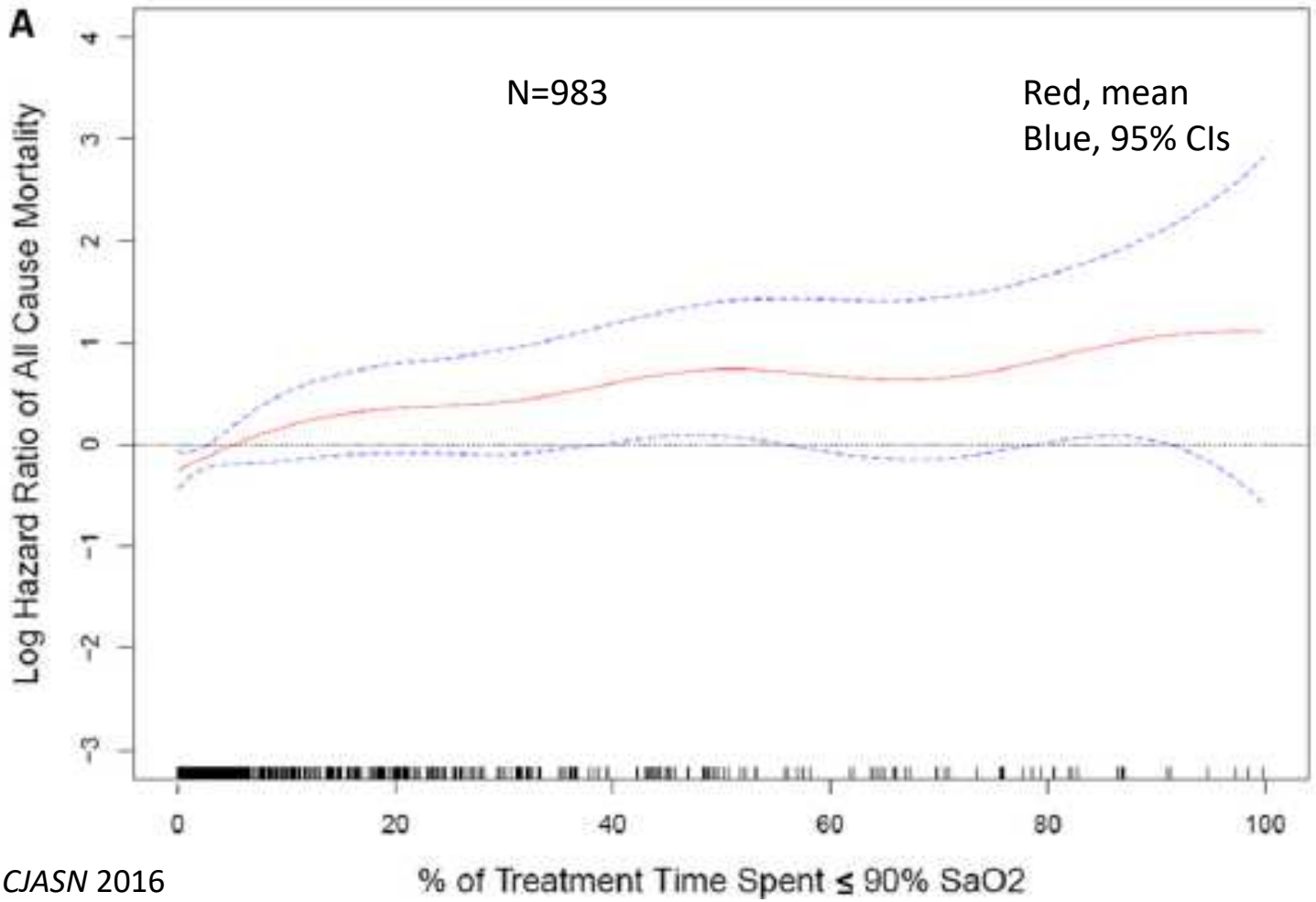
Campos, *Blood Purif* 2016;41:177–187

Association between mean intradialytic SaO_2 and all-cause mortality



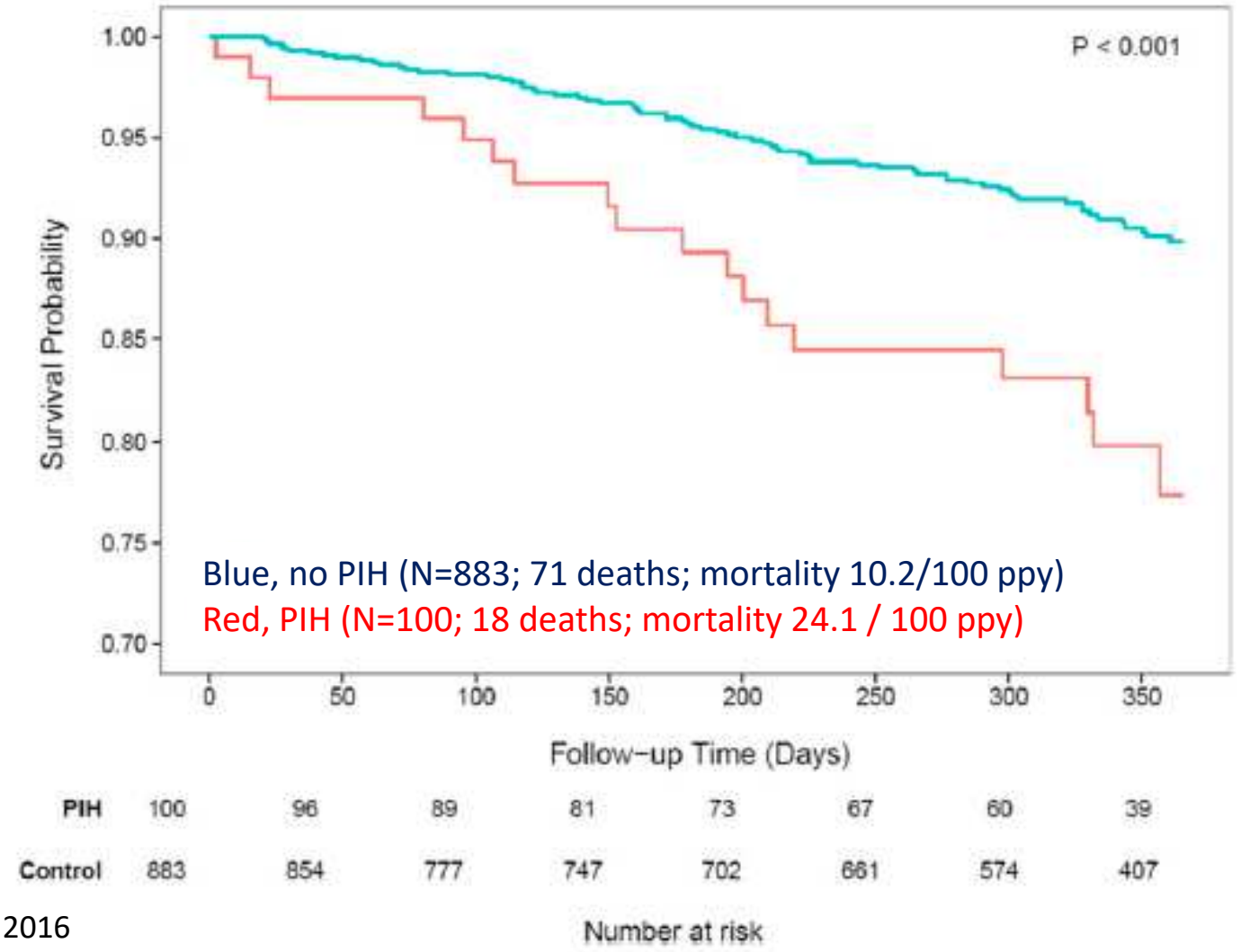
Meyring-Wösten, *CJASN* 2016

Association between % HD treatment time spent ≤ 90% SaO_2 and all-cause mortality



Meyring-Wösten, *CJASN* 2016

Prolonged intradialytic hypoxemia (PIH) is associated with higher all-cause mortality



Meyring-Wösten, *CJASN* 2016

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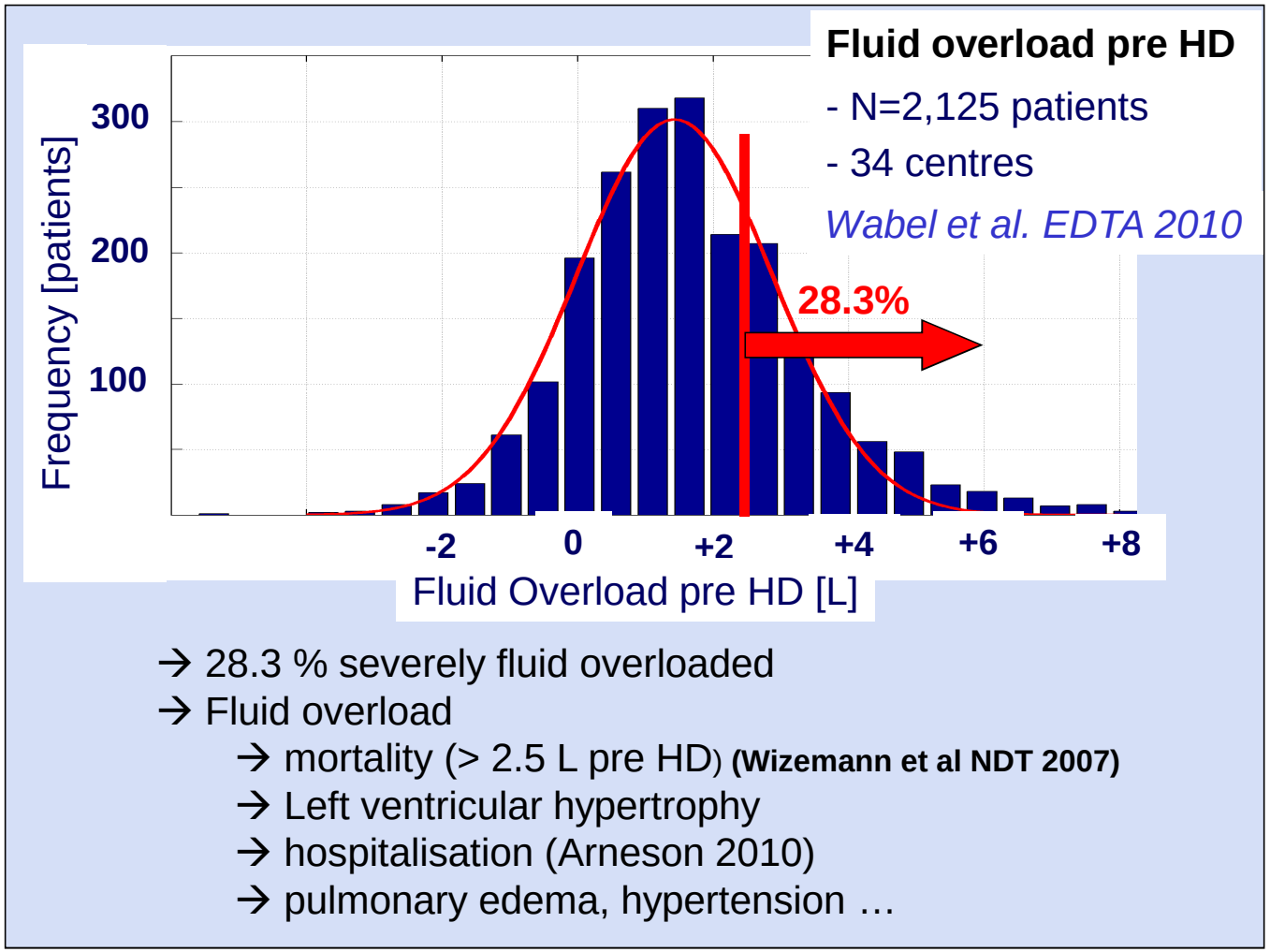
Prevalence of fluid overload in HD patients / Europe (determined by bioimpedance)



→ 28.3 % severely fluid overloaded
→ Fluid overload
- → mortality (> 2.5 L pre HD) **(Wizemann et al NDT 2007)**
- → Left ventricular hypertrophy
- → hospitalisation (Arneson 2010)
- → pulmonary edema, hypertension …

Courtesy of P. Wabel

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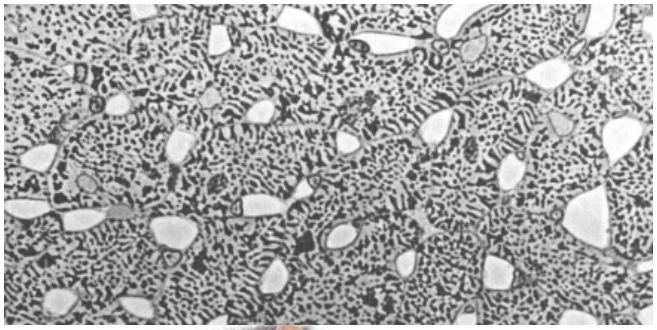
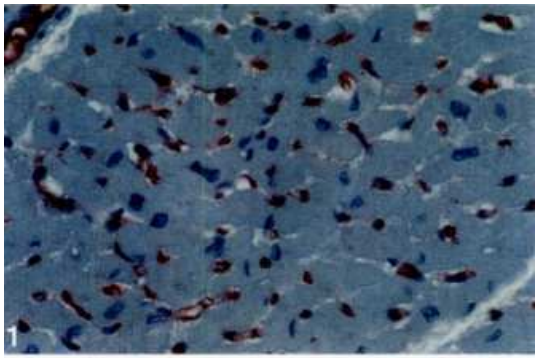
Myocardial capillary rarefication in uremia

Amann, KI 1992

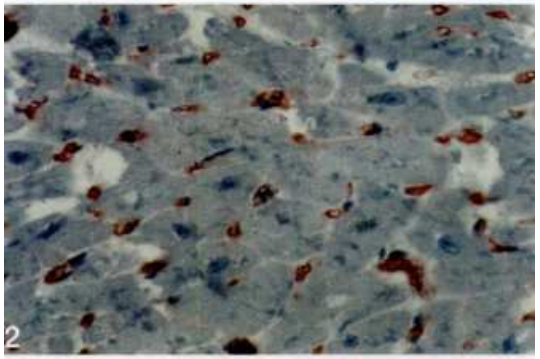
Amann, JASN 1998

Control rat



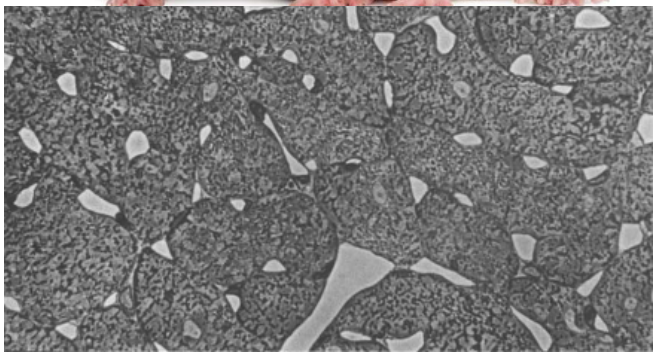


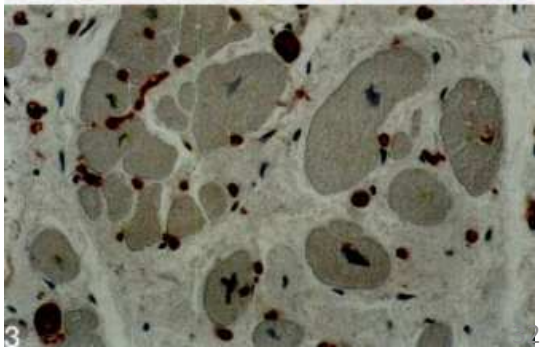
Control patient



Hypertensive patient

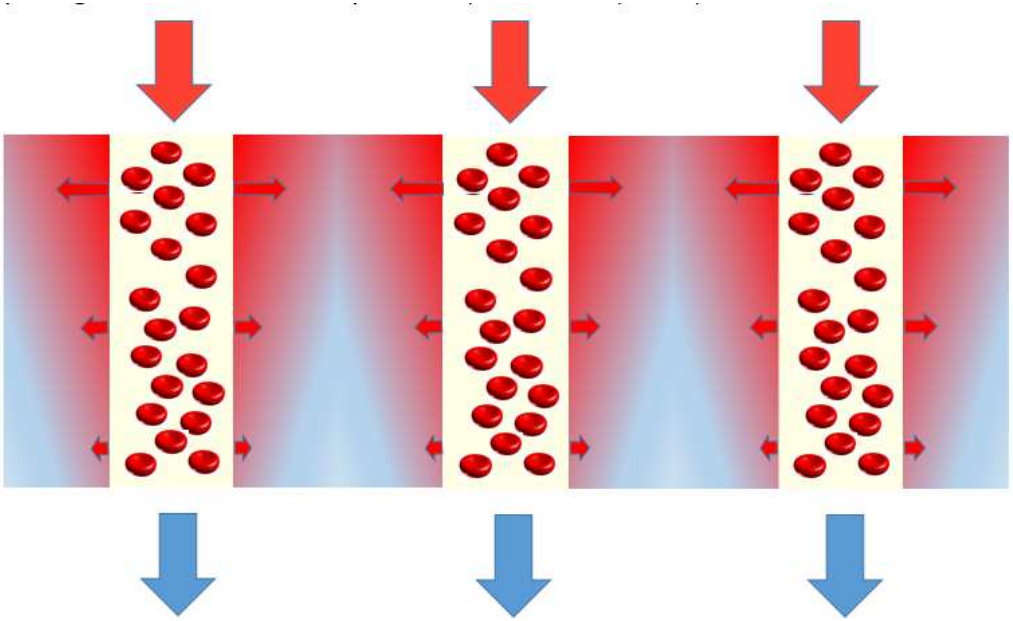
Uremic rat





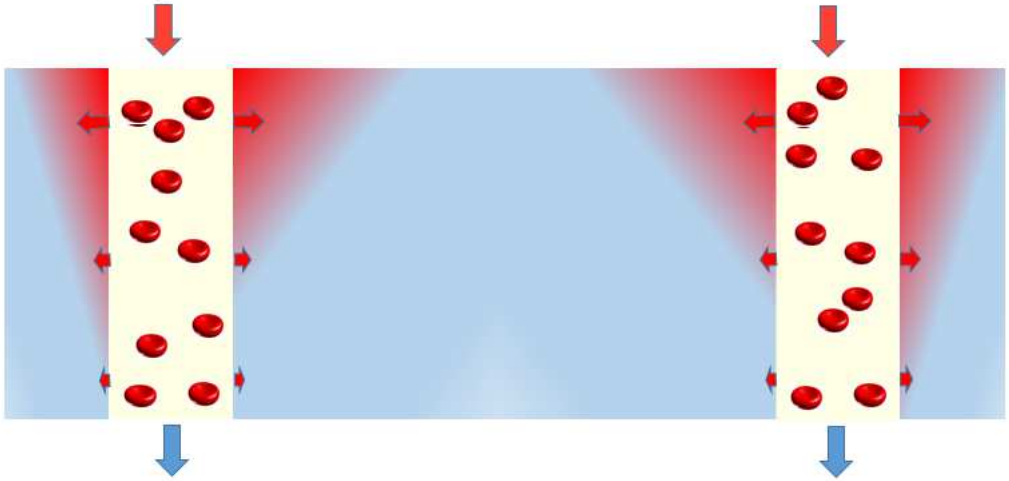
Uremic patient

- Adequate cardiac output
- No anemia
- No fluid overload
- No capillary rarefication



Normal

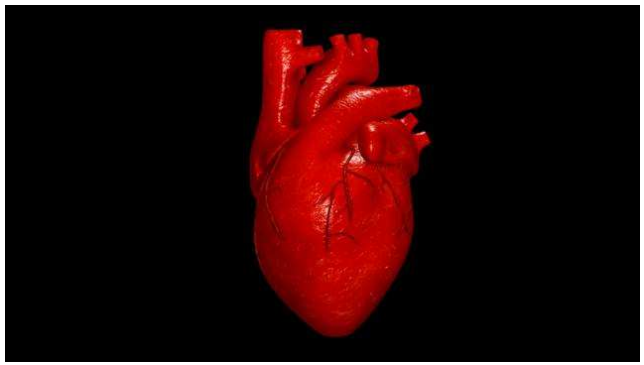
- Low cardiac output
- Anemia
- Fluid overload (intravascular; interstitial)
- Capillary rarefication



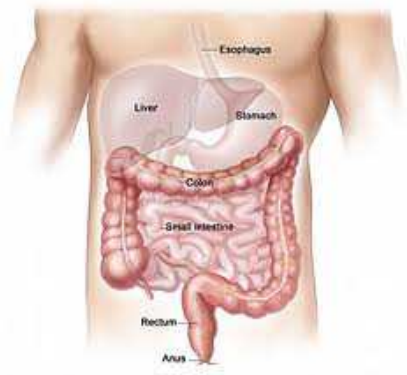
Uremia

Organs with a particularly vulnerable microcirculation

- Heart

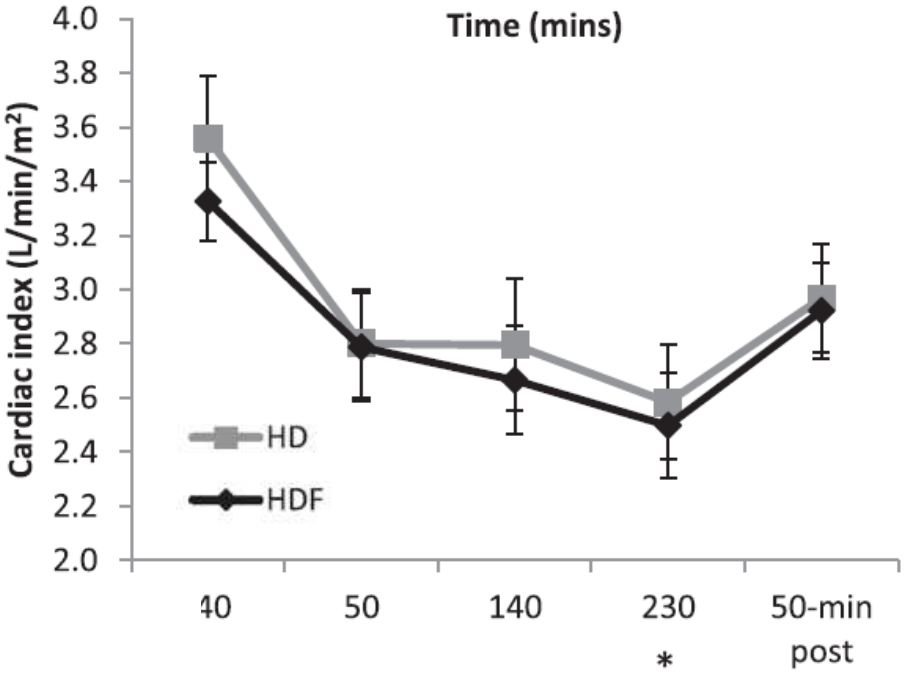


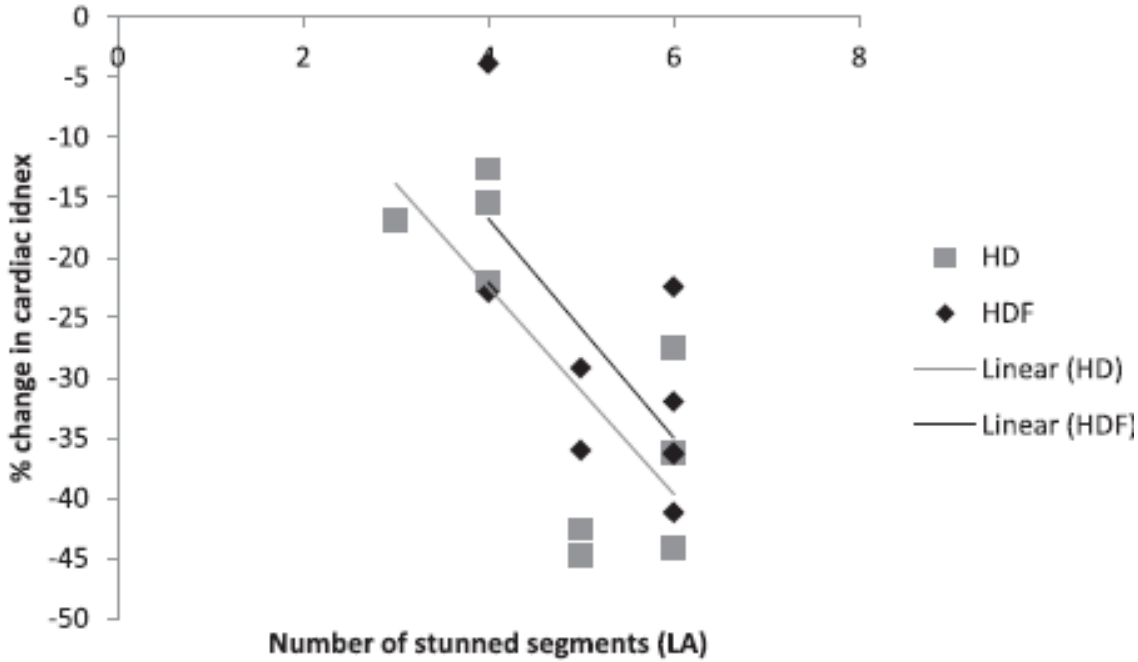
- Gut



- Brain

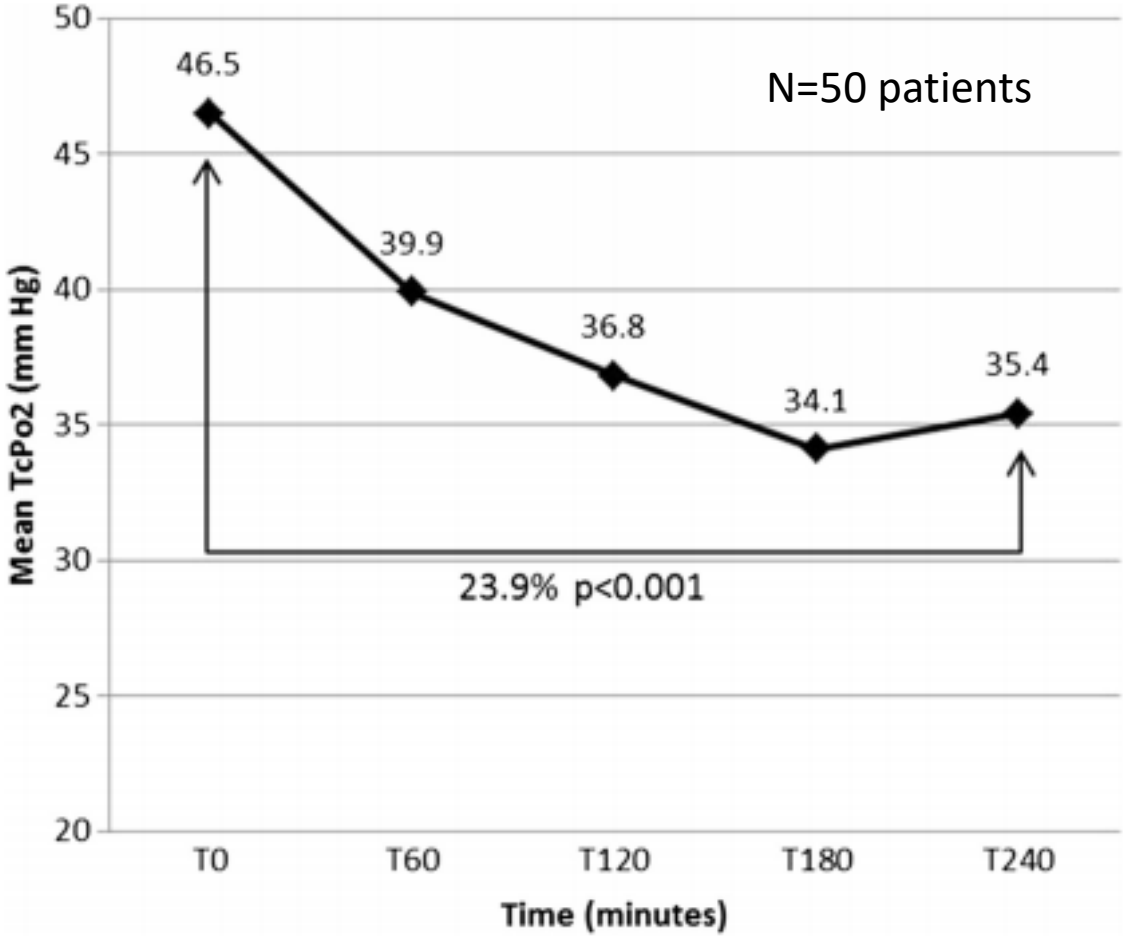
Myocardial stunning and cardiac index during HD / HDF





Buchanan, JASN 2016

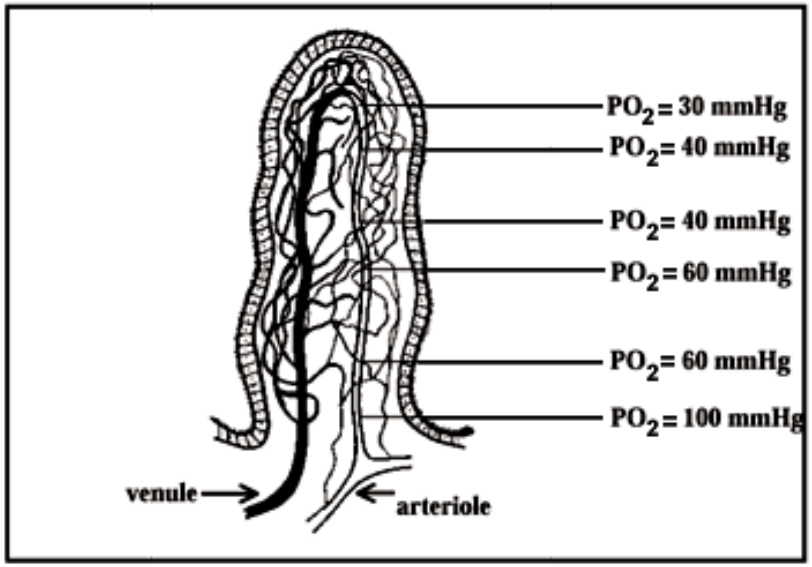
Intradialytic transcutaneous oxygen pressure ($TcPO_2$)



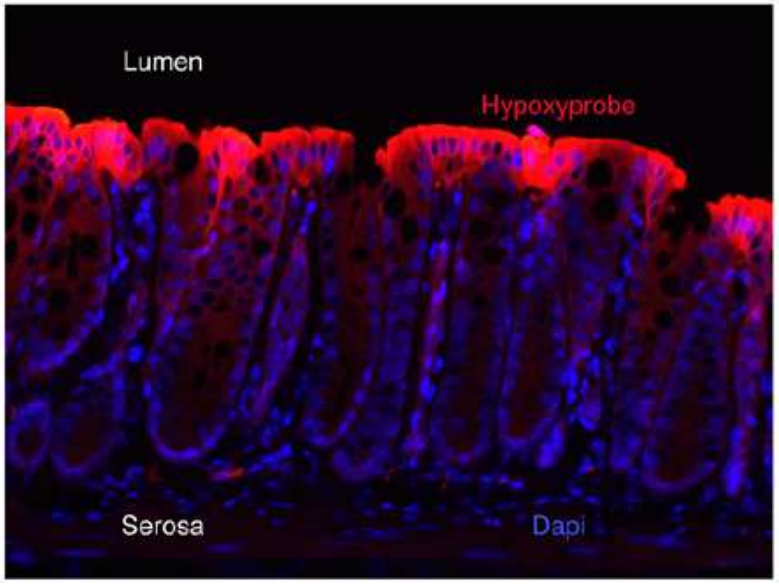
Severe ischemia ($TcPO_2$ < 30 mmHg) and critical ischemia ($TcPO_2$ < 10 mmHg) occurred during dialysis in 47.1% and 15.5%, respectively.

Benhamou, BMC Nephrology 2014

Intestinal mucosa integrity is susceptible to hypoxia



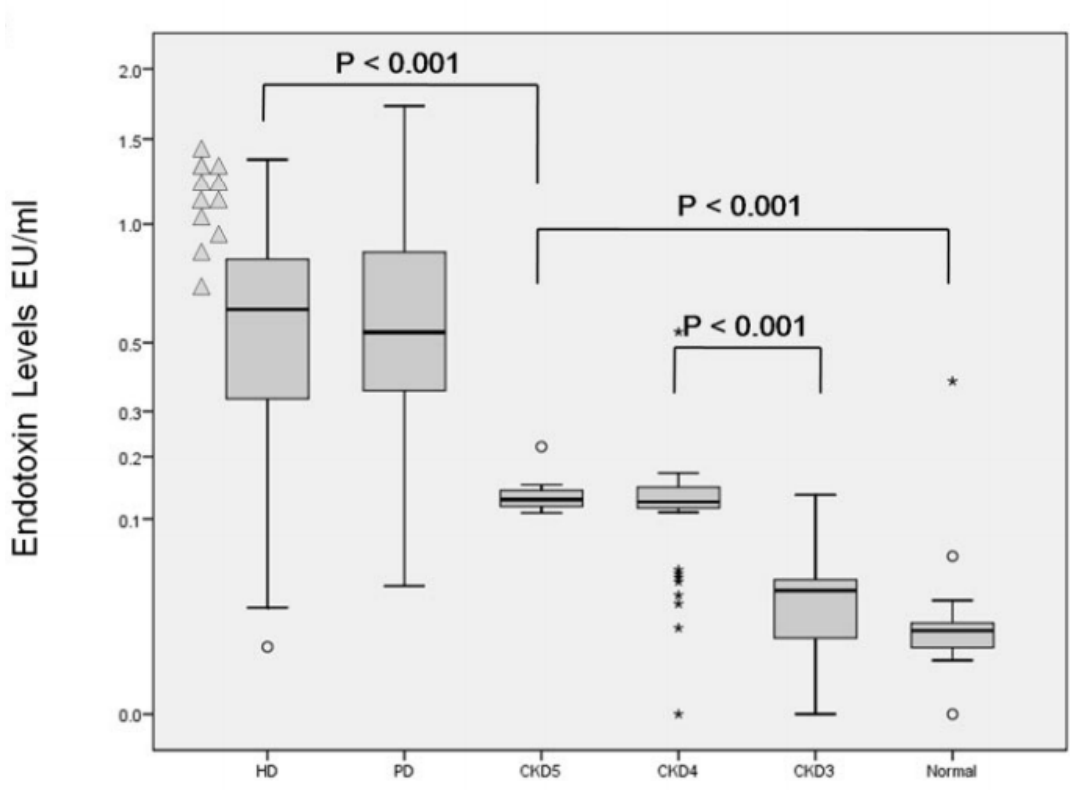
Figueiredo, 2002



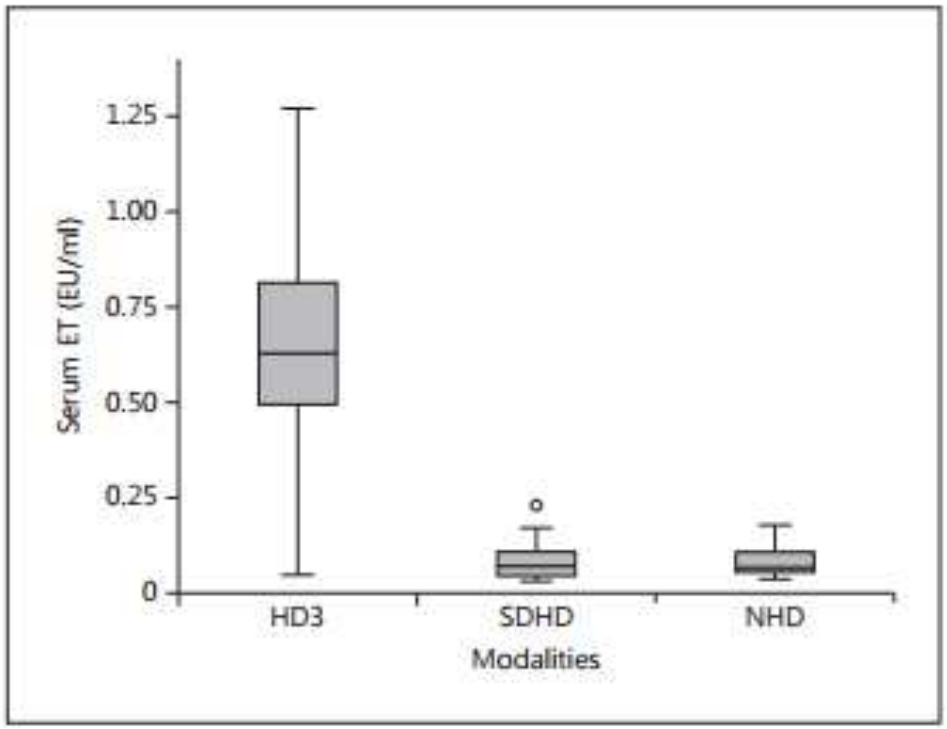
Glover, JCI 2016

The intestinal villi microvascular architecture is characterized by a countercurrent exchange of oxygen from arteriole to adjacent venule along its length (oxygen shunting)

Increased endotoxin levels in ESRD and thrice weekly hemodialysis and PD

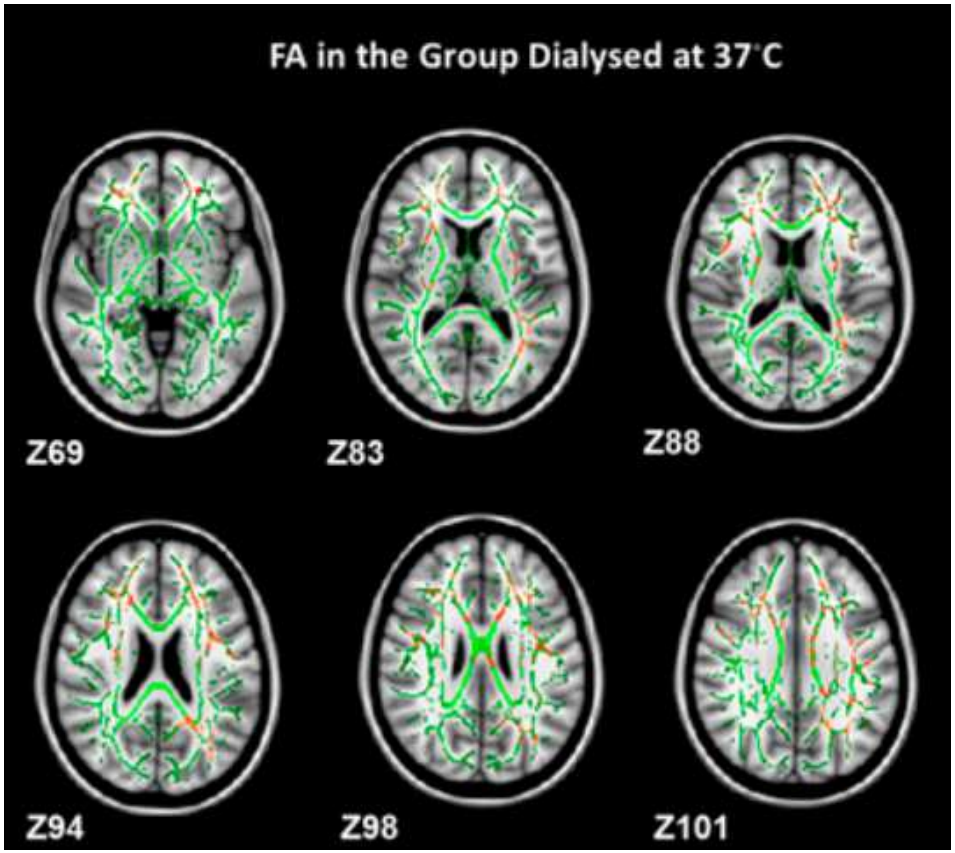


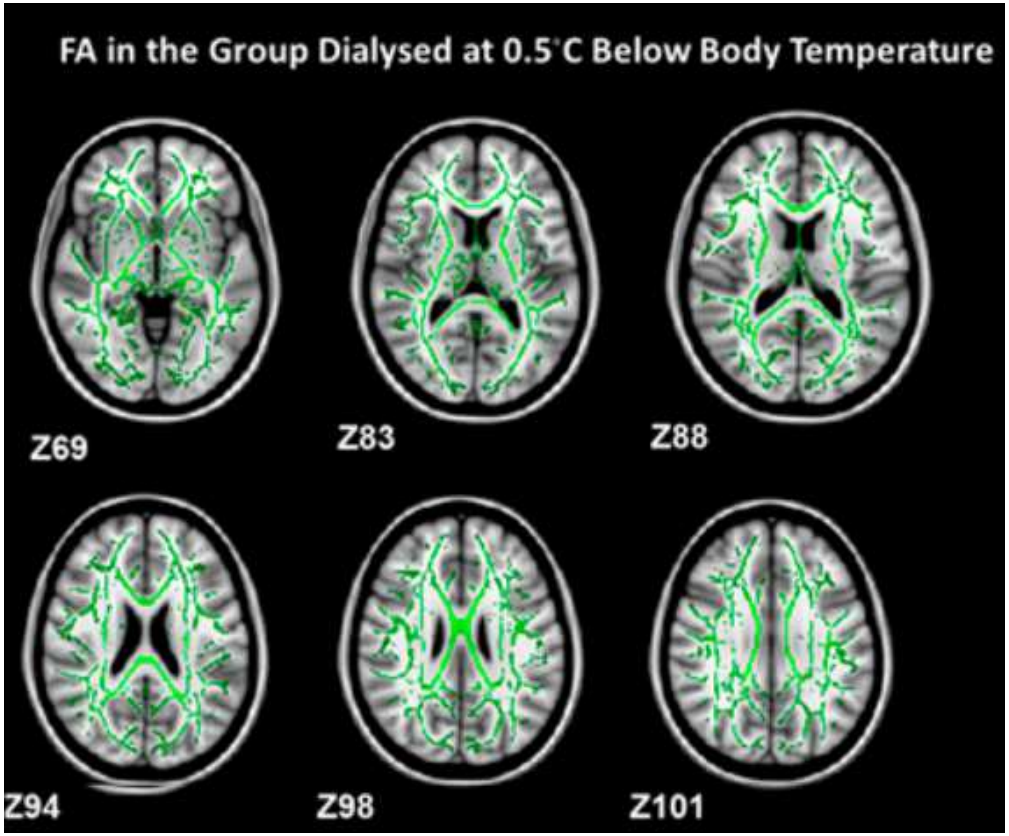
McIntyre, CJASN 2011



Jefferies, Nephron Clin Pract 2014

White matter lesions in brains of HD patients after 1 year on dialysis





Eldehni, JASN 2916

How to improve tissue oxygen supply?

- Impaired pulmonary oxygen uptake
  - Increased lung water
  - Sleep apnea
- Reduced convective oxygen transport
  - Cardiac insufficiency
  - Anemia
  - Lower arterial oxygen saturation
- Impaired tissue oxygen diffusion
  - Interstitial fluid overload
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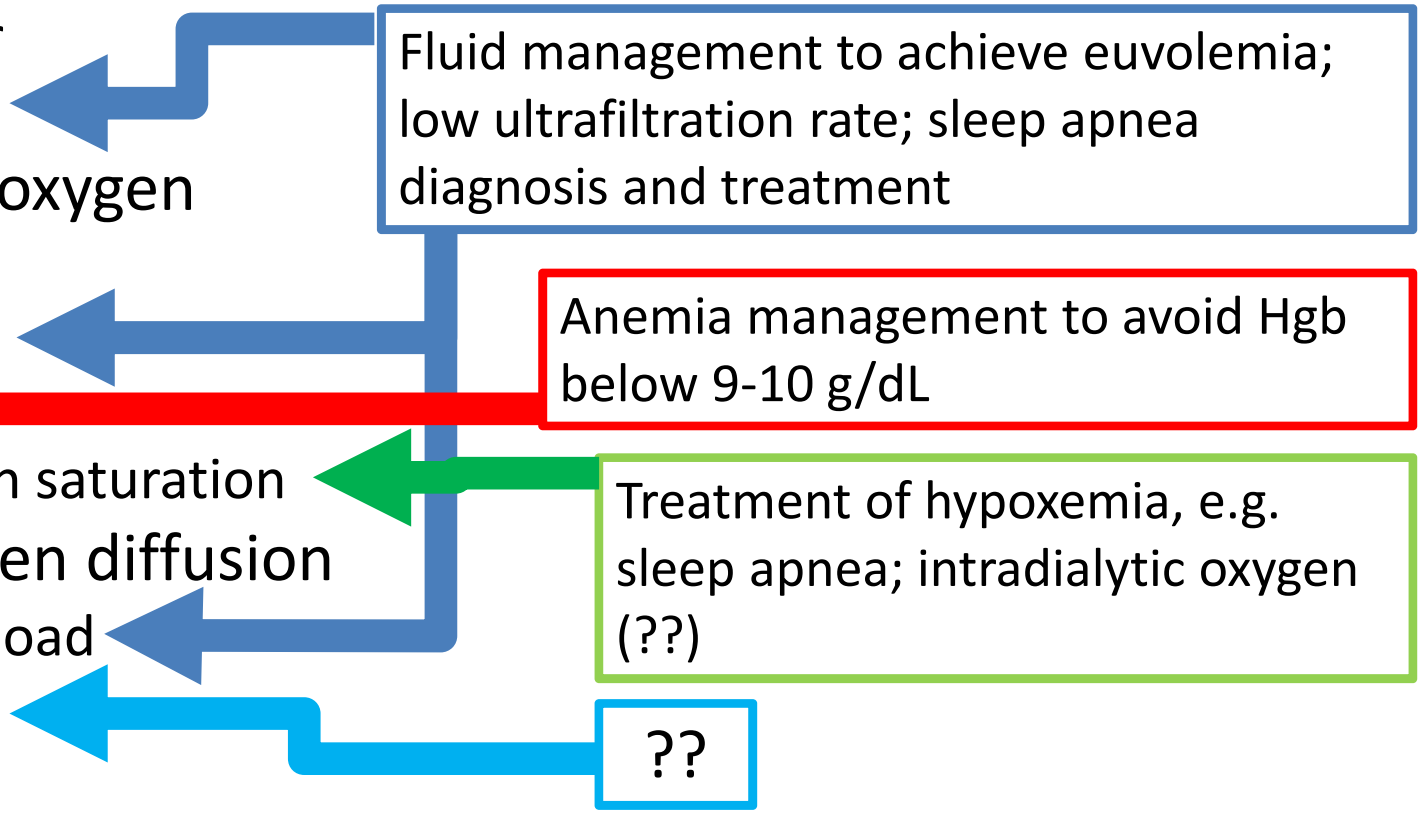

Summary

- Oxygen supply to tissues and organs is impaired in hemodialysis patients due to multiple pathological alterations
- Particularly susceptible organs are the heart, gut, and brain
- Fluid management and means to increase intradialytic hemodynamic stability (e.g. cool dialysate; biofeedback ultrafiltration control) are key to improve oxygen supply to tissues and organs
- Research into hypoxemia and its treatment in ESRD patients is urgently needed

Oxygen in Maintenance Hemodialysis Patients – is it relevant at all?

thank you
gracias
merci
danke
obrigado
dziękuję
teşekkür ederim
go raibh maith agat
mochchakkeram
sukriya
kop khun krap
terima kasih
ngiyabonga
bedankt
спасибо
謝謝
شكراً جزيلاً
감사합니다
ありがとう
ευχαριστώ
мерси
arigatō
dakujem
grazie
takk
dank je
tapadh leat
hvala
mauruuru
sagolun
Баярлалаа
рахмат
хвала