ULM SFB 1149 TRAUMA

ulm university universität ulm

Übersichtsarbeit

Sauerstofftherapie in der Intensiv- und Notfallmedizin

Jörn Grensemann, Valentin Fuhrmann, Stefan Kluge

Deutsches Ärzteblatt | Jg. 113 | Heft 27–28 | 9. Juli 2018

Vorlesungen

über die

Rettungsmittel

beim

Scheintode

und in

plötzlichen Lebensgefahren.

Joseph Bernt,

Doctor der Heilkunde, k. k. ordentlichem und öffentlichen Professor der Staatsarzneikunde an der hohen Schule zu Wien, auswärtigem Mitgliede der k. k. Akademie der Wissenschaften, Literatur und Künste zu Padua.

Wien, 1837.

Einige Schriftsteller sind der Meinung, daß in gewissen Fällen des Scheintodes geschwindere und sicherere Hülfe geleistet werde, wenn man das reine Sauerstoffgas in die Lungenzellchen bringt; es komme hier alles darauf an, eine so große Menge davon auf einmal dem Blute zu nähern, daß dasselbe seinen Kreislauf aus den Lungenzellchen durch die Lungenvenen in das linke Herz fortsetze, um durch die Einwirkung des oxygenirten Blutes einen starken und entscheidenden Herzschlag hervorzubringen. Geschehe dieser, so erfolge ein solcher zur nämlichen Zeit auch im rechten Herzen, wodurch neues Blut in die Lungenzellchen gebracht wird, um dort sich von neuem mit Sauerstoffgas zu verbinden.

le

Weil MH & Shubin H: **The "VIP" approach to the bedside management of shock.**
JAMA 1969;207:337-40
"…v̲entilate (oxygen administration), i̲nfuse (fluid resuscitation), p̲ump (vasoactive drugs).."

Vincent JL & De Backer D: **Circulatory Shock.**
NEJM 2013;369:1726-34
". "…administration of oxygen should be started immediately to increase oxygen delivery and prevent pulmonary hypertension..."

SFB 1149 TRAUMA

ulm university universität ulm

„For as a candle burns much faster indephlogisticated (oxygen-enriched) than incommon air, so we might live out too fast, and the animal powers be too soon exhausted in this pure kind of air. A moralist, at least, may say, that the air which nature has provided for us is as good as we deserve.“

***In:*THE DISCOVERY OF OXYGEN, section 3:**

„Experiments and Observations on Different Kinds of Airs“

Joseph Priestley 1733- 1804

SFB 1149 TRAUMA

ulm university universität ulm

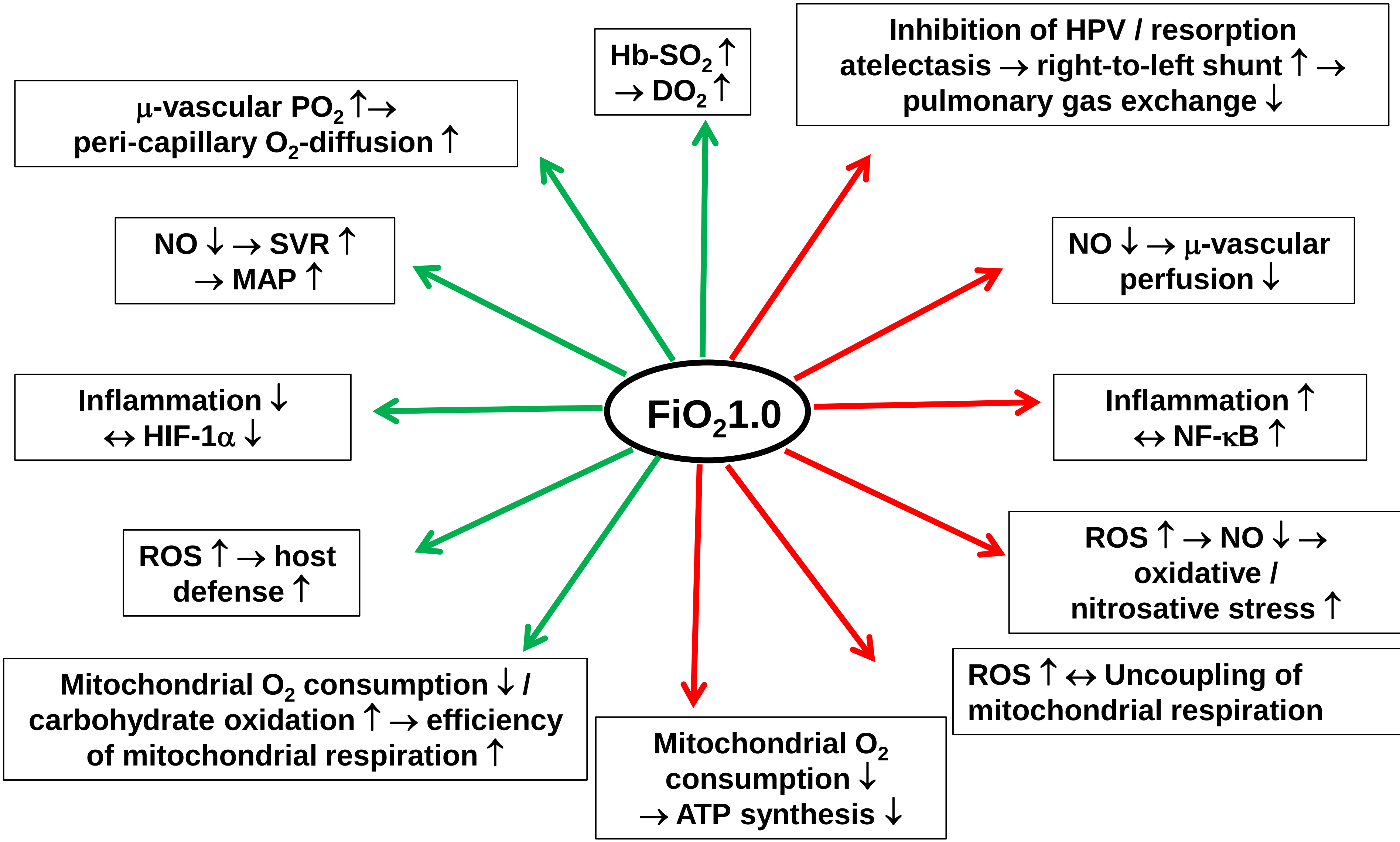
Cornet et al:
The potential harm of oxygen therapy in mdeical emergencies.
Crit Care 2013;17:313

In medical emergencies, supplemental oxygen is often administrated routinely. Most paramedics and physicians believe that high concentrations of oxygen are life-saving [1]. Over the last century, however, a plethora of studies point to possible detrimental effects of hyperoxia induced by supplemental oxygen in a variety of medical emergencies. This viewpoint provides a historical overview and questions the safety of routine high-dose oxygen administration and is based on pathophysiology and (pre)clinical findings in various medical emergencies.

SFB 1149 TRAUMA

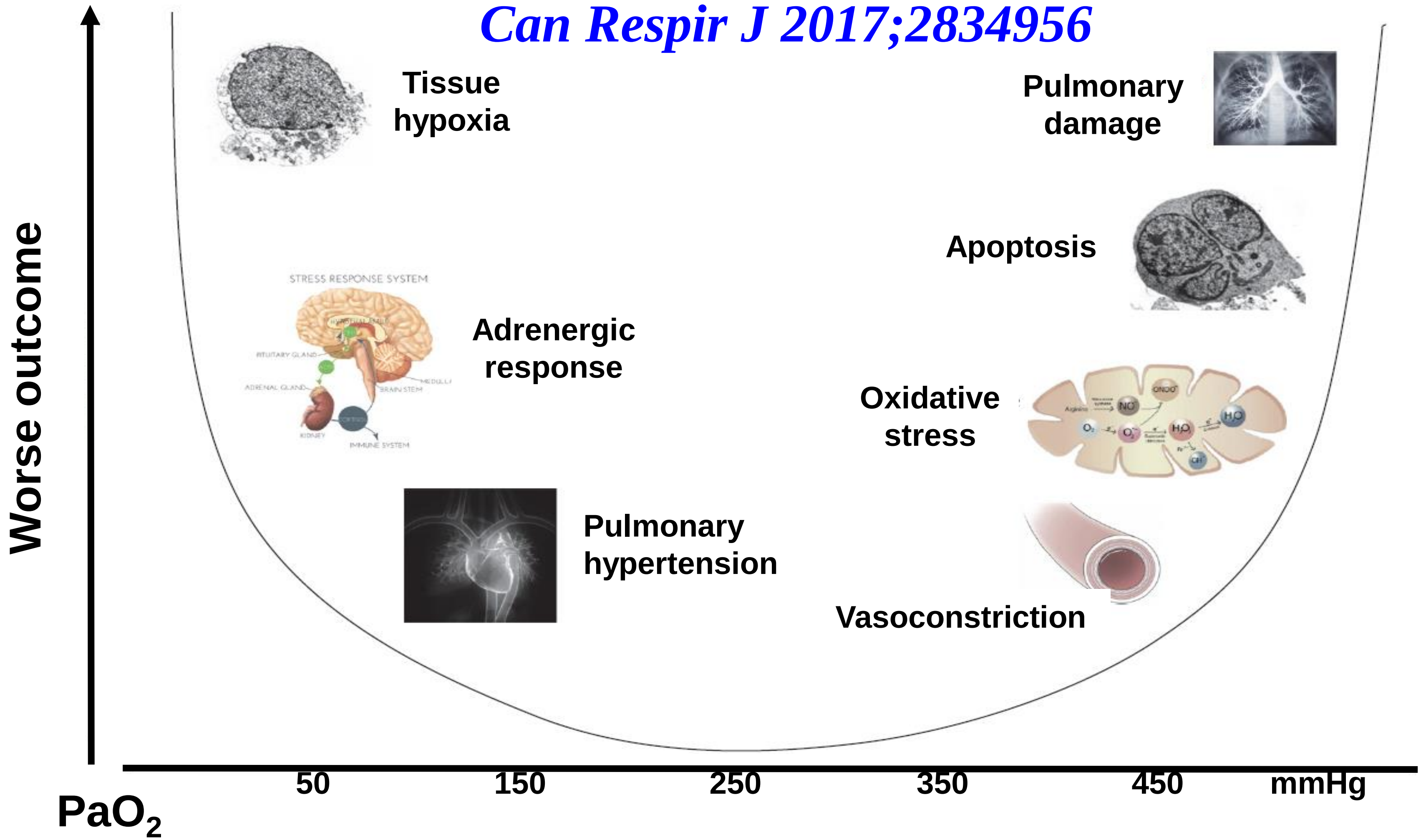
ulm university universität ulm

Asfar, Singer, Radermacher: Understanding the benefits and harms of oxygen therapy. *Intensive Care Med 2015;41:1118*



Vincent JL et al: Harmful effects of hyperoxia in postcardiac arrest, sepsis, traumatic brain injury, or stroke: the importance of individualized oxygen therapy in critically ill patients.

Can Respir J 2017;2834956



Warum ist O_2 ein Gift? Die Radikale

Dienstag, 15. Juni 2004

MENSCH UND GESUNDHEIT

RESPIRATION / Die Luft lässt den Menschen leben – und sterben

Das Atmen ist ein „Pakt mit dem Teufel"

Aggressive Sauerstoff-Atome sind für das Altern verantwortlich – Freitaucher minutenlang unter Wasser

Wir tun es, ohne daran zu denken. Zum Glück müssen wir das auch nicht. Nur wenn uns die Luft wegbleibt, vor Schreck oder unter Wasser, spüren wir, dass wir ohne Atem verloren sind. Die unbewusste Körperfunktion lässt uns altern und ist mit schuld an Leiden wie Krebs.

WALTER SCHMIDT

Vom ersten Schrei als Baby, durch den sich unsere Lungen entfalten, bis zum letzen Atemzug mit – angenommen – 75 Jahren holen wir rund 710 000 Millionen Mal Luft. Jede Minute etwa 18 Atemzüge, jeden Tag rund 26 000. Bei einem halben Liter Luft je Atemzug in Ruhe atmen wir in unserem Leben fast 355 000 Kubikmeter ein – so viel, dass man damit ein 70 Meter aufragendes Hochhaus mit der Grundfläche eines Fußballfeldes füllen könnte. „Hier atme ich und kann nicht anders" – so ließe sich in

Meist läuft das Atmen unbewusst. Nur unter Wasser merkt man, dass der Mensch Luft zum Leben braucht. Archivfoto

braucht das Hirn weniger Sauerstoff als bei Normal-Temperatur.

Wenn das Atmen etwas so Heikles ist, wieso hat sich der Mensch darauf eingelassen? Es war ein Kompromiss. „Wir haben uns im Laufe der Evolution angewöhnt, unsere Energie über die Oxidation von Nährstoffen, vor allem von Zuckern wie der Glukose, zu gewinnen", klärt Claus-Martin Muth auf. Beim Verbrennen der Zuckermoleküle in den Kraftwerken der Zelle, den Mitochondrien, entstehen Wasser, Kohlendioxid und der Energielieferant Adenosintriphosphat (ATP).

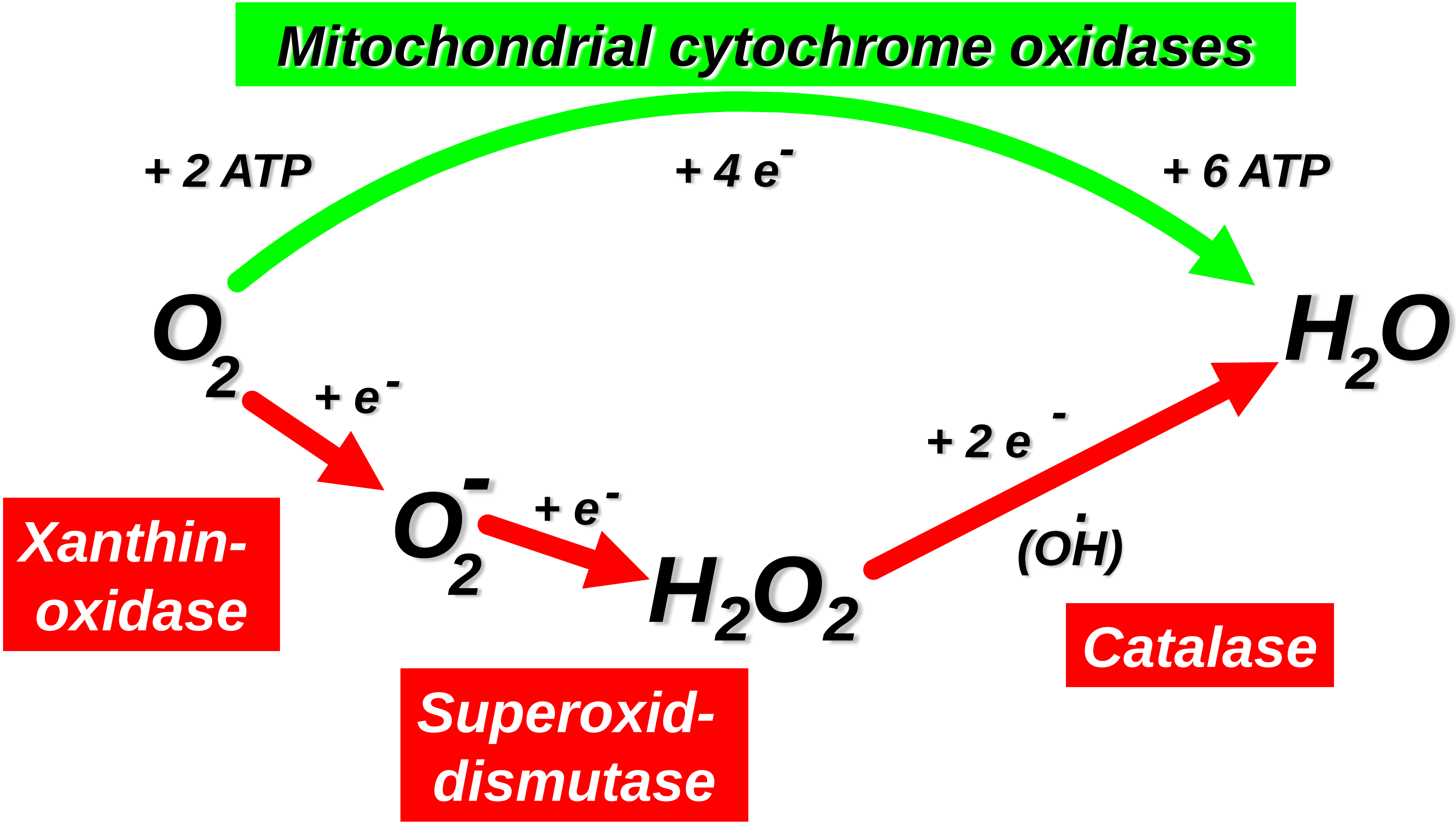
Leben ohne Sauerstoff

Diese Prozedur erwies sich als effektiv, zwingend war sie nicht. Ursprünglich waren die Organismen ohne Sauerstoff ausgekommen, der in der Ur-Atmosphäre nur in Spuren vorkam. Selbst heute noch gibt es Tiefsee-Bakterien, die anaerob, also ohne Sauerstoff, leben und ihre Energie aus Schwefelverbindungen gewinnen. Dann kamen die grünen Pflanzen auf und entließen als Abfallprodukt ihrer Photosynthese

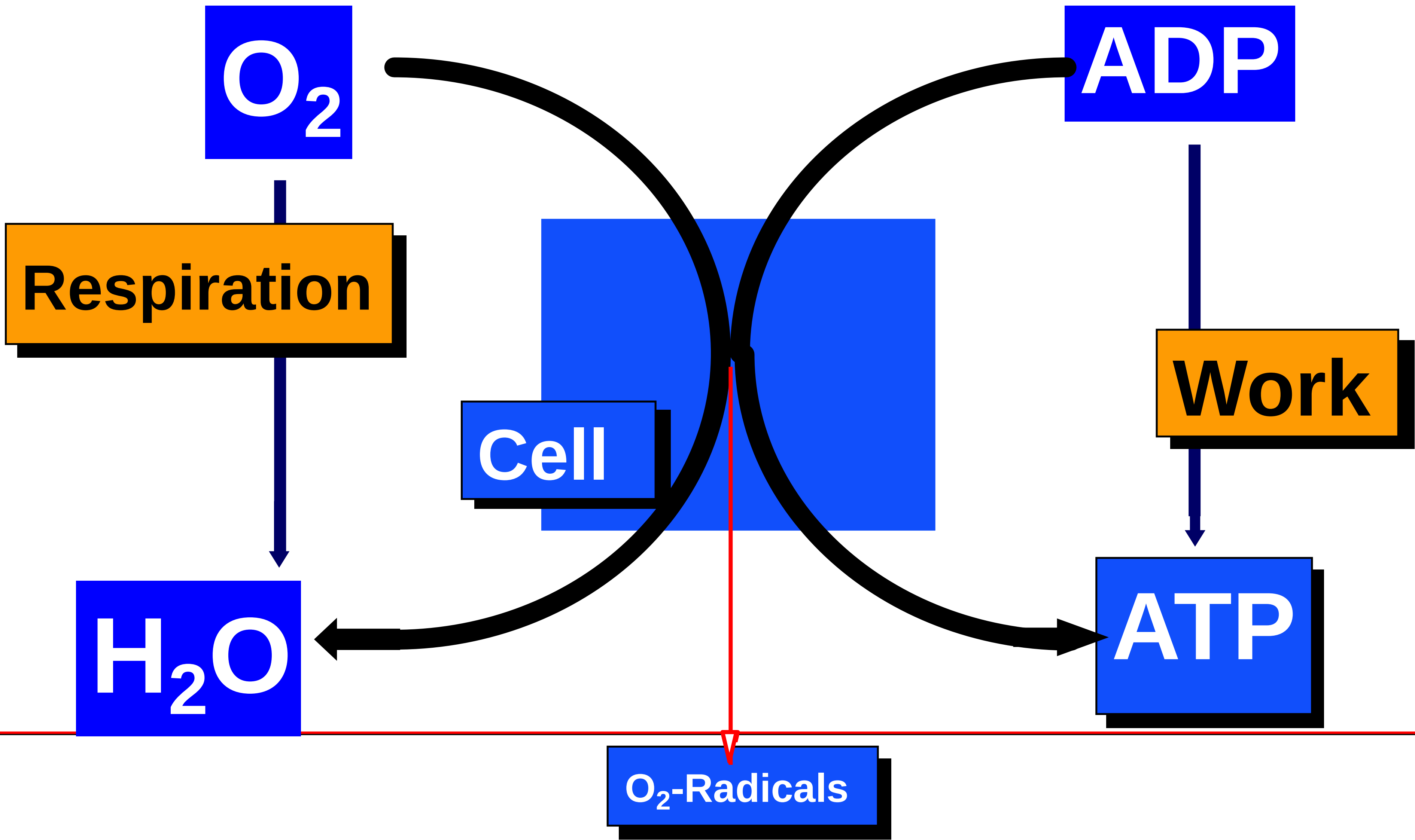
SFB 1149 TRAUMA

ulm university universität ulm

Warum ist O_2 ein Gift? Die Radikale

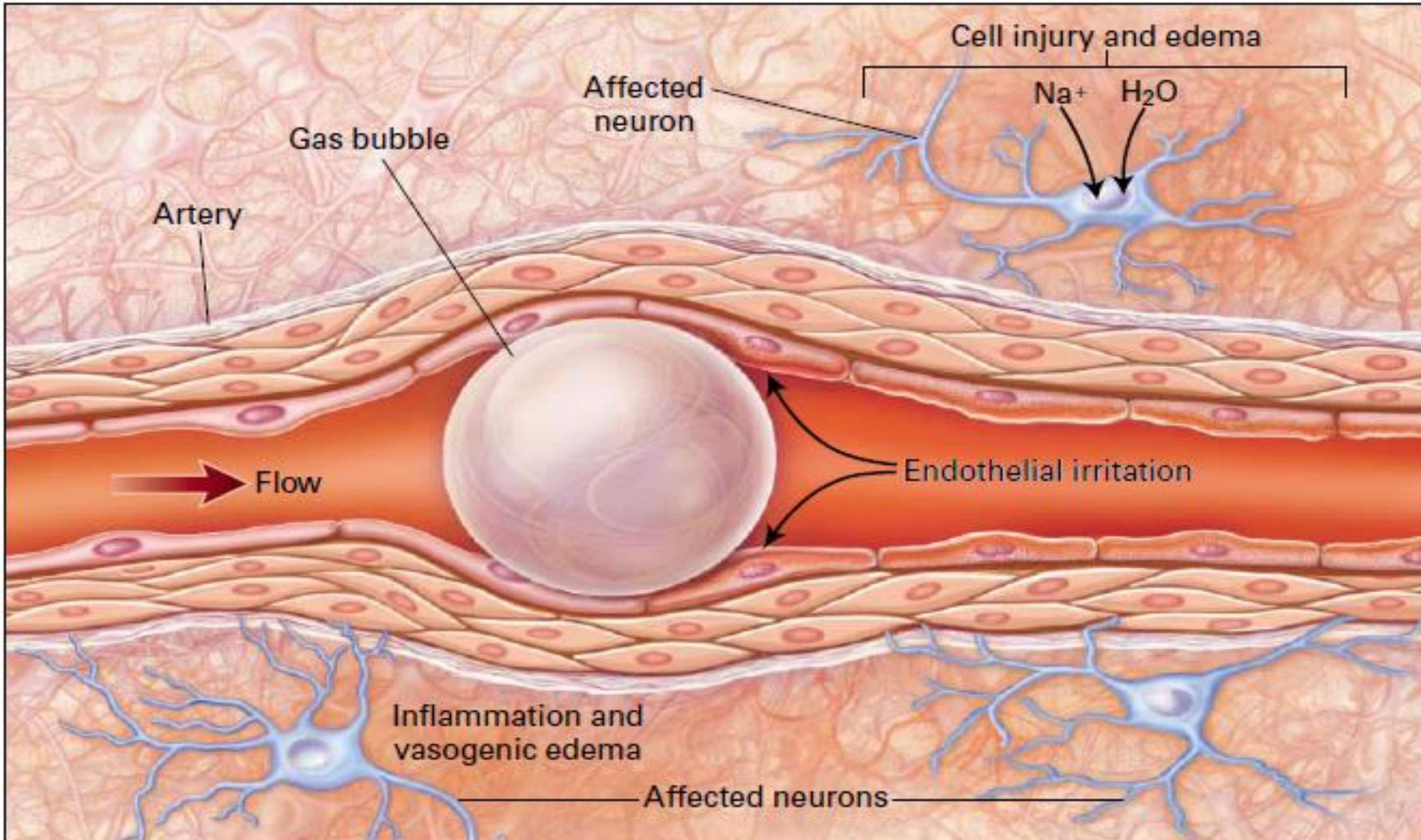


Warum ist O_2 ein Gift? Die Radikale



100 % O_2: Absolute Indikation!

Muth & Shank: **Gas embolism. NEJM 2000;342:476-82**

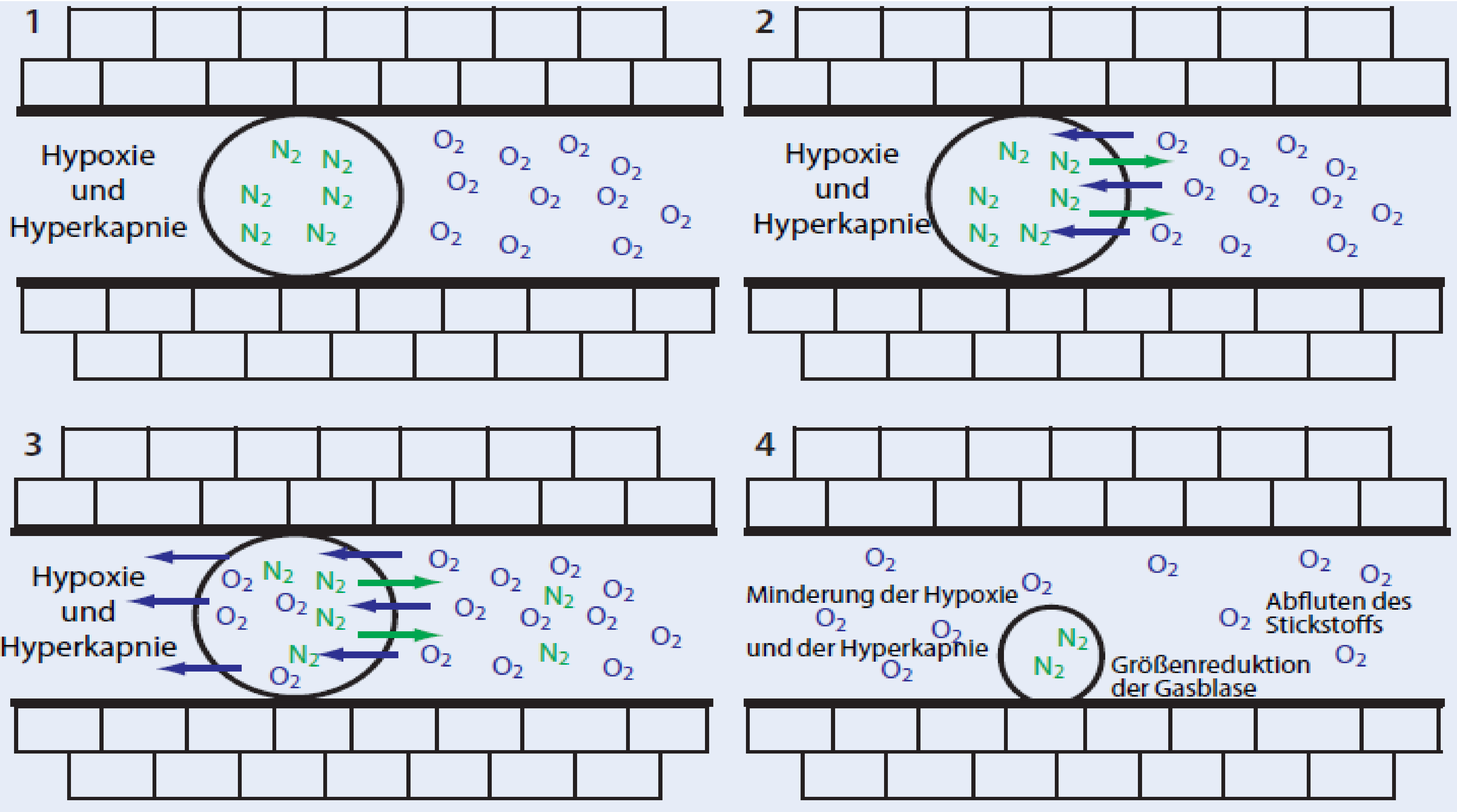


SFB 1149 TRAUMA

ulm university universität ulm

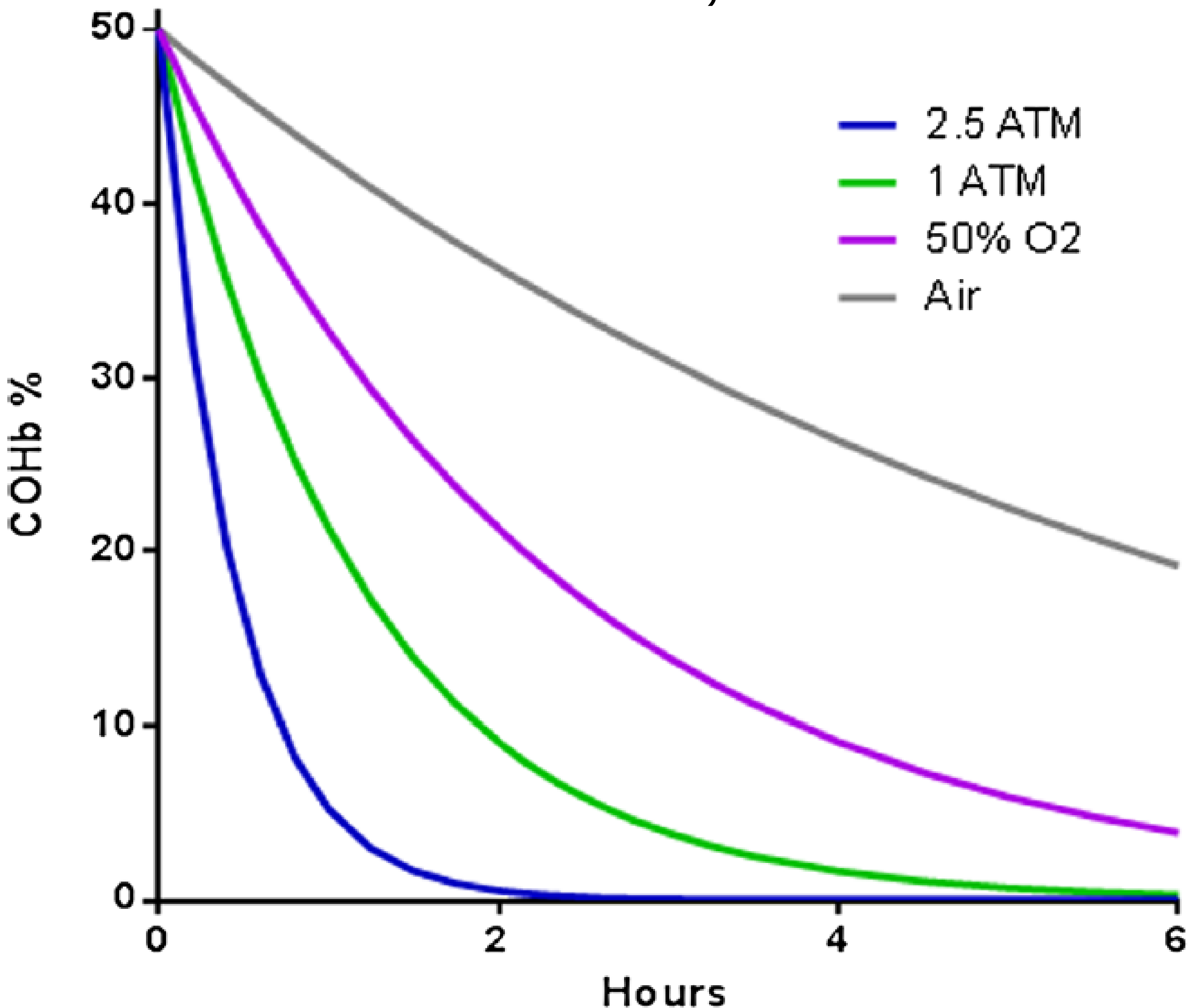
100 % O_2: Absolute Indikation!

Piepho… Muth: Sauerstofftherapie nach Tauchunfall. *Anaesthesist 2007;56:44*



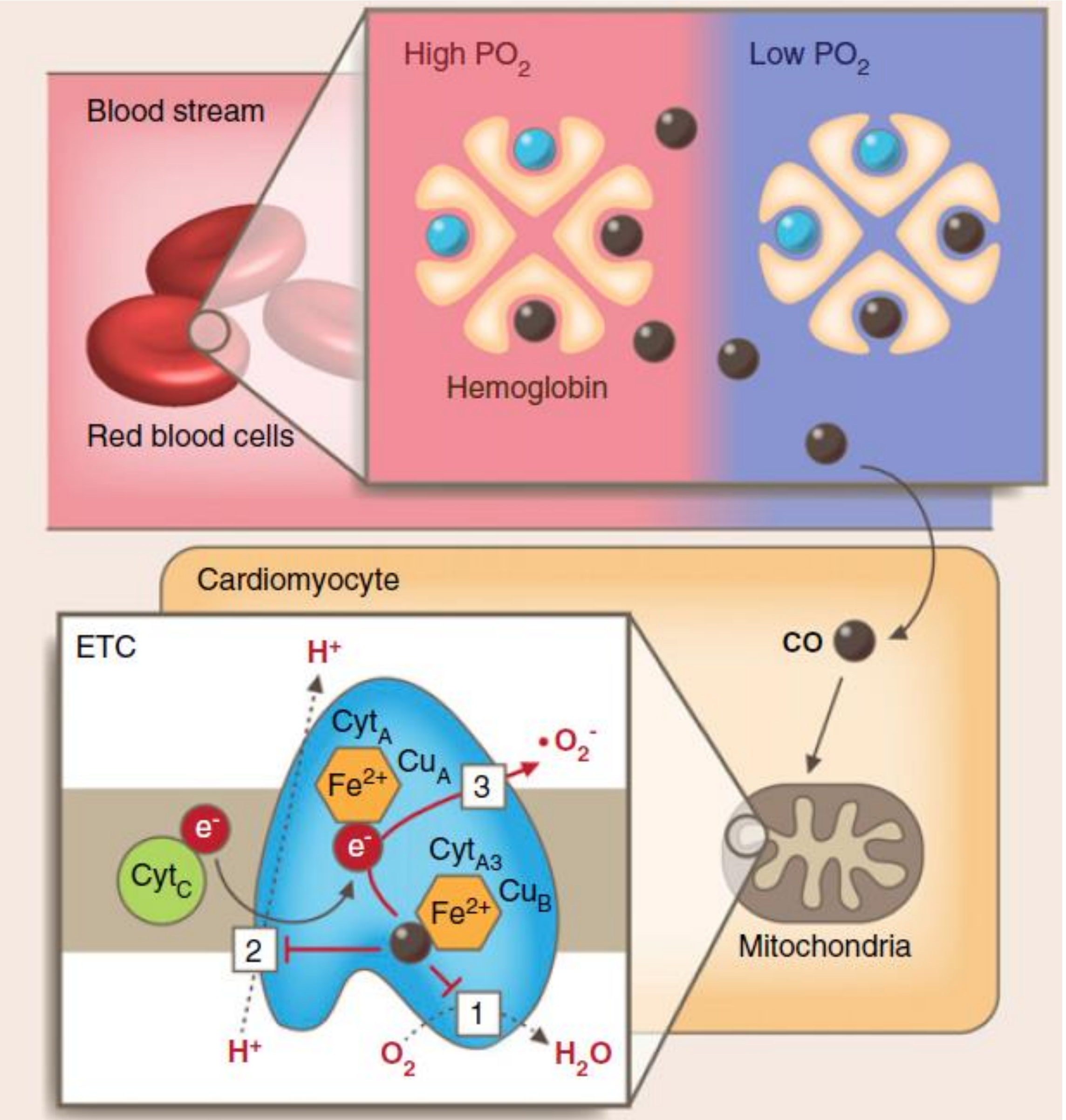
100 % O_2: Absolute Indikation!

Chiew & Buckley: **Carbon monoxide poisoning in the 21st century.**
Crit Care 2014;18:221



100 % O_2: Absolute Indikation!

Rose et al:
Carbon monoxide poisoning: pathogenesis, management, and future directions of therapy.
AJRCCM 2017;195:596-606

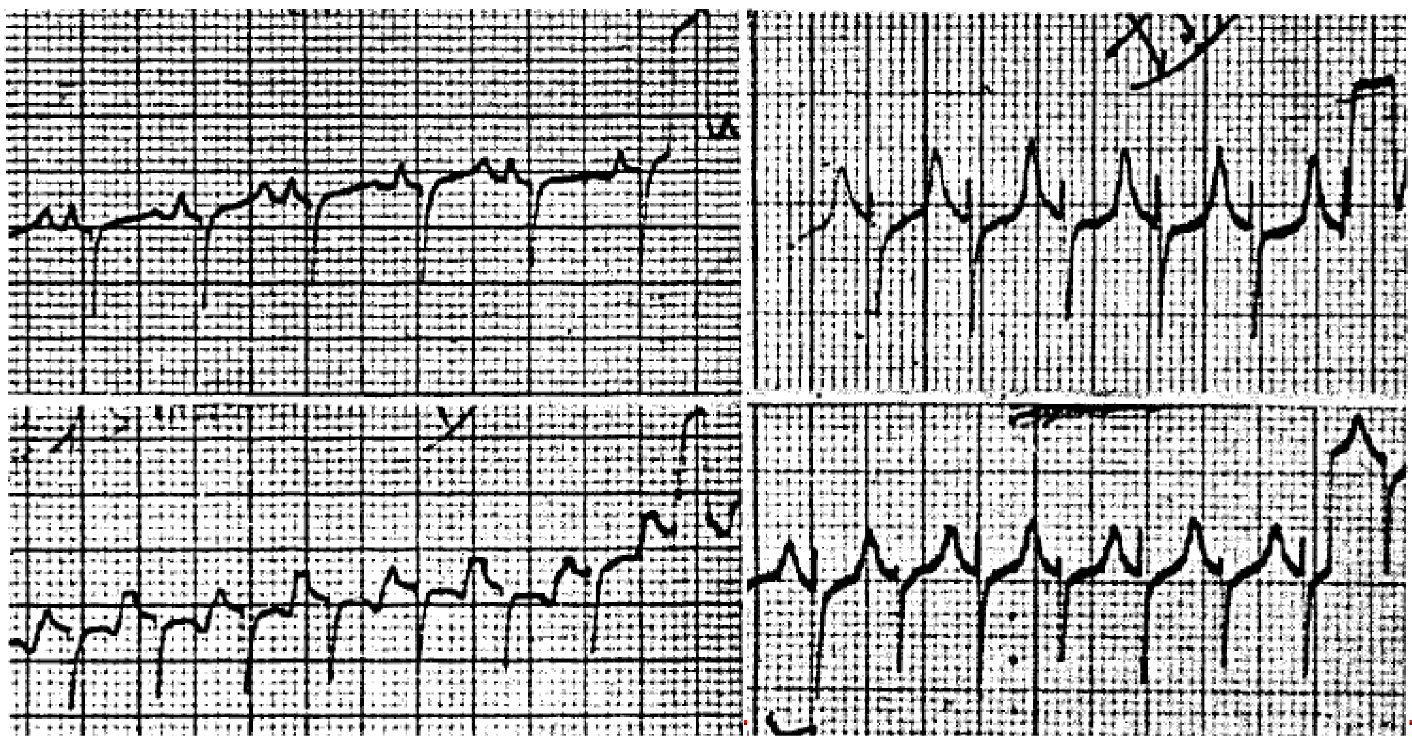


Hyperoxie verlängert das „*window of opportunity*“ bei Hypoxie oder Ischämie

Boerema I, et al*: Life without blood. *Ned Tijdschr Geneeskd 1960;104:949-54

Hb 6.3
1 bar

Hb 4.5
1 bar

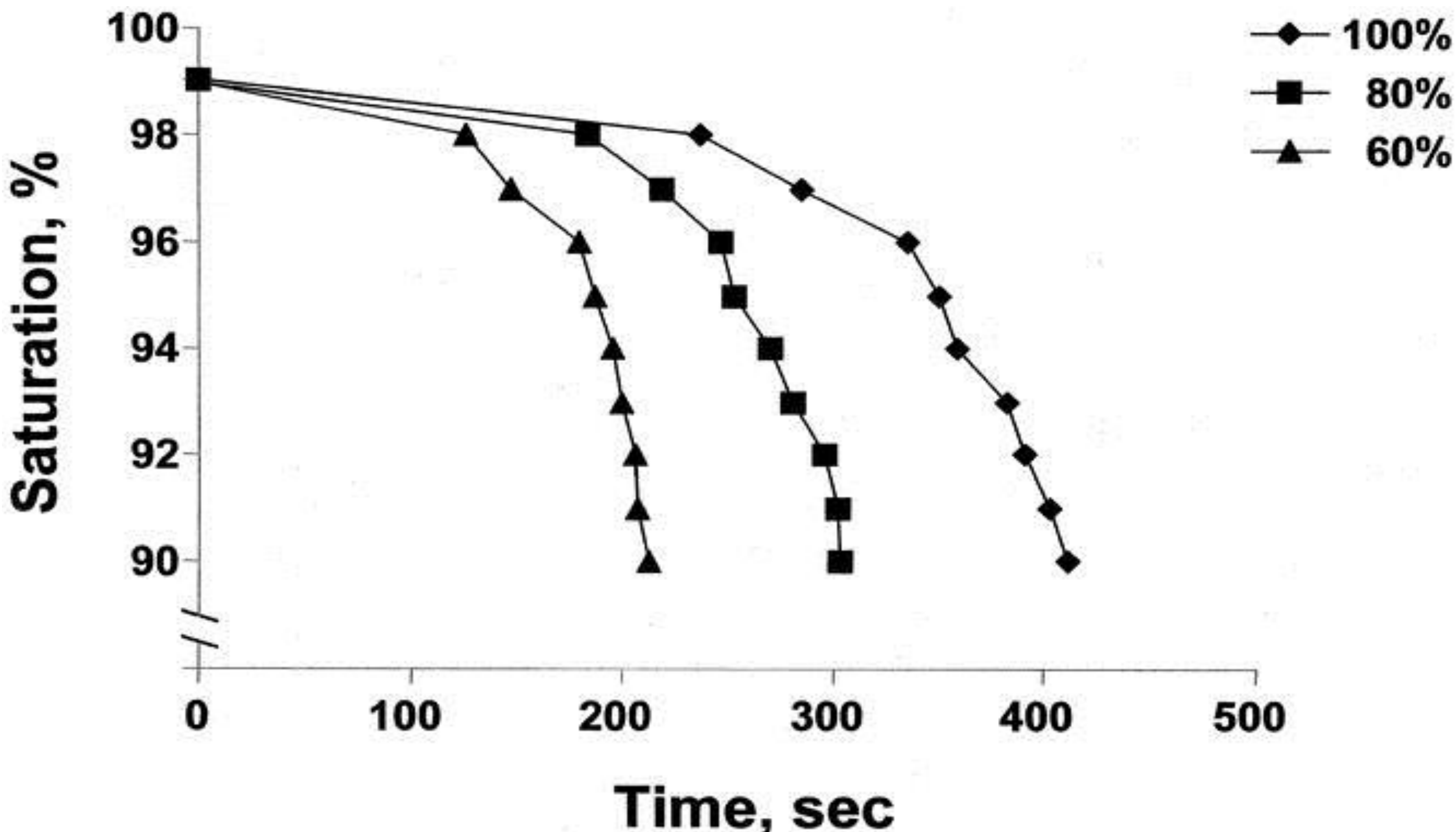


Hb 1.5
1 bar

Hb 0.5
3 bar

Hyperoxie verlängert das „*window of opportunity*“ bei Hypoxie oder Ischämie

Edmark et al: **Optimal oxygen concentration during induction of general anesthesia. *Anesthesiology 2003;98:28***



Das „window of opportunity“

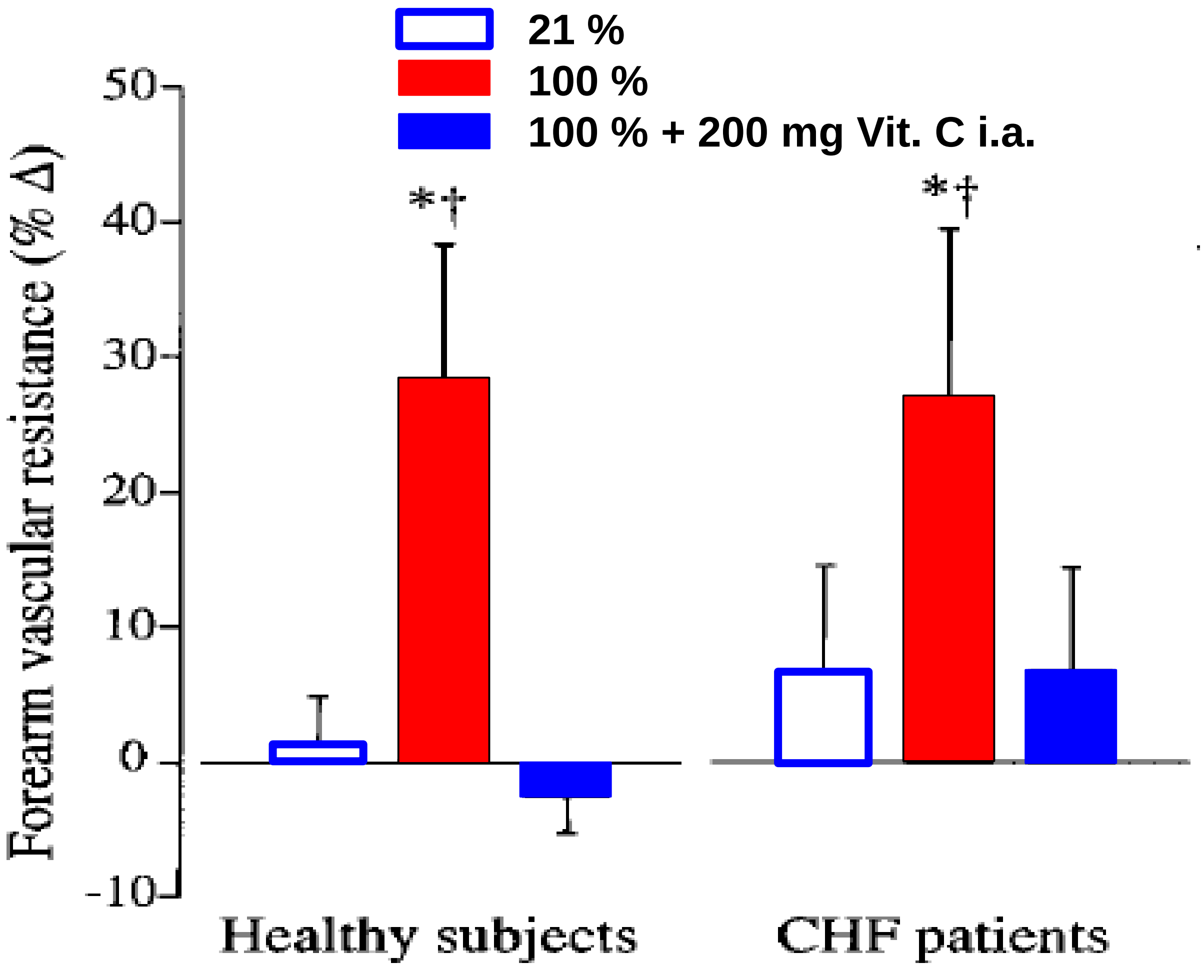
Horvat…Swan, Ganz: **Effect of oxygen breathing on pacing-induced angina pectoris and other manifestations of coronary insufficiency.** ***Circulation 1972;45:837***

Pt	HR (beats/min)		Angina present	
	Air	O_2	Air	O_2
1	125	125	Yes	No
2	130	130	Yes	No
3	160	160	Yes	No
4	105	105	Yes	No
5	158	158	Yes	No
6	135	135	Yes	No
7	145	145	Yes	No
8	120	120	Yes	Yes
9	153	153	Yes	Yes
10	125	125	Yes	No
11	114	114	Yes	No

Hyperoxie und Blutfluss

Hyperoxie und Blutfluss

Mak et al: **Vitamin C prevents hyperoxia-mediated vasoconstriction and impairment of endothelium-dependent vasodilation.** ***AJP 2002;282:H2414***

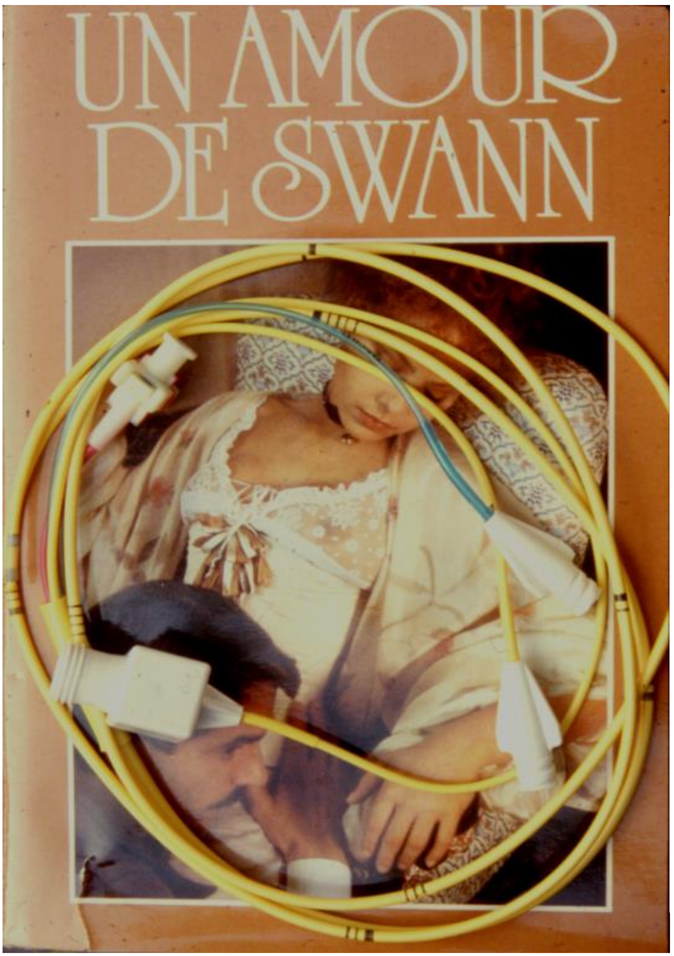


SFB 1149 TRAUMA

ulm university universität ulm

Hyperoxie und Blutfluss

Ganz…Swan: **Coronary hemodynamics and myocardial oxygen metabolism during oxygen breathing in patients with and without coronary artery disease. *Circulation 1972;45:763***

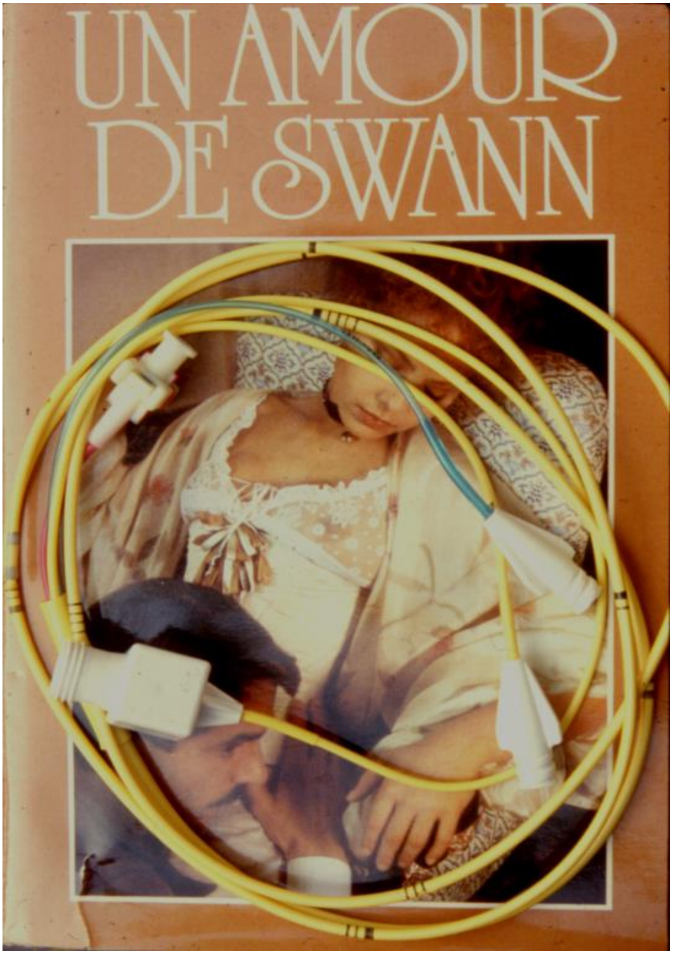


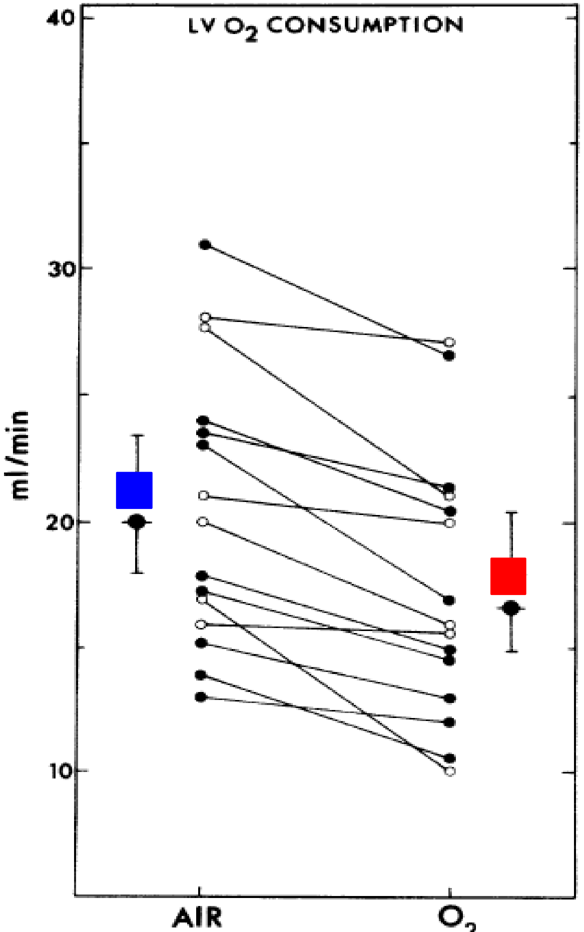
	HR (beats/min)	MABP (mm Hg)	CI (liters/min/m²)	CSBF (ml/min)
		n=6	*Subjects with normal coronary arteries*	
Air	79 ± 10	106 ± 6	3.6 ± 0.3	158 ± 11
O_2	72 ± 7	107 ± 5	3.2 ± 0.4	131 ± 13
P	0.01–0.05	NS	0.01–0.05	<0.01
		n=9	*Subjects with coronary artery disease*	
Air	75 ± 5	93 ± 9	2.9 ± 0.1	151 ± 14
O_2	69 ± 5	99 ± 4	2.6 ± 0.1	138 ± 14
P	<0.01	<0.01	<0.01	<0.01

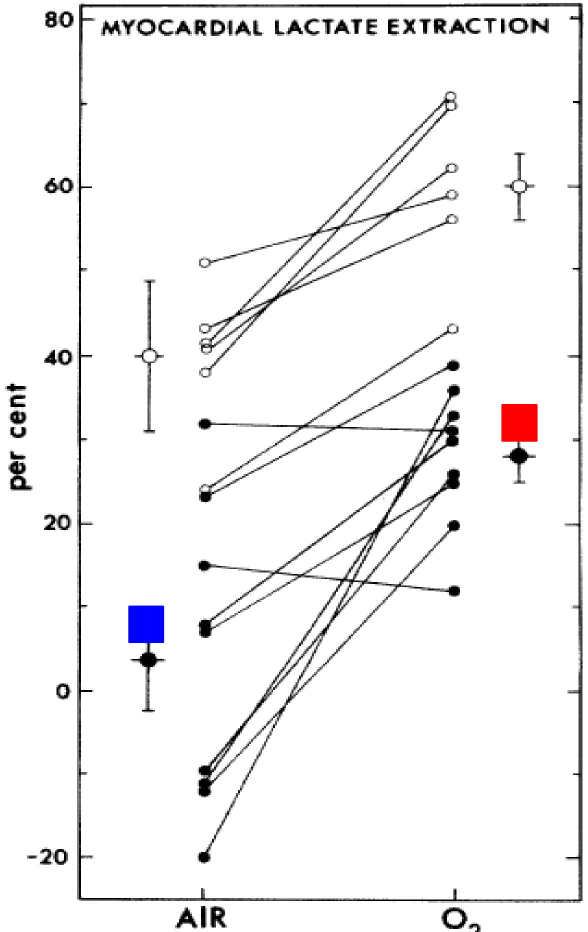
Hyperoxie und Stoffwechsel

Hyperoxie und Stoffwechsel

Ganz…Swan: **Coronary hemodynamics and myocardial oxygen metabolism during oxygen breathing in patients with and without coronary artery disease.** ***Circulation 1972;45:763***







Hyperoxie und ACS

SFB 1149 TRAUMA

ulm university universität ulm

Hyperoxie und ACS

Stub et al:

Air versus oxygen in ST-segment-elevation myocardial infarction.

Circulation 2015;131:2143-50

STEMI assessment paramedic

Pre-hospital

8 L/min O_2 face mask

∅ O_2 unless $S_{tc}O_2$ < 94 %

STEMI confirmation physician

In-hospital

8 L/min O_2 face mask PCI

∅ O_2 unless $S_{tc}O_2$ < 94 % PCI

SFB 1149 TRAUMA

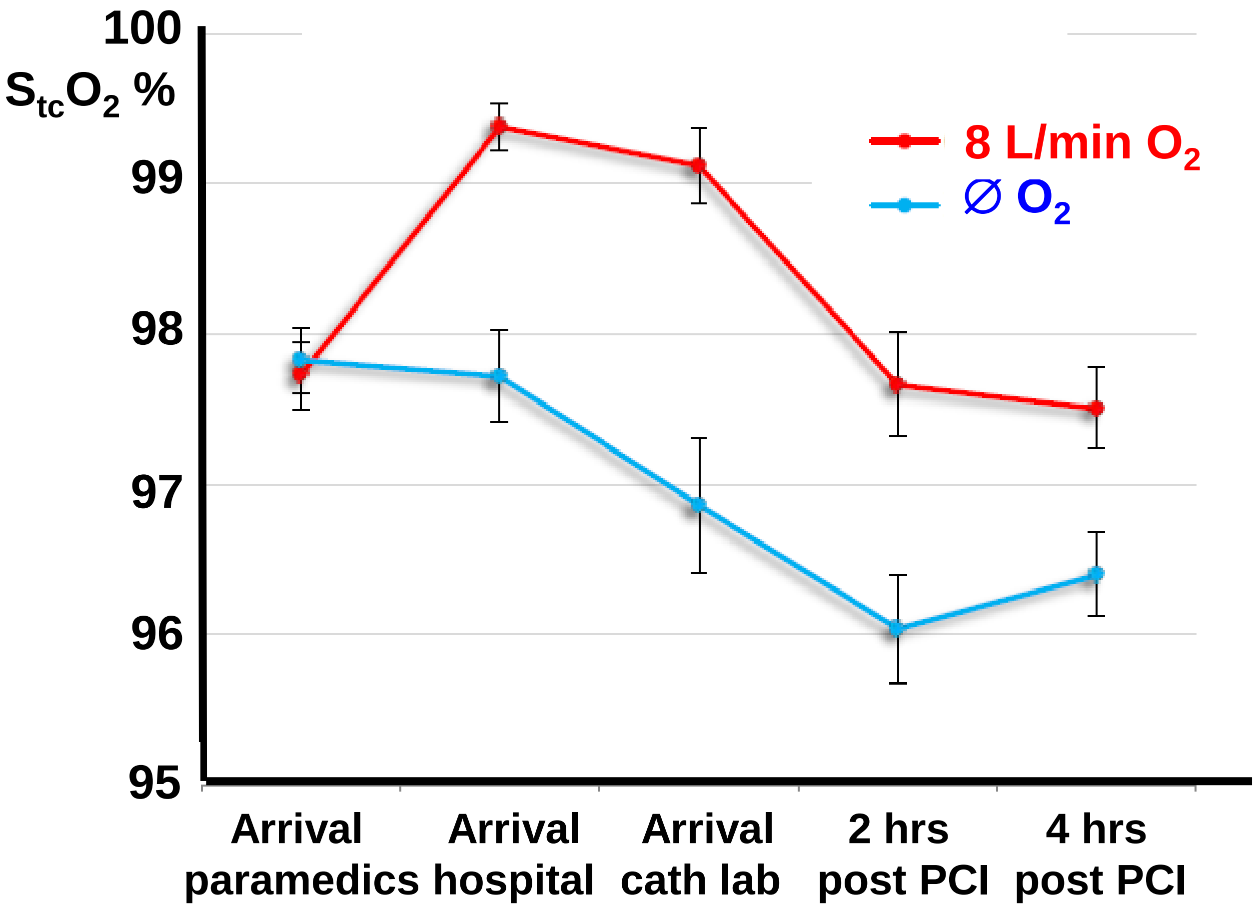
ulm university universität ulm

Hyperoxie und ACS

Stub et al:

Air versus oxygen in ST-segment-elevation myocardial infarction.

Circulation 2015;131:2143-50



Hyperoxie und ACS

Stub et al:

Air versus oxygen in ST-segment-elevation myocardial infarction.

Circulation 2015;131:2143-50

	Hyperoxia	Normoxia	P-value
Mean peak CPK [U/L]	1948 (1721-2205)	1543 (1348-1776)	0.01
Peak troponin [micg/L]	57 (48-69)	48 (40-58)	0.18
Arrhythmia [%]	40	31	0.05
Recurrent MI (at hospital discharge) [%]	5.5	0.9	< 0.01
Infarct size @ 6 mo [g]	20 (10-30)	13 (5-24)	0.04

Hyperoxie und ACS

Stub et al:

Air versus oxygen in ST-segment-elevation myocardial infarction.

Circulation 2015;131:2143-50

	Hyperoxia	Normoxia	P-value
Mean peak CPK [U/L]	1948 (1721-2205)	1543 (1348-1776)	0.01
Peak troponin [micg/L]	57 (48-69)	48 (40-58)	0.18
Arrhythmia [%]	40	31	0.05
Recurrent MI (at hospital discharge) [%]	5.5	0.9	< 0.01
Infarct size @ 6 mo [g]	20 (10-30)	13 (5-24)	0.04
Mortality [%]	1.8	4.5	0.11

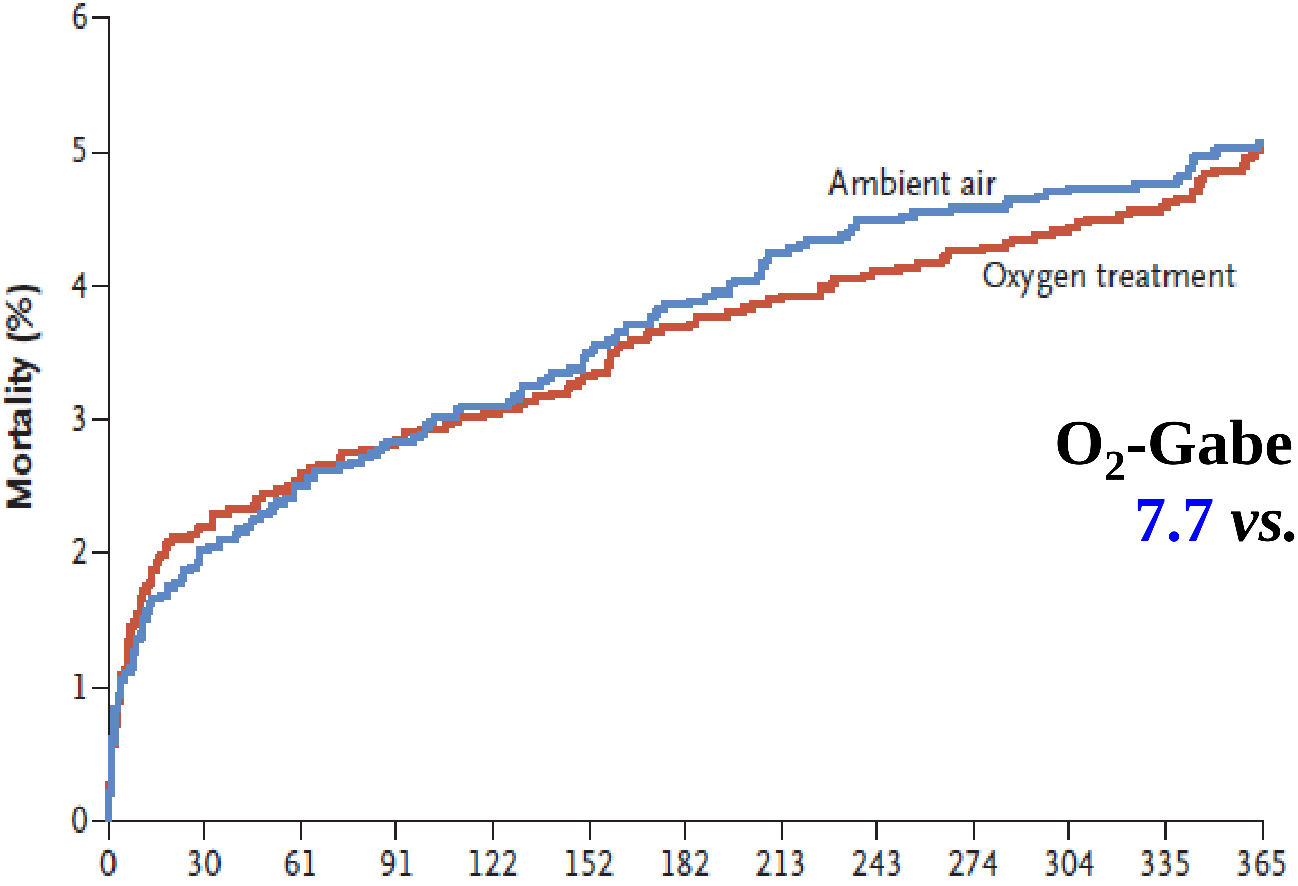
Hyperoxie und ACS

Hofmann et al:

Oxygen therapy in suspected acute myocardial infarction.

NEJM 2017;377:1240-9

6226 Patienten, Symptome < 6 h, $SO_2 \geq$ 90%, Air *vs.* 6 L/min O_2 über 6-12 h



O_2-Gabe wegen Hypoxämie:

7.7 *vs.* 1.9 % (p<0.001)

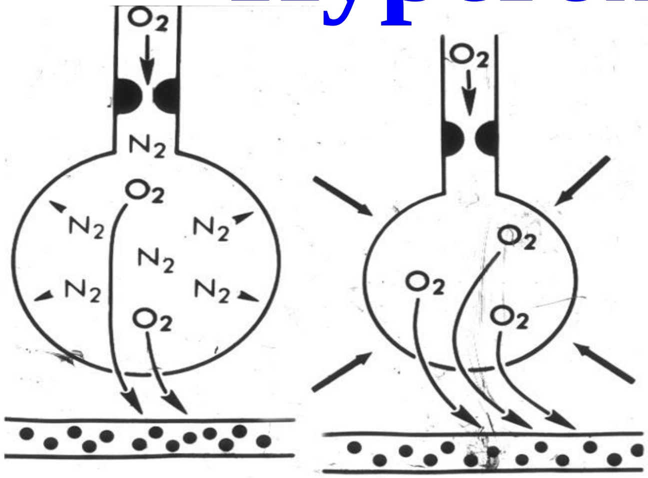
Hyperoxie und Lunge

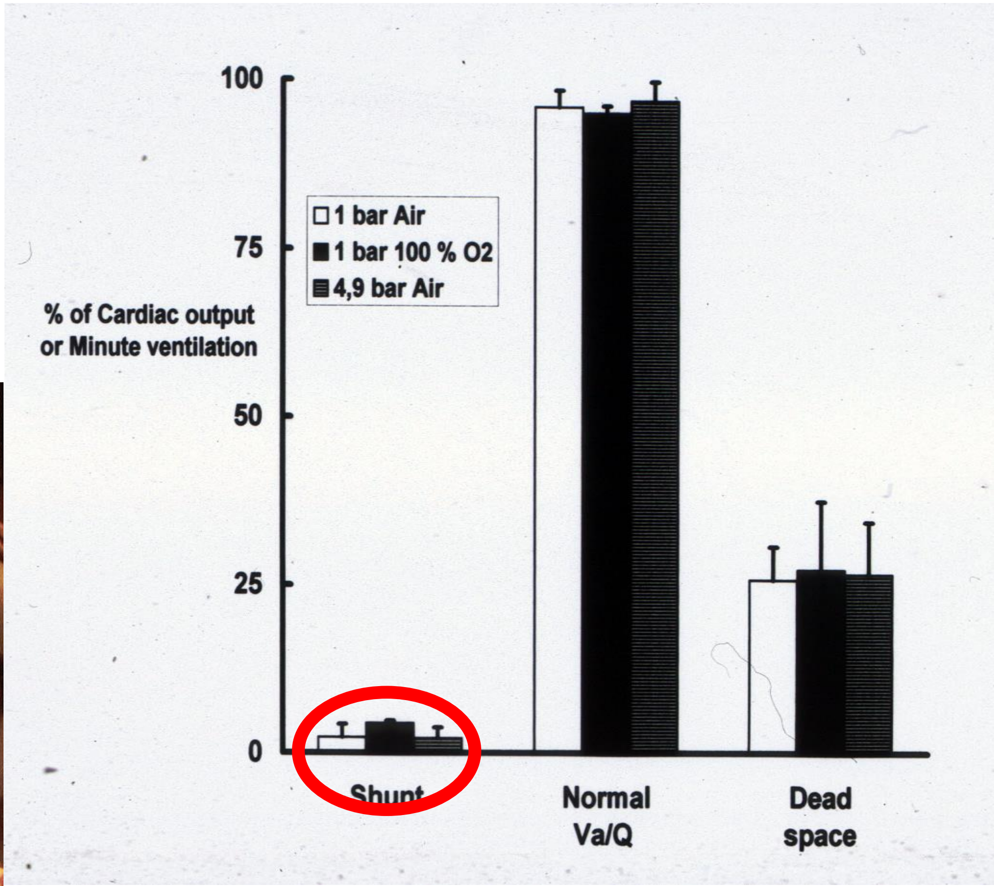
Oxygène – Sauerstoff

Meerschweinchen längere Zeit Sauerstoff exponiert ▸ Tod durch Lungenödem

Antoine Lavoisier 1743-1794

Hyperoxie und Lunge

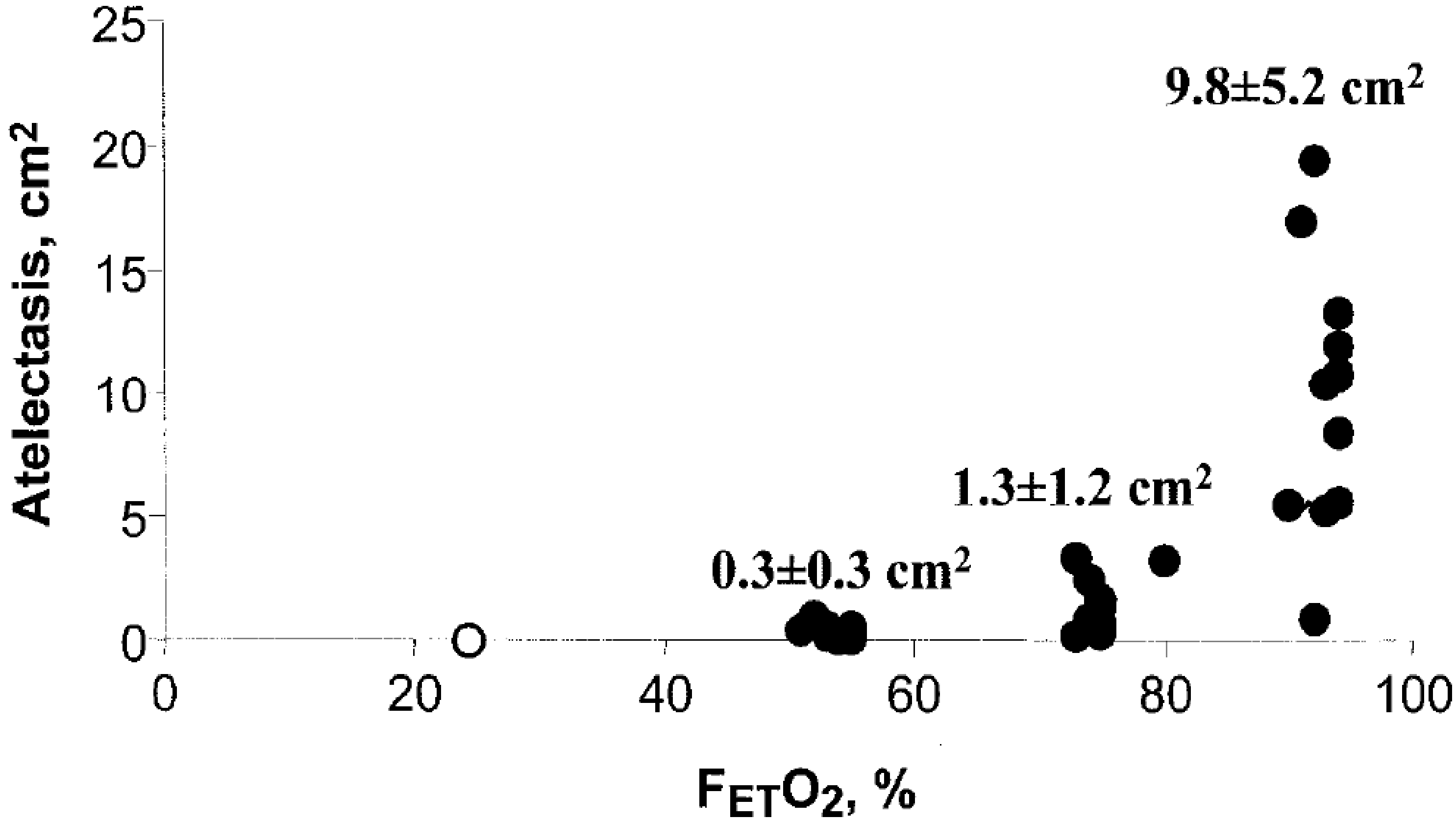




Calzia et al:
Hyperoxia may be beneficial.
CCM 2010;38:S559-68

Hyperoxie verlängert das *„window of opportunity“* bei Hypoxie oder Ischämie

Edmark et al: **Optimal oxygen concentration during induction of general anesthesia.** ***Anesthesiology 2003;98:28***



Sauerstoff Druck in Atmosph. (absol.)	Wirkungsdauer	Tierspezies	Symptome
0,6	mehrere Monate	Hund, Affe	geringe Anämie
1,2	2—3 Tage	Hund, Katze	†
1,2	täglich 6—8 Stunden während mehrerer Wochen	Hund, Affe	Wohlbefinden
3	20—48 Minuten	Mensch	Wohlbefinden
3	50 Minuten	Mensch	Krämpfe
5	2—6 Stunden	Ratte, Hund	† unter Lungenerscheinungen
8	10—15 Minuten	Ratte	Krämpfe
8	45—75 Minuten	Ratte	†

Bornstein A et al (1912) Dtsch Med Wochenschr 32:1495-1497

Hyperoxie und Lunge

- 100% O_2 over 25 h: modest reduction of vital capacity, symptoms of tracheitis at 6 h

Comroe et al. JAMA 1945

- 100% O_2 over 6-12 h, A-aDO_2, Compliance, extravascular lung water unchanged

De Water et al. N Eng J Med 1970

- 100% O_2 over 6 h, symptoms of tracheitis

Sackner et al. Ann Intern Med 1975

- 95% O_2 over 17 h, increased albumin levels in BAL fluid

Davis et al. N Eng J Med 1983

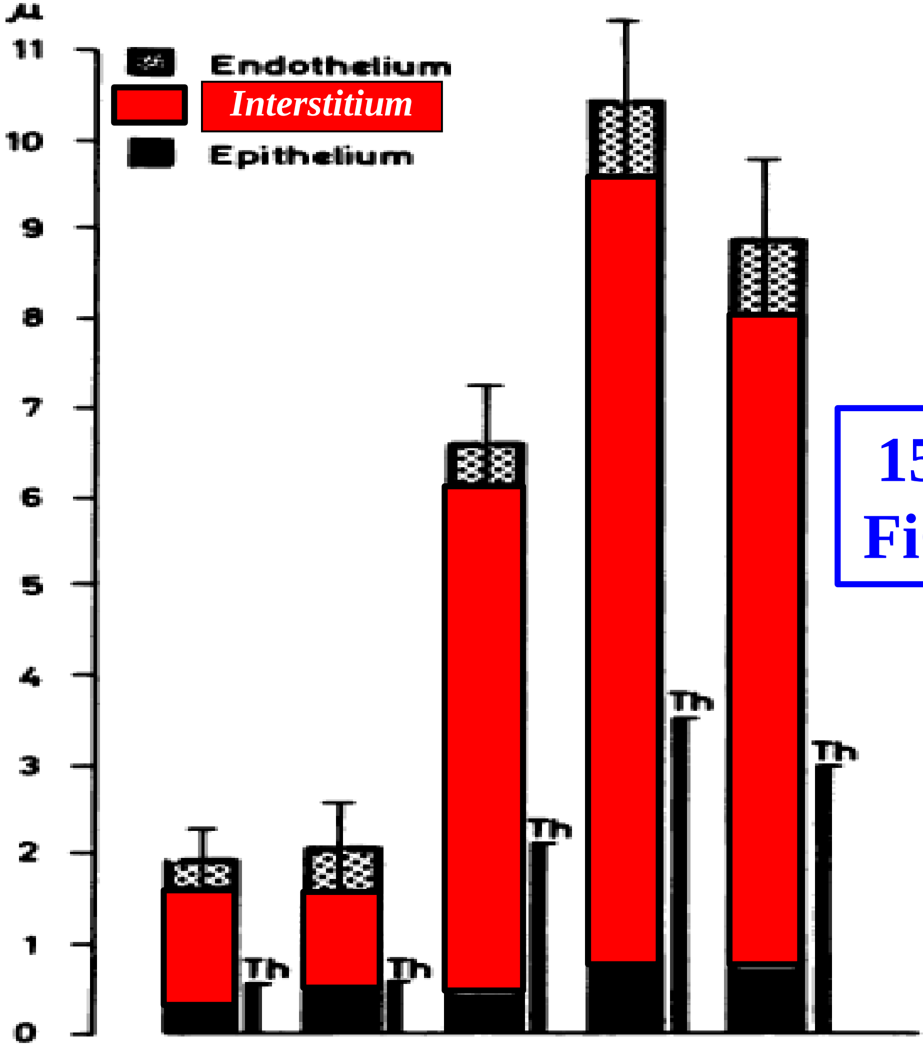
- 100 vs. 30% O_2 over 8 h, normal bronchoscopy

Kotani et al. Anesthesiology 2000

Hyperoxie und Lunge

Kapanci et al: **Oxygen pneumonitis in man.** ***Chest 1972;62:162***

Gould et al: **Oxygen pneumonitis in man.** ***Lab Invest 1972;26:499***

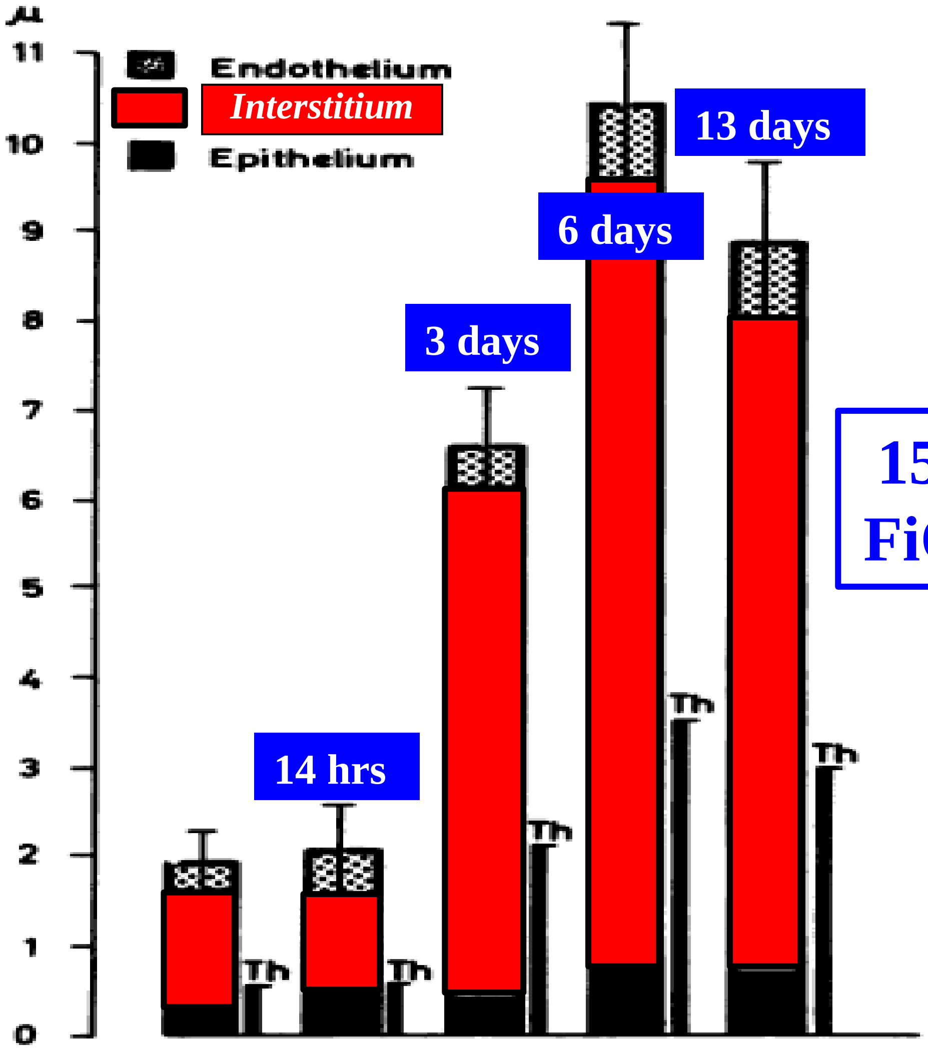


15 mechanically ventilated patients
FiO_2 60 – 100 %, 14 hours – 30 days

Hyperoxie und Lunge

Kapanci et al: **Oxygen pneumonitis in man.** ***Chest 1972;62:162***

Gould et al: **Oxygen pneumonitis in man.** ***Lab Invest 1972;26:499***



15 mechanically ventilated patients
FiO_2 60 – 100 %, 14 hours – 30 days

Hyperoxie und Lunge

Elmer et al:

Exposure to high concentrations of inspired oxygen does not worsen lung injury after cardicc arrest.

Crit Care 2015;19:105

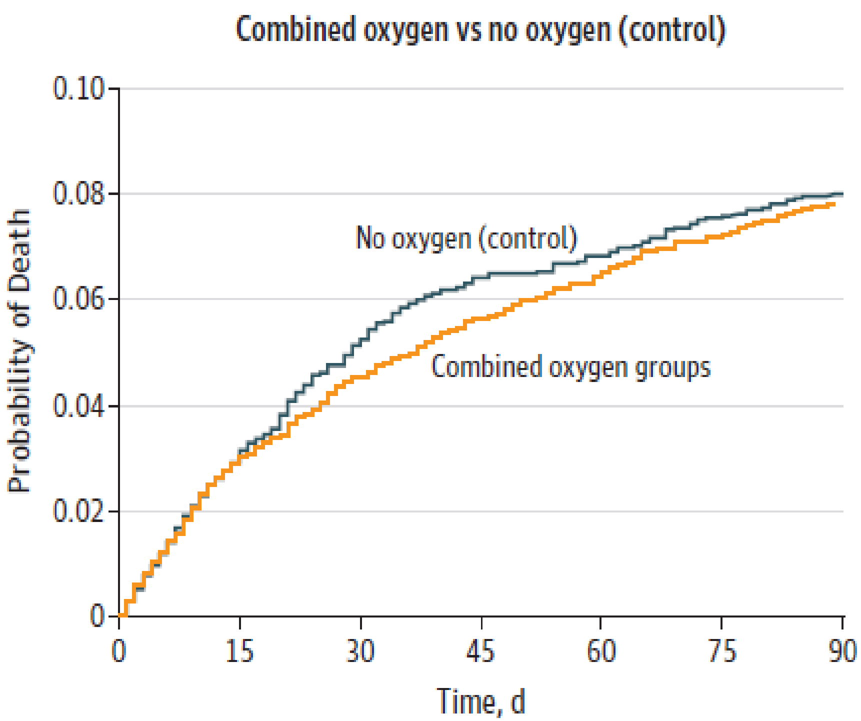
“…Higher exposure to inhaled oxygen in the first *24 hours after cardiac arrest* was *not associated with deterioration in gas exchange or pulmonary compliance*… but ….*decreased survival and worse neurological outcome*.“

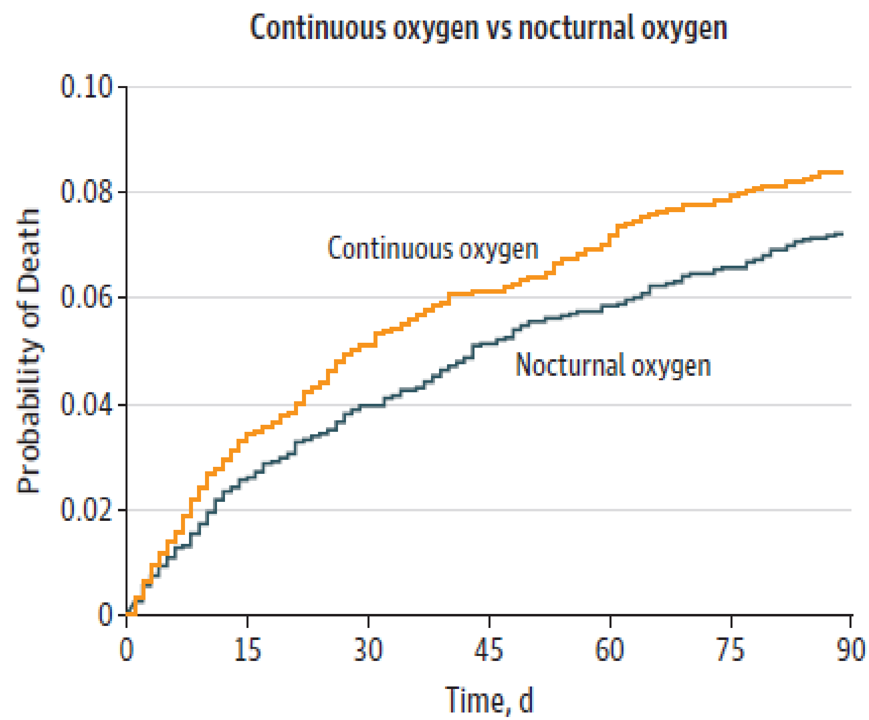
Hyperoxie und Stroke

Roffe et al: **Effect of routine low-dose oxygen supplementation on death and disability in adults with acute stroke. *JAMA 2017;318:1125***

8003 Patienten; 2-3 L/min O_2 per Nasensonde 72 h nach Apoplex, nachts/kontinuierlich/$S_{tc}O_2$ < 93%; Neurologie 3, 6, 12 Monate

$\Rightarrow$ ∅ Effekt!





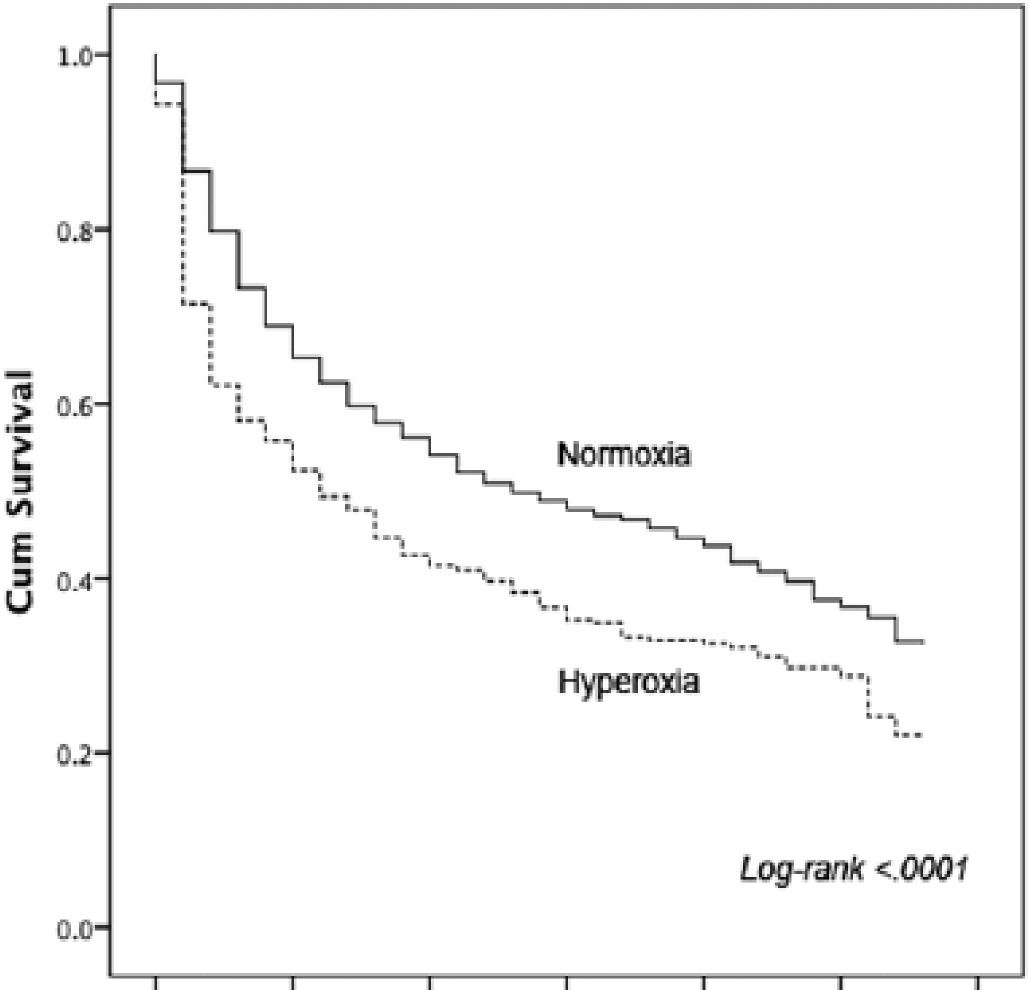
ULM SFB 1149 TRAUMA

ulm university universität ulm

Hyperoxie und Stroke

Rincon et al: **Hyperoxemia and long-term outcome after traumatic brain injury.** ***Crit Care Med 2014;42:387***

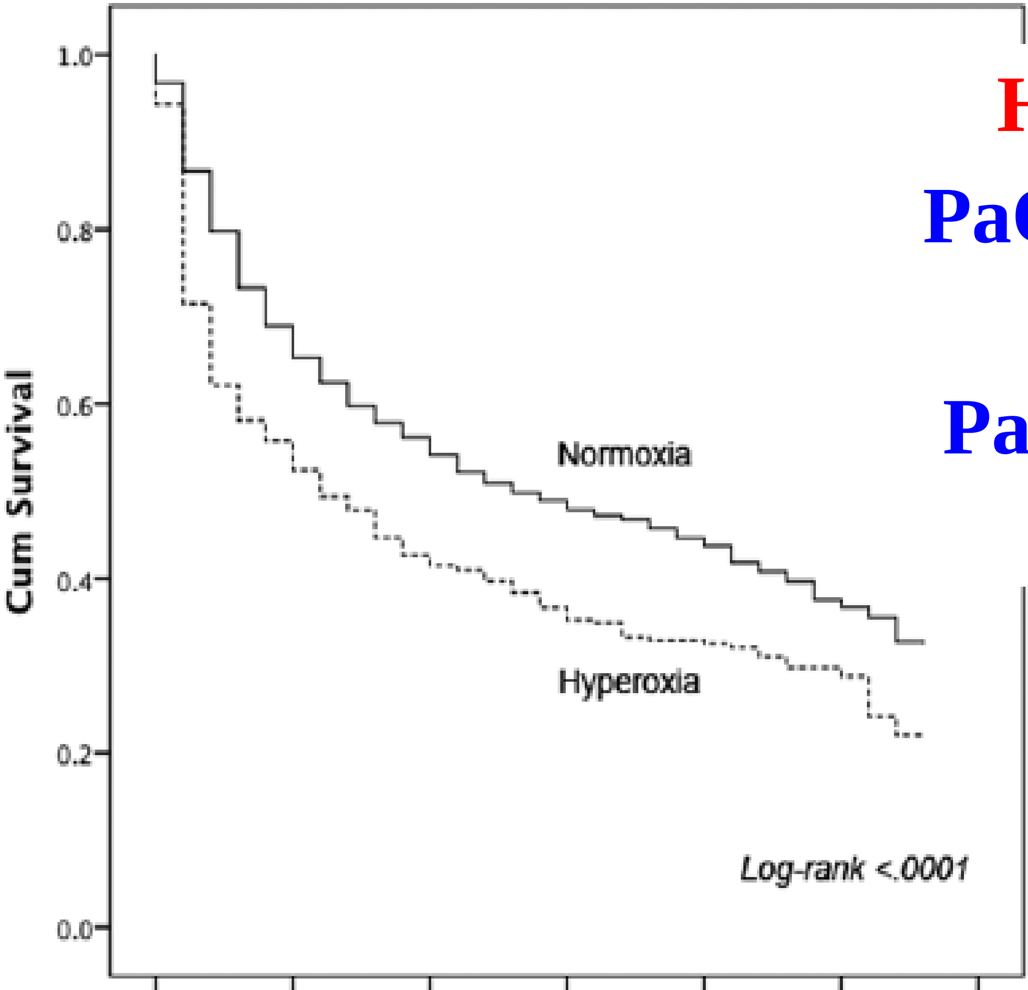
n=2894 (AIS 19%; SAH 32%; ICH 49%)



Hyperoxie und Stroke

Rincon et al: Hyperoxemia and long-term outcome after traumatic brain injury. _Crit Care Med 2014;42:387_

n=2894 (AIS 19%; SAH 32%; ICH 49%)



Hyperoxia (n = 1084) ≅

PaO_2 > 300 mmHg → 60 %

Hypoxia (n = 450) ≅

PaO_2 < 60 mmHg → 53 %

SAH, ICB, AIS ∅

Hyperoxie und SAB

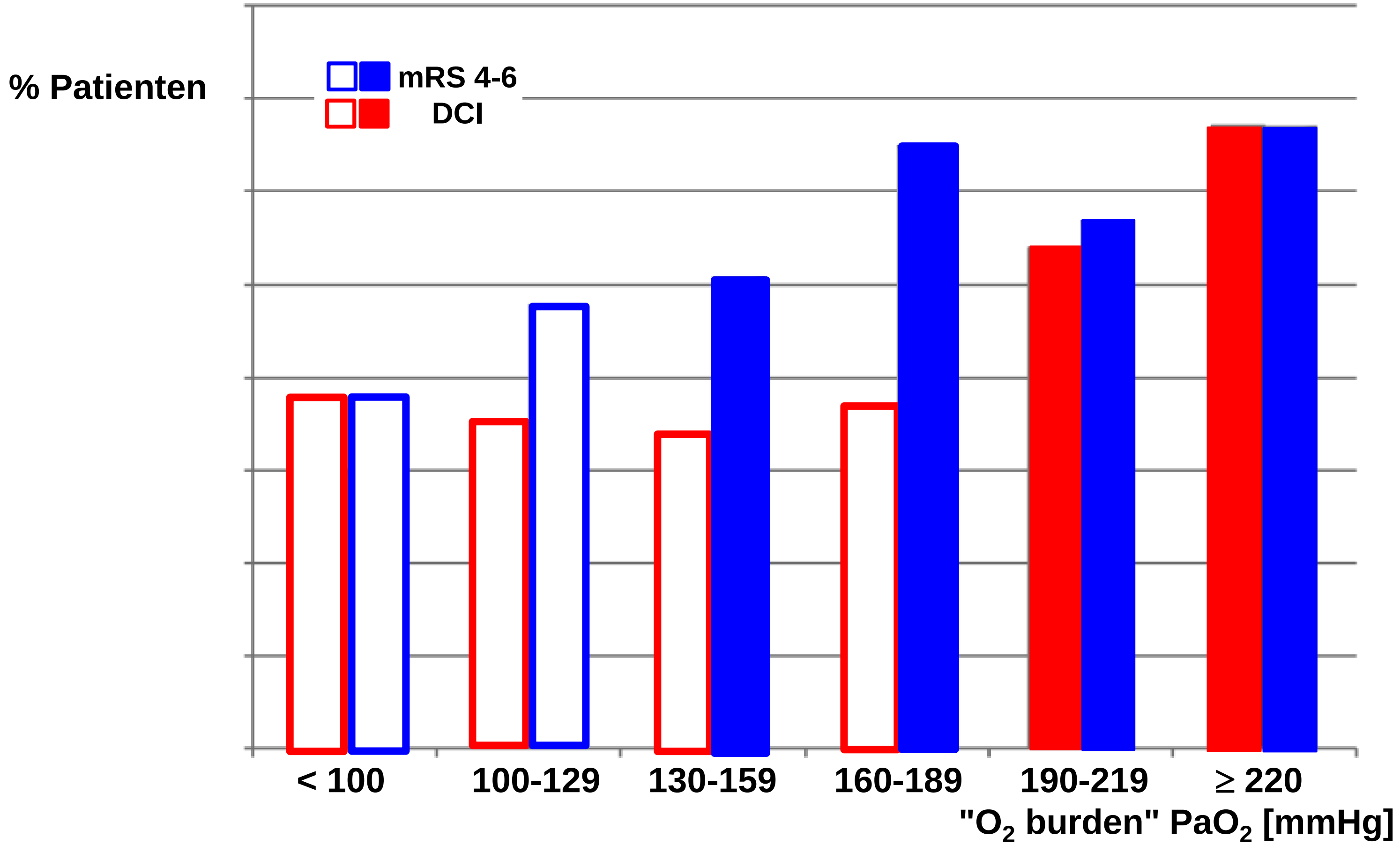
SFB 1149 TRAUMA

ulm university universität ulm

Hyperoxie und SAB

Jeon et al: **Hyperoxemia may be related to *delayed cerebral ischemia* and poor outcome after subarachnoidal haemorrhage.**
J Neurol Neurosurg Psychiatry 2014;85:1301

Single-Center, prospektiv; n=252; "O_2 burden" = AUC PaO_2 bis 2 Wo

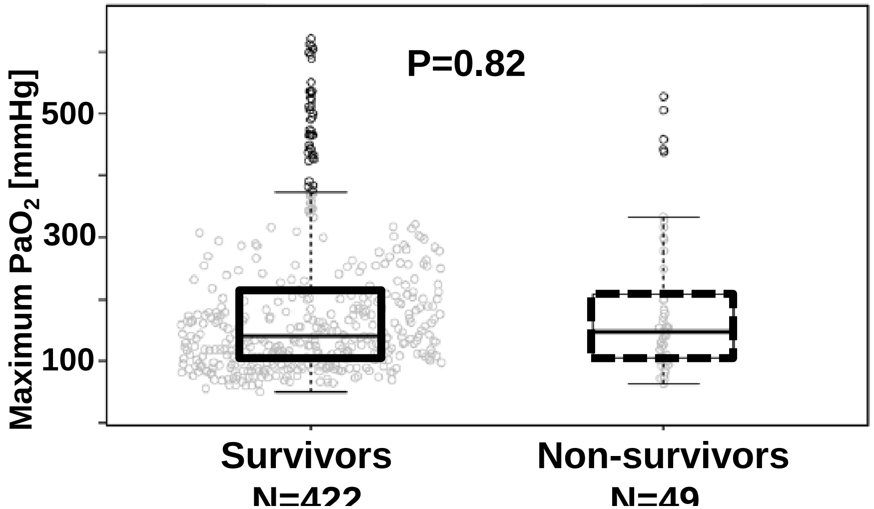


Hyperoxie und SHT

Hyperoxie und SHT

Russel et al: **Early exposure to hyperoxia and mortality in critically ill patients with severe traumatic injuries.** ***BMC Pulm Med 2017;17:29***

Retrospektiv; n=471 (TBI: n=266); ISS 29 (18-36); GCS 11 (8-15); beatmet; PaO_2 24 h

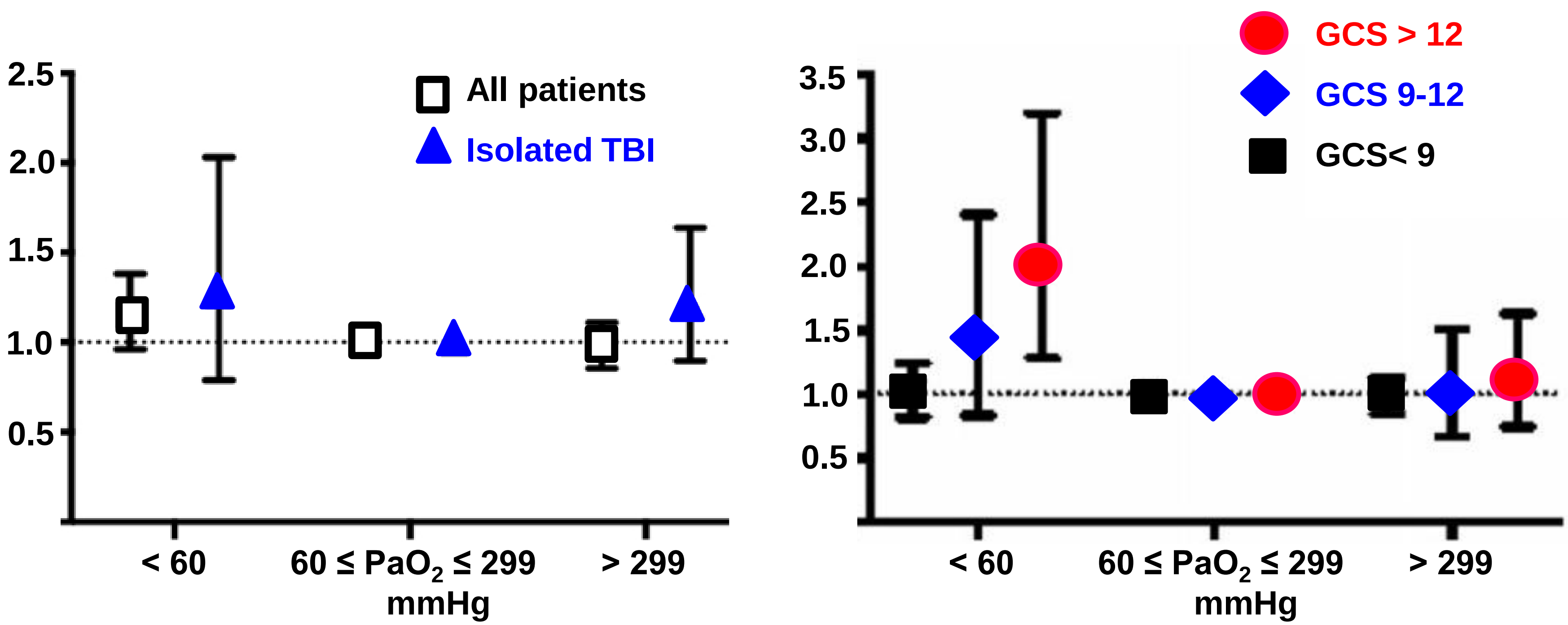


"… In the subgroup with head trauma (n=266)…maximum PaO_2 was not associated with increased mortality"

Hyperoxie und SHT

Ó Briain et al: **Early Hyperoxia in patients with traumatic brain injury admitted to intensive careintensive care in Australia and New Zealand: a retrospective multicenter cohort study.** ***Neurocrit Care 2018;29:443***

N = 24.148 (16 y); GCS 8 [3-13]; beatmet; PaO_2 24 h



SFB 1149 TRAUMA

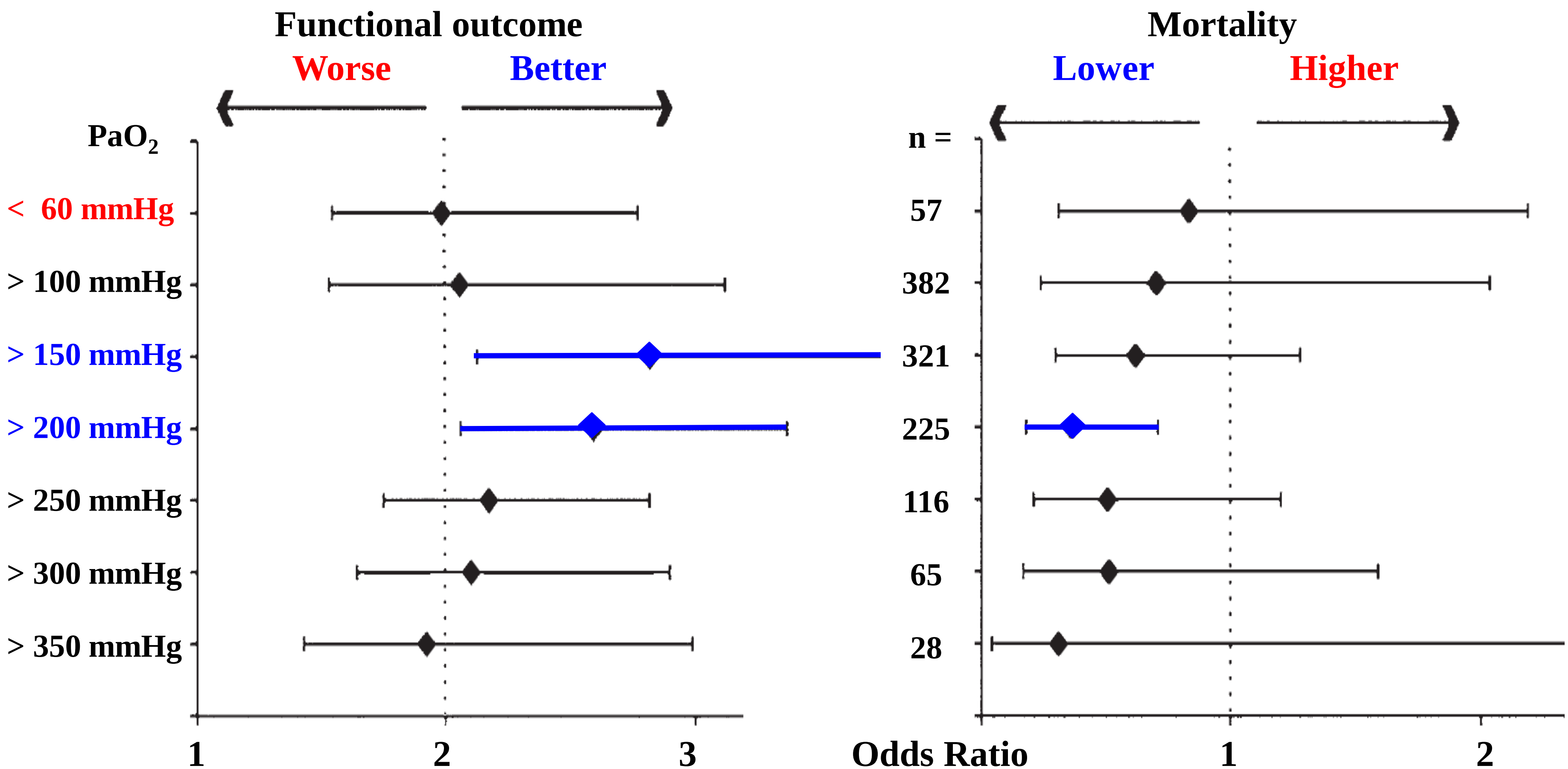
ulm university universität ulm

Hyperoxie und SHT

***Alali et al:* Matching early arterial oxygenation to long-term outcome in severe traumatic brain injury: target values.**

J Neurosurg 2019doi: 10.3171/2018.10.JNS18964

Post hoc COBRIT trial; n=417; GCS 3; GOSE 6 months; PaO_2 24 h



Perioperative Hyperoxie

SFB 1149 TRAUMA

ulm university universität ulm

Berrios-Torres et al:

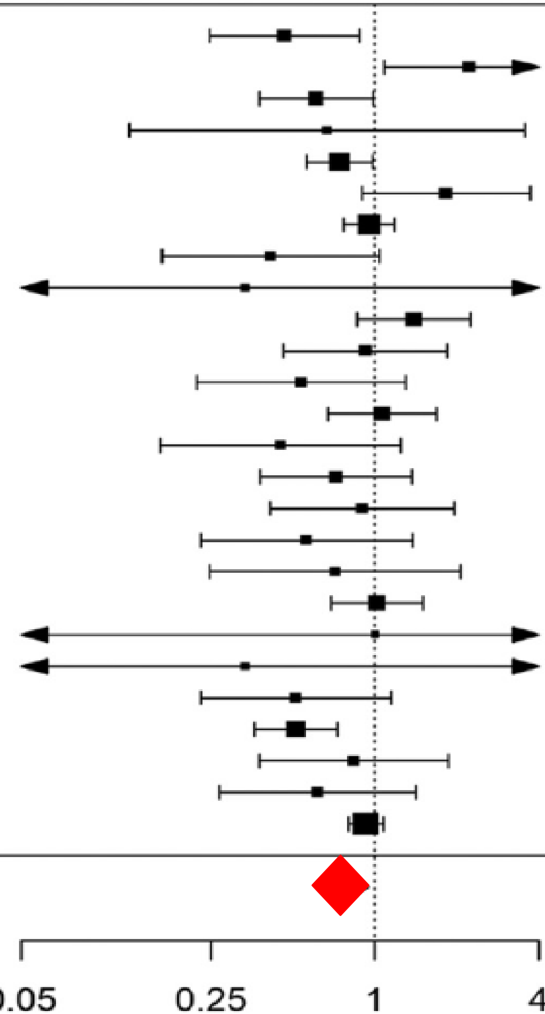
Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017

JAMA Surgery 2017;152:784

"….Increased FiO_2 should be administered during surgery and after extubation in the immediate postoperative period for patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation…"

Cohen et al: Effect of intraoperative Hyperoxia on the incidence of surgical site infections: a meta-analysis. *BJA 2018;120:1176*

Author(s) and year	NO. SSI / Total no. High Fio_2	NO. SSI / Total no. Low Fio_2	Weight	Relative risk (95% CI)
Greif 2000	13/250	28/250	3.76%	0.46 (0.25, 0.88)
Pryor 2004	20/80	9/80	3.10%	2.22 (1.08, 4.58)
Belda 2005	22/148	35/143	5.39%	0.61 (0.38, 0.98)
Mayzler 2005	2/19	3/19	0.72%	0.67 (0.13, 3.55)
Myles 2007	77/997	106/1015	8.81%	0.74 (0.56, 0.98)
Gardella 2008	17/69	10/74	3.19%	1.82 (0.90, 3.70)
Meyhoff 2009	131/685	141/701	10.21%	0.95 (0.77, 1.18)
Bickel 2011	6/107	14/103	2.11%	0.41 (0.16, 1.03)
Golfam 2011	0/30	1/30	0.21%	0.33 (0.01, 7.87)
Scifres 2011	35/288	26/297	5.39%	1.39 (0.86, 2.25)
Thibon 2012	15/226	15/208	3.32%	0.92 (0.46, 1.84)
Chen 2013	5/30	19/61	2.25%	0.54 (0.22, 1.29)
Duggal 2013	34/416	32/415	5.63%	1.06 (0.67, 1.68)
Schietroma 2013	5/86	11/85	1.78%	0.45 (0.16, 1.24)
Stall 2013	14/119	19/116	3.70%	0.72 (0.38, 1.36)
Williams 2013	10/77	12/83	2.75%	0.90 (0.41, 1.96)
Schietroma 2014	6/40	11/41	2.20%	0.56 (0.23, 1.37)
Habib 2015	5/40	7/40	1.65%	0.71 (0.25, 2.06)
Kurz 2015	45/285	42/270	6.81%	1.02 (0.69, 1.49)
Wasnik 2015	0/32	0/32	0.14%	1.00 (0.02, 48.92)
Fariba 2016	0/61	1/61	0.21%	0.33 (0.01, 8.03)
Schietroma 2016a	7/42	14/43	2.64%	0.51 (0.23, 1.14)
Schietroma 2016b	31/119	61/120	7.45%	0.51 (0.36, 0.73)
Tajne 2016	10/120	12/120	2.64%	0.83 (0.37, 1.85)
Vallabha 2016	8/94	13/94	2.48%	0.62 (0.27, 1.42)
Kurz 2017	295/2896	314/2853	11.48%	0.93 (0.80, 1.08)
RE model (Q=42.7, df=25, *P*=0.015; I^2=41.4%)			100.00%	0.81 (0.70, 0.94)

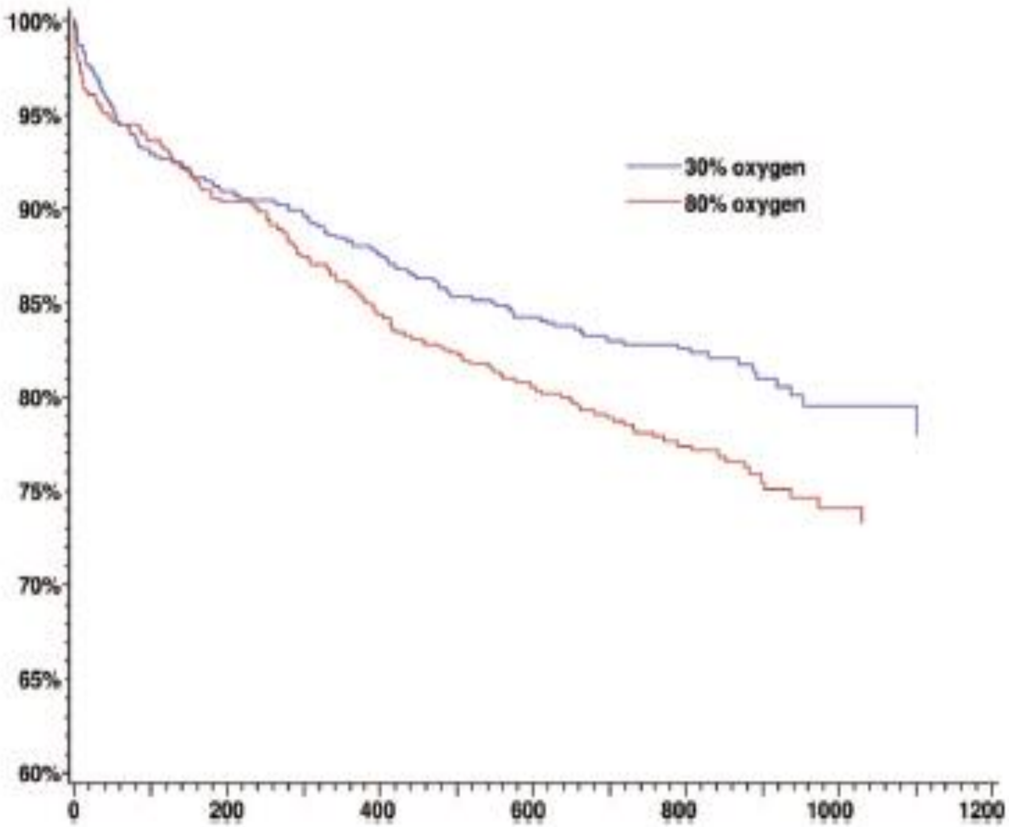


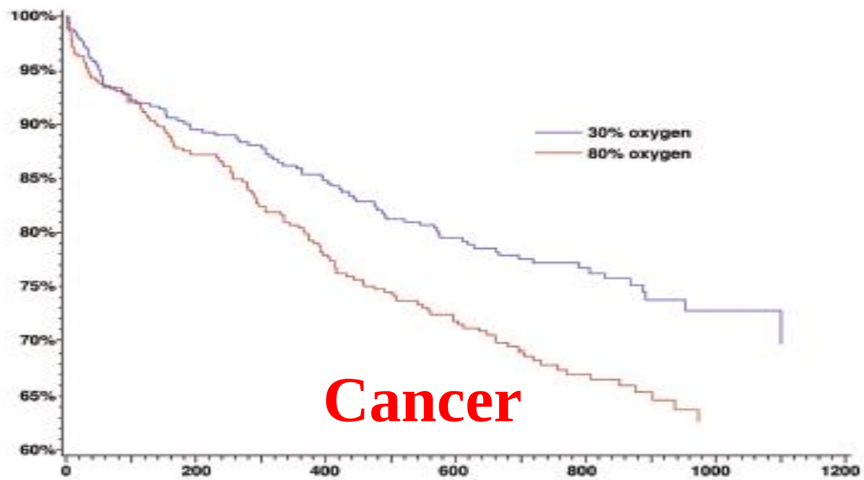
Meta-Analyse von 26 RCT mit 14.710 Patienten!

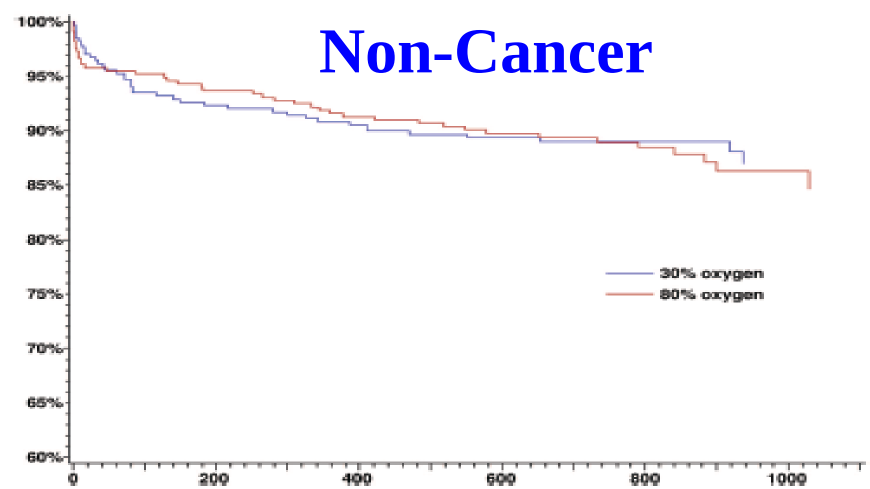
OR 0.81 (0.70-0.94), p=0.00057

Meyhoff et al: Increased long-term mortality after a high perioperative inspiratory oxygen fraction during abdominal surgery: follow-up of a randomized clincial trial. *Anesth Analg 2012;115:849*

1400 Patienten, Notfall- und Elektiv-Laparotomie, 30% / 80 % O_2 bis 2 h post OP; *Follow-up 2 Jahre!*







Hyperoxie und Sepsis

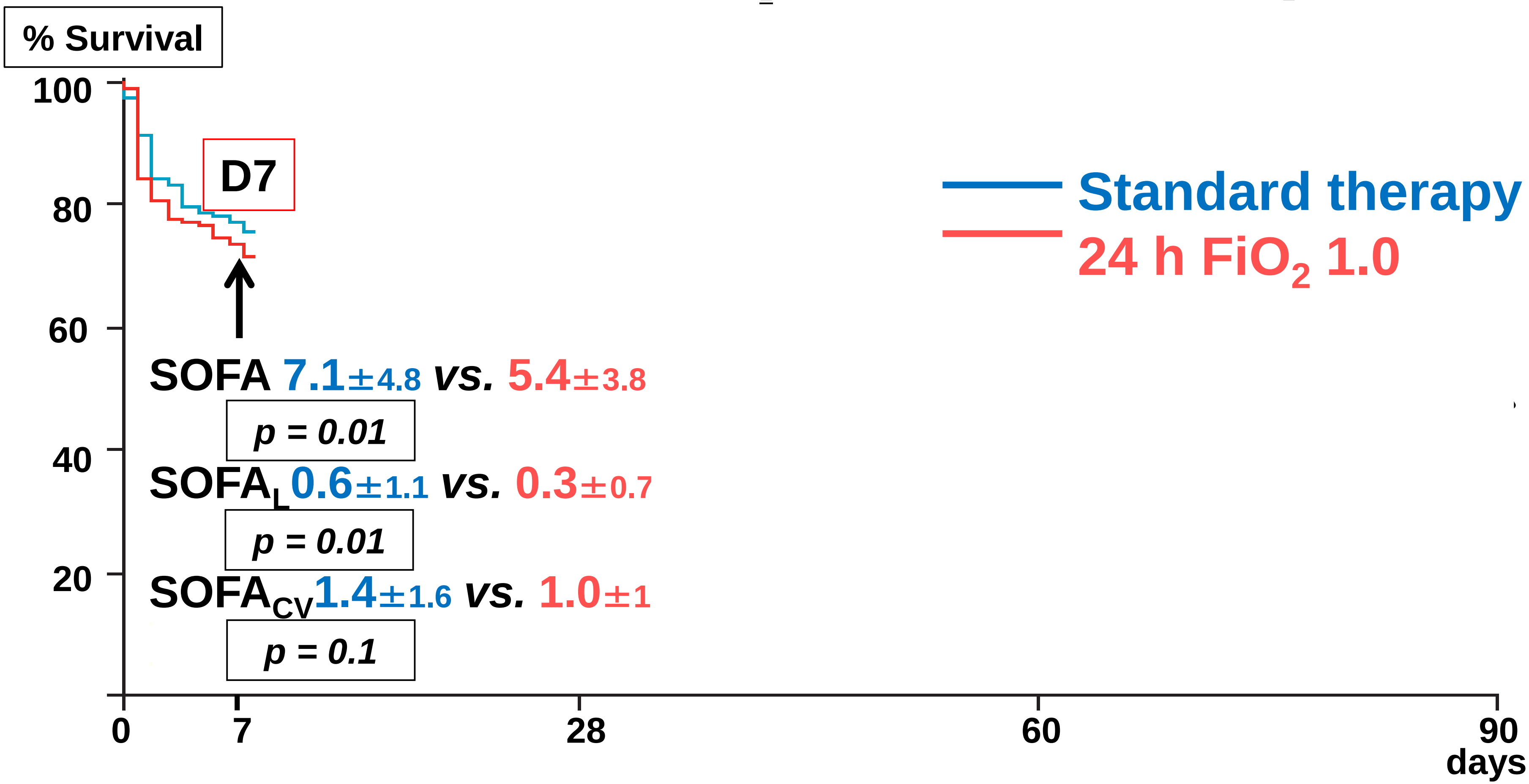
Hyperoxie und Sepsis

Asfar, Schortgen….Radermacher:

Hyperoxia and hypertonic saline in patients with septic shock (HYPER2S): a two-by-two factorial, multicentre, randomised, clinical trial.

Lancet Respir Med 2017;180-90

442 Patienten mit sept. Schock; 24 h FiO_2 1.0 *vs.* Standardtherapie (SO_2=88-95%)



SFB 1149 TRAUMA

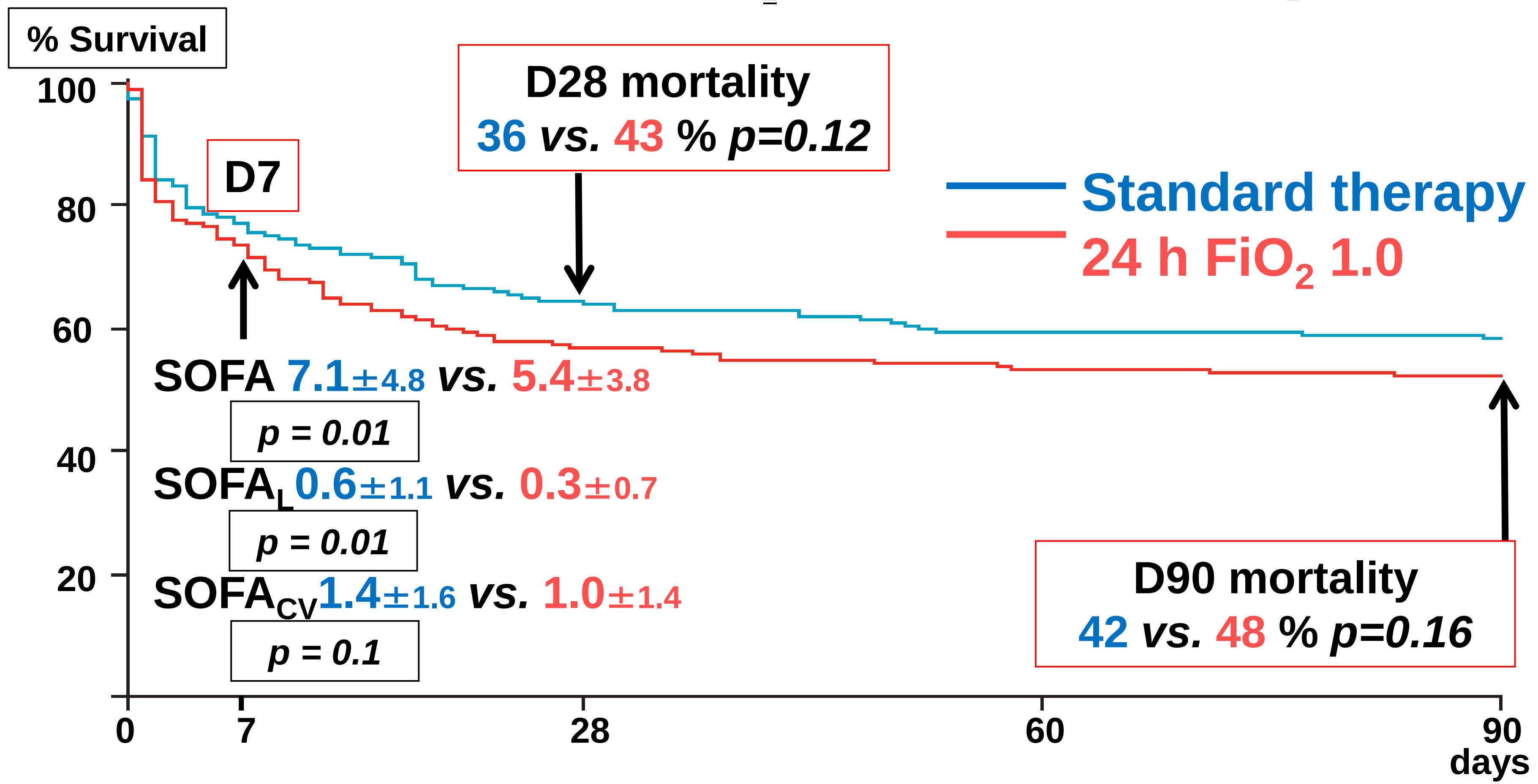
Hyperoxie und Sepsis

Asfar, Schortgen….Radermacher:

Hyperoxia and hypertonic saline in patients with septic shock (HYPER2S): a two-by-two factorial, multicentre, randomised, clinical trial.

Lancet Respir Med 2017;180-90

442 Patienten mit sept. Schock; 24 h FiO_2 1.0 *vs.* Standardtherapie (SO_2=88-95%)



Hyperoxie und Sepsis

Demiselle et al:

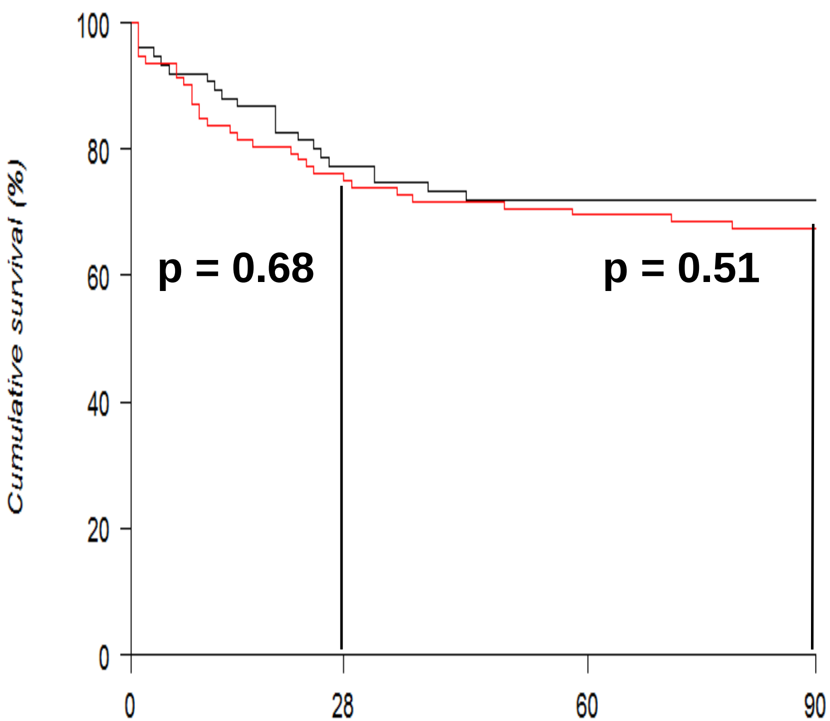
A post hoc analysis of the HYPER2S trial using the Sepsis-3 criteria.

AIC 2018;8:90

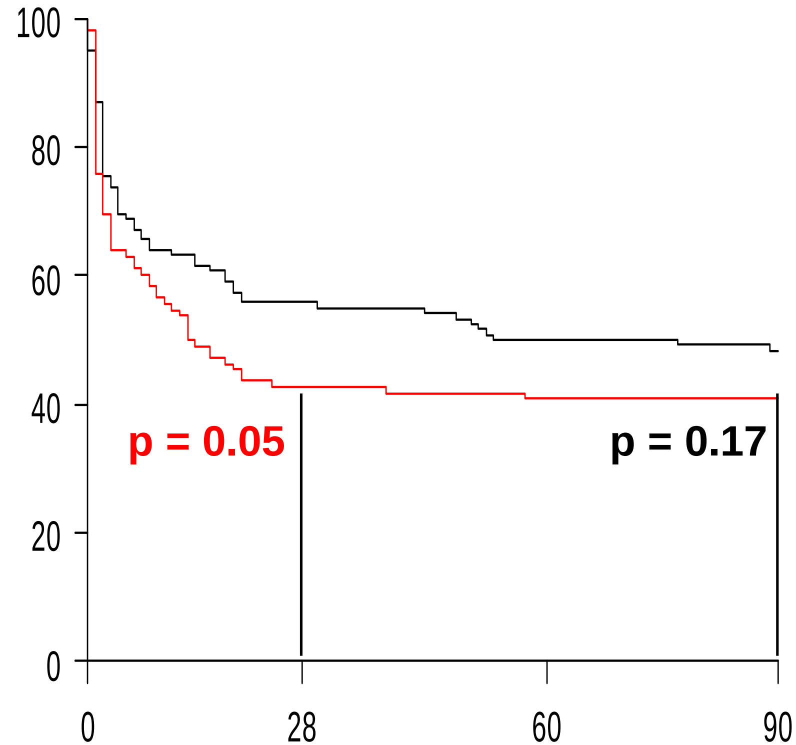
Hyperoxia

Normoxia

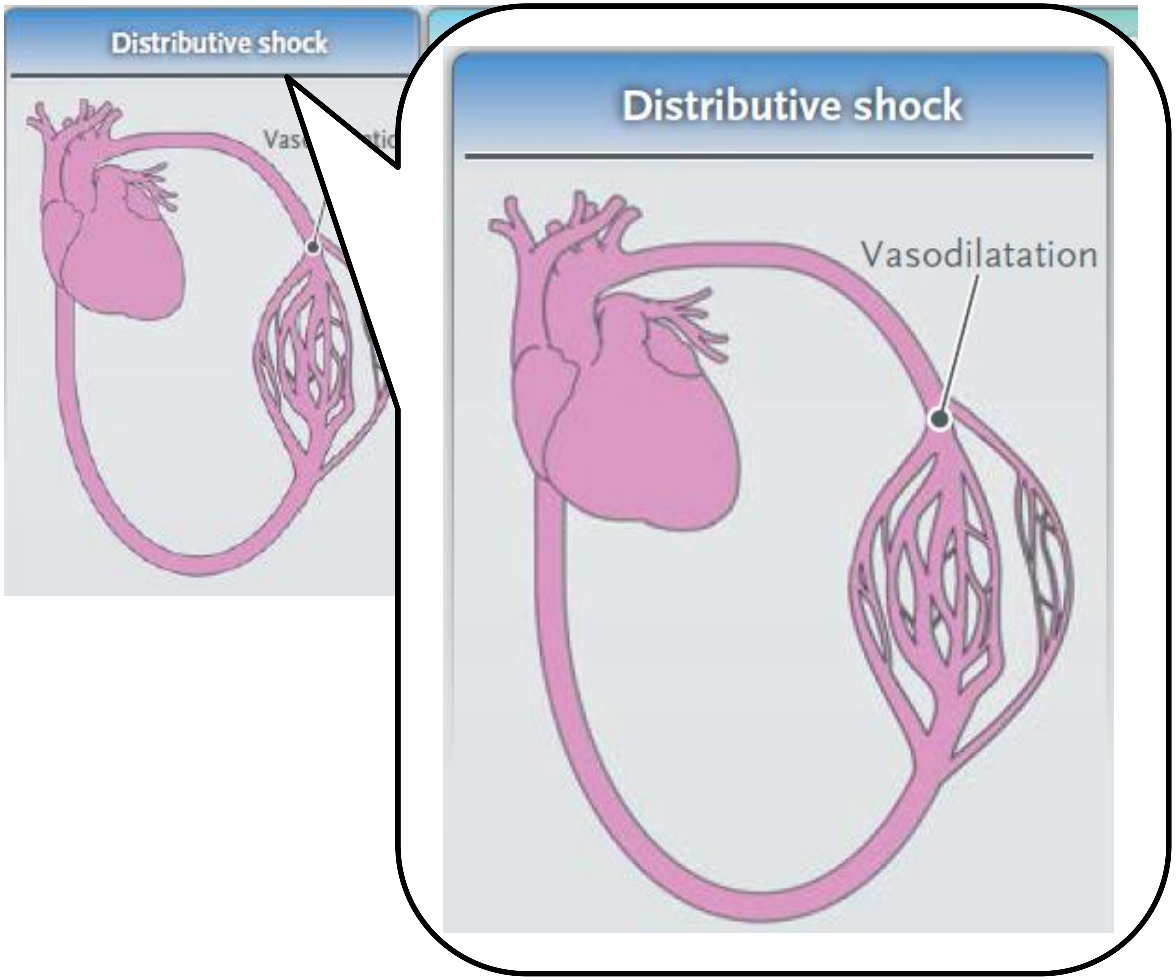
Lactate ≤ 2 mmol/L



Lactate > 2 mmol/L



Vincent & De Backer:
Circulatory Shock.
NEJM 2013;369:1726



"…the main deficit lies in the periphery, with decreased… vascular resistance and *altered oxygen extraction*…"

Hyperoxie und CPR

SFB 1149 TRAUMA

ulm university universität ulm

Hyperoxie und CPR

Roberts et al:

Association between early hyperoxia exposure after resuscitation from cardiac arrestand neurological disability: a prospective multi-center protocol-derived cohort study.

Circulation 2018;138:2864

105/280 (38%) patients, PaO_2 > 300 mmHg during the initial 6 h after ROSC; Poor outcome = Rankin Scale > 3 (70% of patients)

- **77% *vs.* 65% PaO_2 > 300 mmHg ⇒ poor neurological function [relative risk 1.23 (95% CI 1.11-1.35)])**
- **1-h longer duration ⇒ 3% increase in risk of poor neurological outcome [relative risk 1.03 (95% CI 1.02-1.05)]**
- **association with poor neurological outcome PaO_2 > 300 mmHg**

SFB 1149 TRAUMA

ulm university universität ulm

Hyperoxie und CPR

Ebner et al:

Association between partial pressure of oxygen and neurological outcome in out-of-hospital cardiac arrest patients: an explorative analysis of a randomized trial.

Crit Care 2019;23:30

Post hoc **analysis** ***Target Temperature Management*****; 939 patients with ROSC; Cerebral Performance Category ("good" = 1-2; "poor" = 3-5) at 6 months; ("hyperoxemia" = PaO_2 > 300 mmHg vs. "hypoxemia" = PaO_2 < 60 mmHg)**

Although exposure to hyperoxemia and hypoxemia…was common…, we found….NOT to be INDEPENDENTLY ASSOCIATED with neurological outcome at 6-month….s-Tau at 48 or 72 h after ROSC…NOT INDICATE a PaO_2 THRESHOLD…for onset of poor neurological outcome.

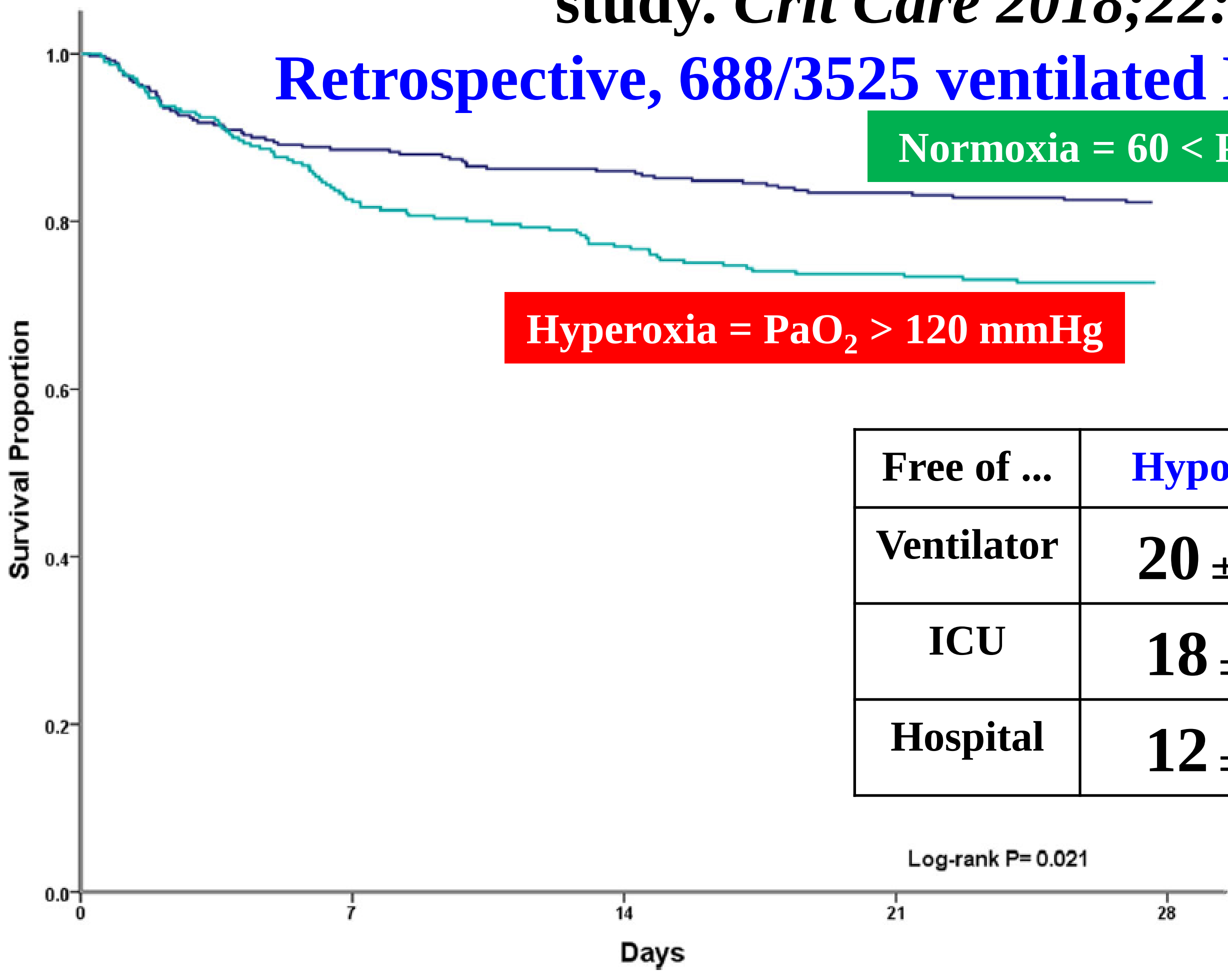
SFB 1149 TRAUMA

ulm university universität ulm

Hyperoxie und Outcome: ER

Page et al:* Emergency department hyperoxia is associated with increased mortality in mechanically ventilated patients: a cohort study. *Crit Care 2018;22:9

Retrospective, 688/3525 ventilated ER patients



Free of ...	Hypoxia	Normoxia	Hyperoxia
Ventilator	20 ± 10	18 ± 10	14 ± 11
ICU	18 ± 9	17 ± 10	13 ± 11
Hospital	12 ± 9	11 ± 9	9 ± 9

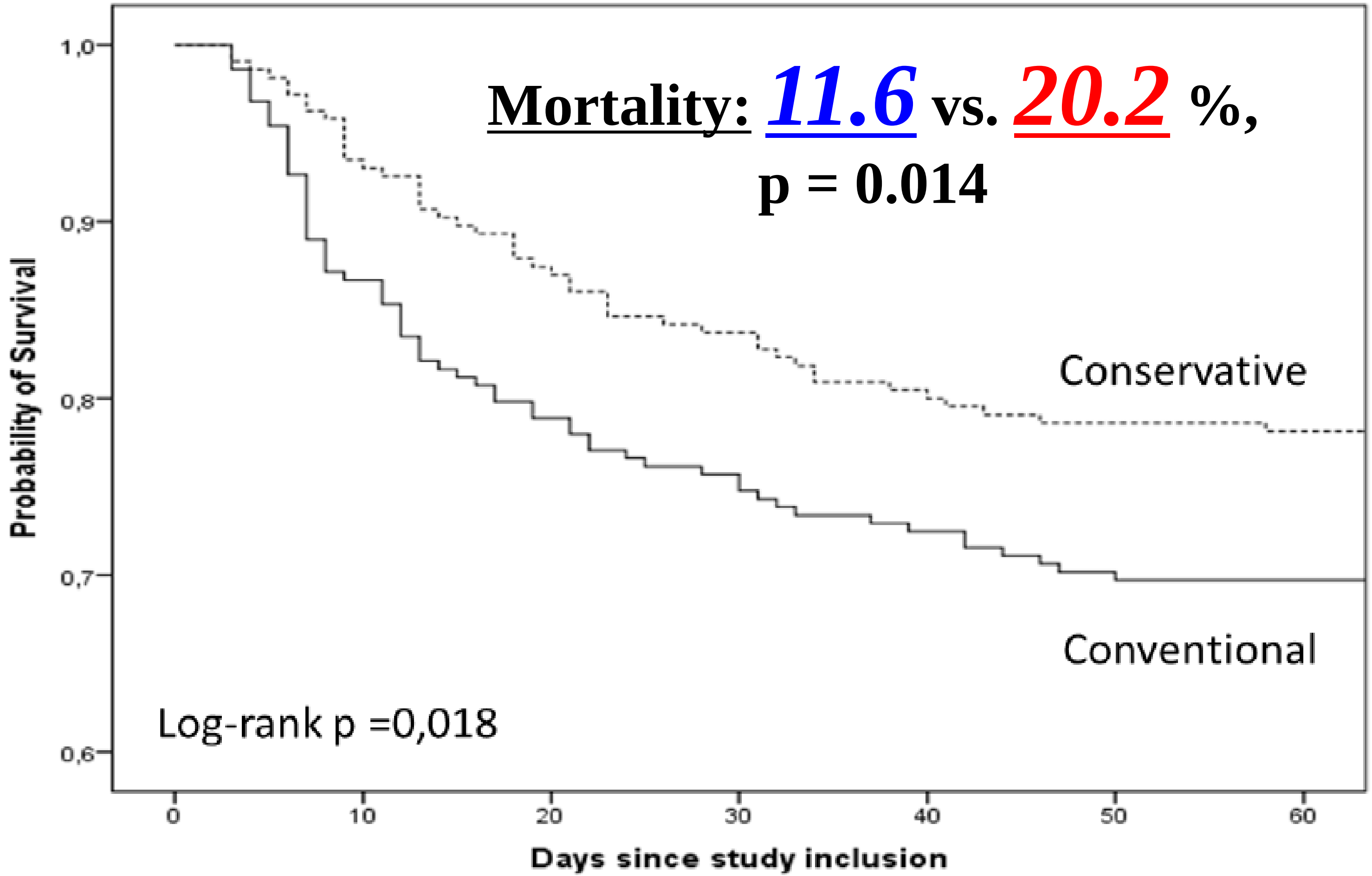
SFB 1149 TRAUMA ULM

ulm university universität ulm

Hyperoxie und Outcome

Girardis et al: **Effect of *conservative* vs. *conventional* oxygen therapy on mortality among patients in an intensive care unit. *JAMA* 2016;316:1583-9**

434 Patienten, PaO_2/SaO_2 70-100 mmHg/94-98 % vs. PaO_2/SaO_2 -150 mmHg/97-100%



Hyperoxie und Outcome

Girardis et al: Effect of *conservative* vs. *conventional* oxygen therapy on mortality among patients in an intensive care unit. *JAMA* 2016;316:1583-9

434 Patienten, PaO_2/SaO_2 70-100 mmHg/94-98 % vs. PaO_2/SaO_2 -150 mmHg/97-100%

	Conservative	Conventional	p-value
Shock	8 (3.7 %)	23 (10.6 %)	0.006
Liver failure	4 (1.9 %)	14 (6.4 %)	0.02
Bacteremia	11 (5.1 %)	22 (10.1 %)	0.049

Hyperoxie und Outcome

Girardis et al: **Effect of *conservative* vs. *conventional* oxygen therapy on mortality among patients in an intensive care unit. *JAMA* 2016;316:1583-9**

434 Patienten, PaO_2/SaO_2 70-100 mmHg/94-98 % vs. PaO_2/SaO_2 -150 mmHg/97-100%

Aber:

Abgebrochen wegen "*slow recruitment*"; *nur*

- 30% Schock (20% Sept. Schock)

- 67 % MV

- 15 % AKI

SFB 1149 TRAUMA

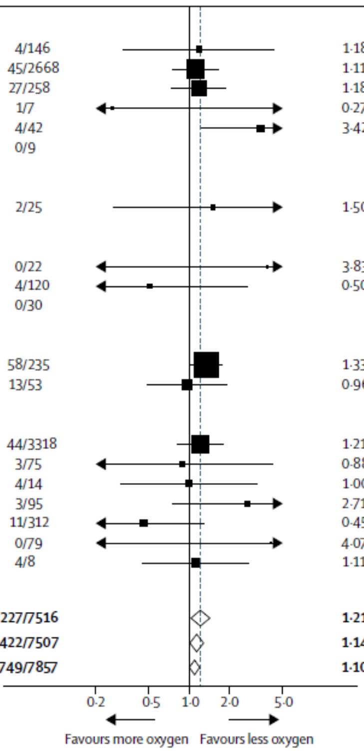
ulm university universität ulm

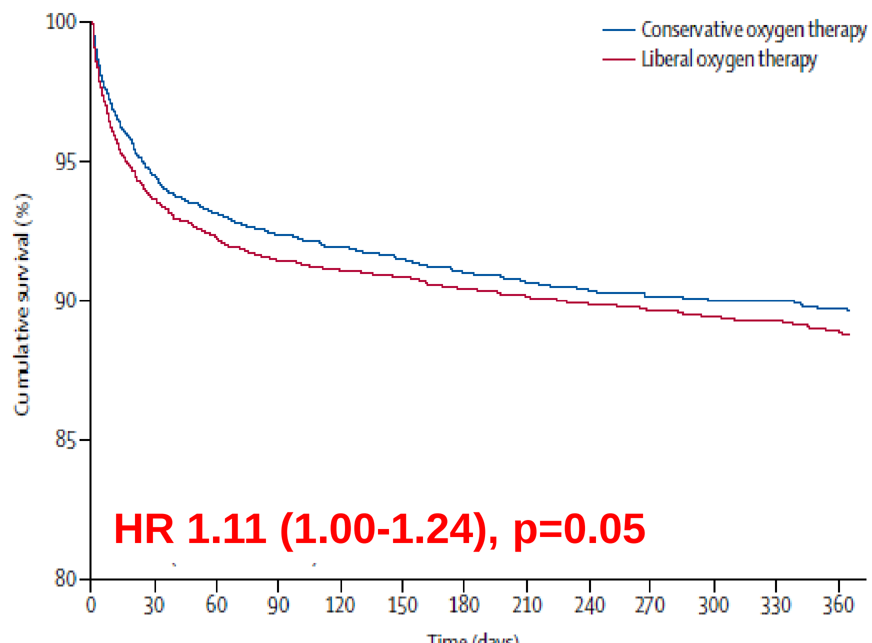
Hyperoxie und Outcome

Chu et al: Mortality and morbidity in acutely il adults treated with liberal versus conservative oxygen therapy (IOTA): a systemic review and meta-analysis. *Lancet 2018;391:1693*

Meta-Analyse von 25 RCT mit 16.037 Patienten!

	Setting	Liberal (n/N)	Conservative (n/N)	RR (95% CI)	% weight
Neurological (stroke–traumatic brain injury)					
Ali et al (2014)[44,66]	Stroke	5/155	4/146	1·18 (0·32–4·30)	1·6
Roffe et al (2017)[59]	Stroke	50/2668	45/2668	1·11 (0·75–1·66)	16·6
Ronning et al (1999)[56]	Stroke	36/292	27/258	1·18 (0·74–1·89)	11·9
Singhal et al (2005)[58]	Stroke (ischaemic)	0/9	1/7	0·27 (0·01–5·70)	0·3
NCT00414726	Stroke (ischaemic)	14/43	4/42	3·42 (1·22–9·54)	2·5
Shi et al (2017)[65]	Stroke (ischaemic)	0/9	0/9	(Excluded)	0
Sepsis					
NCT02378545 (2015)	Sepsis	3/25	2/25	1·50 (0·27–8·22)	0·9
Emergency surgery					
Butler et al (1987)[46]	Limb ischaemia	1/17	0/22	3·83 (0·17–88·62)	0·3
Schietroma et al (2016)[57]	Perforated peptic ulcer	2/119	4/120	0·50 (0·09–2·70)	0·9
NCT02687217	Acute appendicitis	0/30	0/30	(Excluded)	0
Critical care (mixed medical-surgical)					
Girardis et al (2016)[47]	Critical illness	80/243	58/235	1·33 (1·00–1·78)	32·1
Panwar et al (2016)[53]	Critical illness	12/51	13/53	0·96 (0·48–1·90)	5·6
Cardiac (myocardial infarction–cardiac arrest)					
Hofmann et al (2017)[48]	Myocardial infarction	53/3311	44/3318	1·21 (0·81–1·80)	16·8
Khoshnood et al (2015)[49]	Myocardial infarction (STEMI)	3/85	3/75	0·88 (0·18–4·24)	1·1
Kuisma et al (2006)[50]	Cardiac arrest	4/14	4/14	1·00 (0·31–3·23)	1·9
Rawles et al (1976)[55]	Myocardial infarction	9/105	3/95	2·71 (0·76–9·73)	1·6
Stub et al (2012)[60]	Myocardial infarction (STEMI)	5/312	11/312	0·45 (0·16–1·29)	2·4
Ukholkina et al (2005)[61]	Myocardial infarction	1/58	0/79	4·07 (0·17–98·10)	0·6
Young et al (2014)[62]	Cardiac arrest	5/9	4/8	1·11 (0·45–2·75)	3·2
$P_{interaction}=0·97$					
In-hospital mortality, overall (I^2=0%, p=0·020)		**283/7555**	**227/7516**	**1·21 (1·03–1·43)**	**100**
30-day mortality, overall (I^2=0%, p=0·033)		**484/7546**	**422/7507**	**1·14 (1·01–1·28)**	**100**
Mortality at longest follow-up, overall (I^2=0%, p=0·044)		**828/7897**	**749/7857**	**1·10 (1·00–1·20)**	**100**





Number at risk

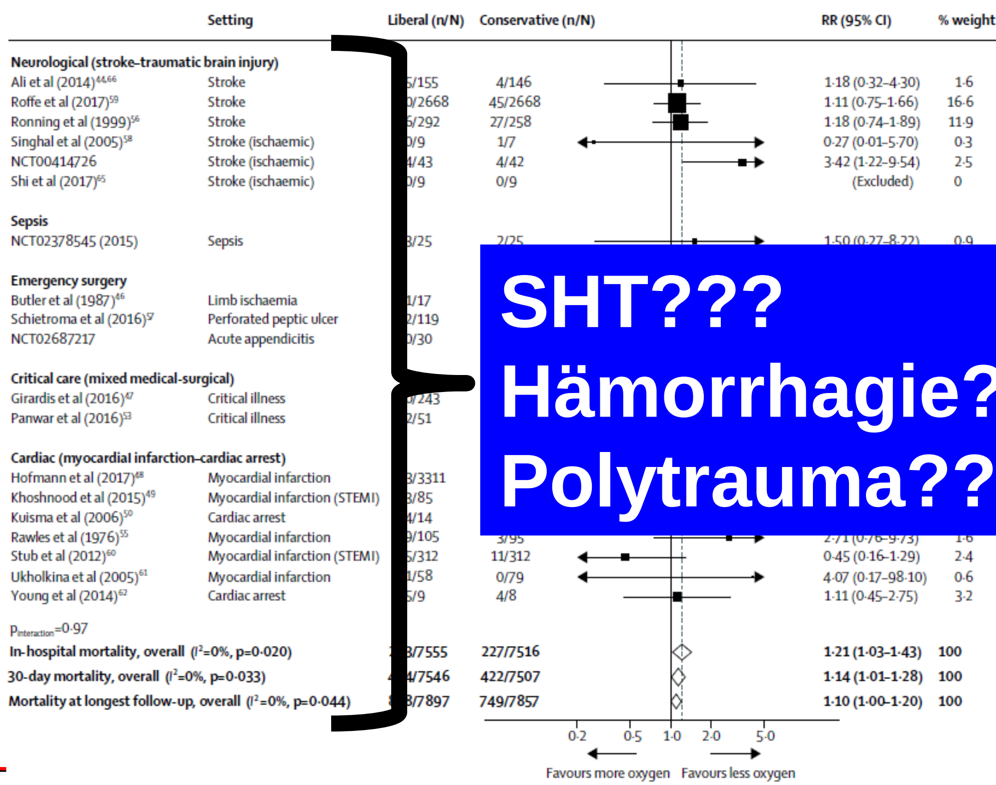
	0	30	60	90	120	150	180	210	240	270	300	330	360
Conservative	6900	6484	6372	6130	3542	3527	3507	3372	3361	3352	3345	3344	3334
Liberal	6943	6450	6345	6119	3564	3554	3539	3402	3390	3381	3370	3365	3351

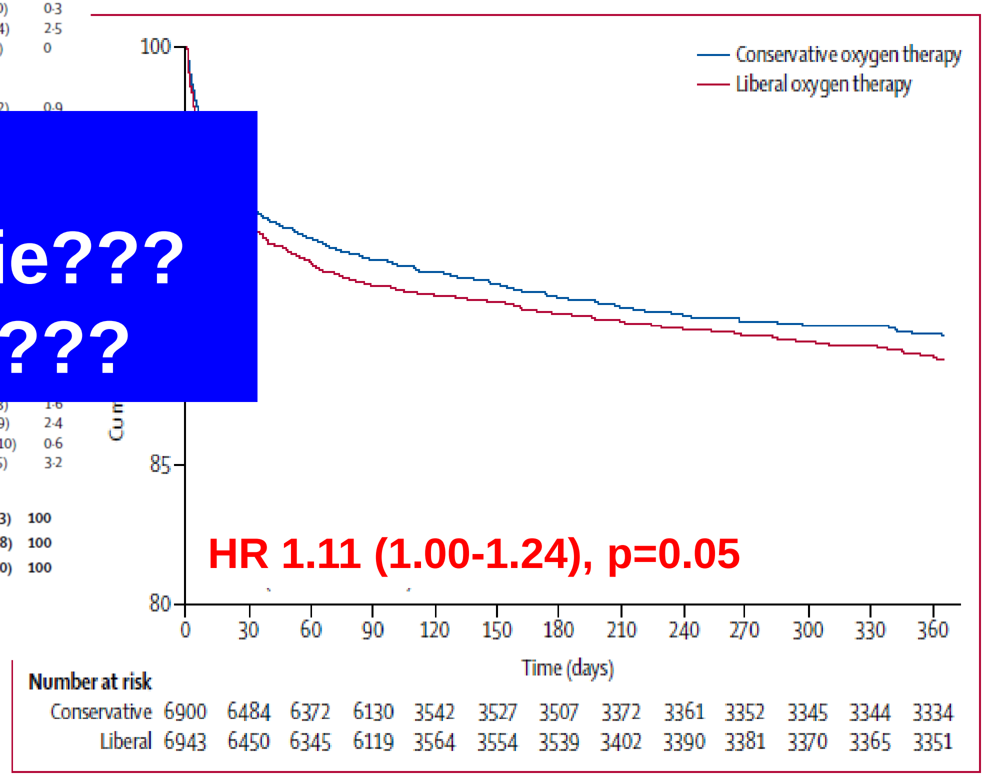
universität ulm zmfu

Hyperoxie und Outcome

Chu et al:* Mortality and morbidity in acutely il adults treated with liberal versus conservative oxygen therapy (IOTA): a systemic review and meta-analysis. *Lancet 2018;391:1693

Meta-Analyse von 25 RCT mit 16.037 Patienten!





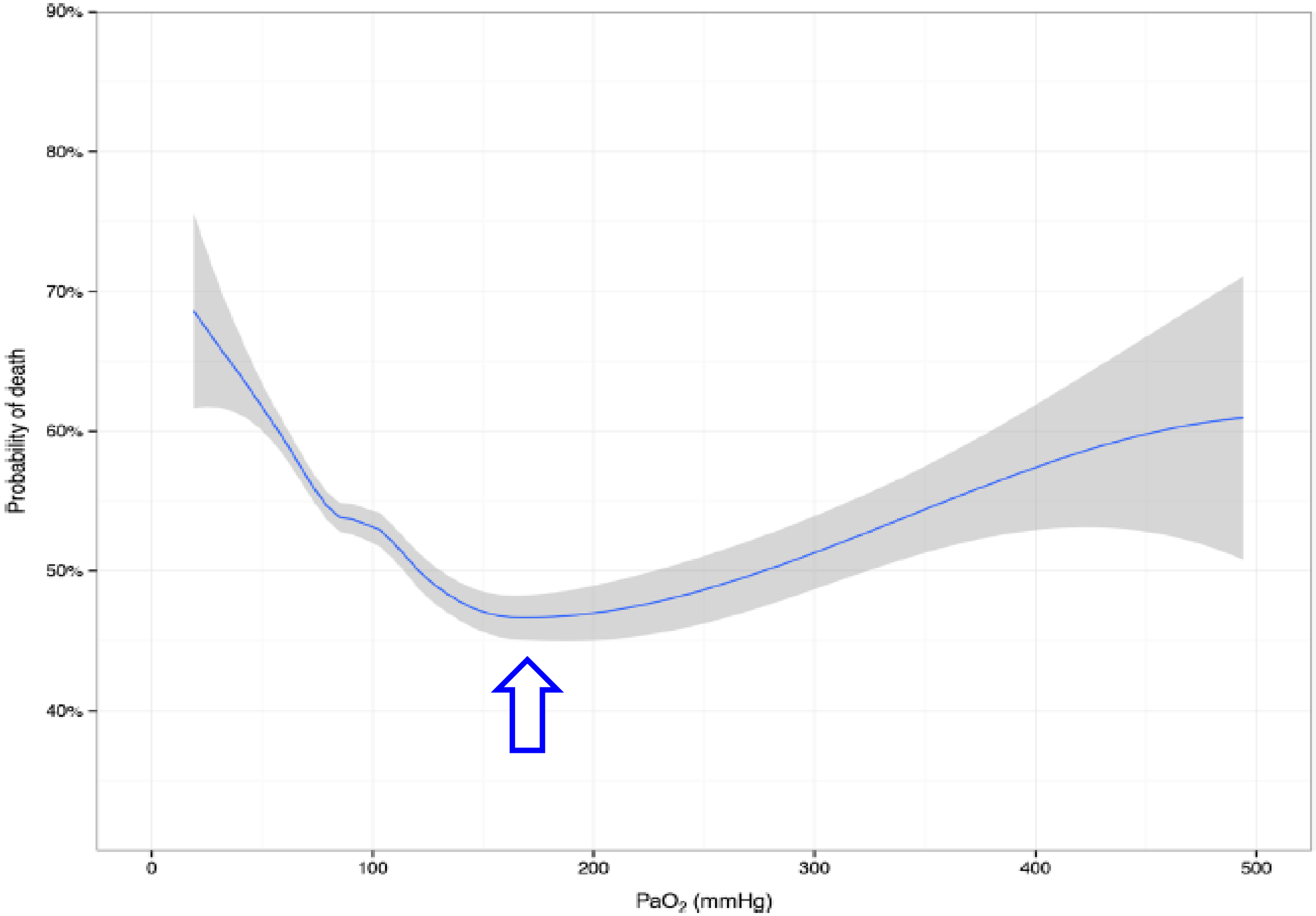
HR 1.11 (1.00-1.24), p=0.05

SHT???
Hämorrhagie???
Polytrauma???

Der optimale PO_2?

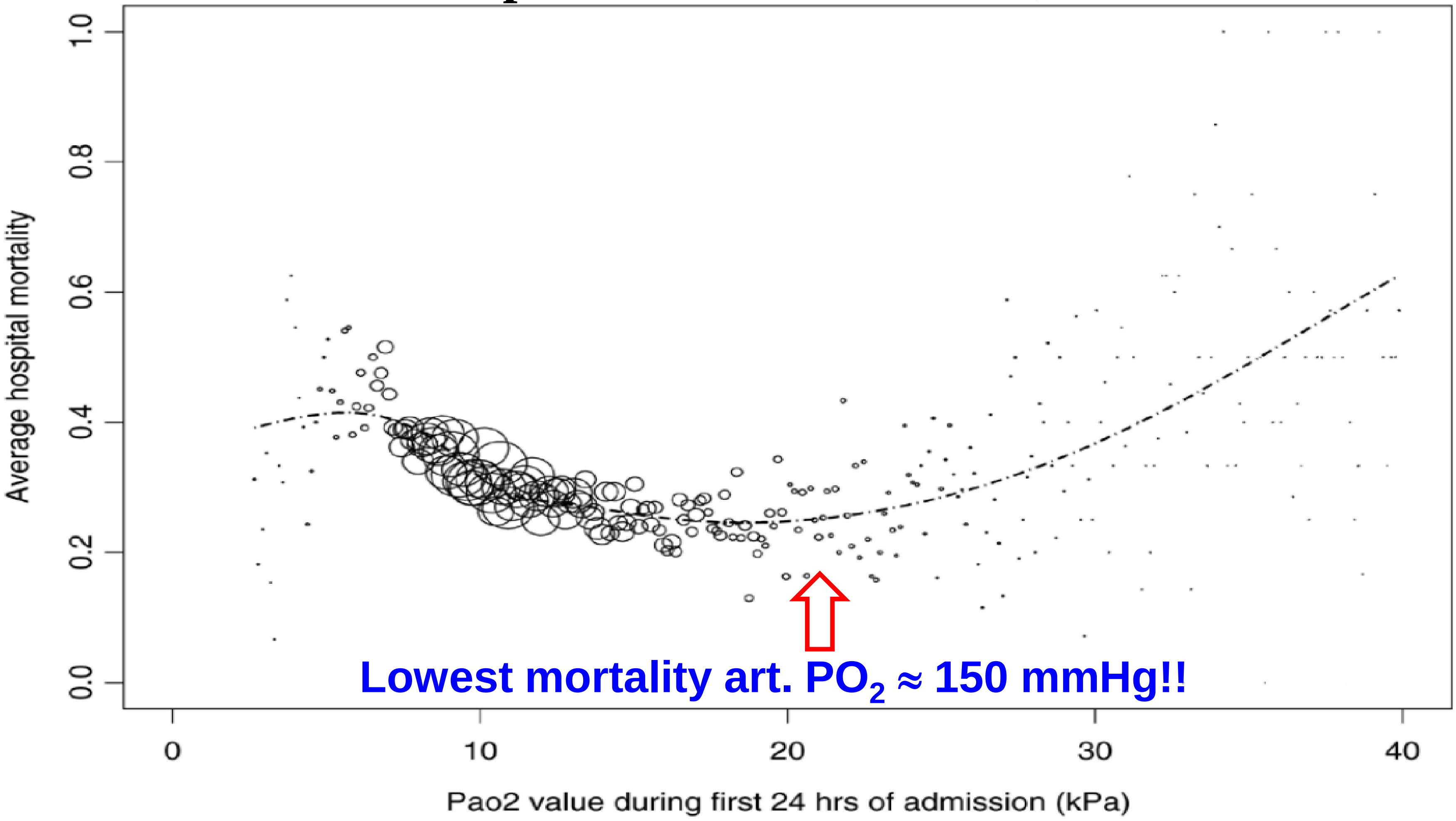
Helmerhorst et al: **Associations of arterial carbon dioixde and arterial oxygen concentrations with hospital mortaltiy after resuscitation from cardiac arrest.** ***Crit Care 2015;19:348***

6496 Patienten!



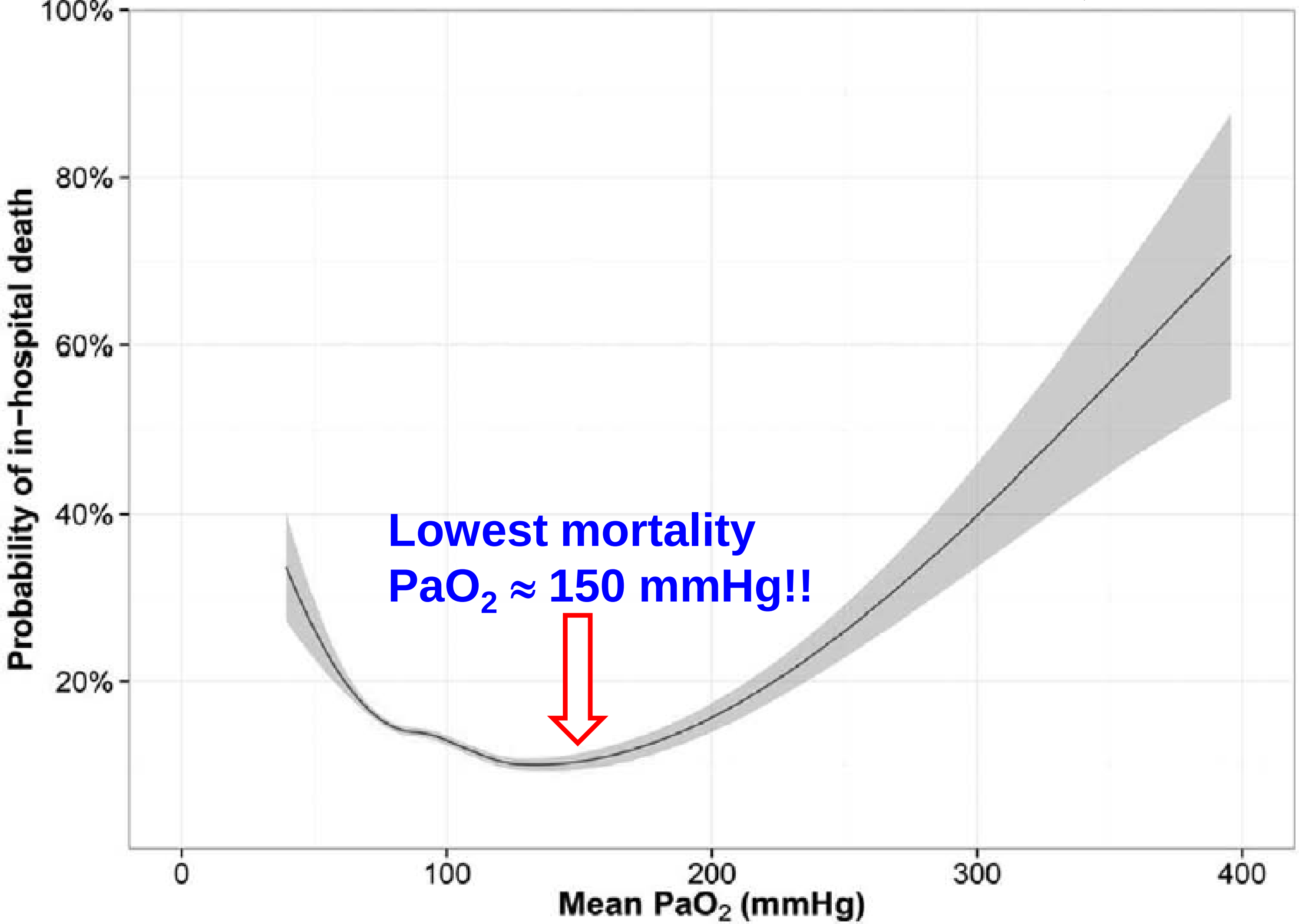
Der optimale PO_2?

de Jonge et al: **Association between administered oxygen, arterial partial oxygen pressure and mortality in mechanically ventilated intensive care patients.** ***Crit Care 2008;12:R156***



Der optimale PO_2?

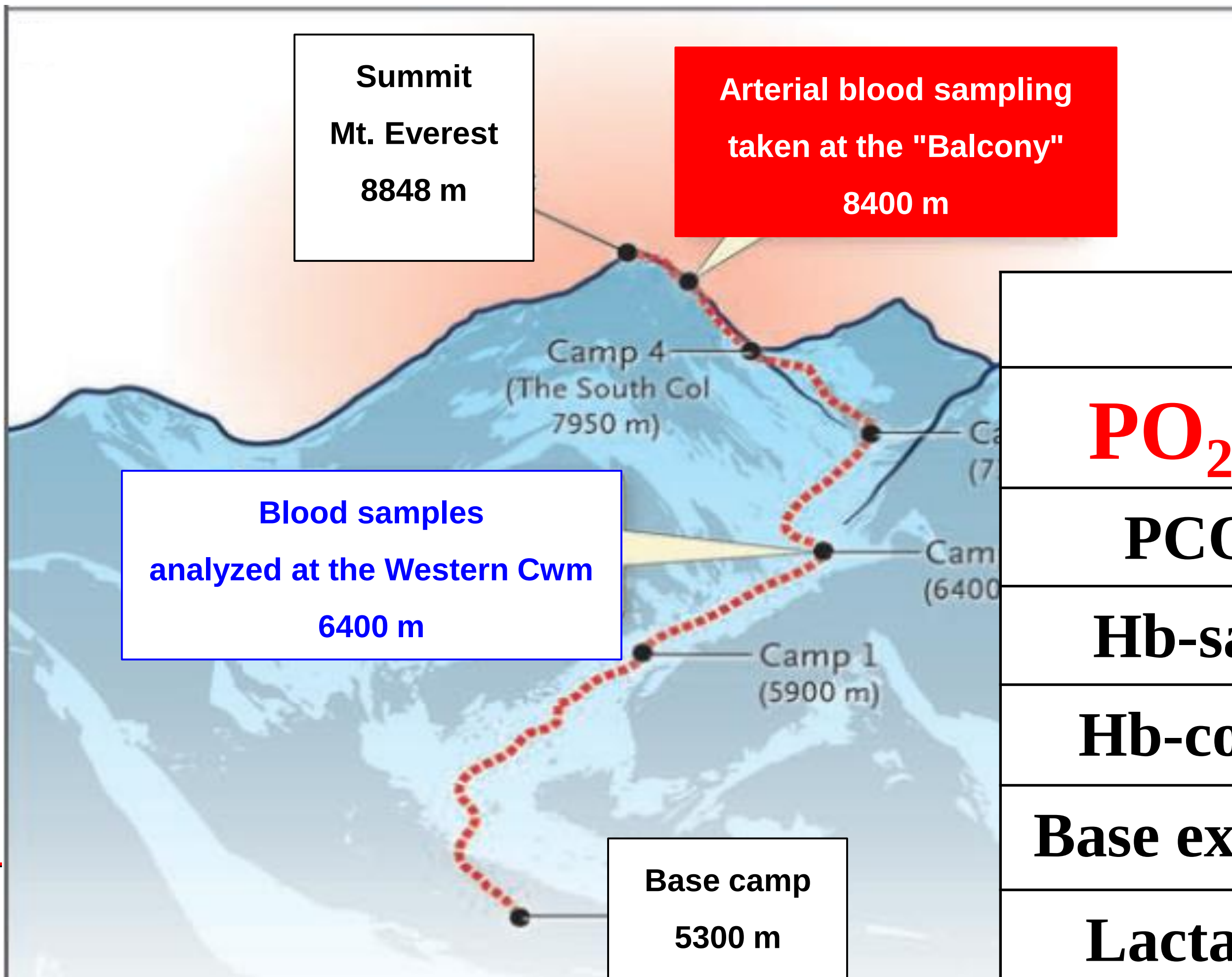
Helmerhorst et al: **Metrics of arterial hyperoxia and associated outcomes in critical care.** ***Crit Care Med 2017;45:187-95***



Der minimale PO_2?

Messner & Habeler bestiegen den Mt. Everest *ohne* O_2!

Grocott et al: **Arterial blood gases and oxygen content in climbers on Mount Everest. *NEJM 2009;340:160***



pH	7.53
PO_2 [mmHg]	25
PCO_2 [mmHg]	13
Hb-saturation %	54
Hb-content [g/dL]	19
Base excess [mmol/L]	-6.9
Lactate [mmol/L]	2.2

SFB 1149 TRAUMA

ulm university universität ulm

Der minimale PO_2?

Messner & Habeler bestiegen den Mt. Everest *ohne* O_2!

***Bailey:* The last „oxygenless“ ascent on Mt. Everest.**

Br J Sport Med 2001;35:294

„…assuming an increase in height by 3 cm/year and a NE-drift by 6 cm/year….a climber with a maximal VO_2 of 3.5 metabolic equivalents… would therefore have to make his assault… about 39460 AD…A winter assault would need ….before 29107 AD…. These dates could be extended by 85 years if the snow melted….

Whether the predictions are correct, only time will tell!

https://www.youtube.com/watch?v=gxtM-gdp0Fk

The Sweet, 1978

Love is like oxygen

You get too much you get too high

Not enough and you're gonna die

Love gets you high