Cosa chiedo alla PtO_2

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NEURO UPDATE TORINO
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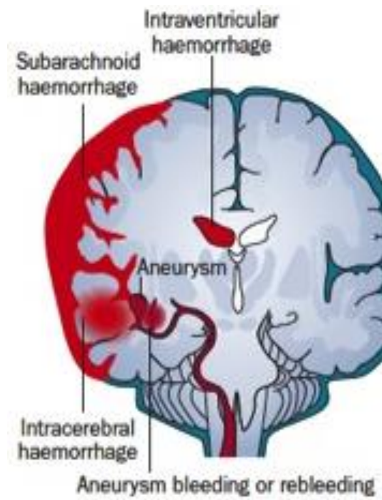
Disclosures

- Research grants
  - Swiss National Science Foundation
  - European ERA-NET NEURO
  - Novartis Foundation for Biomedical Research
  - Nestle Health Science Research

- Consultant fees
  - Nestle Health Science Research
  - Integra Neurosciences, Europe
  - Bard Medical, Europe
  - Carag AG, Switzerland

Primary brain injury



Secondary insults

ISCHEMIA/HYPOXIA
↓ Perfusion; ↓ Oxygen

EDEMA
↑ ICP

ENERGY DYSFUNCTION
↑ metabolism (seizures, T°); ↓ glucose

Annals of Intensive Care — Bouzat P, Sala N, Payen JF, **Oddo M. 2013**

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Functional neuro-physiologic exploration

Brain multimodal monitoring

EDEMA
↑ ICP

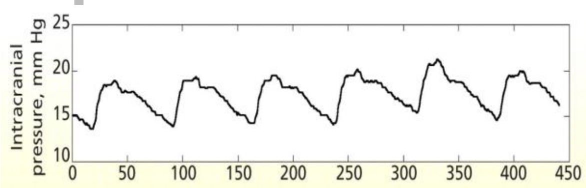
ISCHEMIA/HYPOXIA
↓ Perfusion; ↓ Oxygen

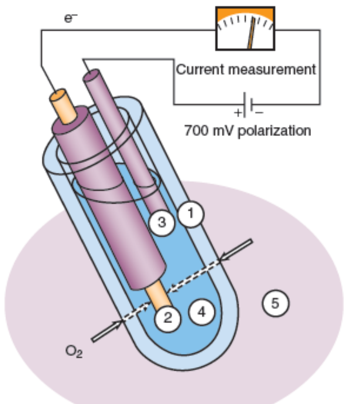
ENERGYDYSFONCTION
↑ metabolism (seizures, T°); ↓ glucose

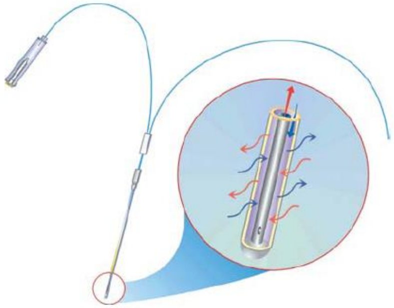
Intracranial pressure (ICP)

Brain tissue oxymetry ($PbtO_2$)

Cerebral microdialysis







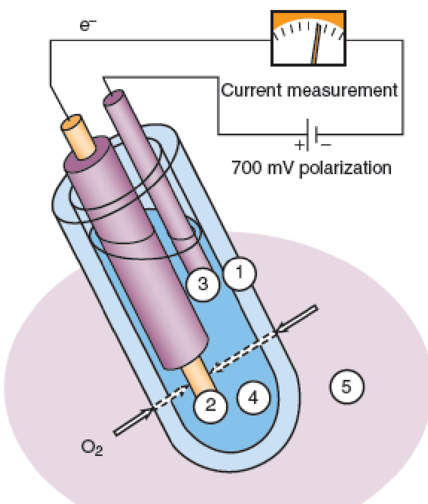
Oddo M, Villa F, Citerio G. Brain multimodality monitoring. *Curr Opin Crit Care* **2012**

neurocritical care society Neurocrit Care
DOI 10.1007/s12028-014-0024-6

REVIEW ARTICLE

Monitoring of Brain and Systemic Oxygenation in Neurocritical Care Patients

Mauro Oddo · Julian Bösel · and the Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring



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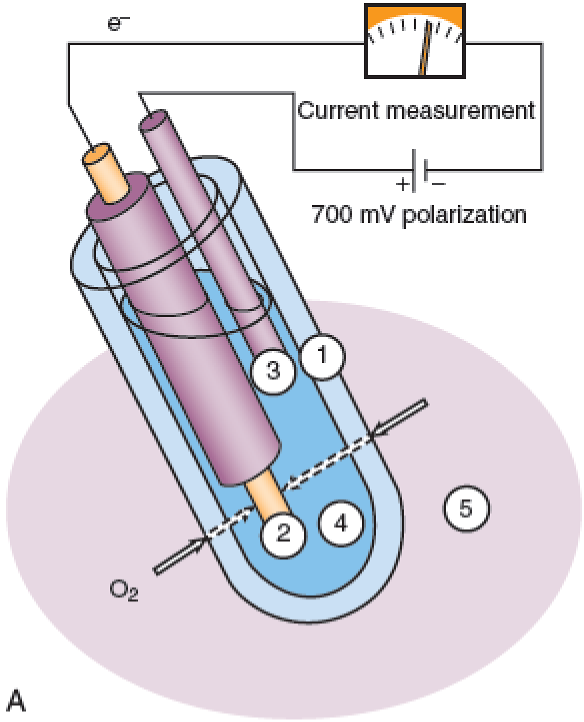
Technology

- Polarographic Clark-type cell with reversible electrochemical electrodes
  - Constant calibration of the system to patient temperature
  - **Licox $PbtO_2$ probe (Integra)**
  - **Neurovent PTO (Raumedic)**

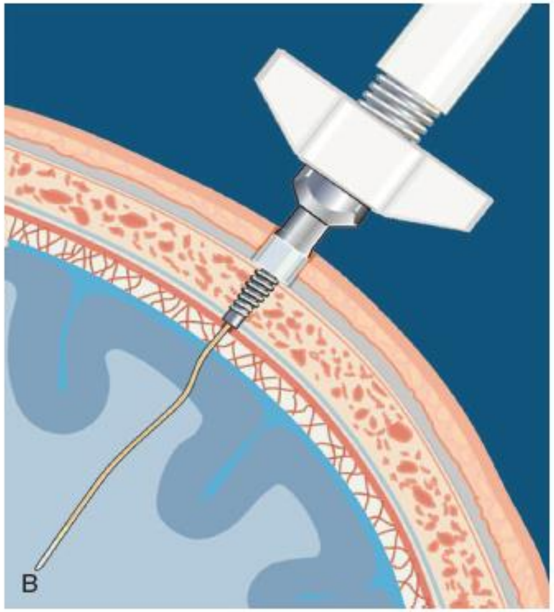


A

Oddo M, LeRoux PD. Brain tissue oxygen. In Monitoring in Neurocritical Care Chapter 35. Elsevier.

Catheter insertion

- Small intra-parenchymal catheter (0.5 mm diameter)
- Via a multiple-lumen bolt
  - Integra bolt
  - Raumedic



- Via a tunnelisation during craniotomy
- Combined monitoring of ICP, Brain Temp, neurochemistry (cerebral microdialysis)

Oddo M, LeRoux PD. Brain tissue oxygen. In Monitoring in Neurocritical Care Chapter 35. Elsevier.

Catheter location

Intracranial Pathology	Catheter Location
Traumatic brain injury	
Diffuse injury	Right frontal lobe
Focal injury (subdural hematoma, contusion)	Pericontusional tissue
Subarachnoid hemorrhage	Expected distribution area of the parent artery of the aneurysm, at highest risk for developing symptomatic vasospasm and delayed ischemia
Cerebral infarction	Area of lesion, at distance from the infarcted tissue

Oddo M, LeRoux PD. Brain tissue oxygen. In Monitoring in Neurocritical Care Chapter 35. Elsevier.

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Physiologic determinants of $PbtO_2$

	Baseline (n = 14)	Oxygen Challenge (n = 14)		MAP Challenge (n = 12)		Hyperventilation Challenge (n = 12)	
		End Value	Change	End Value	Change	End Value	Change
MAP (mm Hg)	89 (83–95)	94 (90–99)[a]	5 (1–9)	103 (97–109)[c]	10 (6–14)	94 (86–101)	1 (−4–6)
ICP (mm Hg)	12 (9–15)	10 (7–13)[b]	−2 (−3– −1)	11 (7–15)	1 (−1–2)	7 (5–10)[a]	−2 (−3–0)
CPP (mm Hg)	77 (70–84)	84 (78–91)[b]	7 (3–11)	92 (85–100)[c]	9 (5–13)	86 (79–93)	3 (−2–8)
P_aCo_2 (mm Hg)	39 (37–40)	39 (37–41)	0 (−2–2)	39 (36–42)	0 (−1–1)	33 (31–36)[c]	−6 (−8– −3)
P_aO_2 (mm Hg)	127 (103–150)	441 (363–518)[c]	314 (257–371)	498 (450–545)	33 (−22–88)	426 (356–495)	−31 (−85–23)
P_vO_2 (mm Hg)	45 (40–49)	50 (42–58)[a]	6 (1–10)	55 (41–68)	7 (−1–14)	39 (34–44)[a]	−8 (−14– −2)*
CBF (mL/100 gm/min)	23.9 (16.5–31.2)	18.5 (12.2–24.8)[a]	−5.4 (−9.2– −1.5)	25.8 (17.3–34.3)[a]	7.3 (1.3–13.2)	13.1 (8.4–17.8)[a]	−6.1 (−11.4– −.7)
C_aO_2 (mL O_2/100 mL)	14.6 (13.9–15.4)	15.9 (15.1–16.7)[c]	1.3 (1.2–1.4)	16.0 (15.2–16.9)	.2 (0–.4)	15.7 (14.7–16.6)	−.1 (−.3–.1)
C_vO_2 (mL O_2/100 mL)	11.3 (10.5–12.1)	11.8 (10.8–12.9)[a]	.6 (.1–1.1)	12.2 (11.2–13.1)	.6 (−1.2)	10.4 (9.4–11.4)[b]	−1.1 (−1.8– −.3)
$AVDO_2$ (mL O_2/100 mL)	3.4 (2.5–4.2)	4.1 (3.1–5.0)[a]	.7 (.2–1.2)	3.9 (2.9–4.8)	−.4 (−.9–.1)	5.3 (4.2–6.4)[a]	1.0 (.2–1.7)
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$_{loc}CMRO_2$ (mL O_2/100 gm/min)	.81 (.46–1.16)	.71 (.41–1.01)	−.10 (−.22–.02)	1.00 (.59–1.42)	.25 (−.04–.54)	.73 (.38–1.08)	−.04 (−.22–.15)
$P_{bt}O_2$ (mm Hg)	22.9 (17.2–28.6)	77.0 (58.1–96.0)[c]	54.1 (37.3–70.9)	100.1 (77.4–122.9)[b]	19.7 (10.0–29.5)	73.5 (53.1–93.8)	−11.7 (−25.6–2.3)
$P_{bt}O_2$ (mL O_2/100 gm)	.07 (.05–.09)	.23 (.17–.29)[c]	.16 (.11–.21)	.30 (.23–.37)[b]	.06 (.03–.09)	.22 (.16–.28)	−.04 (−.08–.01)

Rosenthal G et al. Crit Care Med 2008

Physiologic determinants of $PbtO_2$

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Rosenthal G et al. Crit Care Med 2008

$$PbtO_2 \approx CBF \times (PaO_2 - PvO_2)$$

$PbtO_2$
Normal 25-40 mmHg
Hypoxia <15-20 mmHg

↓ CBF, CPP

↓ PaO_2, systemic oxygenation

↓ PvO_2, oxygen transport, Hgb

Rosenthal G et al. Crit Care Med 2008

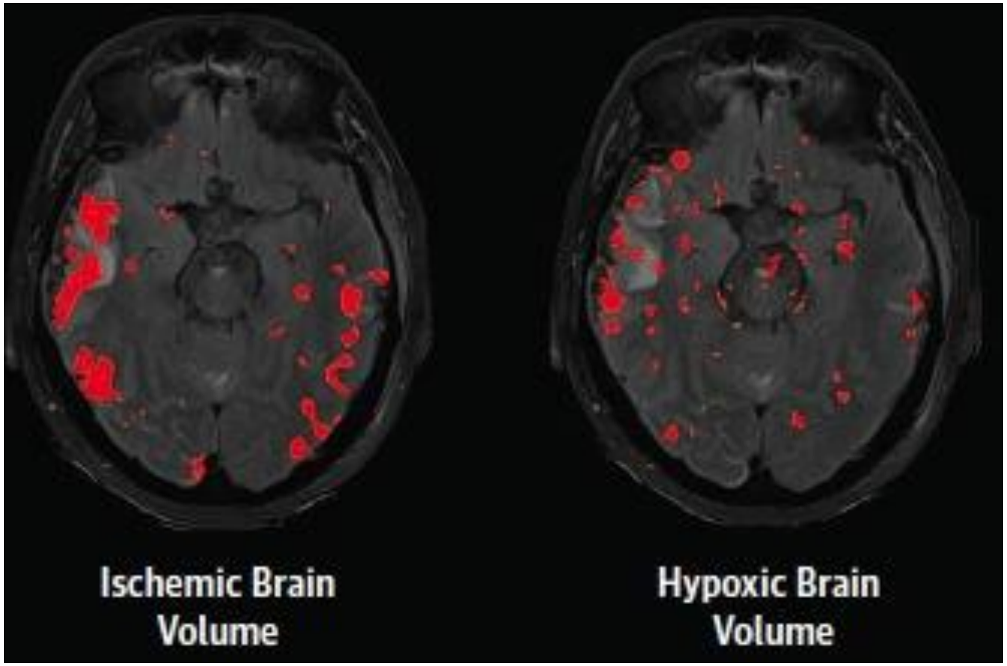
Research

JAMA Neurol. 2016;73(5):542-550. doi:10.1001/jamaneurol.2016.0091
Published online March 28, 2016.

Original Investigation

Pathophysiologic Mechanisms of Cerebral Ischemia and Diffusion Hypoxia in Traumatic Brain Injury

Tonny V. Veenith, FRCA; Eleanor L. Carter, FRCA; Thomas Geeraerts, PhD; Julia Grossac, MD; Virginia F. J. Newcombe, PhD; Joanne Outtrim, MSc; Gloria S. Gee, AS; Victoria Lupson, BSc; Rob Smith, PhD; Franklin I. Aigbirhio, PhD; Tim D. Fryer, PhD; Young T. Hong, PhD; David K. Menon, PhD; Jonathan P. Coles, PhD



Key Points

Question Do cerebral ischemia and diffusion hypoxia have distinct pathophysiologic mechanisms in traumatic brain injury (TBI)?

Findings In this case-control study using oxygen 15–labeled and fluorine 18–labeled fluoromisonidazole positron emission tomography in 10 patients with TBI and 20 controls, tissue hypoxia after TBI was not confined to regions with structural abnormality and could occur in the absence of conventional ischemia.

Meaning This physiologic signature is consistent with microvascular ischemia and is a target for novel neuroprotective strategies.

JAMA Neurol. 2016;73(5):542-550. doi:10.1001/jamaneurol.2016.0091
Published online March 28, 2016.

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$PbtO_2 \approx CBF \times (PaO_2 - PvO_2)$

$PbtO_2$

Normal 25-40 mmHg

Hypoxia <15-20 mmHg

↓ CBF, CPP

↓ PaO_2, systemic oxygenation

↓ PvO_2, oxygen transport, Hgb

↑ barriers to oxygen diffusion

Oddo M, LeRoux PD. Brain tissue oxygen. In Monitoring in Neurocritical Care Chapter 35. Elsevier.

JOURNAL OF NEUROTRAUMA 31:630–641 (April 1, 2014)

DOI: 10.1089/neu.2013.3104

Physiological Complexity of Acute Traumatic Brain Injury in Patients Treated with a Brain Oxygen Protocol: Utility of Symbolic Regression in Predictive Modeling of a Dynamical System

Pradeep K. Narotam,[1,6] John F. Morrison,[2,6] Michael D. Schmidt,[3,4] and Narendra Nathoo[5,6]

JOURNAL OF NEUROTRAUMA 31:630–641 (April 1, 2014)

DOI: 10.1089/neu.2013.3104

SR-Model of TBI

Parameter	*Boundary conditions or tolerance range*	*Criticality*	
		Low brain oxygen	*Mortality*
$PbtO_2$	18–25 mm Hg	<25 mm Hg	<18 mm Hg
ICP	15–22 mm Hg	>23–27 mm Hg	>37mm Hg
CPP	60–75 mm Hg	<60 mm Hg >85 mm Hg	

Clinical utility of $PbtO_2$ monitoring

1. CPP management
   a. MAP target
   b. Cerebral autoregulation and individual CPP target
   c. Induced hypertension and triple H therapy
2. ICP control
   a. Choice of osmotic agent (mannitol vs. hypertonic saline)
   b. Timing for decompressive craniectomy
3. Hemoglobin threshold for blood transfusion
   a. Treatment of anemia in patients with impaired cerebrovascular reserve (poor-grade SAH)
4. Management of mechanical ventilation
   a. PaO_2/FiO_2 ratio, PEEP
   b. Optimal $PaCO_2$ target

Oddo M, LeRoux PD. Brain tissue oxygen. In Monitoring in Neurocritical Care Chapter 35. Elsevier.

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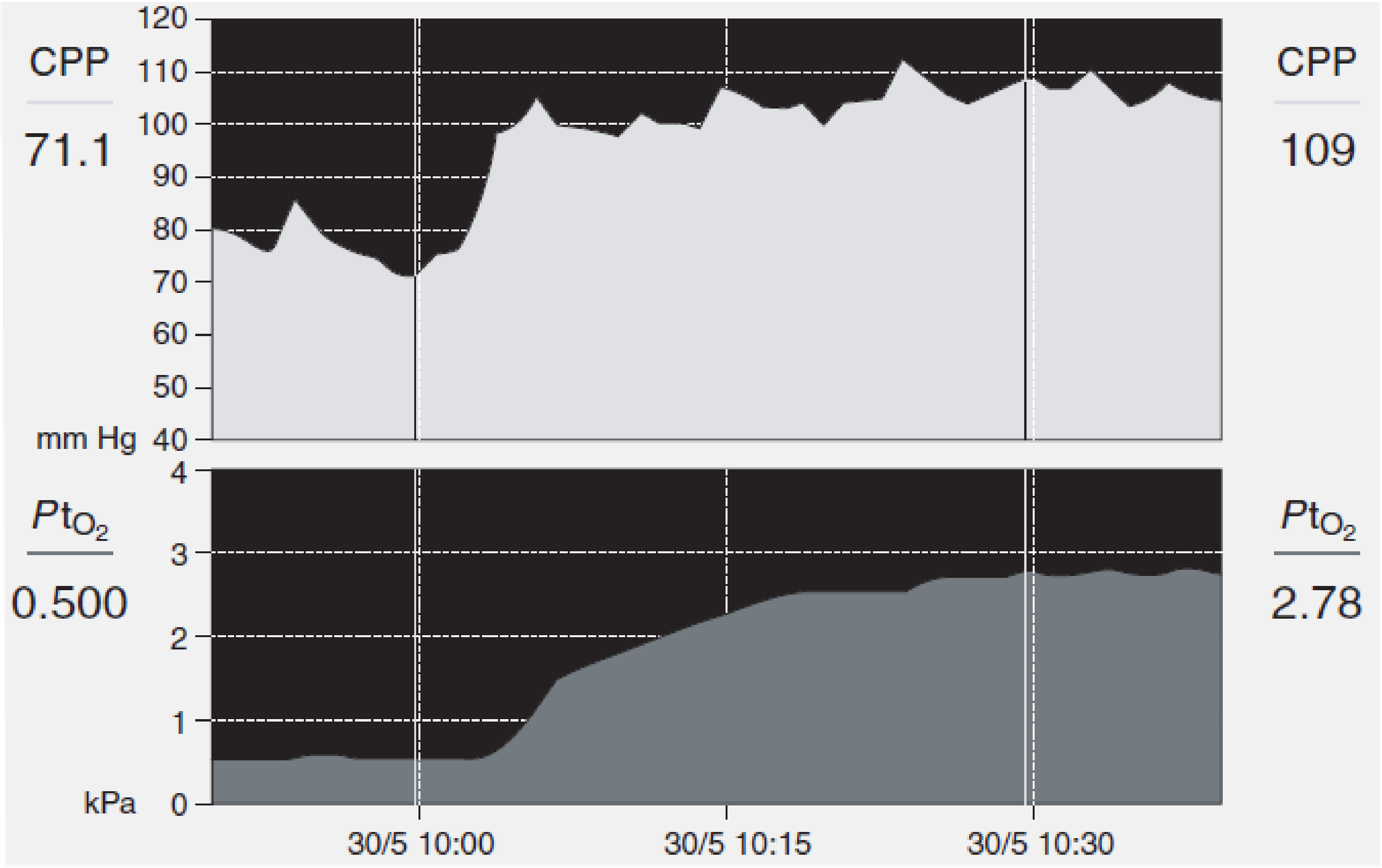
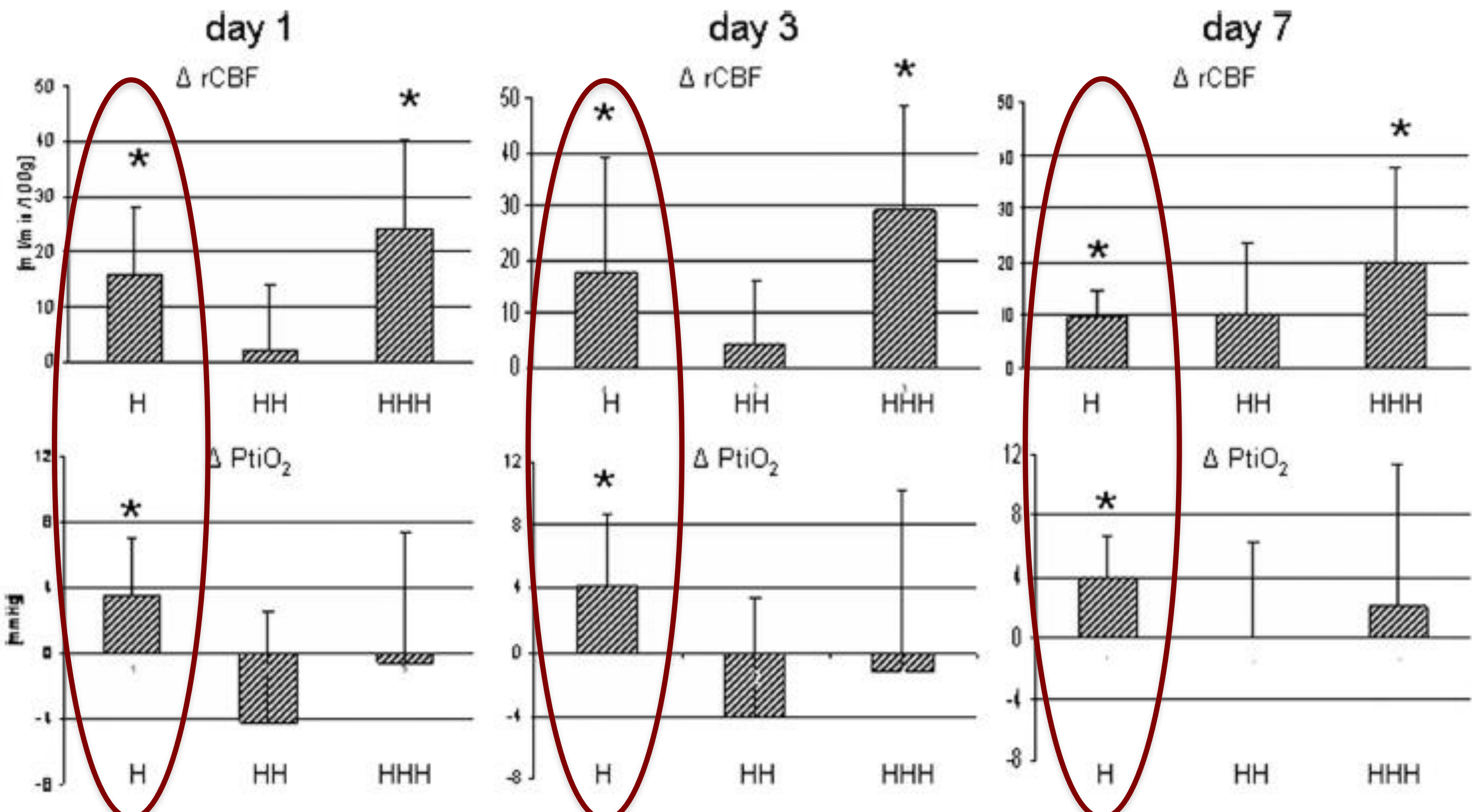
MAP/CPP augmentation



Johnston A Crit Care Med 2005; Raabe A J Neurosurgery 2005; Jaeger M Crit Care Med 2006; Nortje J Br J Anaesth 2006; Jaeger M Crit Care Med 2010

$PbtO_2$ response to MAP/CPP augmentation after SAH



H= induced hypertension alone   HH= hypervolemia-hemodilution   HHH= H + HH

Muench E et al. Crit Care Med 2007

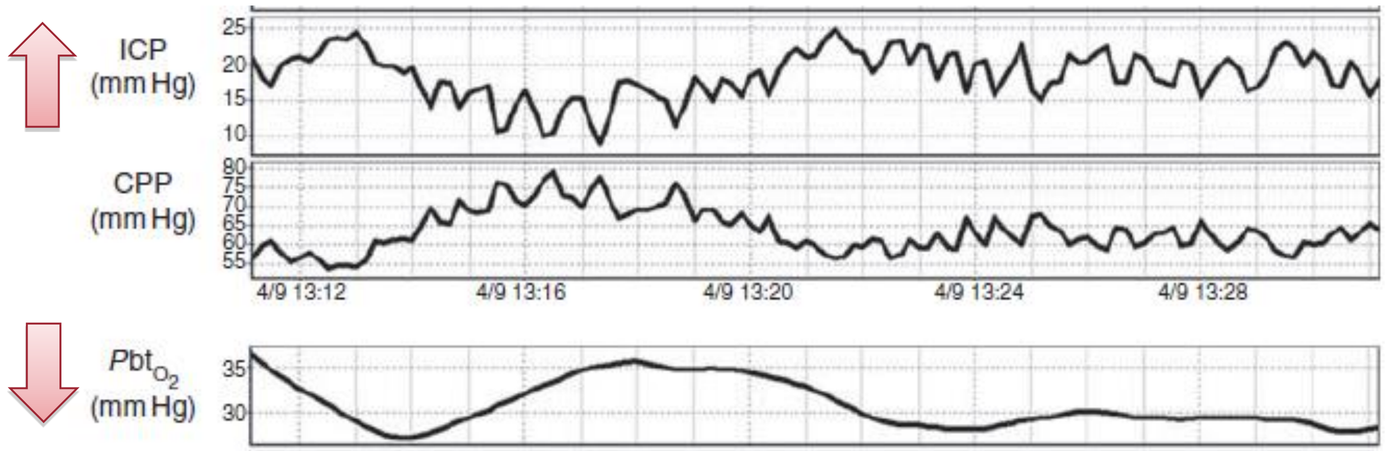


TABLE 5. Outcome in Patients With Intracranial Hypertension (Intracranial Pressure > 20 mm Hg) and Low Cerebral Perfusion Pressure (< 60 mm Hg) According to the Presence or Absence of Brain Hypoxia ($PbtO_2$ < 15 mm Hg)[a]

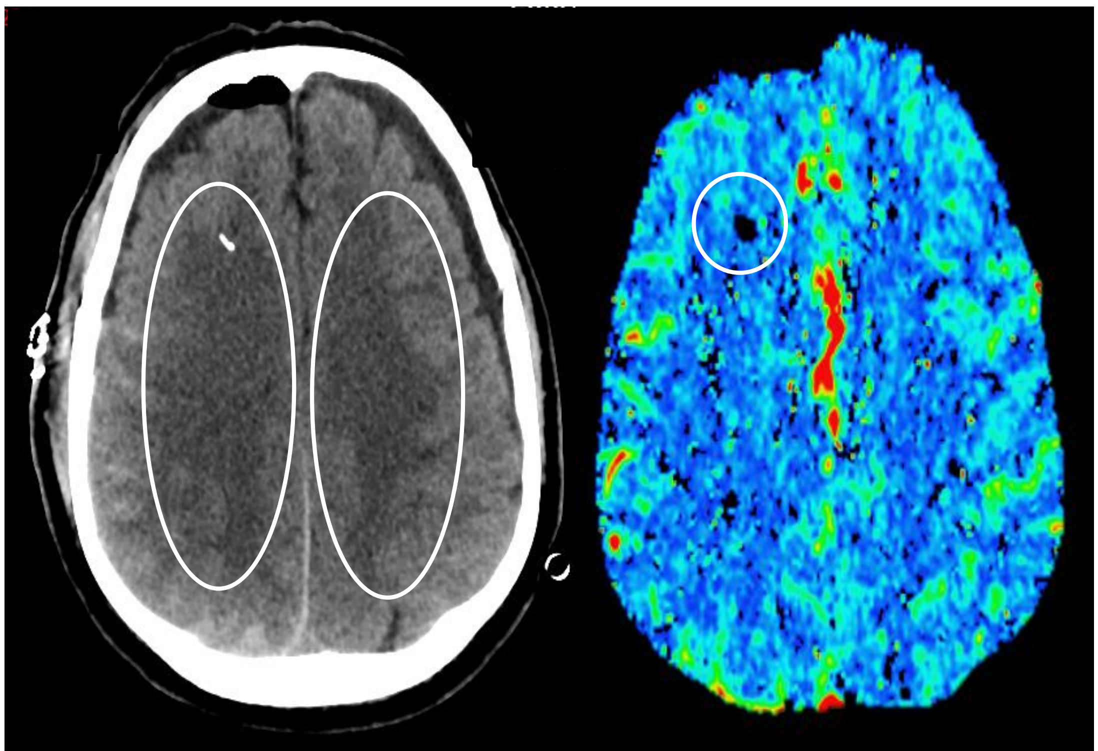
	Patients With Favorable Outcome, n (%)	
	Intracranial Hypertension (n = 74)	Low CPP (n = 75)
Brain hypoxia	20/43 (46)	18/46 (39)
No brain hypoxia	25/31 (81)	24/29 (83)
P	< .01	< .01

N=103 patients with severe TBI monitored with ICP and $PbtO_2$

Oddo M et al. Neurosurgery 2011

Accuracy of Brain Multimodal Monitoring to Detect Cerebral Hypoperfusion After Traumatic Brain Injury*

Pierre Bouzat, MD, PhD[1,2]; Pedro Marques-Vidal, MD, MPH[3]; Jean-Baptiste Zerlauth, MD[4]; Nathalie Sala, MD[1]; Tamarah Suys, RN, MPH[1]; Patrick Schoettker, MD[5]; Jocelyne Bloch, MD[6]; Roy T. Daniel, MD[6]; Marc Levivier, MD[6]; Reto Meuli, MD[4]; Mauro Oddo, MD[1]



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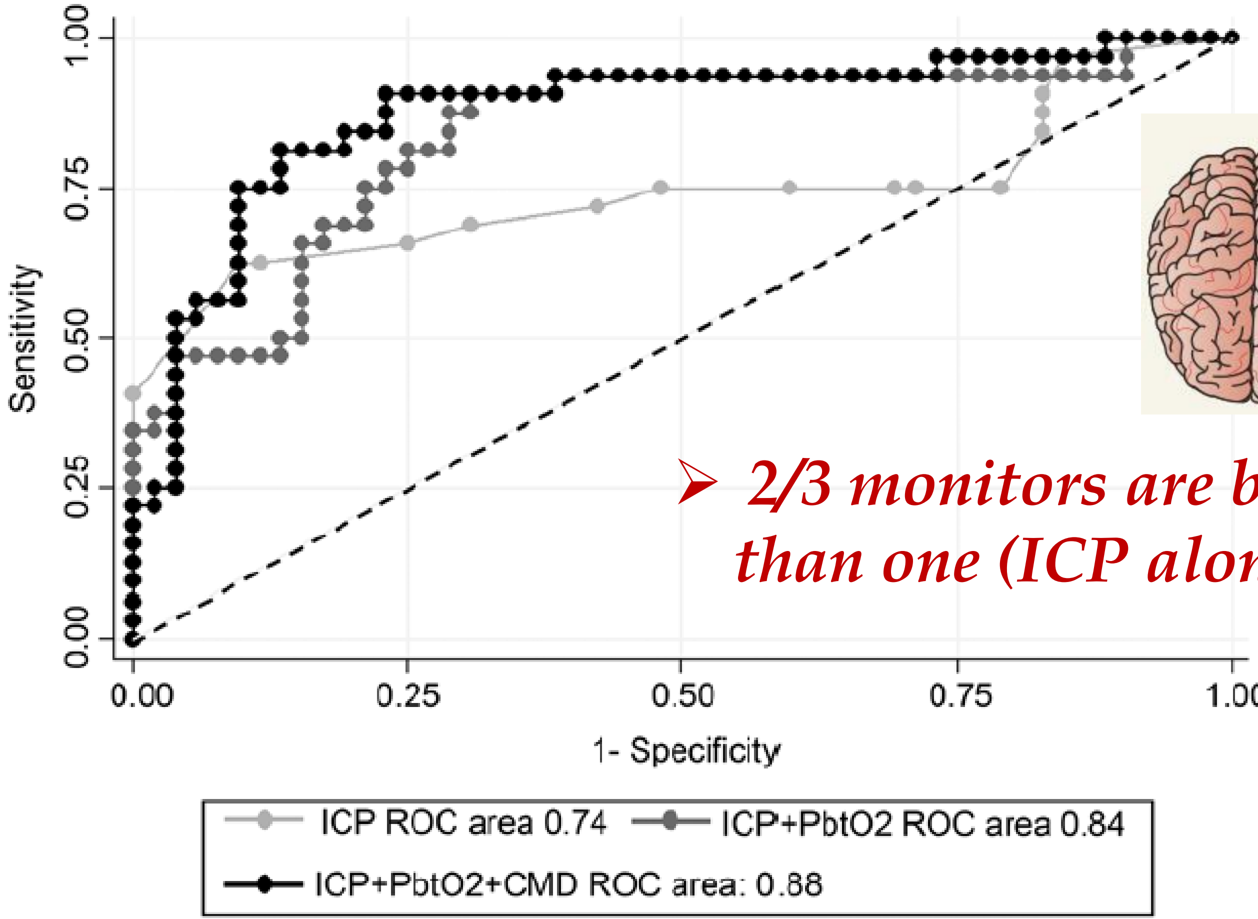
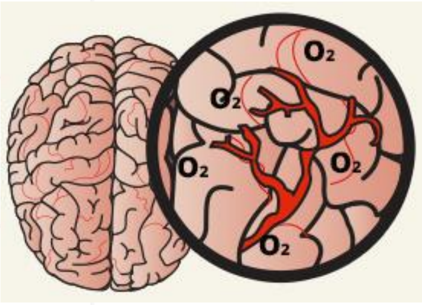




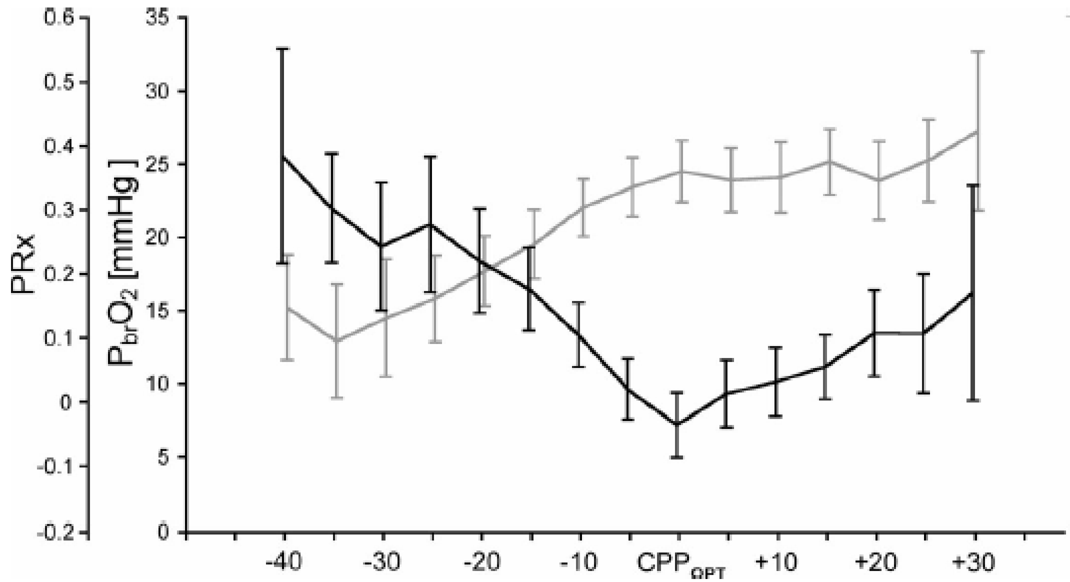
➢ ***2/3 monitors are better than one (ICP alone)***

Index	Variables	Reference
Mx (mean index, TCD-derived)	FVm/CPP	Czosnyka M, *et al.* Monitoring of cerebral autoregulation in head-injured patients. Stroke. 1996;27:1829–34.
PRx (pressure reactivity index)	ICP/MAP	Czosnyka M, *et al.* Continuous assessment of the cerebral vasomotor reactivity in head injury. Neurosurgery. 1997;41:11–7.
LDx (Doppler flowmetry index, laser Doppler flow-derived)	LDF/CPP	Lam JM, *et al.* Monitoring of autoregulation using laser doppler flowmetry in patients with head injury. J Neurosurg. 1997;86:438–45.
ORx (brain tissue oxygen reactivity index)	$PbtO_2$/CPP	Jaeger M, *et al.* Continuous assessment of cerebrovascular autoregulation after traumatic brain injury using brain tissue oxygen pressure reactivity. Crit Care Med. 2006;34:1783–8.
COx (cerebral oximetry index, NIRS-derived, Somanetics)	HbO_2/MAP	Brady KM, *et al.* Continuous time-domain analysis of cerebrovascular autoregulation using near-infrared spectroscopy. Stroke. 2007;38:2818–25.
TOx (tissue oxygenation index, NIRS-derived, Hamamatsu)	TOI/MAP	Steiner LA, *et al.* Near-infrared spectroscopy can monitor dynamic cerebral autoregulation in adults. Neurocrit Care. 2009;10(1):122–8.
HVx (haemoglobin volume index, NIRS-derived, Somanetics)	rTHb/MAP	Lee JK, *et al.* Noninvasive autoregulation monitoring in a Swine model of pediatric cardiac arrest. Anesth Analg. 2012;114(4):825–36.
THx (total haemoglobin reactivity index, NIRS-derived, Hamamatsu)	TH/MAP	Zweifel C, *et al.* Noninvasive monitoring of cerebrovascular reactivity with near infrared spectroscopy in head-injured patients. J Neurotrauma. 2010;27(11):1951–8.
PAx (pressure–amplitude index)	AMP/MAP	Radolovich DK, *et al.* Pulsatile intracranial pressure and cerebral autoregulation after traumatic brain injury. Neurocrit Care. 2011;15(3):379–86.
IAAC (single wave ICP-ABP amplitude correlation)	ICP_{SWA}/ABP_{SWA}	Eide PK, *et al.* Pressure-derived versus pressure wave amplitude-derived indices of cerebrovascular pressure reactivity in relation to early clinical state and 12-month outcome following aneurysmal subarachnoid hemorrhage. J Neurosurg. 2012;116(5):961–71.

Effects of cerebrovascular pressure reactivity-guided optimization of cerebral perfusion pressure on brain tissue oxygenation after traumatic brain injury

Crit Care Med 2010

Matthias Jaeger, MD; Markus Dengl, MD; Jürgen Meixensberger, MD, PhD;
Martin U. Schuhmann, MD, PhD



- ➢ Optimal individual CPP was found in the majority of patients and was correlated to the CPP level = plateau of $PbtO_2$
  - Average $PbtO_2$ at optimal CPP was 24.5 mm Hg
  - Median optimal CPP 70 - 75 mm Hg (*range 60 - 100 mm Hg*)

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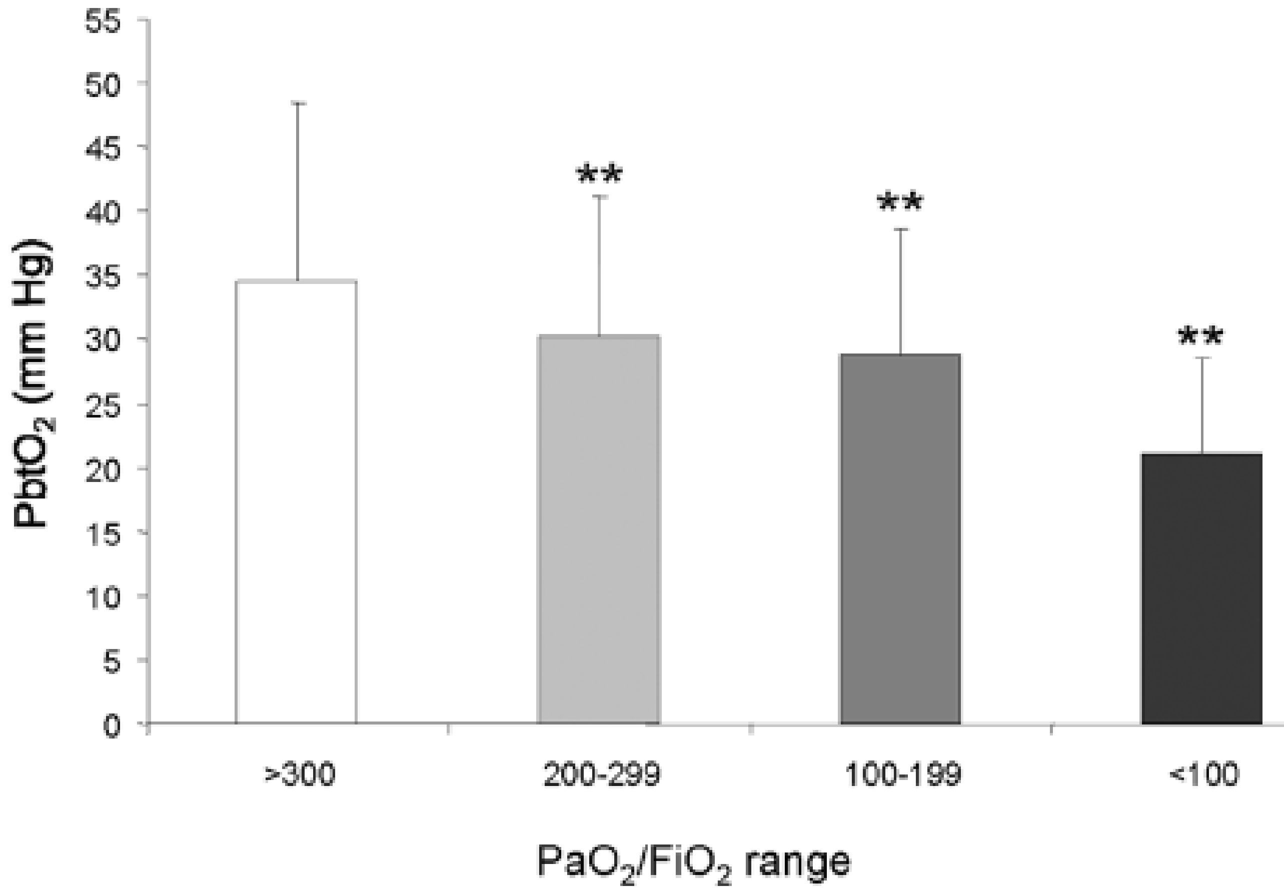
Systemic oxygenation



Neurosurgery 67:338-344, 2010

PENN
Neurosurgery

Hemoglobin Concentration and Cerebral Metabolism in Patients With Aneurysmal Subarachnoid Hemorrhage

Mauro Oddo, Andrew Milby, Isaac Chen, Suzanne Frangos, Eileen MacMurtrie, Eileen Maloney-Wilensky, Michael Stiefel, W. Andrew Kofke, Joshua M. Levine and Peter D. Le Roux

Stroke. 2009;40:1275-1281

Intensive Care Med (2012) 38:1497–1504
DOI 10.1007/s00134-012-2593-1

ORIGINAL

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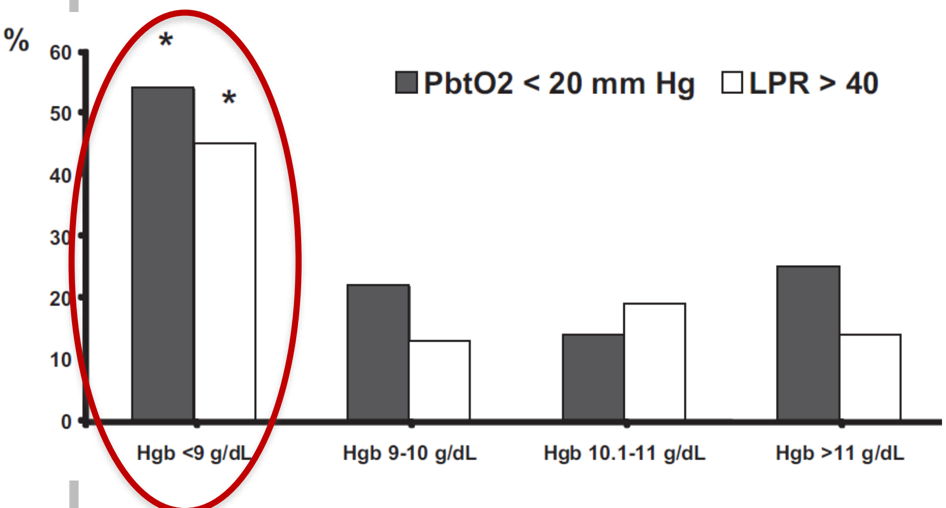
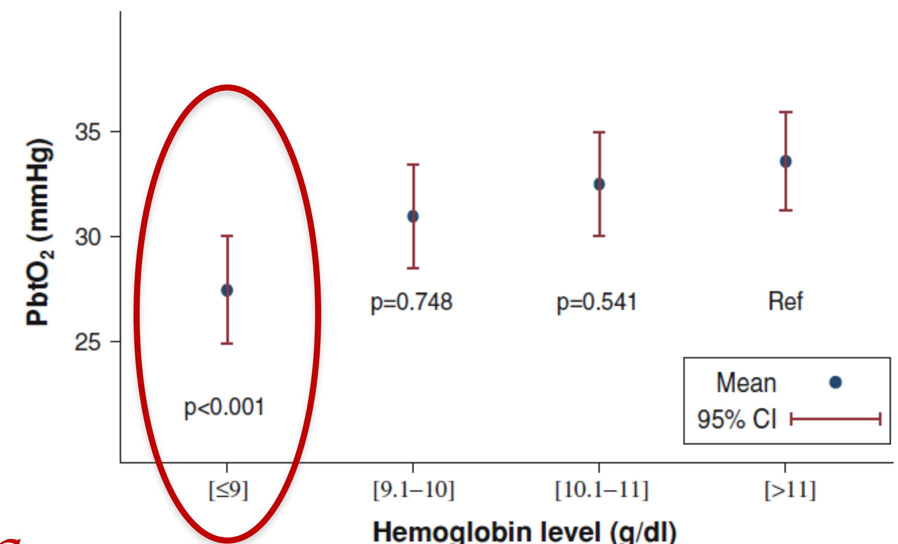
Peter D. Le Roux

Anemia and brain oxygen after severe traumatic brain injury



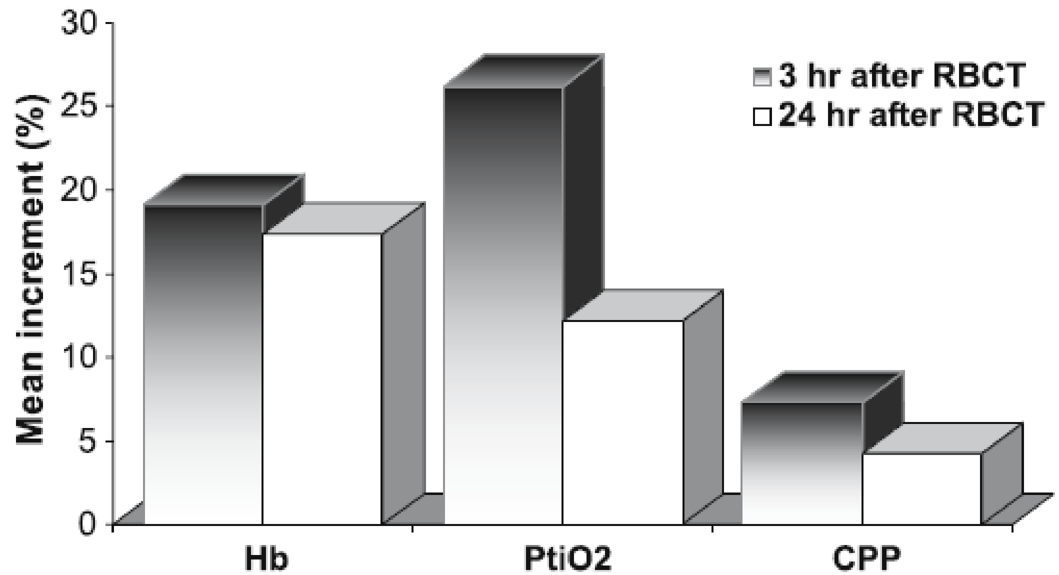


- *Hgb < 9 g/dL → hypoxia*
  - ✓ *PbtO2-targeted RBC transfusion (?)*

CHUV

RBC transfusions increase $PbtO_2$

- Leal-Noval SR
  - Int Care Med 2006



- Leal-Noval SR
  - Crit Care Med 2008
- Zygun D
  - Crit Care Med 2009

Brain Hypoxia Is Associated With Short-term Outcome After Severe Traumatic Brain Injury Independently of Intracranial Hypertension and Low Cerebral Perfusion Pressure

TABLE 6. Independent Predictors of Outcome by Multivariable Analysis[a]

Variable	Adjusted OR for Favorable Outcome	95% CI	Adjusted *P*
Marshall CT classification	0.42	0.25-0.71	.01[e]
Admission GCS	1.21	1.02-144	.03[e]
APACHE II score[b]	0.86	0.73-1.00	.05[e]
Brain hypoxia[c]	0.89	0.79-0.99	.04[e]
Intracranial hypertension[d]	0.99	0.98-1.01	.11

Oddo M et al. Neurosurgery 2011

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Author	Stud y	$PbtO_2$-therapy	ICP/CPP therapy	$PbtO_2$ threshold	Outcome endpoint	Results
Meixensberger 2003	R	52	39	10	6 months GOS	No benefit; 65% vs. 54% (P=0.27)
Stiefel 2005	R	27	26	25	mortality at hospital discharge	Reduced mortality; 25% vs.44% (P<0.05)
Martini 2009	R	123	506	20	FIM at hospital discharge	Worse outcome; FIM 7.6 vs. 8.6 (P<0.01)
Adamides 2009	P	20	10	15	6-month GOS	No difference in outcome
McCarthy 2009	P	81	64	20	3-month GOS	Better outcome; 79% vs. 61% (P=0.09)
Narotam 2009	R	127	41	20	6-month GOS	Better outcome; GOS 3.5 vs. 2.7 (P=0.01)
Spiotta 2010	R	70	53	20	3-month GOS	Better outcome; 64% vs. 40% (P=0.01)
Fletcher 2010	R	21	20	20	morbidity	Higher cumulative fluid balance and vasopressor use, higher rate of pulmonary edema
Green 2013	R	37	37	20	mortality	No benefit; 65% vs. 54% (P=0.34)

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DOI 10.1007/s12028-014-0024-6

REVIEW ARTICLE

Monitoring of Brain and Systemic Oxygenation in Neurocritical Care Patients

Mauro Oddo · Julian Bösel · and the Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring

$SjvO_2$ monitoring

– Safety

- 4 single-center studies specifically tested safety issues
  - <u>15% rate of bacterial colonization</u> susceptible to induce CRI in 1 study
  - <u>Catheter provided accuracy beyond 24 hrs in 1 study</u>
  - <u>Technical complications (catheter could not be calibrated) in 5/18 (28%) patients</u>
  - *No studies on SAH patients*

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$SjvO_2$ monitoring

– Reliability

- Proper position 26/32 (81%) pts (1 study)
- Correspondence rates when bilateral SjvO2 monitoring is performed
  - 1 study (Lam, 1996)
    - Good (80-100%) 9/13
    - Moderate (50-80%) 2/13
    - Poor 2/13
  - 1 study (Metz 1998 JCBFM)
    - SjvO2 variability rate 1.5-21.5%
  - 1 study (Stocchetti)
    - $SjvO_2$ differences of more than 15% in half of the patients

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Study	P	I	O
Fandino, 1999	TBI (n=9)	**PbtO2 vs. SjO2**	Low correlation between SjvO2 and PbtO2 during CO2 reactivity test. **In comparison to SjvO2, PbtO2 more accurately detects focal ischemic events**
Gupta, 1999	TBI (n=13)	**PbtO2 vs. SjO2**	In areas without focal pathology, good correlation between changes in SjVO2 and PbO2 (r2 = 0.69, P < 0.0001). **In areas with focal pathology, no correlation between SjVO, and PbO2 (r2 =0.07, P = 0.23). PbtO2 reflects regional brain oxygenation better than jugular bulb oximetry**.
Kiening, 1996	TBI (n=15)	**PbtO2 vs. SjO2**	**The "time of good data quality" was 95% in brain PtiO2 vs. 43% in SjvO2; PtiO2 monitoring could be performed twice as long as SjvO2 monitoring.**
Meixensberger , 1998	TBI (n=55)	**PbtO2 vs. SjO2**	**Analyzing reliability and good data quality PbtO2 (up to 95%) was superior to SjvO2 (up to 50%).**

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Near-infrared spectroscopy

- Technical problems (extra-cranial contamination)
- Lack of standardization
- No established target values, just intra-individual trends
- Very poor data quality in NICU patients
- Integration into MMM concept possible

BRAIN HYPOXIA

$PbO_2 < 20$ mm Hg

↓

1. ICP > 20 mm Hg

- treat elevated ICP

↓

2. Titrate CPP threshold

- ↑ MAP ~ 10 mm Hg (norepinephrine)

↓

3. Check PaO_2/FiO_2

- if ARDS, ↑ PEEP 2-4 cmH_2O
- adjust ventilatory parameters ($PaCO_2$)

↓

4. If Hgb < 9 g/dL

- give RBC transfusion

Bouzat P, Sala N, Payen JF, Oddo M. Annals of Intensive Care 2013

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