Norepinephrine in septic shock…

Prof. Zsolt Molnár

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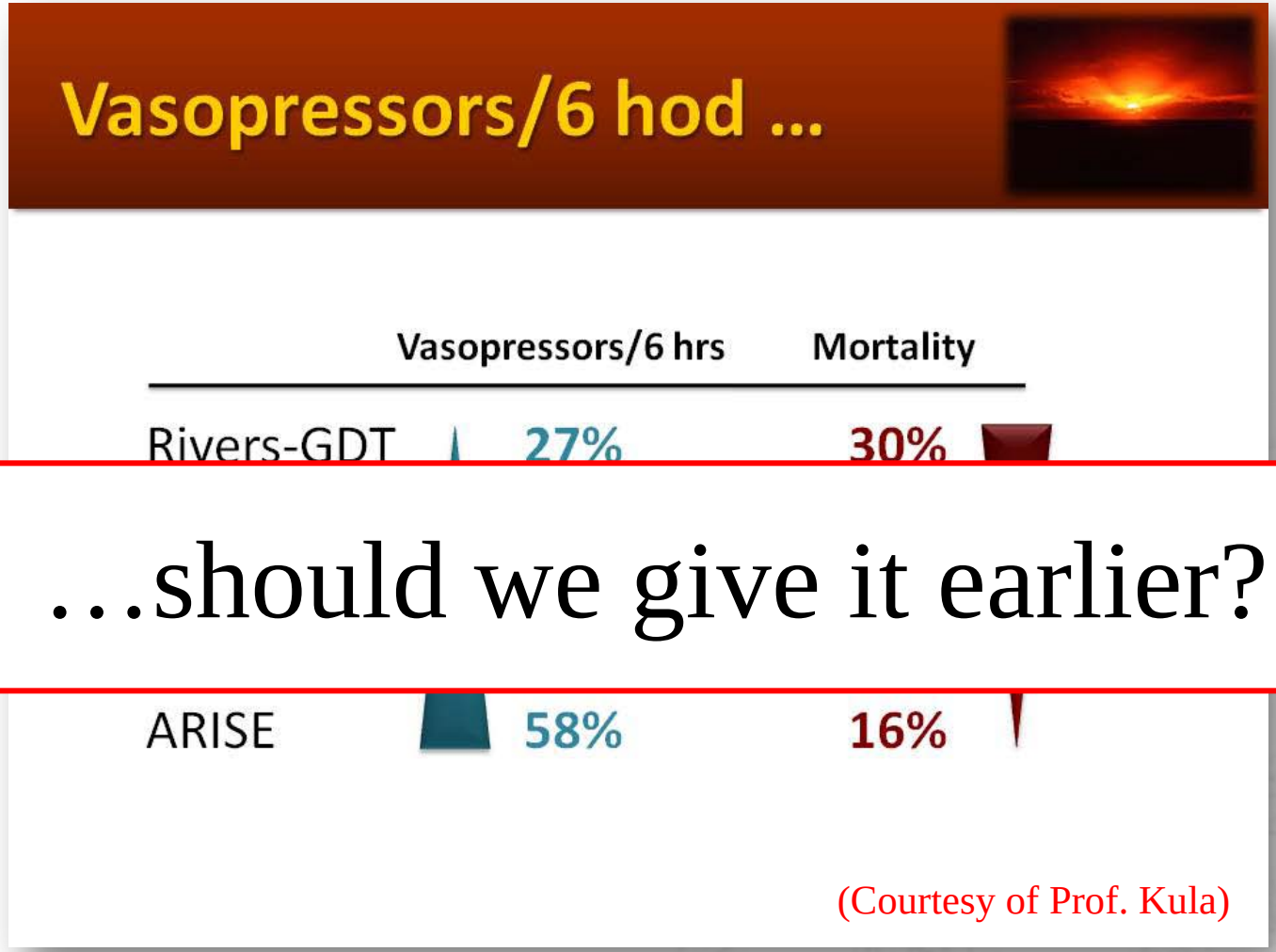
University of Szeged, Hungary

A few months ago…



…should we give it earlier?

Case - 1

- 69 year old female
- IDDM, hypertension
- Vomiting, diarrhea for 3 days
- Admission with UTI via A&E to a medical ward
- Tx: AB
- ICU referral: general deterioration, hypotension (70/… mmHg)

ICU assessment at 13:45

pCO2: 28.4

pH: 7.185

HCO3: 10.5

Laktát: 6.9

pH	7.185	(--)
PCO_2	28.4	mmHg (-)
PO_2	63.8	mmHg (-)
BE	-16.4	mmol/L
$cHCO_3^-$	10.5	mmol/L
$cHCO_{3\,st}^-$	12.0	mmol/L
SO_2	85.5	%
Glu	20.3	mmol/L (++)
Na^+	142.1	mmol/L
K^+	4.26	mmol/L
Lac	6.9	mmol/L (++)
Ca^{2+}	0.827	mmol/L (--)
Cl^-	Nincs kalibrálva	
tHb	10.7	g/dL (-)
Hct	35.9	%
COHb	0.7	%
MetHb	0.6	%
HHb	14.3	% (+)
O_2Hb	84.4	% (-)

ICU admission at 14:00

- Oxigén + 500 ml RL + Norepinephrine (10 µ/min)

↑pH

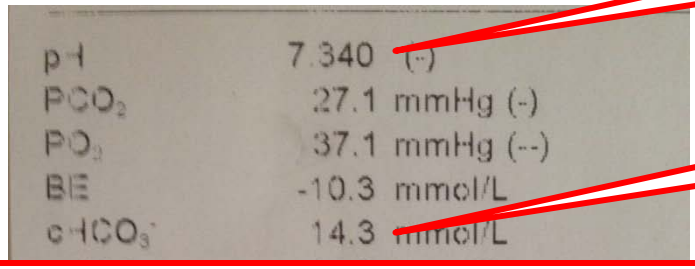
↑HCO3

↓Laktát

pH	7.276 (-)
PCO_2	26.9 mmHg (-)
PO_2	91.5 mmHg
BE	-13.1 mmol/L
$cHCO_3^-$	12.3 mmol/L
$cHCO_3^-{}_{st}$	14.1 mmol/L
SO_2	96.1 %
Glu	21.4 mmol/L (++)
Na^+	140.7 mmol/L
K^+	4.23 mmol/L
Lac	3.7 mmol/L (+)
Ca^{2+}	0.870 mmol/L (--)
Cl^-	Nincs kalibrálva
tHb	9.9 g/dL (-)
Hct	33.2 % (-)
COHb	0.5 % (-)
MetHb	0.6 %
HHb	3.8 %
O_2Hb	95.1 %

After CVC insertion at 14:30

- Oxigen + 1000 ml RL + Norepinephrine (10 µ/min)
- CV-blood gas



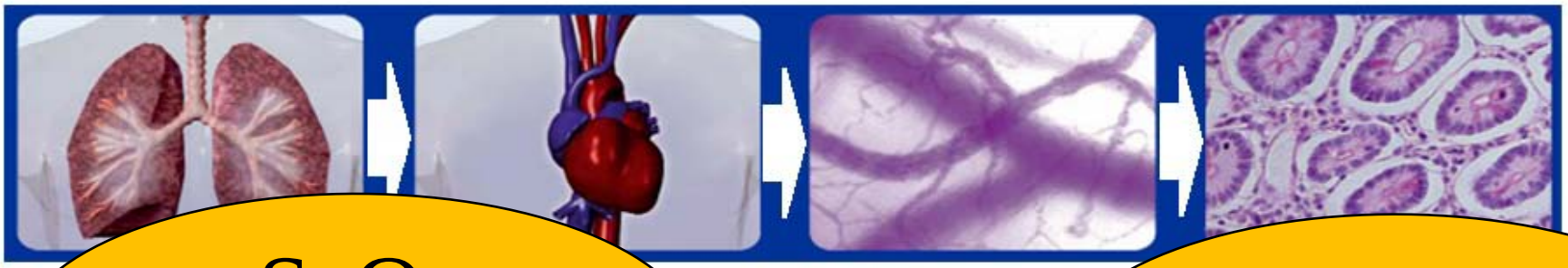
↑pH

↑HCO3

NA and my practice:
In severe hypotension – start immediately and then taper it down

Pathophysiology

Why patients get into trouble?



SaO_2 ~100%

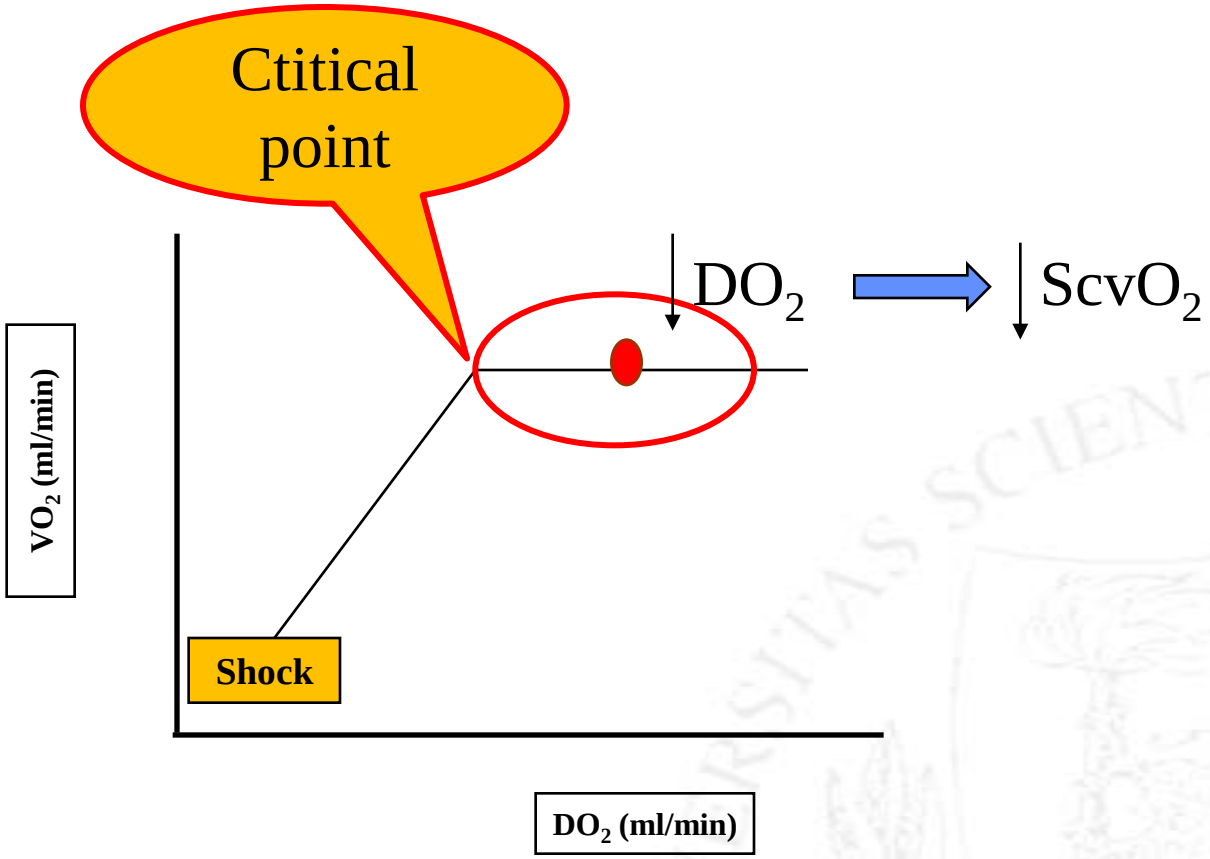
xygen

$ScvO_2$ ~70%

For adequte assessment
Evaluation of physiology (VO_2/DO_2) is needed

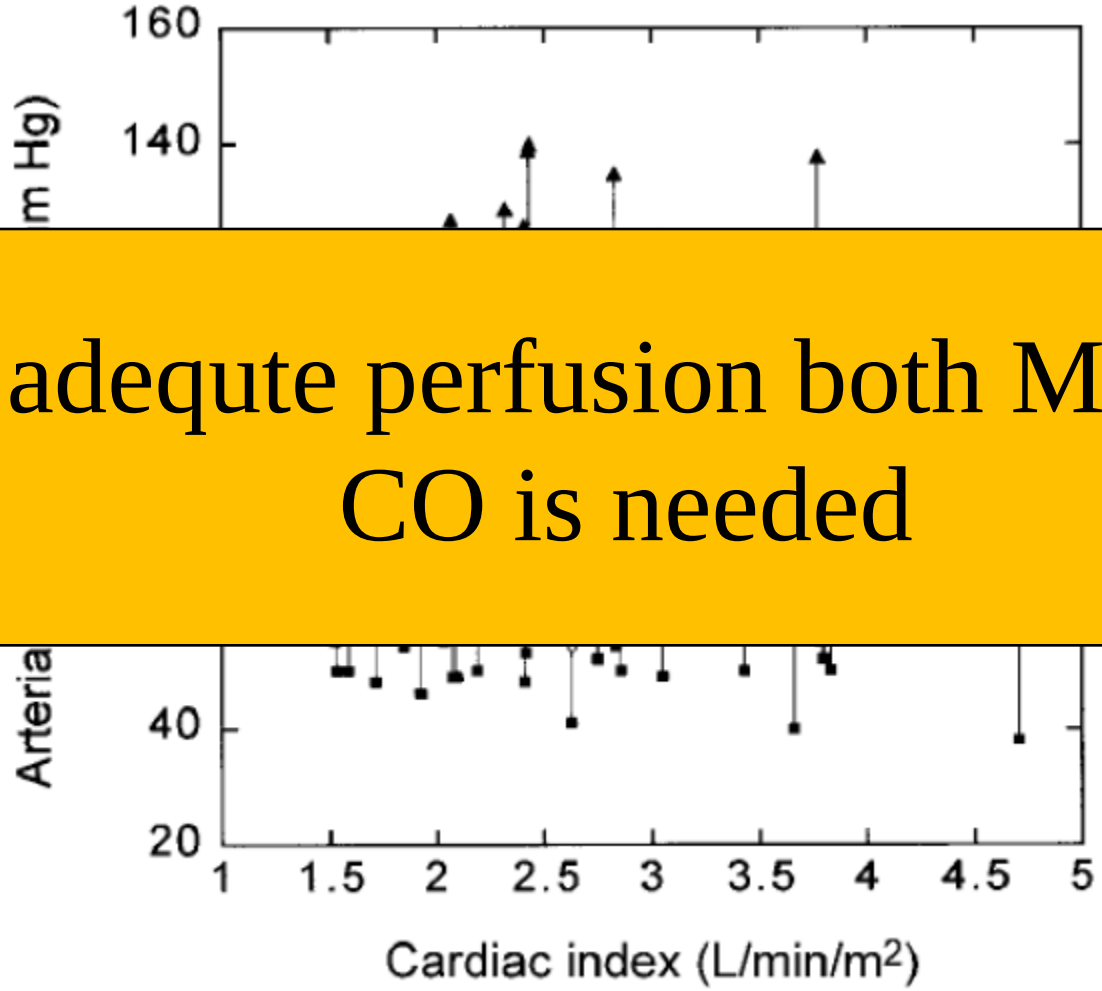
Analgesia, anaesthesia, IPPV

VO_2/DO_2 and $ScvO_2$



Blood pressure and cardiac output

Linton RA, et al. *J Cardiothorac Vasc Anesth* 2002; 16: 4-7.



For adequte perfusion both MAP and CO is needed

Intensive Care Med (2014) 40:1795–1815
DOI 10.1007/s00134-014-3525-z

Maurizio Cecconi
Daniel De Backer
Massimo Antonelli
Richard Beale
Jan Bakker
Christoph Hofer
Roman Jaeschke
Alexandre Mebazaa
Michael R. Pinsky
Jean Louis Teboul
Jean Louis Vincent
Andrew Rhodes

Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine

Table 4 Summary of the consensus statements—part 2

No.	Statement/recommendation	GRADE level of recommendation; quality of evidence	Type of statement
13.	We recommend further hemodynamic assessment (such as assessing cardiac function) to determine the type of shock if the clinical examination does not lead to a clear diagnosis	Ungraded	Best practice
14.	We suggest that, when further hemodynamic assessment is needed, echocardiography is the preferred modality to initially evaluate the type of shock as opposed to more invasive technologies	Level 2; QoE moderate (B)	Recommendation
15.	In complex patients, we suggest to additionally use pulmonary artery catheterization or transpulmonary thermodilution to determine the type of shock	Level 2; QoE low (C)	Recommendation
16.	We recommend early treatment, including hemodynamic stabilization (with fluids and vasopressors if needed) and treatment of the shock etiology, with frequent reassessment of response	Ungraded	Best practice
17.	We recommend arterial and central venous catheter insertion in shock not responsive to initial therapy and/or requiring vasopressor infusion	Ungraded	Best practice
18.	In patients with a central venous catheter, we suggest measurements of $ScvO_2$) and V-$ApCO_2$ to help assess the underlying pattern and the adequacy of cardiac output as well as to guide therapy	Level 2; QoE moderate (B)	Recommendation
19.	We recommend serial measurements of blood lactate to guide, monitor, and assess	Level 1; QoE low (C)	Recommendation
20.	We suggest the techniques to assess regional circulation or microcirculation for research purposes only	Level 2; QoE low (C)	Recommendation

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 4, 2010 VOL. 362 NO. 9

Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D., Didier Chochrad, M.D., Cesar Aldecoa, M.D., Alexandre Brasseur, M.D., Pierre Defrance, M.D., Philippe Gottignies, M.D., and Jean-Louis Vincent, M.D., Ph.D., for the SOAP II Investigators*

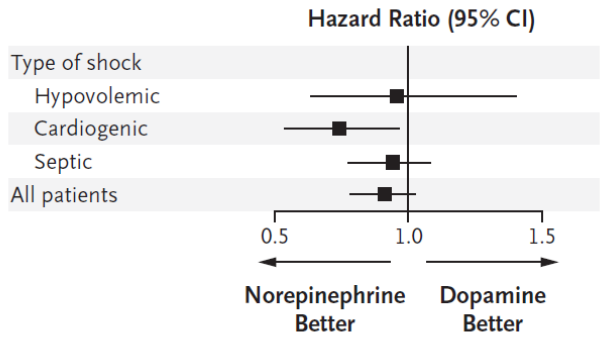


Figure 3. Forest Plot for Predefined Subgroup Analysis According to Type of Shock.

A total of 1044 patients were in septic shock (542 in the dopamine group and 502 in the norepinephrine group), 280 were in cardiogenic shock (135 in the dopamine group and 145 in the norepinephrine group), and 263 were in hypovolemic shock (138 in the dopamine group and 125 in the norepinephrine group). The P value for interaction was 0.87.

Intensive Care Med
DOI 10.1007/s00134-015-3850-x

SEVEN-DAY PROFILE PUBLICATION

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Christoph Hofer
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Sameer Jog
Michael Sander
Claudia Spies
Jean-Yves Lefrant
Daniel De Backer
on behalf of the FENICE Investigators
and the ESICM Trial Group

Fluid challenges in intensive care: the FENICE study

A global inception cohort study

Table 3 Indications and variables used to predict fluid responsiveness ($N = 2213$)

Indication	n (%)
Hypotension	1211 (58.7 [56.7–60.8])
Weaning vasopressor	146 (7.1 [6.0–8.2])
Cardiac output	62 (3.0) [2.3–3.7]
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Lactate	128 (6.2 [5.2–7.2])
$SvO_2/ScvO_2$	10 (0.5 [0.2–0.8])
SVV/PPV	37 (1.8 [1.3–2.4])
CVP/PAOP	60 (2.9 [2.2–3.6])

59%

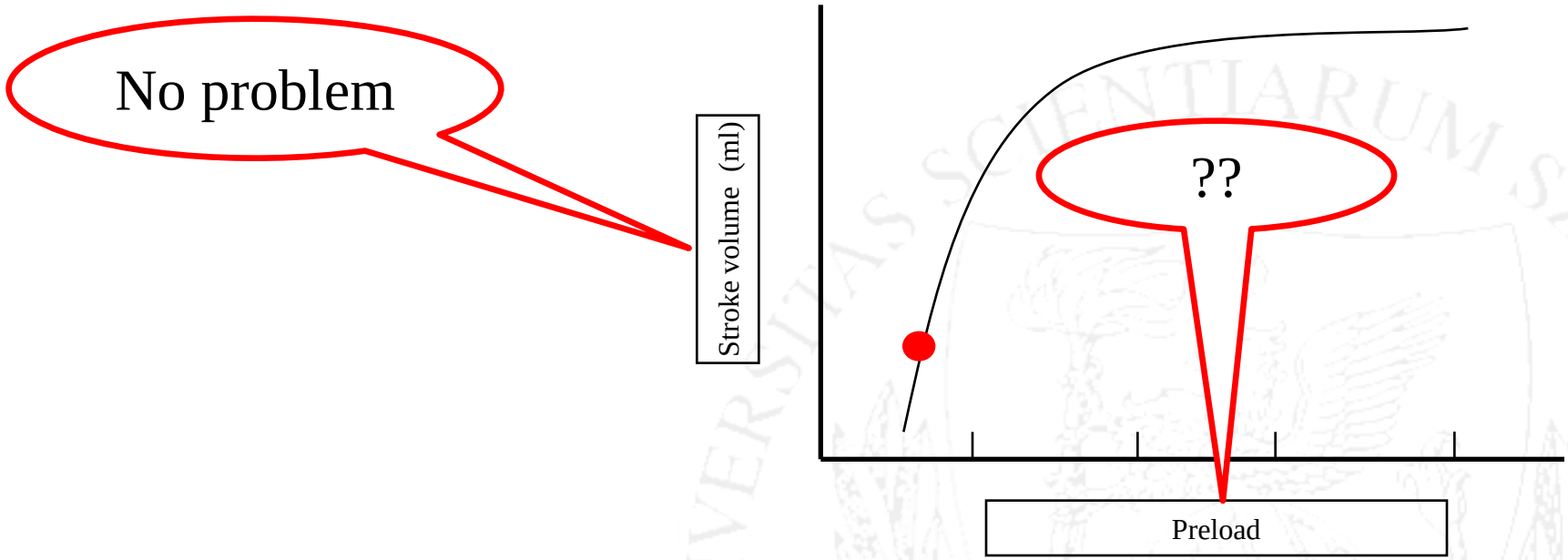
Pioneers

- Otto Frank (1865-1944):
  - Physiologist (Leipzich)
  - Zur Dynamik des Herzmuskels, Z Biol 32 (1895) 370

- Ernest Starling (1866-1927):
  - University College London
  - Starling forces, hormones, etc.

Hemodynamics

- Otto Frank, Ernest Starling – 1914: „Law of the heart”
  - „Within physiological limits, the force of contraction is directly proportional to the initial length of the muscle fiber”

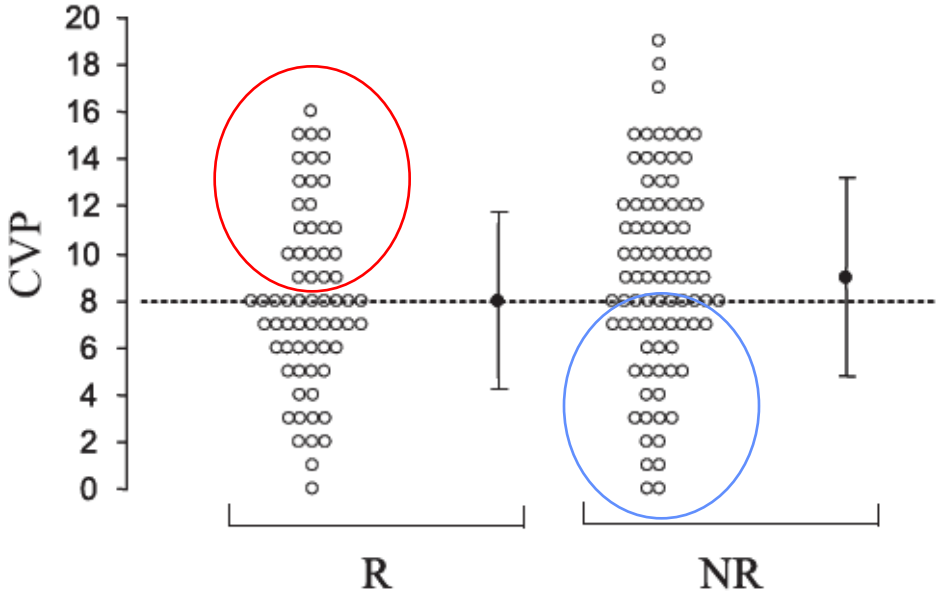


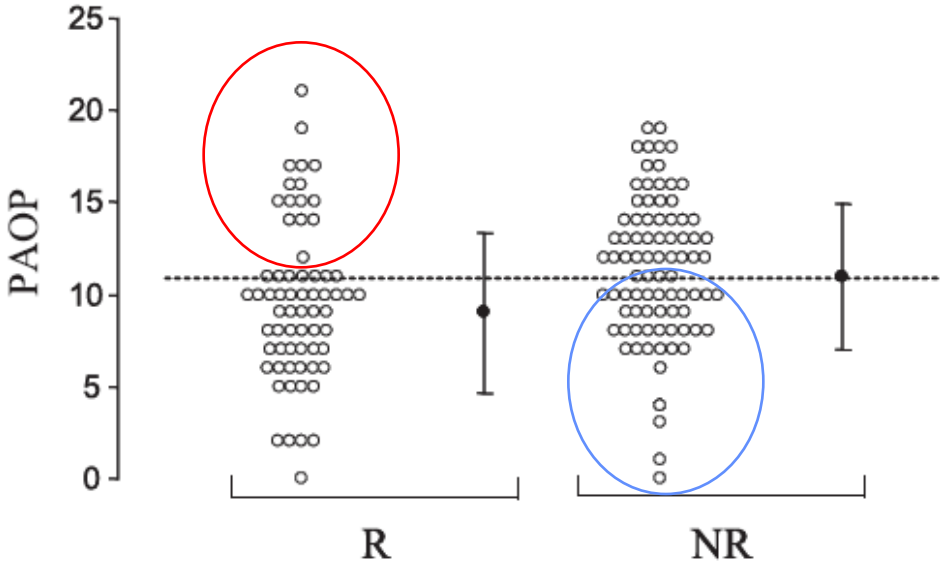
Starling EH. The Linacre Lecture on the Law of the Heart. London; 1918
Starling EH. *J R Army Med Corps*. 1920; 34: 258-262

Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge

Osman D, et al. *Crit Care Med* 2007; 35: 64-8

Pre-infusion values

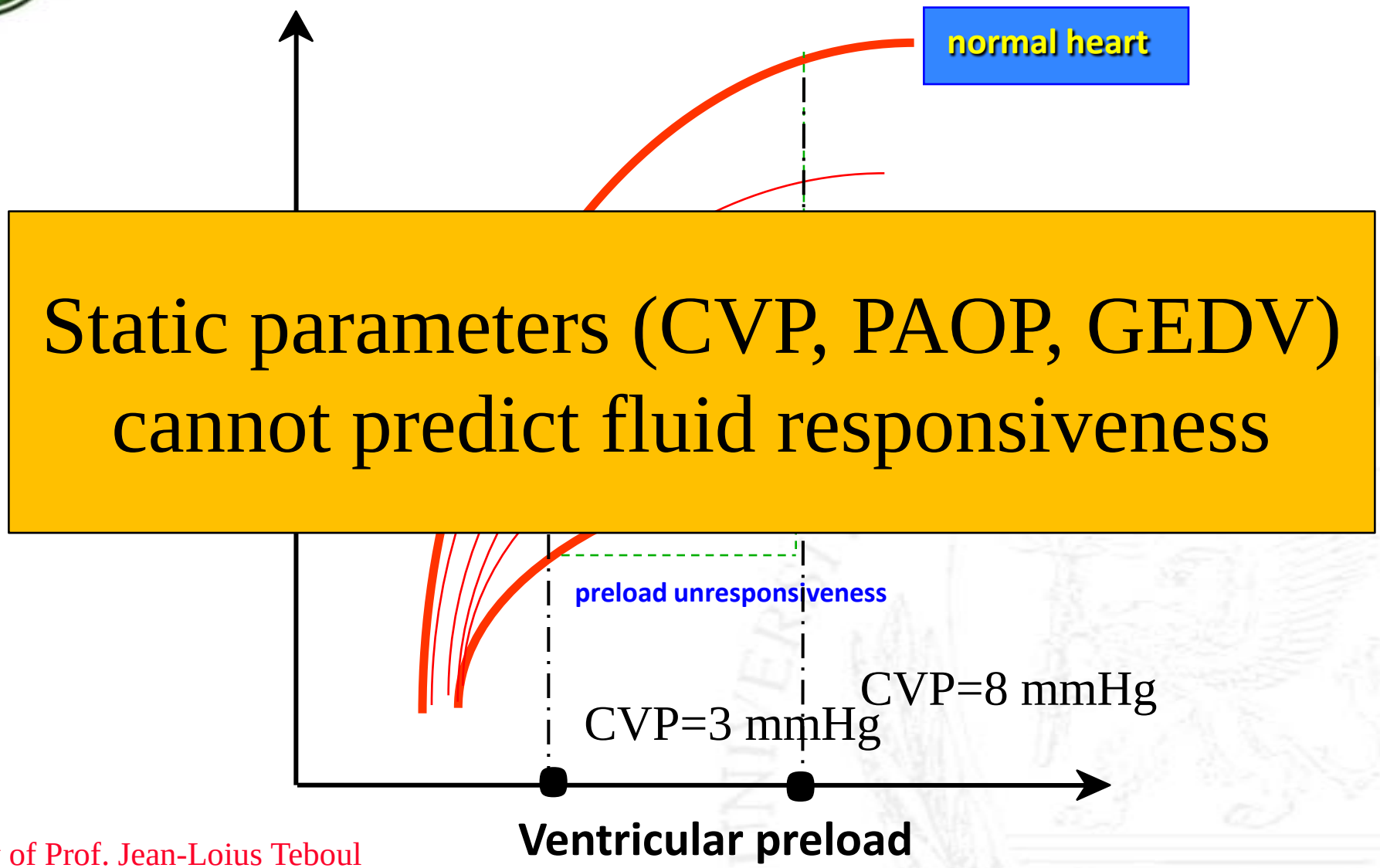




- CVP:
  - Sens: 62% (95% CI, 49–73%)
  - Spec: 54% (95% CI, 43–65%)

- PAOP:
  - Sens: 77% (95% CI, 65–87%)
  - Spec: 51% (95% CI, 40–62%)

„One size does not fit all!”

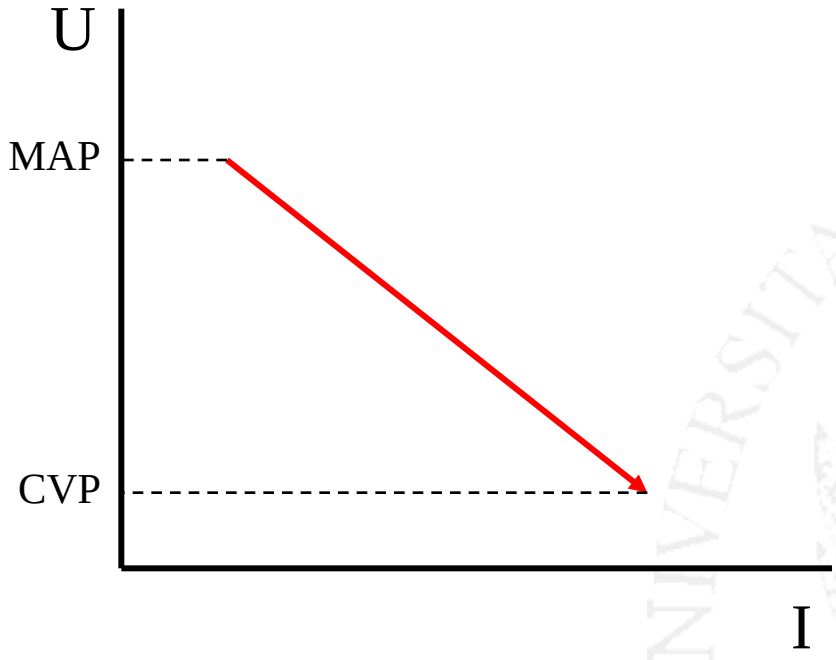


Static parameters (CVP, PAOP, GEDV) cannot predict fluid responsiveness

Courtesy of Prof. Jean-Loius Teboul

A thought on SVR…

- Ohm's law: $$R = \frac{U}{I}$$

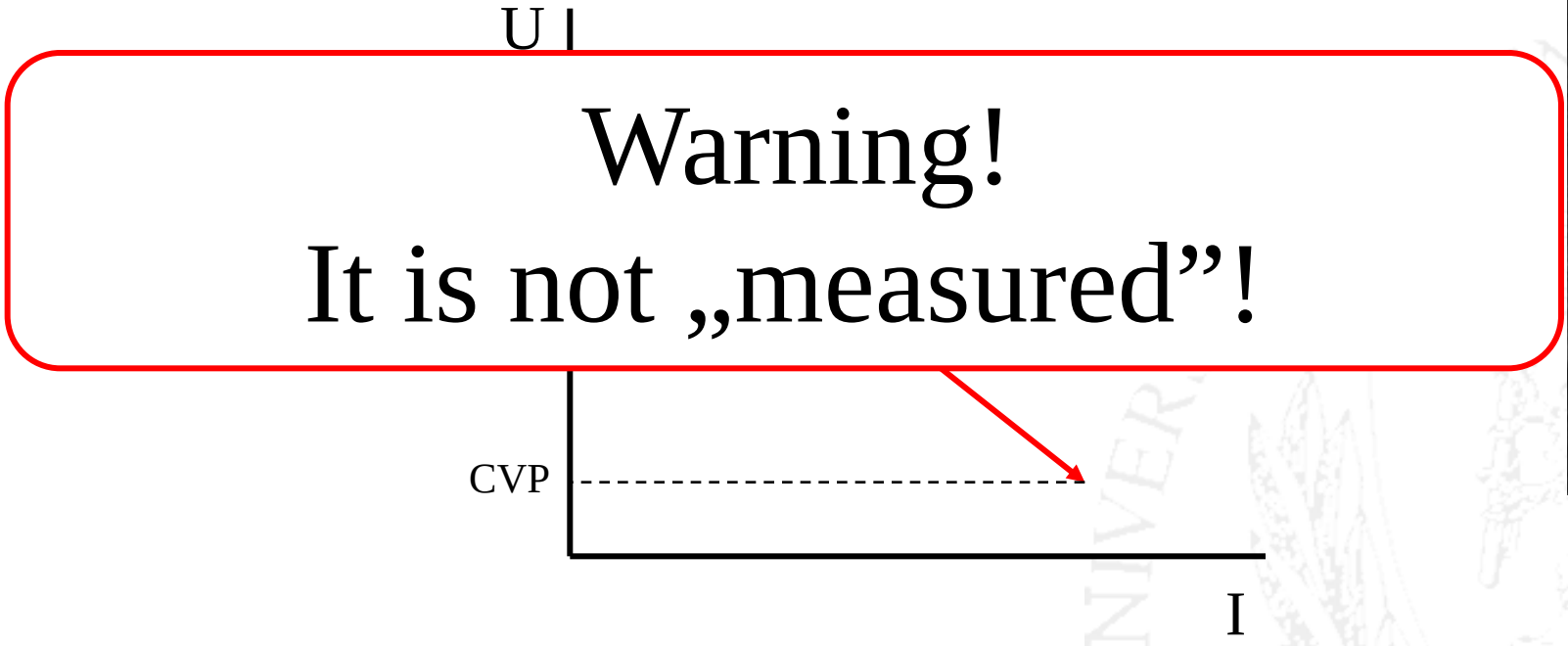


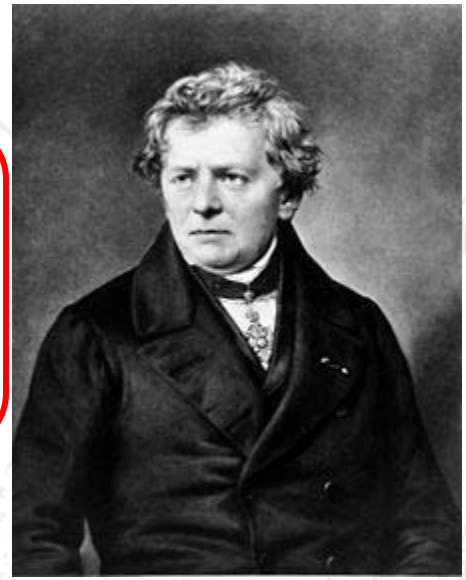
Georg Ohm
1789-1854

A thought on SVR…

- Ohm's law:

$$SVR = \frac{U}{I} = \frac{MAP - CVP}{CO} \cdot K$$





Georg Ohm
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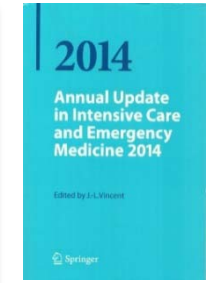
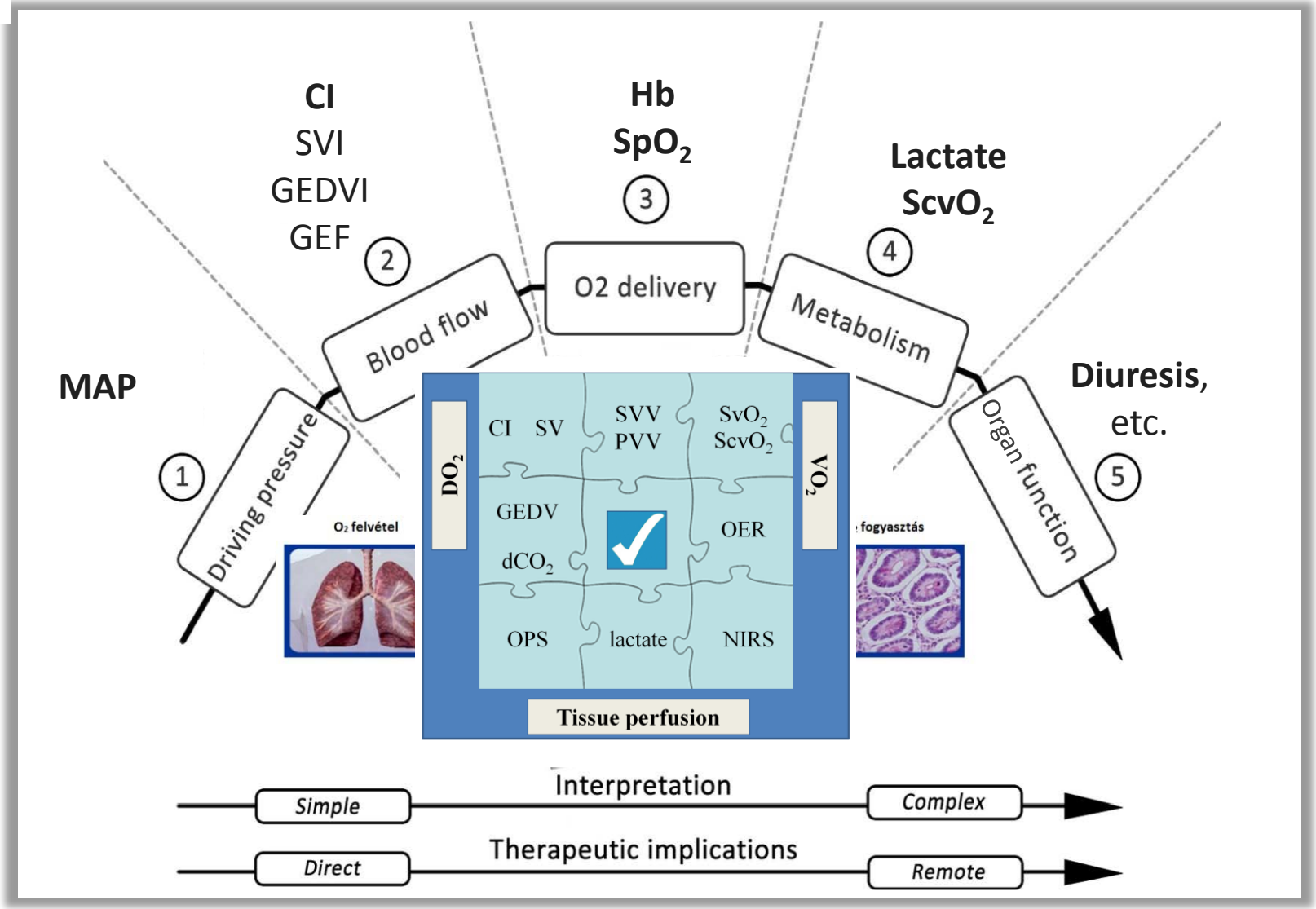
Multimodal hemodynamic monitoring

Tánczos K, Németh M, Molnár Z. *Ann. Up. in Int. Care and Em. Med*. 2014, pp:355



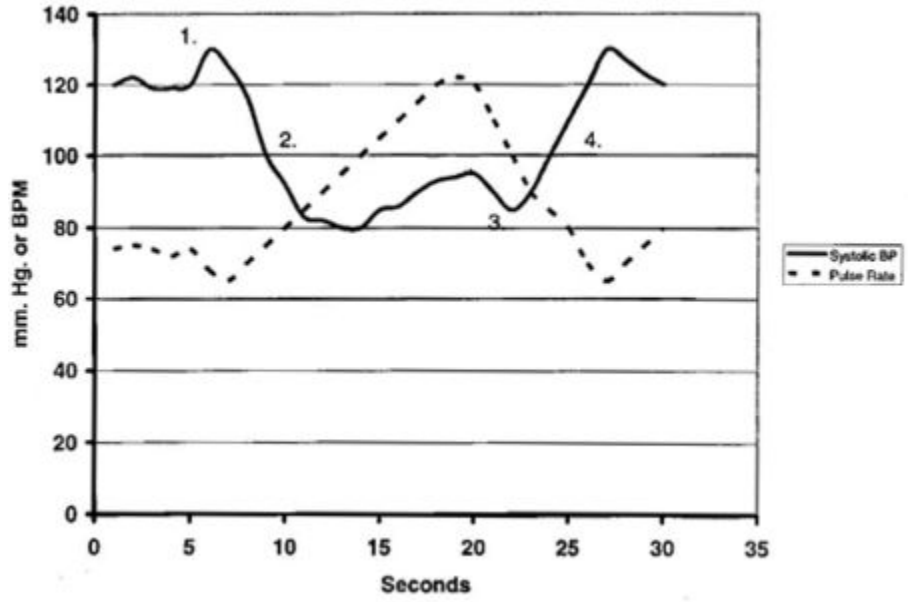


Fluid responsiveness

Heart-lung interactions

- Antonio Maria Valsalva (1666-1723)
  - Physician, phylosopher, artist
  - Anatomy of the ear

- Valsalva maneuvre:

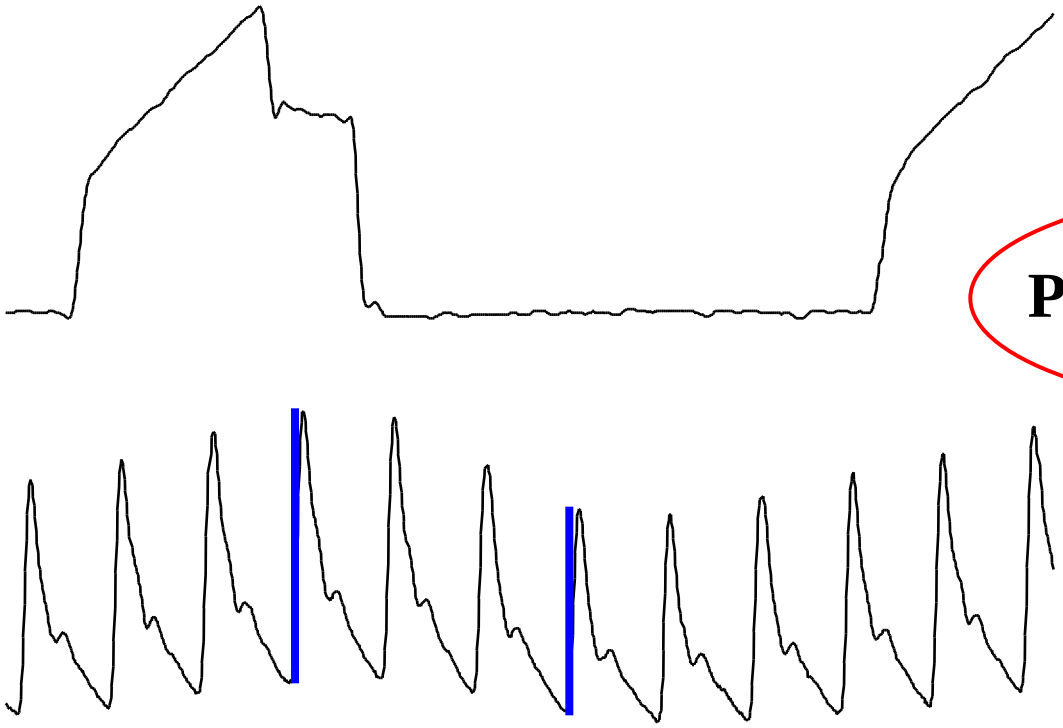


IPPV = series of Valsalva-maneuvers

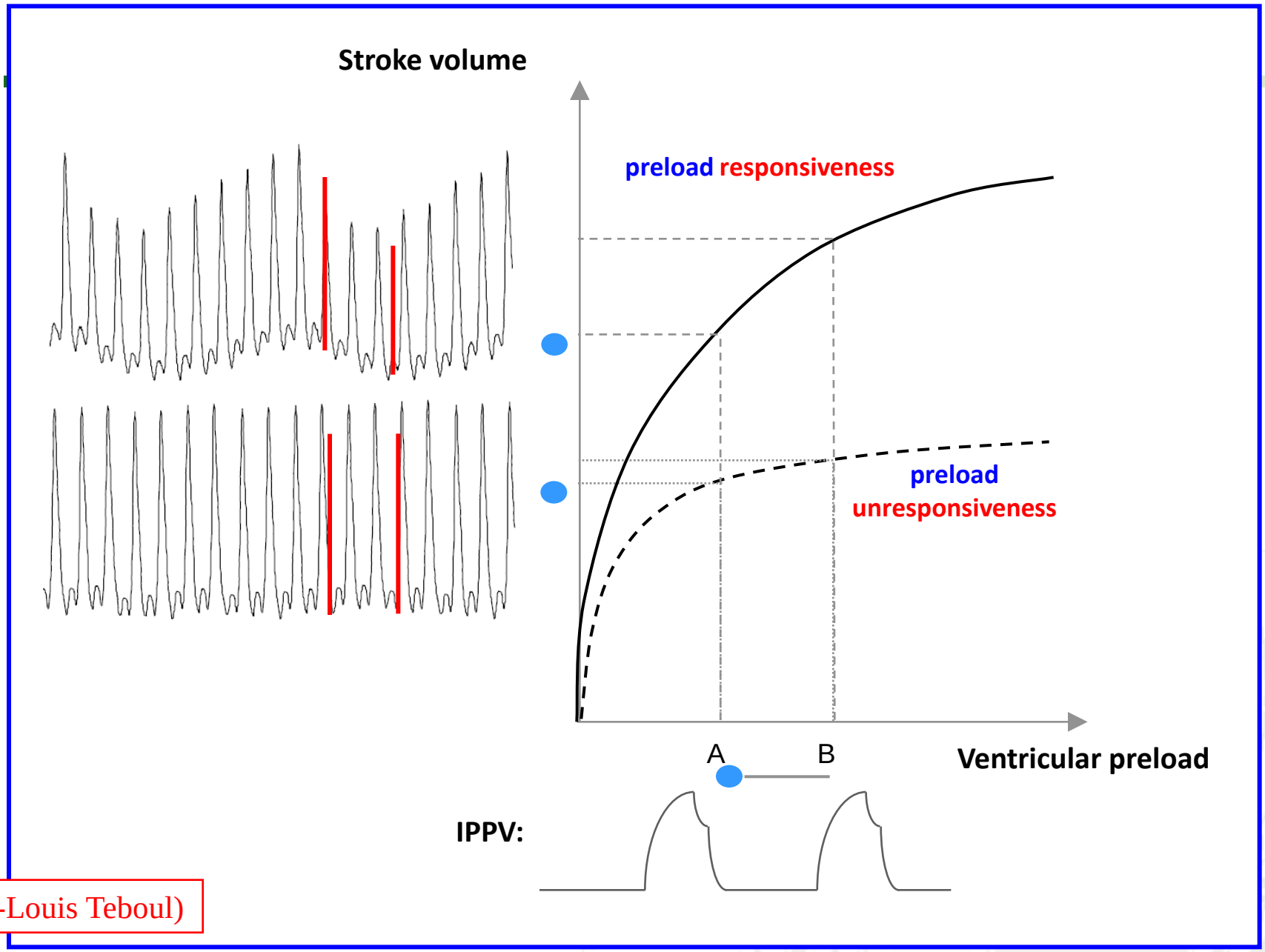
Clinical Use of Respiratory Changes in Arterial Pulse Pressure to Monitor the Hemodynamic Effects of PEEP

FRÉDÉRIC MICHARD, DENIS CHEMLA, CHRISTIAN RICHARD, MARC WYSOCKI, MICHAEL R. PINSKY, YVES LECARPENTIER, and JEAN-LOUIS TEBOUL

AM J RESPIR CRIT CARE MED 1999;159:935–939



$$PPV = \frac{PP_{max} - PP_{min}}{(PP_{max} + PP_{min}) / 2}$$



(Courtesy of Jean-Louis Teboul)

Devices


Edwards Lifesciences
Vigileo
PULSION
Medical Systems
PulsioFlex
178 cm 123 kg
SVV 2
SVRI 1902
dPmx 342

Salzwedel et al. Critical Care 2013, 17:R191
http://ccforum.com/content/17/5/R191

CRITICAL CARE

RESEARCH Open Access

Perioperative goal-directed hemodynamic therapy based on radial arterial pulse pressure variation and continuous cardiac index trending reduces postoperative complications after major abdominal surgery: a multi-center, prospective, randomized study

Cornelie Salzwedel[1†], Jaume Puig[2†], Arne Carstens[3], Berthold Bein[3], Zsolt Molnar[4], Krisztian Kiss[4], Ayyaz Hussain[5], Javier Belda[2], Mikhail Y Kirov[5], Samir G Sakka[6] and Daniel A Reuter[1*]

ProAQT-outcome study

Salzwedel C, et al. *Crit Care* 2013; 17: R191

Figure 1a: Algorithm for initial assessment.

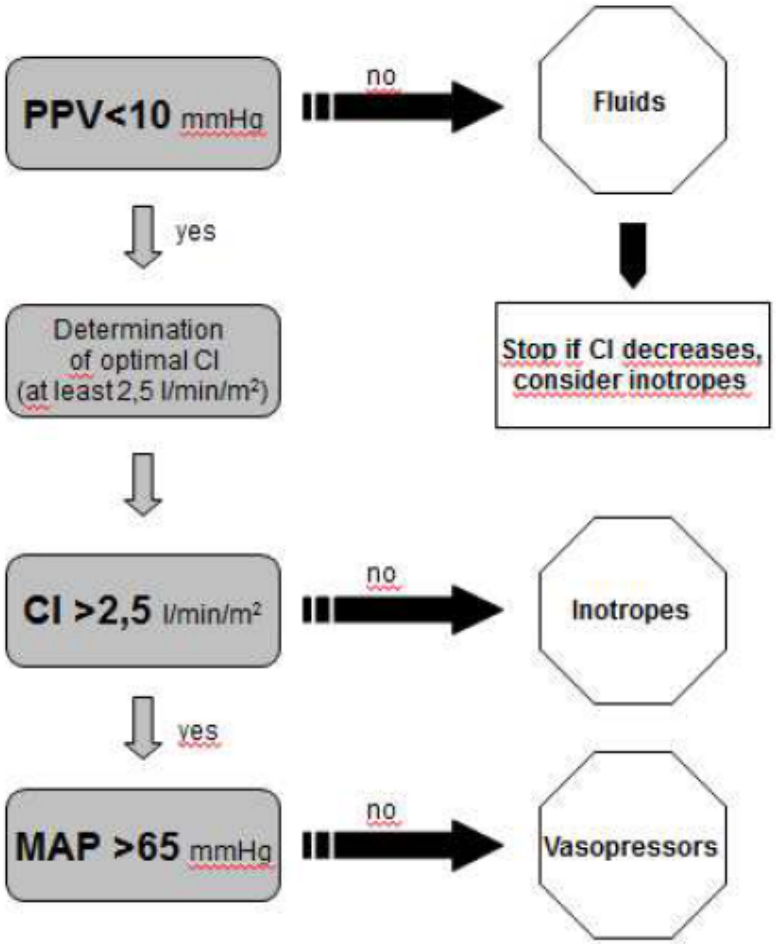
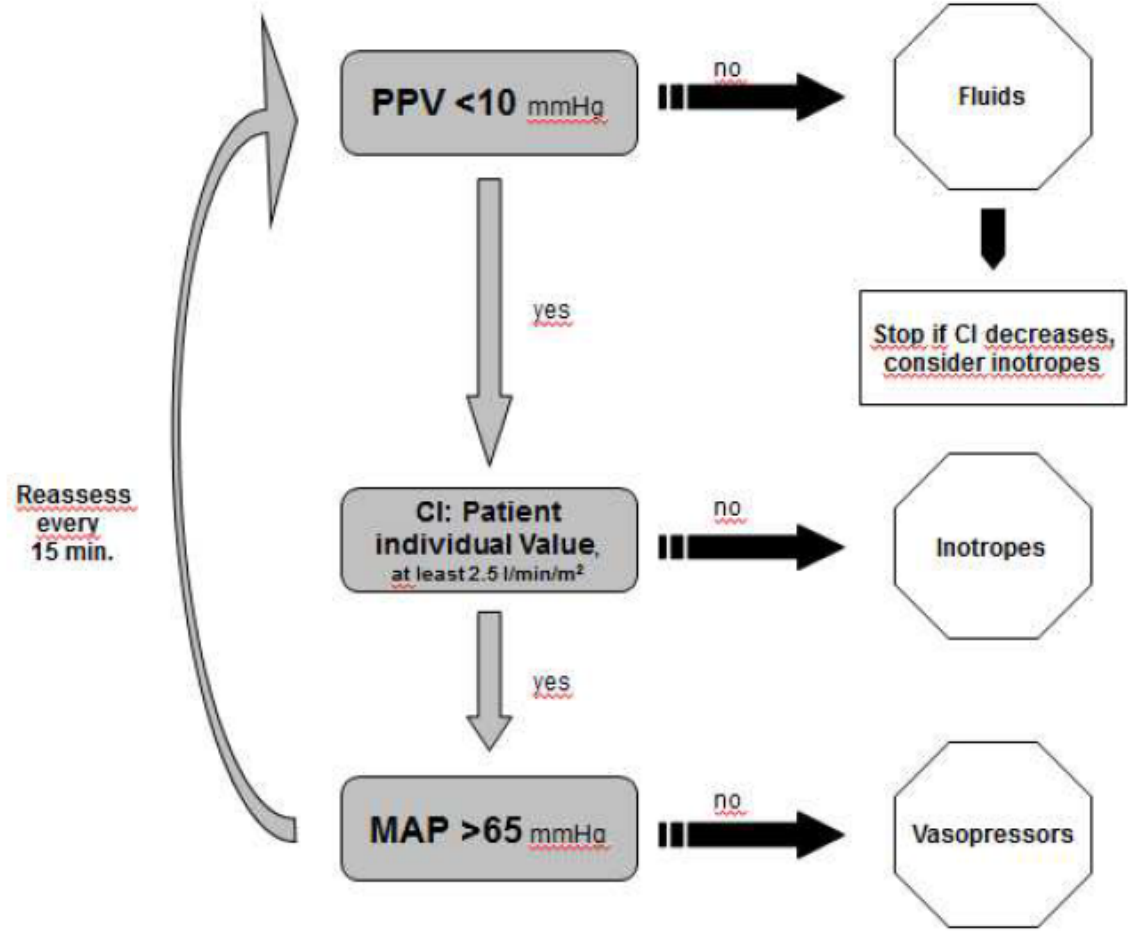
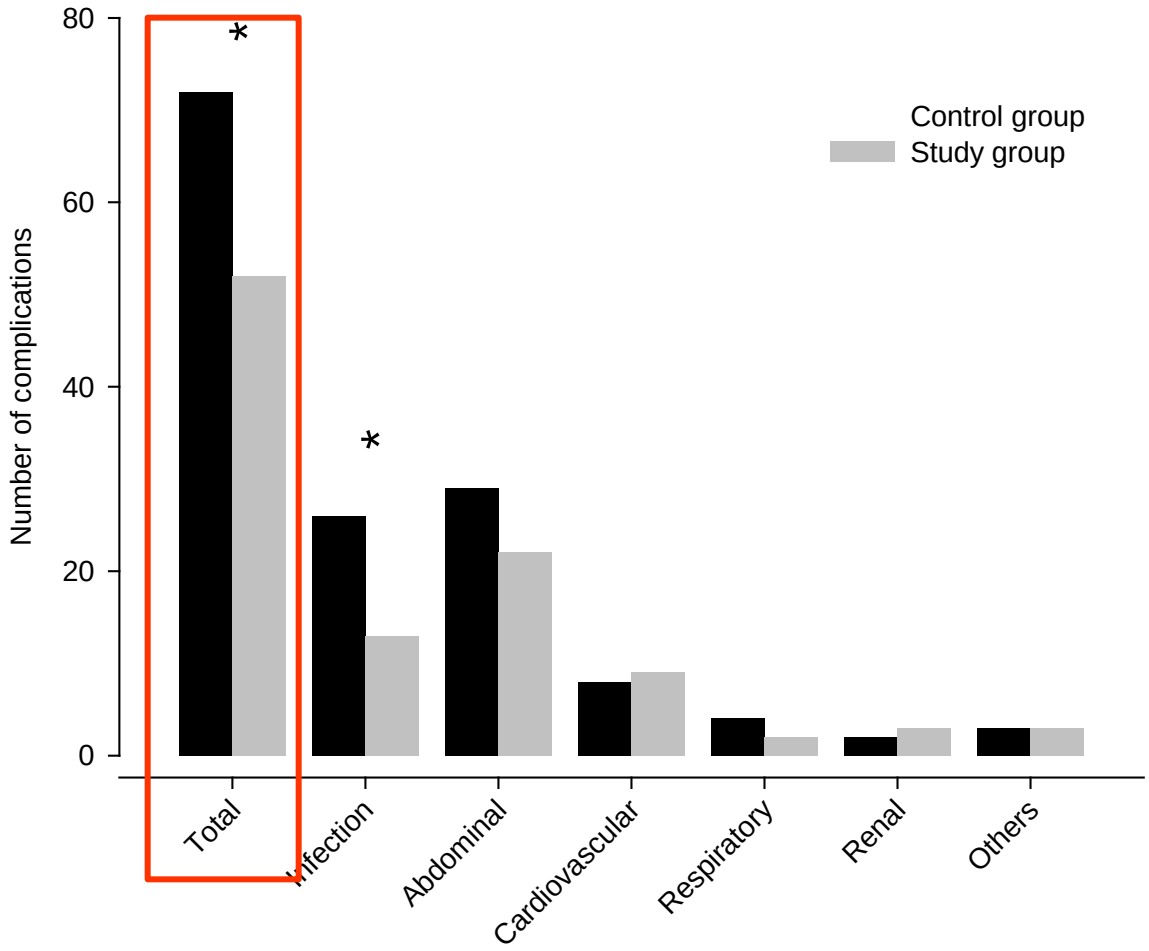


Figure 1b: Algorithm for further evaluation.



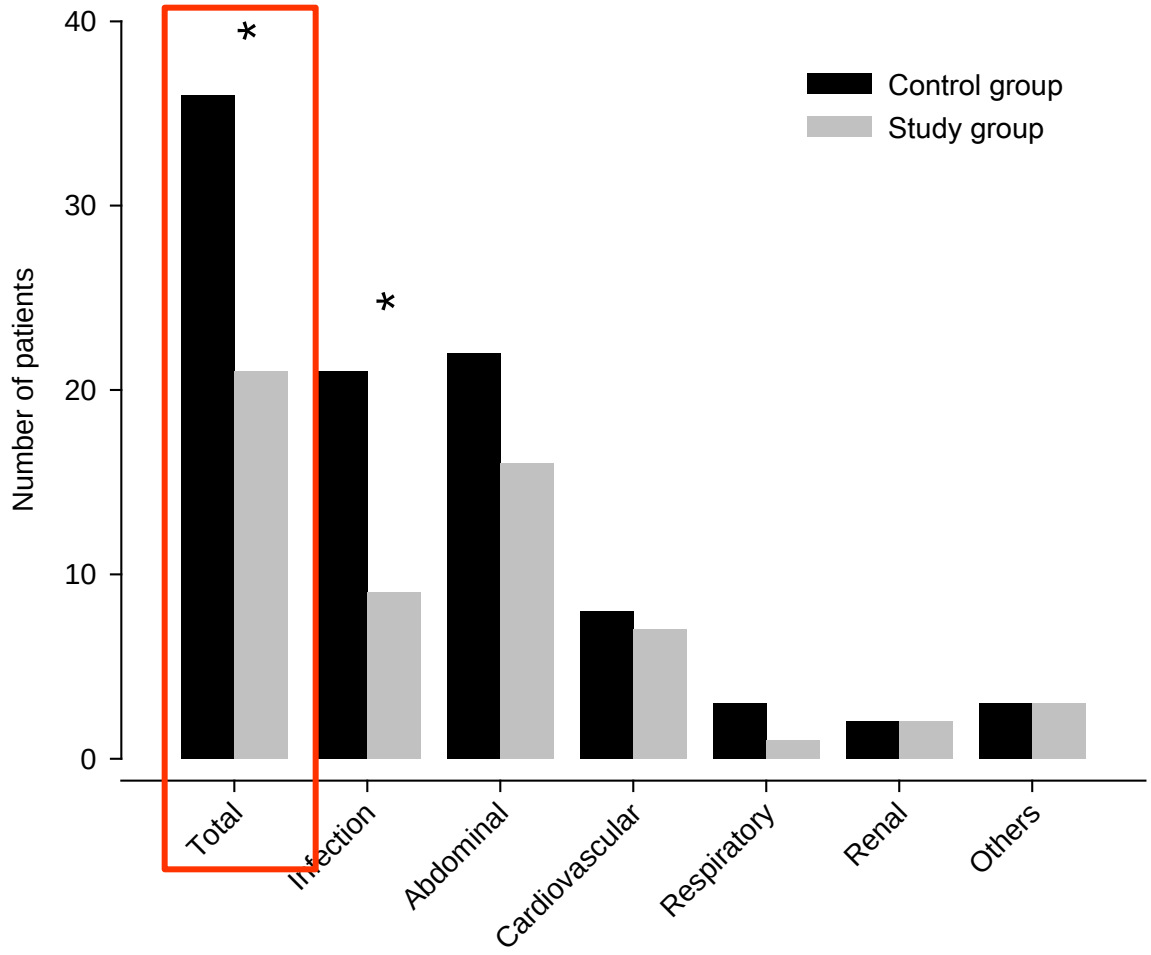
Number of complications

Salzwedel C, et al. *Crit Care* 2013; 17: R191



Number of patients with complications

Salzwedel C, et al. *Crit Care* 2013; 17: R191



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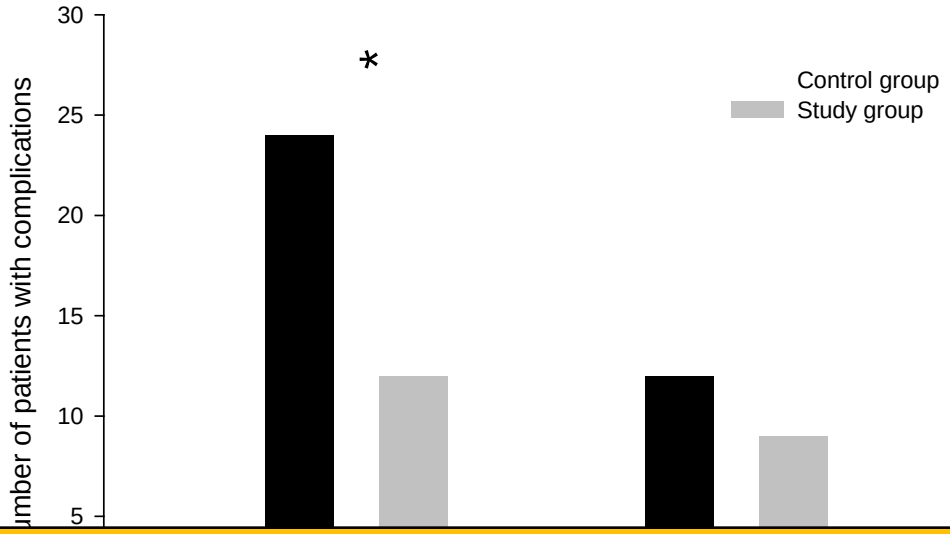
Salzwedel C, et al. *Crit Care* 2013; 17: R191



Not every patient would benefit from this (i.e.: a certain) approach

Salzwedel et al. Critical Care 2013, 17:R191
http://ccforum.com/content/17/5/R191

CRITICAL CARE

RESEARCH Open Access

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Conclusions: This multi-center study demonstrates that hemodynamic goal-directed therapy using pulse pressure variation, cardiac index trending and mean arterial pressure as the key parameters leads to a decrease in postoperative complications in patients undergoing major abdominal surgery.

Effect of a Perioperative, Cardiac Output–Guided Hemodynamic Therapy Algorithm on Outcomes Following Major Gastrointestinal Surgery

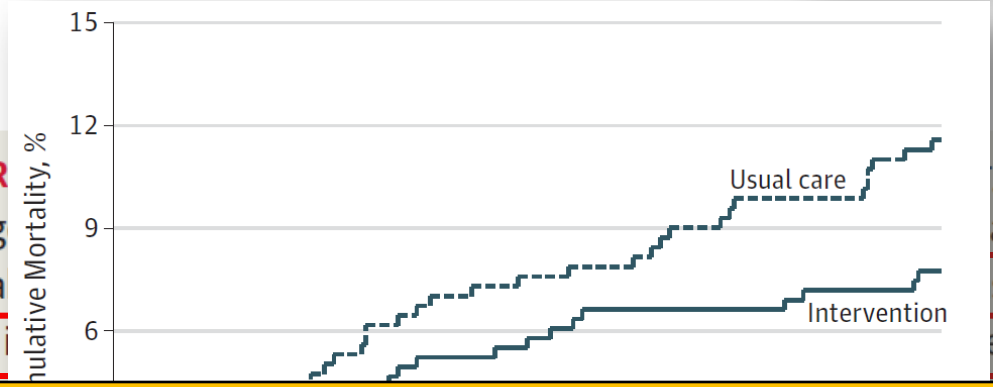
A Randomized Clinical Trial and Systematic Review

Rupert M. Pearse, MD; David A. Harrison, PhD; Neil MacDonald, FRCA; Michael A. Gillies, FRCA; Mark Blunt, FRCA; Gareth Ackland, PhD; Michael P. W. Grocott, MD; Aoife Ahern, BSc; Kathryn Griggs, MSc; Rachael Scott, PhD; Charles Hinds, FRCA; Kathryn Rowan, PhD; for the OPTIMISE Study Group

JAMA. 2014;311(21):2181-2190.

CONCLUSIONS AND R
gastrointestinal surg
compared with usua
mortality. However, i

going major
algorithm
s and 30-day
es that the



„…although could not show significant reduction in the primary outcome of the complication rate at 30 days in the cardiac output guided group, but there was a measurable treatment effect, and at 180 days there was a non-significant reduction in mortality.”

(Quote from the ESICM interview with Rupert Pearse)

What are we actually using?

Intensive Care Med
DOI 10.1007/s00134-015-3850-x

SEVEN-DAY PROFILE PUBLICATION

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A global inception cohort study

Table 3 Indications and variables used to predict fluid responsiveness ($N = 2213$)

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Hypotension	1211 (58.7 [56.7–60.8])
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CVP/PAOP	60 (2.9 [2.2–3.6])

59%

Hemodynamic variable used to predict fluid responsiveness	n	% Of category	% All
No variable used	945		42.7 [40.6–44.8]
Any variable used	1268		57.3 [55.2–59.4]

43%

Cannesson et al. Critical Care 2011, 15:R197
http://ccforum.com/content/15/4/R197

CRITICAL CARE

RESEARCH Open Access

Hemodynamic monitoring and management in patients undergoing high risk surgery: a survey among North American and European anesthesiologists

Maxime Cannesson[1*], Gunther Pestel[2], Cameron Ricks[1], Andreas Hoeft[3] and Azriel Perel[4]

	ASA respondents (n = 237)	ESA respondents (n = 195)
Answer options	**Response percent**	**Response percent**
Invasive arterial pressure	95.4%	89.7%
Central venous pressure	72.6%	83.6%
Non-invasive arterial pressure	51.9%	53.8%
Cardiac output	35.4%	34.9%
Pulmonary capillary wedge pressure	30.8%	14.4%
Transesophageal echocardiography	28.3%	19.0%
Systolic pressure variation	20.3%	23.6%

Ahmad et al. Perioperative Medicine (2015) 4:8
DOI 10.1186/s13741-015-0018-8

Perioperative Medicine

RESEARCH Open Access

Variation in haemodynamic monitoring for major surgery in European nations: secondary analysis of the EuSOS dataset

Tahania Ahmad[1†], Christian M. Beilstein[1†], Cesar Aldecoa[2], Rui P. Moreno[3], Zsolt Molnár[4], Vesna Novak-Jankovic[5], Christoph K. Hofer[6], Michael Sander[7], Andrew Rhodes[8] and Rupert M. Pearse[1,9*]

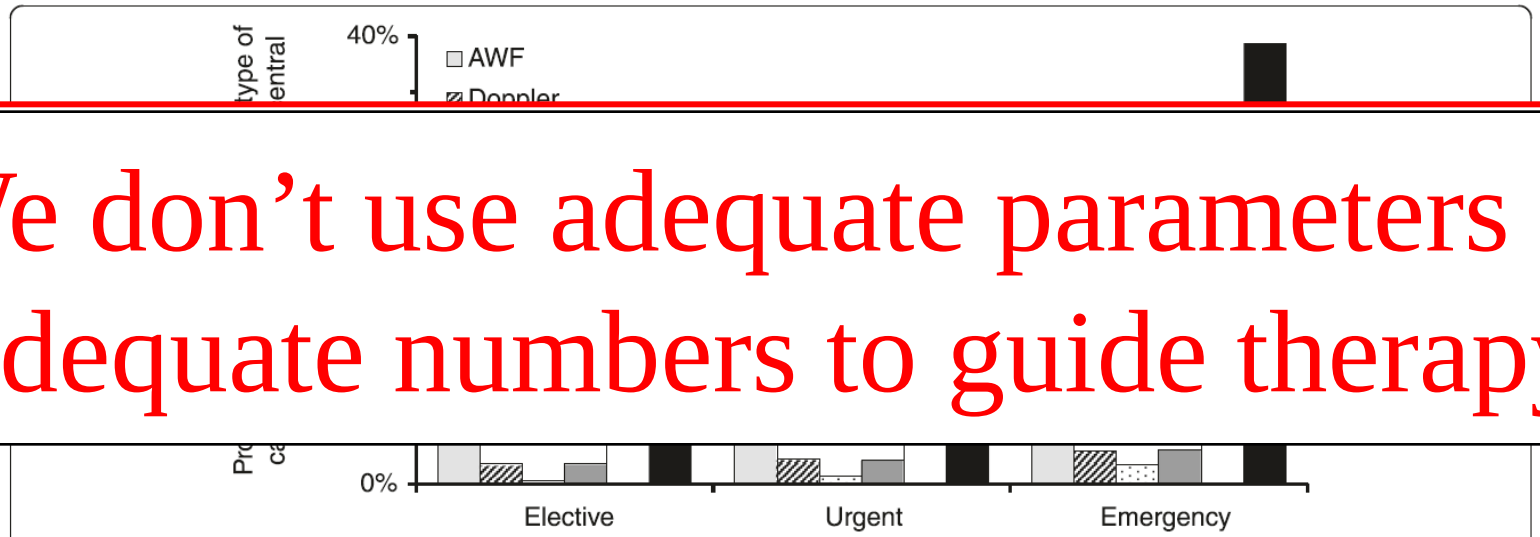
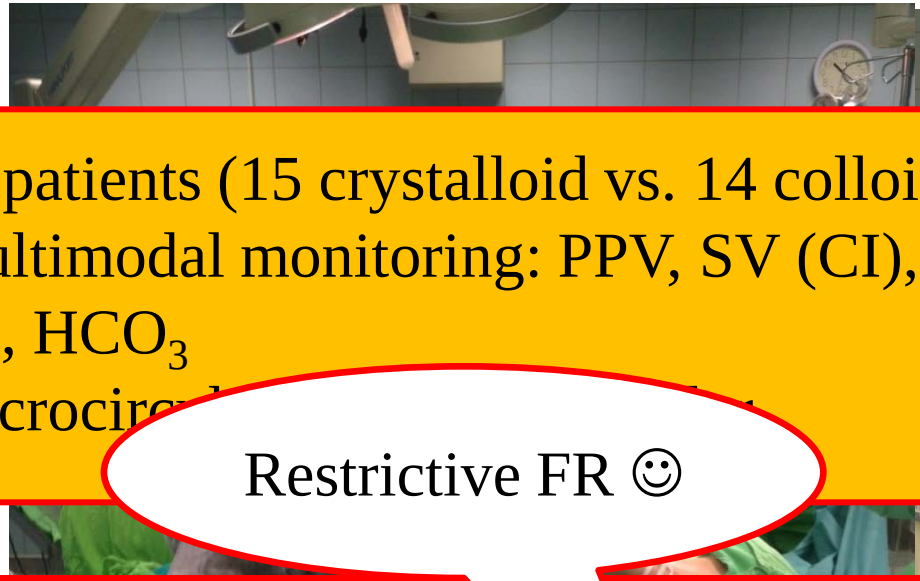


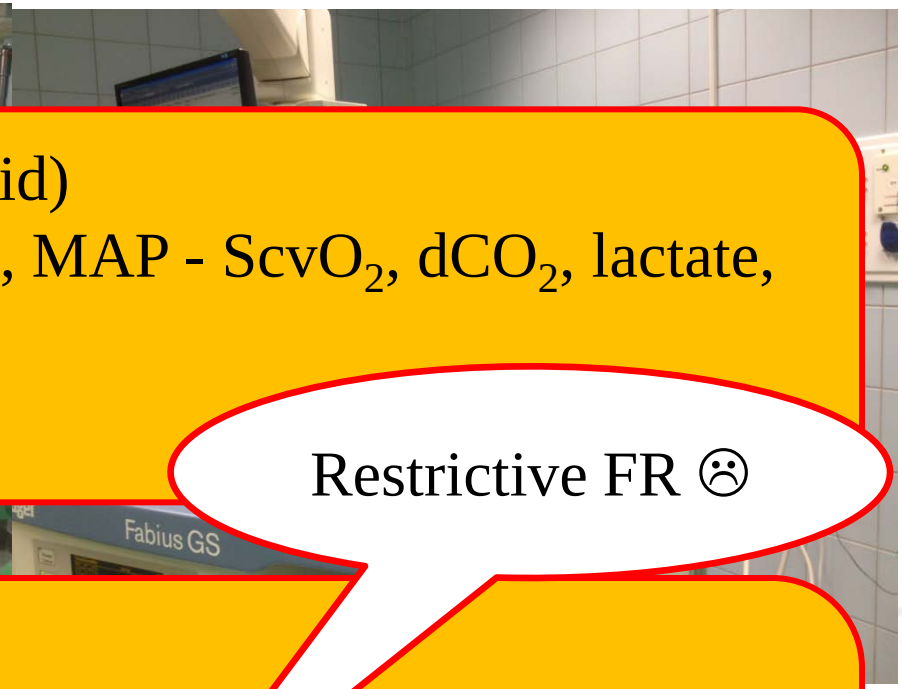
Fig. 1 Use of cardiac output monitoring and central venous catheter per urgency of surgery. Data displayed as percentage per urgency of surgery. *AWF* arterial waveform analysis, *Doppler* Doppler ultrasound, *PAC* pulmonary artery catheter, *COM* cardiac output monitoring, *CVC* central venous catheter

We don't use adequate parameters in adequate numbers to guide therapy

Does the „multimodal concept” work?

Multimodal monitoring during free-flap surgery: Crystalloid vs. Colloid (PRCT)





- 29 patients (15 crystalloid vs. 14 colloid)
- Multimodal monitoring: PPV, SV (CI), MAP - $ScvO_2$, dCO_2, lactate, pH, HCO_3
- Microcirc

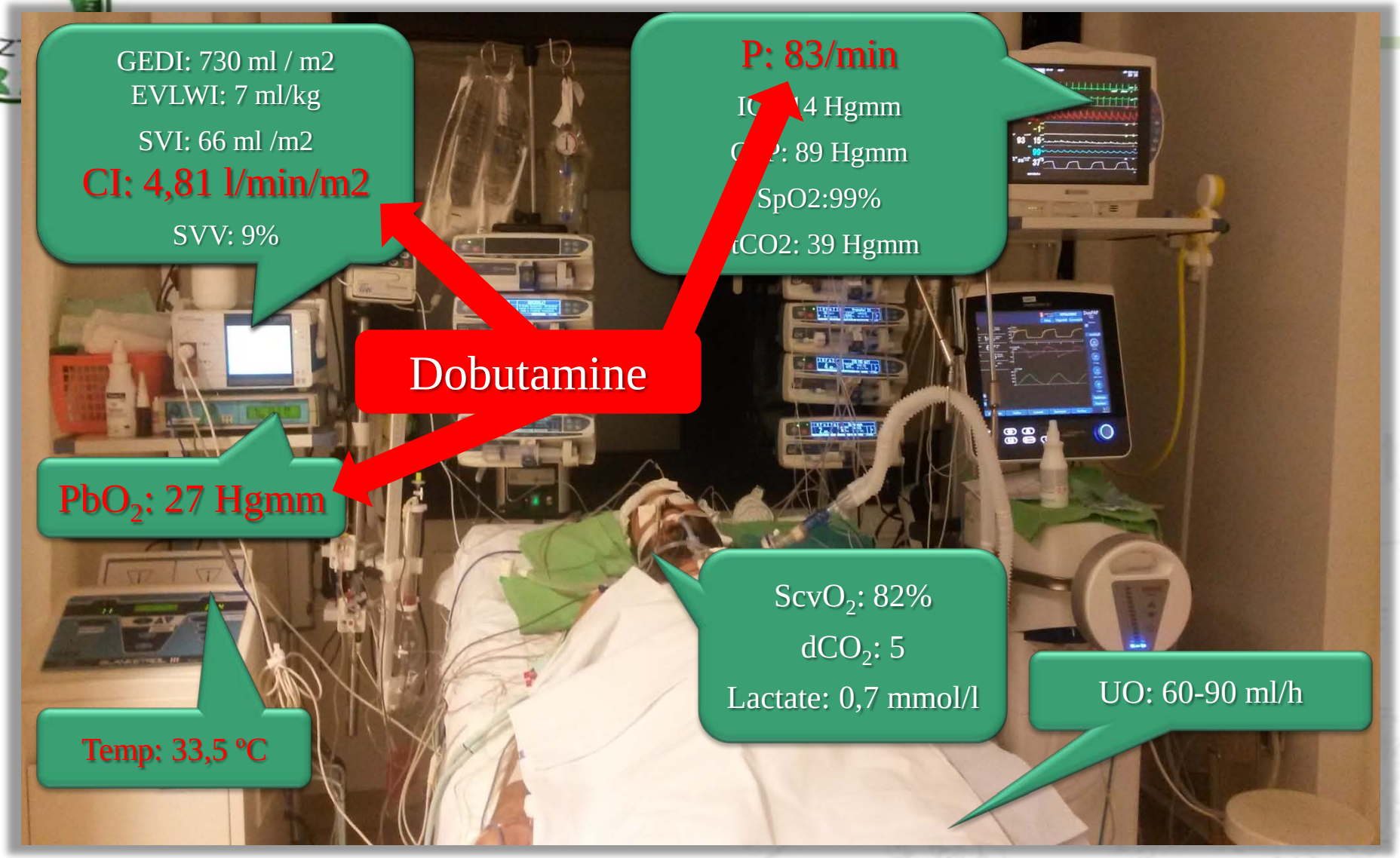
Restrictive FR ☺

Restrictive FR ☹

Length of surgery (mean): hours
Maintenance fluid: 1 ml/kg/h
Boluses:
- Crystalloid group: 1600 ml (min=500, max=5000 ml)
- Coloid group: 560 ml (min=450, max=1500 ml)

No difference in outcome variables

Multimodal monitoring on the ICU



Instead of protocolized management:

frontiers in
PUBLIC HEALTH

MINI REVIEW ARTICLE
published: 30 April 2014
doi: 10.3389/fpubh.2014.00034

The multimodal concept of hemodynamic stabilization

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frontiers in
MEDICINE

SPECIALTY GRAND CHALLENGE ARTICLE
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Individualized goal directed perioperative care – the way to go!

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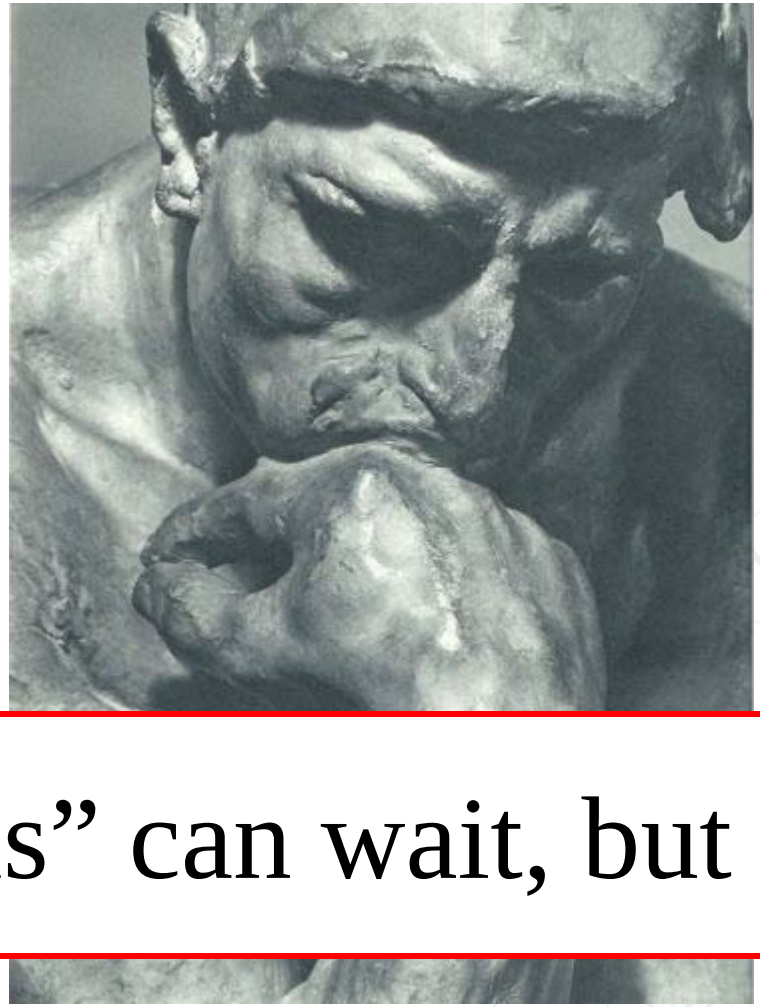
Thinking has no alternative!



„Diagnosis” can wait, but cells can’t!

Auguste Rodin: The Thinker, 1880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