



The high risk surgical patient

Prof. Zsolt Molnár

zsoltmolna@gmail.com

Department of Anaesthesia and Intensive Therapy

University of Szeged
Hungary

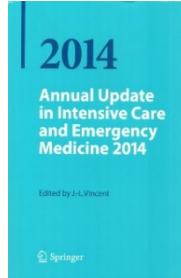
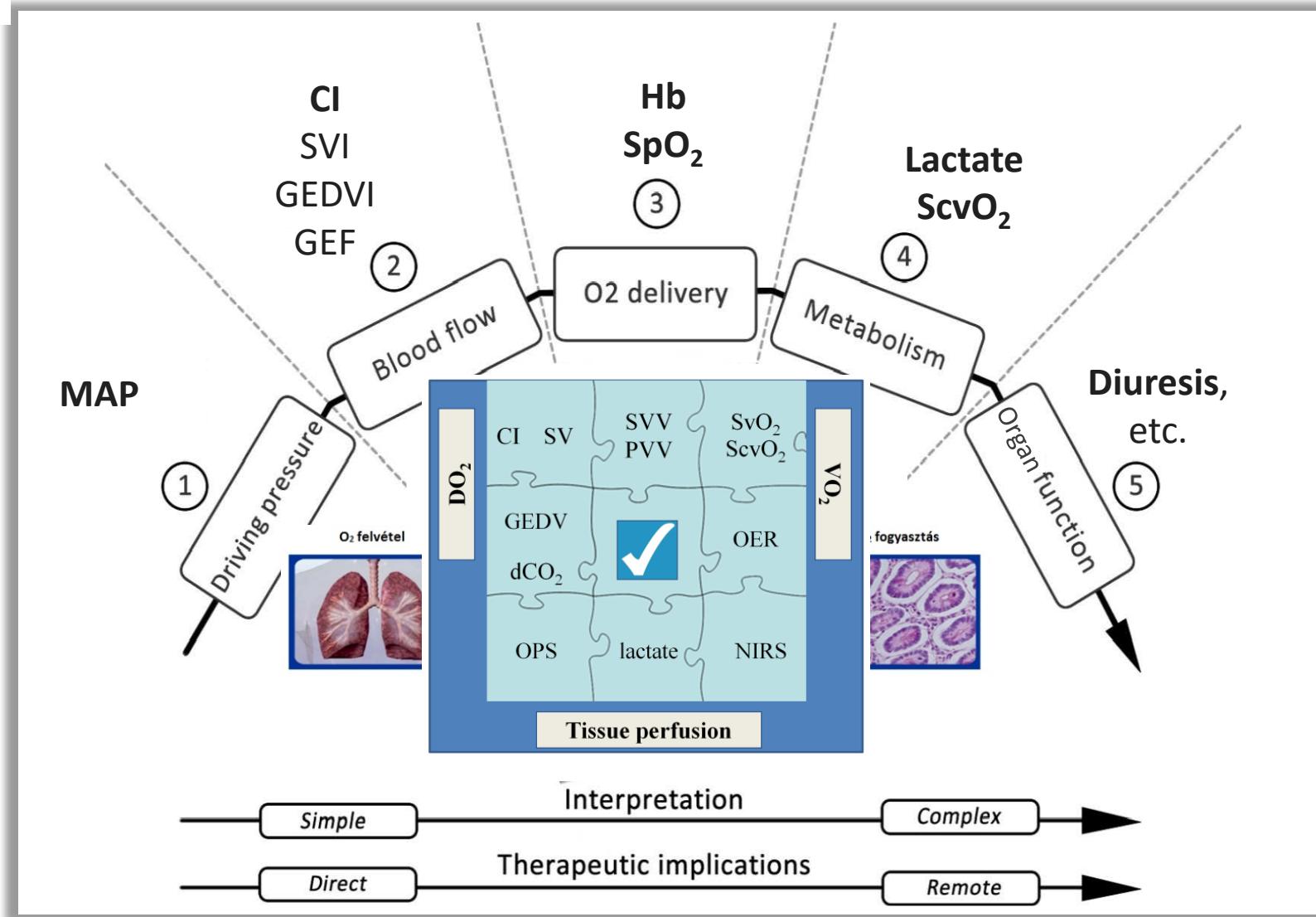


1ST INTERNATIONAL INTER-CONGRESS
CONFERENCE OF THE POLISH SOCIETY
OF ANAESTHESIOLOGY AND INTENSIVE THERAPY
**PITFALLS IN ANAESTHESIOLOGY
AND INTENSIVE THERAPY**

ZAKOPANE, 11–12 December 2015 r.

Multimodal hemodynamic monitoring

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





Is it important in the perioperative setting?



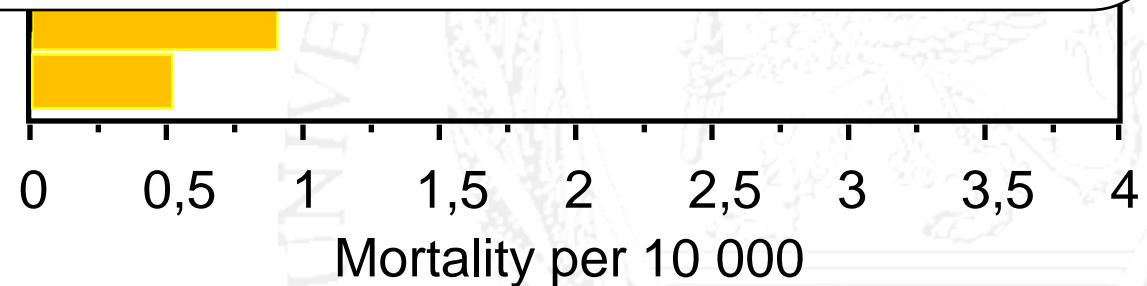
Mortality and anaesthesia

Beecher & Todd (1954)
Hingson et al. (1956)
Clifton & Hotten (1963)
Harrison (1978)
Turnbull et al. (1980)
Hovi-Viander (1980)
Lunn & Muchin (1982)



Anaesthesia has become safe
but...

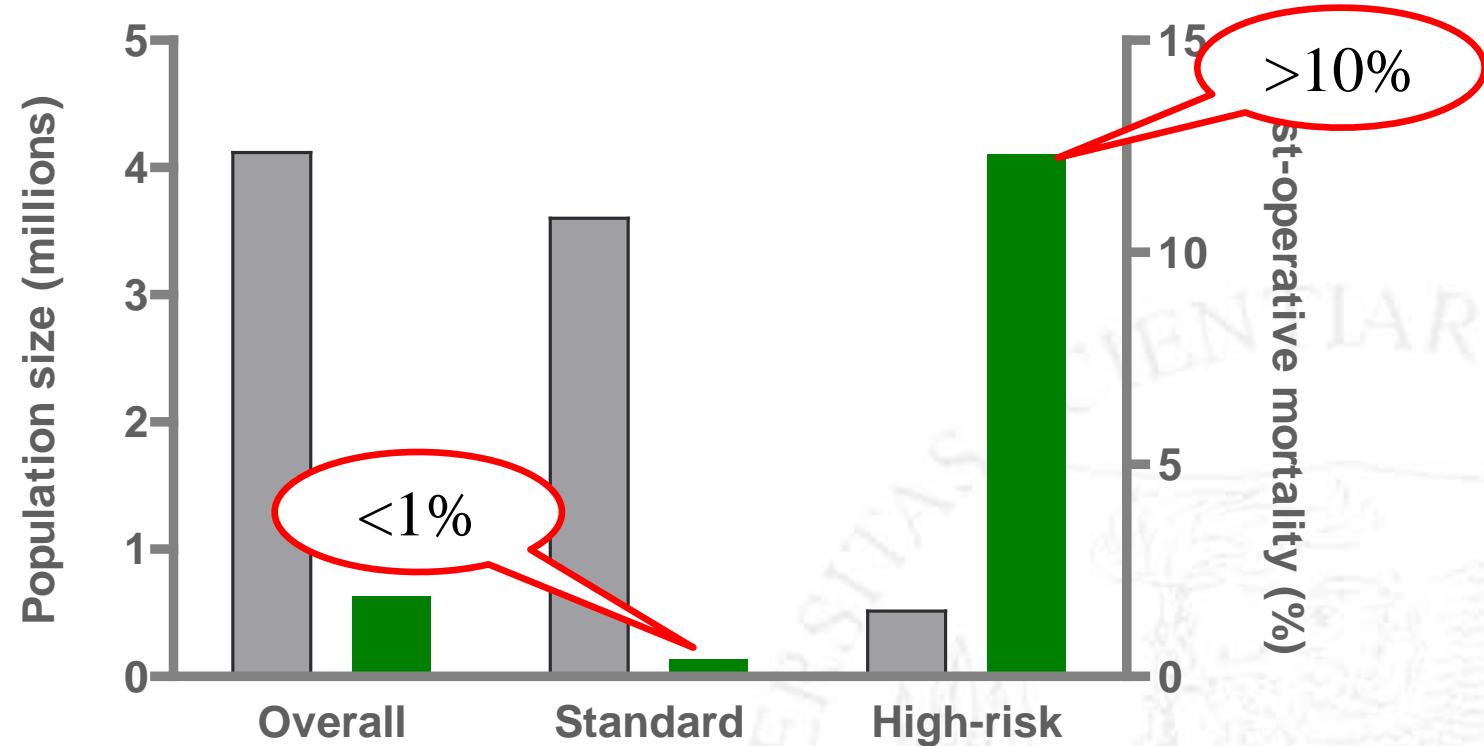
Newland (2002)
Lienhart (2006)



Identification and characterisation of the high-risk surgical population in the United Kingdom

Rupert M Pearse¹, David A Harrison², Philip James³, David Watson¹, Charles Hinds¹, Andrew Rhodes⁴, R Michael Grounds⁴ and E David Bennett⁴

Critical Care 2006, 10:R81



Higher mortality in high risk patients is hidden
by the large number of cases



Mortality after surgery in Europe: a 7 day cohort study

Rupert M Pearse, Rui P Moreno, Peter Bauer, Paolo Pelosi, Philipp Metnitz, Claudia Spies, Benoit Vallet, Jean-Louis Vincent, Andreas Hoeft, Andrew Rhodes, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology*

Lancet 2012; 380: 1059-65

	Number of patients	Median days in hospital (IQR)	Number admitted to critical care	Percentage admitted to critical care (95% CI)	Number died in hospital	Percentage died in hospital (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p value
Belgium	1486	3.0 (1.0-6.0)	136	9.2% (7.7-10.6)	47	3.2% (2.3-4.1)	0.89 (0.65-1.21)	1.65 (0.81-3.40)	0.17
Croatia	1767	4.0 (2.0-7.0)	166	9.4% (8.0-10.8)	131	7.4% (6.2-8.6)	2.17 (1.77-2.67)	1.89 (0.94-3.80)	0.07
Cyprus	45	1.0 (1.0-3.0)	0	0	1	2.2% (0.0-6.7)	0.62 (0.09-4.48)	0.82 (0.04-16.70)	0.90
Czech Republic	434	4.0 (2.0-9.0)	21	4.8% (2.8-6.9)	10	2.3% (0.9-3.7)	0.64 (0.34-1.21)	1.30 (0.23-7.46)	0.77
Denmark	1000	2.0 (1.0-5.0)	36	3.6% (2.4-4.8)	32	3.2% (2.1-4.3)	0.90 (0.62-1.29)	1.16 (0.52-2.61)	0.72
Estonia	727	3.0 (1.0-6.0)	51	7.0% (5.2-8.9)	11	1.5% (0.6-2.4)	0.42 (0.23-0.76)	0.60 (0.16-2.28)	0.45
Finland	1071	2.0 (1.0-5.0)	43	4.0% (2.8-5.6)	21	2.0% (1.1-2.8)	0.54 (0.35-0.85)	0.44 (0.19-1.05)	0.06
France	2278	3.0 (1.0-6.0)	132	5.8% (4.8-6.8)	73	3.2% (2.5-3.9)	0.90 (0.70-1.16)	1.36 (0.72-2.56)	0.34
Germany	5284	4.0 (2.0-9.0)	611	11.6% (10.7-12.4)	133	2.5% (2.1-2.9)	0.70 (0.57-0.86)	0.85 (0.50-1.43)	0.54
Greece	1803	3.0 (2.0-7.0)	63	3.5% (2.7-4.3)	65	3.6% (2.7-4.5)	1.01 (0.78-1.33)	1.20 (0.66-2.16)	0.55
Hungary	621	4.0 (2.0-7.0)	44	7.1% (5.1-9.1)	20	3.2% (1.8-4.6)	0.90 (0.57-1.43)	1.23 (0.43-3.50)	0.69
Iceland	162	2.0 (1.0-4.0)	15	9.3% (4.8-13.8)	2	1.2% (0.0-3.0)	0.34 (0.08-1.37)	0.47 (0.07-3.41)	0.46
Ireland	856	3.0 (1.0-6.0)	66	7.7% (5.9-9.5)	55	6.4% (4.8-8.1)	1.86 (1.39-2.49)	2.61 (1.30-5.27)	0.007
Italy	2673	3.0 (2.0-7.0)	200	7.5% (6.5-8.5)	141	5.3% (4.4-6.1)	1.51 (1.24-1.84)	1.70 (0.97-2.97)	0.06
Latvia	302	4.0 (2.0-8.0)	19	6.3% (3.5-9.1)	65	21.5% (16.9-26.2)	7.44 (5.55-9.97)	4.98 (1.22-20.29)	0.025
Lithuania	375	3.0 (2.0-5.0)	14	3.7% (1.8-5.7)	10	2.7% (1.0-4.3)	0.74 (0.39-1.40)	1.21 (0.21-6.95)	0.83
Netherlands	1627	3.0 (1.0-6.0)	126	7.7% (6.4-9.0)	32	2.0% (1.3-2.7)	0.55 (0.38-0.78)	0.63 (0.28-1.41)	0.26
Norway	689	3.0 (1.0-6.0)	31	4.5% (3.0-6.1)	10	1.5% (0.6-2.4)	0.40 (0.21-0.75)	0.51 (0.17-1.49)	0.22
Poland	397	5.0 (2.0-7.5)	8	2.0% (0.6-3.4)	71	17.9% (14.1-21.7)	5.91 (4.48-7.79)	6.92 (2.37-20.27)	0.0004
Portugal	1489	3.0 (1.0-7.0)	103	6.9% (5.6-8.2)	61	4.1% (3.1-5.1)	1.16 (0.88-1.53)	1.43 (0.72-2.83)	0.31
Romania	1298	5.0 (3.0-8.0)	209	16.1% (14.1-18.1)	88	6.8% (5.4-8.2)	1.97 (1.55-2.51)	3.19 (1.61-6.29)	0.001
Serbia	85	5.0 (3.0-7.0)	1	1.2% (0.0-3.5)	2	2.4% (0.0-5.6)	0.65 (0.16-2.67)	1.06 (0.11-10.04)	0.96
Slovakia	1156	3.0 (2.0-7.0)	22	1.9% (1.1-2.7)	129	11.2% (9.3-13.0)	3.41 (2.76-4.20)	2.15 (0.91-5.07)	0.08
Slovenia	518	3.0 (1.0-7.0)	13	2.5% (1.2-3.9)	15	2.9% (1.5-4.3)	0.81 (0.48-1.37)	1.12 (0.30-4.22)	0.86
Spain	5433	3.0 (1.0-7.0)	677	12.5% (11.6-13.3)	208	3.8% (3.3-4.3)	1.08 (0.91-1.28)	1.39 (0.89-2.18)	0.15
Sweden	1314	2.0 (1.0-6.0)	42	3.2% (2.2-4.2)	24	1.8% (1.1-2.6)	0.50 (0.33-0.77)	0.58 (0.23-1.49)	0.26
Switzerland	1019	4.0 (2.0-8.0)	79	7.8% (6.1-9.4)	20	2.0% (1.1-2.8)	0.54 (0.35-0.86)	0.86 (0.25-2.97)	0.81
UK	10630	2.0 (1.0-6.0)	671	6.3% (5.9-6.8)	378	3.6% (3.2-3.9)	1.00

Odds ratios (OR) referenced against the UK and adjusted for age, American Society of Anesthesiologists' score, urgency of surgery, grade of surgery (minor, intermediate, major), surgical specialty, and the presence of either metastatic disease or cirrhosis in a two-level binary logistic regression model (with patient at the first level and hospital at the second).

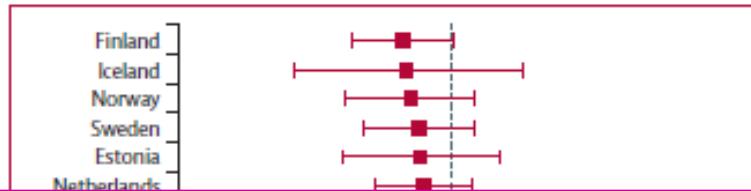
Table 2: Relation between country and in-hospital mortality



Mortality after surgery in Europe: a 7 day cohort study

Rupert M Pearse, Rui P Moreno, Peter Bauer, Paolo Pelosi, Philipp Metnitz, Claudia Spies, Benoit Vallet, Jean-Louis Vincent, Andreas Hoeft, Andrew Rhodes, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology*

Lancet 2012; 380: 1059-65



Interpretation The mortality rate for patients undergoing inpatient non-cardiac surgery was higher than anticipated. Variations in mortality between countries suggest the need for national and international strategies to improve care for this group of patients.



There is room for improvement!

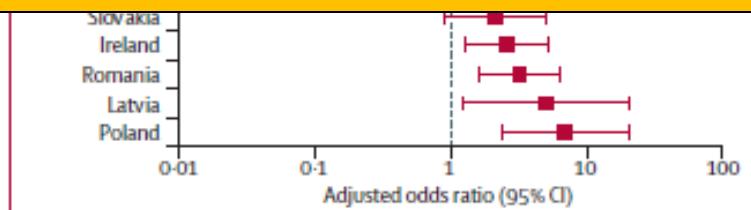


Figure 3: Adjusted odds ratio for death in hospital after surgery for each country

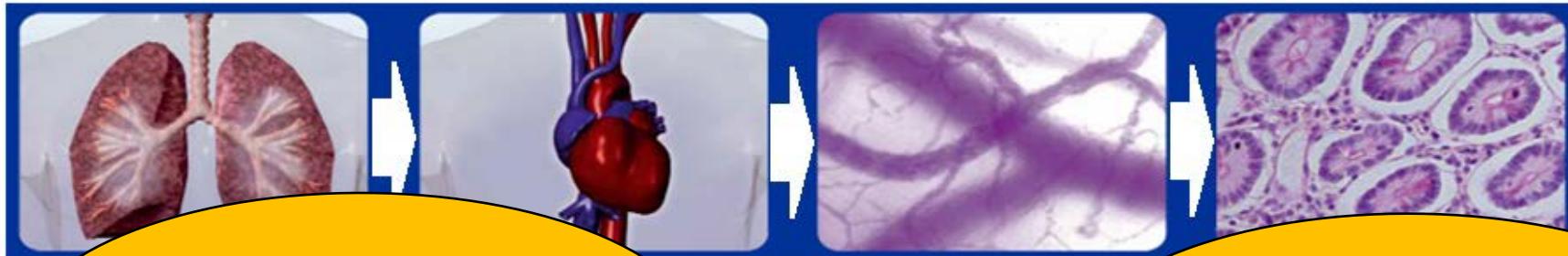


Pathophysiology





Why patients get into trouble?



SaO_2
100%

oxygen

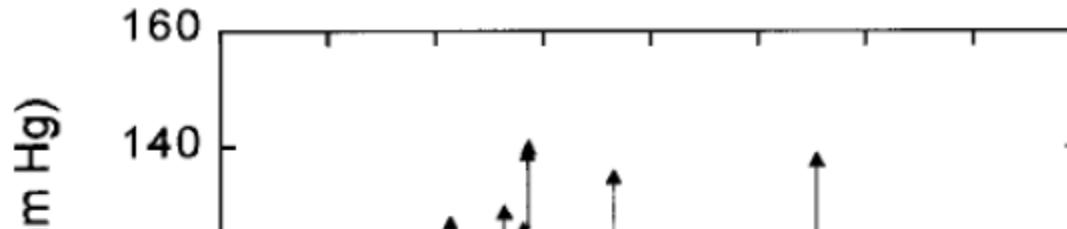
ScvO_2
70%

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

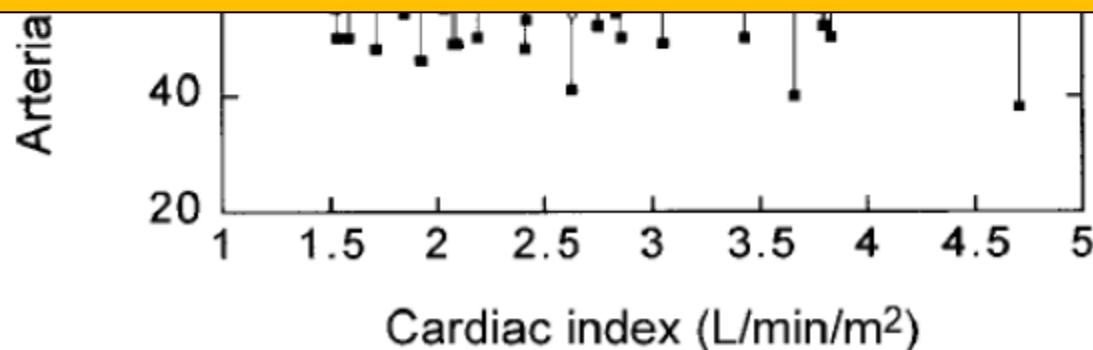
↑
Analgesia, anaesthesia, IPPV

Blood pressure and cardiac output

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



For adequate perfusion both MAP and CO is needed



Maurizio Cecconi
Christoph Hofer
Jean-Louis Teboul
Ville Pettila
Erika Wilkman
Zsolt Molnar
Giorgio Della Rocca
Cesar Aldecoa
Antonio Artigas
Sameer Jog
Michael Sander

Fluid challenges in intensive care: the FENICE study

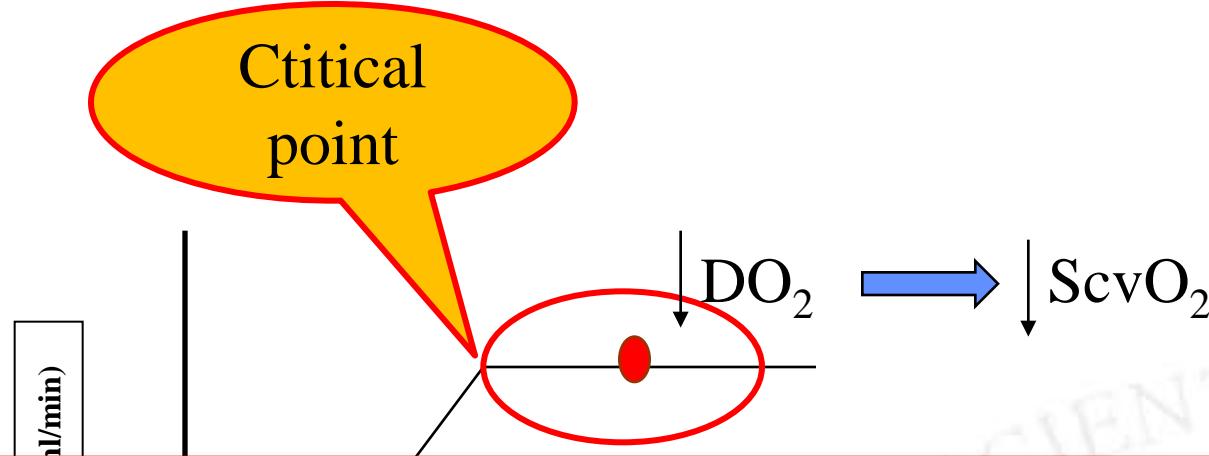
A global inception cohort study

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

Indication	<i>n</i> (%)
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]
Oliguria	372 (18.0 [16.4–19.6])
Skin mottling	36 (1.7 [1.2–2.2])
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%

Oxygen debt during anaesthesia



Hypothesis:

Intraoperative hypotension – hypovolemia,
or anaesthesia caused vasodilatation?

RESEARCH ARTICLE

Open Access

Continuous central venous oxygen saturation assisted intraoperative hemodynamic management during major abdominal surgery: a randomized, controlled trial

András Mikor^{1*}, Domonkos Trásy¹, Márton F Németh¹, Angelika Osztroluczki¹, Szilvia Kocsi², Ildikó Kovács¹, Gábor Demeter¹ and Zsolt Molnár¹

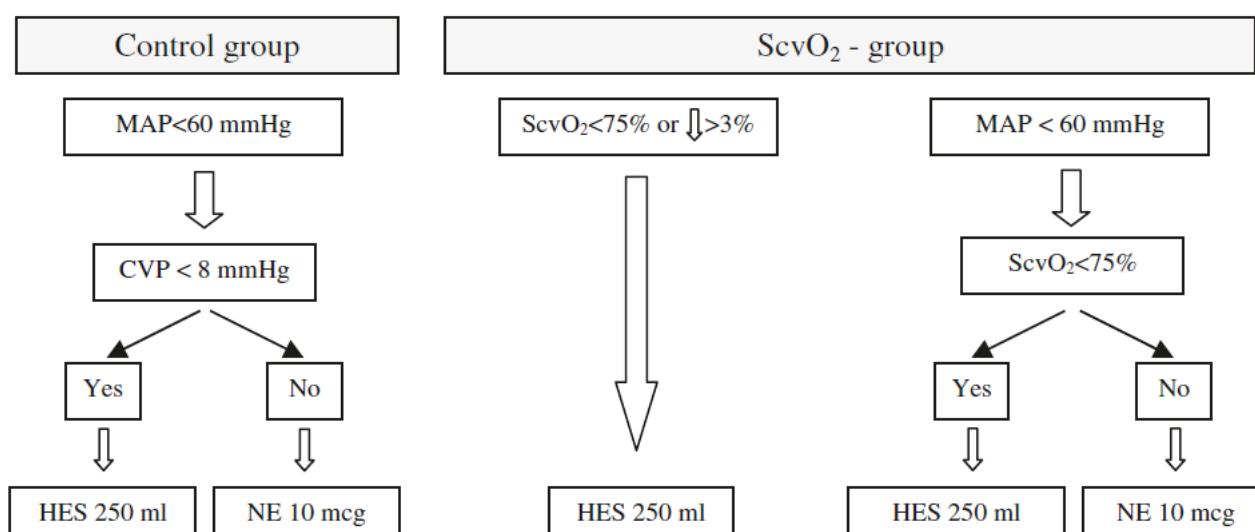


Fig. 1 Flowchart of the study design. MAP: mean arterial pressure, CVP: central venous pressure, ScvO₂: central venous oxygen saturation, HES: hydroxyethyl starch, NE: norepinephrine



RESEARCH ARTICLE

Open Access

Continuous central venous oxygen saturation assisted intraoperative hemodynamic management during major abdominal surgery: a randomized, controlled trial

András Mikor^{1*}, Domonkos Trásy¹, Márton F Németh¹, Angelika Osztroluczki¹, Szilvia Kocsi², Ildikó Kovács¹, Gábor Demeter¹ and Zsolt Molnár¹

Table 2 Intraoperative interventions. Data are shown as mean \pm SD or median (interquartile)

	ScvO ₂ (n = 38)	Control (n = 41)	p
Crystalloid (ml/h)	1126 \pm 471	1049 \pm 431	0.46
Colloid (ml/h)	279 (161)	107 (250)	<0.001*
Number of patients needing vasopressor	11	15	0.47
Dose of vasopressor (mcg/h)	37 (107)	18 (73)	0.84
Number of patients receiving blood transfusion	24	15	0.02*
Blood loss during the operation (ml)	973 \pm 473	983 \pm 574	0.99

*: p<0.05



RESEARCH ARTICLE

Open Access

Continuous central venous oxygen saturation assisted intraoperative hemodynamic management during major abdominal surgery: a randomized, controlled trial

András Mikor^{1*}, Domonkos Trásy¹, Márton F Németh¹, Angelika Osztroluczki¹, Szilvia Kocsi², Ildikó Kovács¹, Gábor Demeter¹ and Zsolt Molnár¹

	ScvO ₂ (n=38)	Control (n=41)	p	
Number of patients with complications	10	19	0.07	
PaO₂/FiO₂	> 300 Hgmm	4	3	0.62
	200-300 Hgmm	24	15	0.02*
	100-200 Hgmm	10	22	0.01*
	< 100 Hgmm	0	1	0.52
28 day survival (S/NS)	37/1	33/8	0.018*	



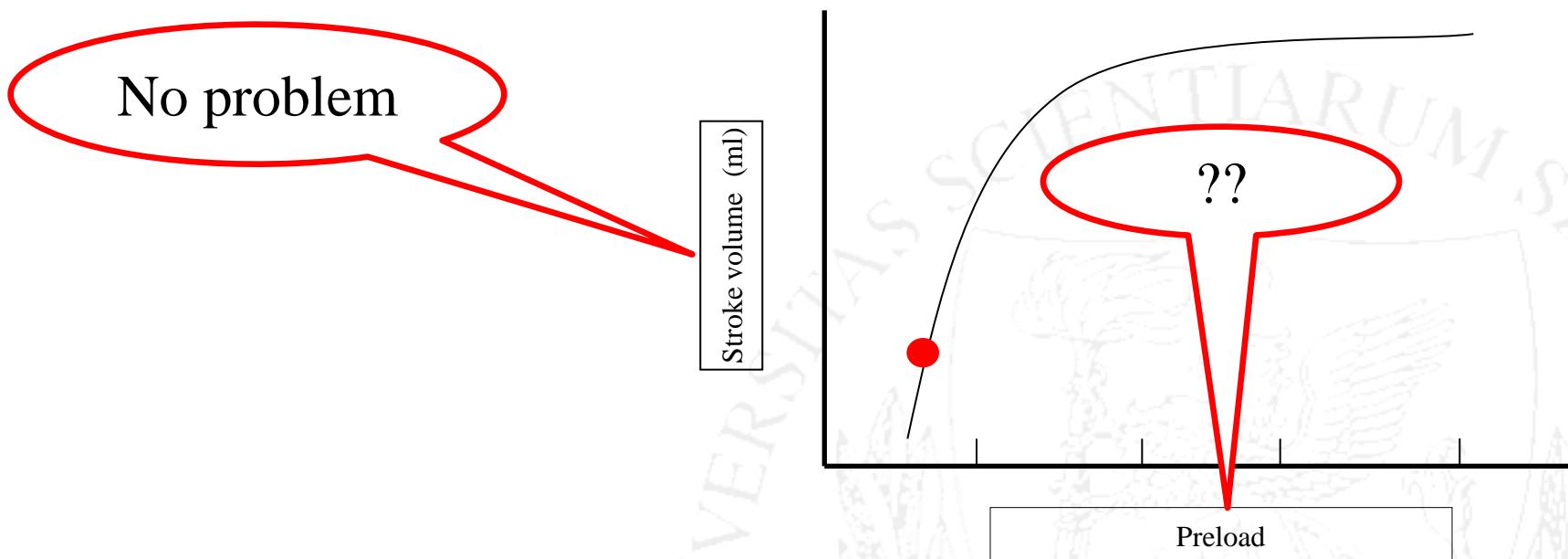
Pioneers

- Otto Frank (1865-1944):
 - Physiologist (Leipzig)
 - 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”

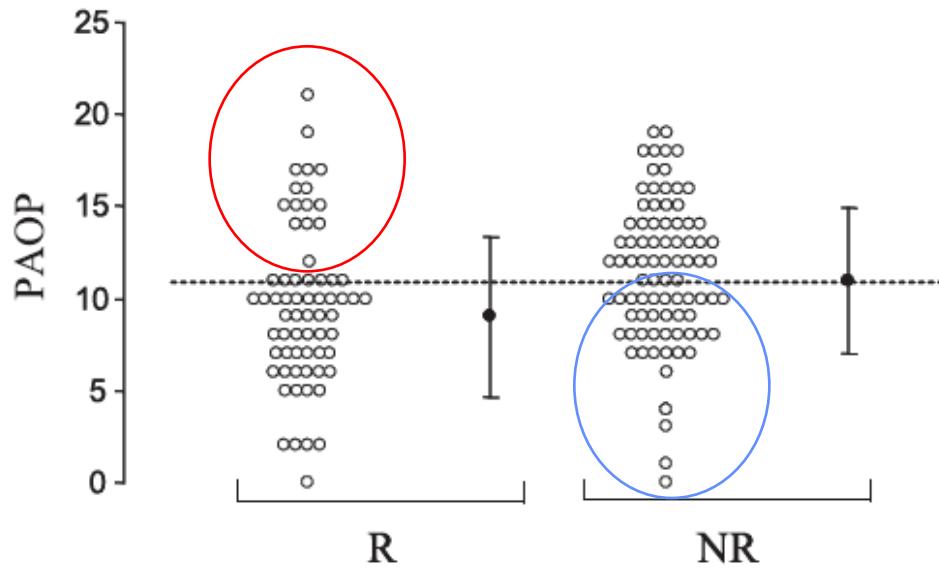
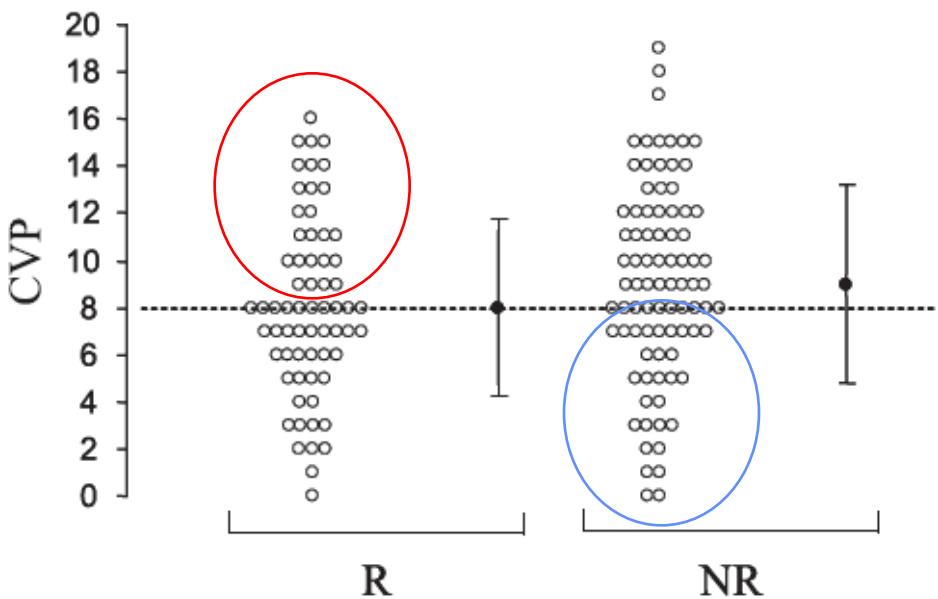


Starling EH. The Linacre Lecture on the Law of the Heart. London; 1918
Starling EH. *J R Army Med Corps.* 1920; 34: 258-262

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

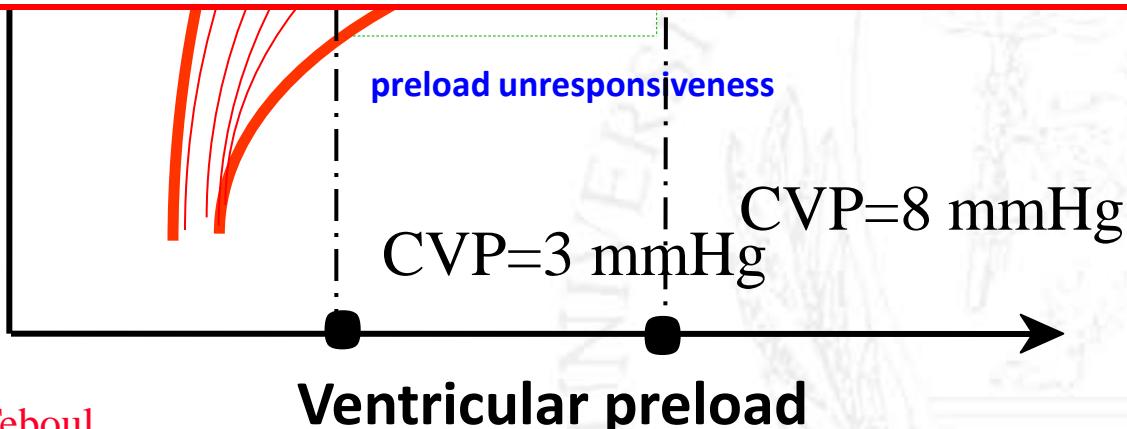


- CVP:
 - Sens: 62% (95% CI, 49–73%)
 - Spec: 54% (95% CI, 43–65%)

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

„One size does not fit all!”

„Evidence based” protocols/guidelines
based on studies utilising static
parameters is a waste of space!





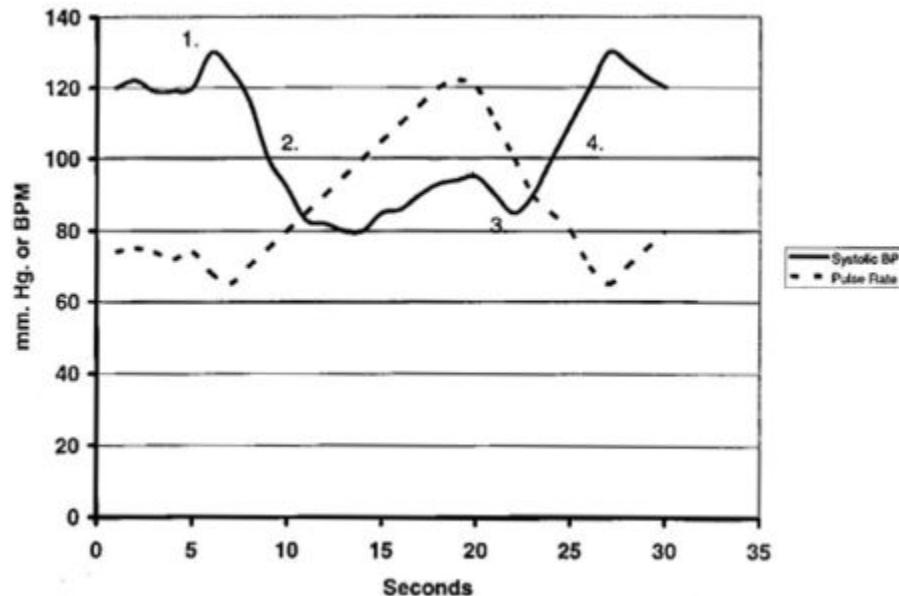
Applying physiology at the bedside





Heart-lung interactions

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



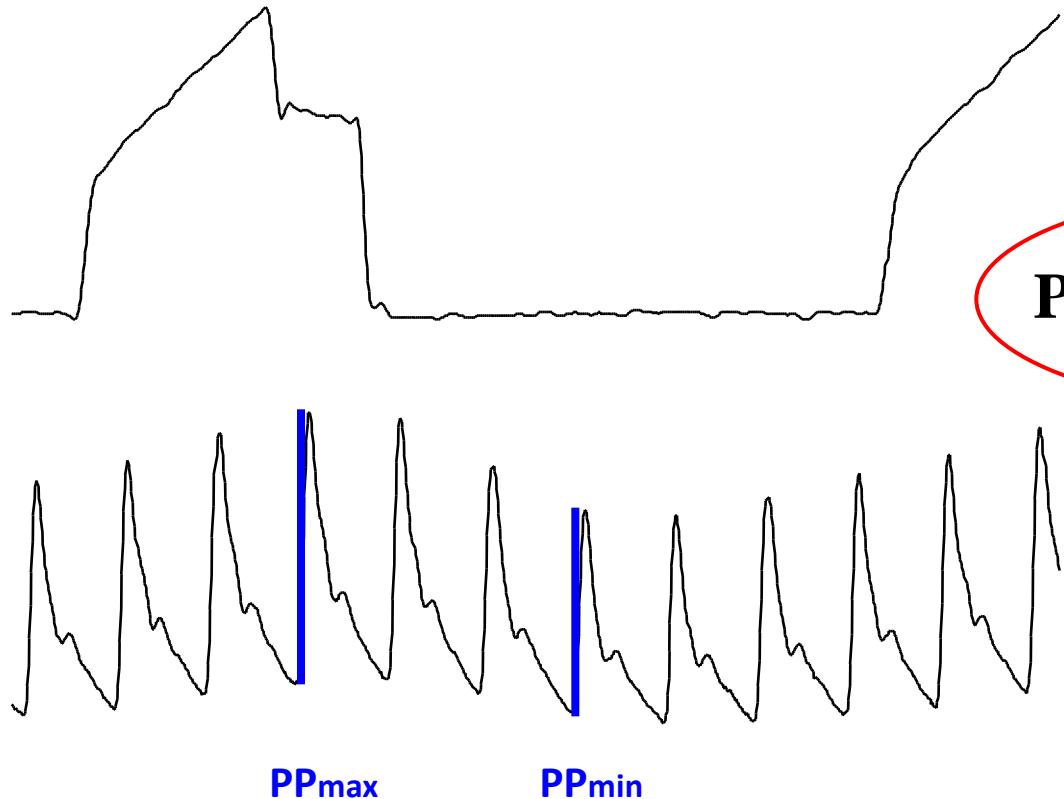


IPPV = series of Valsalva-maneuvers

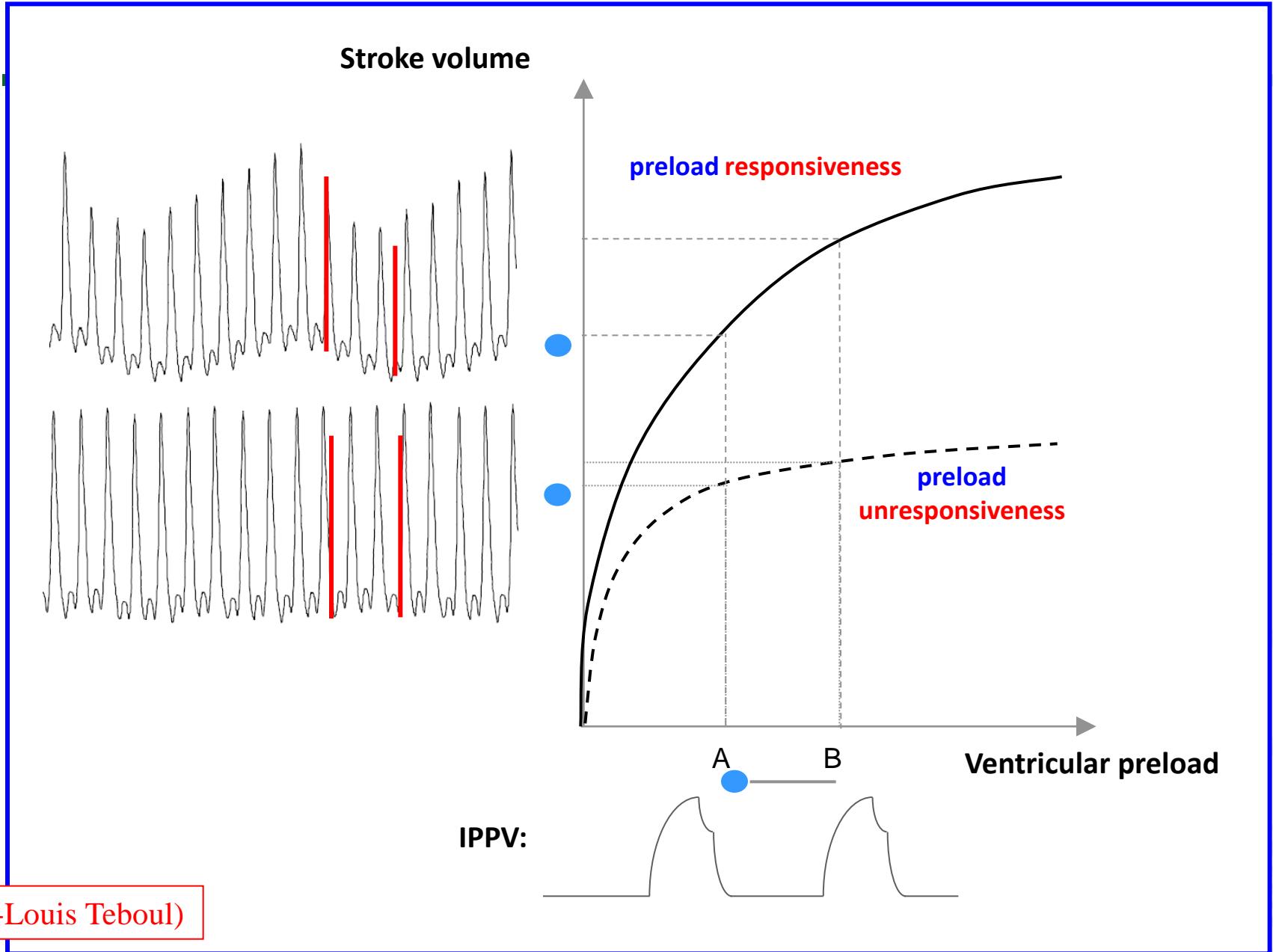
Clinical Use of Respiratory Changes in Arterial Pulse Pressure to Monitor the Hemodynamic Effects of PEEP

FRÉDÉRIC MICHAUD, DENIS CHEMLA, CHRISTIAN RICHARD, MARC WYSOCKI, MICHAEL R. PINSKY,
YVES LECARPENTIER, and JEAN-Louis TEBOL

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



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





Devices





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

Cornelia Salzwedel^{1†}, Jaume Puig^{2†}, Arne Carstens³, Berthold Bein³, Zsolt Molnar⁴, Krisztian Kiss⁴, Ayyaz Hussain⁵, Javier Belda², Mikhail Y Kirov⁵, Samir G Sakka⁶ and Daniel A Reuter^{1*}

ProAQT-outcome study

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

Figure 1a: Algorithm for initial assessment.

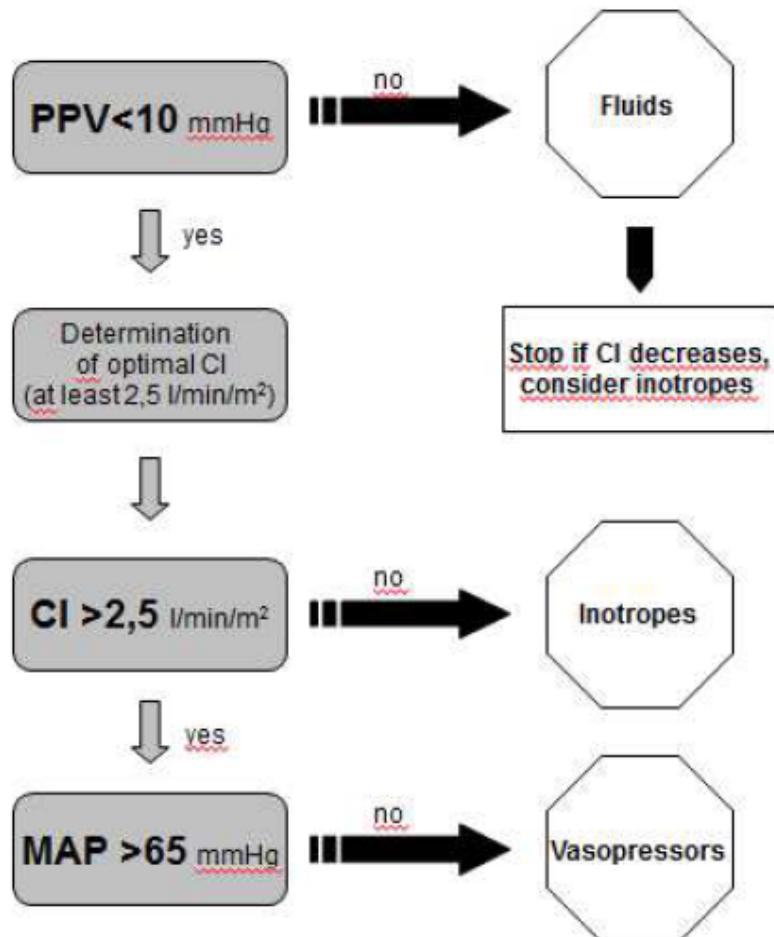
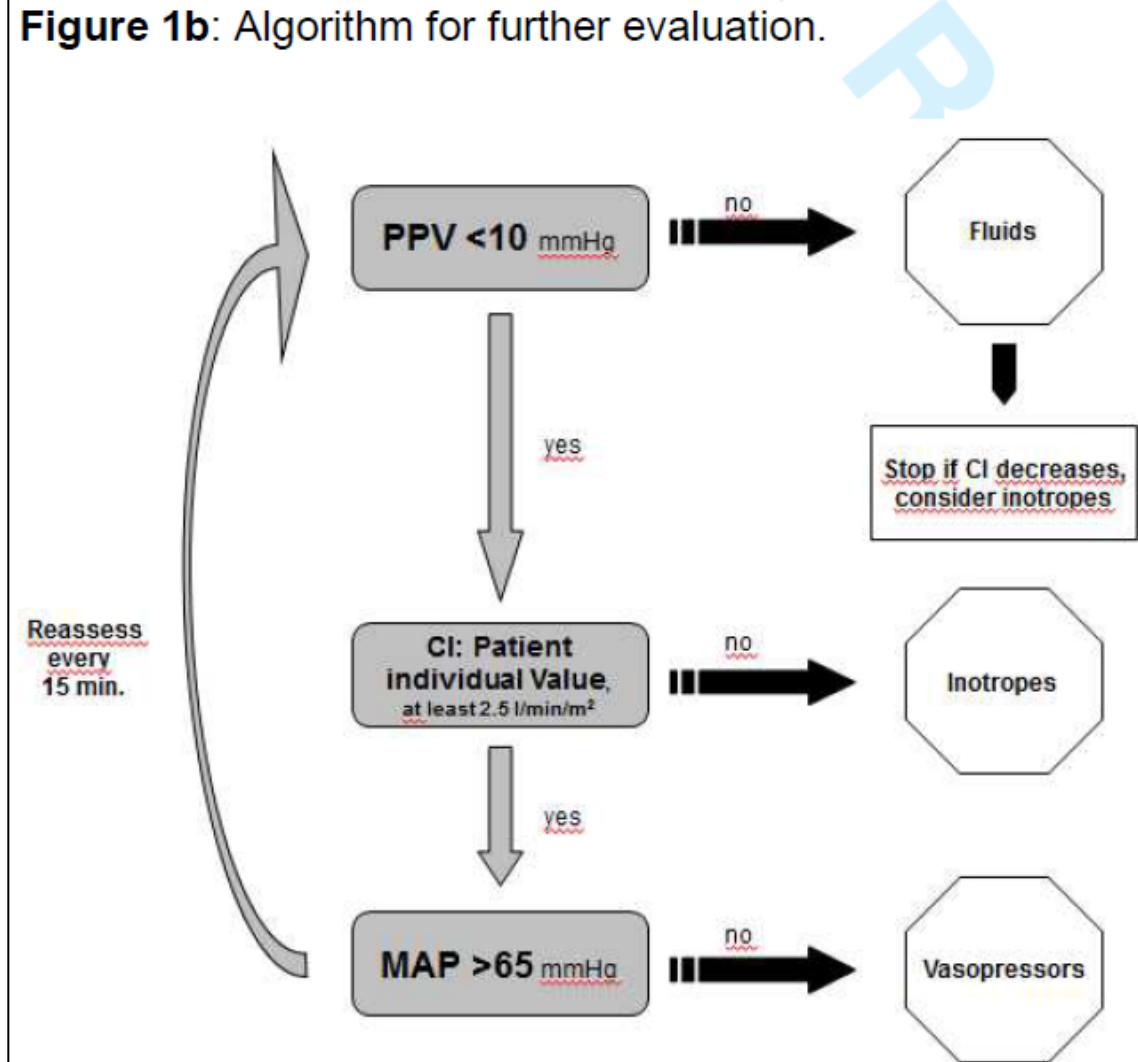


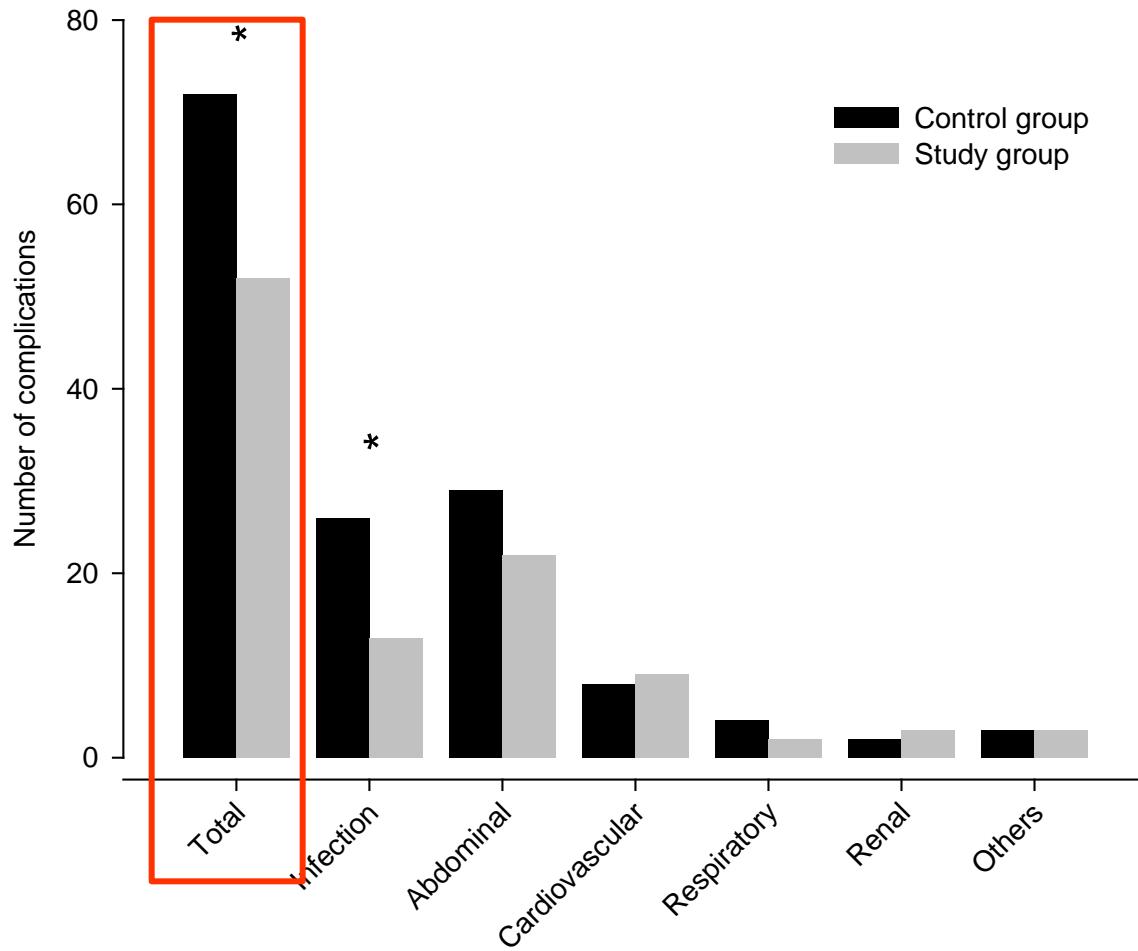
Figure 1b: Algorithm for further evaluation.





Number of complications

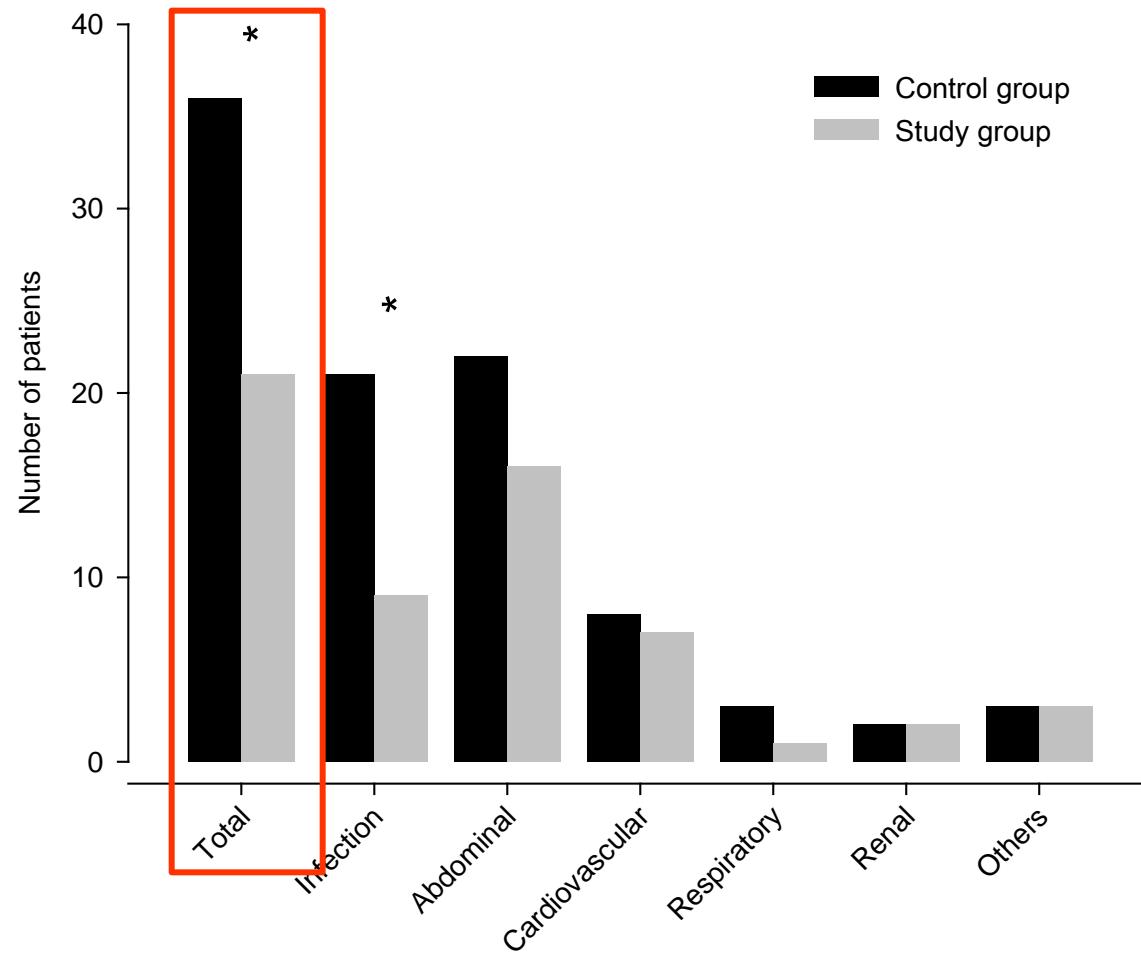
Salzwedel C, et al. *Crit Care* 2013; 17: R191





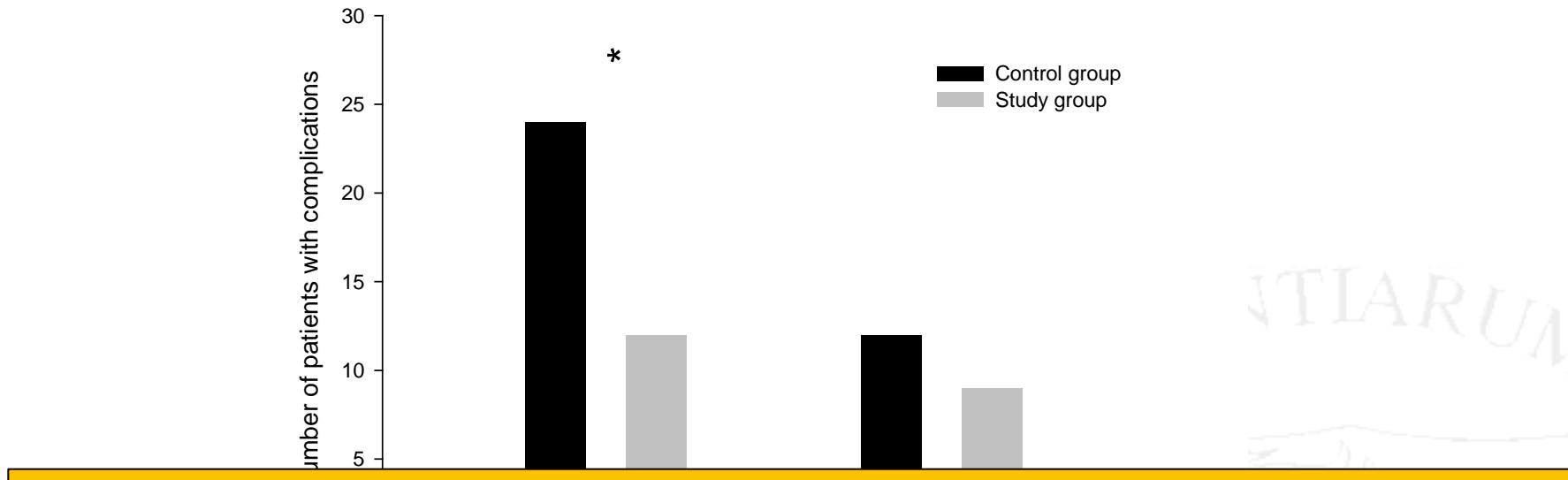
Number of patients with complications

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



Number of patients with complications

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



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



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

Cornelia Salzwedel^{1†}, Jaume Puig^{2†}, Arne Carstens³, Berthold Bein³, Zsolt Molnar⁴, Krisztian Kiss⁴, Ayyaz Hussain⁵, Javier Belda², Mikhail Y Kirov⁵, Samir G Sakka⁶ and Daniel A Reuter^{1*}

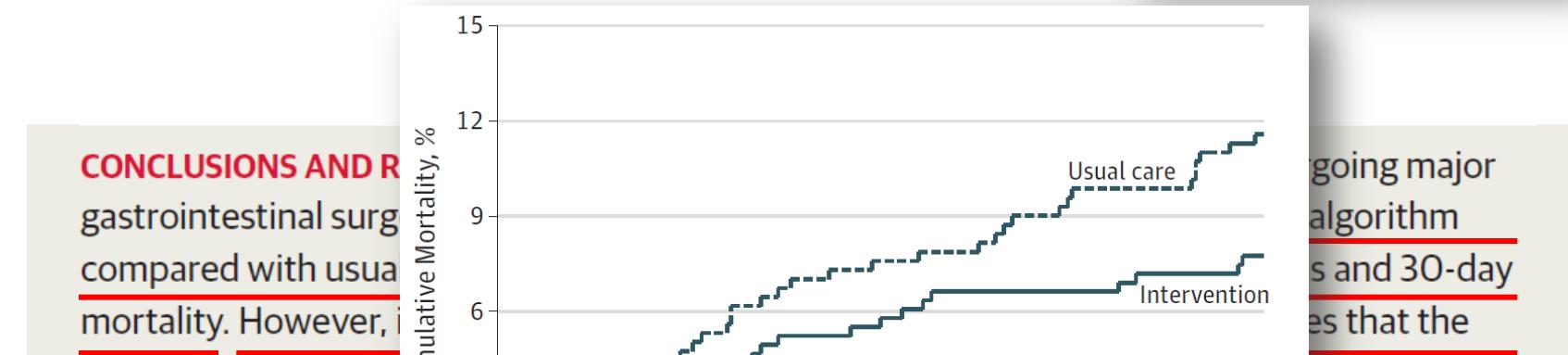
Conclusions: This multi-center study demonstrates that hemodynamic goal-directed therapy using pulse pressure variation, cardiac index trending and mean arterial pressure as the key parameters leads to a decrease in postoperative complications in patients undergoing major abdominal surgery.



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.



„...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?

Maurizio Cecconi
 Christoph Hofer
 Jean-Louis Teboul
 Ville Pettila
 Erika Wilkman
 Zsolt Molnar
 Giorgio Della Rocca
 Cesar Aldecoa
 Antonio Artigas
 Sameer Jog
 Michael Sander

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	<i>n</i> (%)
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]
Oliguria	372 (18.0 [16.4–19.6])
Skin mottling	36 (1.7 [1.2–2.2])
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])

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



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 Pestel², Cameron Ricks¹, Andreas Hoeft³ and Azriel Perel⁴

Answer options	ASA respondents (n = 237)	ESA respondents (n = 195)
	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%



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 Aldecoa², Rui P. Moreno³, Zsolt Molnár⁴, Vesna Novak-Jankovic⁵, Christoph K. Hofer⁶, Michael Sander⁷, Andrew Rhodes⁸ and Rupert M. Pearse^{1,9*}



Conclusion
five rec...

Why don't we use it?



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

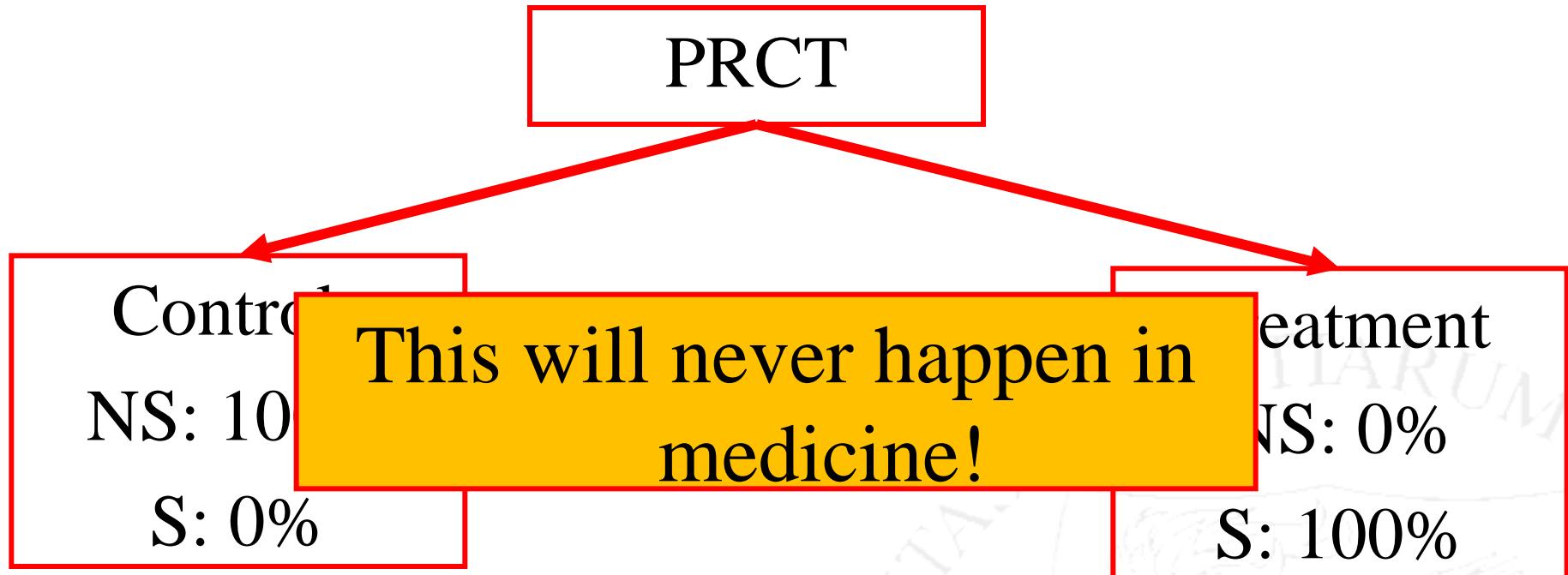


PRCTs and EBM





PRCTs vs. the individual patient



- Patients are different (co-morbidities, individual response, etc)
- Disease definitions don't mean homogenous groups
- Practice variations between centers



Multicenter, randomized, controlled trials evaluating mortality in intensive care: Doomed to fail?

Gustavo A. Ospina-Tascón, MD; Gustavo Luiz Büchele, MD; Jean-Louis Vincent, MD, PhD

(Crit Care Med 2008; 36:1311–1322)

- PRCTs till 2006:
 - 72 PRCT with mortality being the primary end-point
 - 10 positive
 - 7 negative
 - 55 no difference

We should abandon randomized controlled trials in the intensive care unit

Jean-Louis Vincent, MD, PhD, FCCM

(Crit Care Med 2010; 38[Suppl.]:S534–S538)



Monocentric vs. multicenter

(Courtesy of Prof. J-L Vincent)

Small study
(monocentric or a few centers)

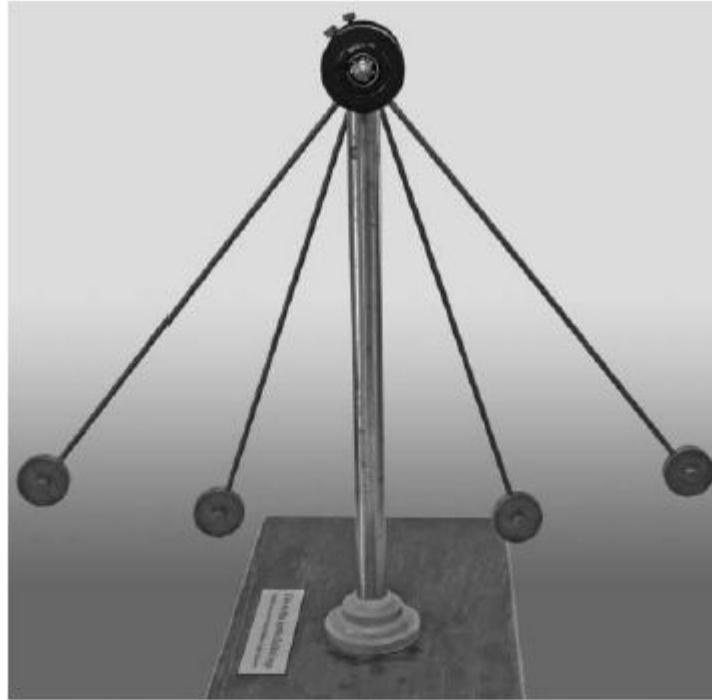


Unless *all details* (patients&care) are standardised – one center will „kill” the other, hence „non-significant” results are inevitable

Large study
(many centers)

Pendulum effect

Good



3. ábra. A Berzsenyi Dániel Főiskolán készített, továbbfejlesztett Eötvös-féle fizikai inga.

Bad

Lóránd Eötvös, 1891



Pendulum effect

„Critical care medicine and research to a large degree seems more and more like a gigantic pendulum in the center of an insane asylum. Each swing imagined to be something new...and we will continue to clap and drue at each pass of the pendulum insane as that may be...

Reminds me of the old saying "Frequently wrong, but never in doubt"

/Charlie Phillips, 2015/

„Sticking to the principles of pathophysiological rationale is the best remedy against the pendulum-induced motion sickness”

/Azriel Perel, 2015/

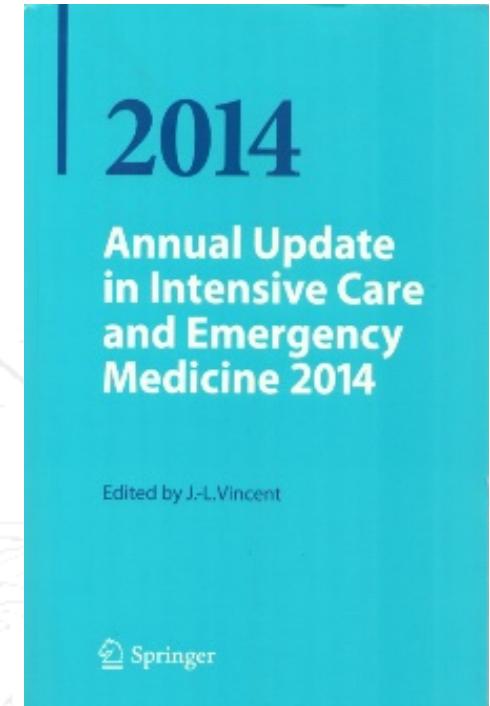
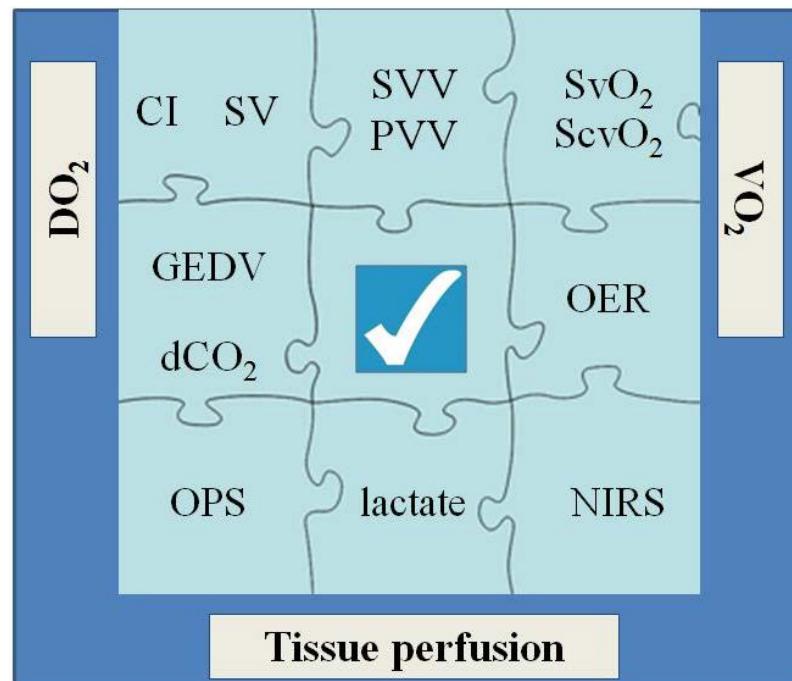




Solving the hemodynamic puzzle

Tánczos K, Németh M, Molnár Z

Ann. Up. in Int. Care and Em. Med. 2014, pp:355



Does it work?



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

- 29 patients (15 crystalloid vs. 14 colloid)
- Multimodal monitoring: PPV, SV (CI), MAP - ScvO₂, dCO₂, lactate, pH, HCO₃
- Microcirculation

Restrictive FR ☺

Restrictive FR ☹

Length of surgery (mean): hours

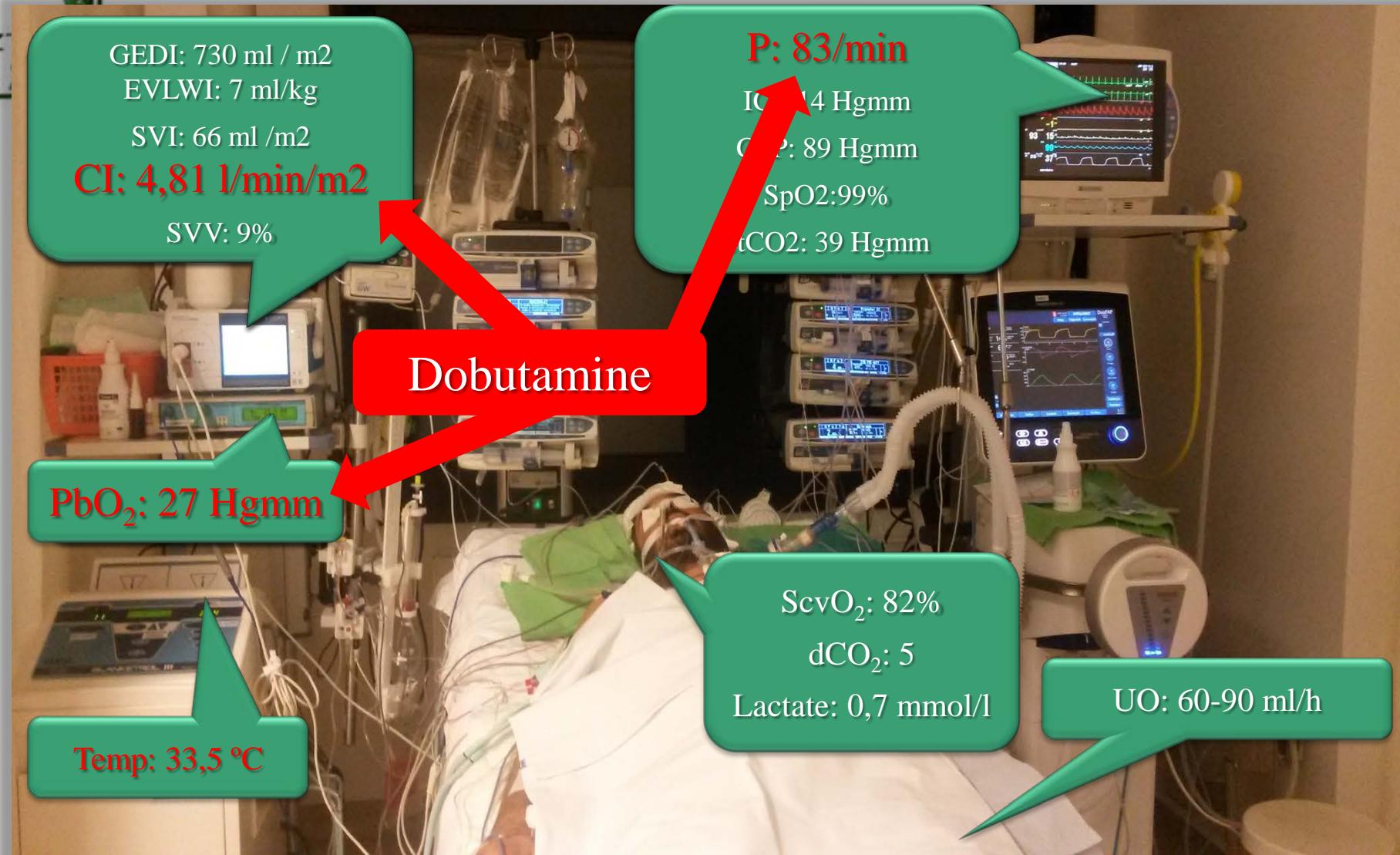
Maintenance fluid: 1 ml/kg/h

Boluses:

- Crystalloid group: 1600 ml (min=500, max=5000 ml)
- Colloid group: 560 ml (min=450, max=1500 ml)

No difference in outcome variables

Multimodal monitoring on the ICU

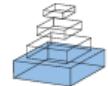




Instead of protocolized management:

frontiers in
PUBLIC HEALTH

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



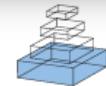
The multimodal concept of hemodynamic stabilization

Krisztián Tánczos, Márton Németh and Zsolt Molnár *

Department of Anaesthesiology and Intensive Therapy, University of Szeged, Szeged, Hungary

frontiers in
MEDICINE

SPECIALTY GRAND CHALLENGE ARTICLE
published: 08 April 2015
doi: 10.3389/fmed.2015.00022



Individualized goal directed perioperative care – the way to go!

Zsolt Molnár *

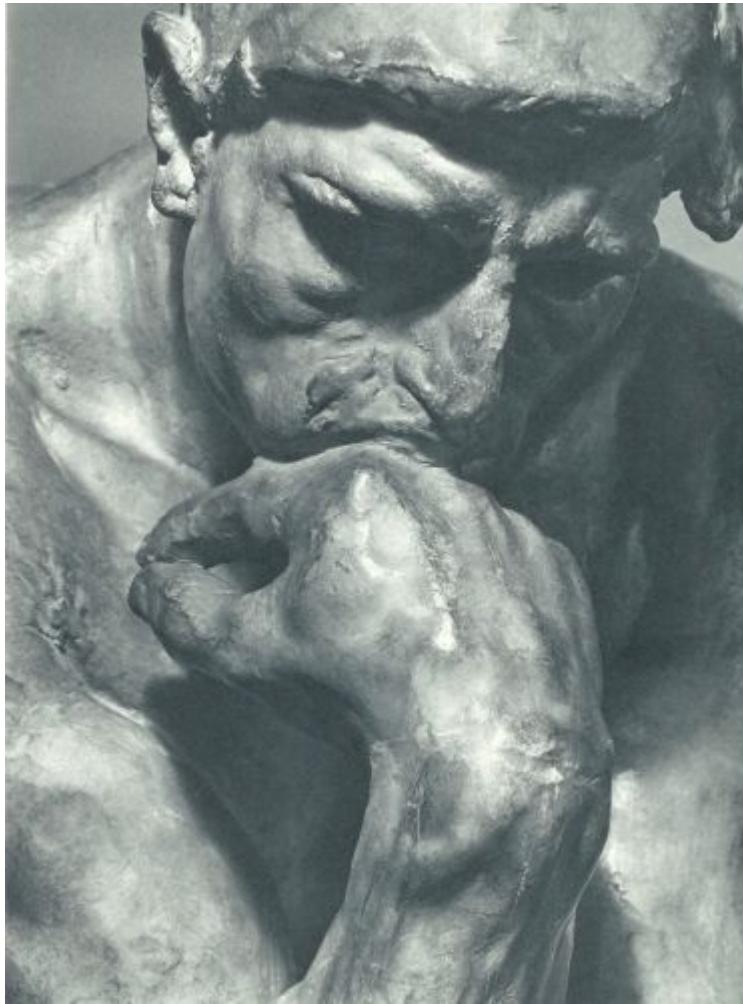
Department of Anaesthesiology and Intensive Therapy, Faculty of Medicine, University of Szeged, Szeged, Hungary

*Correspondence: zsoltmolna@gmail.com

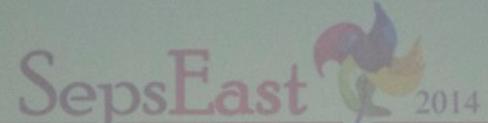
UNI



Thinking has no alternative!



Auguste Rodin: The Thinker, 1880



Free for junior doctors (<29)!

www.sepseast.eu

Budapest, 9-11 November 2016

