Critical Care Medicine
Limited Overview

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Overview of Selected Topics

- Resuscitation from Shock
  - Surviving Sepsis Guidelines
    - Earlier use of vasopressors
    - Choice of fluid
  - Resuscitation targets (pressure, flow, function)
    - Determinants of organ blood flow regulation
      - Tissue perfusion pressure
      - Vasoplegia = low diastolic arterial pressure
    - Dynamic parameters of volume responsiveness and vasomotor tone

I will not discuss:

Mechanical ventilation

Heart-Lung Interactions

Acute kidney injury

Antibiotic stewardship

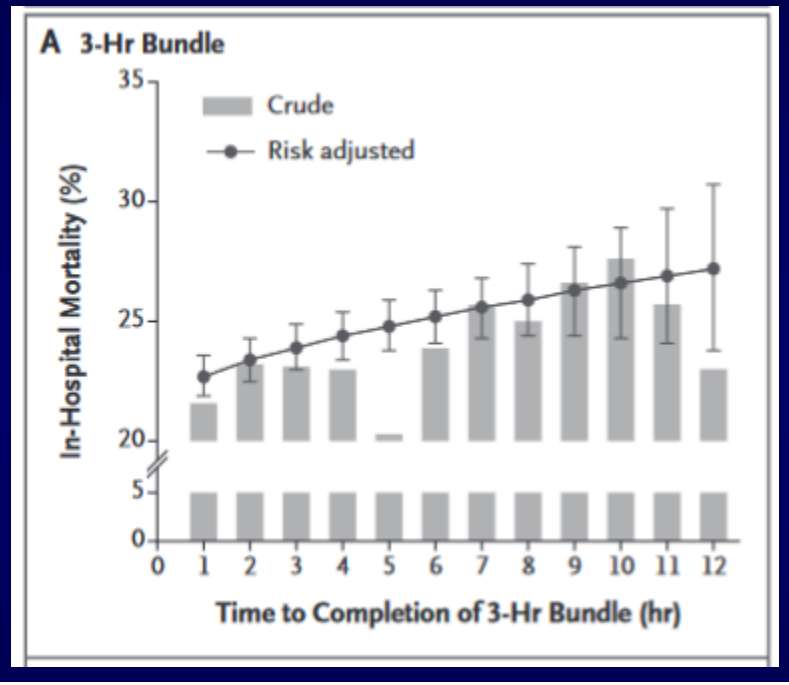
Nutrition

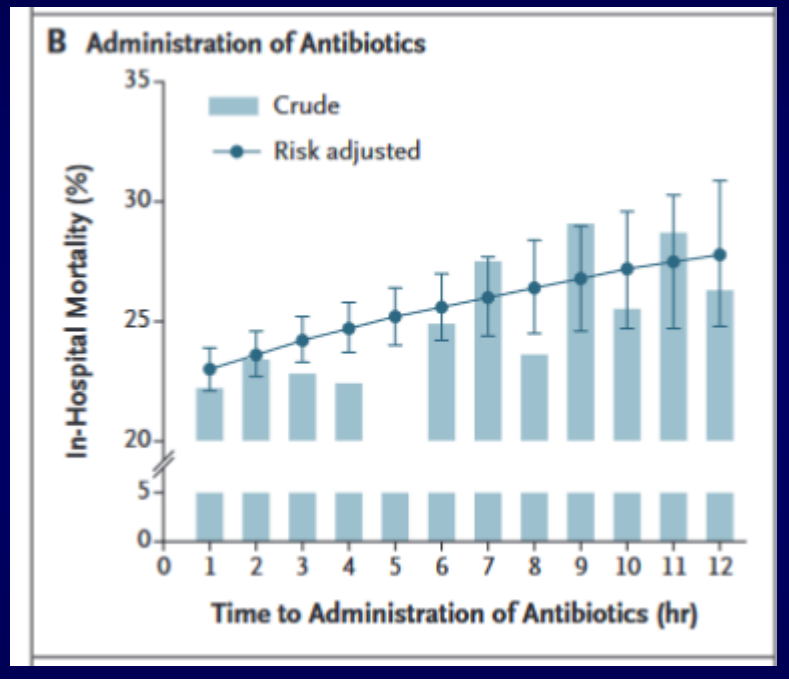
Neurotrauma

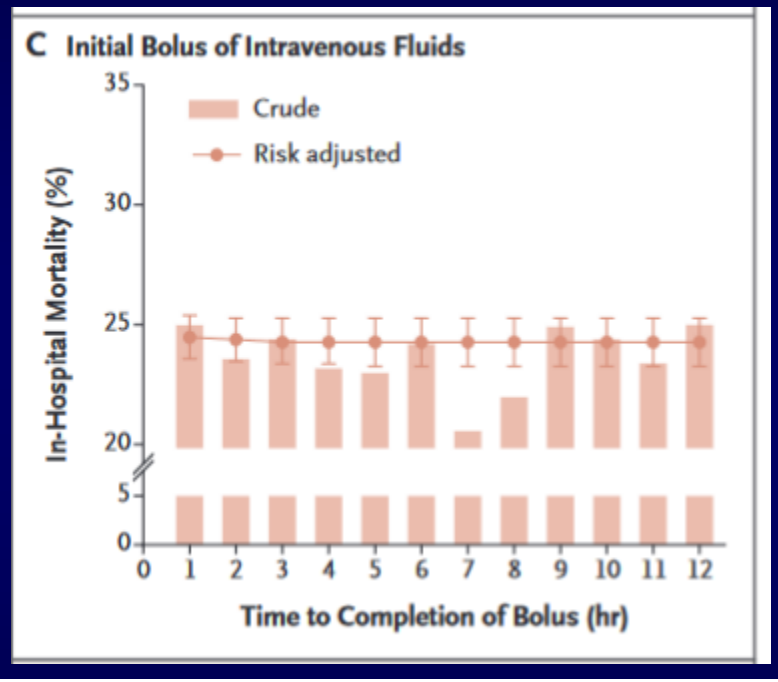
Resuscitation from Circulatory Shock

- Priorities depend on etiology
  - In septic shock mortality is inversely related to time of starting appropriate antibiotics, not fluid resuscitation
  - In all forms of circulatory shock, persistent hypotension is a cumulative ischemia burden
- Not all fluids are created equal
- Avoid fluid over-resuscitation
- Hypotension is bad, start vasopressors early to minimize both hypotension time and total fluid overload

Early Identification and Treatment from Sepsis in Children







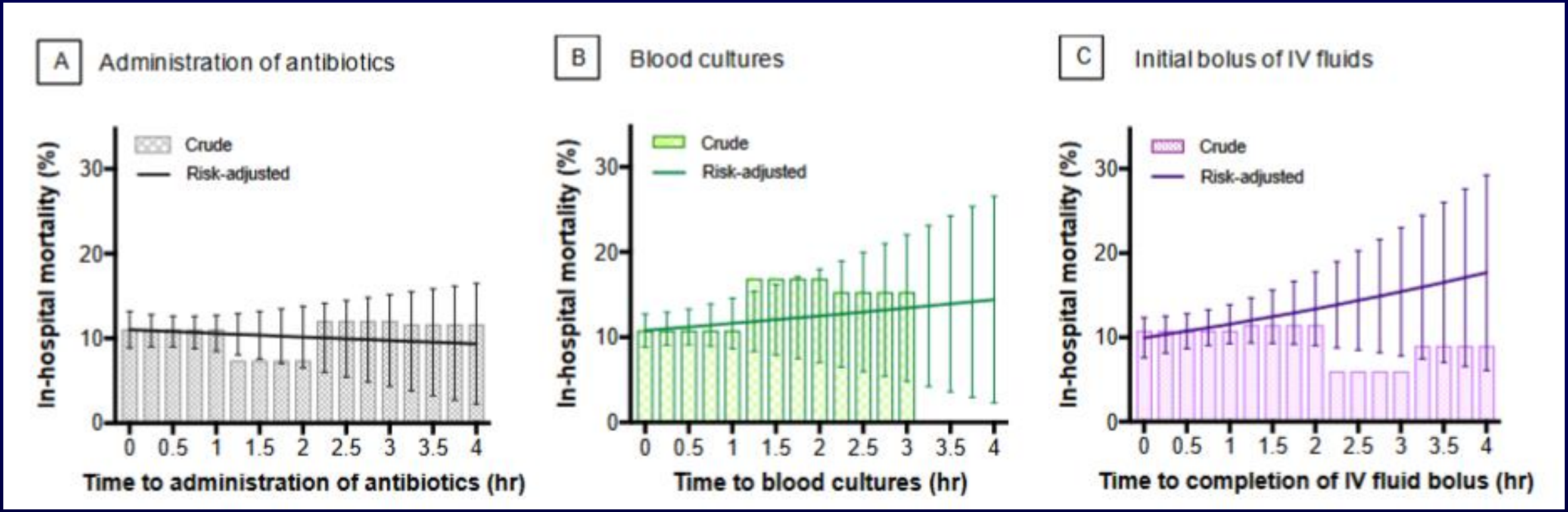
It was the earlier administration of antibiotics that drove survival, Not fluid resuscitation

Seymour et al. N Engl J Med 376 2235-44, 2017

Impact of the components of SSG Bundles

New York Sepsis Care Mandate

1179 patients with sepsis



SSG **downgraded** 30 ml/kg to a suggestion

ESICM review suggests personalizing fluid resuscitation

Evans et al. JAMA 320:358-67, 2018

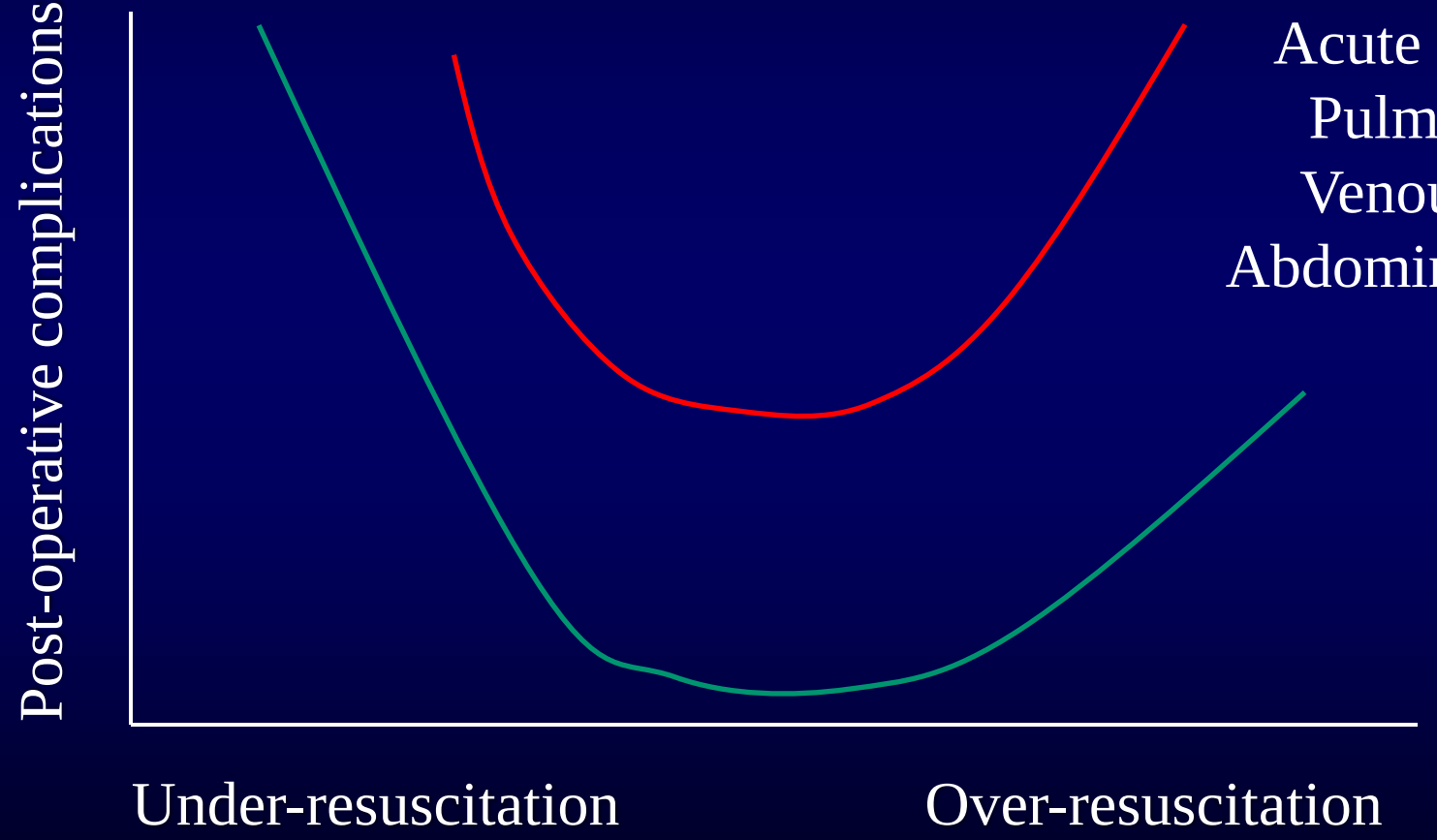
Why Not Give Volume to Every Unstable Patient as Primary Resuscitation Therapy?

	Responders / Non-Responders	% Responders
Calvin (Surgery 81)	20 / 8	71 %
Schneider (Am Heart J 88)	13 / 5	72 %
Reuse (Chest 90)	26 / 15	63 %
Magder (J Crit Care 92)	17 / 16	52 %
Diebel (Arch Surgery 92)	13 / 9	59 %
Diebel (J Trauma 94)	26 / 39	40 %
Wagner (Chest 98)	20 / 16	56 %
Tavernier (Anesthesiology 98)	21 / 14	60 %
Magder (J Crit Care 99)	13 / 16	45 %
Tousignant (A Analg 00)	16 / 24	40 %
Michard (AJRCCM 00)	16 / 24	40 %
Feissel (Chest 01)	10 / 9	53 %
Mean	**211 / 195**	**52 %**

Michard & Teboul. Chest 121:2000-8, 2002

Relation between fluid loading and complications during high-risk surgery

One must to be precise when giving fluids



Acute cor pulmonale
Pulmonary edema
Venous congestion
Abdominal hypertension

Bellamy. BJA 97:755-7, 2006

Sepsis in European intensive care units: Results of the SOAP study*

Jean-Louis Vincent, MD, PhD, FCCM; Yasser Sakr, MB, BCh, MSc; Charles L. Sprung, MD; V. Marco Ranieri, MD; Konrad Reinhart, MD, PhD; Herwig Gerlach, MD, PhD; Rui Moreno, MD, PhD; Jean Carlet, MD, PhD; Jean-Roger Le Gall, MD; Didier Payen, MD; on behalf of the Sepsis Occurrence in Acutely Ill Patients Investigators

Table 7. Multivariate, forward stepwise logistic regression analysis in sepsis patients (n = 1177), with intensive care unit mortality as the dependent factor

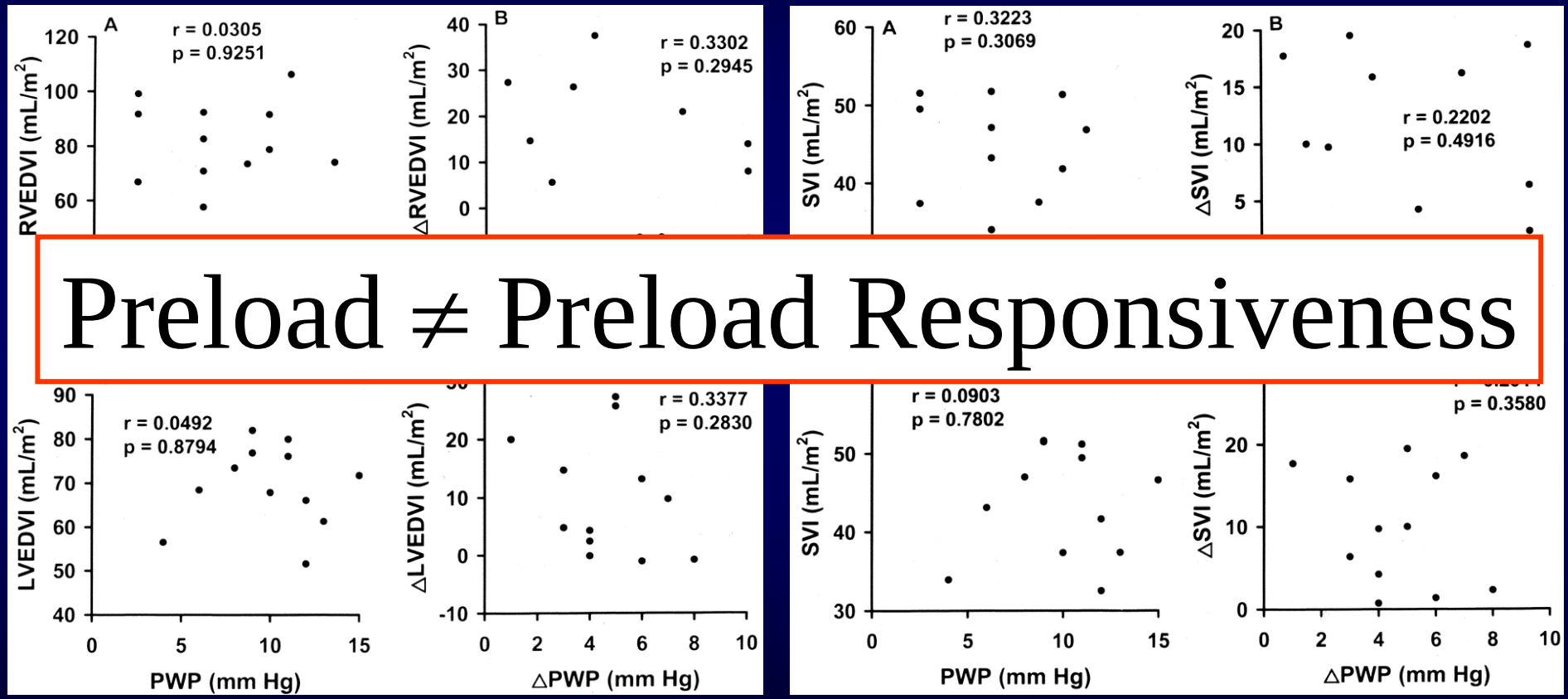
	OR (95% CI)	*p* Value
SAPS II score[a] (per point increase)	1.0 (1.0–1.1)	<.001
Cumulative fluid balance[b] (per liter increase)	1.1 (1.0–1.1)	.001
Age (per year increase)	1.0 (1.0–1.0)	.001
Initial SOFA score (per point increase)	1.1 (1.0–1.1)	.002
Blood stream infection	1.7 (1.2–2.4)	.004
Cirrhosis	2.4 (1.3–4.5)	.008
Pseudomonas infection	1.6 (1.1–2.4)	.017
Medical admission	1.4 (1.0–1.8)	.049
Female gender	1.4 (1.0–1.8)	.044

Vincent et al. Crit Care Med 34:344-53, 2006

Functional Hemodynamic Questions

- Is my patient in compensated shock?
- **Will cardiac output increase with fluid resuscitation, and if so, by how much?**
- Is arterial tone increased, normal or decreased?
- Is the heart able to maintain an adequate output under pressure without high filling pressures?

Neither CVP or Ppao reflect Ventricular Volumes or Tract Preload-Responsiveness

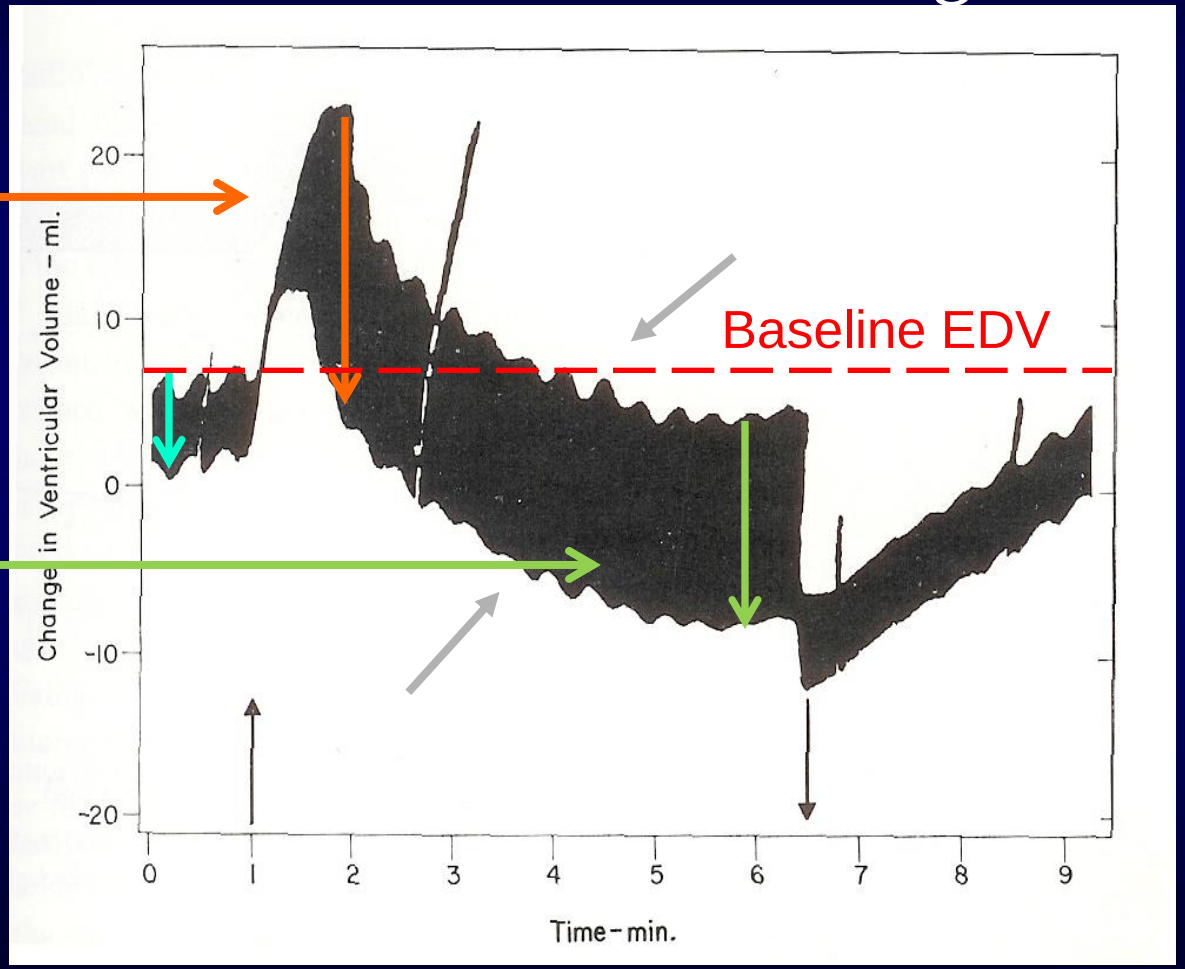


Kumar et al. Crit Care Med 32:691-9, 2004

Starling versus Anrep
Preload versus Contractility
Heterometric v. Homeometric autoregulation of the heart

Starling

Anrep



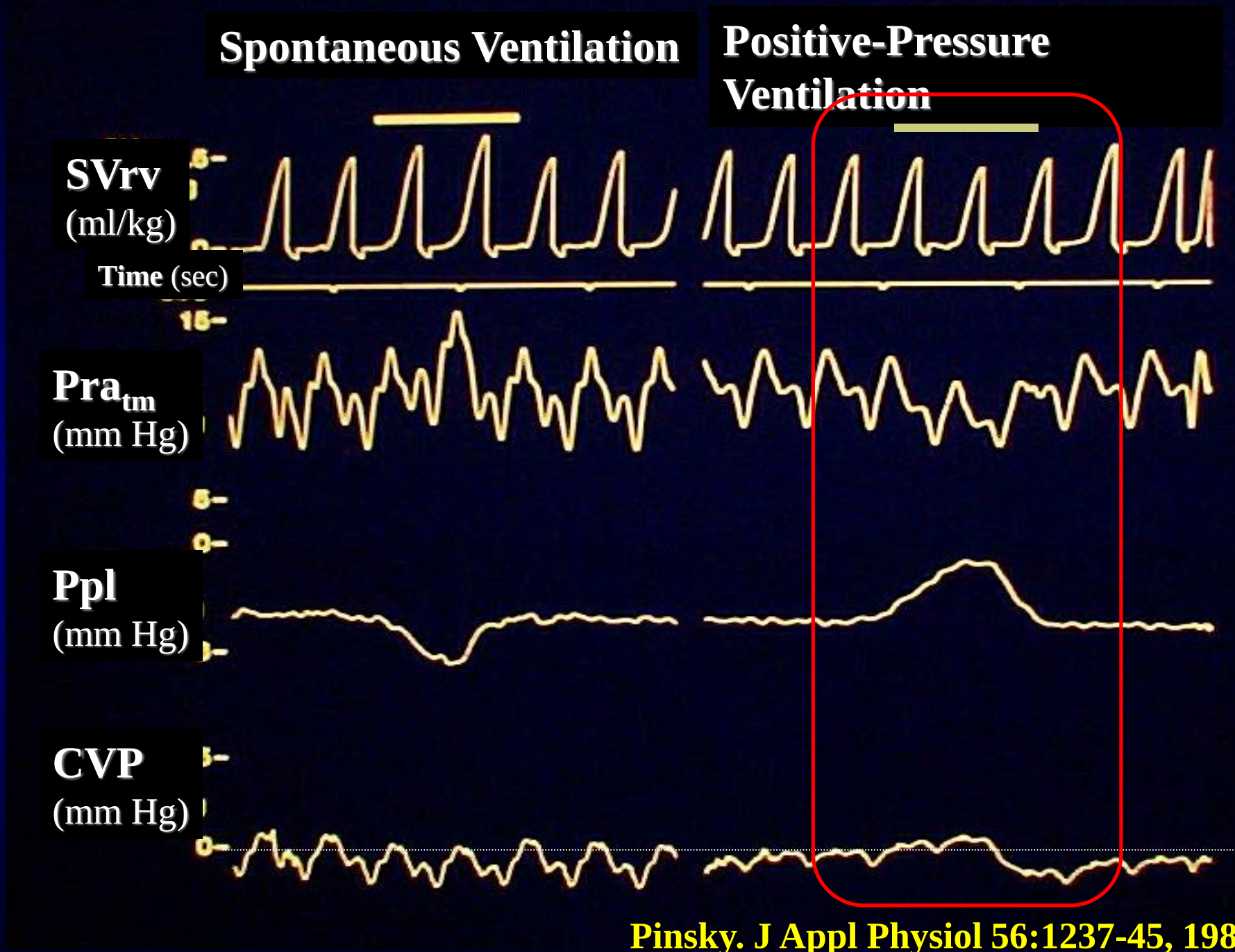
But Starling and Anrep Mechanisms are Short Term Adaptations to acute stress (~2 hr)

Acute Care Medicine

Long Term Adaptations are Hypertrophy and Dilation (days/weeks)

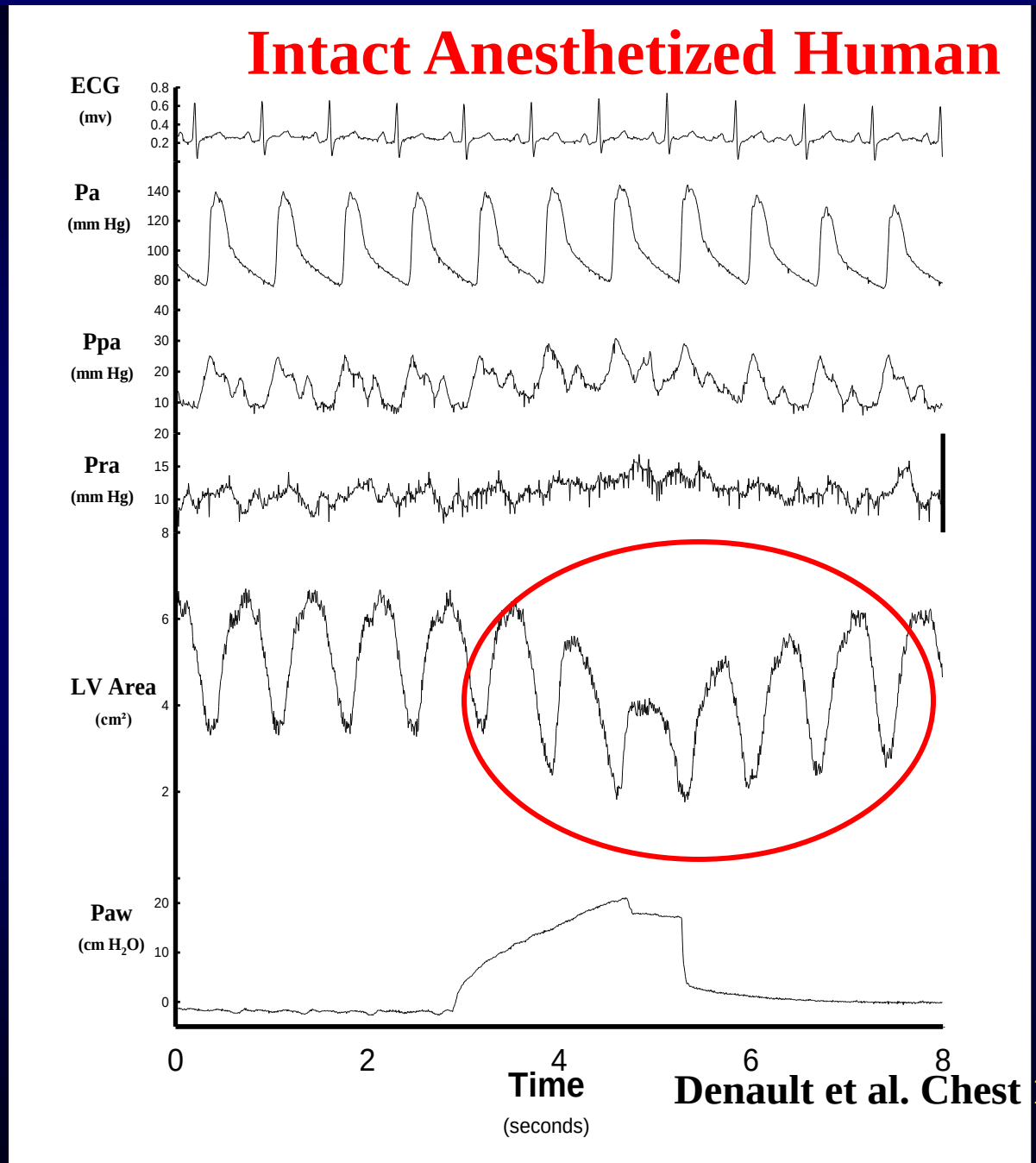
Sudden increase and decrease in venous return

Rosenblueth et al. Arch Int Physiol 67: 358, 1959



Pinsky. J Appl Physiol 56:1237-45, 1984

Effect of Positive-Pressure Ventilation on LV Volumes and Pressure



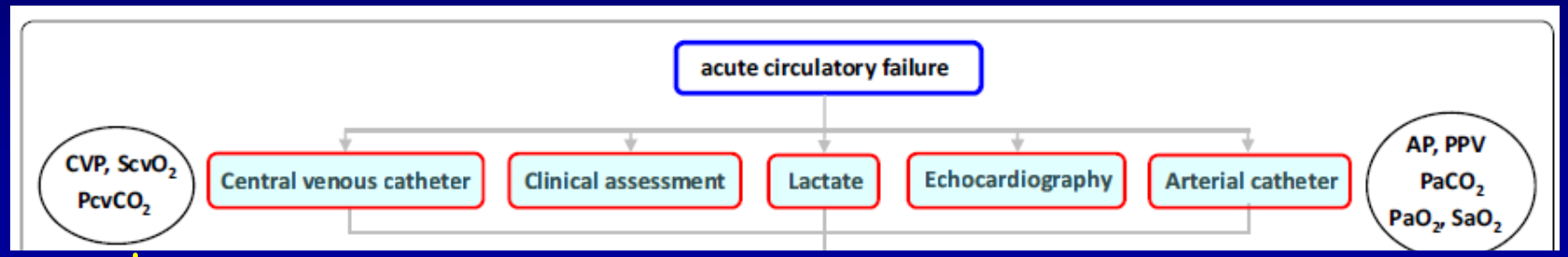
Denault et al. Chest 1999; 116:176-86

Intensive Care Med (2016) 42:1350–1359

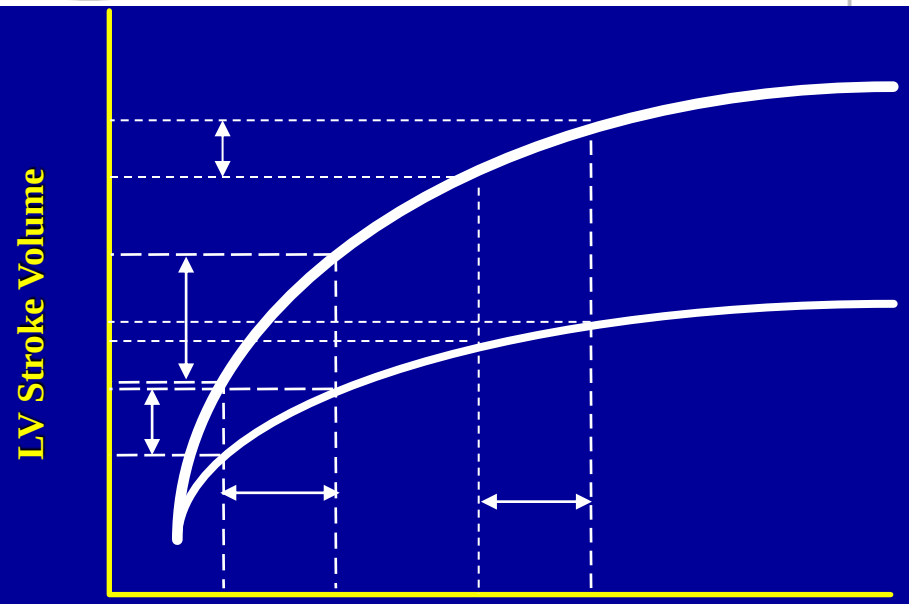
CONFERENCE REPORTS AND EXPERT PANEL

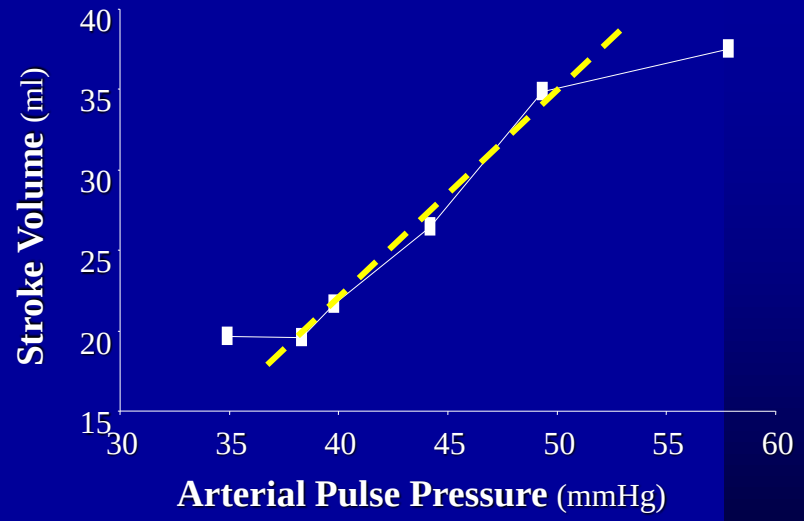
Less invasive hemodynamic monitoring in critically ill patients

Jean-Louis Teboul[1*], Bernd Saugel[2], Maurizio Cecconi[3], Daniel De Backer[4], Christoph K. Hofer[5], Xavier Monnet[1], Azriel Perel[6], Michael R. Pinsky[7], Daniel A. Reuter[2], Andrew Rhodes[3], Pierre Squara[8], Jean-Louis Vincent[9] and Thomas W. Scheeren[10]



PPV

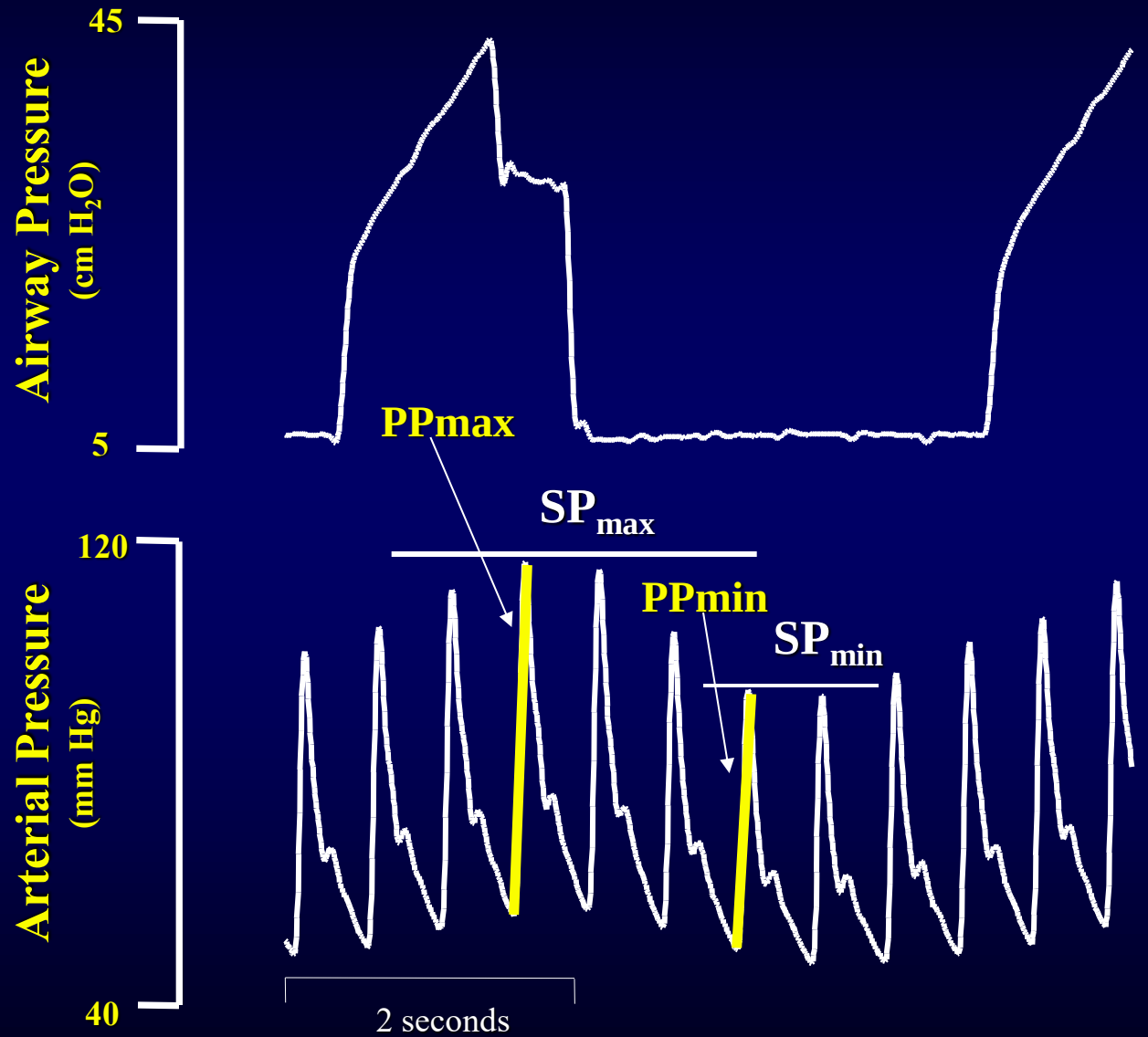




Michard et al. Am J Respir Crit Care Med 162:134-8, 2000

Marquez et al. Crit Care Med 36:3001-7, 2008

Definitions: Δ Pulse Pressure & Δ Systolic Pressure

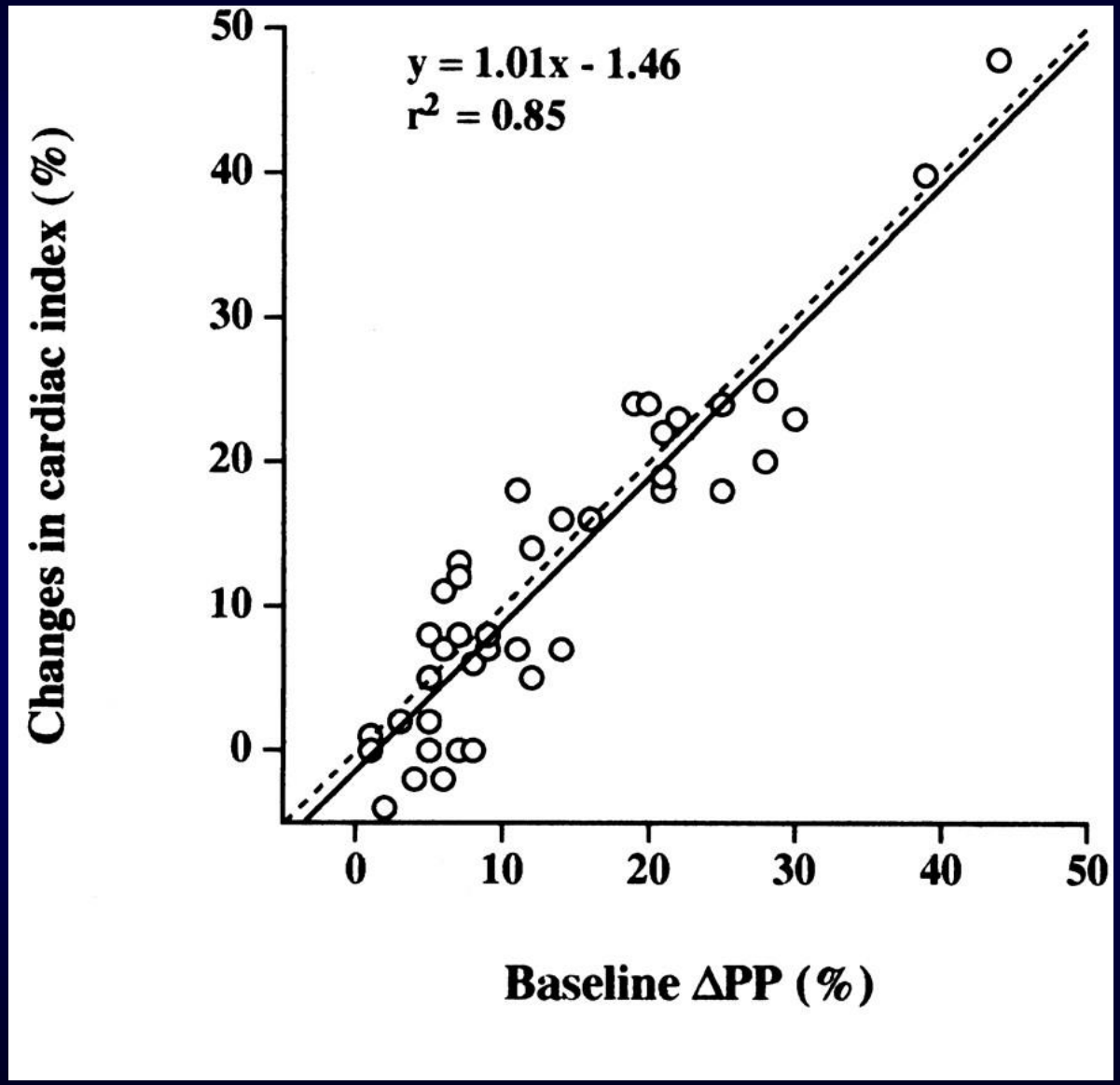


Δ Pulse Pressure (PP) = PPmax-Ppmin

PPV = (PPmax-PPmin)/PPmean

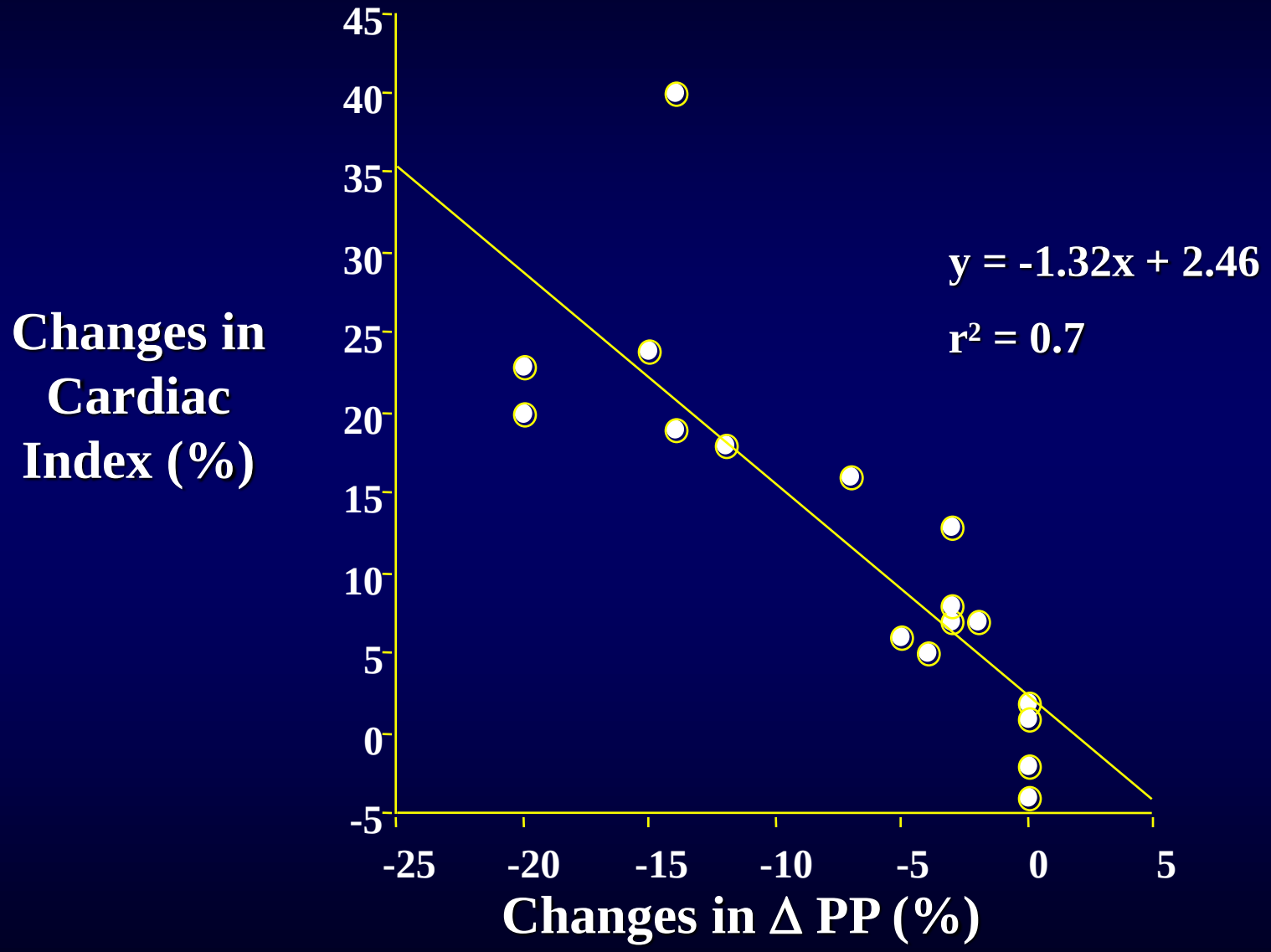
Michard et al. Am J Respir Crit Care Med 159:935-9, 1999

Baseline Δ PP Predicts Volume Responsivenessin Hypotensive Septic Patients



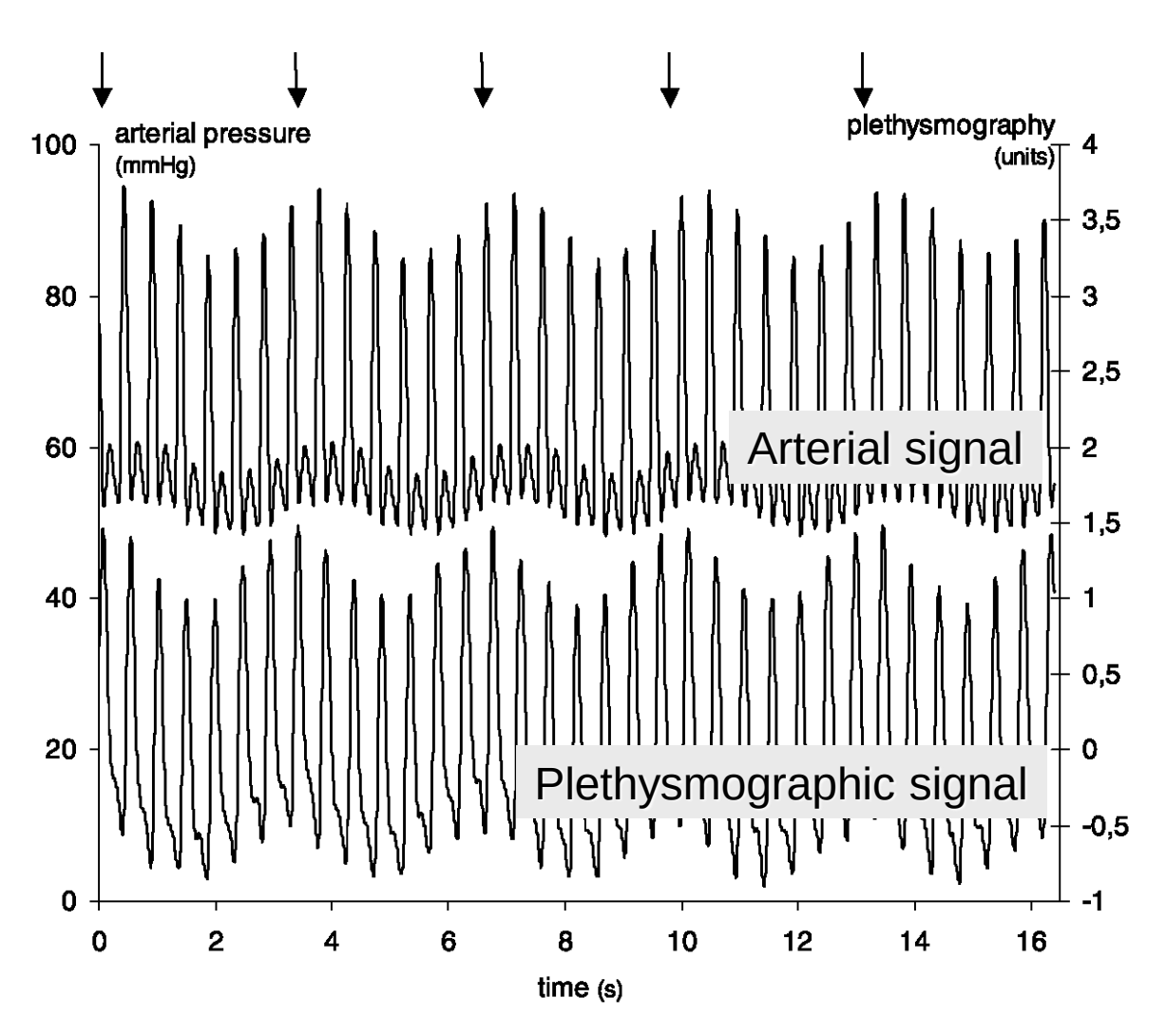
Michard et al. Am J Respir Crit Care Med 162:134-8, 2000

Changes in Δ PP Predict Changes in Cardiac Index in Septic Shock



Michard et al. Am J Respir Crit Care Med 162:134-8, 2000

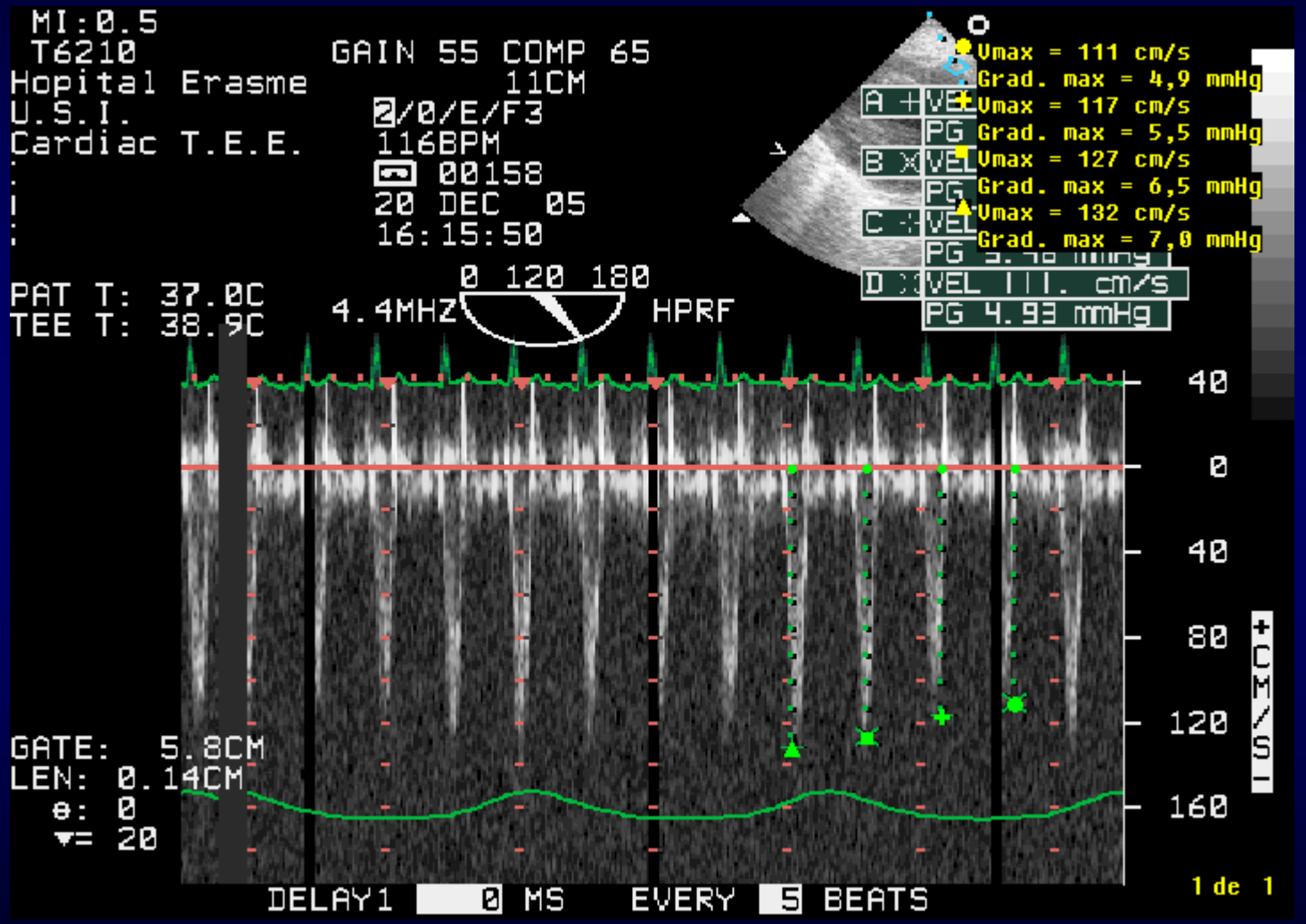
Arterial versus Plethysmographic Dynamic Indices to Predict Volume Responsiveness in Hypotensive Patients



Cut-off values:
ΔPP: 13%
ΔP_{pleth}: 9%

Natalini et al. Anesth Analg 103:1182-8, 2006

Respiratory variations in aortic flow



Feissel et al. Chest 119:867-72, 2001

Applicability of pulse pressure variation: how many shades of grey?

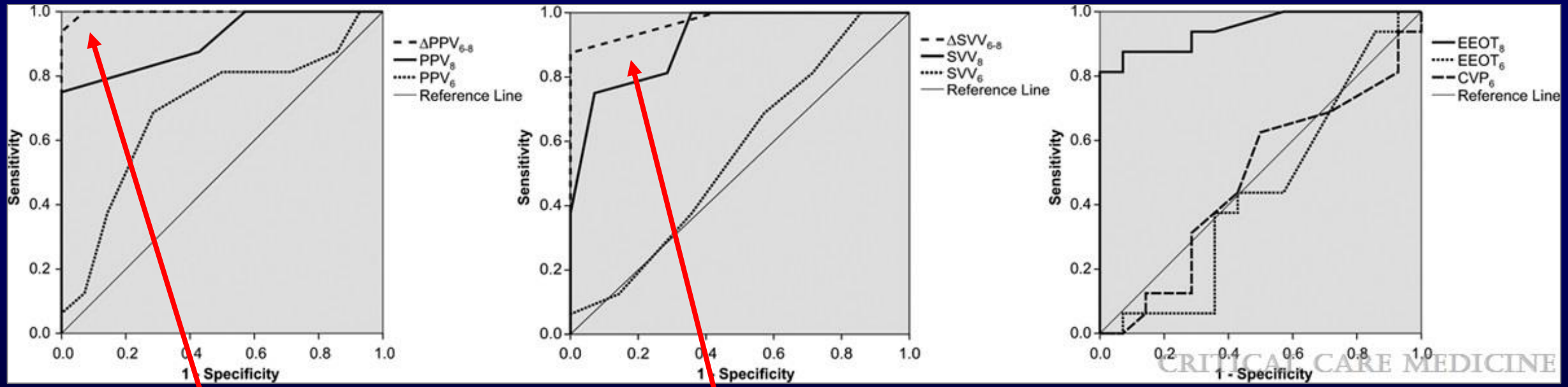
Frederic Michard[1*], Denis Chemla[2] and Jean-Louis Teboul[3]

Critical Care (2015) 19:144

	False positive	False negative
L **Low** HR/RR ratio (Extreme bradycardia or high frequency ventilation)		✓
I **Irregular** heart beats	✓	
M **Mechanical** ventilation with low tidal volume		✓
I **Increased** abdominal Pressure (Pneumoperitoneum)	✓	
T **Thorax** open		✓
S **Spontaneous** breathing	✓	✓

Tidal Volume Challenge

- Measure PPV or SVV during 6 ml/kg then after increasing Vt to 8 ml/kg for 20 seconds (ΔPPV_{6-8} or ΔSVV_{6-8})

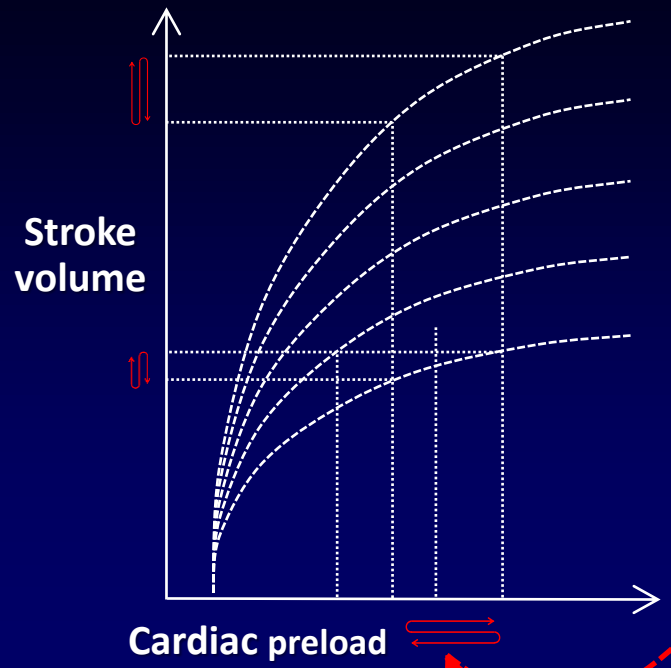


ΔPPV_{6-8} (>3.5%)

ΔSVV_{6-8} (>2.5%)

Myatra et al. Crit Care Med 45:415-21, 2017

Prediction of Fluid Responsiveness



Mimicking a fluid challenge

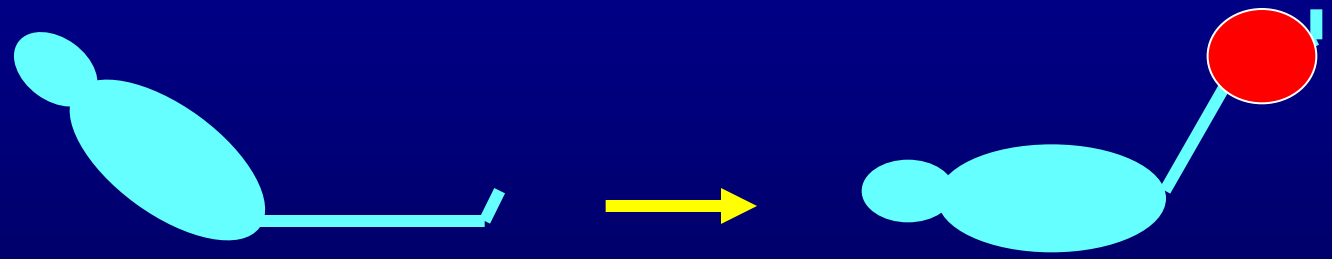
- 2006 — Passive leg raising test
- 2011 — Mini-fluid challenge

Using heart-lung interactions

- 2000 — Pulse pressure variation
- 2004 — Stroke volume variation
- Vena cava collapsibility
- 2009 — End-expiratory occlusion
- 2017 — Tidal volume challenge
- 2017 — Sigh manoeuvre

Monnet, Malbrain & Pinsky, Intensive Care Med 49: 83-6, 2020

The passive leg raising test

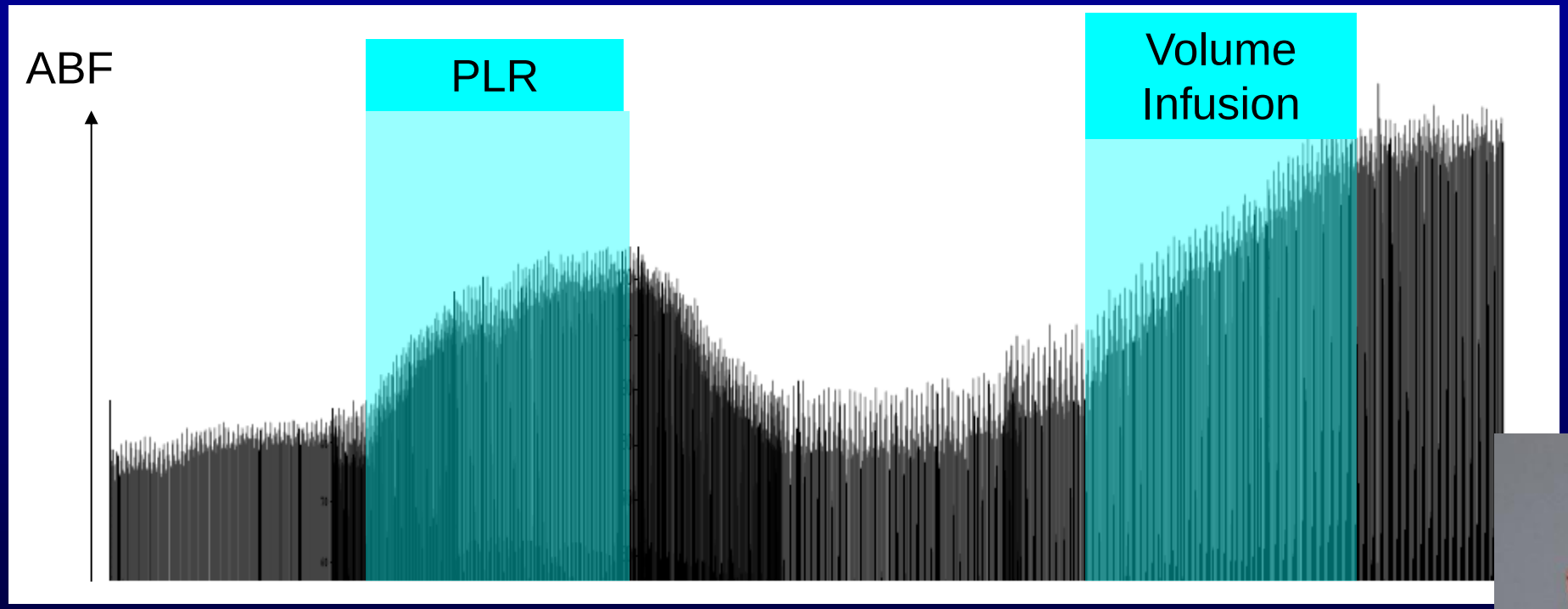


Autotransfusion of ~300 mL of blood

Measurement of cardiac output with fast response device (beat by beat) within 1 min of PLR (transient effect)

Prediction of Fluid Responsiveness

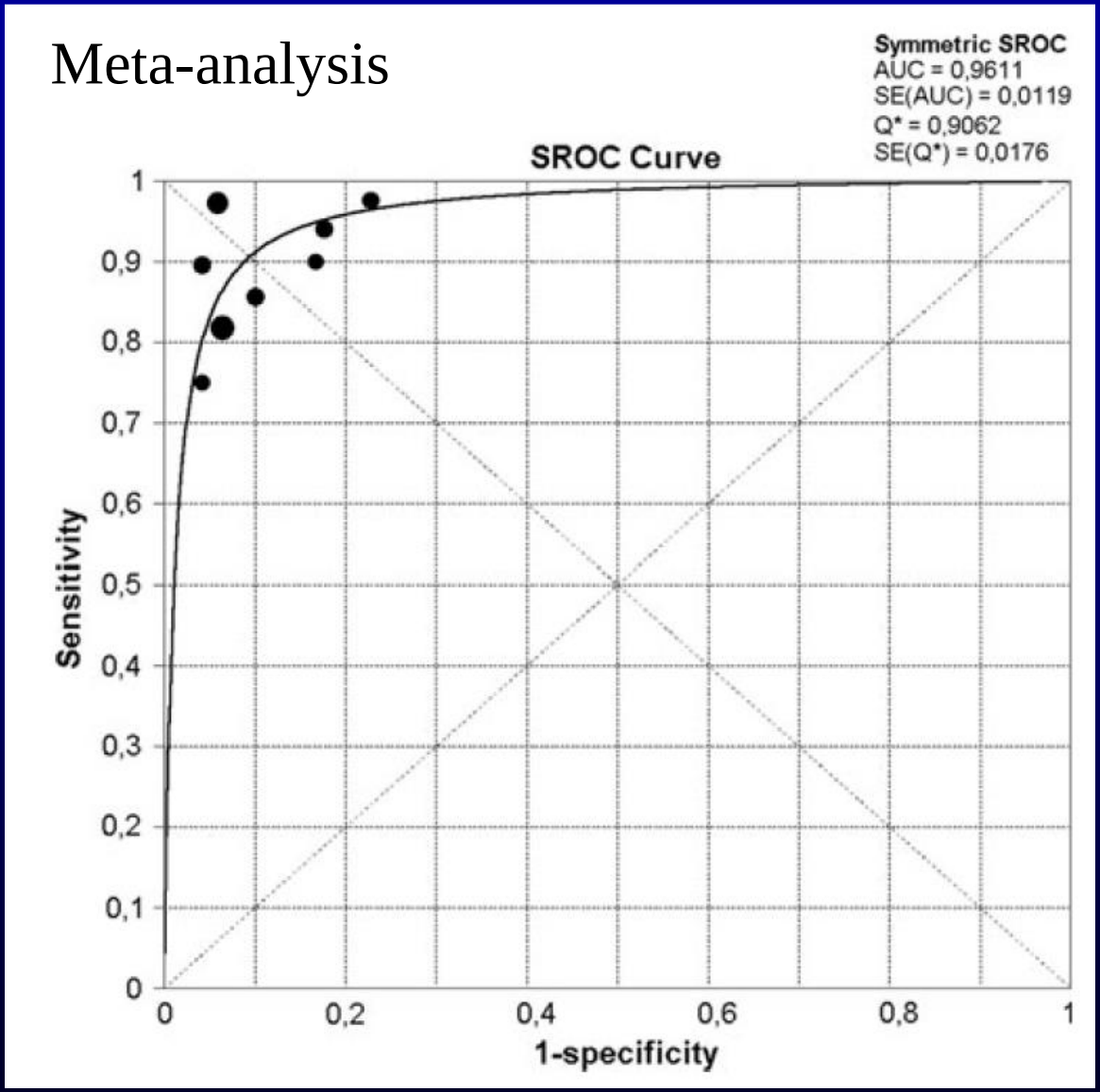
Spontaneous breathing and arrhythmias



The PLR effects occur over a epoch of time encompassing several cardiac and respiratory cycles

Monnet et al. Crit Care Med 34:1402-7, 2006

The passive leg raising test predicts volume responsiveness



9 trials
353 pts

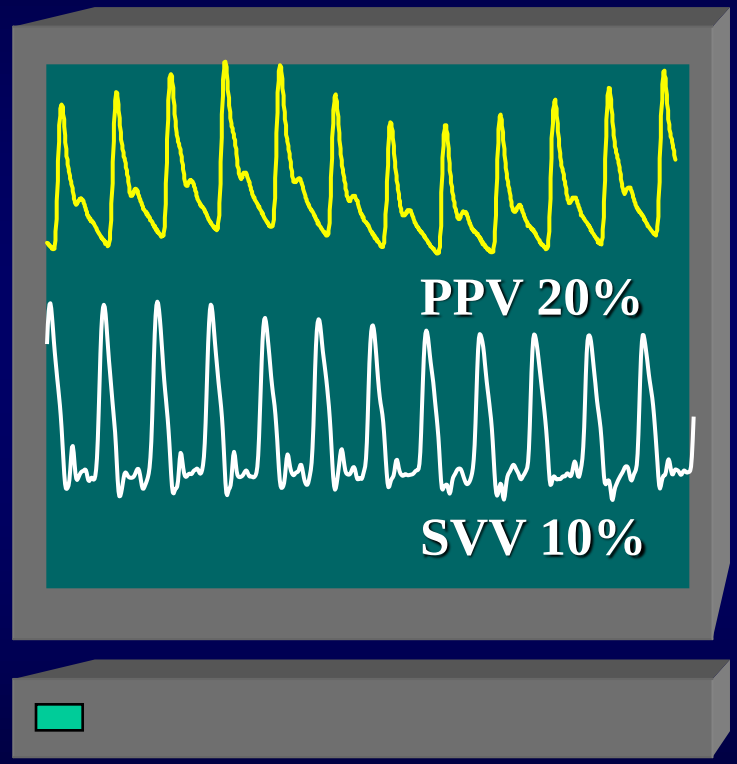
Cavallaro et al. Intensive Care Med 36:1475-82, 2010

How to assess preload-responsiveness in spontaneously breathing patients?

- Volume challenge
- Passive leg raising
  - **DeBacker & Pinsky. Intensive Care Med 33:1111-3, 2007**

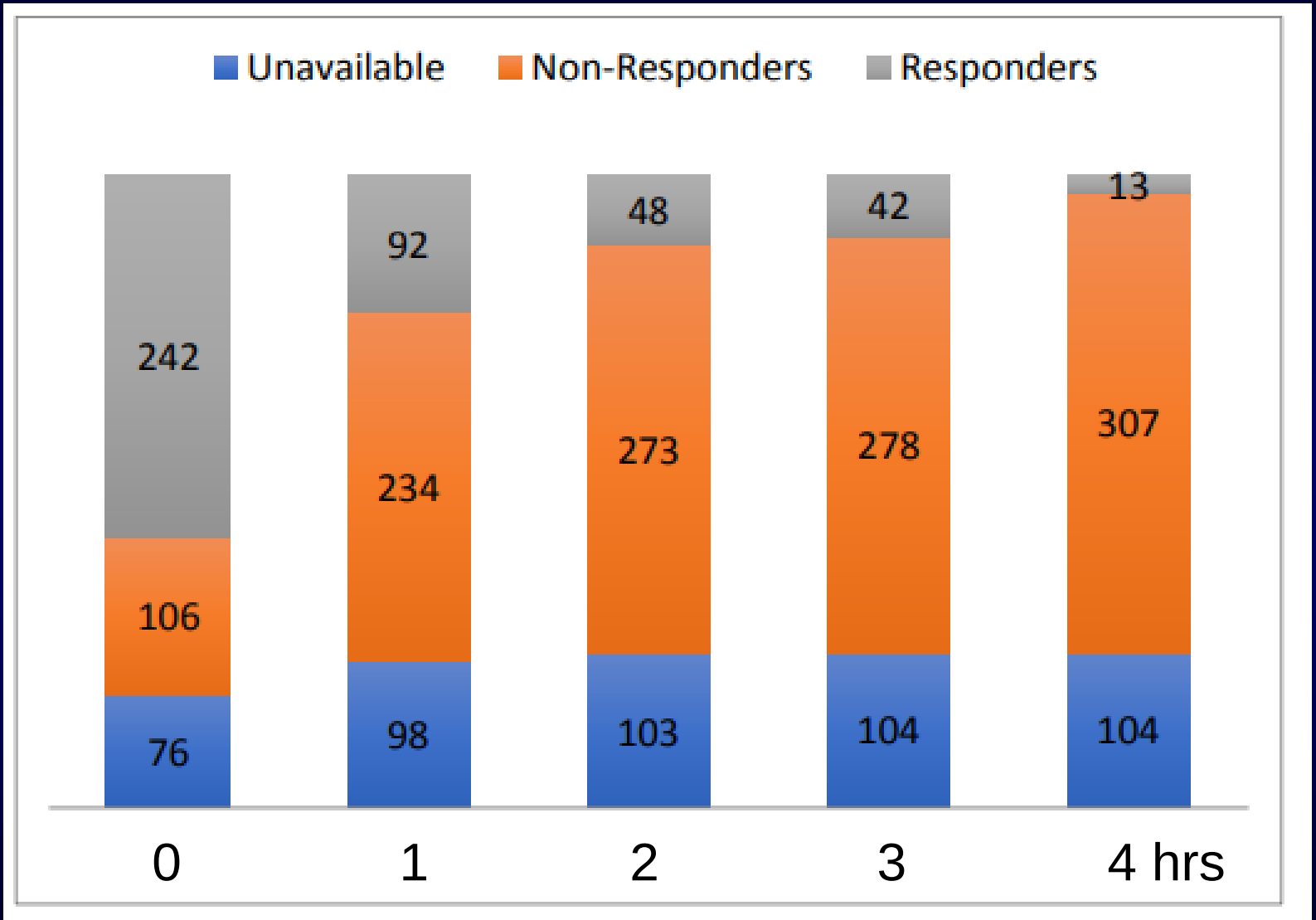
FDA-Approved Devices for Continuous Monitoring of Preload Responsiveness

- **Arterial Pressure**
  - Non-invasive
    - **ClearSight ®, Masimo pleth, CVInsight ®, CNAP ®, LiDCO*rapid* ®**
  - Invasive
    - **Arterial catheterization**
- **Arterial flow**
  - **Esophageal Doppler**
    - **Deltex CardiaQ, USCOM**
  - **Echocardiography, hTEE**
- **Combined Pressure and Flow**
    - Pulse Contour Technology
    - **PiCCO®, LiDCO®, FloTrac®, MostCare ®**



PPV > 13%
SVV > 10%
ΔCO > 10%

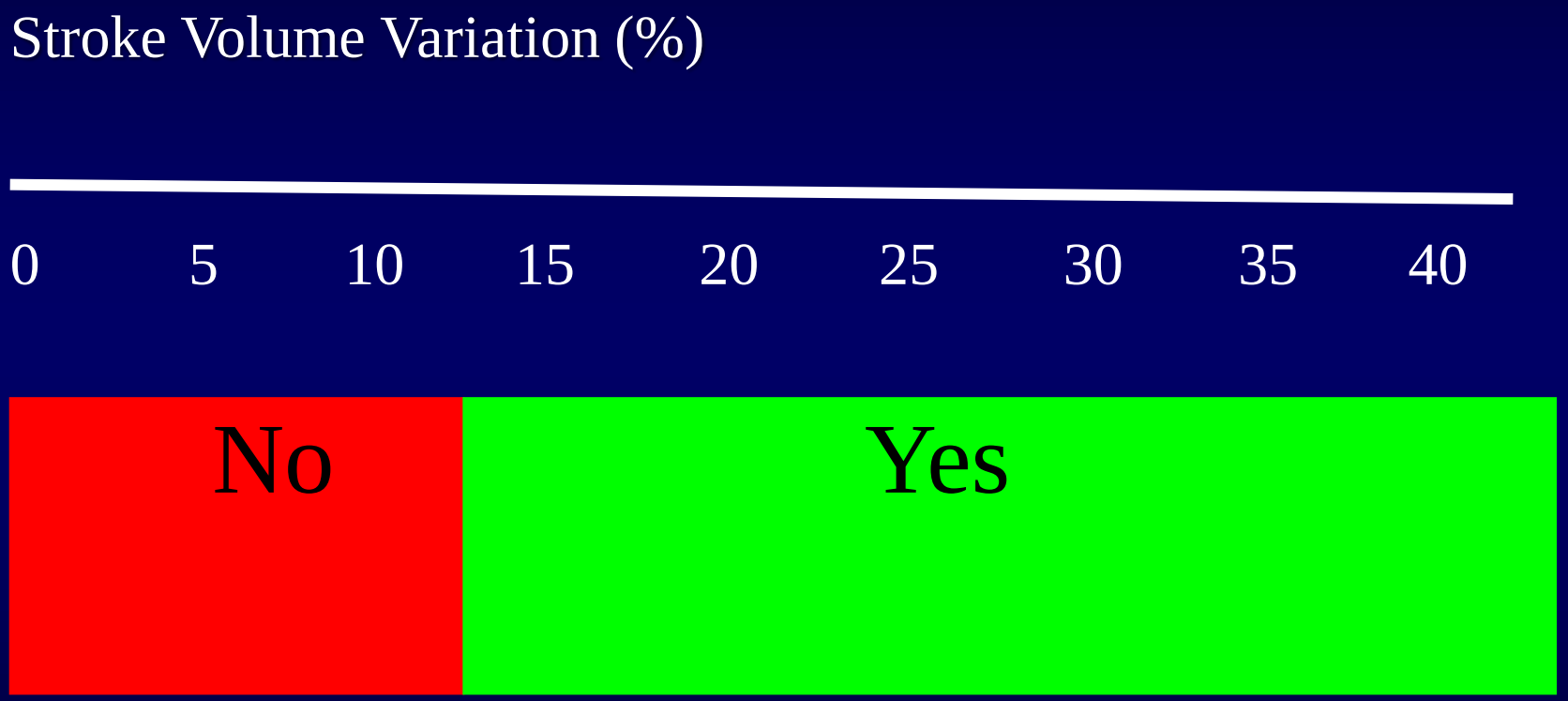
Fluid Responsiveness Changes with Resuscitation



At baseline, 57% of patients were fluid responsive and 25% fluid unresponsive

Hernández et al. JAMA 2019;321:654–64, 2019

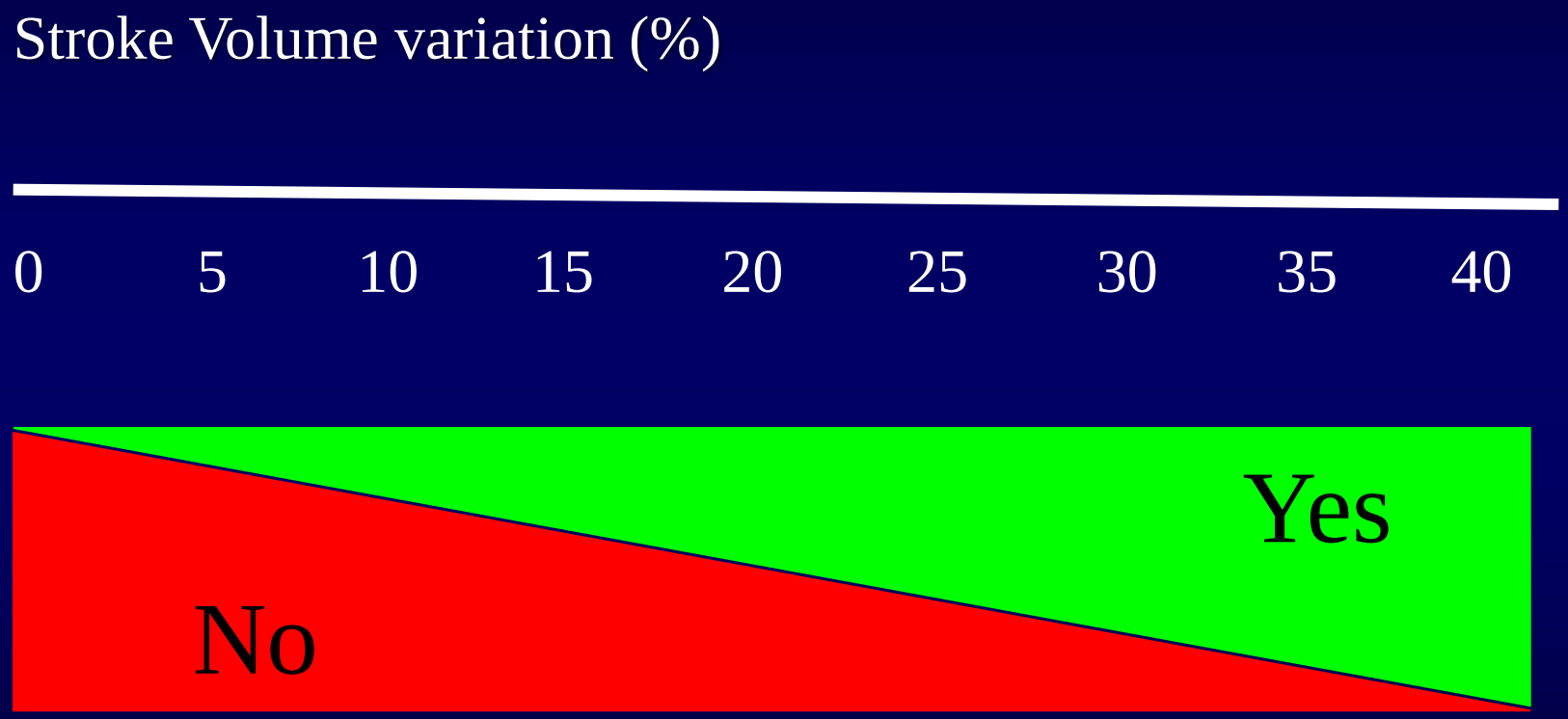
The ideal world…



Likelihood of response to fluids

from D DeBacker

But fluid responsiveness is a continuum,
not an on/off phenomenon!



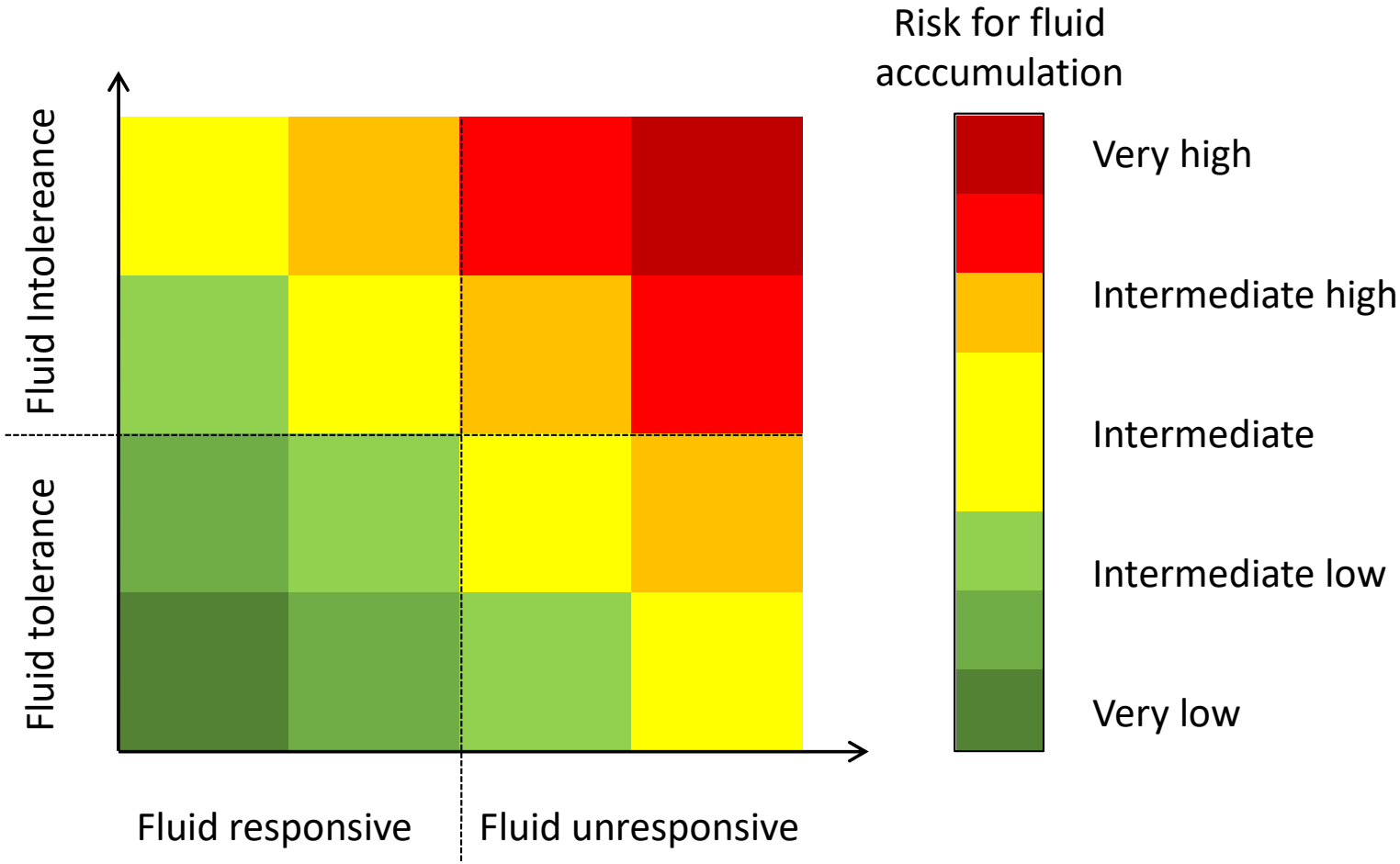
Likelihood of response to fluids

from D DeBacker

Even If Fluid Responsive, Fluids Carry Risk

Intra-abdominal
Cor pulmonale
Hypertension
ARDS

Early septic shock
Acute hemorrhage



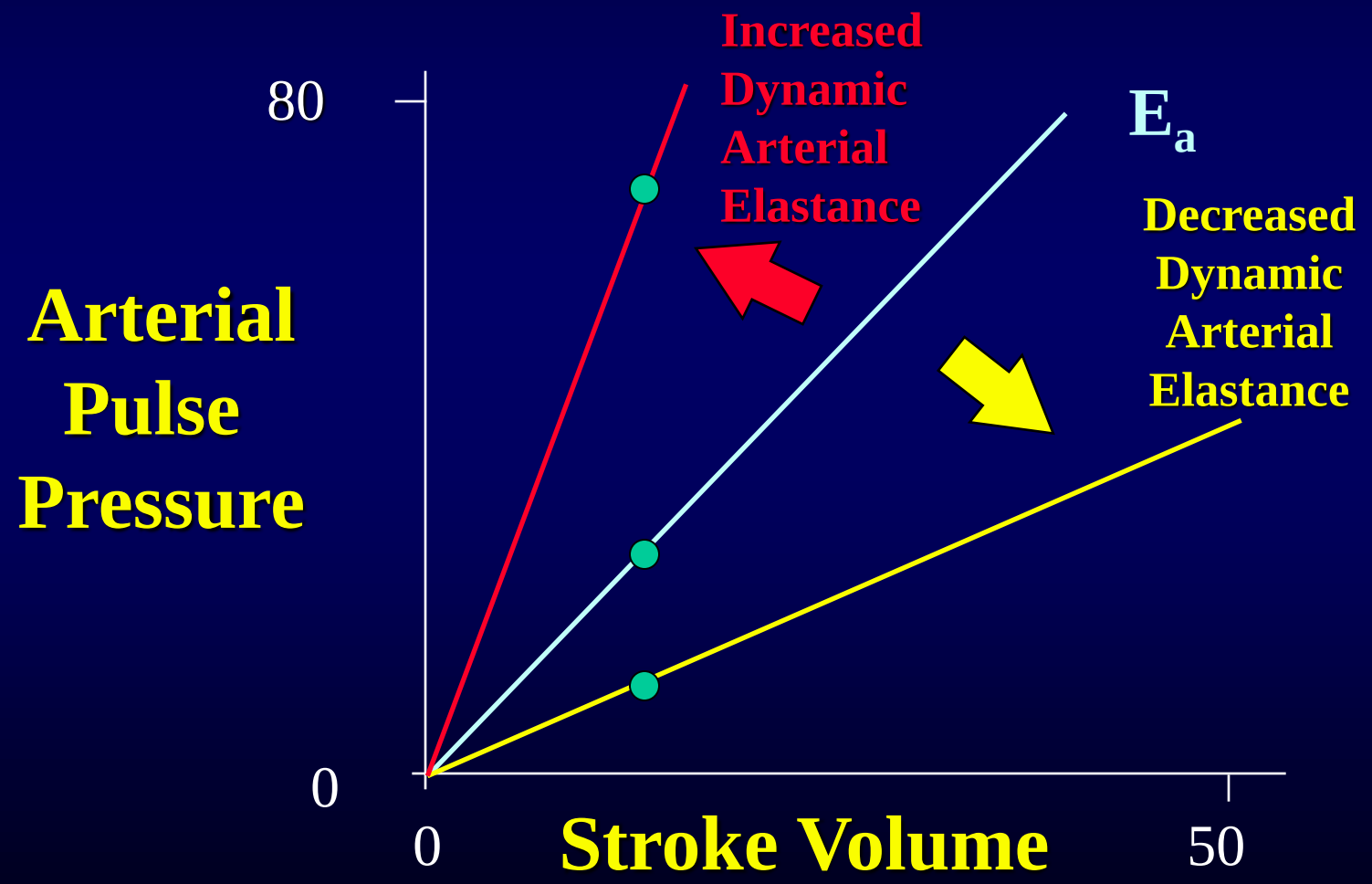
Monnet, Malbrain & Pinsky, Intensive Care Med 49: 83-6, 2020

Functional Hemodynamic Questions

- Is my patient in compensated shock?
- Will cardiac output increase with fluid resuscitation, and if so, by how much?
- **Is arterial tone increased, normal or decreased?**
- Is the heart able to maintain an adequate output under pressure without high filling pressures?

Ventriculo-Arterial Coupling

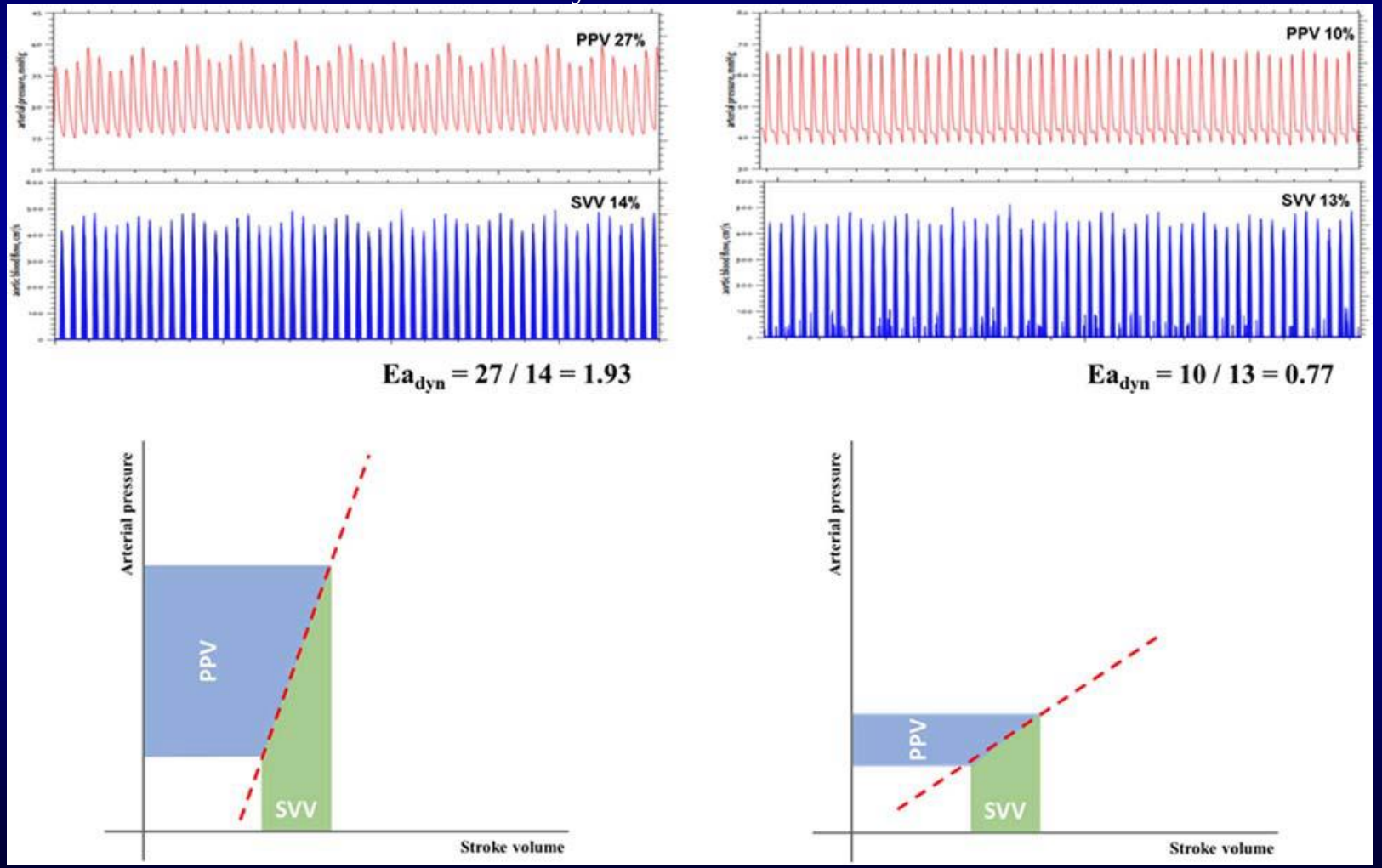
Dynamic Arterial Elastance (E_a) **Defines** the **Gain** in Stroke Volume/Arterial Pressure Relation



Dynamic Parameters to Predict Vasomotor Responsiveness

Ratio of Pulse pressure variation (PPV) and stroke volume variation (SVV)

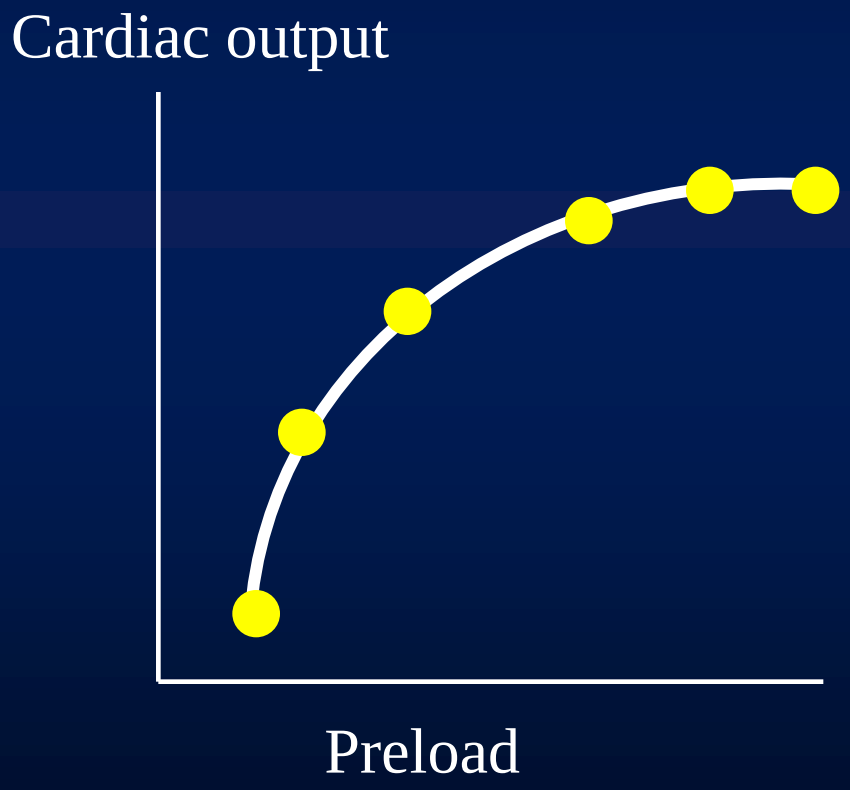
Ea_{dyn} = PPV/SVV

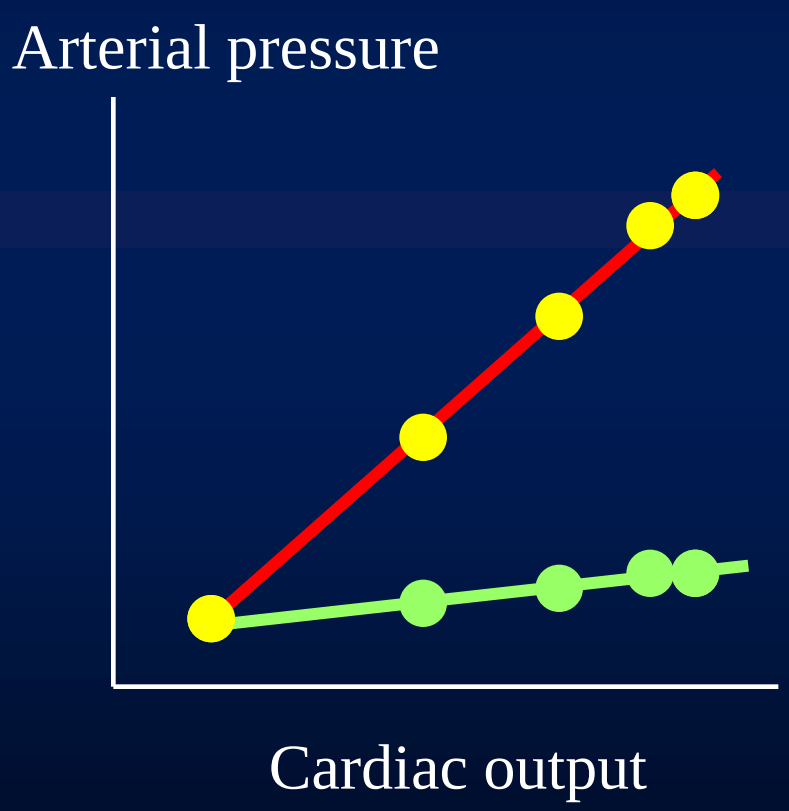


Monge Garcia et al. Intensive Care Med 43:1841-3, 2017

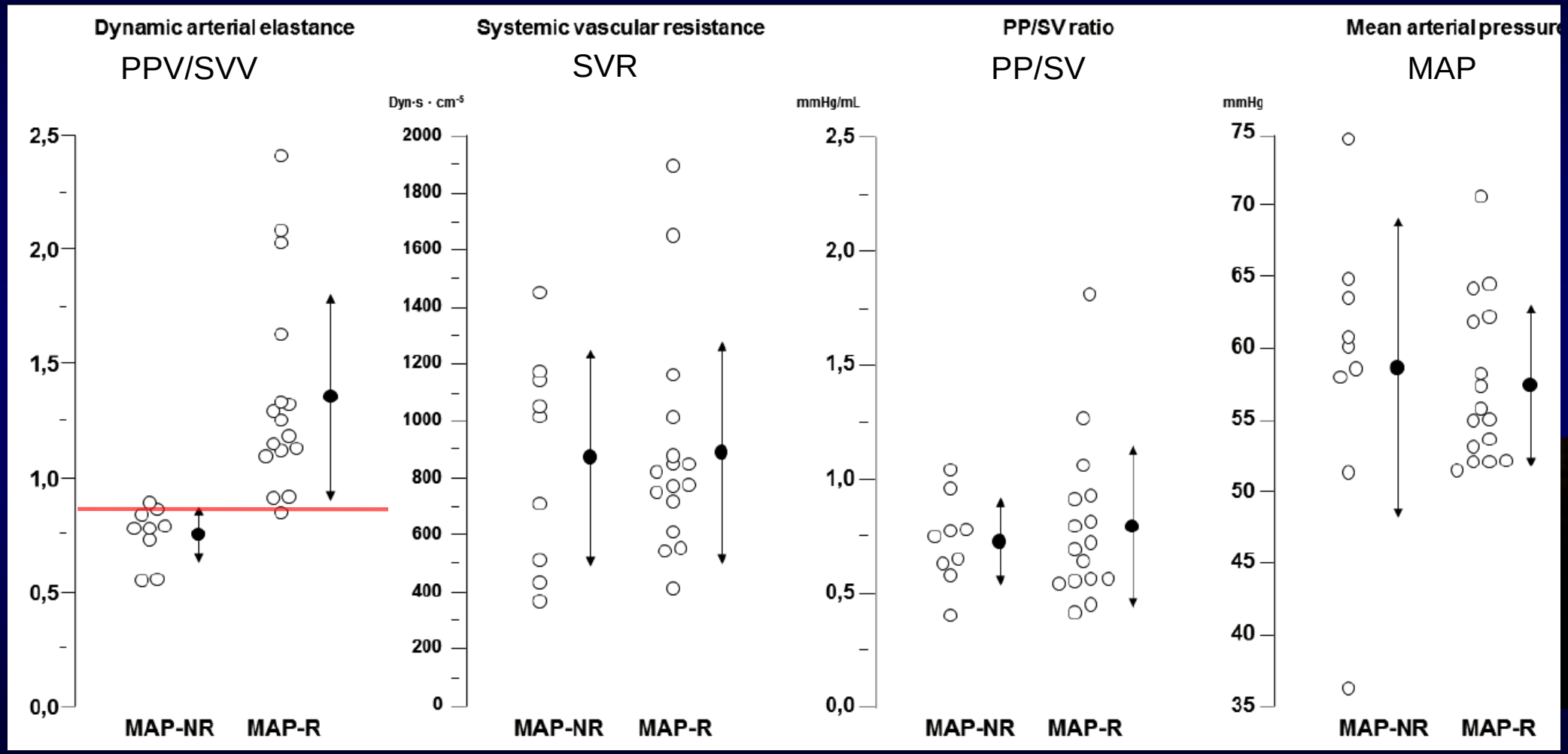
Why is it important to identify a Low Ea?

In a hypotensive patient, if Ea is low, then increasing cardiac output alone will not increase arterial pressure.



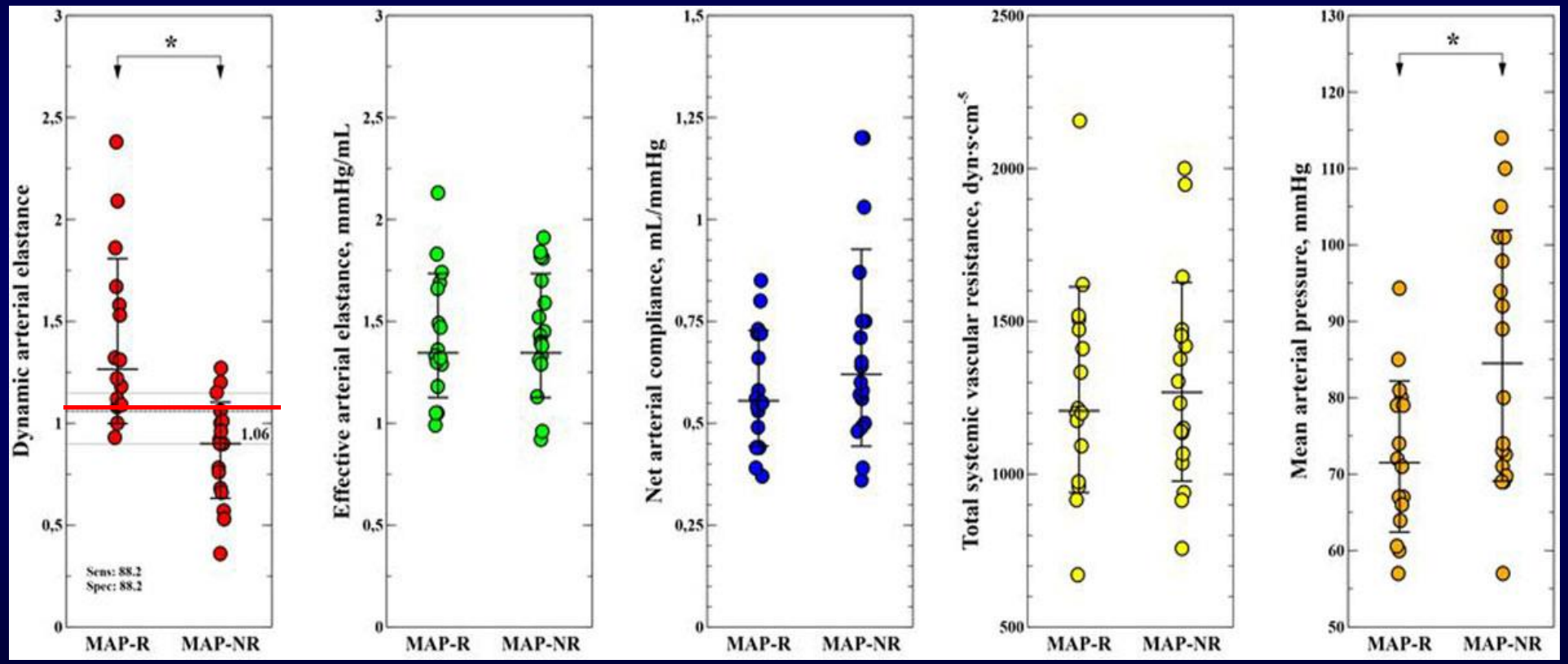


Comparing PPV to SVV as Dynamic Arterial Elastance



Monge et al. Crit Care 15:R15, 2011

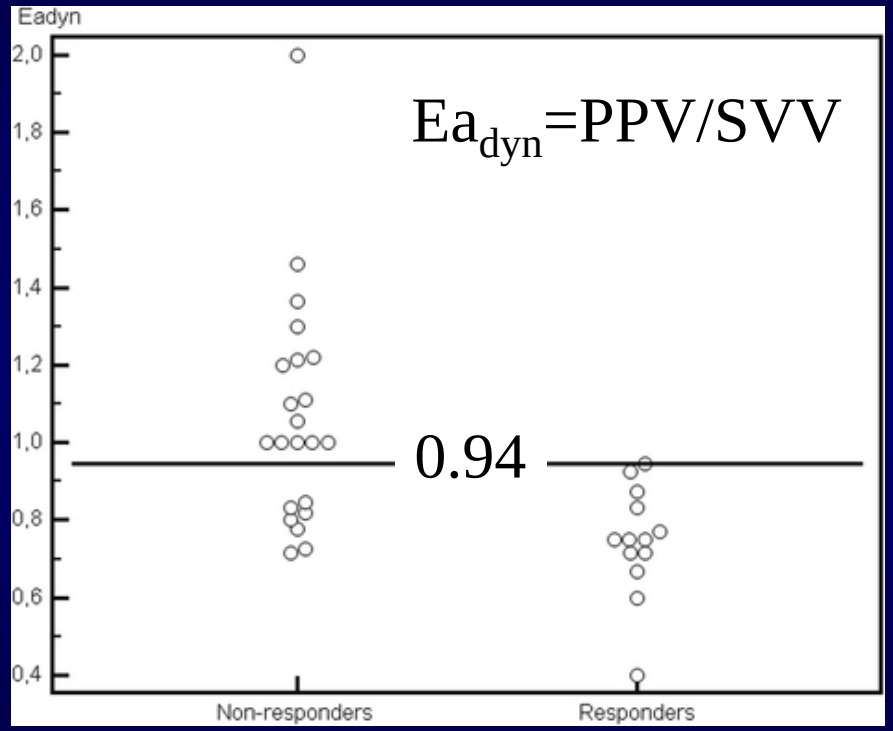
Ea_{dyn} Predict Arterial Pressure Response to Fluid Administration in Spontaneously Breathing Patients



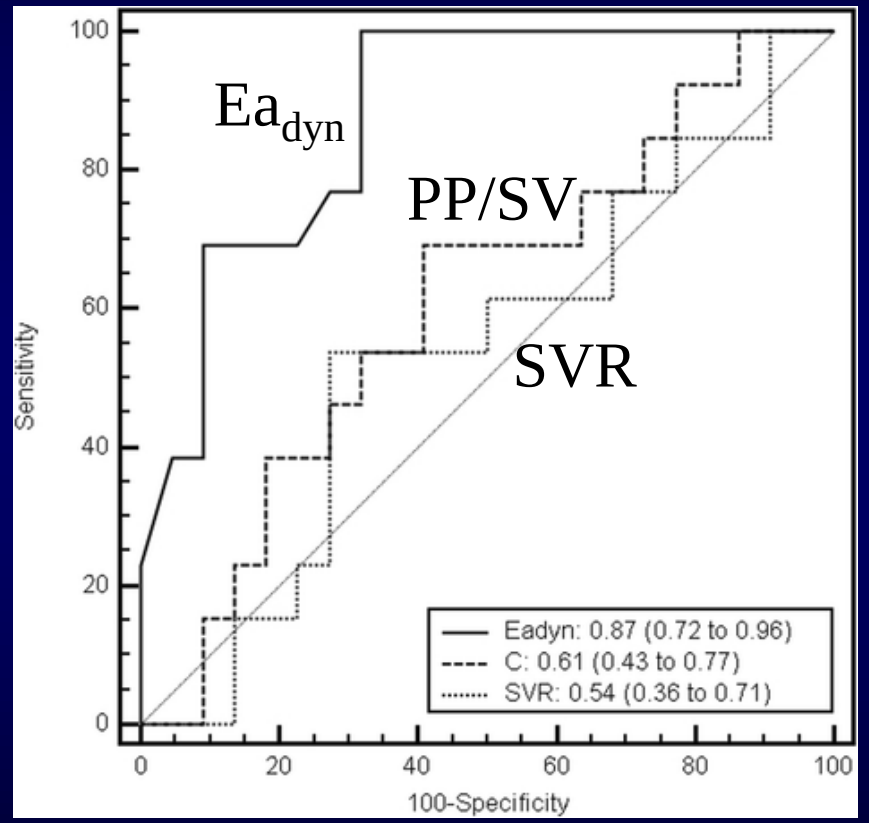
PPV/SVV Ea PP/SV SVR MAP

Cecconi et al. Crit Care 18:P181, 2014

Ea_{dyn} predicts MAP decrease with decreasing norepinephrine in vasoplegic shock



ROC Curve



Non-responder = no change in MAP

SVR=(MAP-CVP)/CO

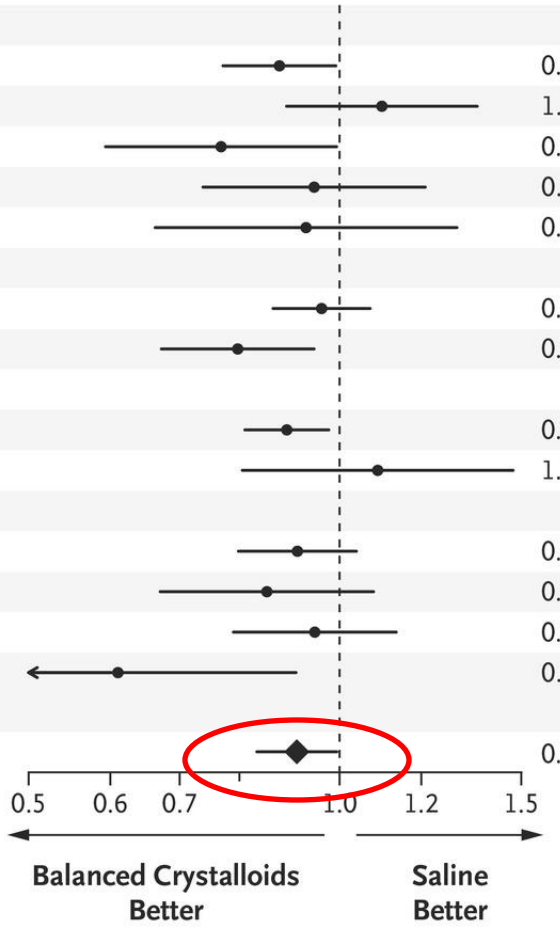
Guinot et al. Crit Care 19:14 2017

What type of fluid?

- Crystalloid
  - Balanced salt solution
  - 0.9N NaCl
- Colloids
  - Albumin
  - ~~Hydroxyethyl starch~~

Balanced Crystalloids versus Saline in Critically Ill Adults

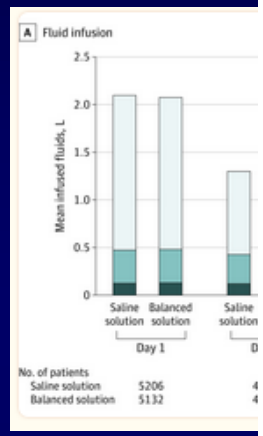
Subgroup	Balanced Crystalloids	Saline	Odds Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no. (%)				
Unit					0.27
Medical	615/2735 (22.5)	659/2646 (24.9)	0.87 (0.77–0.99)	0.04	
Cardiac	202/1470 (13.7)	190/1501 (12.7)	1.10 (0.89–1.36)	0.38	
Neurologic	116/1440 (8.1)	141/1377 (10.2)	0.77 (0.59–0.99)	0.04	
Trauma	131/1640 (8.0)	142/1688 (8.4)	0.95 (0.74–1.21)	0.66	
Surgical	75/657 (11.4)	79/648 (12.2)	0.93 (0.66–1.30)	0.66	
Sepsis					0.06
No	744/6775 (11.0)	756/6691 (11.3)	0.96 (0.86–1.07)	0.47	
Yes	395/1167 (33.8)	455/1169 (38.9)	0.80 (0.67–0.94)	0.01	
Traumatic brain injury					0.24
No	1034/7244 (14.3)	1118/7195 (15.5)	0.89 (0.81–0.98)	0.01	
Yes	105/698 (15.0)	93/665 (14.0)	1.09 (0.81–1.47)	0.58	
Categories of kidney function					0.19
Normal	476/5596 (8.5)	514/5561 (9.2)	0.91 (0.80–1.04)	0.16	
Acute kidney injury	315/574 (54.9)	316/537 (58.8)	0.85 (0.67–1.08)	0.18	
Chronic kidney disease	301/1388 (21.7)	307/1360 (22.6)	0.95 (0.79–1.13)	0.55	
Previous renal-replacement therapy	47/384 (12.2)	74/402 (18.4)	0.61 (0.41–0.91)	0.01	
Overall	1139/7942 (14.3)	1211/7860 (15.4)	0.91 (0.83–0.99)	0.04	

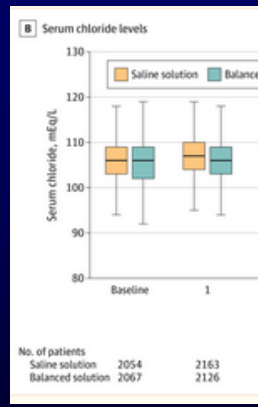


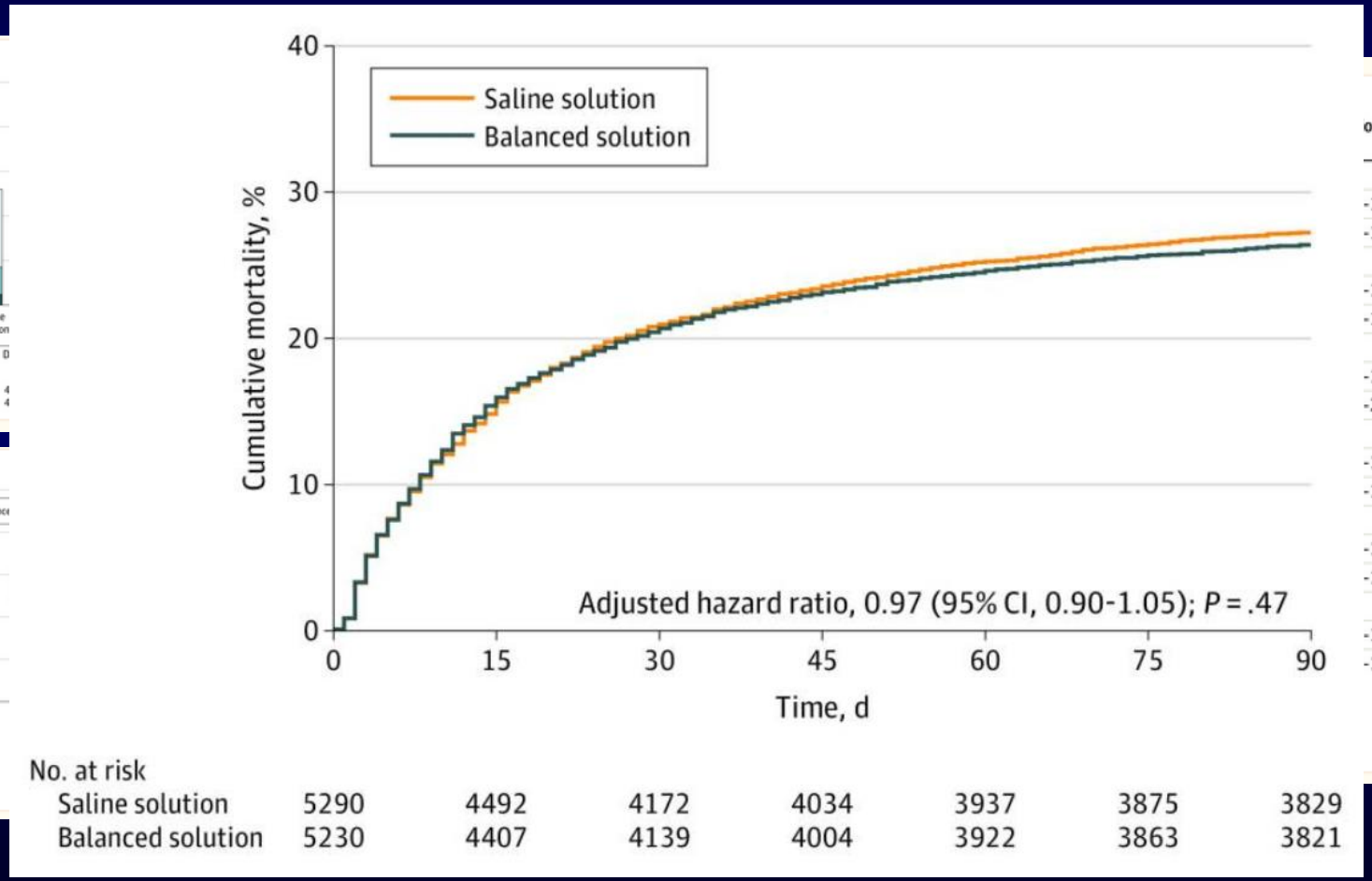
2350 patients

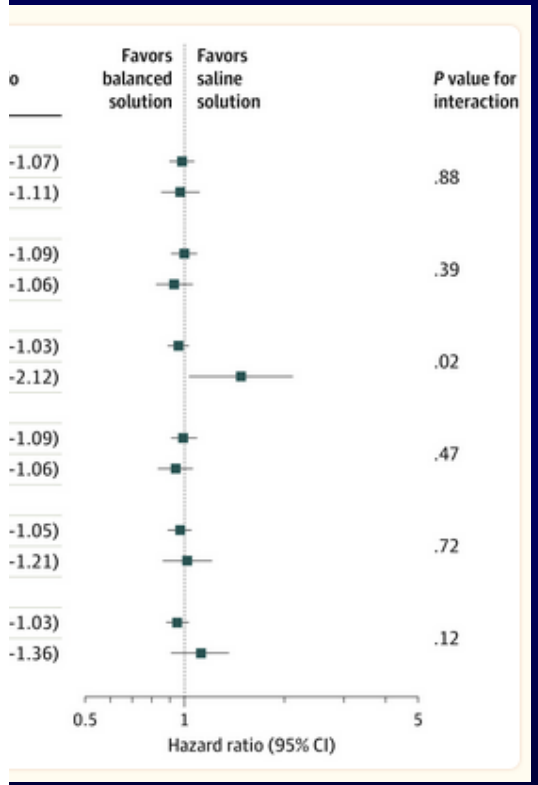
Semler et al. N Engl J Med 378: 829-39, 2018

BaSICS randomized trial of saline v. balanced salt solution





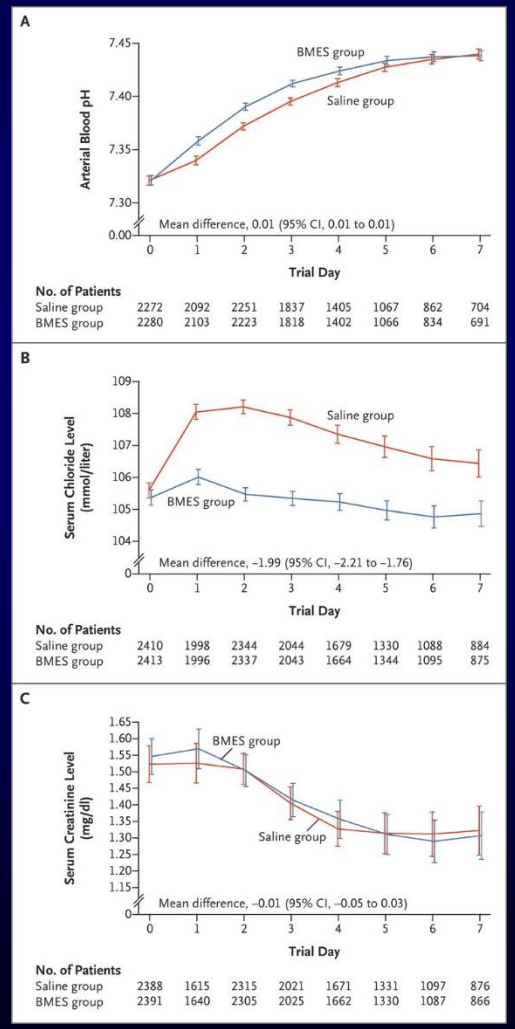


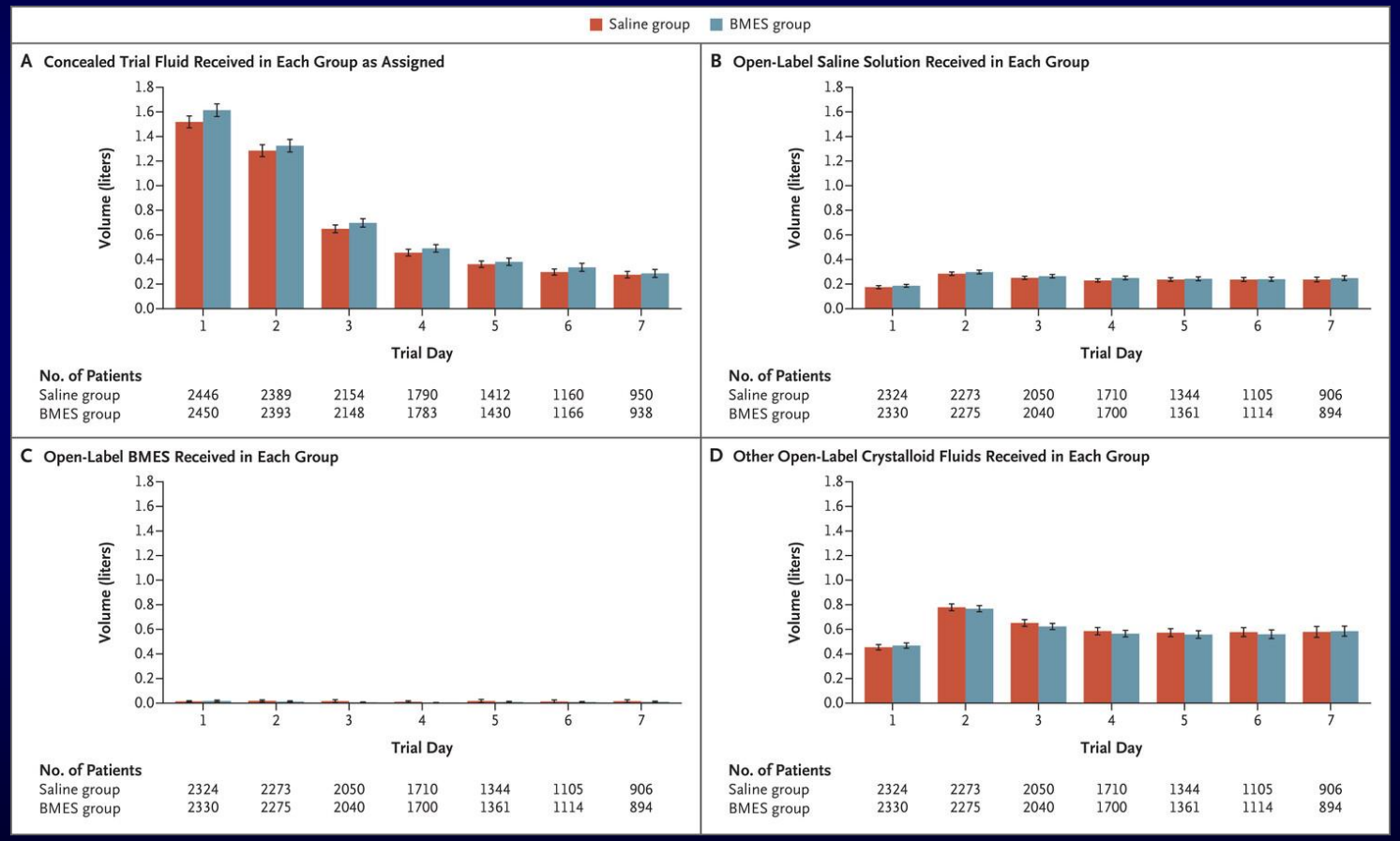


Balanced salt 5230 patients, NaCl 5290 patients

Zampieri et al. JAMA 326:1-12, 2021

ANZICS Double blind randomized trial of saline v. balanced salt solution

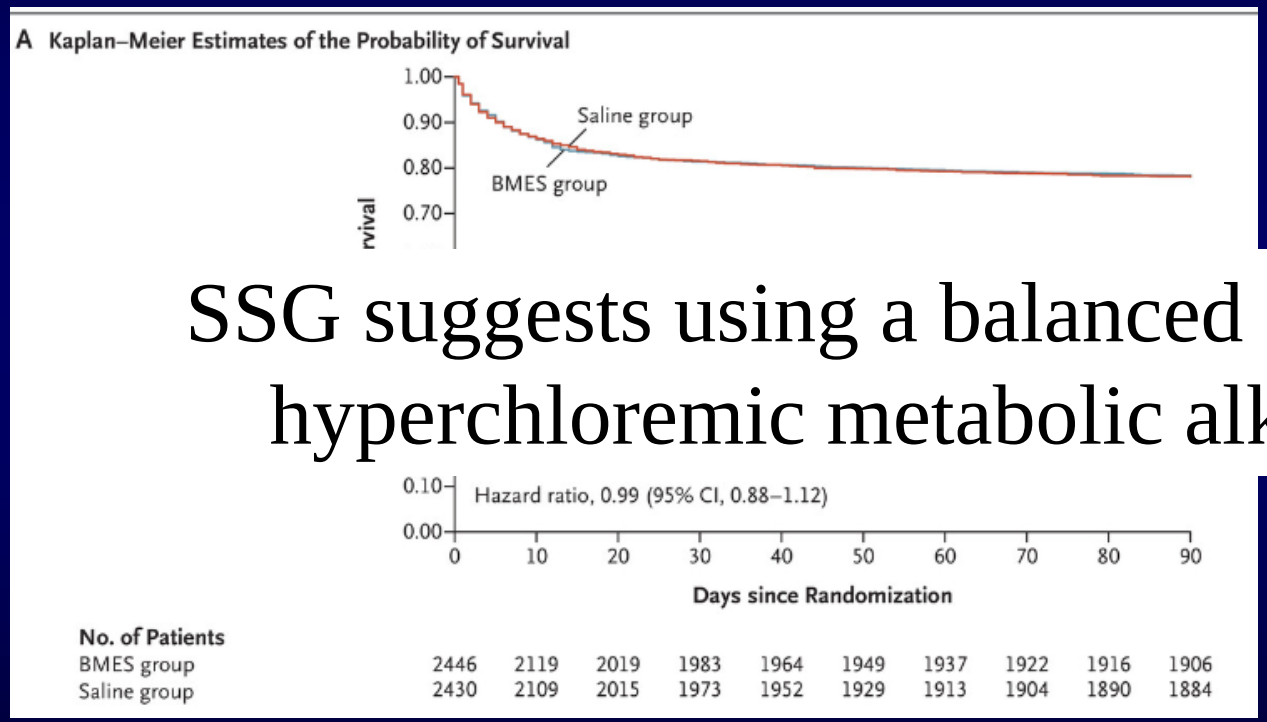


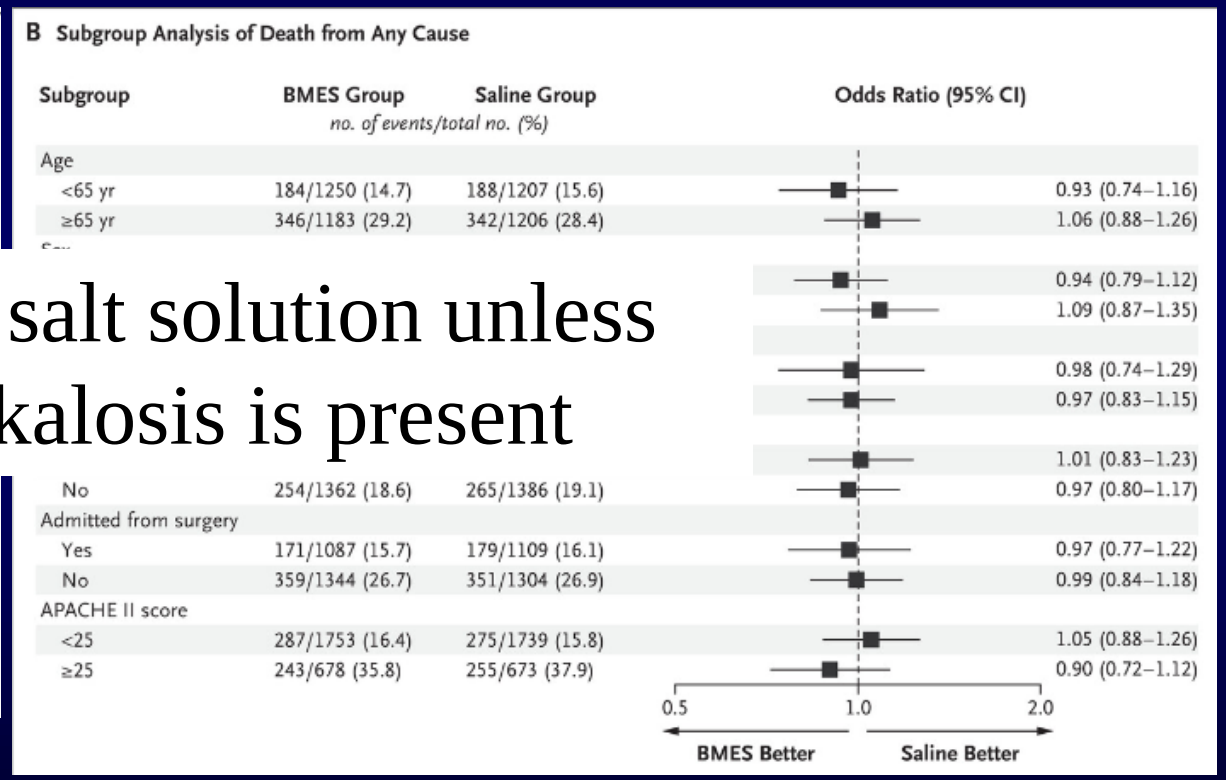


4654 patients

Finfer et al. N Engl J Med 386: 815-26, 2022

ANZICS Double blind randomized trial of saline v. balanced salt solution

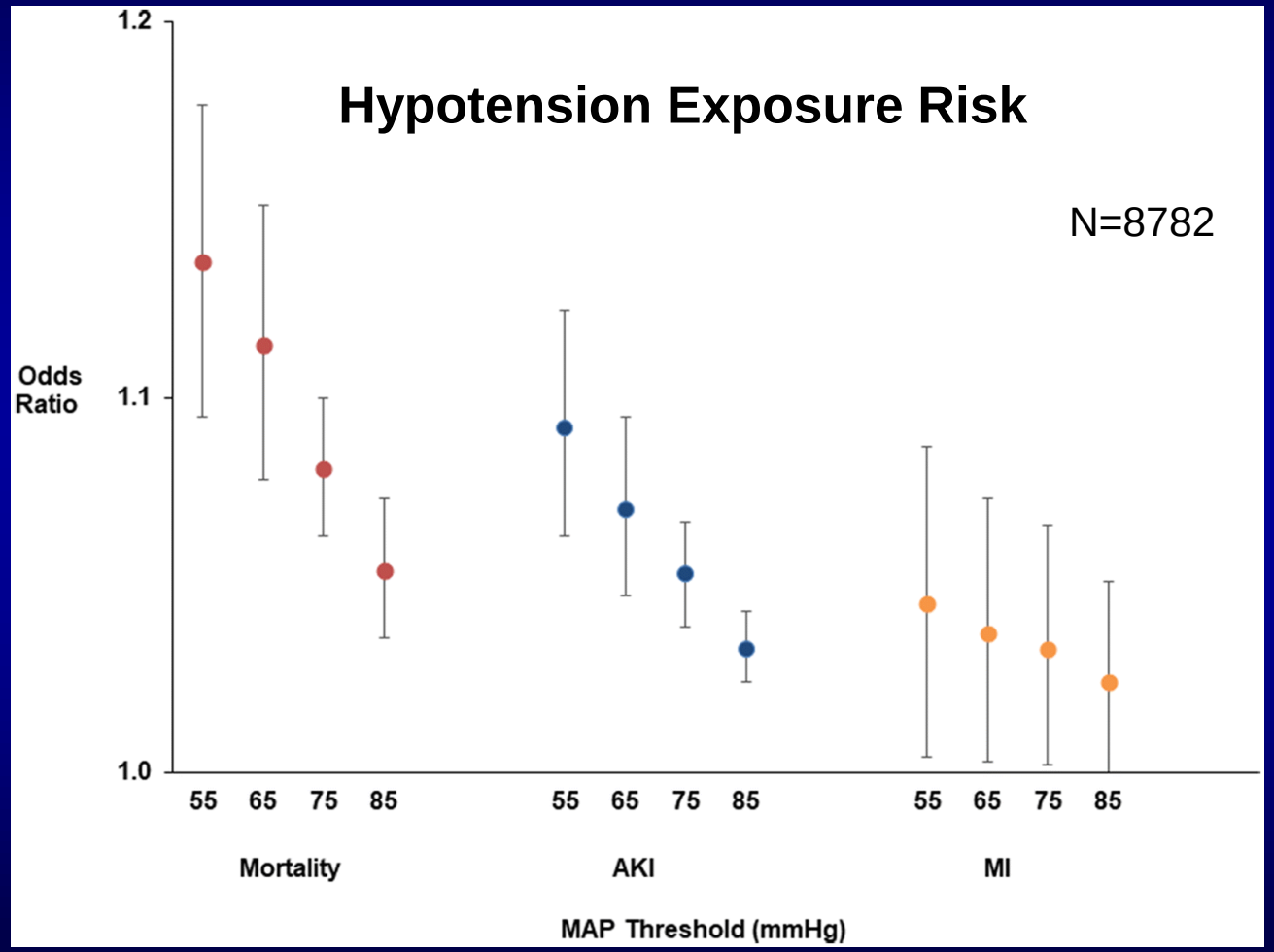




SSG suggests using a balanced salt solution unless hyperchloremic metabolic alkalosis is present

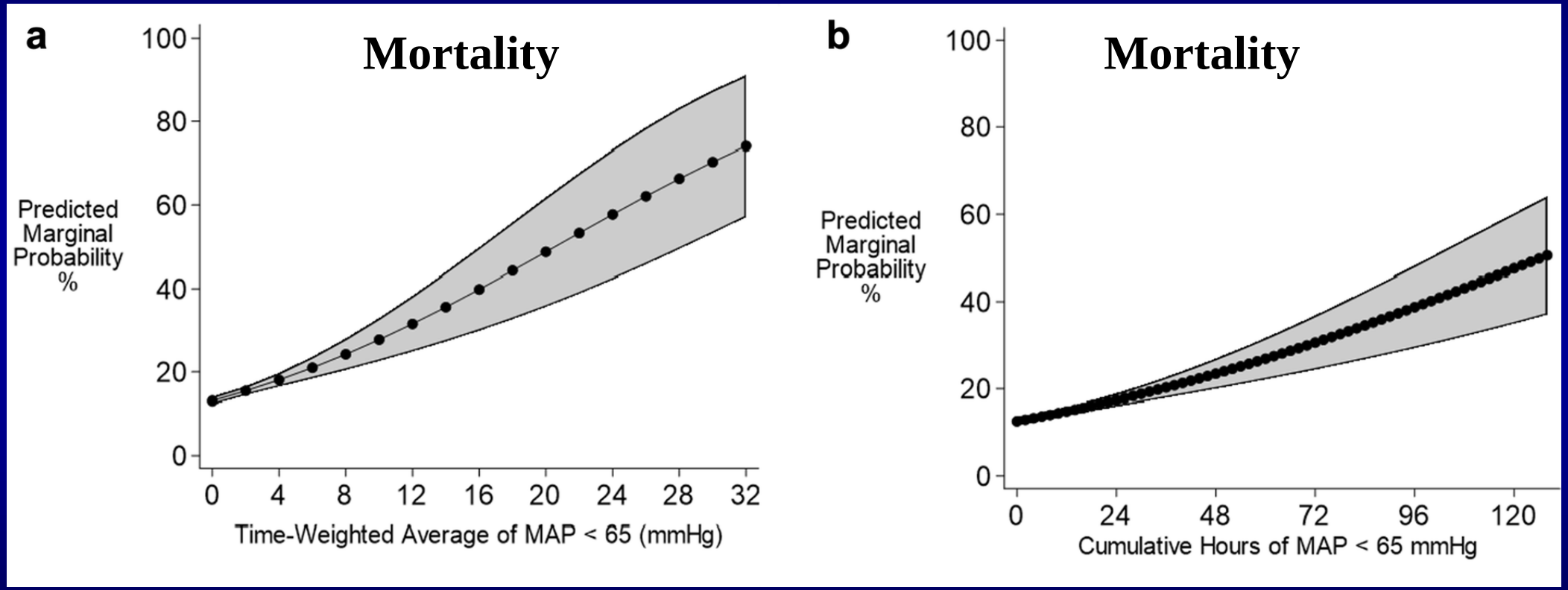
Finfer et al. N Engl J Med 386: 815-26, 2022

Association between ICU hypotension and in-hospital morbidity in septic patients



Maheshwari et al. Intensive Care Med 44:857-67, 2018

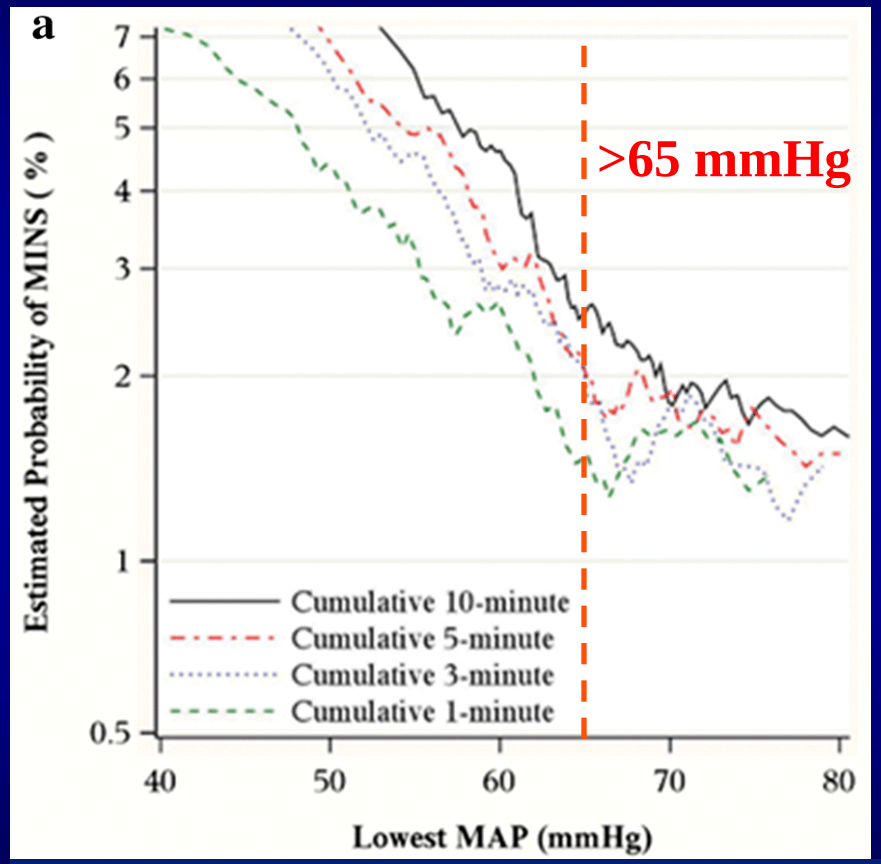
Duration of ICU Hypotension and In-Hospital Mortality in Septic Patients

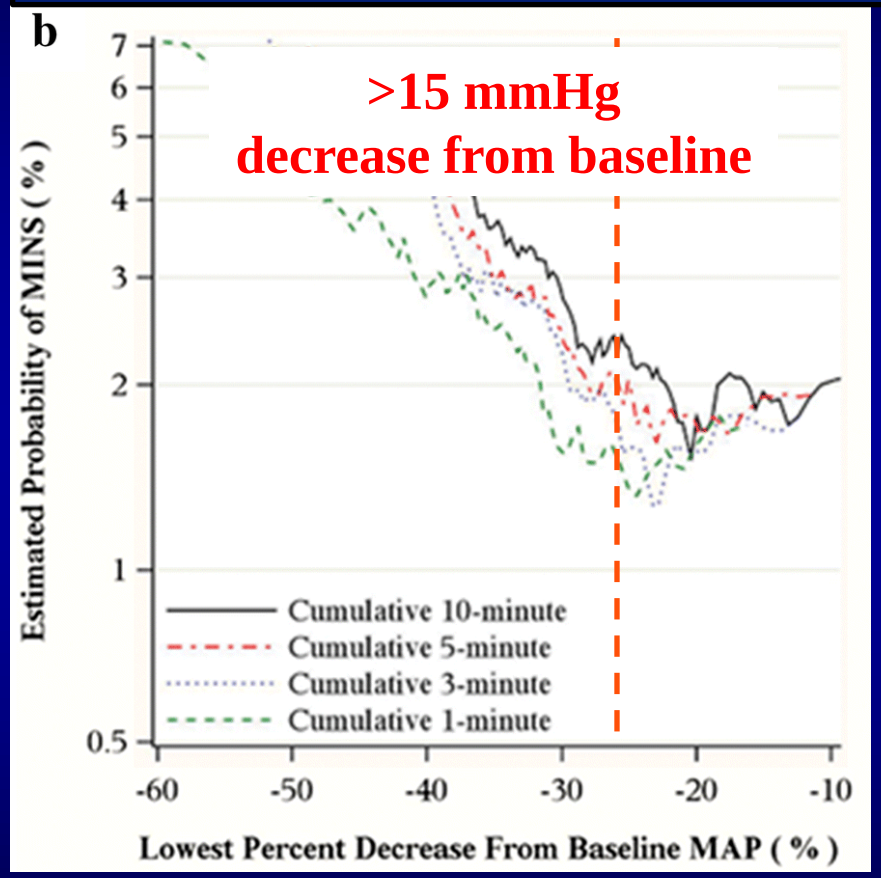


N=8782

Maheshwari et al. Intensive Care Med 44:857-67, 2018

Relationship between Perioperative Hypotension and Myocardial Injury



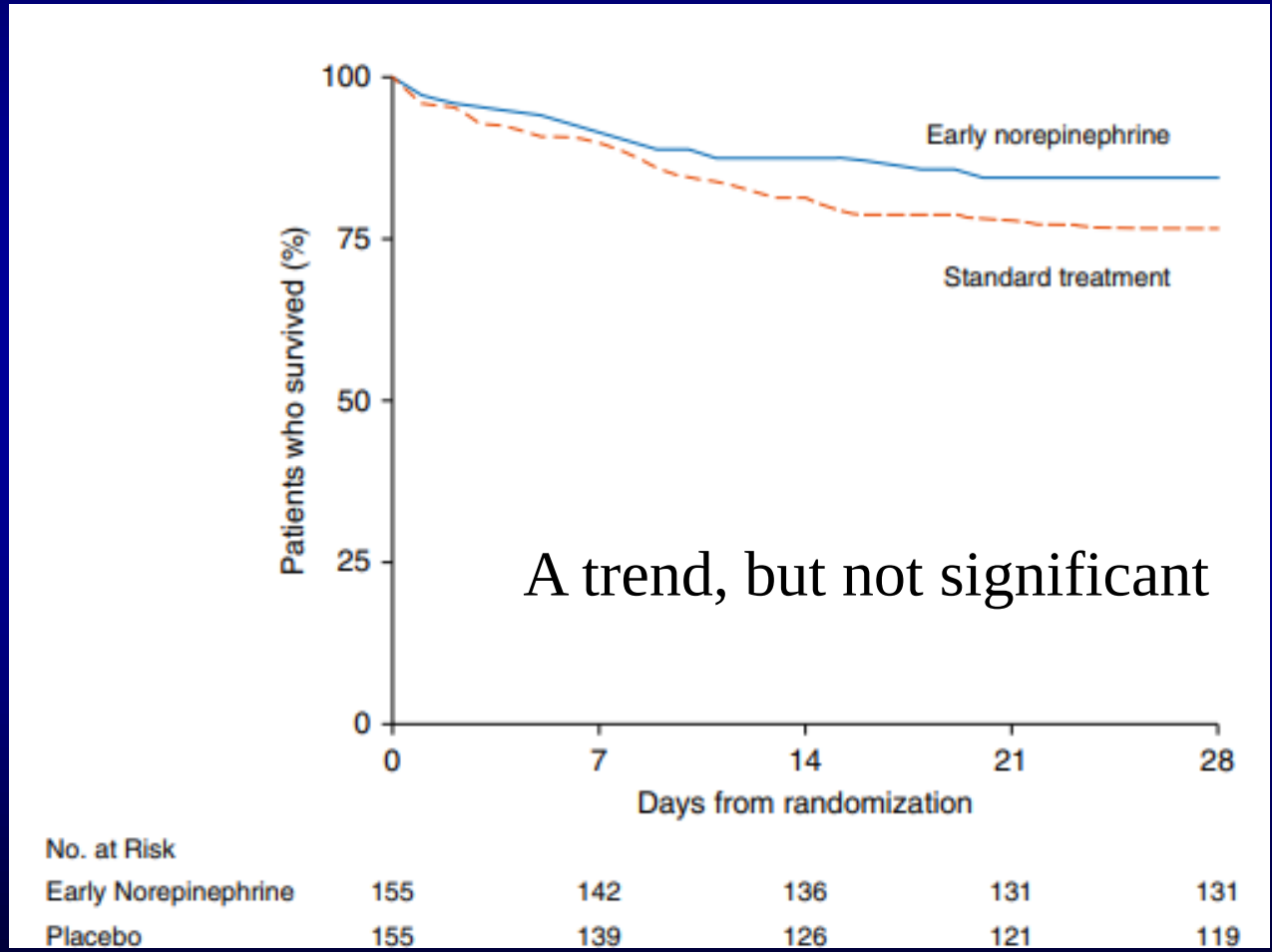


Sessler & Khanna. Intensive Care Med 44:811-22, 2018

Early Use of Norepinephrine in Sepsis with Hypotension Resuscitation

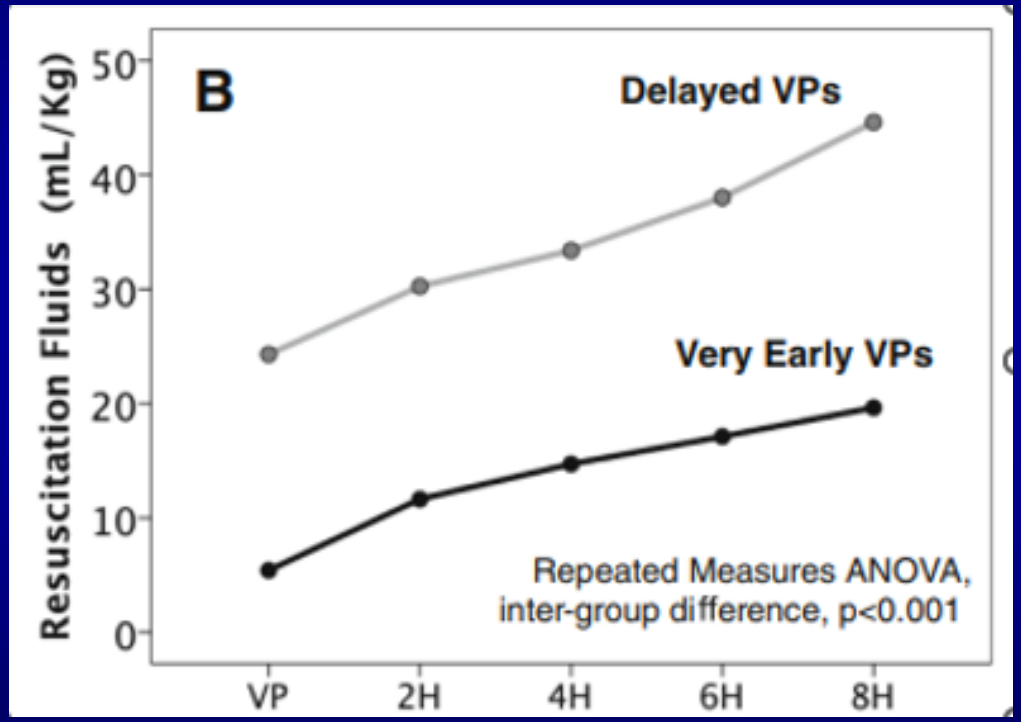
- Single center randomized double-blind placebo-controlled trial
- 310 adult patients in septic shock
- 155 early norepinephrine, 155 control (received NE if hypotensive after 30 ml/kg fluids)
- Early norepinephrine
  - *Decreased time with MAP <60 mmHg at 6 hr*
  - *Lower incidence of ACPE and arrhythmias*
    - **Permpikul et al. Am J Respir Crit Care Med 199:1097-1105, 2019**

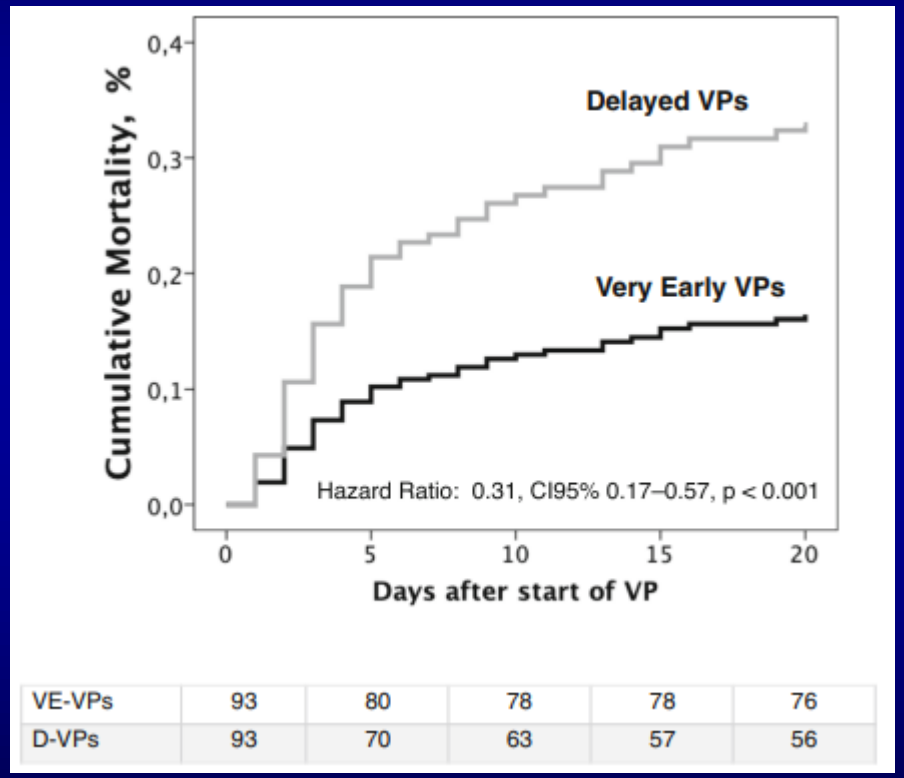
Early Use of Norepinephrine in Sepsis with Hypotension Resuscitation



Permpikul et al. Am J Respir Crit Care Med 199:1097-1105, 2019

Early Use of Norepinephrine in Sepsis with Hypotension Resuscitation





VE-VPs	93	80	78	78	76
D-VPs	93	70	63	57	56

SSG suggests starting vasopressors early if no response to initial fluid bolus

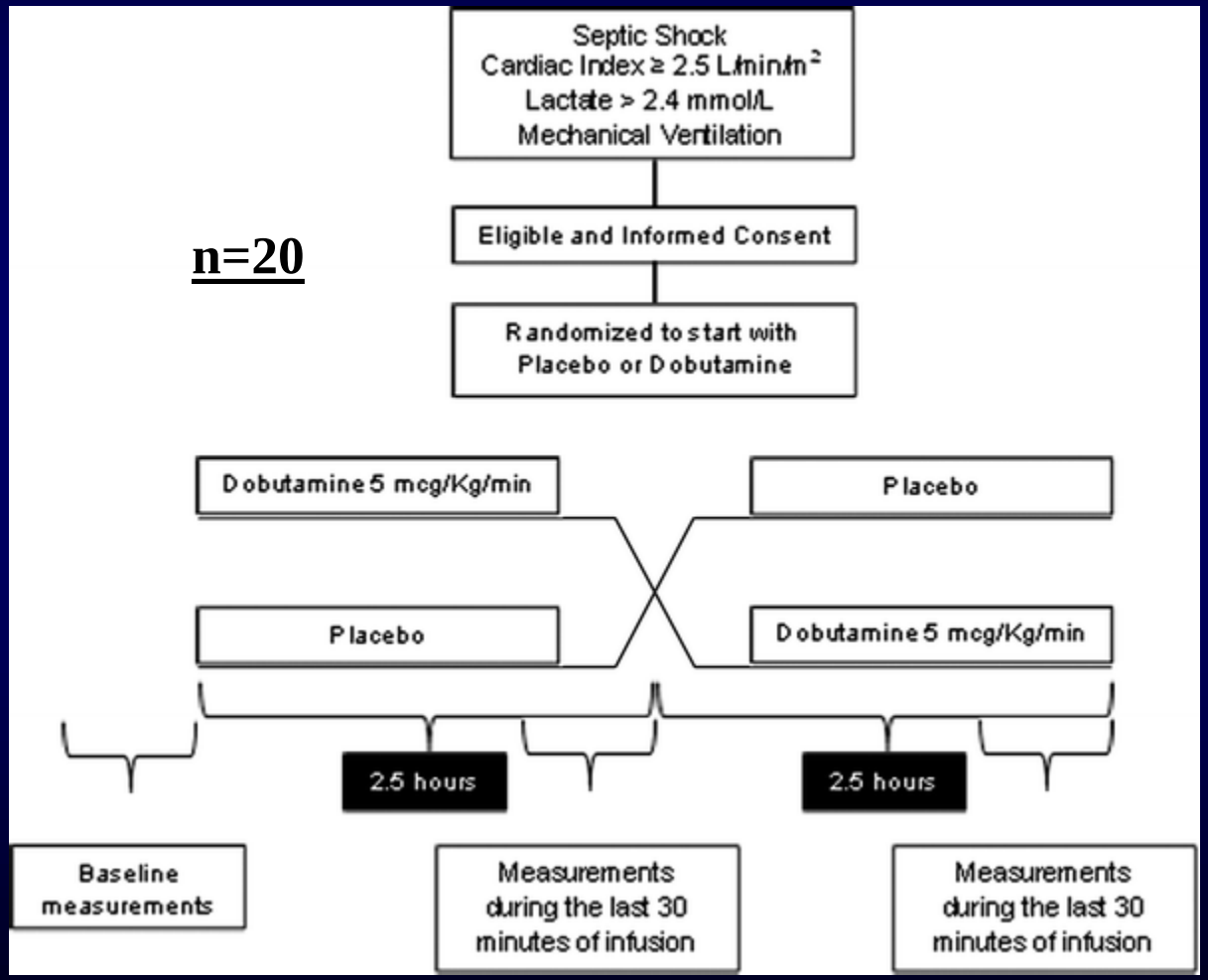
ESICM review also agrees with this suggestion to minimize fluid overload

Ospina-Tascon et al. Crit Care 24:52, 2020

What Drives Tissue Perfusion

- Is it mean arterial pressure?
- Is it cardiac output?
- Is it local metabolic demand?
- Is it blunted by severe injury, sepsis and surgical trauma?

Do Macro-Circulatory Parameters Reflect Organ Perfusion?



Hernandez et al. Intensive Care Med 39:1435-43, 2013

Do Macro-Circulatory Parameters Reflect Organ Perfusion?

Macro-circulatory Parameters

Parameter	Placebo	Dobutamine	*p* value
Heart rate (bpm)	93 (84-108)	108 (97-122)	<0.01
Mean arterial pressure (mmHg)	71 (68-80)	69 (65-75)	0.52
Central venous pressure	13 (11-16)	11 (9-14)	0.13
Pulmonary Artery Occlusion P	13 (10-15)	12 (10-15)	0.15
Cardiac index (l/min/m^2)	3.7 (3.2-4.1)	4.2 (3.5-5.0)	<0.01
LV ejection fraction (%)	63 (58-72)	74 (64-78)	0.02
Pulse pressure variation (%)	6 (2-8)	6 (3-8)	0.16
Urine output (ml)	90 (51-119)	52 (25-220)	0.39
Norepi dose (mcg/kg/min)	0.15 (0.07-0.33)	0.16 (0.06-0.42)	0.39

Hernandez et al. Intensive Care Med 39:1435-43, 2013

Do Macro-Circulatory Parameters Reflect Organ Perfusion?

Metabolic-related Perfusion Parameters

Parameter	Placebo	Dobutamine	*p* value
Mixed venous O_2 saturation (%)	77 (72-81)	78 (75-81)	0.05
Mixed venous-arterial pCO_2 gradient (mm Hg)	3.3 (1.5-3.8)	3.6 (0.4-4.6)	0.45
Arterial lactate (mmol/l)	2.8 (2.4-3.9)	2.8 (2.4-4.0)	0.20
O_2 Delivery (ml/min/m^2)	566 (374-722)	717 (419-771)	0.02
O_2 Consumption (ml/min/m^2)	129 (100-156)	140 (106-167)	0.35
ICG plasma disappearance rate*	18.8 (11.7-24.6)	14.4 (9.5-25.6)	0.03
ICG retention rate at 15 min (%)	6.0 (2.8-17.4)	11.5 (2.3-24.3)	0.06
Gastric-arterial pCO_2 (mmHg)	13 (7-18)	13 (7-29)	0.52
Intraabdominal pressure (mmHg)	12 (8-16)	12 (9-17)	0.39

*(%/min)

Hernandez et al. Intensive Care Med 39:1435-43, 2013

Do Macro-Circulatory Parameters Reflect Organ Perfusion?

Sublingual Microcirculatory Parameters

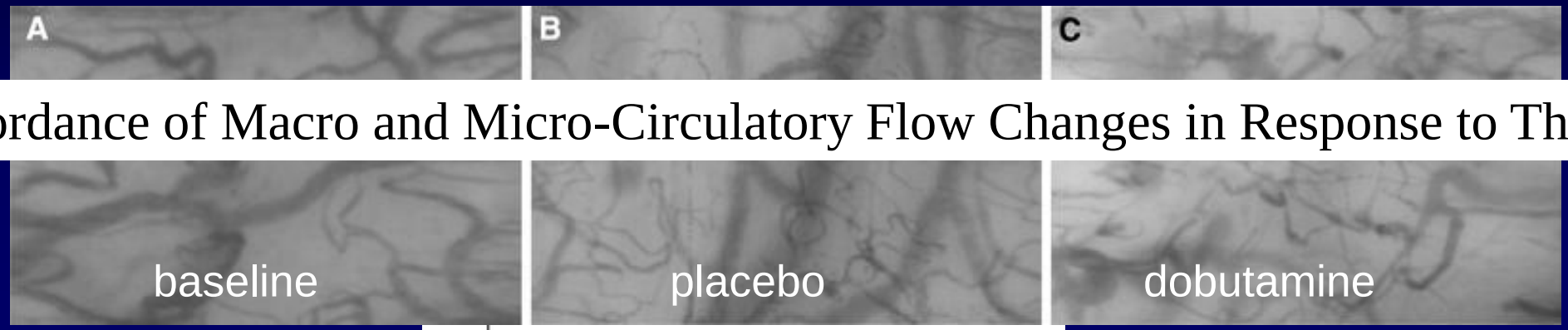
Parameter	Placebo	Dobutamine	*p* value
Total microcirculatory density (n/mn)	11.8 (10.2-12.5)	11.9 (9.7-12.5)	0.91
Perfused vessel density (n/mn)	9.1 (7.9-9.9)	9.1 (7.9-10.1)	0.24
Proportion of perfused microvessels (%)	75 (69-79)	79 (72-84)	0.09
Microvascular flow index	2.1 (1.9-2.5)	2.1 (1.8-2.5)	0.73
Heterogeneity of microvascular flow	0.58 (0.46-0.73)	0.47 (0.40-0.86)	0.52

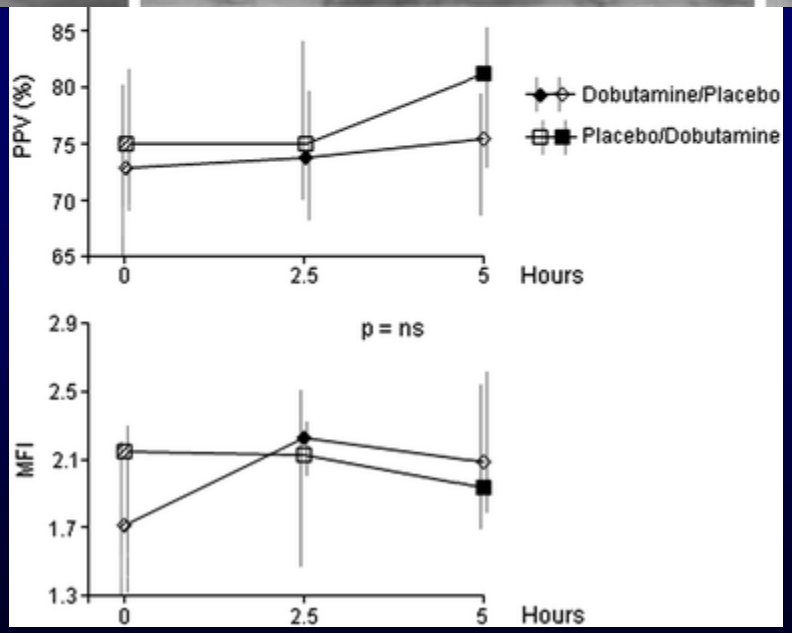
*(%/min)

Hernandez et al. Intensive Care Med 39:1435-43, 2013

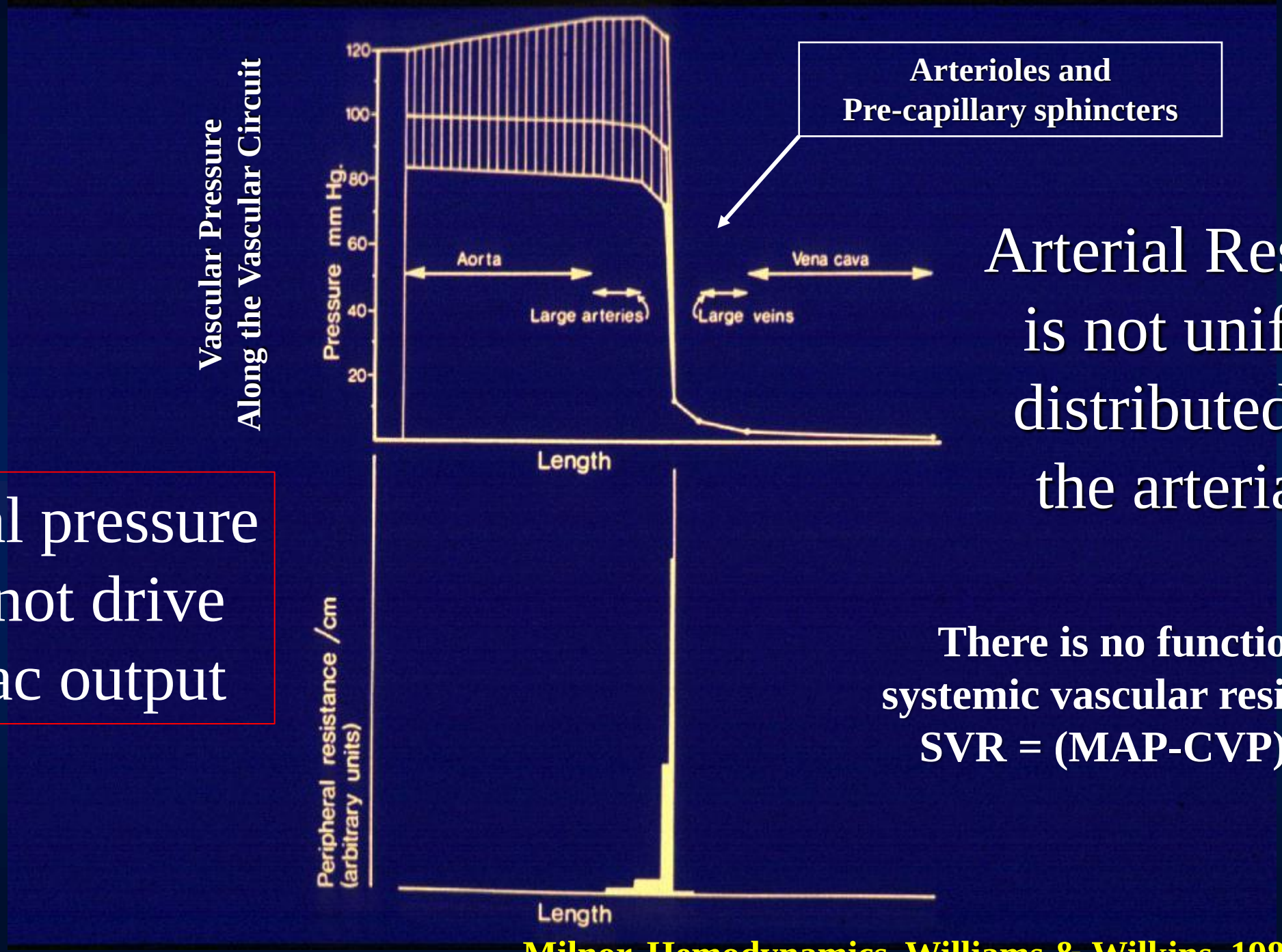
Do Macro-Circulatory Parameters Reflect Organ Perfusion?

Discordance of Macro and Micro-Circulatory Flow Changes in Response to Therapy





Hernandez et al. Intensive Care Med 39:1435-43, 2013



Arterial pressure does not drive cardiac output

Arterial Resistance is not uniformly distributed along the arterial tree

There is no functional systemic vascular resistance
SVR = (MAP-CVP)/CO

Milnor. Hemodynamics. Williams & Wilkins, 1982

Regulation of Organ Blood Flow

- High input pressure (arterial pressure)
- High intra-organ input resistance
  - Small artery arterial tone, precapillary arterioles
  - Tissue interstitial pressure
- Primary Method to Increase Organ Blood Flow:
  - local vasodilation in metabolically active tissues
  - passive increase in arterial inflow

Cardiac output important only to maintain pressure

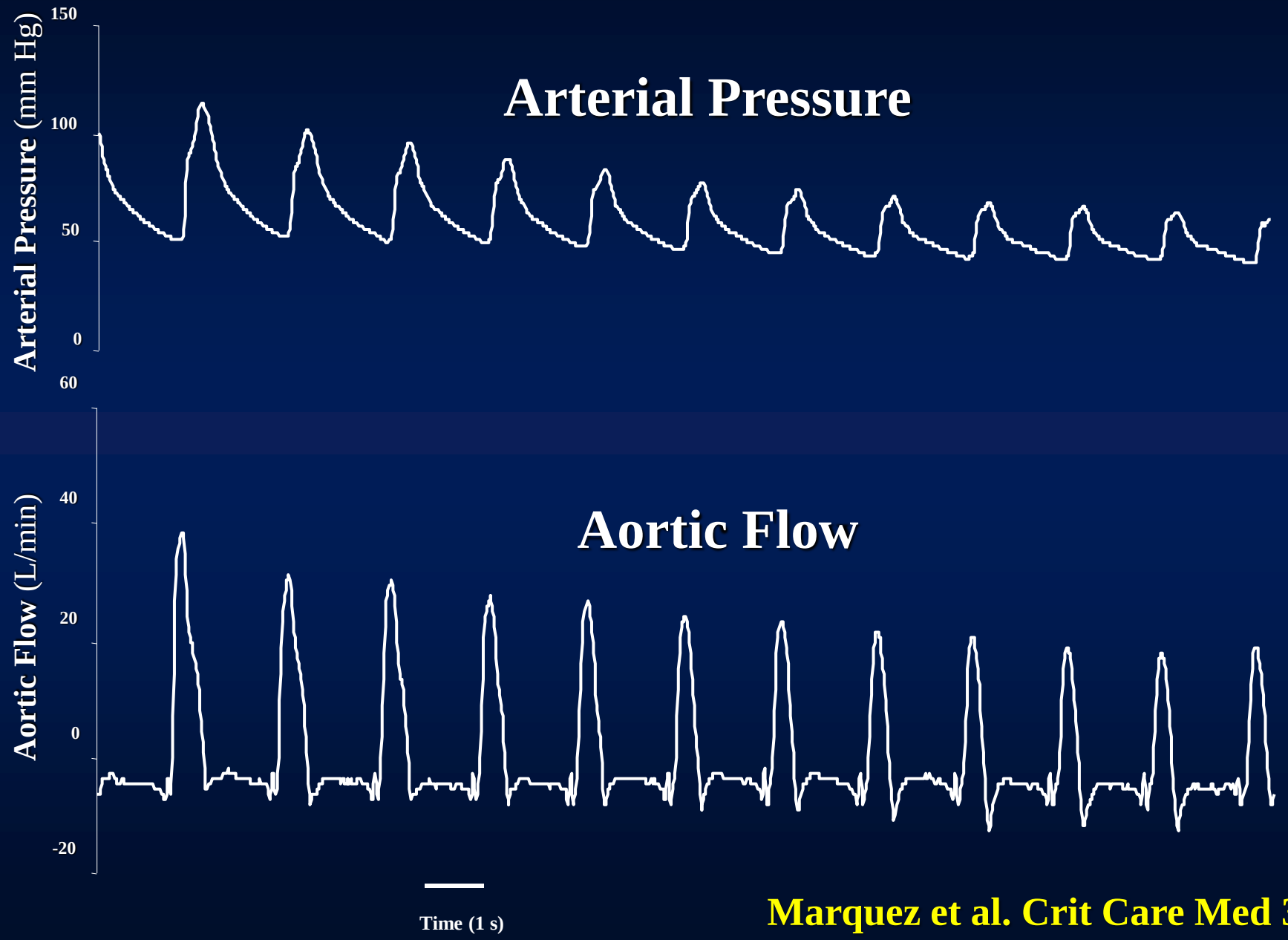
Rationale for Defense of Arterial Pressure

Allows autoregulation of blood flow distribution

Corollary:

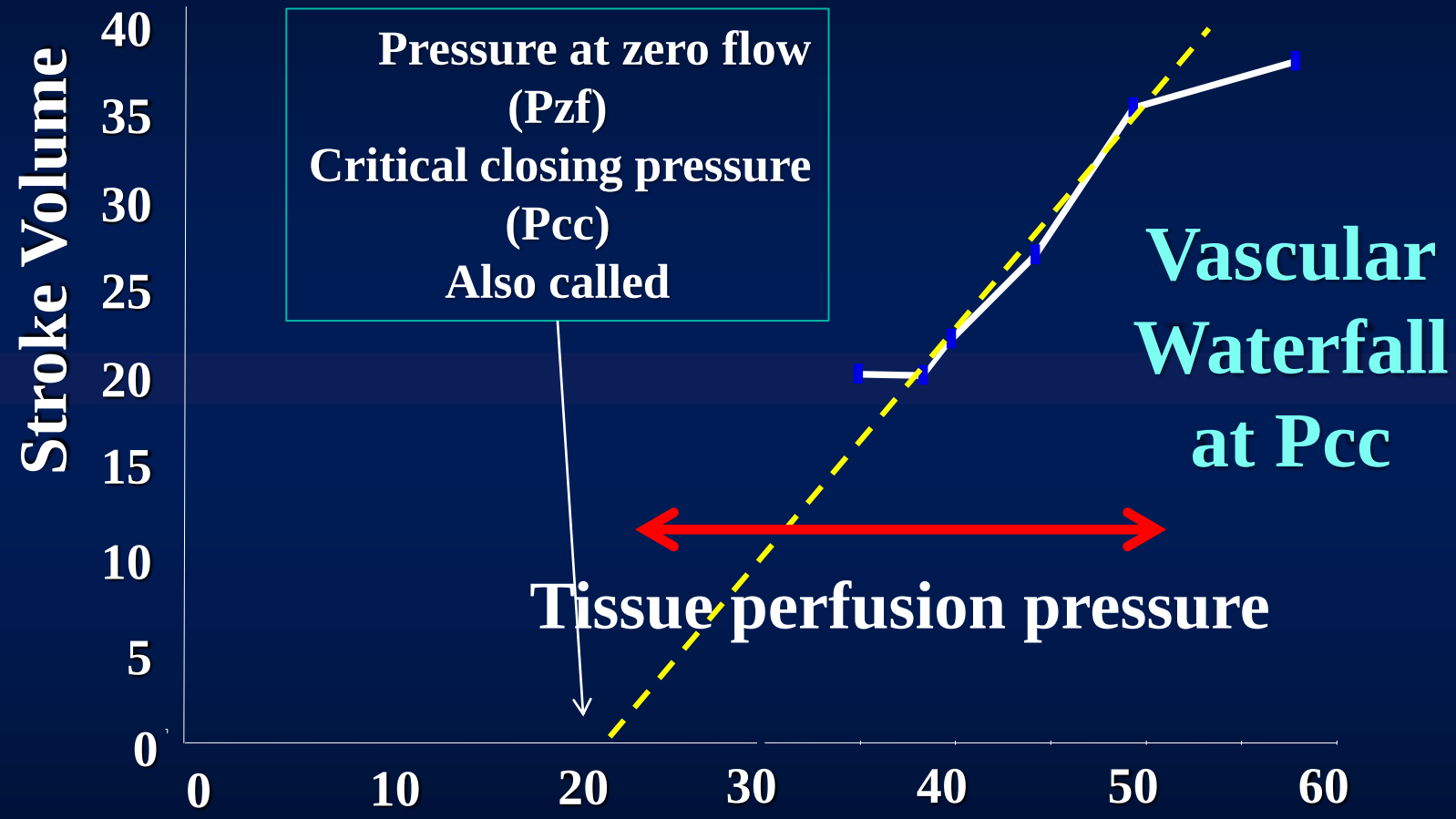
Systemic Hypotension induces Loss of Autoregulation despite Intact Autonomic and Local Reflex Mechanisms

Effect of IVC Occlusion on Aortic Flow and Arterial Pressure in Humans



Marquez et al. Crit Care Med 36:3001-7, 2008

Relation Between Stroke Volume and Pulse Pressure During IVC Occlusion in Man



Marquez et al. Crit Care Med 36:3001-7, 2008

Vascular Waterfall

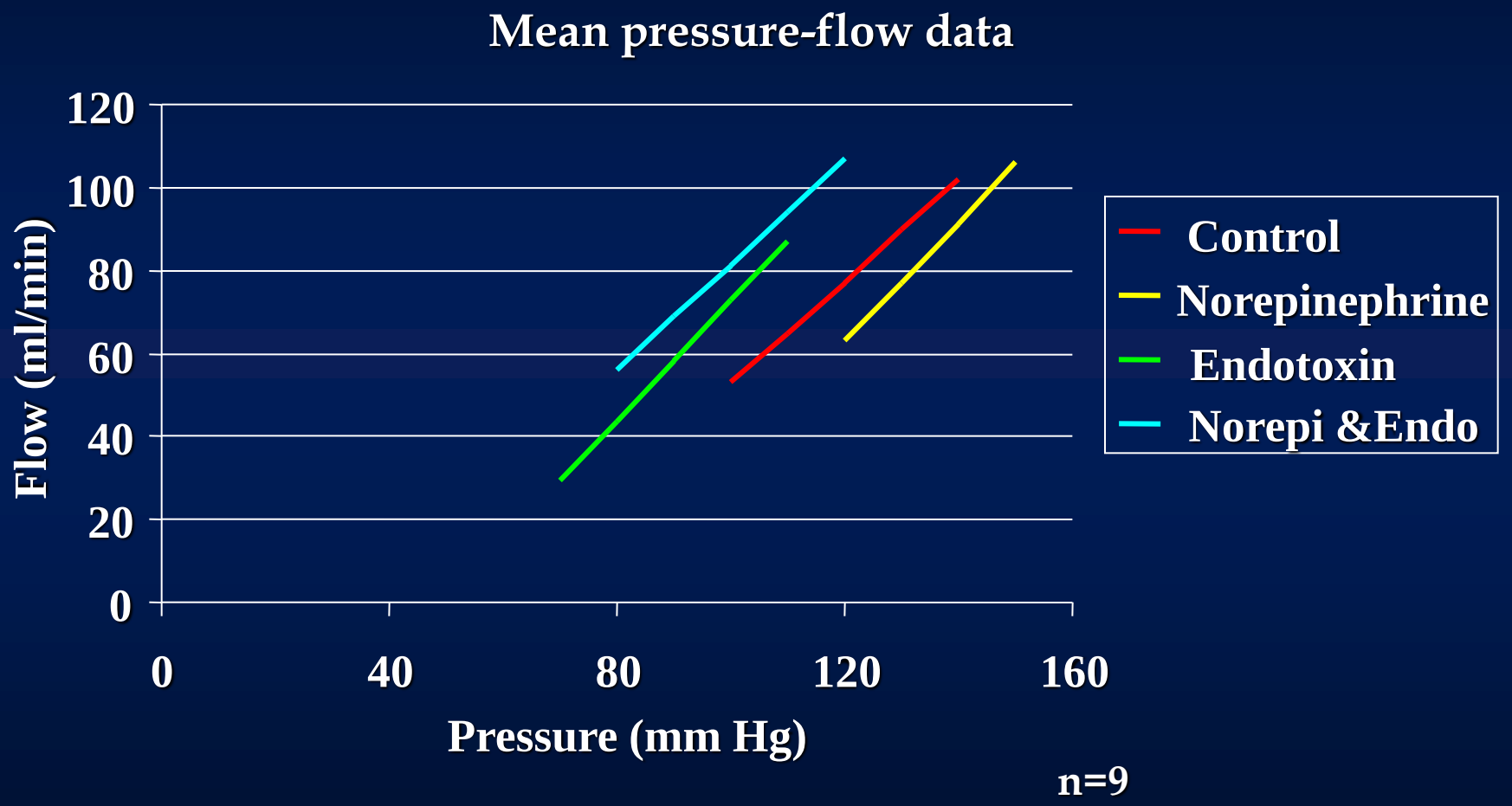
Rate of water flow is independent of how far it falls once it falls over the edge

Significance of Critical Closing Pressures in the Arterial Circuit

- Arterial resistance << Total Peripheral Resistance
- Explains autoregulation: Tissue Perfusion Pressure
- Arterial driving pressure ≈ MAP – Pcc

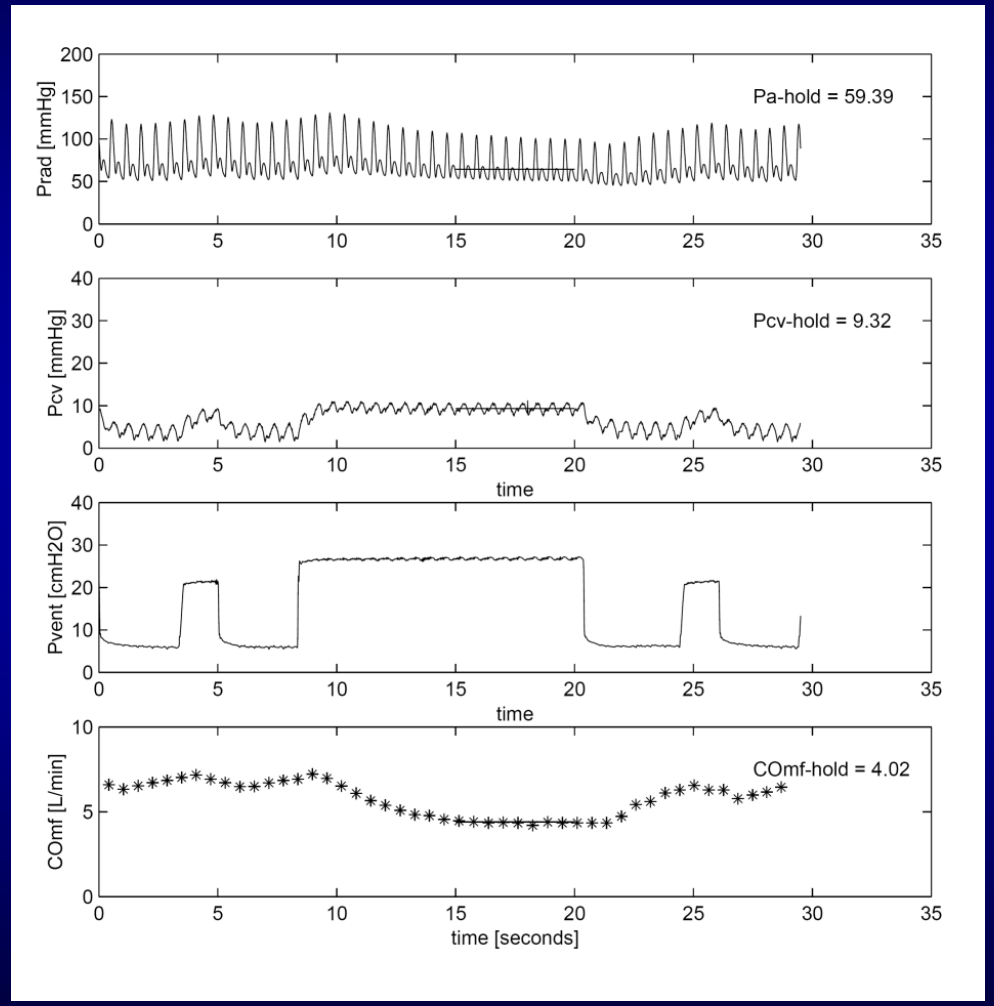
Pinsky et al. Crit Care 28:127, 2024

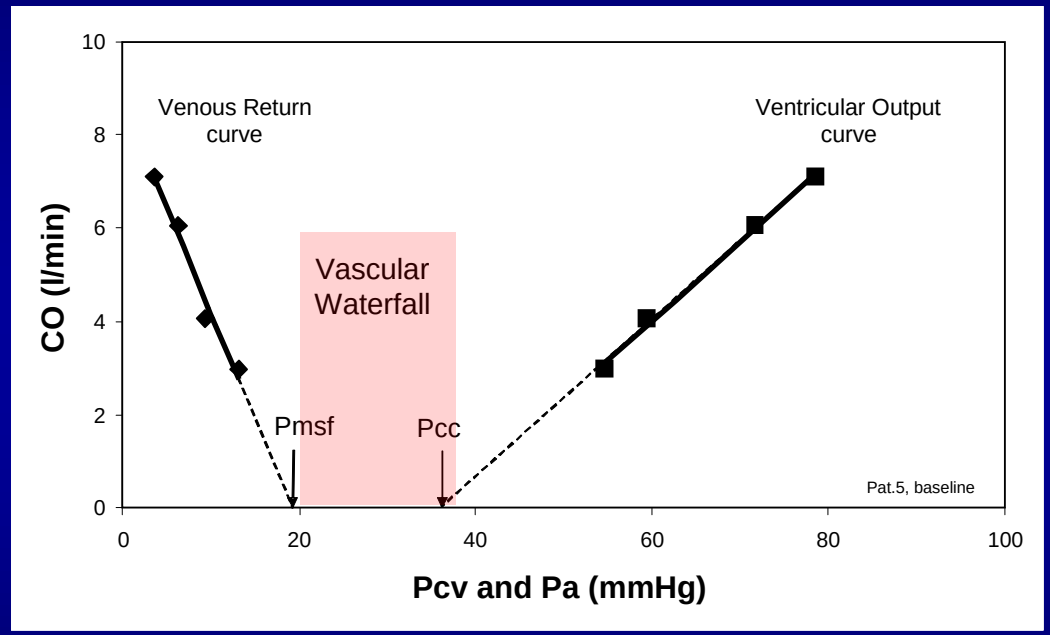
Endotoxin and Renal Blood Flow



Bellomo et al. Am J Respir Crit Care Med 159:1186-92, 1999

Arterial Pressure at zero flow (Pcc) and Mean Systemic Pressure (Pmsf) are Not the Same



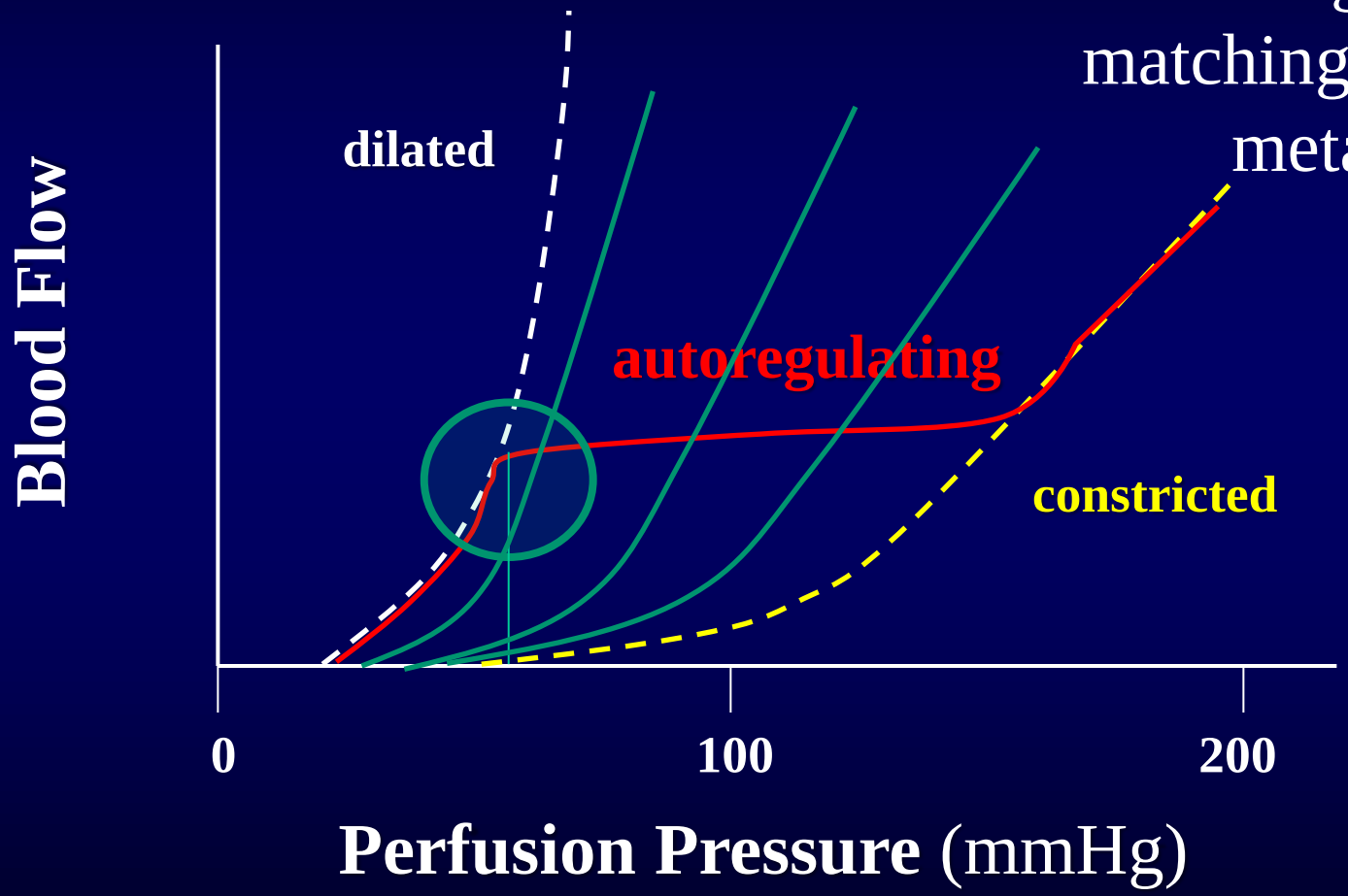


Pcc ≈ 35-45 mmHg

Maas et al. Anes Analg 114:803-11, 2012

Organ Specific Autoregulation

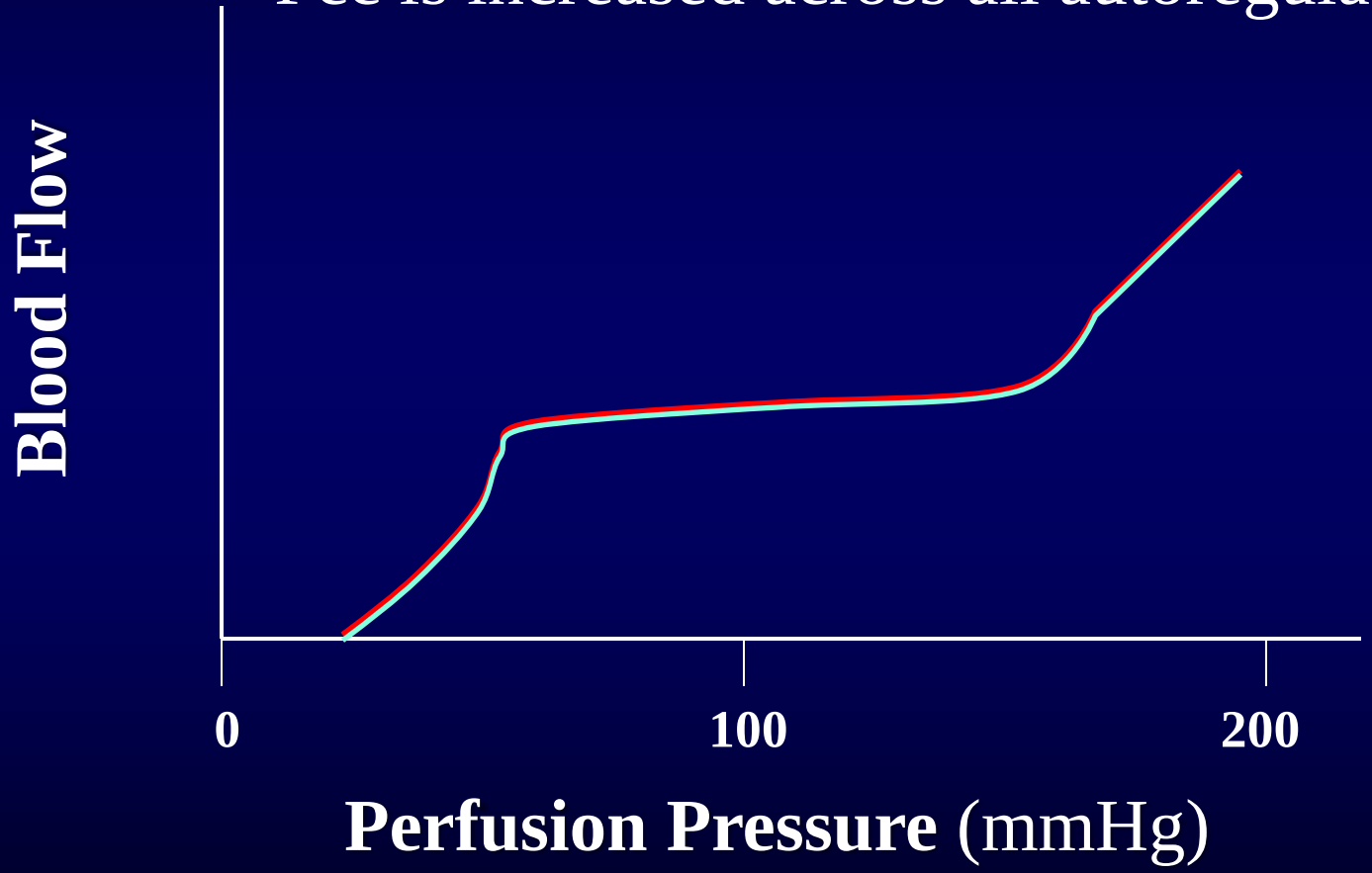
Autoregulation occurs by matching driving pressure to metabolic demand



Kato & Pinsky. Ann Intensive Care 5:41, 2015

Autoregulation shifted with Essential Hypertension

Pcc is increased across all autoregulatory values



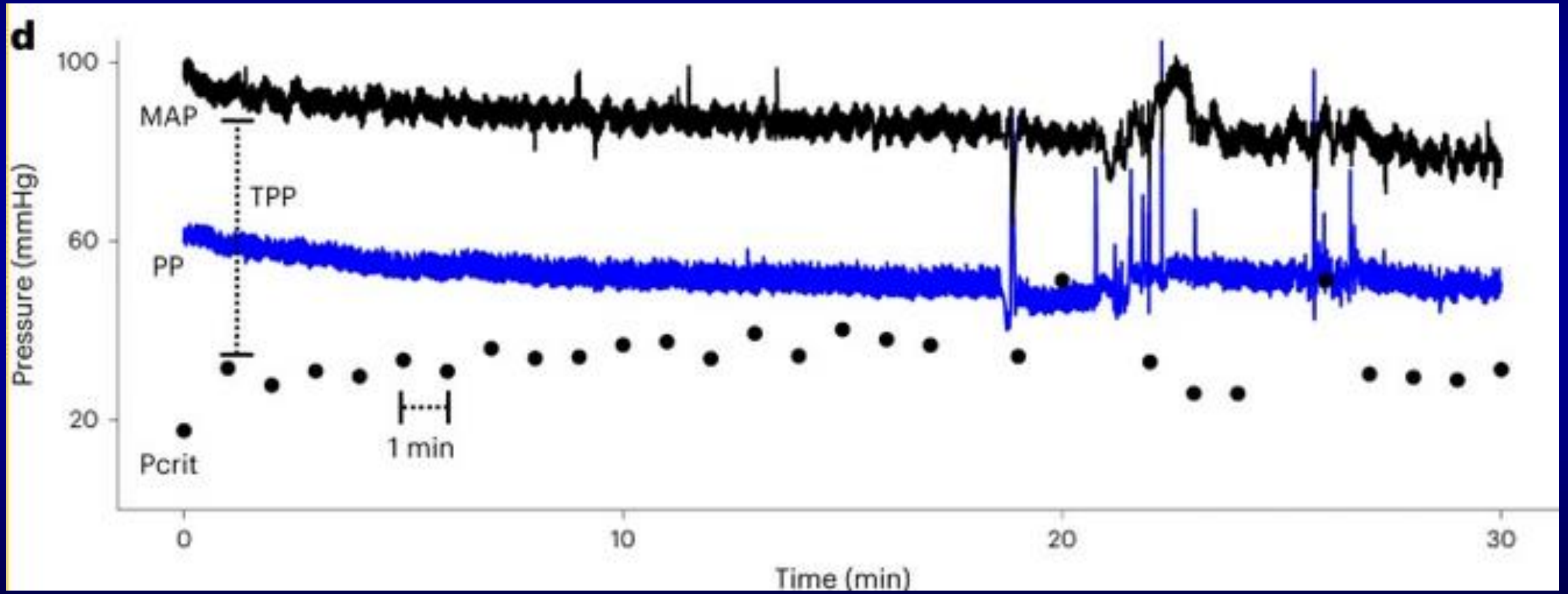
Kato & Pinsky. Ann Intensive Care 5:41, 2015

Tissue Perfusion pressure enable continuous hemodynamic evaluation and risk prediction in the ICU

- Tissue perfusion pressure = MAP – Pcrit (critical closing pressure)
- Analyzed 5,988 Cardiac ICU admissions, externally validated on 864 admission from another hospital
- Plot change in CO and MAP to zero CO to define Pcrit
- Replace CO with *k x PP x HR* during 1 minute of breathing

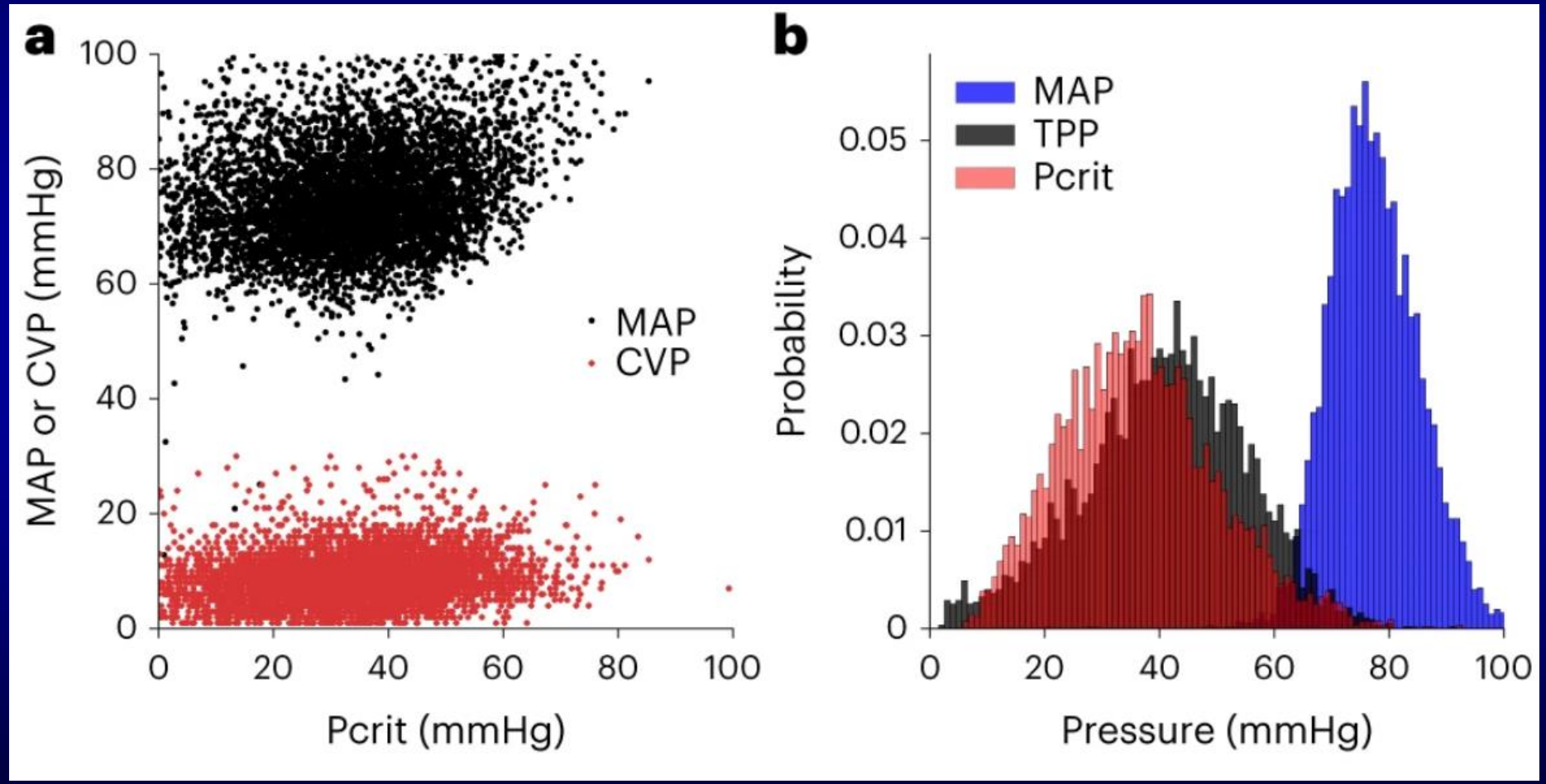
Chandraesekhar et al. Nat Med 29:1998-2006, 2023

Tissue Perfusion pressure enable continuous hemodynamic evaluation and risk prediction in the ICU



Chandraesekhar et al. Nat Med 29:1998-2006, 2023

Tissue Perfusion pressure enable continuous hemodynamic evaluation and risk prediction in the ICU

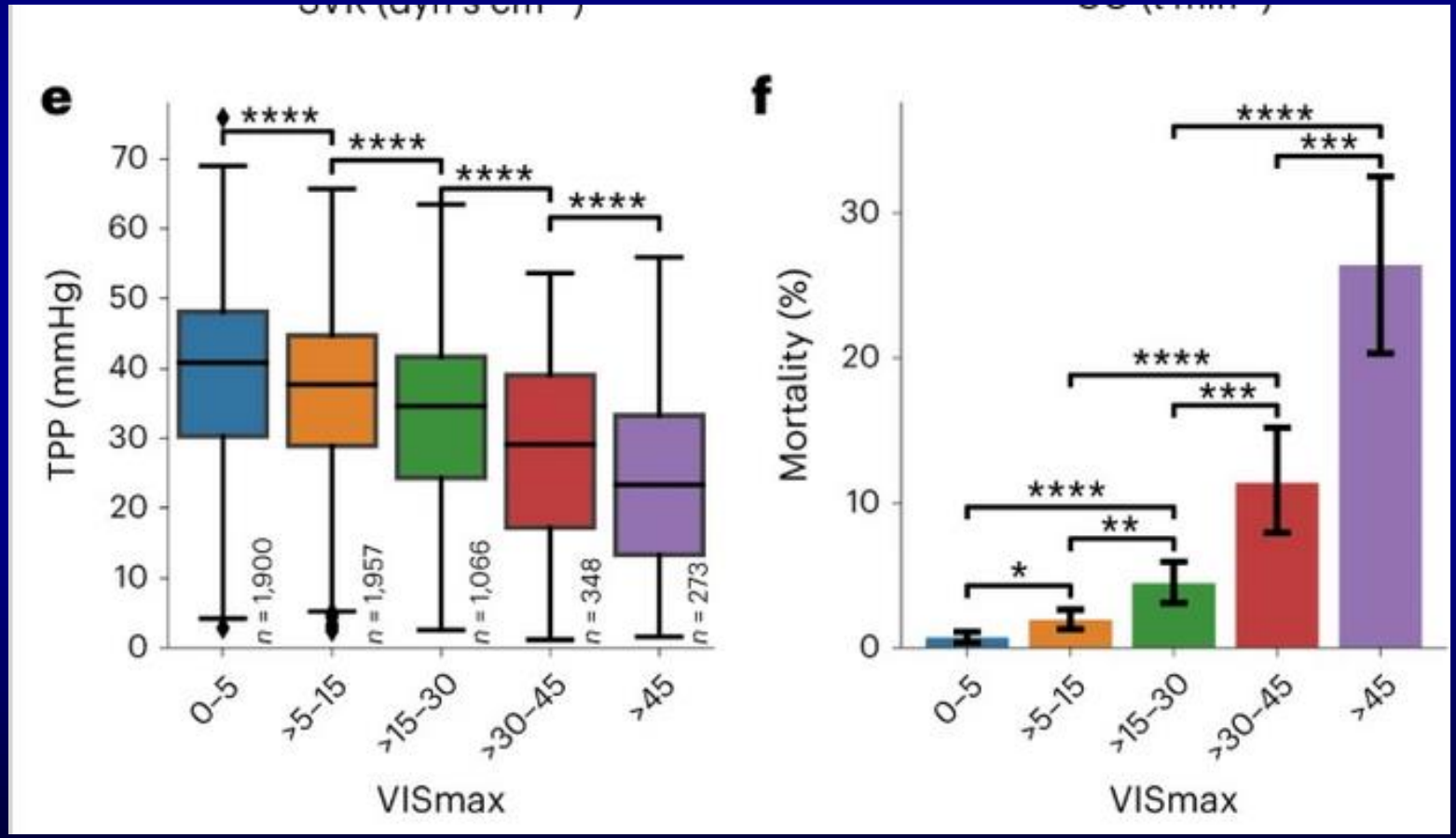


Chandraesekhar et al. Nat Med 29:1998-2006, 2023

Tissue Perfusion pressure (TPP) enables continuous hemodynamic evaluation and risk prediction in the ICU

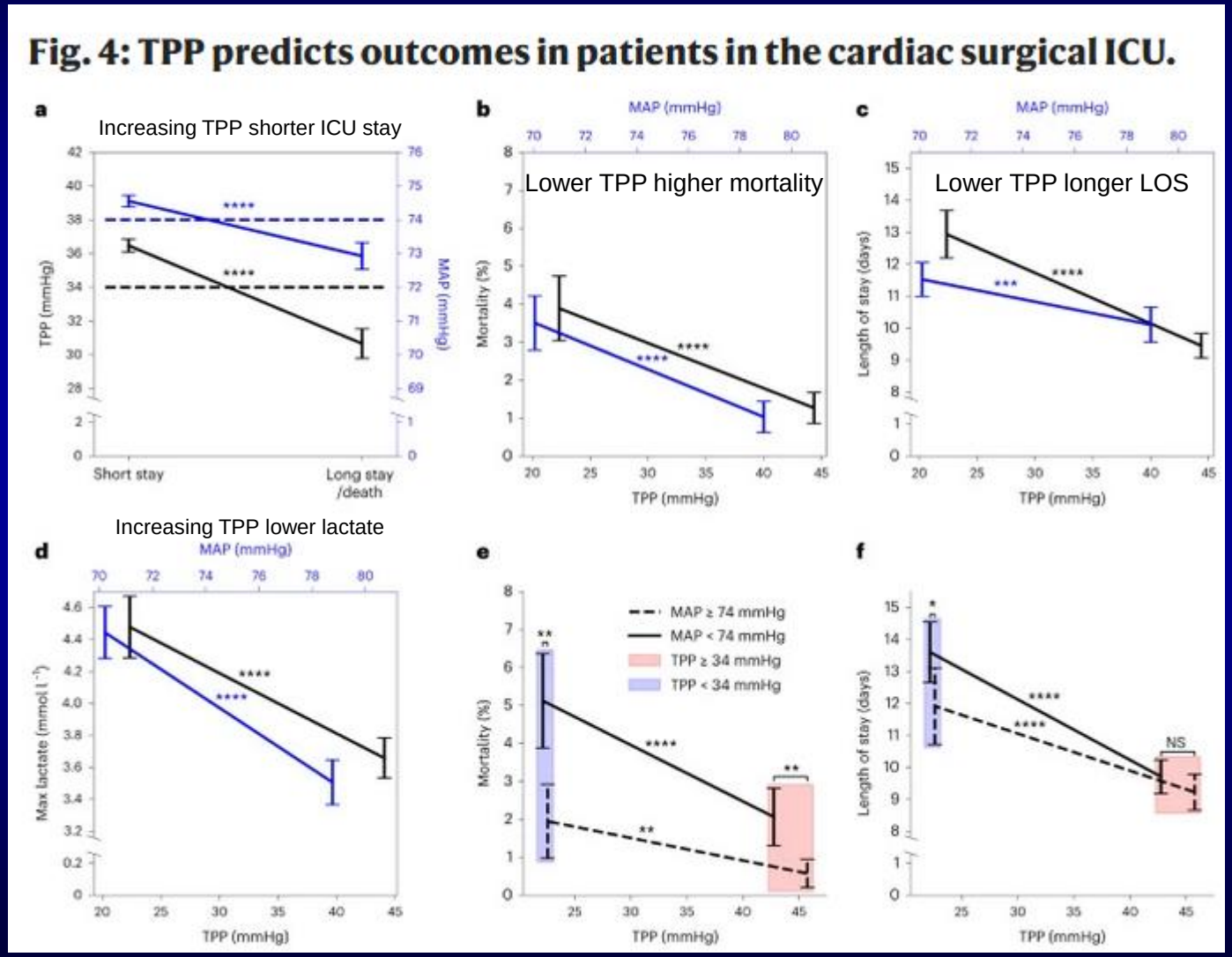
Vasopressor infusion score (VIS)

Higher TPP, Lower VISmax **Higher VISmax, higher mortality**



Chandraesekhar et al. Nat Med 29:1998-2006, 2023

Tissue Perfusion pressure enable continuous hemodynamic evaluation and risk prediction in the ICU



MAP > 74 mmHg

MAP <74 mmHg

TPP > 34 mmHg

TPP < 34 mmHg

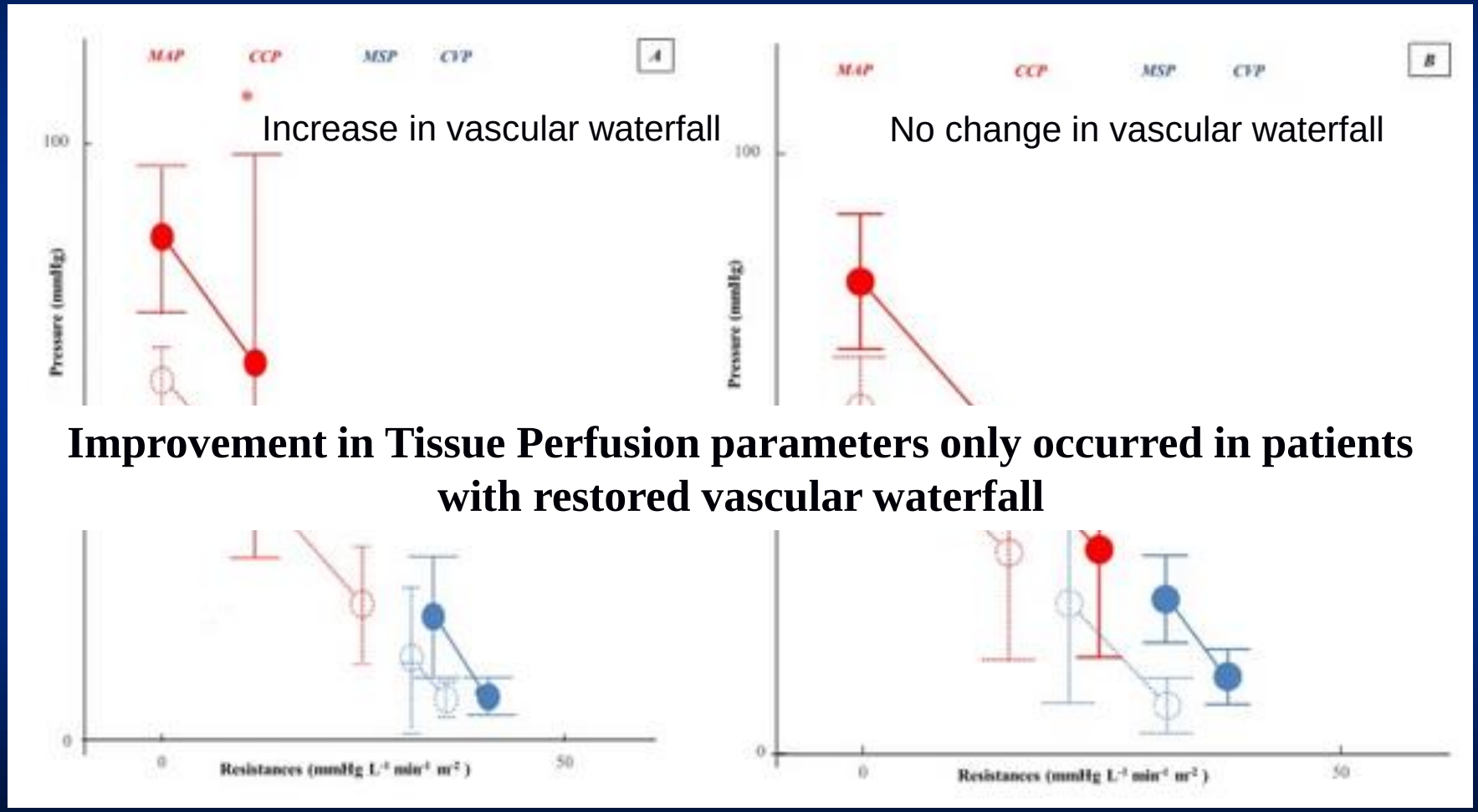
Chandraesekhar et al. Nat Med 29:1998-2006, 2023

Effect of norepinephrine on tissue perfusion in vasoplegic hypotension

- 30 post-cardiac surgery vasoplegic patients
- Measured MAP, Pcc, mean systemic pressure (Pms) and CVP
- Tissue perfusion pressure = MAP-Pcc
- Vascular waterfall = Pcc-Pms
- Driving pressure for venous return = Pms-CVP
- Gave norepinephrine to increase MAP in all (59 to 80 mmHg)

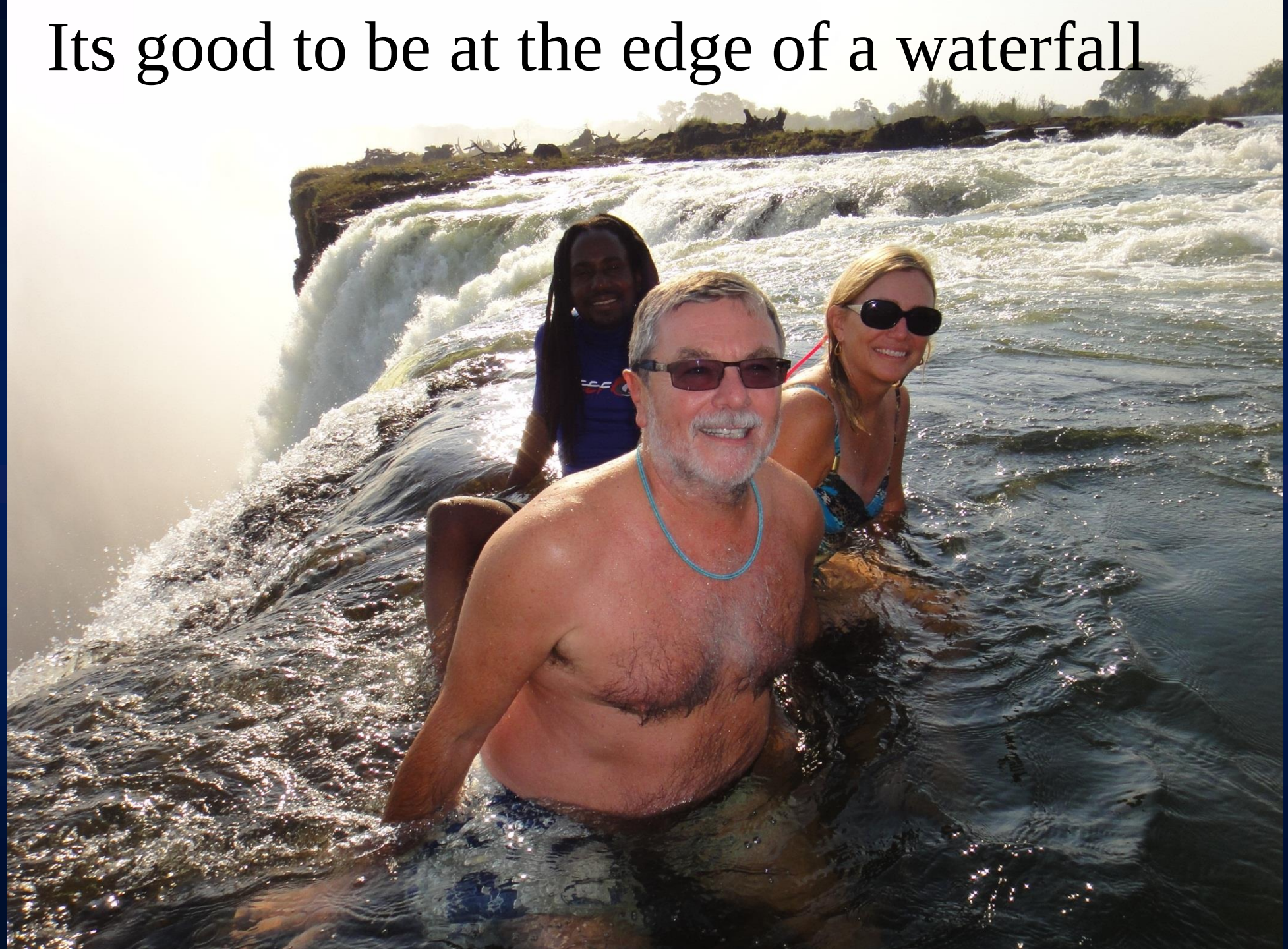
Andrei et al. Intensive Care Med Exper 11:22, 2023

Effect of norepinephrine on tissue perfusion in vasoplegic hypotension



Andrei et al. Intensive Care Med Exper 11:22, 2023

Its good to be at the edge of a waterfall



Effect of Increasing MAP and CO on Tissue Blood Flow

- In otherwise healthy patients in acute hemorrhagic shock, immediate resuscitation improves tissue perfusion:

Circulatory Doncordance

- In sepsis and prolonged circulatory shock/vasoplegia little to no relation between changes in macro and microcirculatory flow

Circulatory Discordance

- Is this due to loss of TPP and an effective vascular waterfall?

Hemodynamic Monitoring: Tools or Toys?

No monitoring device, no matter how insightful its information, will improve patient outcomes

Unless coupled with a treatment which itself improves outcomes


Pinsky et al. Critical Care (2022) 26:294
https://doi.org/10.1186/s13054-022-04173-z

Critical Care

REVIEW Open Access

Effective hemodynamic monitoring

Michael R Pinsky[1*], Maurizio Cecconi[2,3], Michelle S. Chew[4], Daniel De Backer[5], Ivor Douglas[6], Mark Edwards[7], Olfa Hamzaoui[8], Glenn Hernandez[9], Greg Martin[10], Xavier Monnet[11], Bernd Saugel[12], Thomas W. L. Scheeren[13], Jean-Louis Teboul[14] and Jean-Louis Vincent[15]

- Monitoring of high-risk patients likely to have untoward events
  - ECG for acute coronary syndrome
  - SpO_2 for COVID19 triage
- Guiding preemptive resuscitation in high-risk surgical patients
  - Preoptimization in pre-identified high-risk patient subgroups
- Monitoring response to therapy and avoiding over resuscitation
  - Functional hemodynamic monitorng for Shock salvage and Optimization phases
- AI-featurization of vital signs to predict untoward event
  - hypotension, tachycardia and sepsis

Pinsky et al. Crit Care 26:294, 2022

Monitoring-based Treatments that Improve Outcomes

Table 1 Outcome effectiveness targets for hemodynamic monitoring-guided acute care*

Setting	Monitor-treatment	Outcome
Perioperative	Pre-optimization (CO)	Reduced complications
		Reduced ventilator time
		Reduced ICU/hospital LOS
	Functional hemodynamic monitoring	Decreased infused volume
		Decreased lac-time
	Hypotension prediction	Decreased hypotension time
Emergency Department	Sepsis resuscitation SSG	Decreased mortality
	Functional hemodynamic monitoring sepsis	Decreased infused volume
		Lower lac-time
		Decrease hypotension time
ICU resuscitation	Functional hemodynamic monitoring sepsis	Decreased infused volume
		Decreased hypotension time
ICU management	Stabilization/de-escalation (Eadyn)	Rapid norepinephrine weaning

*_CO_ cardiac output, _Eadyn_ dynamic arterial elastance, _ICU_ intensive care unit, _LOS_ length of stay, _lac-time_ duration of time serum lactate is > 2.0 mmol/l, _SSG_ surviving sepsis guidelines

Pinsky et al. Crit Care 26:294, 2022

Ramp-Up Approach to Monitoring

Intensive Care Med (2016) 42:1350–1359

CONFERENCE REPORTS AND EXPERT PANEL

Less invasive hemodynamic monitoring in critically ill patients

Jean-Louis Teboul[1*], Bernd Saugel[2], Maurizio Cecconi[3], Daniel De Backer[4], Christoph K. Hofer[5], Xavier Monnet[1], Azriel Perel[6], Michael R. Pinsky[7], Daniel A. Reuter[2], Andrew Rhodes[3], Pierre Squara[8], Jean-Louis Vincent[9] and Thomas W. Scheeren[10]

- **Continuous invasive**
  - Arterial catheterization, central venous, PAC, TPTD

Teboul et al. Intensive Care Med 42:1350-9, 2016

Causes of Cardiovascular Insufficiency Can Be Obscure and Multifactorial

- Hypovolemia
  - Blood loss, third space, diarrhea/v
  - Decreased vasomotor tone decrea
- Vasoplegia
  - Sepsis, spinal shock, anaphylaxis
- Impaired LV stroke volume
  - Decreased contractility: ischemia, myocardial depression
  - Impaired filling: RV failure, pulmonary embolism, tamponade

Volume
Pressors
Inotropes

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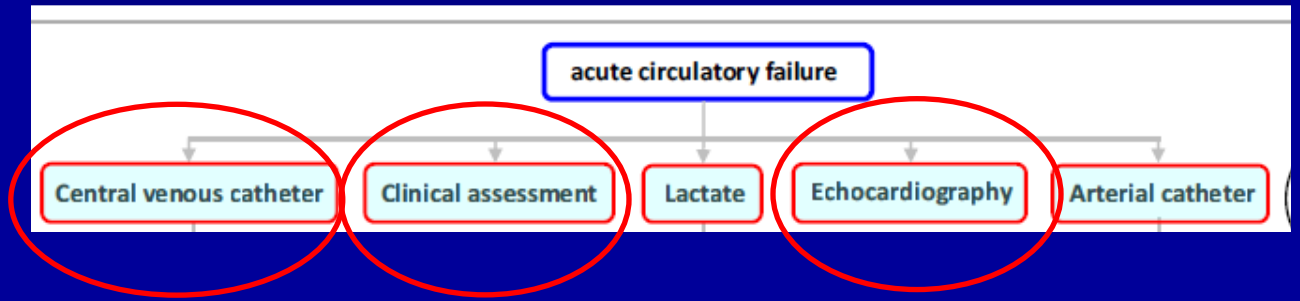

CVP is very important or assessing RV function And the back pressure to organ blood flow

Interment measure of several aspects of Cardiac Function

$ScvO_2$, $PcvCO_2$ and Pv-aCO_2 gap

REVIEW Open Access

Effective hemodynamic monitoring

Michael R. Pinsky[1*], Maurizio Cecconi[2,3], Michelle S. Chew[4], Daniel De Backer[5], Ivor Douglas[6], Mark Edwards[7], Olfa Hamzaoui[8], Glenn Hernandez[9], Greg Martin[10], Xavier Monnet[11], Bernd Saugel[12], Thomas W. L. Scheeren[13], Jean-Louis Teboul[14] and Jean-Louis Vincent[15]

Critical Care (2022) 26:294

In some forms of distributive shock, $ScvO_2$ can be > 70% despite ongoing CVI due to impairment of oxygen extraction [84, 86]. A v-aPCO_2 > 6 mmHg (or > 0.8 kPa) identifies patients for whom an increase in CO may be beneficial in sustaining organ perfusion despite a SvO_2 > 70%. If the v-aPCO_2 is < 6 mmHg (or < 0.8 kPa), it is unlikely that increasing CO would reverse organ hypoperfusion.

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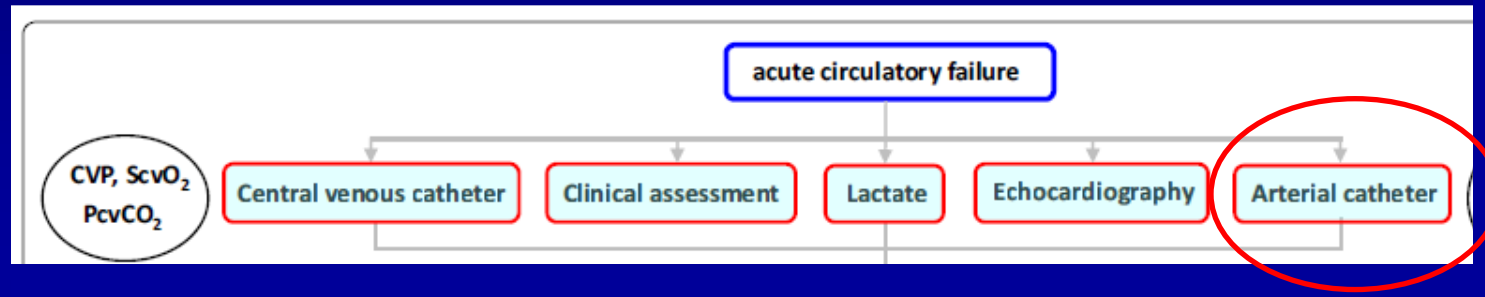
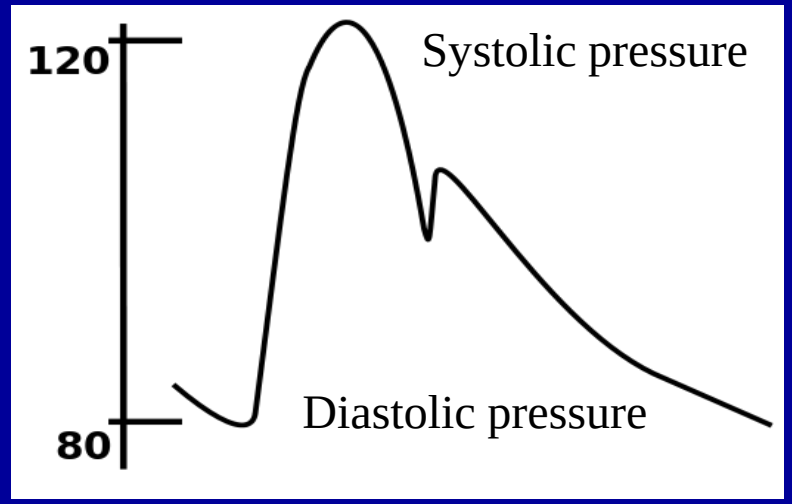




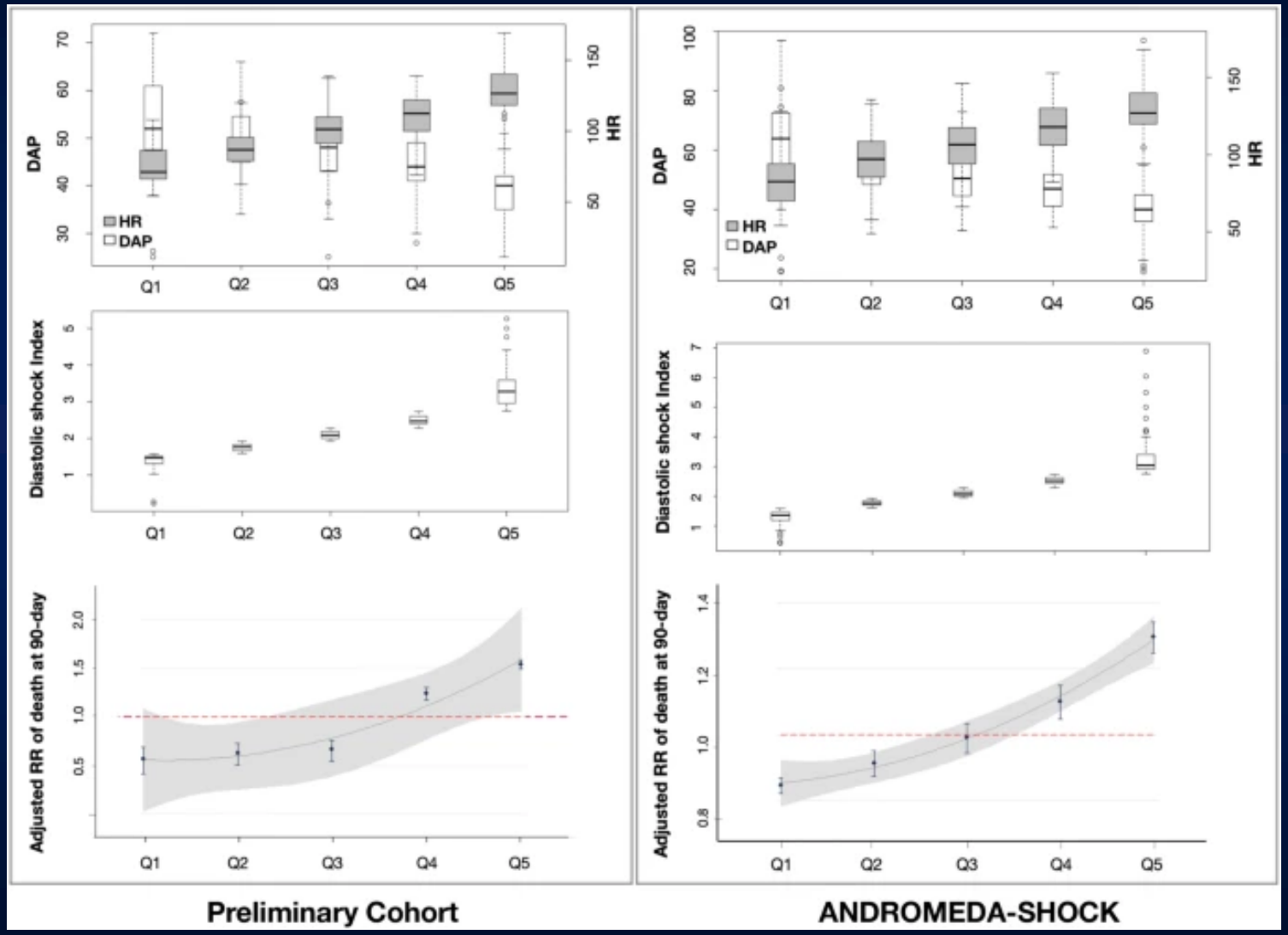
Diastolic pressure is a function of vasomotor tone and HR

Diastolic Shock Index

- Diastolic shock index: HR/Diastolic pressure
- Examined DSI to outcomes during early septic shock
  - **Andromeda-Shock** randomized clinical trial n=424
  - Measured DSI at before start of vasopressors (Pre-VPs/DSI) and at vasopressor start (VPs/DSI)
- Risk of death progressively increased as either diastolic pressure, HR or DSI increased
- MAP and SV/PP (shock index) showed poor correlation

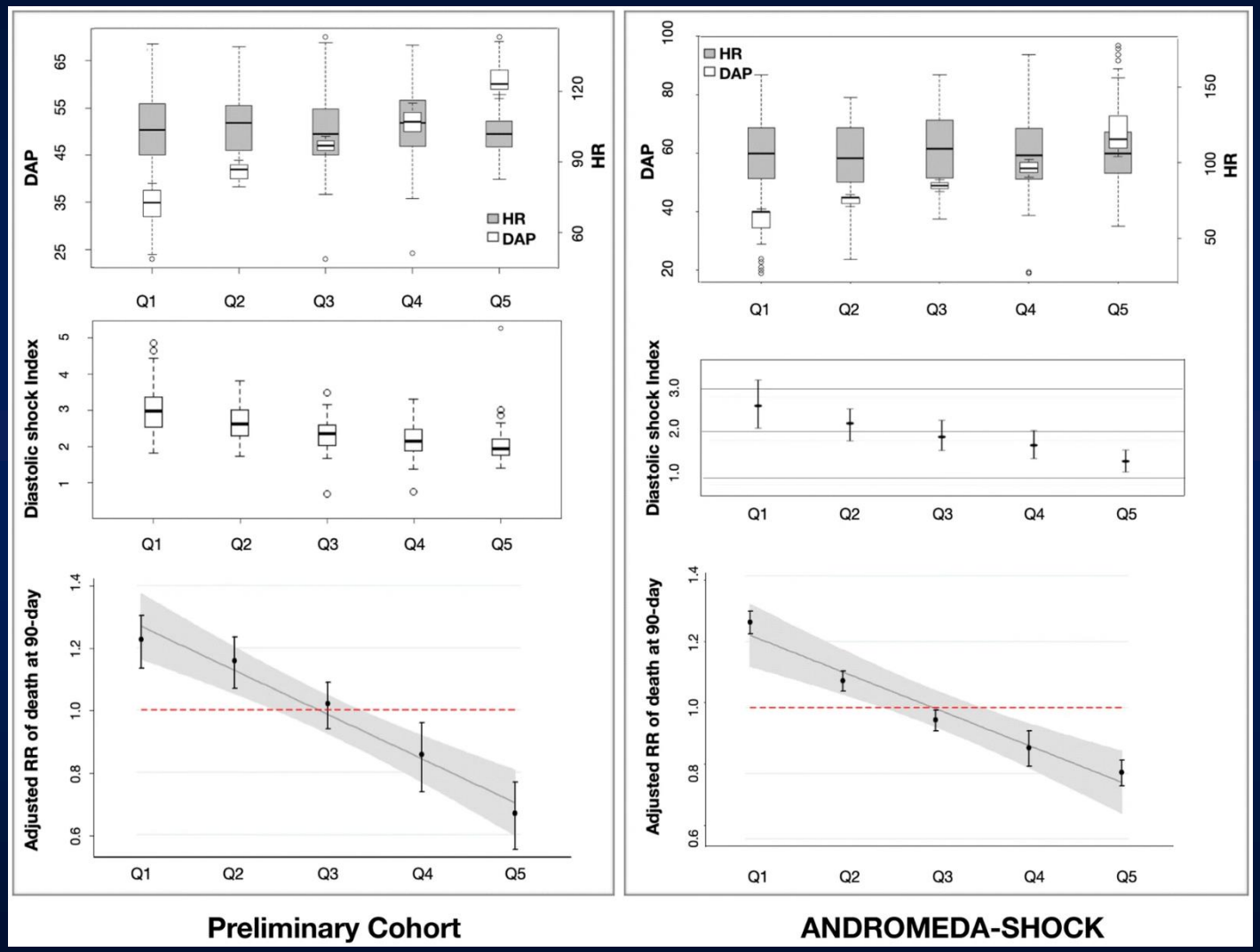
Ospina-Tascon et al. Ann Crit Care 10:41, 2020

Diastolic Shock Index



Ospina-Tascon et al. Ann Crit Care 10:41, 2020

Diastolic Shock Index: Constant HR

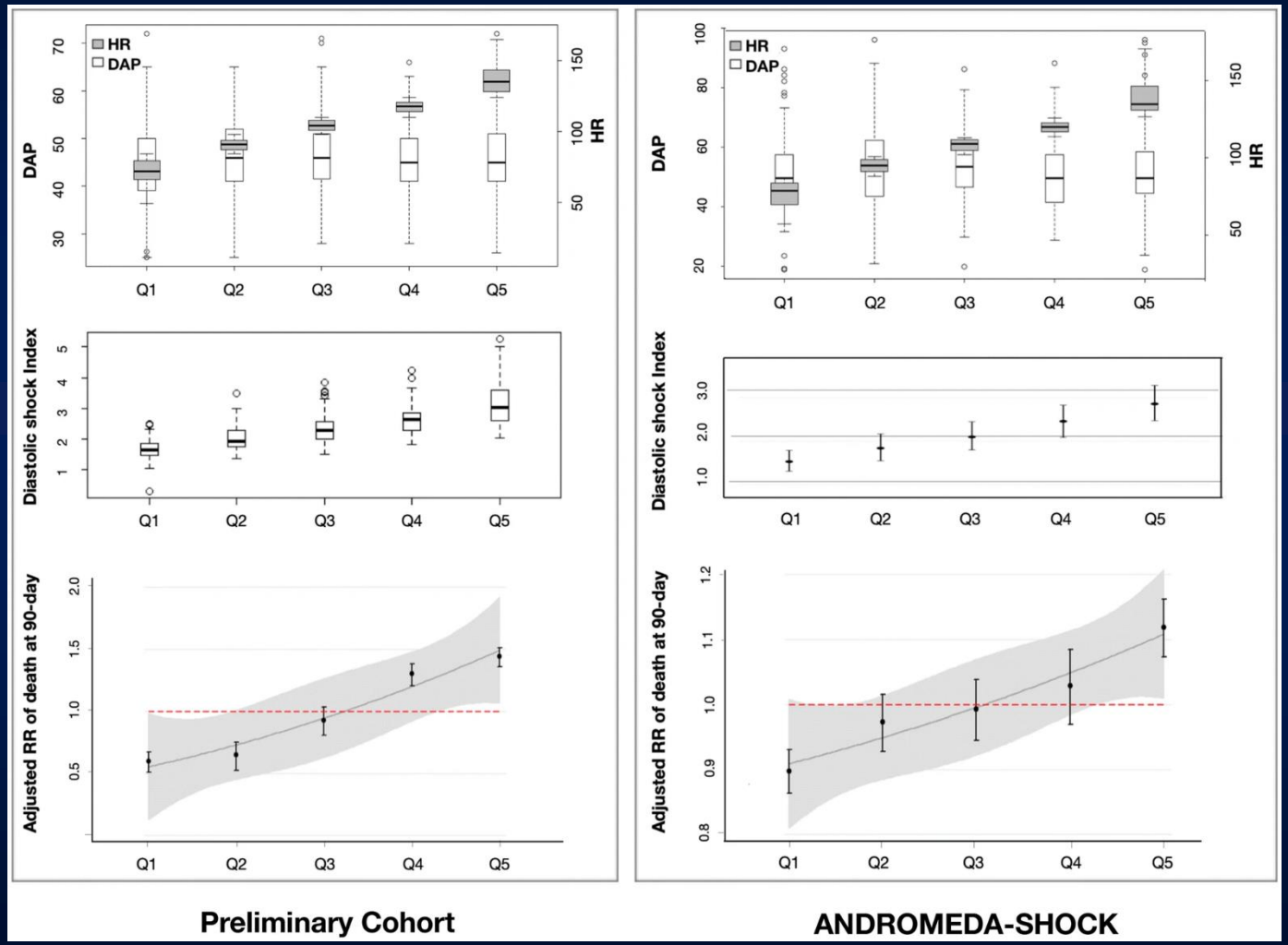


As diastolic pressure decreases for the same HR, risk of death increases

DSI >2

Ospina-Tascon et al. Ann Crit Care 10:41, 2020

Diastolic Shock Index: Constant Diastolic Pressure



As HR increases for the same diastolic pressure, risk of death increases

DSI >2

Ospina-Tascon et al. Ann Crit Care 10:41, 2020

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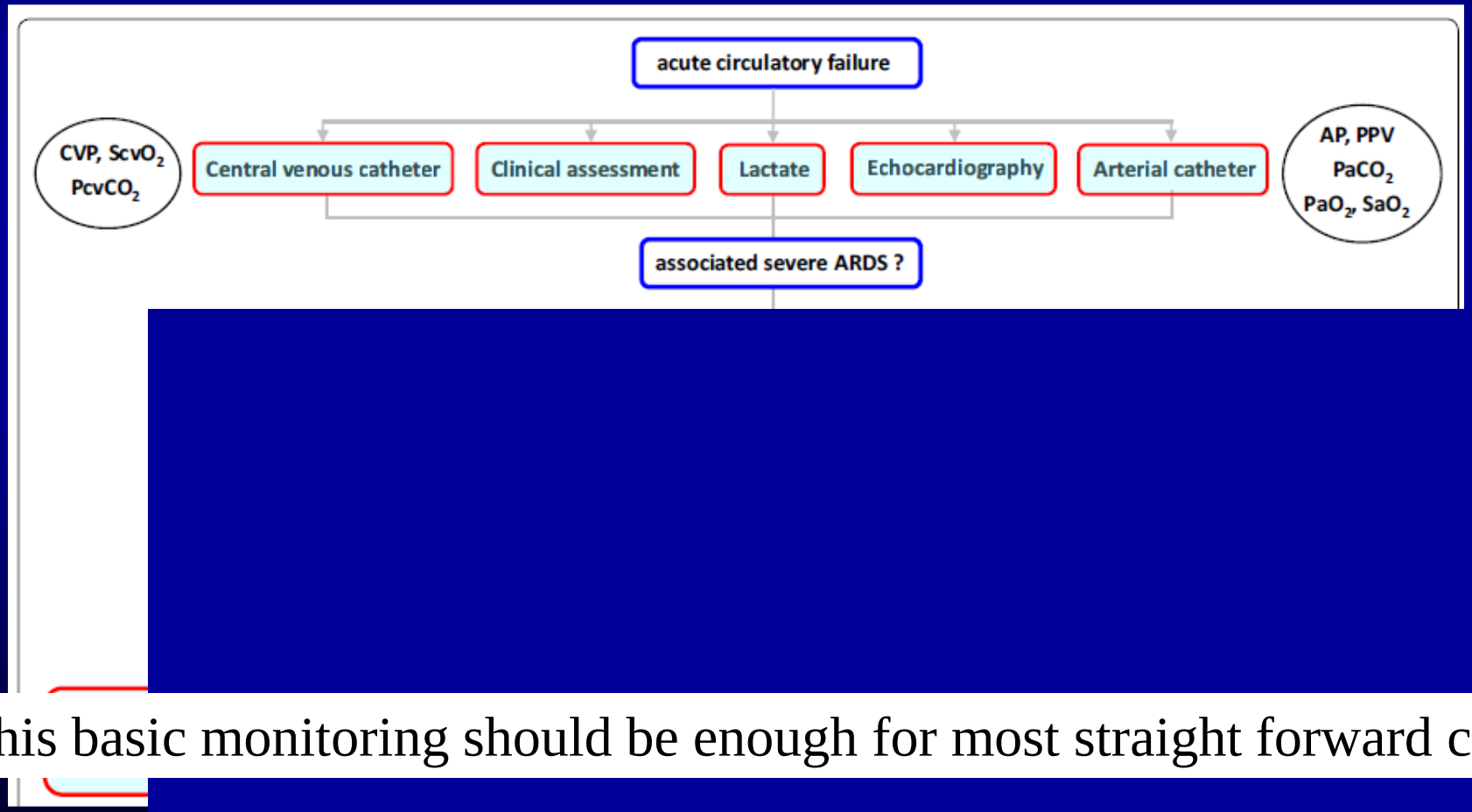

This basic monitoring should be enough for most straight forward cases

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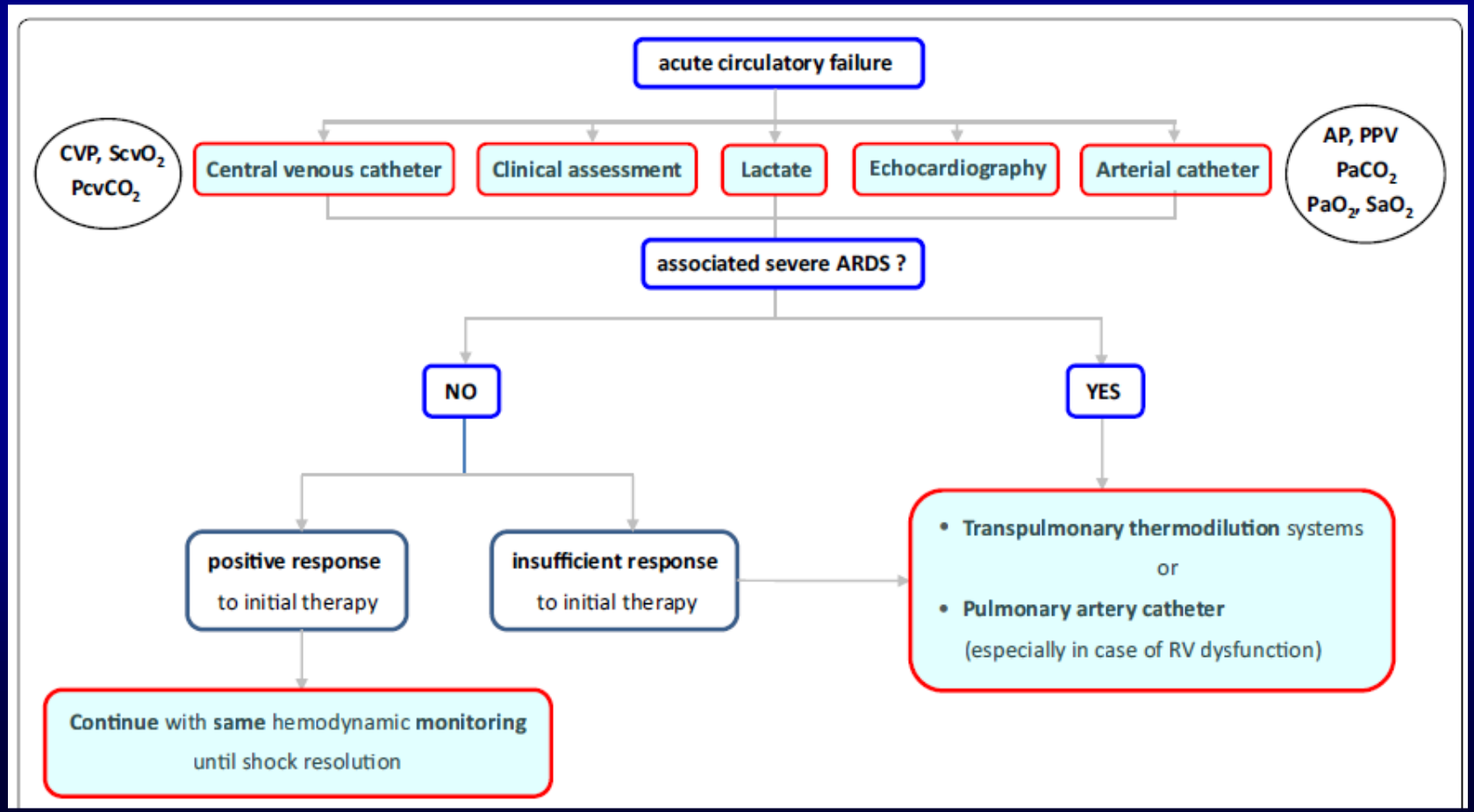
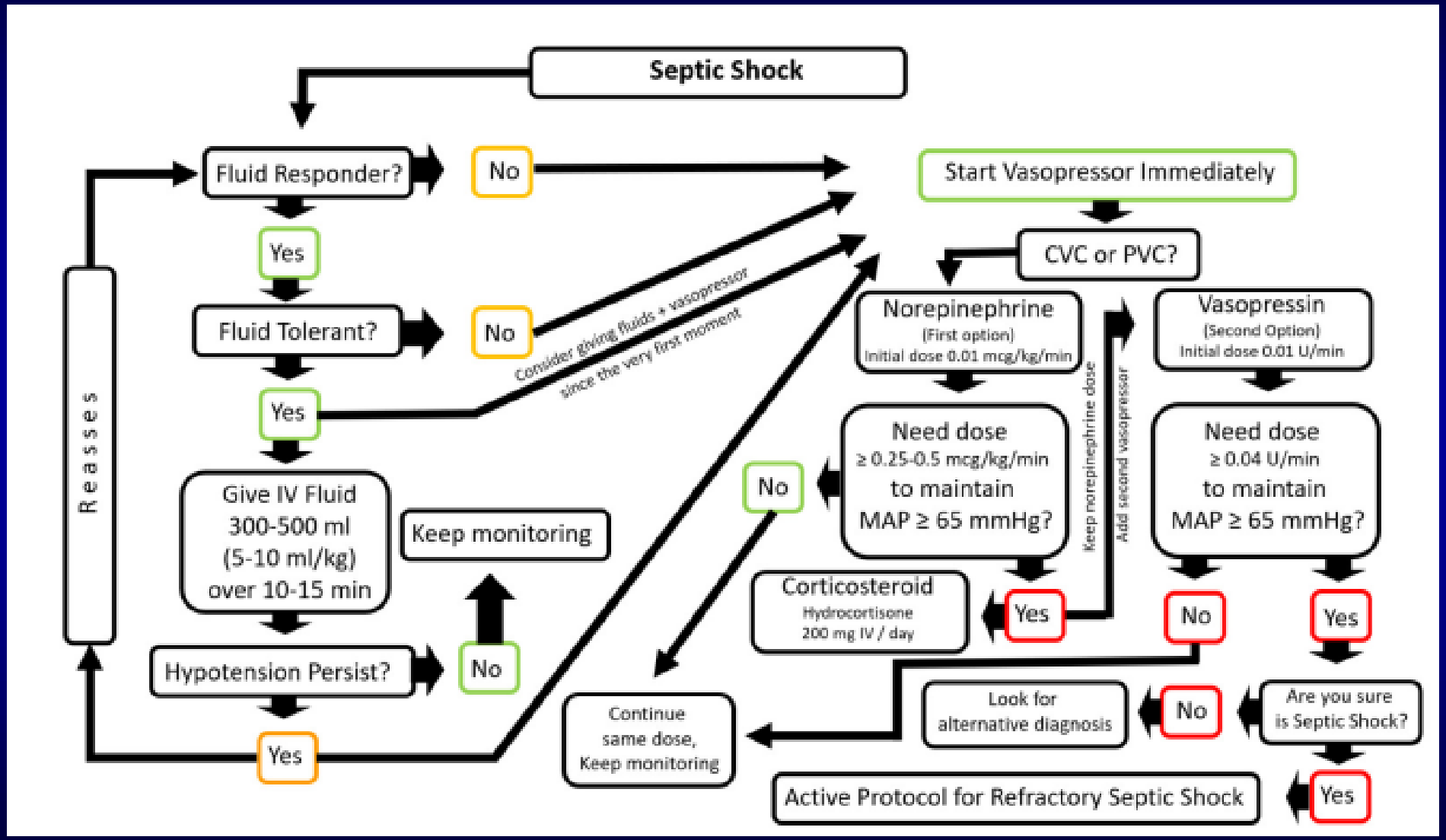


Fluids and Early Vasopressors



Sanchez E, Pinsky MR, et al. J Crit Care Med 9:138-47, 2023

Intensive Care Med (2014) 40:1795–1815

CONFERENCE REPORTS AND EXPERT PANEL

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

We suggest the use of **transpulmonary thermodilution** or **PAC**

in patients with severe shock especially in the case of associated **ARDS**

Level 2; QoE low (C)

REVIEW Open Access

Effective hemodynamic monitoring

Michael R. Pinsky[1*], Maurizio Cecconi[2,3], Michelle S. Chew[4], Daniel De Backer[5], Ivor Douglas[6], Mark Edwards[7], Olfa Hamzaoui[8], Glenn Hernandez[9], Greg Martin[10], Xavier Monnet[11], Bernd Saugel[12], Thomas W. L. Scheeren[13], Jean-Louis Teboul[14] and Jean-Louis Vincent[15]

Critical Care (2022) 26:294

The causes of ARDS can be complex and causes of death are multiple, making it difficult to demonstrate any benefit on survival from hemodynamic therapeutic protocols. Since no monitoring device has been demonstrated to cause harm per se, it seems unreasonable to manage such complex patients without appropriate invasive hemodynamic tools since clinical and biochemical signs are often misleading [80, 84]. Bedside echocardiographic evaluation is necessary to diagnose and direct the management of these patients in both a static and dynamic fashion but is not well suited to continual monitoring.

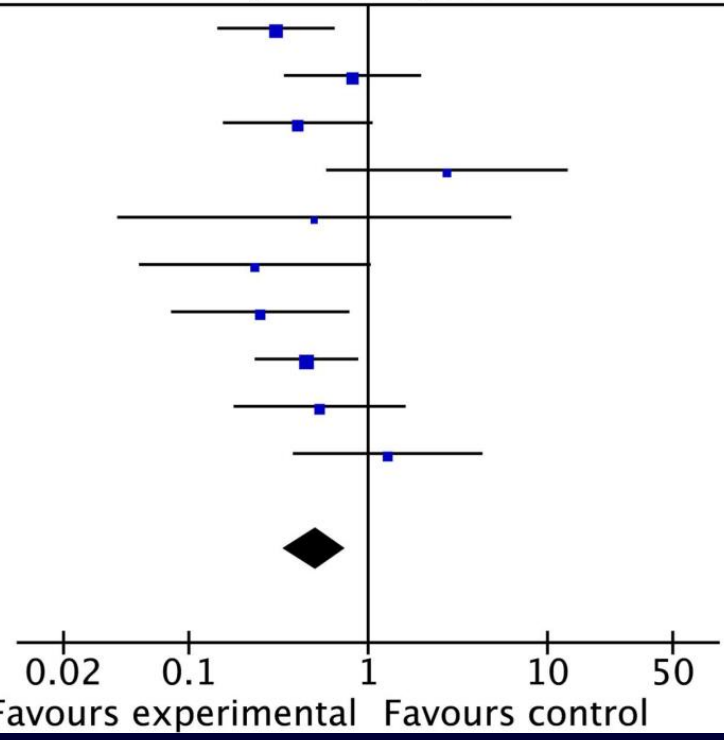
Effects of Goal-Directed Therapy based on Dynamic Parameters on post-surgical outcomes

A Meta-analysis of randomized controlled trials

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Benes 2010 (30)	18	60	35	60	16.0%	0.31 [0.14, 0.65]
Forget 2010 (29)	23	41	25	41	13.2%	0.82 [0.34, 1.97]
Goepfert 2013 (28)	34	50	42	50	11.7%	0.40 [0.15, 1.06]
Harten 2008 (27)	7	14	4	15	5.6%	2.75 [0.58, 12.98]
Kapoor 2008 (31)	1	13	2	14	2.3%	0.50 [0.04, 6.28]
Lopes 2007 (10)	7	17	12	16	6.0%	0.23 [0.05, 1.03]
Mayer 2010 (32)	6	30	15	30	9.1%	0.25 [0.08, 0.79]
Salzwedel 2013 (22)	21	79	36	81	18.3%	0.45 [0.23, 0.88]
Scheeren 2013 (25)	12	26	16	26	9.6%	0.54 [0.18, 1.62]
Zhang Ju 2012 (24)	12	40	5	20	8.3%	1.29 [0.38, 4.34]
Total (95% CI)		**370**		**353**	**100.0%**	**0.51 [0.34, 0.75]**
Total events	141		192			

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 12.47$, df = 9 (P = 0.19); $I^2 = 28\%$

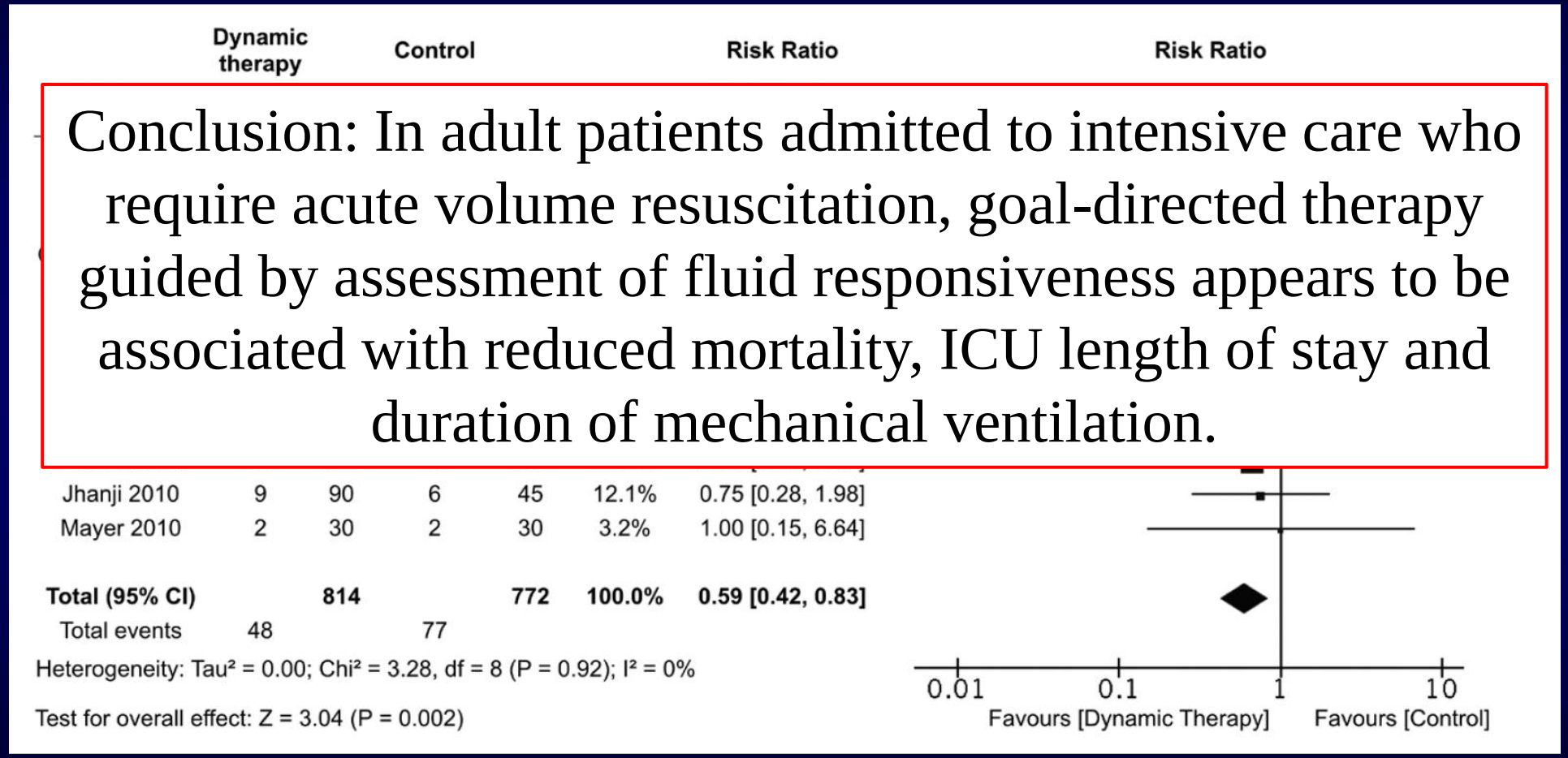
Test for overall effect: Z = 3.35 (P = 0.0008)



Benes et al. Crit Care 18:584, 2014

Use of Dynamic Variables to Drive Sepsis Resuscitation

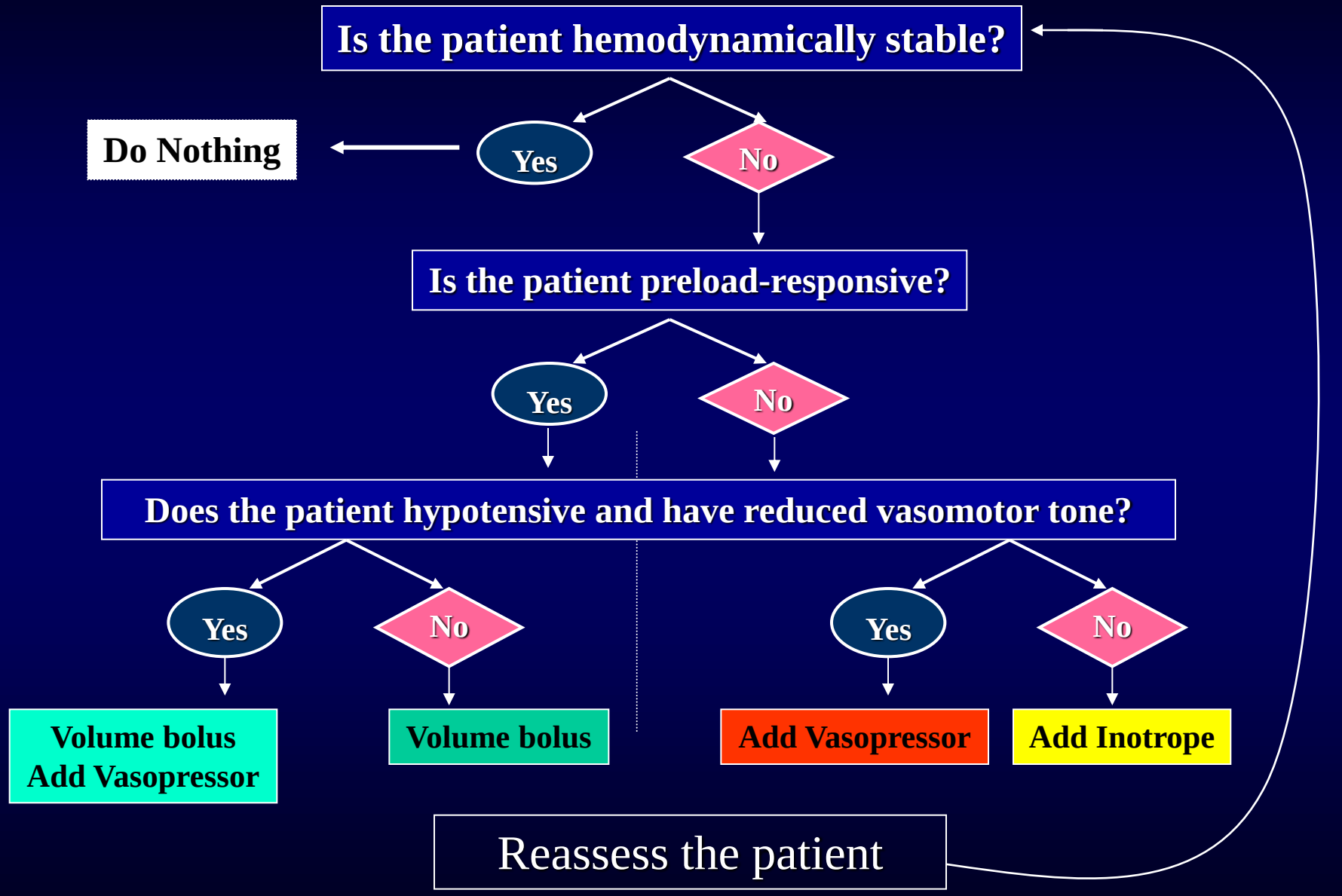
Conclusion: In adult patients admitted to intensive care who require acute volume resuscitation, goal-directed therapy guided by assessment of fluid responsiveness appears to be associated with reduced mortality, ICU length of stay and duration of mechanical ventilation.



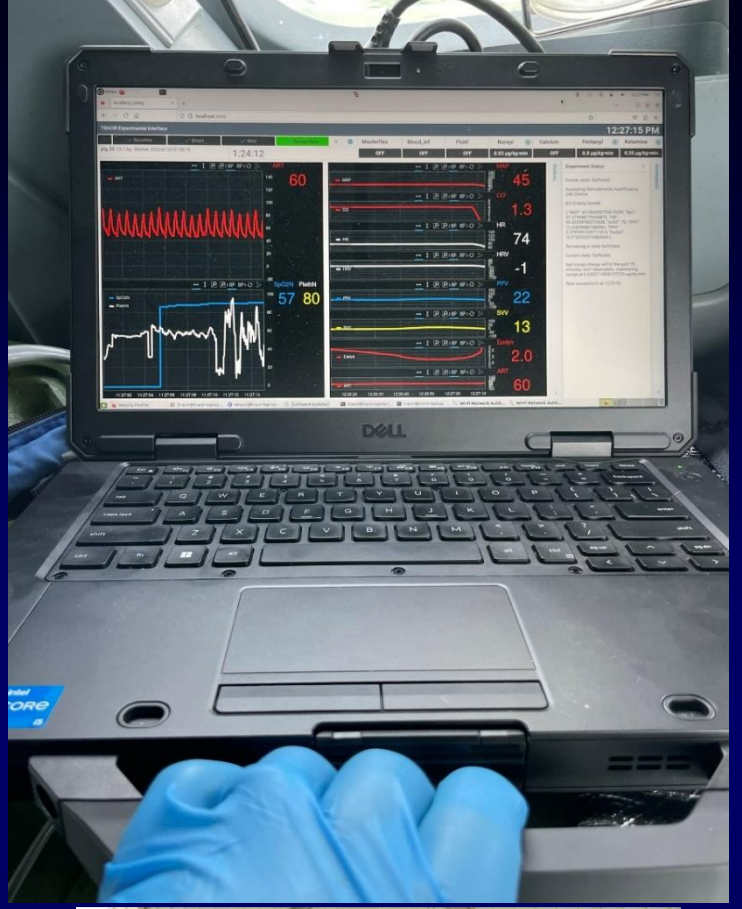
Bednarczyk et al. Crit Care Med 45:1538-45, 2017

Precise Resuscitation

Percise Personalized Resuscitation



Pinsky. Protocolized care, *in*: Pinsky & Payen. Functional Hemodynamic Monitoring, pp 381-95, 2004



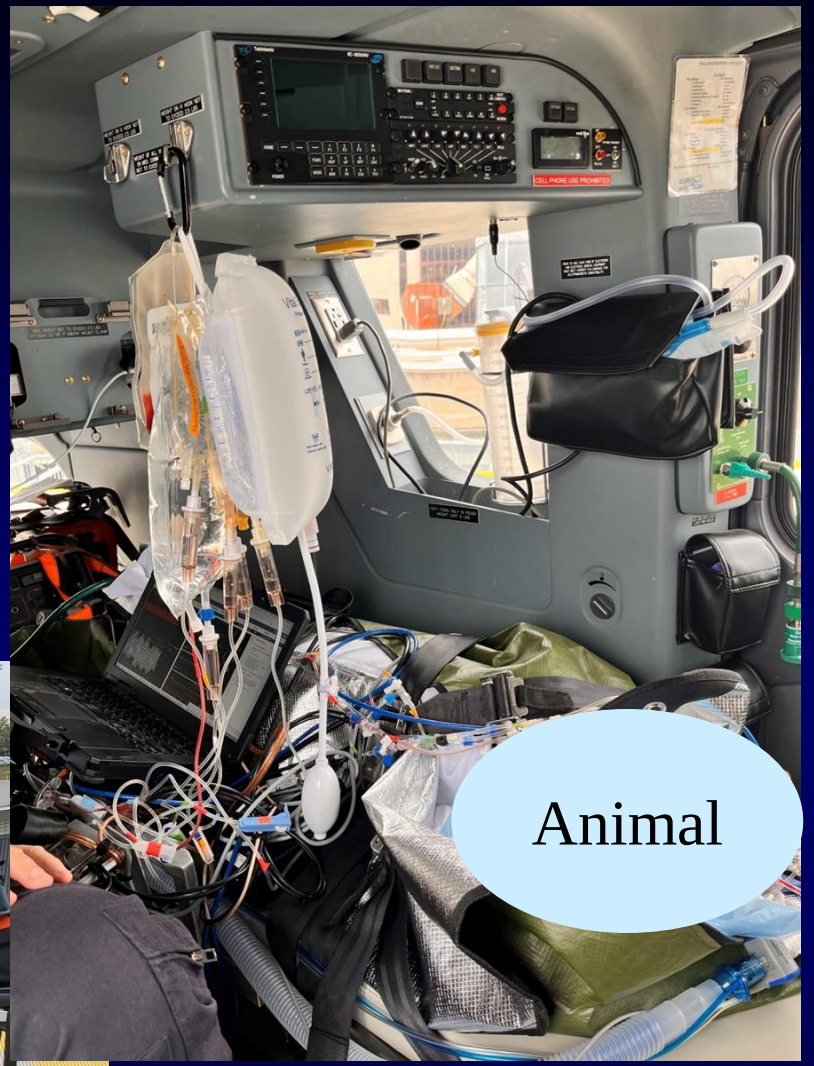
Total Intravenous Anesthesia

Initiate Uncontrolled Hemorrhage two 4x4 cm stellate liver lacerations

Allow MAP < 30 mmHg, close abdomen

Start ReFIT protocol → Package patient with flight crew → transport

Pinsky et al. ICMx 12:44, 2024



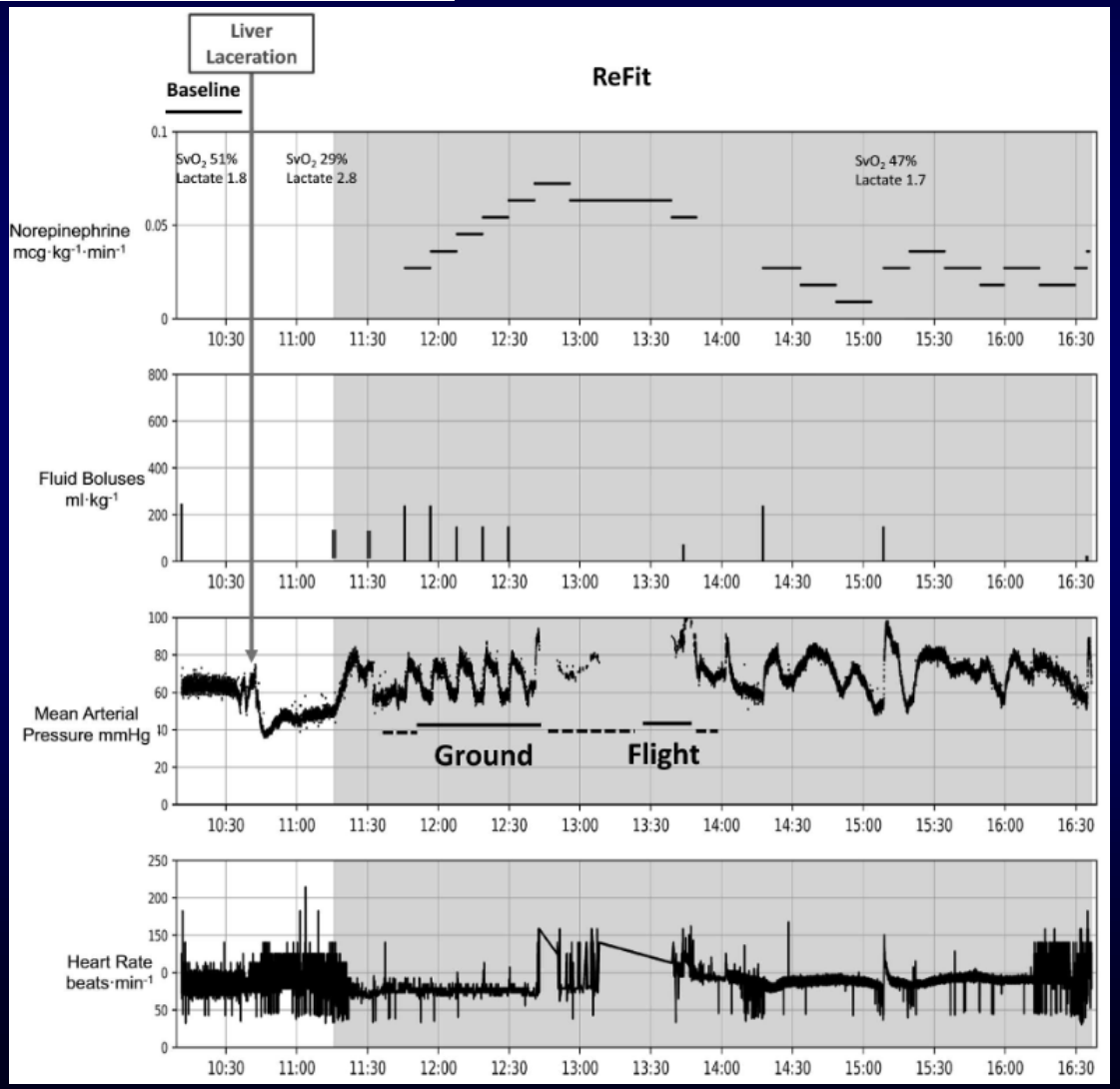
Animal

- Eurocopter
- Single Pilot
- Flight Physi

Pinsky et al. ICMx 12:44, 2024

Autonomous precision resuscitation during ground and air transport of an animal hemorrhagic shock model

Michael R. Pinsky[1,2*], Hernando Gomez[1], Francis X. Guyette[3], Leonard Weiss[3], Artur Dubrawski[4], Jim Leonard[4], Robert MacLachlan[4], Lisa Gordon[1], Theodore Lagattuta[1], David Salcido[3] and Ronald Poropatich[1,2,5]



Pinsky et al. ICMx 12:44, 2024

Pittsburgh Post-Gazette Friday May 24, 2024

Pitt works to extend 'Golden Hour'

Little human intervention needed in lifesaving method developed for battlefield critical care

By Anya Sostek
Pittsburgh Post-Gazette

On four occasions last year, medical helicopters flew over Pittsburgh transporting not injured humans, but wounded pigs.

The pigs — bleeding heavily from the abdomen — were stabilized in the air by an autonomous medical intervention system developed by the University of Pittsburgh as part of a military-funded study with the potential for "groundbreaking" advances in health care.

"What we did with the Department of Defense was try to solve their number one cause of preventable death on the battlefield," said Ronald Poropatich, director of the Pitt Center for Military Medicine. "This is the future of medicine, whether it's military or civilian."

In the five-year proof-of-concept study — published Friday in the journal Intensive Care Medicine Experimental — Pitt researchers and physicians worked with computer scientists at Carnegie Mellon University to build the ReFit (Resuscitation based on Functional Hemodynamic Monitoring) system. About the size of a microwave, the computer system can function as a highly trained

SEE **PITT**, PAGE A-2

Pitt tries to extend the 'Golden Hour'

PITT, FROM A-1

critical care physician, administering fluids, blood and medication without human intervention. It was funded by a $3.712 million grant over four years from the Department of Defense.

In the experiment, four pigs were fully anesthetized in accordance with animal research protocols and then given liver lacerations in a laboratory to mimic a gunshot wound to the abdomen or other non-compressible hemorrhage.

The pigs were allowed to bleed for 30 minutes and then connected to the ReFit system. At this point, a human medical professional still has to manually insert an IV, but after that, no human intervention is required.

Two of the pigs were placed on a stretcher and taken to the hospital helipad, where they flew for several hours around Pittsburgh. The other two pigs were taken via ambulance to the Allegheny County Airport, and then flown on a medical helicopter as far as Kittanning and then back to Oakland.

The ReFit system was able to stabilize the pigs and return them in adequate condition for life-saving surgery.

"For the first time in the history of medicine, we took an animal in a critical state onto a helicopter and autonomously brought it back healthier than when it was placed in emergency transport hours earlier," said Michael Pinsky, professor of critical care, bioengineering and critical and translational medicine at Pitt and lead author of the study. "This has profound implications for trauma resuscitation in the field and of course in military medicine."

In emergency medicine, physicians have long referred to the "golden hour," an idea dating back to World War I that it is critical to get a seriously injured patient to a trauma center within one hour of their injury to avoid death or long-term complications. What ReFit can do is extend that timeline so that patients are stable for much longer — up to five hours in the study — before hospital care. "It is all about extending the golden hour," said Dr. Poropatich. "All we are trying to do is keep the casualty alive long enough to get to an operating room."

Nate Langer/UPMC

The University of Pittsburgh's Dr. Michael Pinsky, left, observes an injured pig being loaded onto a medevac helicopter as part of an experiment using the ReFit system to treat the pig without human intervention.

Although the technology was developed for the military, there are numerous scenarios in civilian medicine where it would be useful. Take the case of a serious car accident in an area of Pennsylvania that is far from a trauma hospital, said Dr. Pinsky: An EMT could insert an IV into a patient and the ReFit system could then administer care equivalent to what they would receive from an experienced physician while they were being transported.

In a military scenario, the technology is well suited for large-scale combat operations with dispersed medical assets, such as the war going on in Ukraine, said Dr. Poropatich, who served in the U.S. Army for 30 years before retiring in 2012 as a colonel. "It's the concept of trauma care in a backpack," he said. "It could provide the technology to resuscitate without having a critical care doctor there with you."

The team at Pitt is working on further advancements to the technology, such as the ability to deliver the ReFit system via a drone, to extend its reach into remote locations. Other research centers, such as Carnegie Mellon, are also working on robotic technology to insert an IV without a human. "There is great interest in making it truly autonomous," said Dr. Poropatich. "Autonomous care in an autonomous aircraft."

To do so, the system will need to be tested on humans, in addition to pigs. While there are aspects of human testing that they plan to begin within this year, full clinical trials are realistically two or three years away, said Dr. Pinsky.

"We at the University of Pittsburgh and especially emergency medicine are completely excited about going to the next level here," he said. "Everyone sees the realistic application of this now — to treat human beings."

Anya Sostek: asostek@post-gazette.com.

Conclusions

- Physiology is alive and well at the bedside, if you look
- Protocols minimize practice variations but may not be best for all patients. A plea for personalization of care.
- Precise resuscitation using dynamic parameters to define volume responsiveness and vasomotor tone will minimize treatment related harm, and can function semi-autonomously
- We have better tools today and a clearer understanding to minimize treatment complications while optimizing recovery of patients with critical illness

Thank You