Les états de choc septique:

des recommandations à la pratique

Prof. Jean-Louis TEBOUL

Medical ICU

Bicetre hospital

University Paris South

France

Early management

- Evaluate the **clinical** severity
- Perform usual **laboratory** tests
- **Begin** as soon as possible:
  - ✓ a **hemodynamic** therapy
  - ✓ an **anti-infectious** therapy

Early management

- Evaluate the **clinical** severity

  - ✓ depth of **hypotension**
  - ✓ **neurologic** disorders
  - ✓ **respiratory distress**

→ **Accelerate** patient's **transfer** to the **ICU**

Early management

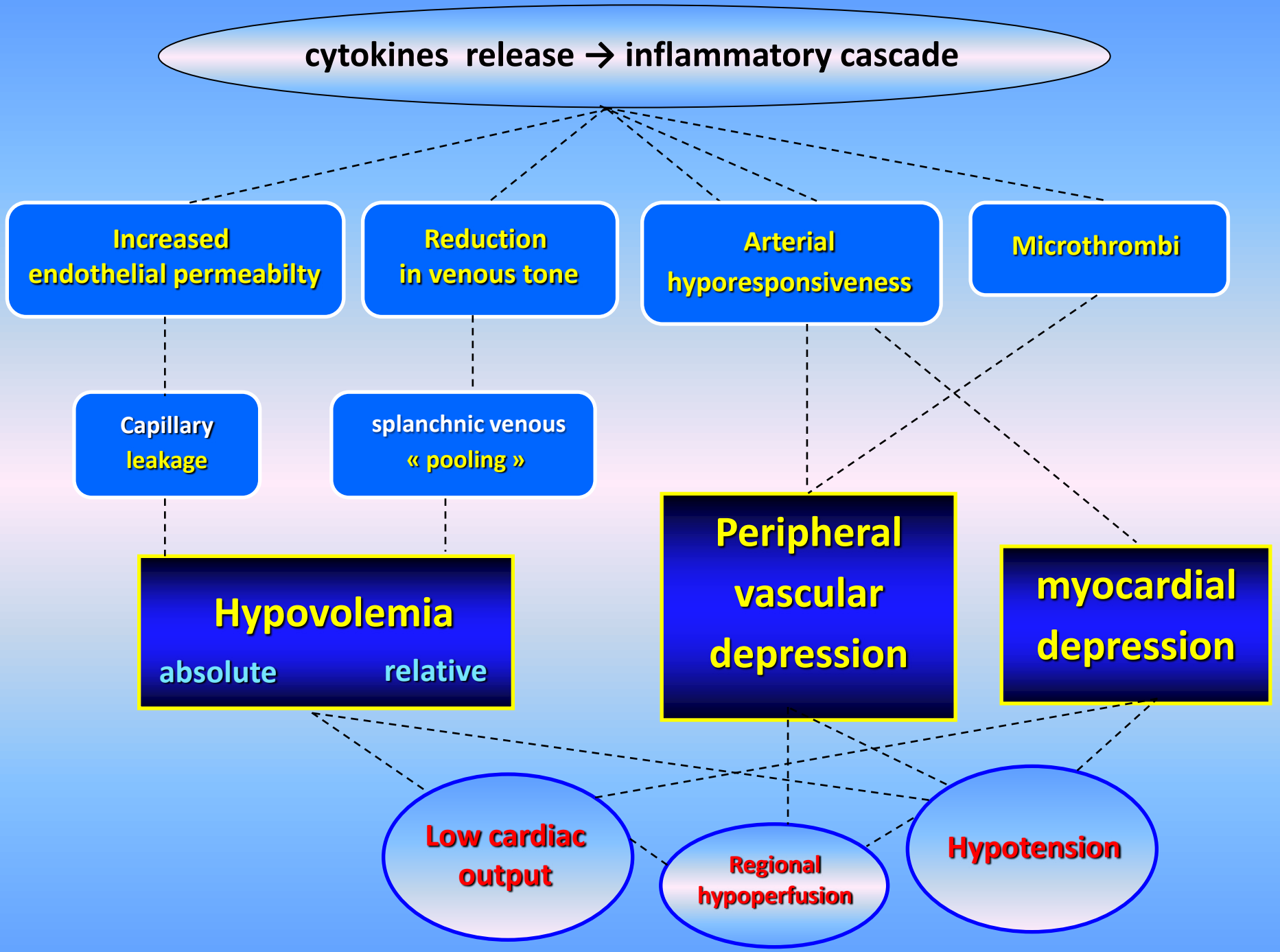
- Evaluate the **clinical** severity
- Perform usual **laboratory** tests
  - Standard **blood samples,** blood **gases**
  - **Blood lactate +++**
  - **Cardiac biomarkers** (BNP, troponin)
  - **Inflammatory biomarkers** (CRP, PCT)
  - **Blood cultures** (2 within a few mins),
  - **Microbiological samples** according to **clinical** suspicion
  - **ECG, cardiac echo** if possible

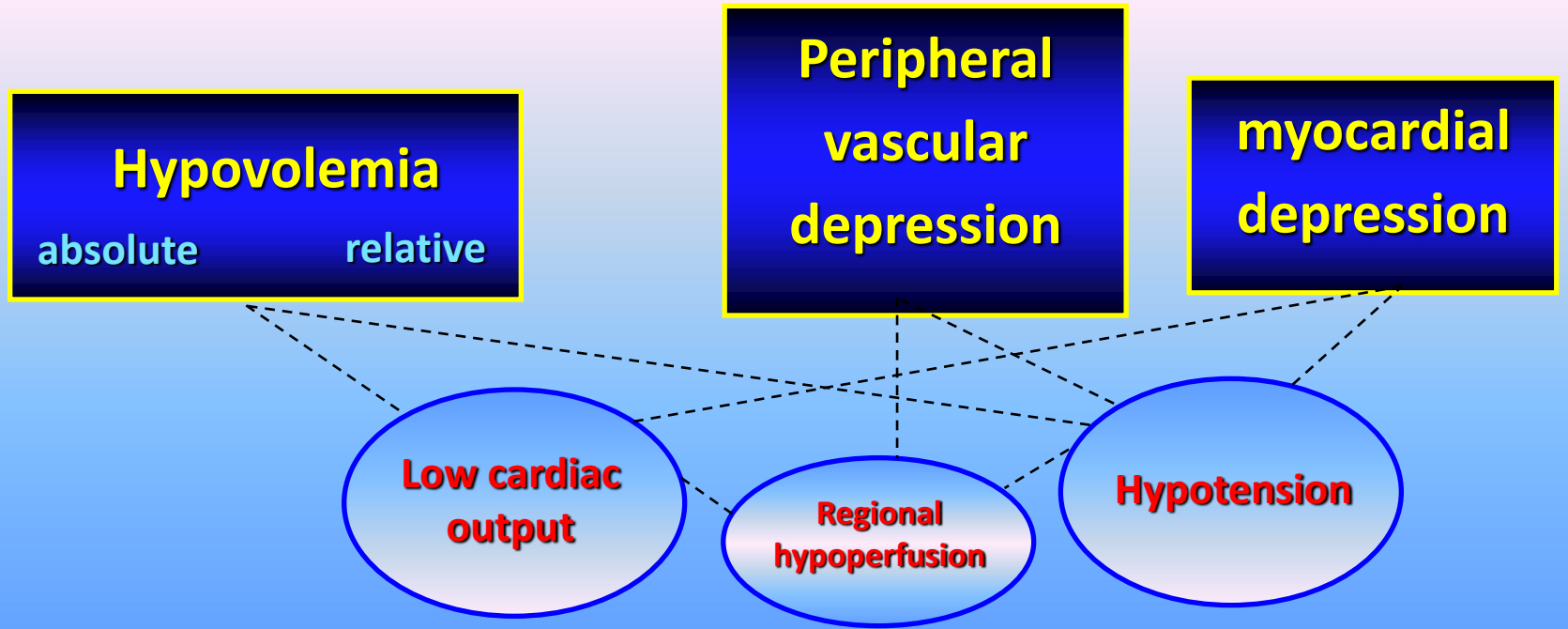
Early management

- Evaluate the **clinical** severity
- Perform usual **laboratory** tests
- **Begin** as soon as possible:
  - ✓ a **hemodynamic** therapy
  - ✓ an **anti-infectious** therapy

Early management

- Evaluate the **clinical** severity
- Perform usual **laboratory** tests
- **Begin** as soon as possible:
  - ✓ a **hemodynamic** therapy
  - ✓ an **anti-infectious** therapy

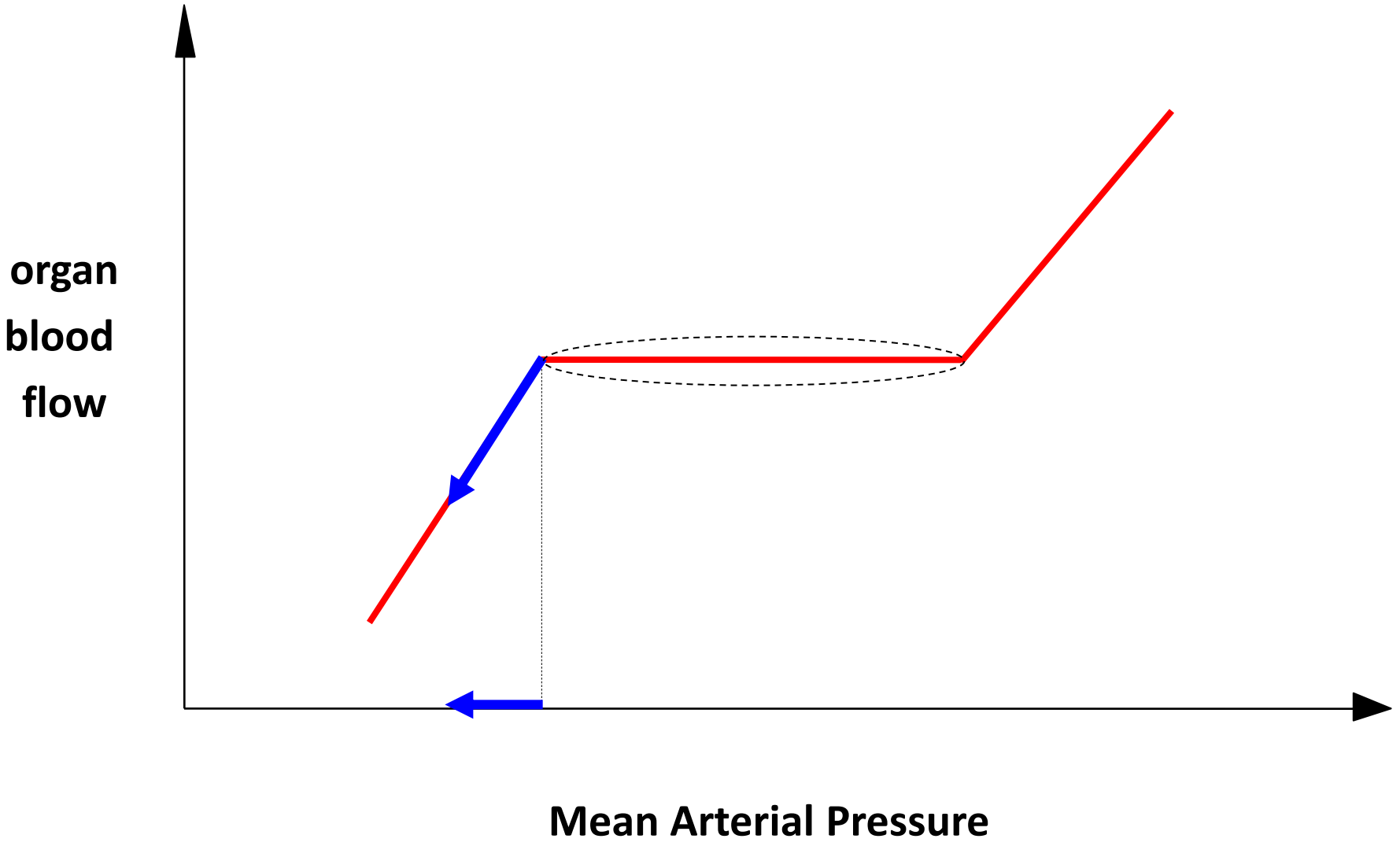

cytokines release → inflammatory cascade
Increased endothelial permeabilty
Reduction in venous tone
Arterial hyporesponsiveness
Microthrombi
Capillary leakage
splanchnic venous « pooling »
Hypovolemia
absolute
relative
Peripheral vascular depression
myocardial depression
Low cardiac output
Regional hypoperfusion
Hypotension


Hypovolemia
absolute
relative
Peripheral vascular depression
myocardial depression
Low cardiac output
Regional hypoperfusion
Hypotension

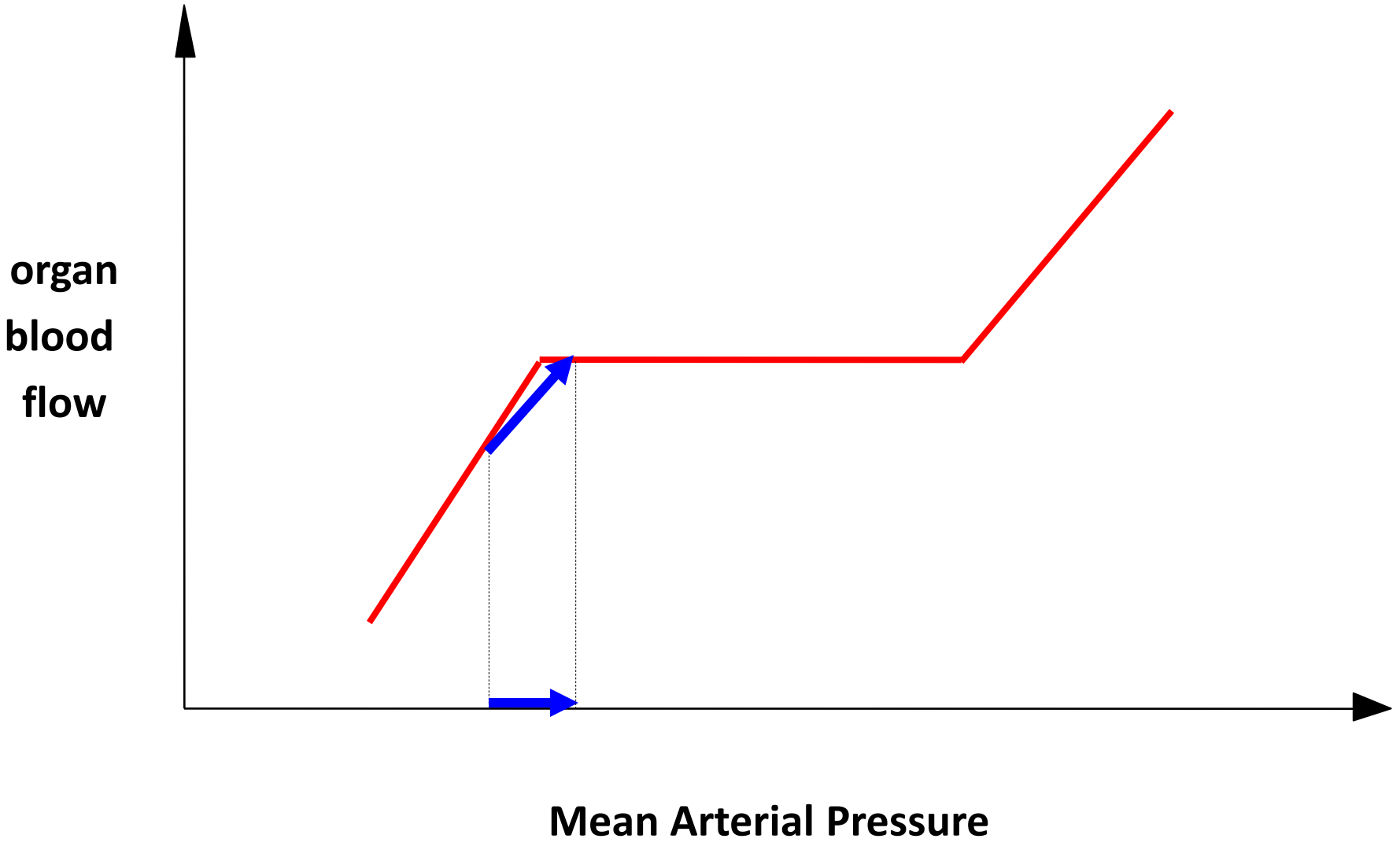
Profound hypotension

Organ hypoperfusion

Autoregulation of organ blood flow



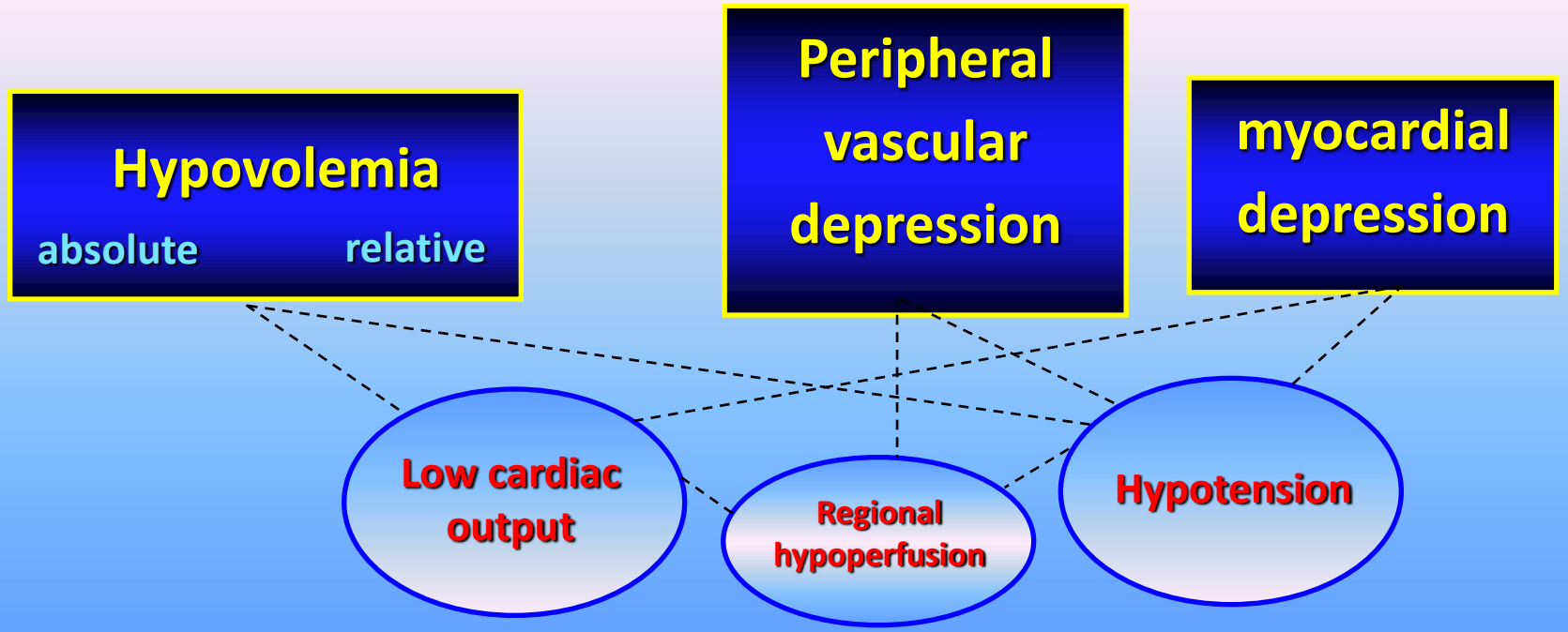
Autoregulation of organ blood flow



Therapeutic goals

Restore as soon as possible tissue perfusion

1) Restore an adequate **mean arterial pressure**
2) Restore an adequate **cardiac output**



Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

Initial resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis-induced hypoperfusion (defined as hypotension persisting after initial fluid challenge or blood lactate $\geq$ 4 mmol/L).

Goals during the first 6h of resuscitation:

(a) Central venous pressure 8-12 mmHg

(b) Mean arterial pressure (MAP) $\geq$ 65 mmHg

(c) Urine output $\geq$ 0.5 mL.kg^{-1} h

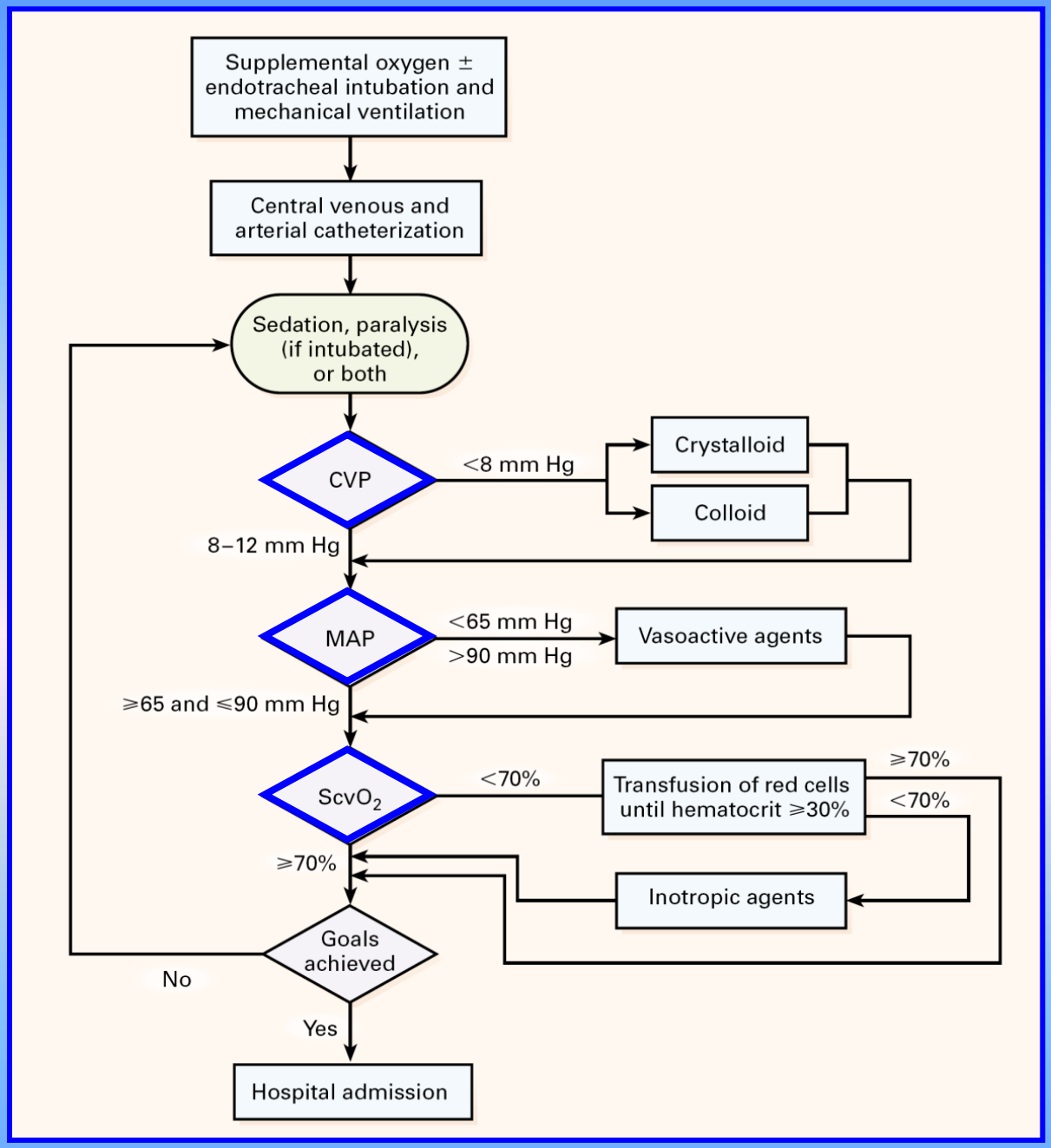
(d) Central venous or mixed venous oxygen saturation 70 or 65%, respectively (grade 1C)

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

N Engl J Med 2001;345:1368-77

Reduced mortality with EGDT (30.5%) *vs.* control (46.5%)



Rivers et al. *New Engl J Med* 2001

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

N Engl J Med 2001;345:1368-77

Caution

The patients of this study were not representative

of septic shock patients

typically encountered elsewhere

The patients of the EGDT study were not representative of septic shock patients typically encountered elsewhere

- Their hemodynamic profile denotes a **hypovolemic** shock rather than a **vasoplegic** shock

Variable and Treatment group	Base Line 0 hr
CVP mmHg	
Standard therapy	6.1 ± 7.7
EGDT	5.3 ± 9.3
MAP mmHg	
Standard therapy	76 ± 24
EGDT	74 ± 27
$ScvO_2$ %	
Standard therapy	49.2 ± 13.3
EGDT	48.6 ± 11.2

Hypovolemic shock

rather than

… **vasoplegic** shock

Rivers et al. *New Engl J Med* 2001

Variable and Treatment group	Base Line 0 hr	6 hrs after the start of therapy	
		Total fluids (mL)	
CVP mmHg			
Standard therapy	6.1 ± 7.7	11.8 ± 6.8	3499 ± 2438
EGDT	5.3 ± 9.3	13.8 ± 4.4	4981 ± 2984
		Any vasopressor (%)	
MAP mmHg			
Standard therapy	76 ± 24	81 ± 18	30.3
EGDT	74 ± 27	95 ± 19	27.4
$ScvO_2$ %			
Standard therapy	49.2 ± 13.3		
EGDT	48.6 ± 11.2		

Hypovolemic shock

rather than

… vasoplegic shock

Rivers et al. *New Engl J Med* 2001

The patients of the EGDT study are not representative of septic shock patients typically encountered elsewhere

- **Their hemodynamic profile denotes a hypovolemic shock rather than a vasoplegic shock**

- Their **low $ScvO_2$ (49%)** suggests **normal** O_2 **extraction** capacities …. **uncommon** in cases of severe sepsis

$ScvO_2$ is rather normal or high in cases of severe sepsis, … even in early sepsis

The patients of the EGDT study are not representative of septic shock patients typically encountered elsewhere

- **Their hemodynamic profile denotes a hypovolemic shock rather than a vasoplegic shock**

- Their **low $ScvO_2$** (**49%**) suggests **normal** O_2 **extraction** capacities …. **uncommon** in cases of severe sepsis

The patients of the EGDT study are not representative of septic shock patients typically encountered elsewhere

One must be cautious before applying the EGDT protocol to every patient with septic shock

Intensive Care Med (2013) 39:165–228

GUIDELINES

R. P. Dellinger
Mitchell M. Levy
Andrew Rhodes
Djillali Annane
Herwig Gerlach
Steven M. Opal
Jonathan E. Sevransky

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock, 2012

Initial resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis-induced hypoperfusion (defined as hypotension persisting after initial fluid challenge or blood lactate ≥ 4 mmol/L).

Goals during the first 6h of resuscitation:

(a) Central venous pressure 8-12 mmHg

(b) Mean arterial pressure (MAP) ≥ 65 mmHg

(c) Urine output ≥ 0.5 mL.kg^{-1} h

(d) Central venous or mixed venous oxygen saturation 70 or 65%, respectively (grade 1C)

It is **strange** that the **SSC** experts have **recommended** this **EGDT** protocol

One must be cautious before applying the EGDT protocol to every patient with septic shock

The EGDT targets are methodologically and **physiologically questionable**

Intensive Care Med (2013) 39:165–228

GUIDELINES

R. P. Dellinger
Mitchell M. Levy
Andrew Rhodes
Djillali Annane
Herwig Gerlach
Steven M. Opal
Jonathan E. Sevransky

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock, 2012

Initial resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis-induced hypoperfusion
r blood lactate ≥ 4 mmol/L).

Central venous pressure 8-12 mmHg

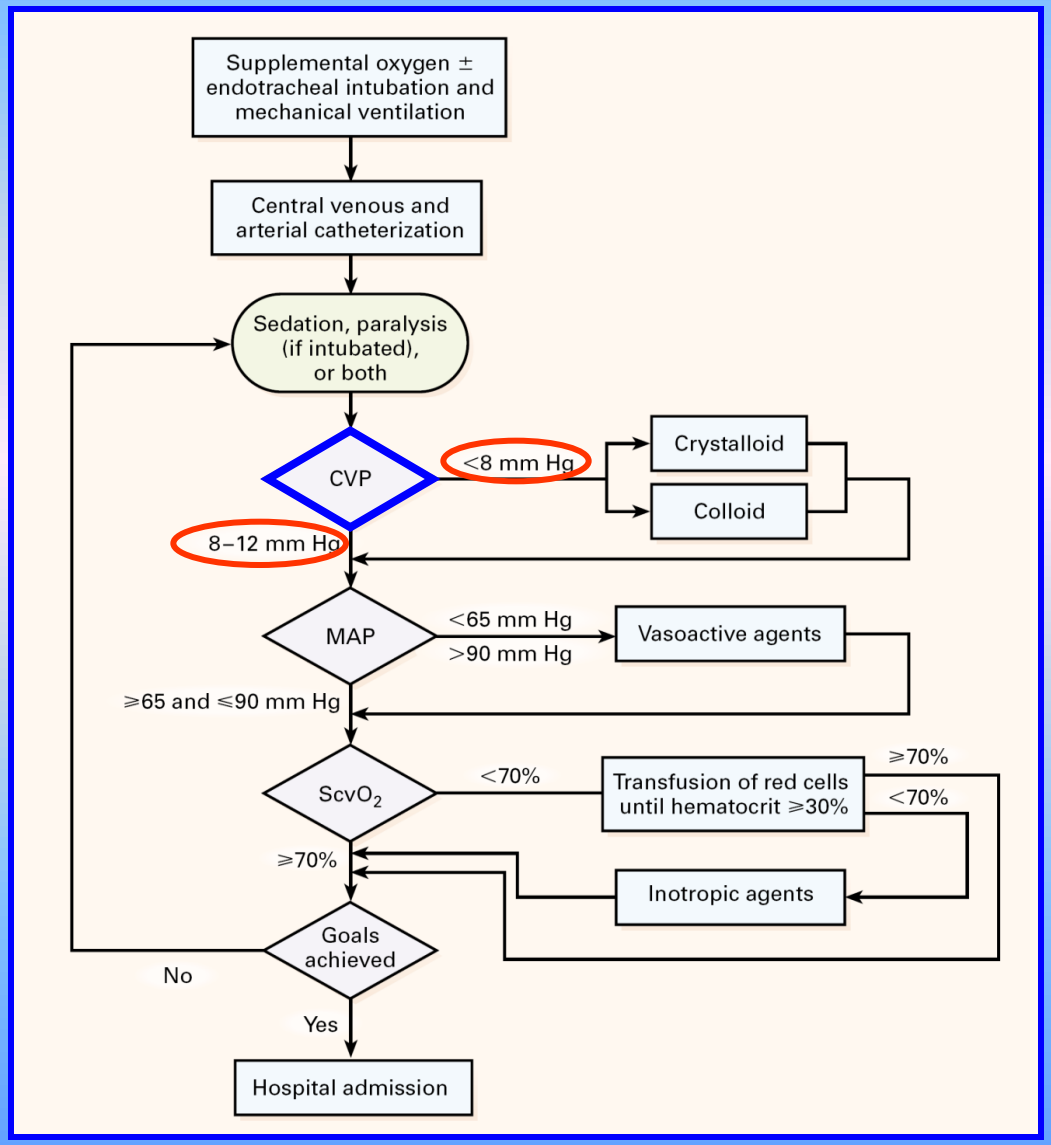
Mean arterial pressure (MAP) ≥ 65 mmHg

Central venous or mixed venous oxygen saturation 70 or 65%

12-15 mmHg if **MV**

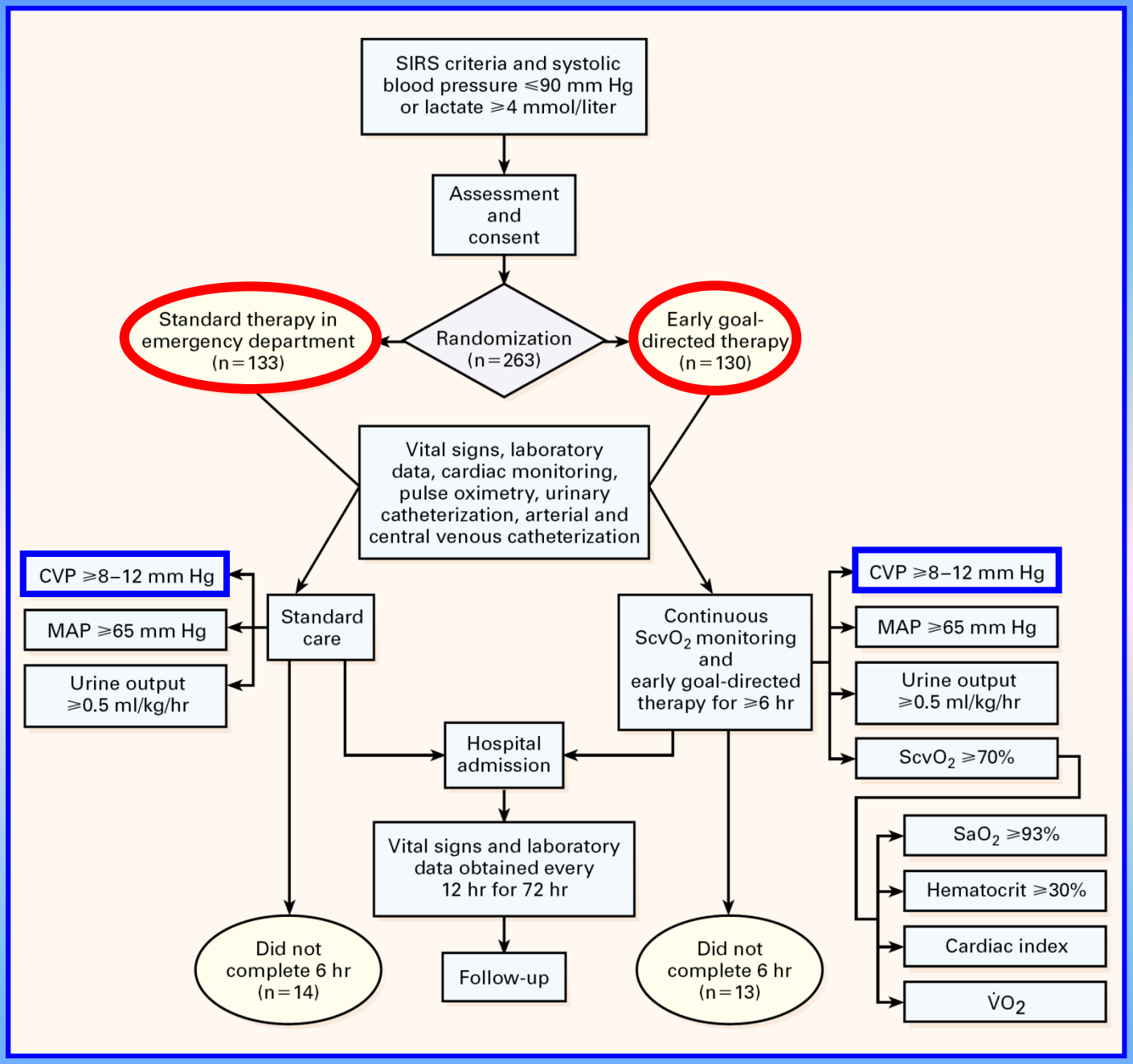
Why CVP?

Why 8 mmHg? Why 12 mmHg?



However:

- **CVP** and the **same cut-off** values in **both** study arms of the EGDT study



Rivers et al. *New Engl J Med* 2001

However:

- **CVP** and the **same cut-off** values in **both** study arms of the EGDT study
- **CVP**: a **not so simple** measurement, which raises many **problems**

  - problem of the anatomic « **zero** » level

  - which CVP value in cases of **PEEP** or **intrinsic PEEP**?

Nothing is **specified** in the **EGDT** study and the **SSC** guidelines!!!

However:

- **CVP** and the **same cut-off** values in **both** study arms of the EGDT study
- **CVP**: a **not so simple** measurement, which raises many **problems**
  - problem of the anatomic « **zero** » level
  - which CVP value in cases of **PEEP** or **intrinsic PEEP**?
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of lung **edema**

CVP 15 mmHg **PAOP 18** mmHg **Pcap ≈ 21** mmHg

Too high value
with high **risks** of **lung edema,**
especially in case of **altered** lung **permeability**

However:

- **CVP** and the **same cut-off** values in **both** study arms of the EGDT study
- **CVP**: a **not so simple** measurement, which raises many **problems**
  - problem of the anatomic « **zero** » level
  - which CVP value in cases of **PEEP** or **intrinsic PEEP**?
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of lung **edema**
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of **organ dysfunction**

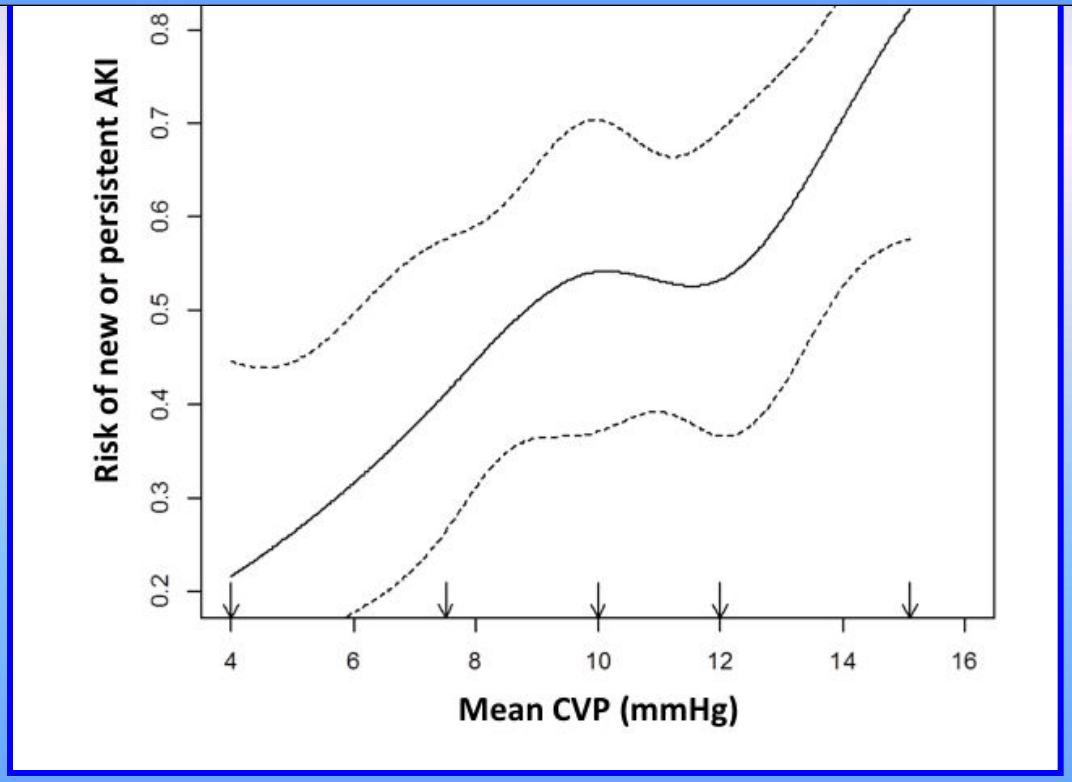
Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study

Matthieu Legrand[1,2*], Claire Dupuis[1], Christelle Simon[1], Etienne Gayat[1,3], Joaquim Mateo[1], Anne-Claire Lukaszewicz[1,2,4] and Didier Payen[1,2,4]

Critical Care 2013, **17**:R278

Association between **elevated CVP** and **AKI**

suggests a role of **venous congestion** in the development of AKI



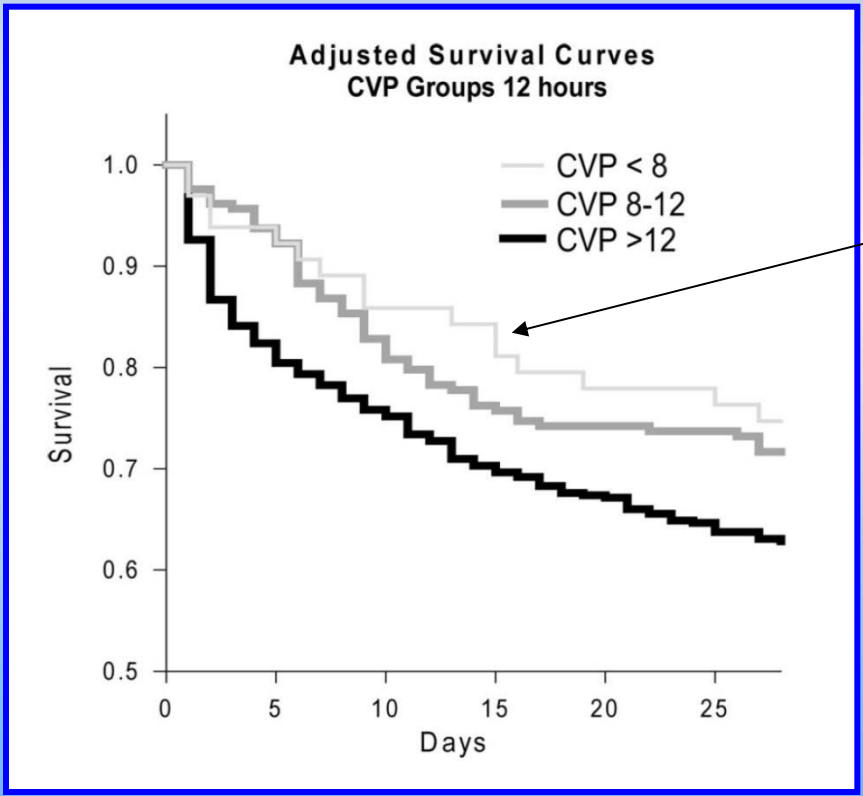
However:

- **CVP** and the **same cut-off** values in **both** study arms of the EGDT study
- **CVP**: a **not so simple** measurement, which raises many **problems**
  - problem of the anatomic « **zero** » level
  - which CVP value in cases of **PEEP** or **intrinsic PEEP**?
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of lung **edema**
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of **organ dysfunction**
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of **mortality**

Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality*

John H. Boyd, MD, FRCP(C); Jason Forbes, MD; Taka-aki Nakada, MD, PhD; Keith R. Walley, MD, FRCP(C); James A. Russell, MD, FRCP(C)

Crit Care Med 2011; 39:259–265



Pts with **CVP < 8 mmHg**
at 12 hrs
had the **highest survival**

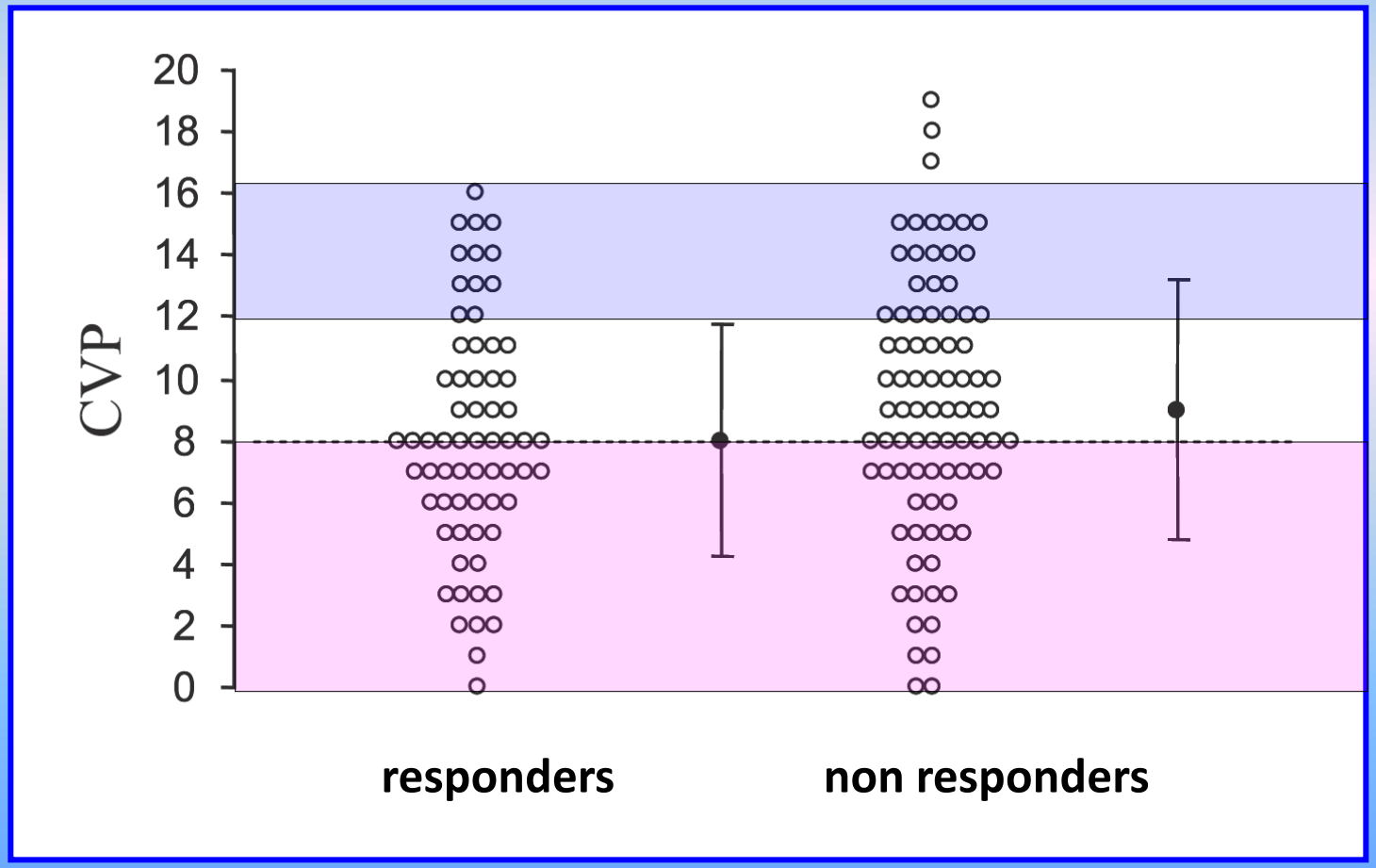
However:

- **CVP** and the **same cut-off** values in **both** study arms of the EGDT study
- **CVP**: a **not so simple** measurement, which raises many **problems**
  - problem of the anatomic « **zero** » level
  - which CVP value in cases of **PEEP** or **intrinsic PEEP**?
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of lung **edema**
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of **organ dysfunction**
- **CVP**: if MV, targeting **12-15** mmHg is at high risks of **mortality**
- **CVP**: **inappropriate** to assess **preload responsiveness**

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

David Osman, MD; Christophe Ridel, MD; Patrick Ray, MD; Xavier Monnet, MD, PhD; Nadia Anguel, MD; Christian Richard, MD; Jean-Louis Teboul, MD, PhD

Crit Care Med 2007; 35:64–68



Does the Central Venous Pressure Predict Fluid Responsiveness? An Updated Meta-Analysis and a Plea for Some Common Sense*

Paul E. Marik, MD, FCCM[1]; Rodrigo Cavallazzi, MD[2]

Crit Care Med 2013; 41:1774-81

1802 pts

43 Citations

- 22 ICU studies
- 20 operating room studies
- 1 human volunteer study

Summary AUC

0.56

Predicting fluid responsiveness with **CVP** is like

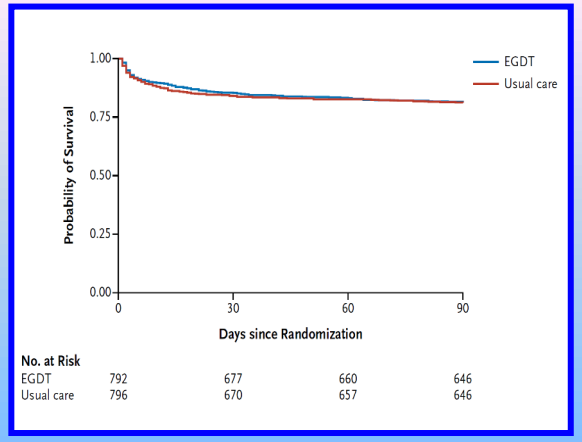
Three **multicenter randomized clinical trials**

Arise

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

N Engl J Med 2014;371:1496-506

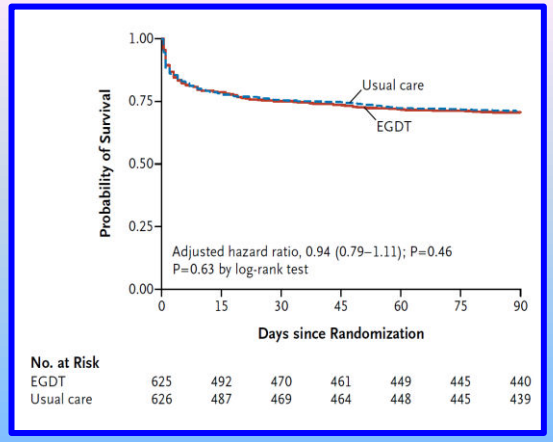


Promise

Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc., David A. Harrison, Ph.D., M. Zia Sadique, Ph.D., Richard D. Grieve, Ph.D., Rahi Jahan, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D., Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, D.M., and Kathryn M. Rowan, Ph.D., for the ProMISe Trial Investigators*

N Engl J Med 2015;372:1301-11

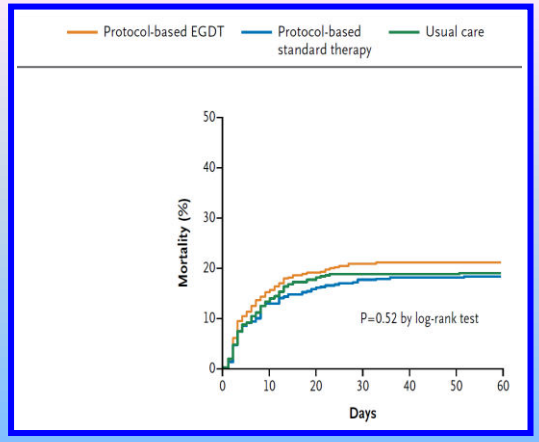


Process

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

N Engl J Med 2014;370:1683-93



No improved survival with **EGDT**

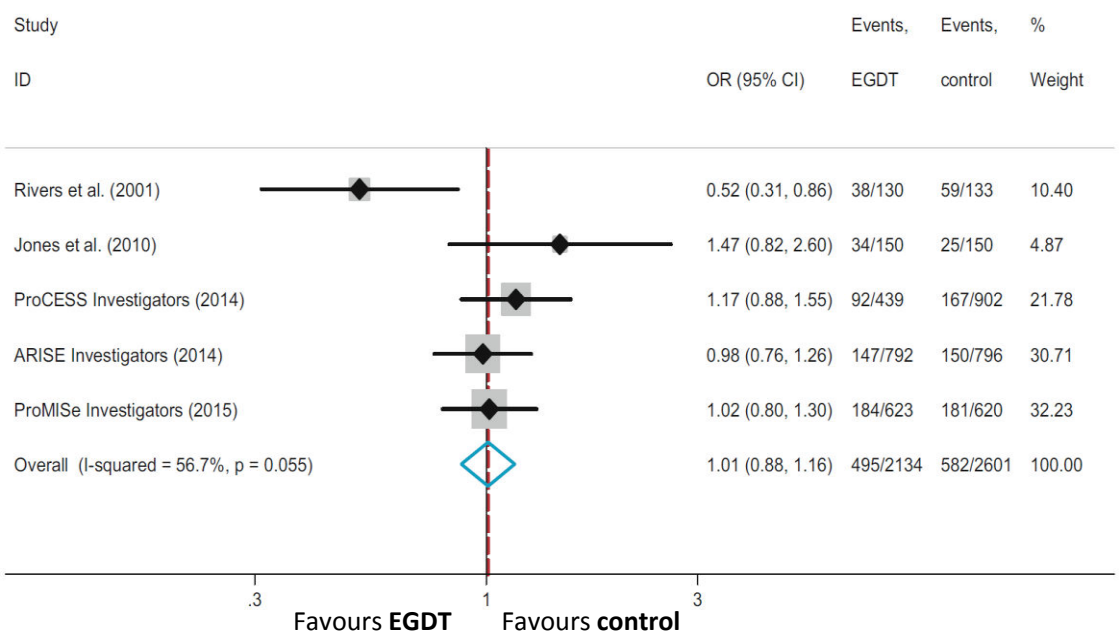
Intensive Care Med
DOI 10.1007/s00134-015-3822-1

SEVEN-DAY PROFILE PUBLICATION

D. C. Angus
A. E. Barnato
D. Bell
R. Bellomo
C.-R. Chong
T. J. Coats
A. Davies

A systematic review and meta-analysis of early goal-directed therapy for septic shock: the ARISE, ProCESS and ProMISe Investigators

Primary **mortality** outcome of each study



Intensive Care Med
DOI 10.1007/s00134-015-3822-1

SEVEN-DAY PROFILE PUBLICATION

D. C. Angus
A. E. Barnato
D. Bell
R. Bellomo
C.-R. Chong
T. J. Coats
A. Davies

A systematic review and meta-analysis of early goal-directed therapy for septic shock: the ARISE, ProCESS and ProMISe Investigators

- Our **meta-analysis does not** show **improved survival** for patients randomised to receive **EGDT** compared to usual or to less invasive alternative haemodynamic resuscitation protocols

- Our findings **do not support** the systematic **use** of **EGDT** in the management of all patients with septic shock or its **inclusion** in the **SSC guidelines**

TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION*:

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L

* *"Time of presentation" is defined as the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of severe sepsis or septic shock ascertained through chart review.*

Therapeutic goals

Restore as soon as possible tissue perfusion

1) Restore an adequate **mean arterial pressure**
2) Restore an adequate **cardiac output**

Hypovolemia → **Volume expansion**

Peripheral vascular depression

- Which **solutions?**
- Which **goals**

myocardial depression → **Inotropes ?**

Therapeutic goals

Restore as soon as possible tissue perfusion

1) Restore an adequate **mean arterial pressure**
2) Restore an adequate **cardiac output**

Hypovolemia

Volume expansion

Peripheral vascular depression

myocardial depression

- Which **solutions?**
- Which **goals**

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

G. Fluid Therapy of Severe Sepsis

1. **Crystalloids** as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D., Laurent Billot, M.Sc., Alan Cass, M.D., Ph.D., David Gattas, M.D., Parisa Glass, Ph.D., Jeffrey Lipman, M.D., Bette Liu, Ph.D., Colin McArthur, M.D., Shay McGuinness, M.D., Dorrilyn Rajbhandari, R.N., Colman B. Taylor, M.N.D., and Steven A.R. Webb, M.D., Ph.D., for the CHEST Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

N Engl J Med 2012;367:1901-11

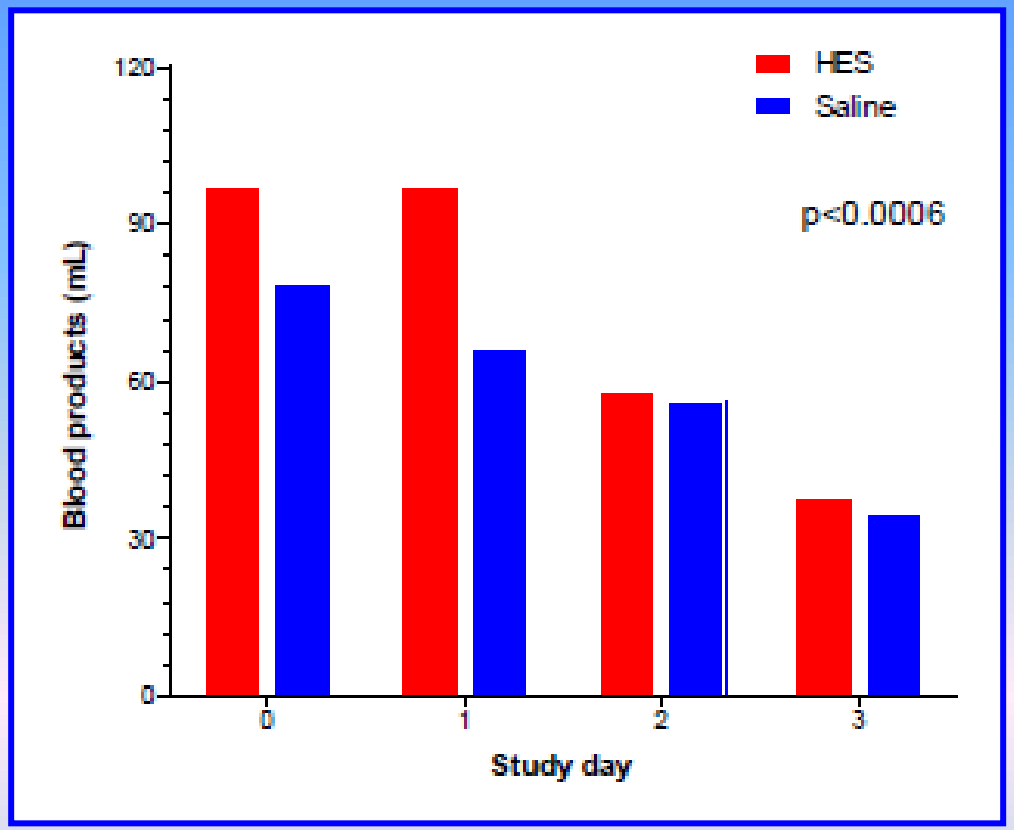
No difference
in terms of **mortality**

Table 2. Outcomes and Adverse Events.*

Variable	HES	Saline	Relative Risk (95% CI)	P Value
Outcome				
Primary outcome of death at day 90 — no./total no. (%)	597/3315 (18.0)	566/3336 (17.0)	1.06 (0.96 to 1.18)	0.26
Secondary outcomes — no./total no. (%)				
Renal outcomes				
RIFLE-R	1788/3309 (54.0)	1912/3335 (57.3)	0.94 (0.90 to 0.98)	0.007
				0.005
				0.12
				0.04

Increased use of **renal replacement therapy**
in the **HES** group

Myburgh et al NEJM 2012



Increased requirements of **blood transfusion**

in the **HES** group

Myburgh et al NEJM 2012

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.42 versus Ringer's Acetate in Severe Sepsis

Anders Perner, M.D., Ph.D., Nicolai Haase, M.D.,
Anne B. Guttormsen, M.D., Ph.D., Jyrki Tenhunen, M.D., Ph.D.,
Gudmundur Klemenzson, M.D., Anders Åneman, M.D., Ph.D.,
Kristian R. Madsen, M.D., Morten H. Møller, M.D., Ph.D., Jeanie M. Elkjær, M.D.,
Lone M. Poulsen, M.D., Asger Bendtsen, M.D., M.P.H., Robert Winding, M.D.,
Morten Steensen, M.D., Pawel Berezowicz, M.D., Ph.D., Peter Søe-Jensen, M.D.,
Morten Bestle, M.D., Ph.D., Kristian Strand, M.D., Ph.D., Jørgen Wiis, M.D.,
Jonathan O. White, M.D., Klaus J. Thornberg, M.D., Lars Quist, M.D.,
Jonas Nielsen, M.D., Ph.D., Lasse H. Andersen, M.D., Lars B. Holst, M.D.,
Katrin Thormar, M.D., Anne-Lene Kjældgaard, M.D., Maria L. Fabritius, M.D.,
Frederik Mondrup, M.D., Frank C. Pott, M.D., D.M.Sci., Thea P. Møller, M.D.,
Per Winkel, M.D., D.M.Sci., and Jørn Wetterslev, M.D., Ph.D.,
for the 6S Trial Group and the Scandinavian Critical Care Trials Group*

N Engl J Med 2012;367:124-34

Increased mortality in the **HES** group

Table 3. Primary and Secondary Outcomes.*

Outcome	HES 130/0.42 (N=398)	Ringer's Acetate (N=400)	Relative Risk (95% CI)	P Value
Primary outcome				
Dead or dependent on dialysis at day 90 — no. (%)	202 (51)	173 (43)	1.17 (1.01–1.36)	0.03
Dead at day 90 — no. (%)	201 (51)	172 (43)	1.17 (1.01–1.36)	0.03
Dependent on dialysis at day 90 — no. (%)	1 (0.25)	1 (0.25)	—	1.00
Secondary outcome measures				
Dead at day 28 — no. (%)	154 (39)	144 (36)	1.08 (0.90–1.28)	0.43
Severe bleeding — no. (%)†	38 (10)	25 (6)	1.52 (0.94–2.48)	0.09
Severe allergic reaction — no. (%)†	1 (0.25)	0	—	0.32
SOFA score at day 5 — median (interquartile range)	6 (2–11)	6 (0–10)	—	0.64
Use of renal-replacement therapy — no. (%)‡	87 (22)	65 (16)	1.35 (1.01–1.80)	0.04

Increased use of **renal replacement therapy** in the **HES** group

Perner et al. NEJM 2012

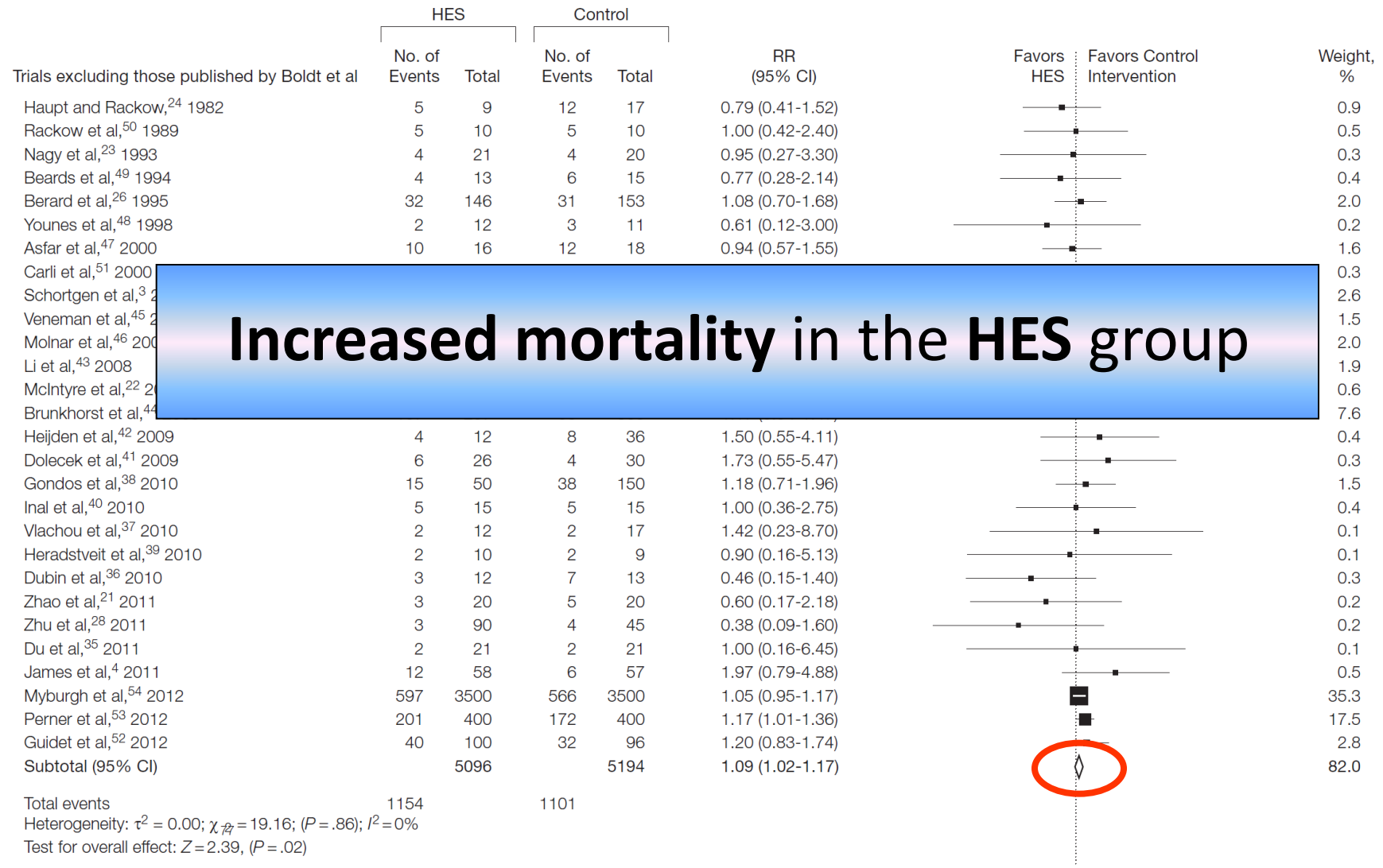
Association of Hydroxyethyl Starch Administration With Mortality and Acute Kidney Injury in Critically Ill Patients Requiring Volume Resuscitation

A Systematic Review and Meta-analysis

Ryan Zarychanski, MD, MSc
Ahmed M. Abou-Setta, MD, PhD
Alexis F. Turgeon, MD, MSc
Brett L. Houston, BSc
Lauralyn McIntyre, MD, MSc
John C. Marshall, MD
Dean A. Fergusson, PhD, MHA

JAMA. 2013;309(7):678-688

Figure 2. Mortality and Hydroxyethyl Starch



Increased mortality in the **HES** group

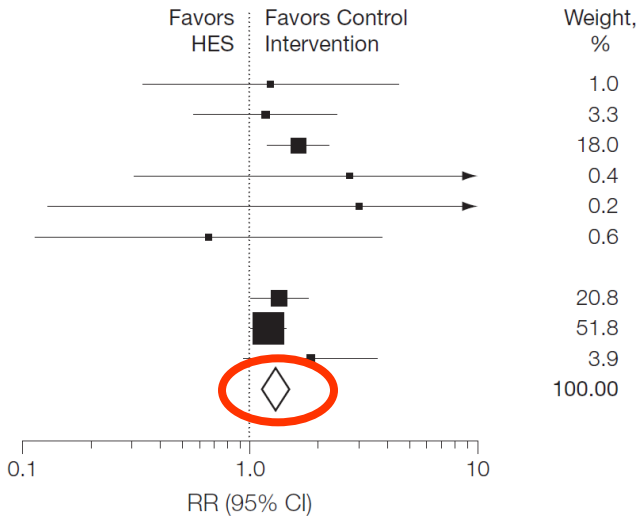
Zarychanski et al JAMA 2013

Figure 3. Renal Replacement Therapy and Hydroxyethyl Starch

Source	HES No. of Events	HES Total	Control No. of Events	Control Total	RR (95% CI)
Berard et al,[26] 1995	5	155	4	152	1.23 (0.34-4.48)
Schortgen et al,[3] 2001	13	65	11	64	1.16 (0.56-2.40)
Brunkhorst et al,[44] 2008	81	297	51	303	1.62 (1.19-2.21)
McIntyre et al,[22] 2008	3	21	1	19	2.71 (0.31-23.93)
Du et al,[35] 2011	1	21	0	21	3.00 (0.13-69.70)
James et al,[4] 2011	2	58	3	57	0.66 (0.11-3.78)
Viachou et al,[37] 2010	0	12	0	17	Not estimable
Perner al,[53] 2012	87	400	65	400	1.34 (1.00-1.79)
Myburgh et al,[54] 2012	235	3500	196	3500	1.20 (1.00-1.44)
Guidet et al,[52] 2012	21	100	11	96	1.83 (0.93-3.59)
Total (95% CI)		**4629**		**4629**	**1.32 (1.15-1.50)**
Total events	448		342		

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_8 = 5.07$; ($P = .75$); $I^2 = 0\%$

Test for overall effect: $Z = 4.08$, ($P < .001$)



Increased use of **renal replacement therapy** in the **HES** group

Zarychanski et al JAMA 2013

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

G. Fluid Therapy of Severe Sepsis

1. **Crystalloids** as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B)

2. **Against** the use of **hydroxyethyl starches** for fluid resuscitation of severe sepsis and septic shock (grade 1B)

Therapeutic goals

Restore as soon as possible tissue perfusion

1) Restore an adequate **mean arterial pressure**
2) Restore an adequate **cardiac output**

Hypovolemia

Volume expansion

Peripheral vascular depression

myocardial depression

- Which **solutions?**
- Which **goals?**

SSC « static » approach

« dynamic » approach

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

SSC « static » approach

« dynamic » approach

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

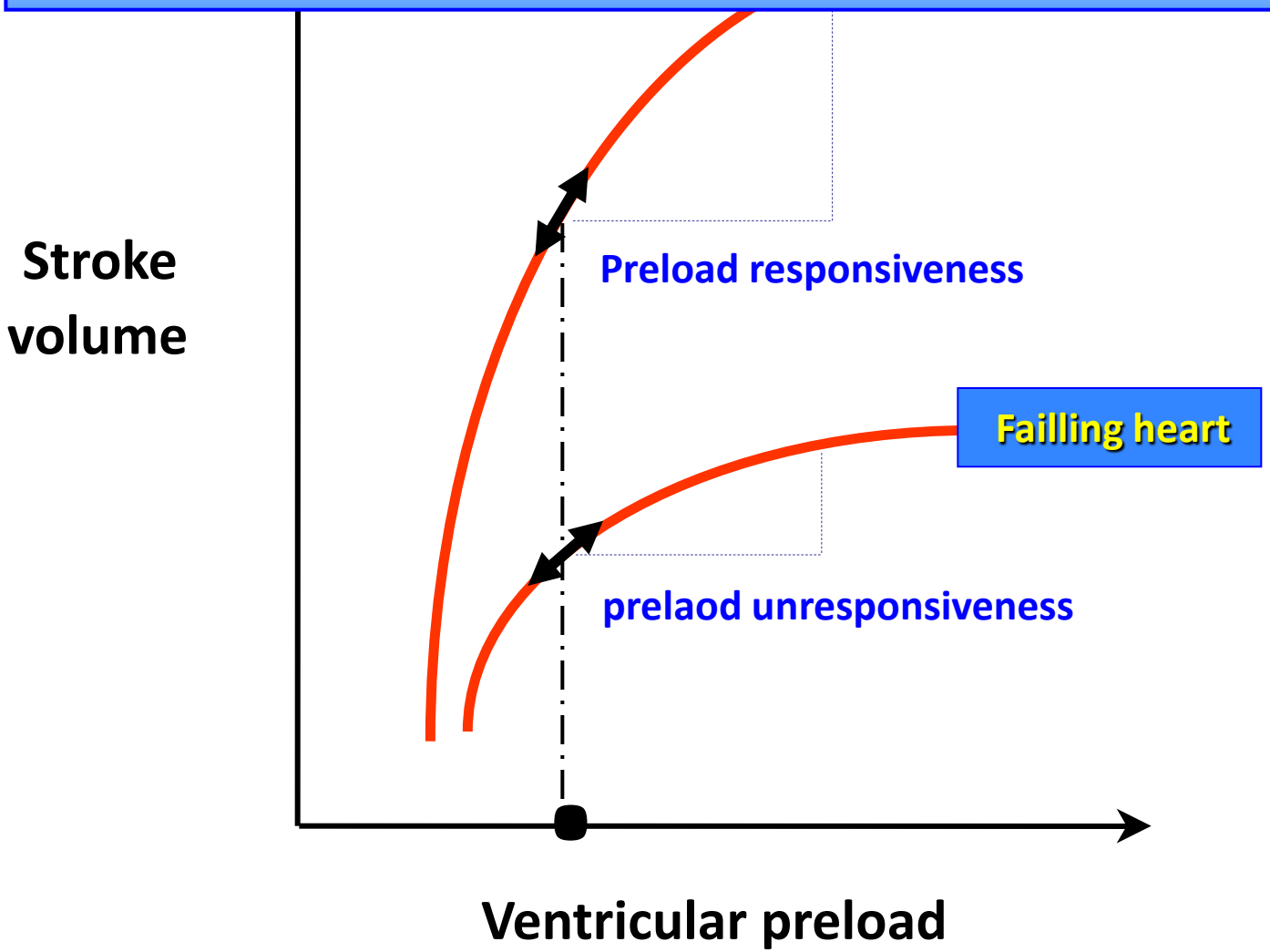
30. We recommend not to target any absolute value of ventricular filling pressure or volume

Level 1; QoE moderate (B)

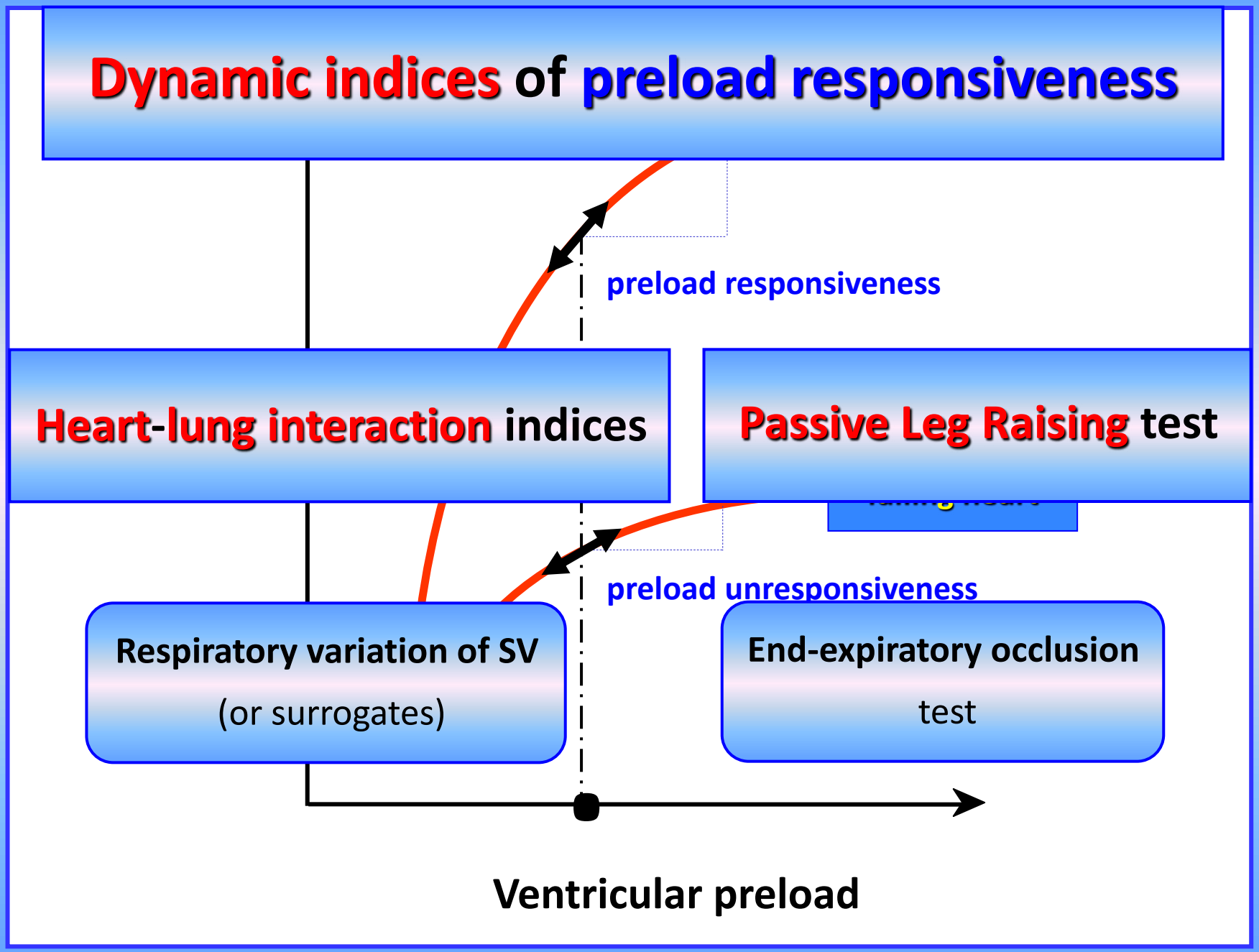
31. We recommend using dynamic over static variables to predict fluid responsiveness, when applicable

Level 1; QoE moderate (B)

Dynamic indices of preload responsiveness



Dynamic indices of preload responsiveness



Patient presenting at the ED for out-of-hospital septic shock

Given that **hypovolemia** is a **constant** feature of **out-of-hospital** septic shock, it is logical to infuse **fluids early** *without using any marker of fluid responsiveness*

- Be **smart** ….. but **not** too much
- **Don't waste** too much **time**

Patient presenting at the ED for out-of-hospital septic shock

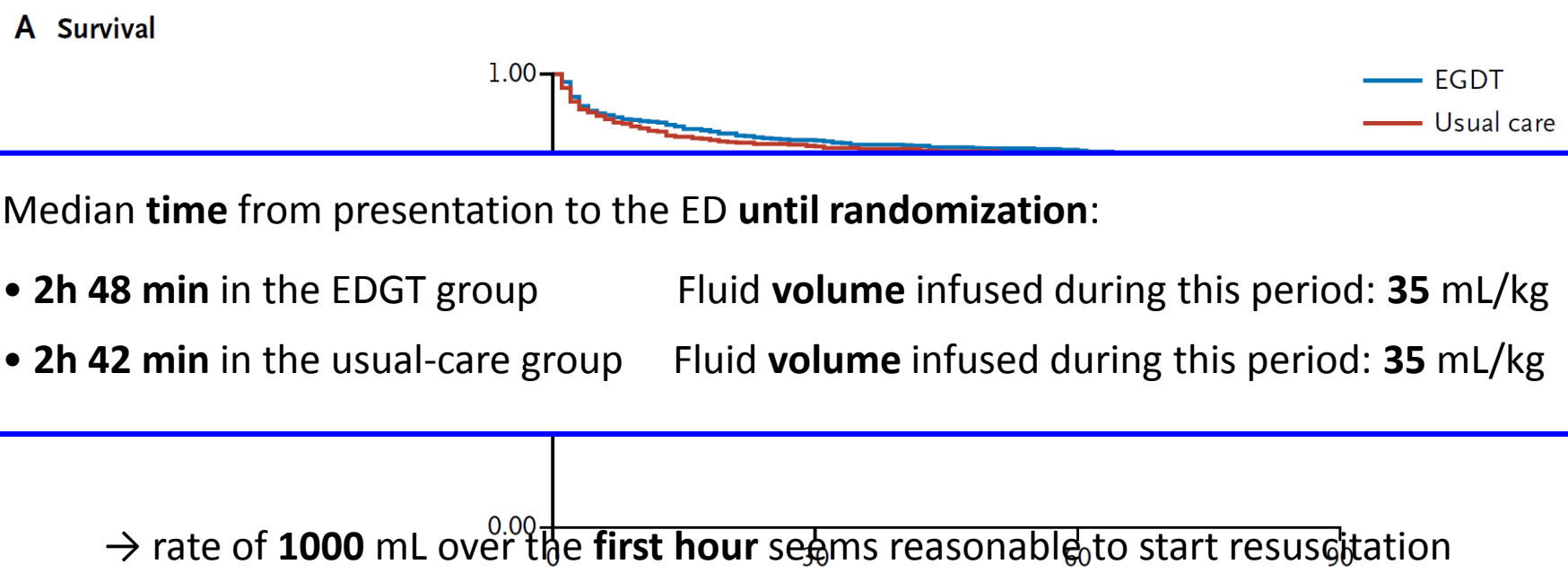
Given that **hypovolemia** is a **constant** feature of **out-of-hospital** septic shock, it is logical to infuse **fluids early** *without using any marker of fluid responsiveness*

→ rate of **1000** mL over the **first hour** seems reasonable to start resuscitation

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

N Engl J Med 2014;371:1496-506



Median **time** from presentation to the ED **until randomization**:

- **2h 48 min** in the EDGT group — Fluid **volume** infused during this period: **35** mL/kg
- **2h 42 min** in the usual-care group — Fluid **volume** infused during this period: **35** mL/kg

→ rate of **1000** mL over the **first hour** seems reasonable to start resuscitation

Patient presenting at the ED for out-of-hospital septic shock

Given that **hypovolemia** is a **constant** feature of **out-of-hospital** septic shock, it is logical to infuse **fluids early** *without using any marker of fluid responsiveness*

→ rate of **1000** mL over the **first hour** seems reasonable to start resuscitation

- **more** if:
  - **low pulse pressure** suggesting a low stroke volume
  - **mottling**, ↗ **capillary refill time**
  - **high** body **temperature**
  - **abdominal** origin of sepsis , evident **fluid losses**
- **less** if appearance of signs of **pulmonary edema** (dyspnea, ↘ SpO_2)

Importance of **clinical** monitoring at this **early** phase

Importance of **individualizing** the patient's care

One size *does not* fit all!!

Patient presenting at the ED for out-of-hospital septic shock

Given that **hypovolemia** is a **constant** feature of **out-of-hospital** septic shock, it is logical to infuse **fluids early** *without using any marker of fluid responsiveness*

→ rate of **1000** mL over the **first hour** seems reasonable to start resuscitation

- **more** if:
  - **low pulse pressure** suggesting a low stroke volume
  - **mottling**, ↗ **capillary refill time**
  - **high** body **temperature**
  - **abdominal** origin of sepsis, evident fluid losses
- **less** if appearance of signs of **pulmonary edema** (dyspnea, ↘ SpO_2)

After the **first hour** of resuscitation, if shock **persists**: assess **fluid responsiveness**

critical care review

Predicting Fluid Responsiveness in ICU Patients*

A Critical Analysis of the Evidence

Frédéric Michard, MD, PhD; and Jean-Louis Teboul, MD, PhD

CHEST 2002, 121:2000-8

Source	Patients	EC	Fluid	Volume	Speed of	Definition of	Rate of Response, %
Calvin et al[2]							71
Schneider et al[3]							72
Reuse et al[4]							63
Magder et al[5]							52
Diebel et al[6]							59
Diebel et al[7]							40
Wagner and Leatherman[8]							56
Tavernier et al[9]							60
Magder and Lag							45
Tousignant et al[11]							40
Michard et al[12]						15%	40
Feissel et al[13]	19	19	HES	8 mL/kg	30	ΔCO > 15%	53
Total	334	406					52

Only **52%** of patients **responded**

to **fluid** administration

in terms of **CO increase**

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

Crit Care Med 2006; 34:344–353

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

Patient presenting at the ED for out-of-hospital septic shock

Given that **hypovolemia** is a constant feature of **out-of-hospital** septic shock, it is logical to infuse **fluids** early *without using any marker of fluid responsiveness*

→ rate of **1000** mL over the **first hour** seems reasonable to start resuscitation

- **more** if:
  - **low pulse pressure** suggesting a low stroke volume
  - **mottling**, ↗ **capillary refill time**
  - **high** body **temperature**
  - **abdominal** origin of sepsis, evident fluid losses
- **less** if appearance of signs of **pulmonary edema** (dyspnea, ↘ SpO_2)

After the **first hour** of resuscitation, if shock **persists**: assess **fluid responsiveness**

- either **PLR** (**echo** or real-time **CO** monitor)
- or **PPV** or **SVV** (if applicable and if **arterial catheter** or **pulse contour CO** monitor)
- or **IVC diameter variation**, if applicable (**echo**)

If presence of **fluid responsiveness** consider **continuation of fluid administration**

If associated **ARDS** or **hypoxemic pneumonia**, also assess **extravascular lung water** and **pulmonary vascular permeability** (transpulmonary thermodilution), or PAOP (PAC)

If absence of fluid responsiveness or evident risks of pulmonary edema

Patient experiencing in-hospital septic shock

Given that **hypovolemia** and **fluid responsiveness** are **less frequent** in **in-hospital** septic shock, and given that **risks** of **fluid overload** might be present

→ rate of **500** mL over the **first 30 min** seems reasonable to start resuscitation

- **more** if:
  - **low pulse pressure** suggesting a low stroke volume
  - **mottling**, ↗ **capillary refill time**
  - **high** body **temperature**
  - **abdominal** origin of sepsis, evident **fluid losses**
- **less** if appearance of signs of **pulmonary edema** (dyspnea, ↘ SpO_2)

After the **first 30 min** of resuscitation, if shock **persists**: assess **fluid responsiveness**

- either **PLR** (**echo** or real-time **CO** monitor)
- or **PPV** or **SVV** (if applicable and if **arterial catheter** or **pulse contour CO** monitor)
- or **IVC diameter variation**, if applicable (**echo**)

If associated **ARDS** or **hypoxemic pneumonia**, also assess **extravascular lung water** and **pulmonary vascular permeability** (transpulmonary thermodilution), or PAOP (PAC)

If presence of **fluid responsiveness** consider **continuation of fluid administration** unless evident risks of pulmonary edema

Therapeutic goals

Restore as soon as possible tissue perfusion

1) Restore an adequate **mean arterial pressure**
2) Restore an adequate **cardiac output**

Hypovolemia

Peripheral vascular depression

myocardial depression

Vasopressors

Vasopressors and septic shock

1- Which first-line **agent**?

2- When to start?

3- Which therapeutic target?

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

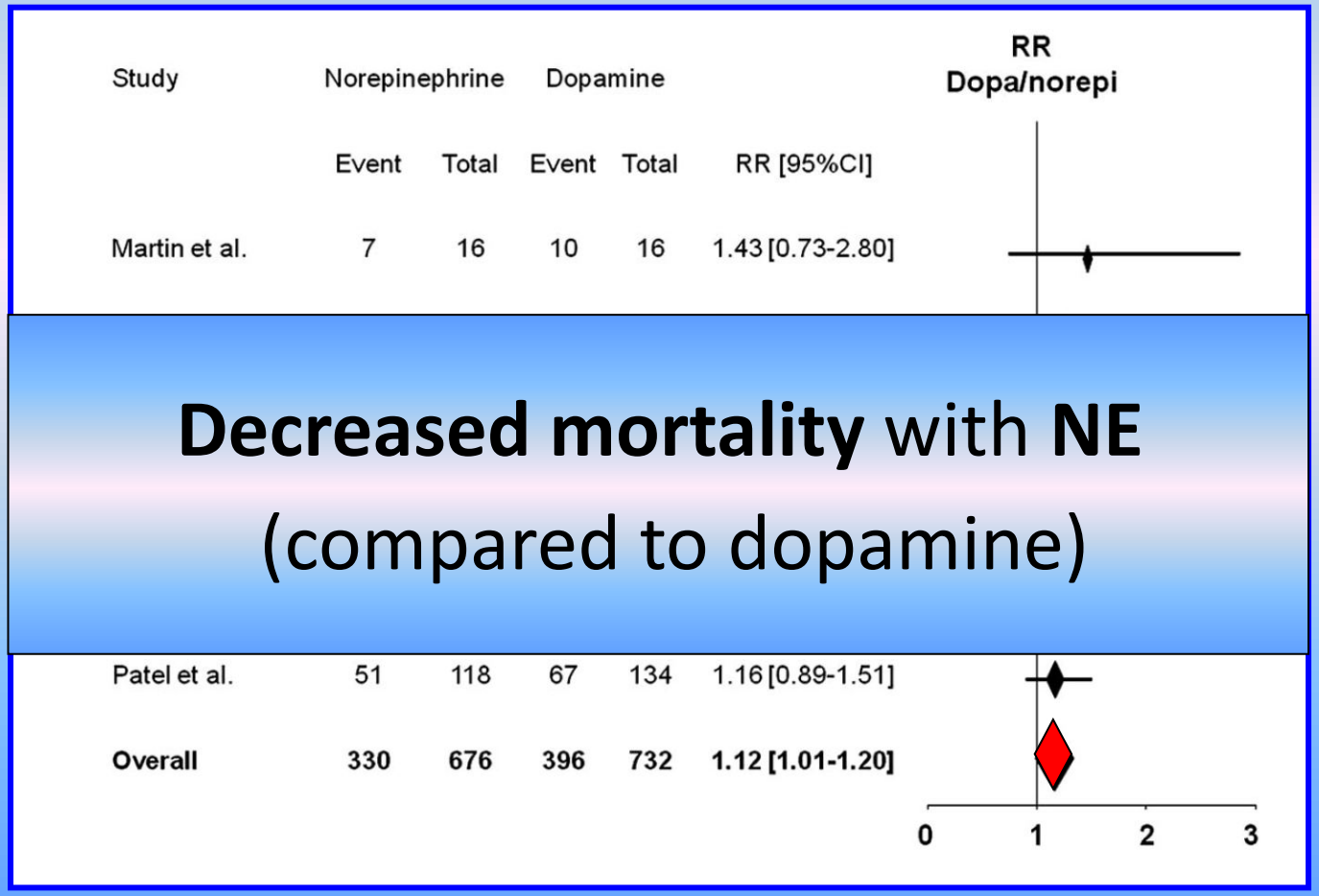
R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

- **Norepinephrine** as the **first choice** vasopressor (1B)

Dopamine versus norepinephrine in the treatment of septic shock: A meta-analysis*

Daniel De Backer, MD, PhD; Cesar Aldecoa, MD; Hassane Njimi, MSc, PhD; Jean-Louis Vincent, MD, PhD, FCCM

Crit Care Med 2012; 40:725–730



Decreased mortality with **NE**

(compared to dopamine)

Vasopressors and septic shock

1- Which first-line **agent**?

2- **When** to **start**?

3- Which therapeutic target?

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

Rationale. Vasopressor therapy is required to sustain life and maintain perfusion in the face of life-threatening hypotension, even when hypovolemia has not yet been resolved.

Adequate fluid resuscitation is a fundamental aspect of the hemodynamic management of patients with septic shock and should ideally be achieved before vasopressors and inotropes are used; however, using vasopressors early as an emergency measure in patients with severe shock is frequently necessary, as when diastolic blood pressure is too low.

Early administration of norepinephrine increases cardiac preload and cardiac output in septic patients with life-threatening hypotension

Olfa Hamzaoui, Jean-François Georger, Xavier Monnet, Hatem Ksouri, Julien Maizel, Christian Richard, Jean-Louis Teboul*

Critical Care 2010, **14**:R142

Norepinephrine increases cardiac preload and reduces preload dependency assessed by passive leg raising in septic shock patients*

Xavier Monnet, MD, PhD; Julien Jabot, MD; Julien Maizel, MD; Christian Richard, MD; Jean-Louis Teboul. MD. PhD

Crit Care Med 2011; 39:689–694

Early initiation of NE

- Increase in **cardiac preload**
- Increase in **CO** in **preload-dependent** patients
- Reduction of the degree of **preload-dependency**

… as **fluid** infusion does

How does **NE impact** the **venous circulation**?

by blood **redistribution**
from **unstressed** to **stressed** volume?

NE **increases CO**

through an **increase** in **Mean Systemic Pressure**

related to blood **redistribution**

from unstressed to stressed volume

This is a good news

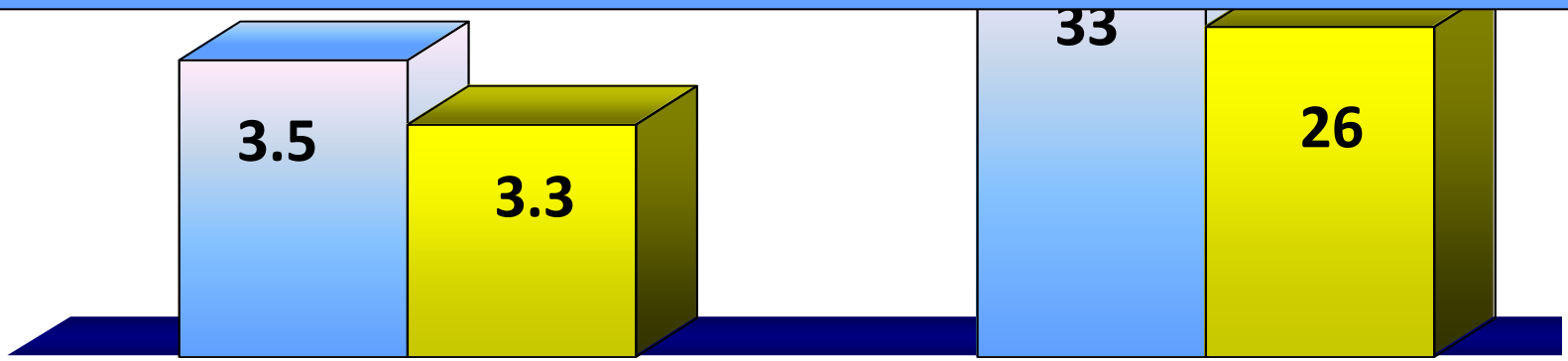
since **unstressed volume** is **abnormally increased**

during sepsis and further **overfilled** by fluid loading

• 16

NE

NE



Cardiac Index

L/min/m^2

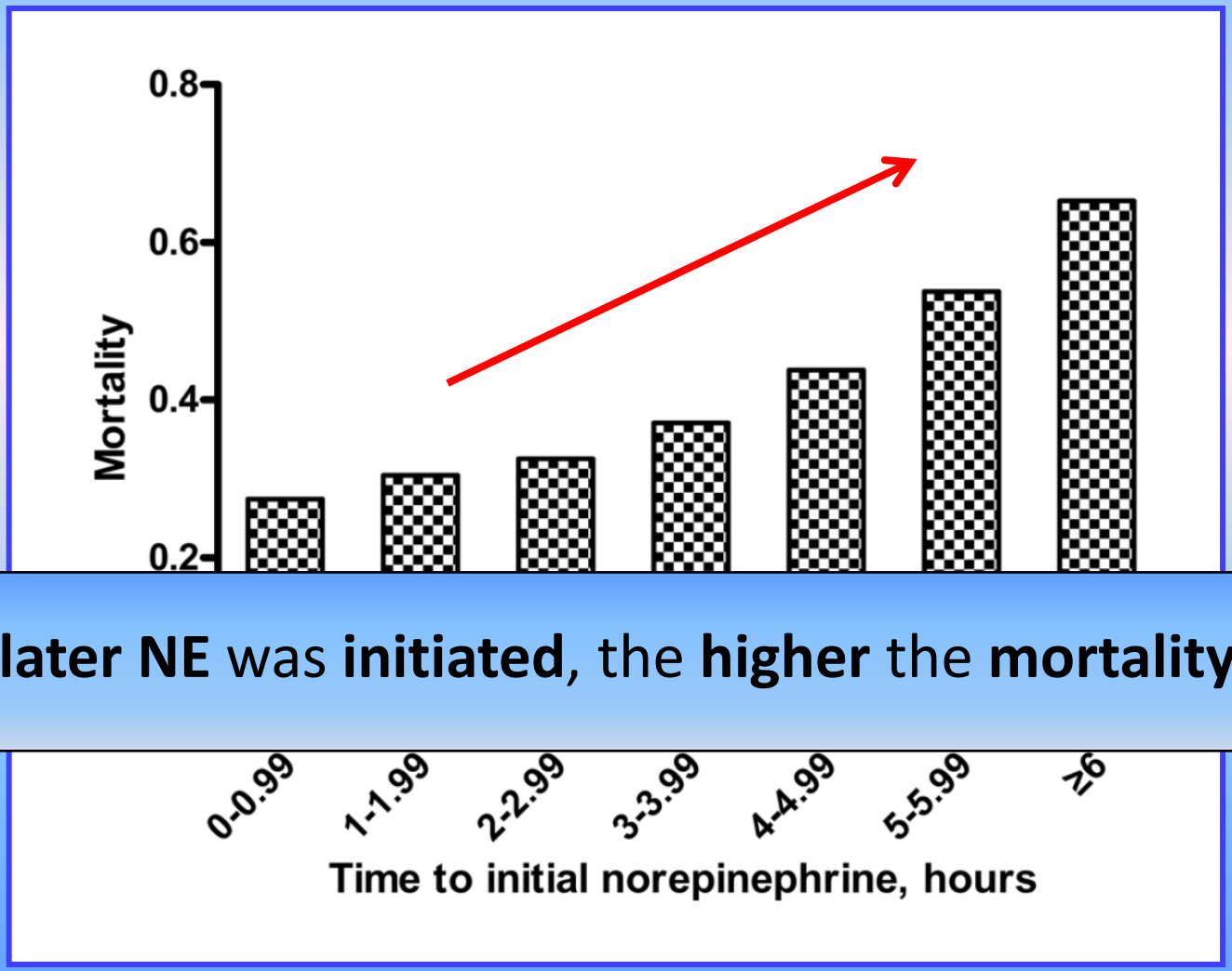
Mean Systemic Pressure

mmHg

Early versus delayed administration of norepinephrine in patients with septic shock

Xiaowu Bai, Wenkui Yu*, Wu Ji, Zhiliang Lin, Shanjun Tan, Kaipeng Duan, Yi Dong, Lin Xu and Ning Li*

Critical Care 2014, **18**:532



The **later NE** was **initiated**, the **higher** the **mortality** rate

Vasopressors and septic shock

1- Which first-line **agent**?

2- **When** to **start**?

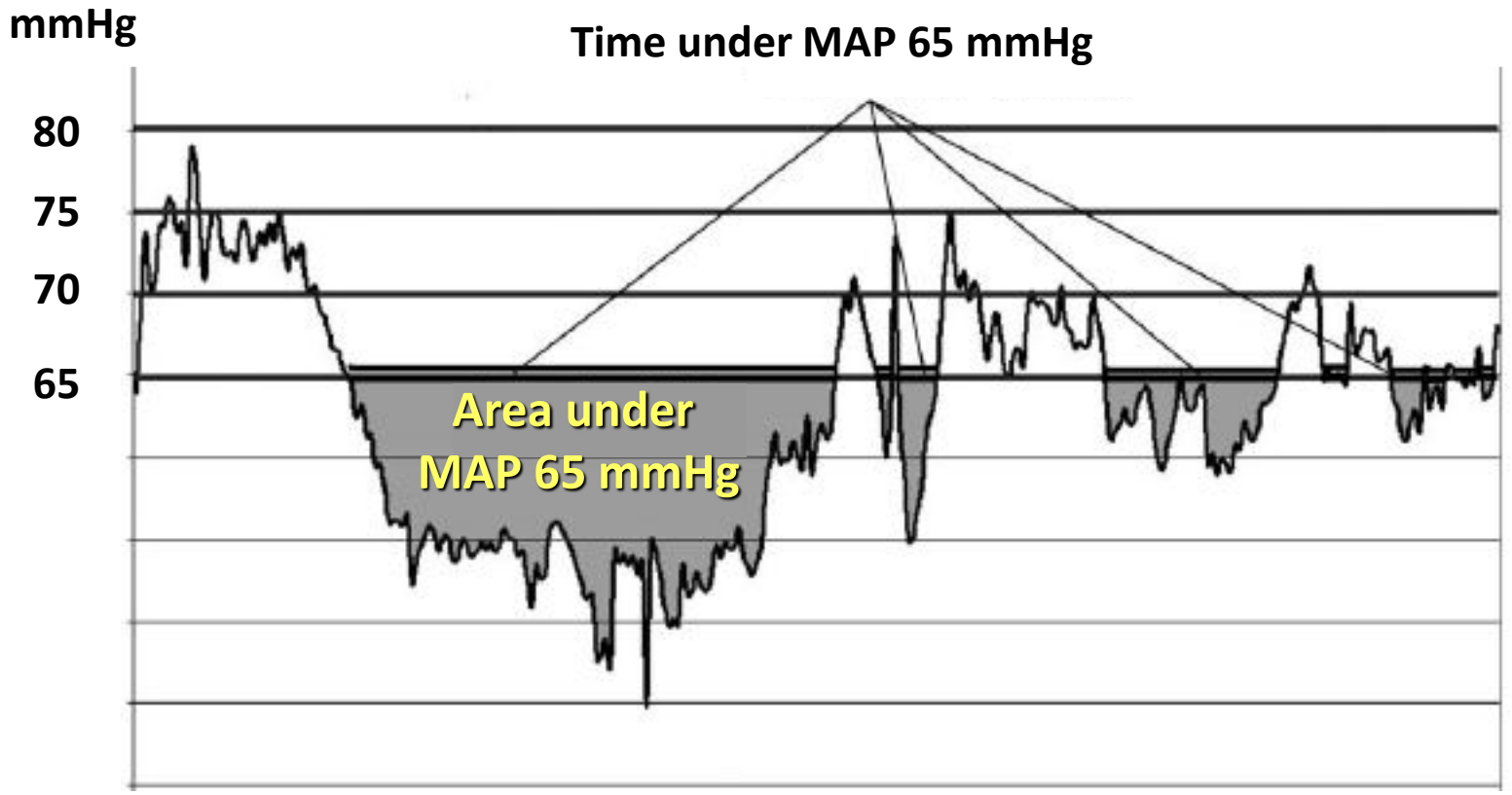
3- Which therapeutic **target**?

Intensive Care Med (2005) 31:1066–1071
DOI 10.1007/s00134-005-2688-z

ORIGINAL

Marjut Varpula
Minna Tallgren
Katri Saukkonen
Liisa-Maria Voipio-Pulkki
Ville Pettilä

Hemodynamic variables related to outcome in septic shock



Area under MAP 65 mmHg **Best predictor of 30-day mortality**

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

Vasopressors

- Vasopressor therapy initially to target a **MAP** of **65** mmHg (grade 1C)

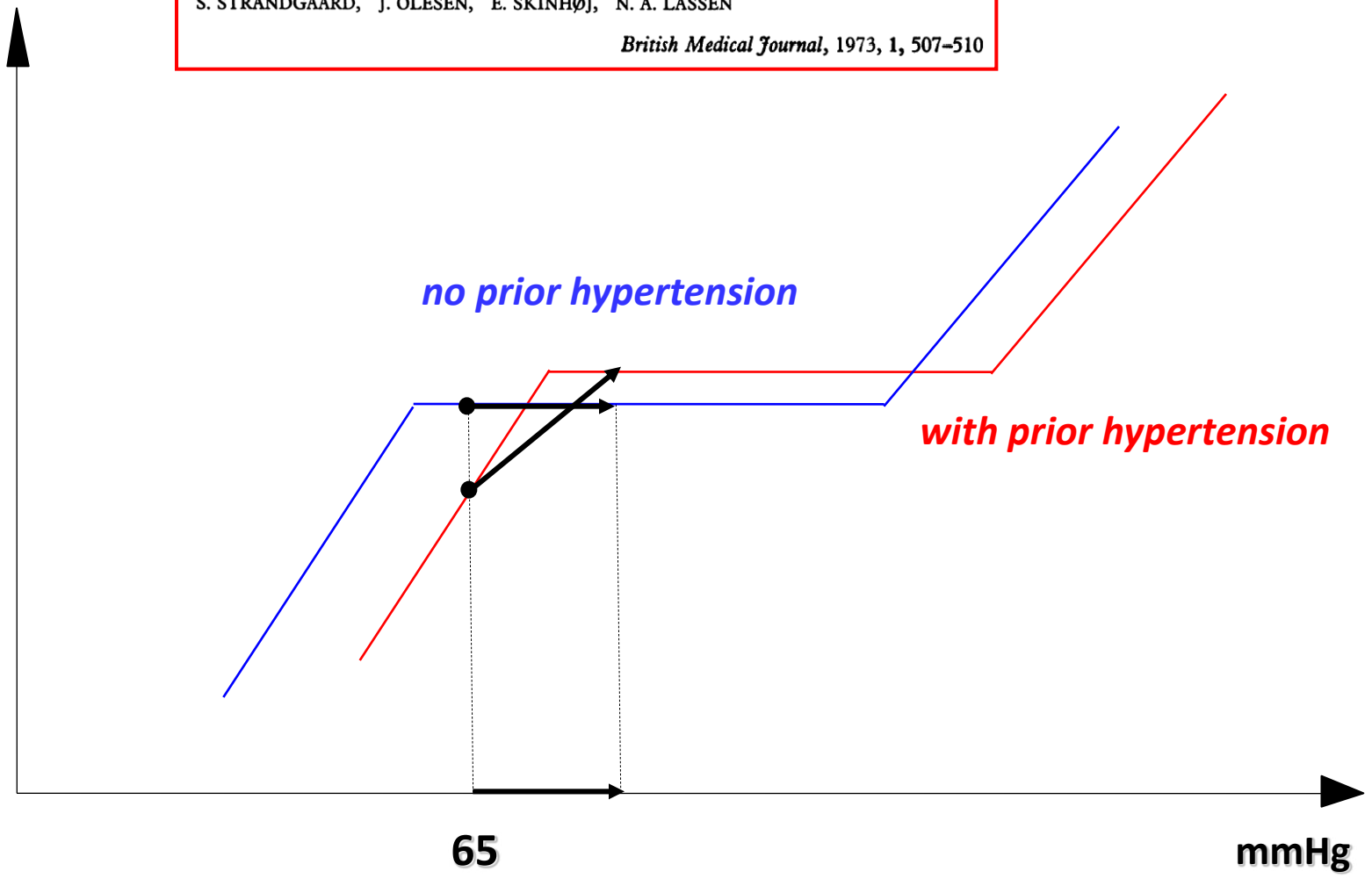
Probably **higher target value** if:

- **History of chronic hypertension**

Autoregulation of Brain Circulation in Severe Arterial Hypertension

S. STRANDGAARD, J. OLESEN, E. SKINHØJ, N. A. LASSEN

British Medical Journal, 1973, **1**, 507–510



The NEW ENGLAND JOURNAL of MEDICINE

BLISHED IN 1812 APRIL 24, 2014 VOL. 370 NO

80-85 mmHg

65-70 mmHg

High versus Low Blood-Pressure Target in Patients with Septic Shock

Pierre Asfar, M.D., Ph.D., Ferhat Meziani, M.D., Ph.D., Jean-François Hamel, M.D., Fabien Grelon, M.D., Bruno Megarbane, M.D., Ph.D., Nadia Anguel, M.D., Jean-Paul Mira, M.D., Ph.D., Pierre-François Dequin, M.D., Ph.D., Soizic Gergaud, M.D., Nicolas Weiss, M.D., Ph.D., François Legay, M.D., Yves Le Tulzo, M.D., Ph.D., Marie Conrad, M.D., René Robert, M.D., Ph.D., Frédéric Gonzalez, M.D., Christophe Guitton, M.D., Ph.D., Fabienne Tamion, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Pierre Guezennec, M.D., Thierry Van Der Linden, M.D., Antoine Vieillard-Baron, M.D., Ph.D., Eric Mariotte, M.D., Gaël Pradel, M.D., Olivier Lesieur, M.D., Jean-Damien Ricard, M.D., Ph.D., Fabien Hervé, M.D., Damien du Cheyron, M.D., Ph.D., Claude Guerin, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Jean-Louis Teboul, M.D., Ph.D., and Peter Radermacher, M.D., Ph.D.,

388 pts

388 pts

Table 2. Clinical Results, Primary and Secondary Outcomes, and Serious Adverse Events.

Variable	Low-Target Group (N = 388)	High-Target Group (N = 388)	P Value
Primary outcome: death at day 28 — no. (%)*	132 (34.0)	142 (36.6)	0.57
Secondary outcomes — no./total no. (%)			
Death at day 90†	164 (42.3)	170 (43.8)	0.74
Survival at day 28 without organ support‡	241 (62.1)	235 (60.6)	0.66
Doubling of plasma creatinine	161 (41.5)	150 (38.7)	0.42
No chronic hypertension	71/215 (33.0)	85/221 (38.5)	0.32
Chronic hypertension	90/173 (52.0)	65/167 (38.9)	0.02
Renal-replacement therapy from day 1 to day 7	139 (35.8)	130 (33.5)	0.50
No chronic hypertension	66/215 (30.7)	77/221 (34.8)	0.36
Chronic hypertension	73/173 (42.2)	53/167 (31.7)	0.046
Serious adverse events — no. (%)			
Any	69 (17.8)	74 (19.1)	0.64
Acute myocardial infarction§	2 (0.5)	7 (1.8)	0.18
Bleeding	42 (10.8)	31 (8.0)	0.22

Benefits in terms of **kidney function** with a **high MAP** target in patients with **chronic hypertension**

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

Target blood pressure in circulatory shock

- We recommend **individualizing** the target blood pressure during shock resuscitation.

  Recommendation Level 1: QoE moderate (B)

- We recommend to **initially target a MAP of ≥ 65 mmHg.**

  Recommendation: Level 1; QoE low (C)

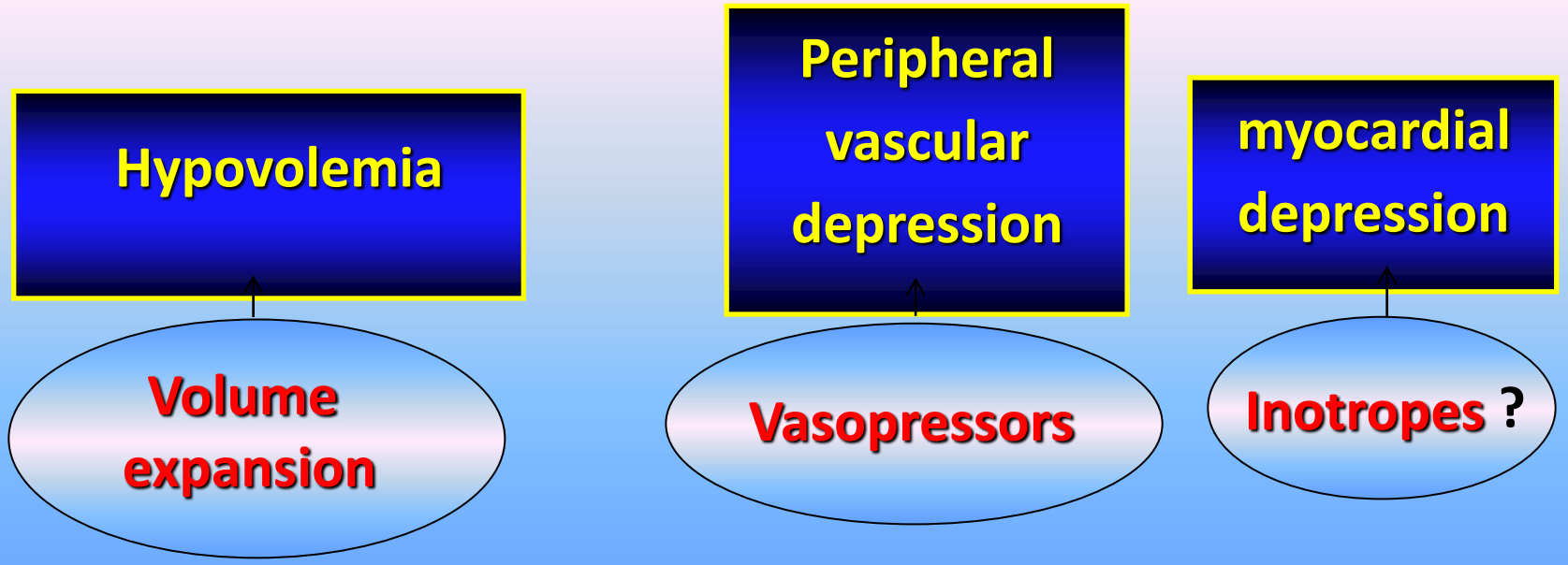
- We suggest a **higher MAP** in septic patients with a **history of hypertension.**

  Recommendation: Level 2; QoE low (B)

Therapeutic goals

Restore as soon as possible tissue perfusion

1) Restore an adequate **mean arterial pressure**
2) Restore an adequate **cardiac output**

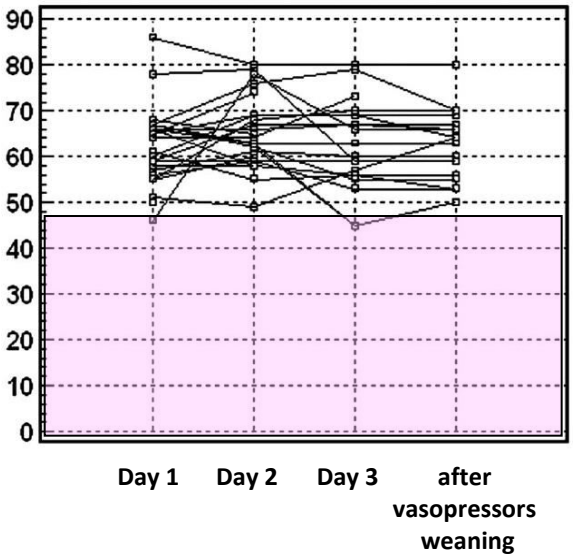


Actual incidence of global left ventricular hypokinesia in adult septic shock

Antoine Vieillard-Baron, MD; Vincent Caille, MD; Cyril Charron, MD; Guillaume Belliard, MD; Bernard Page, MD; François Jardin, MD

Crit Care Med 2008; 36:1701–1706

LV EF %



40% of pts

40% of pts

20% of pts

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 **recommend not to** give inotropes for **isolated impaired** cardiac function

  Level 1; QoE moderate (B)

- We **suggest** that **inotropes** should be added when the **altered** cardiac function is accompanied by a low or **inadequate CO** and signs of **tissue hypoperfusion persist** after preload optimization

  Level 2; QoE low (C)

Take-home messages

- **Pay attention to DAP**
  - **DAP: reflection of arterial tone**

    if DAP is low, the arterial tone is low

    - Helpful to rapidly diagnose **vasoplegic** shock
    - Helpful to urgently initiate a **vasopressor**

Take-home messages

- Pay attention to DAP
- **Pay attention to MAP**
  - **MAP: driving pressure for organ perfusion**
  - **MAP: therapeutic target**
    - ✓ **at least 65 mmHg**
    - ✓ **more if history of chronic hypertension**

Take-home messages

- Pay attention to DAP
- Pay attention to MAP
- **Pay attention** to **Pulse Pressure (PP)**
  - function of **cardiac stroke volume**
  - if PP is **low**, **stroke volume** should be **low**

3 pts (A, B, C) presenting at the ED

A	B	C
65 yo	**65** yo	**65** yo
HR: **100**/min	**HR**: **100**/min	**HR**: **100**/min
SAP: **80** mmHg	**SAP**: **80** mmHg	**SAP**: **50** mmHg
DAP: **60** mmHg	**DAP**: **30** mmHg	**DAP**: **30** mmHg
Low stroke volume + **normal arterial tone**	**Not low stroke volume** + **depressed arterial tone**	**Low stroke volume** + **depressed arterial tone**
hypovolemic or **cardiogenic shock**	**Septic shock** Vasopressor **urgently required**	**Septic shock** with pronounced **hypovolemia** (or **cardiac failure)**

Take-home messages

- Pay attention to DAP
- Pay attention to MAP
- Pay attention to Pulse Pressure (PP)
- **Hypovolemia** always present in **septic shock** but of **variable** degree
- After 500 to 1000 mL of **crystalloids**, assess **fluid responsiveness**

Early management

- Evaluate the **clinical** severity
- Perform **usual non-clinical** tests
- **Begin** as soon as possible:
  - ✓ a **hemodynamic** therapy
  - ✓ an **anti-infectious** therapy

Thank you