Choc septique – 20 ans d'avancées …
JRUR Marseille 2024

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Sebastien PREAU

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Conflits d'intérêts

☑ AOP

☑ Viatris

2016 – 3ème Conférence de Consensus

Society of Critical Care Medicine
The Intensive Care Professionals

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

Endorsing Societies: Academy of Medical Royal Colleges (UK); American Association of Critical Care Nurses; American Thoracic Society (endorsed August 25, 2015); Australian-New Zealand Intensive Care Society (ANZICS); Asia Pacific Association of Criti… Society of Critical C… Caribbean Intensive… Society of Critical C… Critical Care Medicir… Critical Care Society… Intensive Care Societ… Society; European Resuscitation Council; European Society of Clinical Microbiology and Infectious Diseases and its Study Group of Bloodstream Infections and Sepsis; European Society of Emergency Medicine; European Society of Intensive Care Medicine; European Society of Paediatric and Neonatal Intensive Care; German Sepsis Society; Indian Soci… Critical Care …ian Critical Care …ciation for Acute …ensive Care …ian Congress of …iedad Chilena de …edad Peruana de …, Shock Society; Sociedad Argentina de Terapia Intensiva; Society of Critical Care Medicine; Surgical Infection Society; World Federation of Pediatric Intensive and Critical Care Societies; World Federation of Critical Care Nurses; World Federation of Societies of Intensive and Critical Care Medicine.

World Health Organization

Sepsis

Dysfonction d'organe menaçant la vie induite par une reaction inappropriée de l'hôte à une infection

=> Critères diagnostiques …

=> Mortalité hospitalière >10%

Choc septique

Sous ensemble du sepsis avec des anomalies importantes de la circulation sanguine et du métabolisme

=> Critères diagnostiques …

=> Mortalité hospitalière >40%

Singer et al. 2016 JAMA

Le sepsis dans le monde …

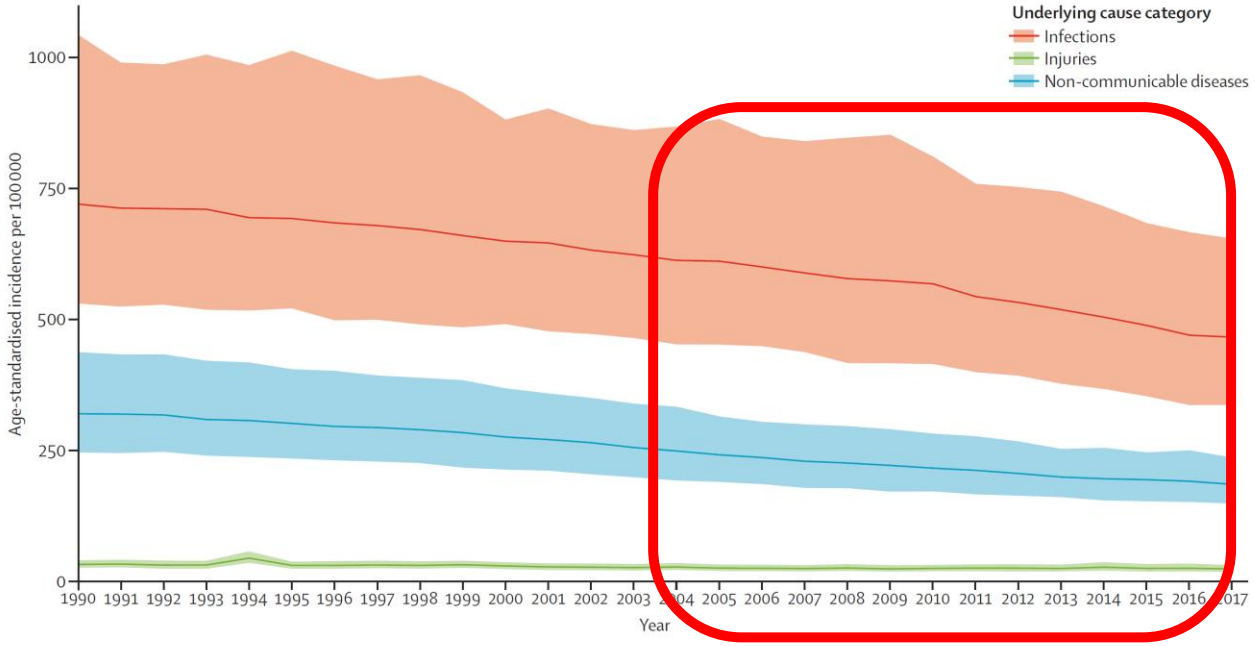
Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study

⇒ **Estimation de 49 million de cas / an**

⇒ **11 million (22%) de décès**

⇒ **Des complications à long terme !**

Rudd K. et al. 2020 Lancet



Incidence globale ↓ de 37% !

Mortalité globale ↓ de 53% !

Des Recommandations internationales …

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Check for updates

Evans L et al. 2021 ICM
SSC Guideline

Dellinger R et al. 2004 CCM
SSC Guideline

Des Recommandations internationales …

« Vraie Vie »

Et les >50% restant ?

Recommandations

Bien traiter les patients « moyens »

Des Recommandations internationales …

« Vraie Vie »

Et les >50% restant ?

EDITORIAL Open Access

Equilibrating SSC guidelines with individualized care

Vincent et al. 2021 Crit Care

EDITO

La prise en charge initiale …

BEST PRACTICE

4 Sepsis and septic shock are medical emergencies, and we **recommend** that treatment and resuscitation begin immediately.

LOW

10 For adults with sepsis or septic shock who require ICU admission, we **suggest** admitting the patients to the ICU within 6 hours.

*Evans L et al. 2021 ICM - **SSC Guideline***

Dellinger R et al. 2004 CCM - ***SSC Guideline***

OBJECTIFS

-

OUTILS

diagnostiques et Thérapeutiques

< 6H …

< 3H …

< 1H …

Les antibiotiques …

Evans L et al. 2021 ICM
*- **SSC Guideline 2021***

Antibiotic Timing

	Shock is present	Shock is absent
Sepsis is definite or probable	Administer antimicrobials **immediately**, ideally within 1 hour of recognition	
Sepsis is possible	Administer antimicrobials **immediately**, ideally within 1 hour of recognition	Rapid assessment* of infectious vs noninfectious causes of acute illness Administer antimicrobials **within 3 hours** if concern for infection persists

VERY LOW

21 For adults with sepsis or septic shock, we **suggest against** using double gram-negative coverage once the causative pathogen and the susceptibilities are known.

Les antibiotiques …

Quel délai ?

Délai <3h ou <1h
Intérêt pour des malades en
sepsis et choc septique

Ferrer et al. 2014 CCM
Pruinelli et al. 2018 CCM
Peltan et al. 2019 Chest
Seymour et al. 2017 NEJM
Liu et al. 2017 AJRCCM
Levy MM et al. 2018 AJRCCM

Délai « trop court »
=>
↗ Risque de
prescriptions abusives

Kanwar al. 2007 Chest
PAC avant après reco ABT<4h

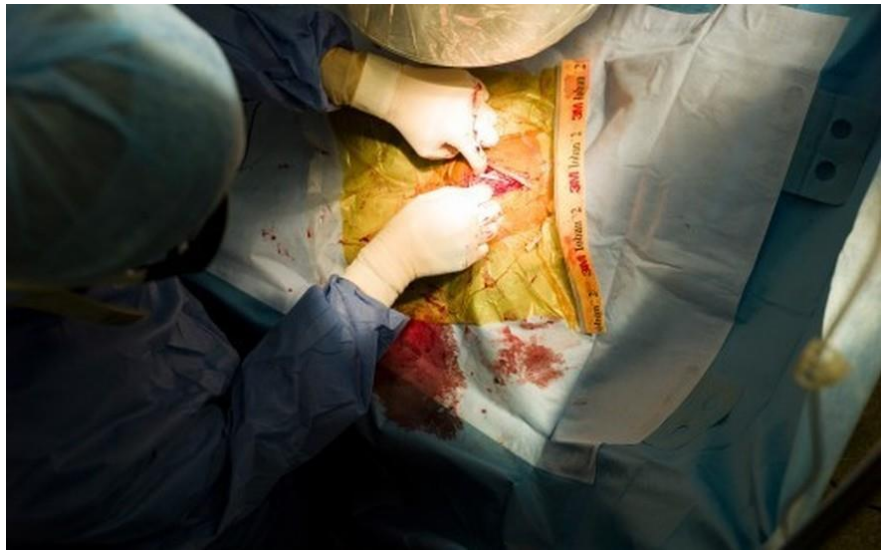
« Sepsis - ICU »
Erreur diagnostique 12 à 41%

Klouwenberg al. 2015 CritCare
Contou al. 2016 CritCare

<u>Préhospitalier</u>
Inutile …

(-) *Alam al. 2018 Lancet Resp Med*
PHANTASi

Le contrôle de l'infection …



Evans L et al. 2021 ICM
*- **SSC Guideline 2021***

BEST PRACTICE

27 For adults with sepsis or septic shock, we **recommend** rapidly identifying or excluding a specific anatomical diagnosis of infection that requires emergent source control and implementing any required source control intervention as soon as medically and logistically practical.

28 For adults with sepsis or septic shock, we **recommend** prompt removal of intravascular access devices that are a possible source of sepsis or septic shock after other vascular access has been established.

BEST PRACTICE

Quels objectifs de perfusion ?

Evans L et al. 2021 ICM
SSC Guideline 2021

!! MODERATE

9 For adults with septic shock on vasopressors, we **recommend** an initial target mean arterial pressure (MAP) of 65 mm Hg over higher MAP targets.

! LOW

7 For adults with sepsis or septic shock, we **suggest** guiding resuscitation to decrease serum lactate in patients with elevated lactate level, over not using serum lactate.

NEW !

! LOW

8 For adults with septic shock, we **suggest** using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion.

Objectif de PAM ≥ 65 mmHg …

Fondamentaux

Hypotension artérielle profonde et prolongée ⇔ Mortalité

Varpula et al. 2005 ICM (65 mmHg)

Dünser et al. 2009 ICM (60-75 mmHg)

Dunser et al. 2009 CritCare

Vincent et al. 2018 AIC

Maheshwari et al. 2018 ICM

Schuurmans et al. 2024 ICM

Seuil optimal variable !
60-85 mmHg

Incertitudes

Un objectif de perfusion ?

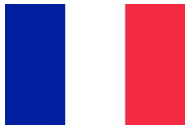
Quel(s) seuil(s) ?

*Asfar et al. 2014 NEJM - **SEPSIS-PAM***
N=776 65±14 ans

*Lamontagne et al. 2016 ICM - **OVATION***
N=118 64±13 ans

*Lamontagne et al. 2020 JAMA - **65***
N=2600 >65 ans (75±7 ans)

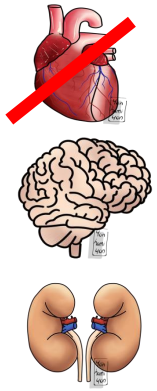
Objectifs de PAM : *RCTs …*



PAM 70-80 mmHg → **PAM 80-90 mmHg**

Asfar et al. 2014 NEJM - *SEPSIS-PAM*
N=776 65±14 ans
Choc septique => NAD 5jours

Pas de différence de mortalité J28
↑ TDR cardiaques ?
↑ éveil en réanimation ?
Bénéfique chez les HTA … sous ARA2 ?

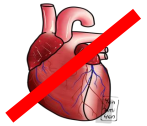


Jouan et al. 2019 AIC Demiselle et al. 2021 CCM
71±11 ans

PAM 65-75 mmHg → **PAM 75-85 mmHg**

Lamontagne et al. 2016 ICM - *OVATION*
N=118 64±13 ans
Choc distributif (70% sepsis)
Vasoconstricteurs ICU ≈2jrs

Etude de faisabilité
↑ TDR cardiaques ?
↑ mortalité chez les >75 ans ?



PAM 65-70 mmHg → **PAM 70-80 mmHg**

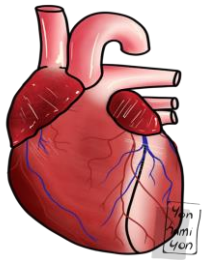
Lamontagne et al. 2020 JAMA - *65*
N=2600 **>65 ans (75±7 ans)**
Choc distributif (78% sepsis)
Vasoconstricteurs ICU ≈4jrs

Tendance à ↑ de mortalité J90
Surtout délétère chez les HTA ?

PAM => Perfusion d'organes ?

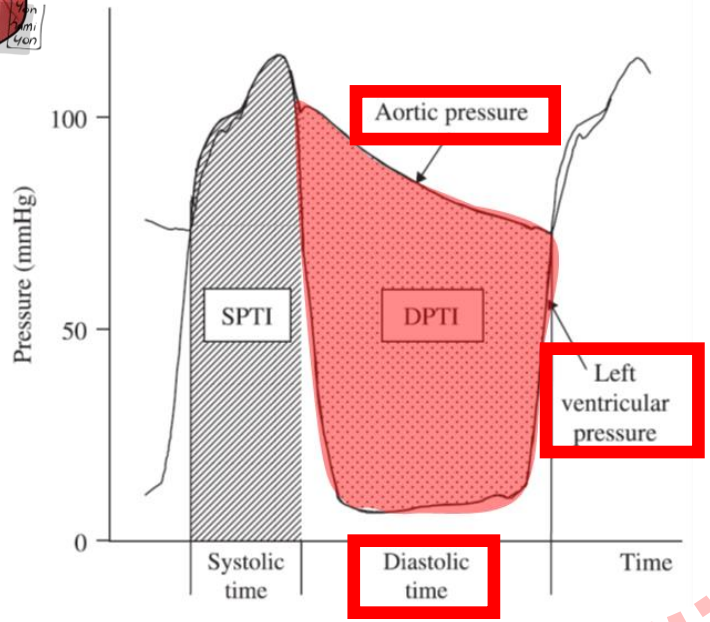
Le débit cardiaque !
Geri et al. 2019 ICM

La PAD

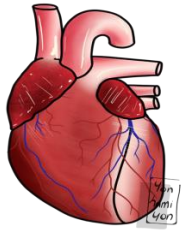


Hamzaoui et Teboul
2018 J of CritCare

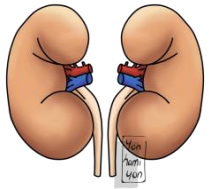
Chemla et al. 2009
Clin Exp Pharmacol Physiol



La pression extravasculaire



Pression thoracique
Zerbib, Slama et al.
2024 AJRCCM

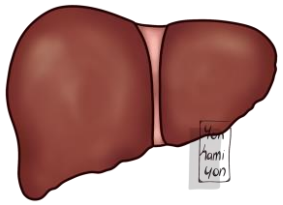


Pression intra-abdominale
Rogers, Garcia
2017 Chest ***REVIEW***

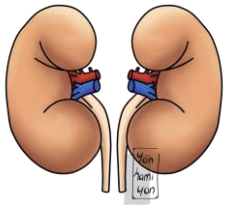
Pression intra-crânienne
Stoccetti, Maas
2014 NEJM ***REVIEW***

La PVC

Panwar et al. 2020 AJRCCM



Herion et al.
1994 J of Hepatol



Geri et al.
2021 JCritCare

Legrand et al.
2013 CritCare

Hussain-Syed et al.
2021 ESC-Heart Failure
REVIEW

Objectif lactatémie normale …

Fondamentaux

Lactatémie normale ≈ 1 mmol/L

Lactate ≠ toxique

Marqueur d'hypoperfusion …

Levy et al. 2005 Lancet

Mégarbane et al. 2010 Clin Toxicol

Hyperlactatémie ⇔ Mortalité

Nichol et al. 2010 Crit Care

Singer et al. 2016 JAMA

Shankar-Hari et al. 2016 JAMA
>1 mmol/L

Wacharasint et al. 2012 Shock
>1,4 mmol/L

Ryoo et al. 2018 CCM
Après réanimation initiale

Cinétique de la lactatémie ⇔ Mortalité

Vincent et al. 2016 CritCare ***REVIEW***

Ryoo et al. 2018 CCM

Nguyen et al. 2004 CCM

Bakker et al. 1996 Am J Surg

Incertitudes

Un objectif de perfusion ?

Cinétique vs Valeur Absolue ?

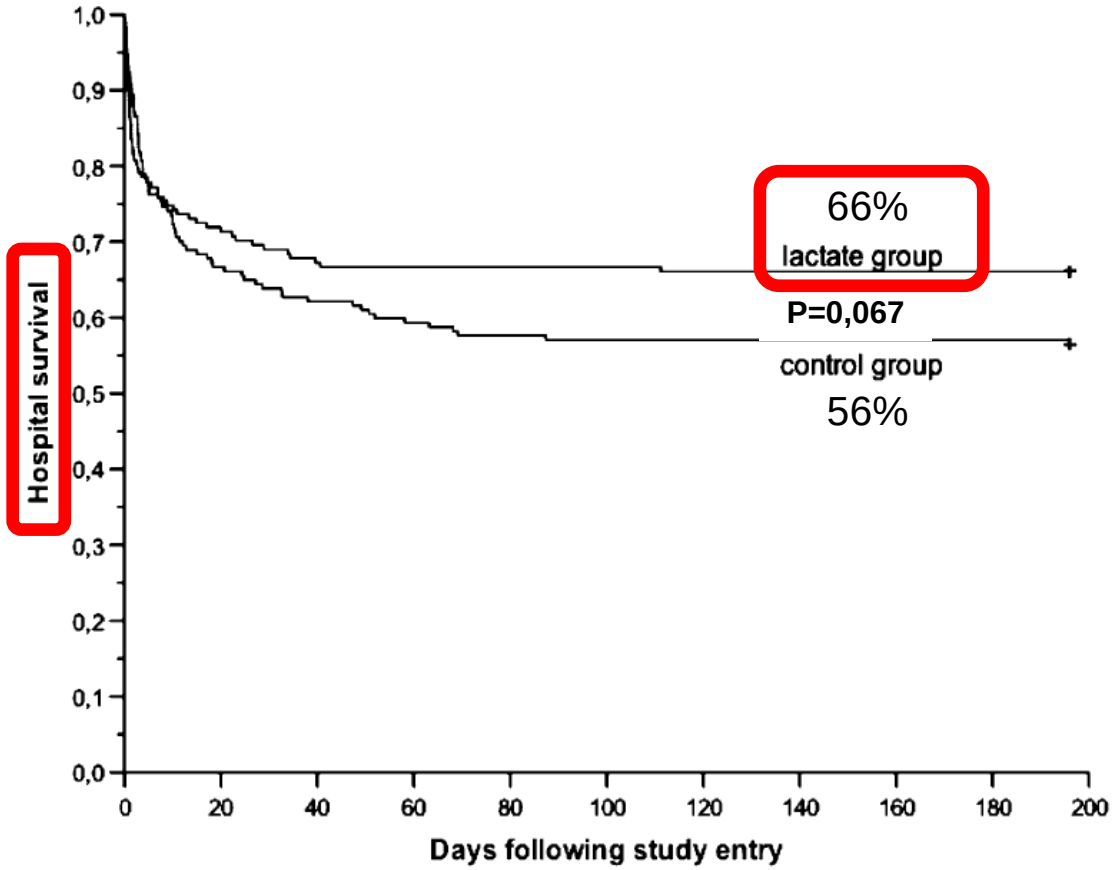
(+ns) *Jones et al. 2010 JAMA* ***EMShockNet***

Puskarich et al. 2011 Acad Emerg Med

(+) *Jansen et al. 2011 AJRCCM* ***RCT***

Early Lactate-Guided Therapy in Intensive Care Unit Patients

Jansen et al.
2010 AJRCCM



Après ajustement / facteurs de risque prédéfinis de mortalité

HR 0,61 (IC 95% 0,43 – 0,87 ; p=0,006)

RCT multicentrique Hollande
348 patients Réanimation
2006 - 2008

Inclusion
ICU
Lactate≥3mmol/L

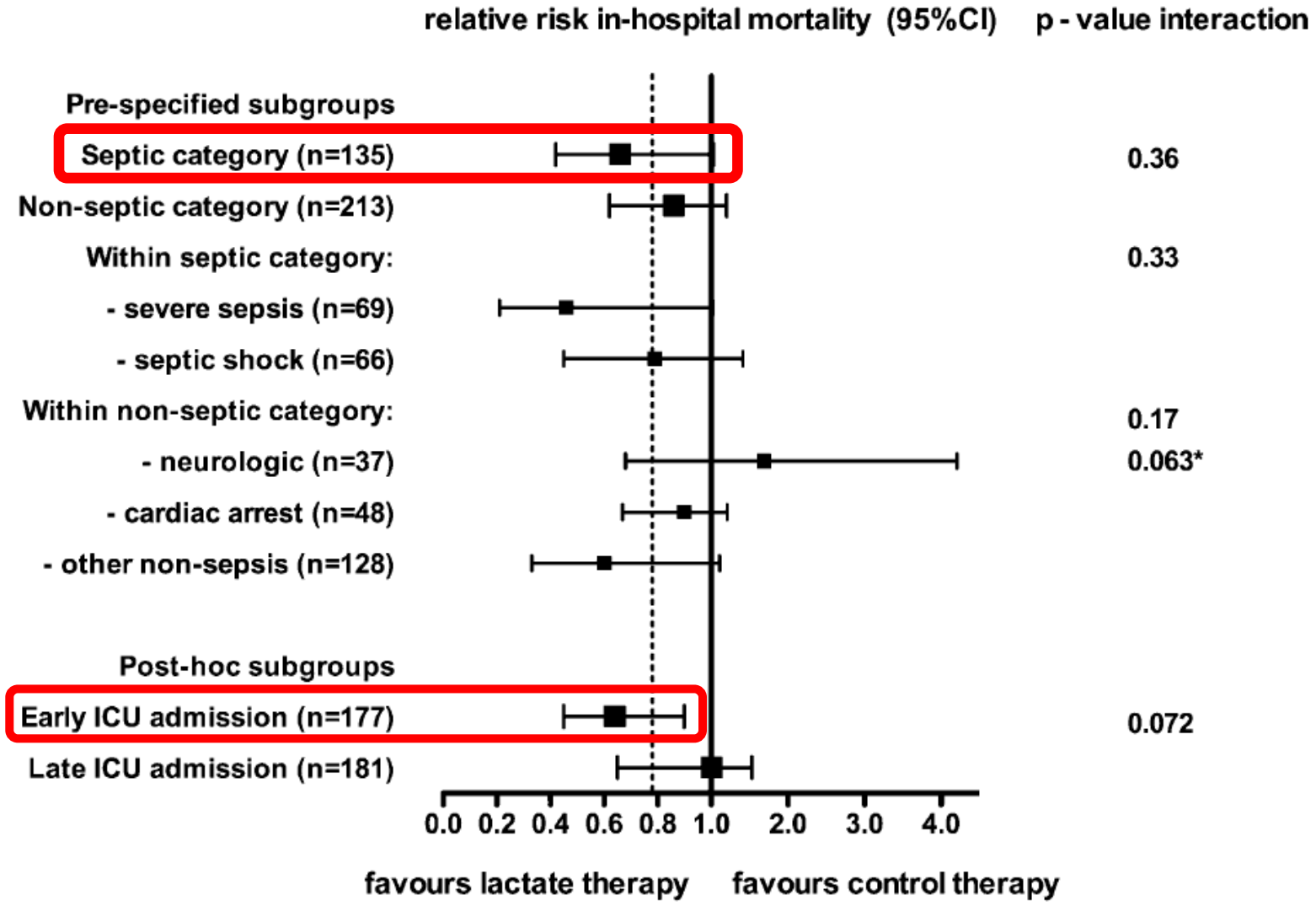
Exclusion
Insuffisance hépato-cellulaire …

Intervention en ouvert

Objectif ↓ ≥20% lactate /2h
Vs
Réanimation sans lactate (excepté celui d'entrée)
Pendant 8 heures

Early Lactate-Guided Therapy in Intensive Care Unit Patients

Jansen et al.
2010 AJRCCM



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ICU
Lactate≥3mmol/L

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Insuffisance hépato-cellulaire …

Intervention en ouvert

Objectif ↓ ≥20% lactate /2h
Vs
Réanimation sans lactate (excepté celui d'entrée)
Pendant 8 heures

D’autres objectifs de perfusion tissulaire …

Fondamentaux

Hypoperfusion tissulaire
⇔ Mortalité

Ait-Oufella et al. 2016 ICM
REVIEW

Jacquet-Lagrèze et al. 2023 CritCare
META-ANALYSIS

Cecconi et al. 2019 ICM
RFE ESICM

Incertitudes

Des objectifs thérapeutiques …

(+ns) *Hernandez et al. 2019 JAMA*
ANDROMEDA-SHOCK

Zampieri et al. 2019 CCM
Post-hoc ANDROMEDA-SHOCK
Bayesian analysis

van Genderen et al. 2015 AJRCCM
LETTER – ***PILOT RCT +***

Pour moins réanimer …

Kattan et al. 2020 AIC
Post-hoc ANDROMEDA-SHOCK

Lavillegrand et al. 2018 ICM

Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28-Day Mortality Among Patients With Septic Shock

The ANDROMEDA-SHOCK Randomized Clinical Trial

Hernandez et al.
2019 JAMA

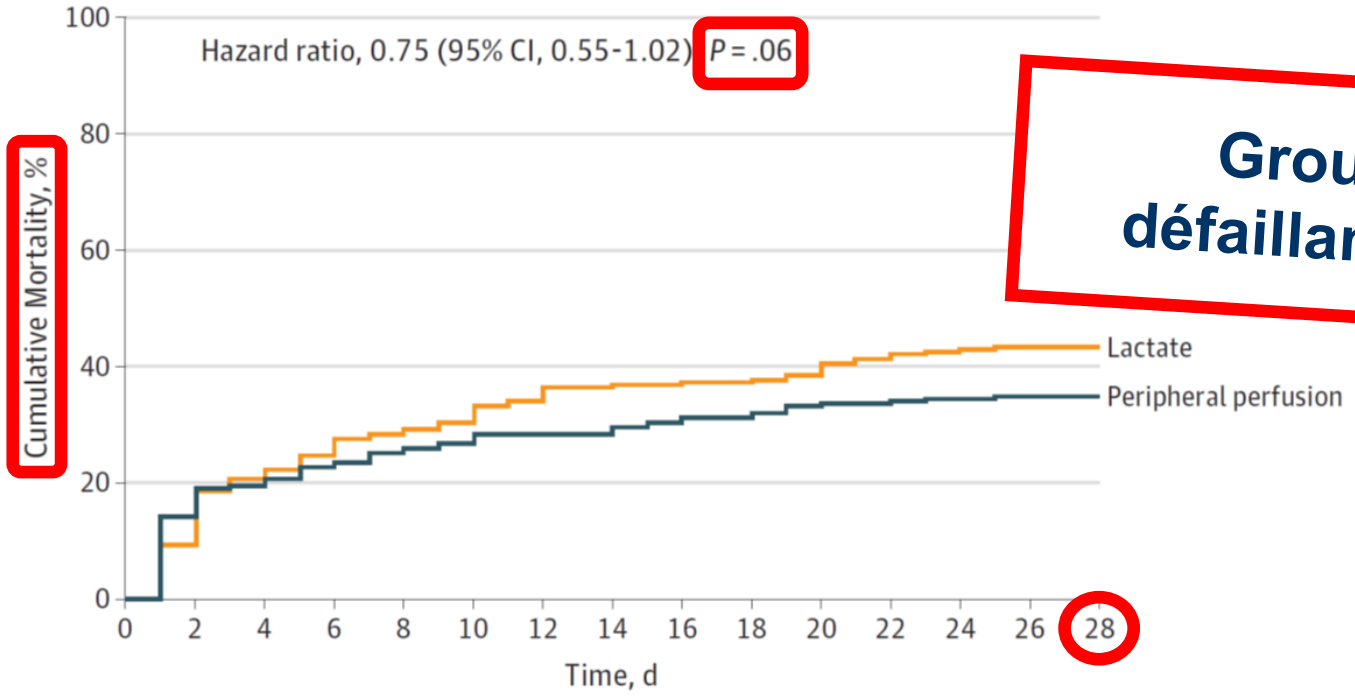
ANDROMEDA-SHOCK

Lactatémie /2h

TRC /30min

Pendant 8h

424 **patients**
Choc Septique-2 <4h
2017 -2018



No. at risk

Lactate	212	192	168	160	152	148	140	135	134	133	130	124	122	120	120
Peripheral perfusion	212	182	171	164	159	155	152	152	148	146	142	141	139	138	138

Groupe TRC => moins de défaillances d'organes à 72h …

⇒ **Personnalisation des traitements HDQ**

Kattan et al. 2020 AIC

Hernandez et al. 2024 AIC

Les outils diagnostiques …

Pas des objectifs mais DES MOYENS pour les atteindre !

Microcirculation

Précharge

Transport en CO2 (deltaCO2)

Œdème pulmonaire

Débit cardiaque

Fonction vasculaire systémique

Fonction cardiaque

Précharge dépendance

Œdème systémique

Transport artériel en O2 (TaO2)

Fonction vasculaire pulmonaire

Le TaO2 comme objectif <6h …

… pour améliorer le pronostic ?

↓ mortalité

Hospitalière
***p* = 0,0009**

À J28
p = 0,0009

À J60
p = 0,0009

Table 4. Treatments Administered.*

Treatment	Hours after the Start of Therapy		
	0–6	7–72	0–72
Total fluids (ml)			
Standard therapy	3499±2438	10,602±6,216	13,358±7,729
EGDT	4981±2984	8,625±5,162	13,443±6,390
P value	<0.001	0.01	0.73
Red-cell transfusion (%)			
Standard therapy	18.5	32.8	44.5
EGDT	64.1	11.1	68.4
P value	<0.001	<0.001	<0.001
Any vasopressor (%)†			
Standard therapy	30.3	42.9	51.3
EGDT	27.4	29.1	36.8
P value	0.62	0.03	0.02
Inotropic agent (dobutamine) (%)			
Standard therapy		16.8	70.6

Avant tout remplissage …

Lactate ≈ 7 mmol/L
SVcO2 ≈ 50 %

Oui,
en 2001 !

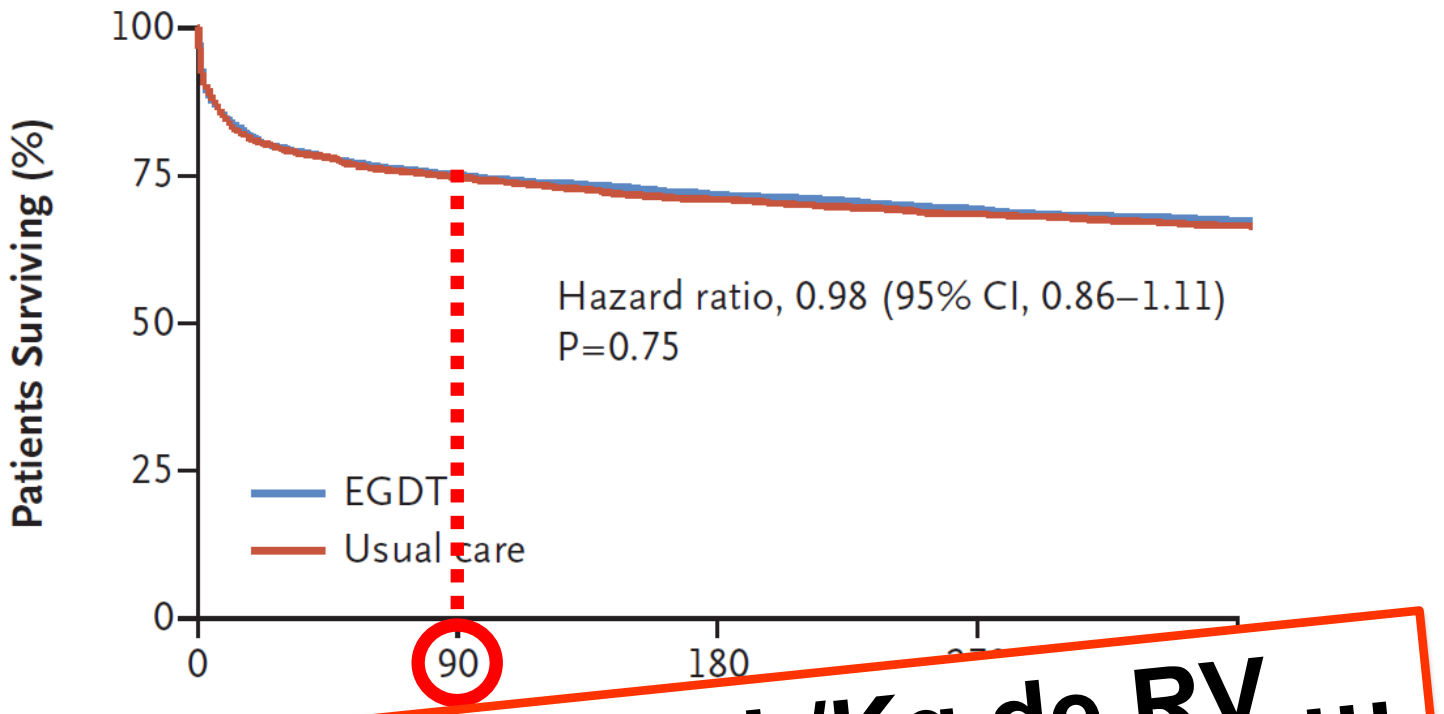
RCT monocentrique
Urgences USA Détroit
263 patients

Sepsis-1 et Choc septique

Rivers et al.
2001 NEJM

Le TaO2 comme objectif <6h …

… pour améliorer le pronostic ?



Après 30 mL/Kg de RV …

Lactate ≈ 4 mmol/L
SVcO2 ≈ 70 %

Non, en 2018 ?

Méta-analyse
3 RCT multicentriques
3723 patients
Réanimations
7 pays 128 hôpitaux

Sepsis-2 et Choc septique

***PRISM** 2018 NEJM*

La ScvO2 comme marqueur pronostique …

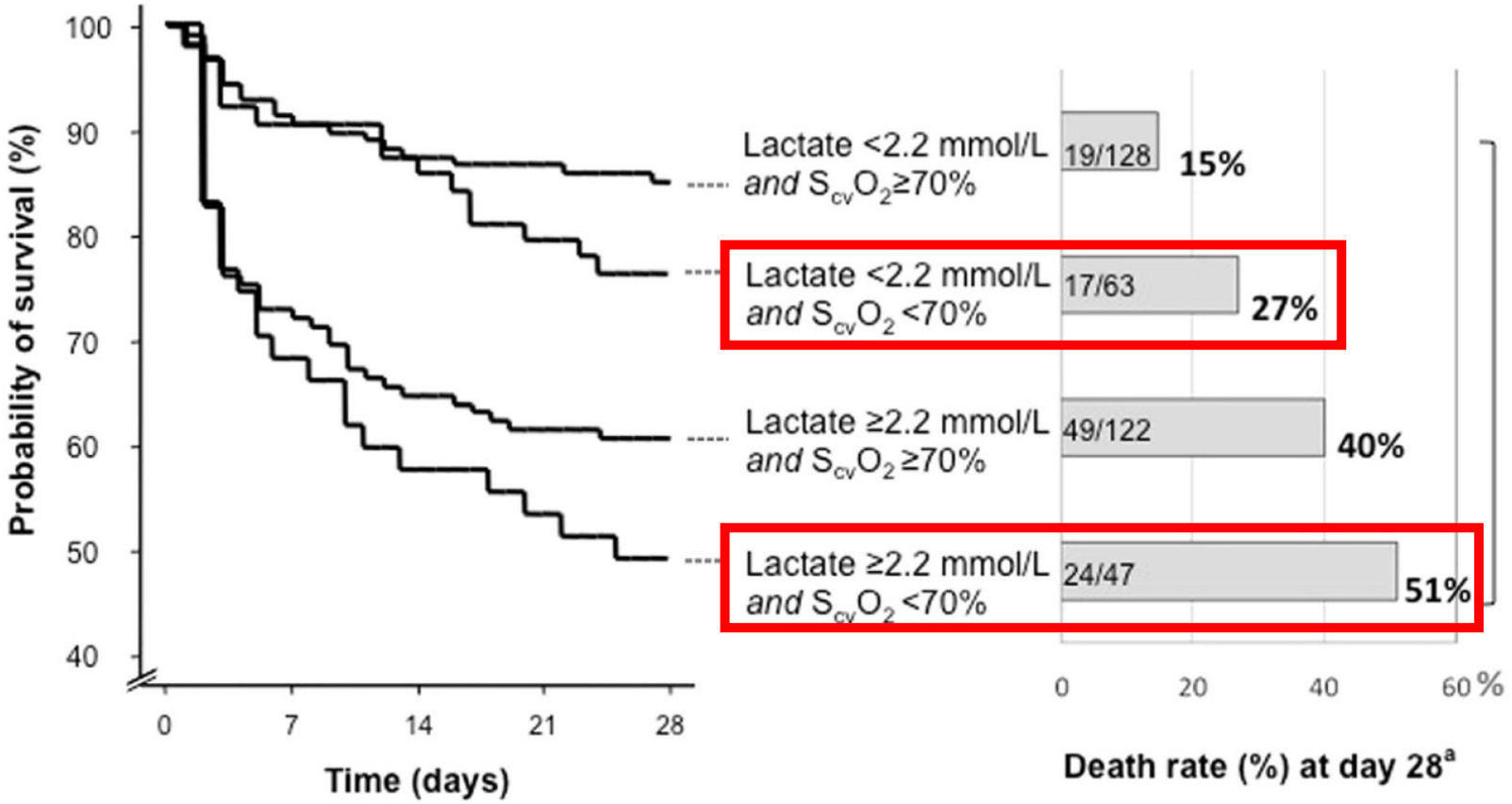
RESEARCH Open Access

Prevalence of low central venous oxygen saturation in the first hours of intensive care unit admission and associated mortality in septic shock patients: a prospective multicentre study

Boulain et al. 2014
Crit Care
OBS-PRO multicentrique

363 patients en choc septique

ScVO2 et lactatémie après réanimation initiale !!



31% des patients avec une ScvO2 <70% ! ⇔ Surmortalité !!!

Quel volume de remplissage vasculaire ?

Evans L et al. 2021 ICM
SSC Guideline 2021

Rhodes A et al. 2017 ICM
SSC Guideline 2016

LOW

5 For patients with sepsis-induced hypoperfusion or septic shock we **suggest** that at least 30 mL/kg of intravenous (IV) crystalloid fluid should be given within the first 3 hours of resuscitation.

2016 STATEMENT

*"We **recommend** that in the initial resuscitation from sepsis-induced hypoperfusion, at least 30ml/kg of intravenous crystalloid fluid be given within the first 3 hours."*

3. **We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS).**

VERY LOW

6 For adults with sepsis or septic shock, we **suggest** using dynamic measures to guide fluid resuscitation, over physical examination, or static parameters alone.

Quels solutés de remplissage vasculaire ?

Evans L et al. 2021 ICM
SSC Guideline 2021

MODERATE

32 For adults with sepsis or septic shock, we **recommend** using crystalloids as first-line fluid for resuscitation.

LOW

33 For adults with sepsis or septic shock, we **suggest** using balanced crystalloids instead of normal saline for resuscitation.

2016 STATEMENT

*"We **suggest** using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock"*

MODERATE

34 For adults with sepsis or septic shock, we **suggest** using albumin in patients who received large volumes of crystalloids.

HIGH

35 For adults with sepsis or septic shock, we **recommend against** using starches for resuscitation.

MODERATE

36 For adults with sepsis and septic shock, we **suggest against** using gelatin for resuscitation.

2016 STATEMENT

*"We **suggest** using crystalloids over gelatins when resuscitating patients with sepsis or septic shock."*

Le remplissage vasculaire …

Fondamentaux

Le RV => Améliore le pronostic des patients les plus graves !

Jamais vraiment démontré …

Latta T. 1832 Lancet
Jane et al. 2018 JAMAnet

Steele et al. 2017 Shock

Débuter le plus vite possible …

Ponikowski 2016 Eur Heart J
Konstantinides 2014 Eur Heart J
Jane et al. 2018 JAMA Net
Pruinelli et al. 2018 CCM

Steele et al. 2017 Shock

L'excès de RV est dangereux !

Andrews et al. 2017 JAMA
Zambia

Malbrain et al. 2018 AIC
Besen et al. 2017 Shock
Marik et al. 2017 ICM

Rudiger et al 2013 Clin Sci

Le RV => Uniquement en cas d'hypoperfusion …

Jane et al. 2018 JAMA Net

Maitland et al. 2011 NEJM
FEAST

Par des Cristalloïdes ! Pas d'Hydroxyléthylamidon ou de gélatine !

Perner et al. 2012 NEJM
6S

Moeller et al. 2016 J crit Care
META-ANALYSE

Le remplissage vasculaire …

Incertitudes

≥ 30 mL/Kg ?
<1h ou <3h ?

PRISM *2018 NEJM*
Pruinelli et al. 2018 CCM
Kattan et al. 2020 AIC
Seymour et al. 2017 NEJM

Intérêt de l'albumine ?
… des cristalloïdes hypertoniq. ?

Caironi P et al. 2014 NEJM
ALBIOS (sepsis)

Asfar et al. 2017
Lancet Respir Med
HYPERS2S

Park et al. 2019 CCM
RASP (cancer + Sepsis)

Après un RV initial, une stratégie restrictive pourrait améliorer le pronostic ?

Meyhoff et al. 2022 NEJM
CLASSIC (N)

Silversides et al. 2018 ICM
META-ANALYSE

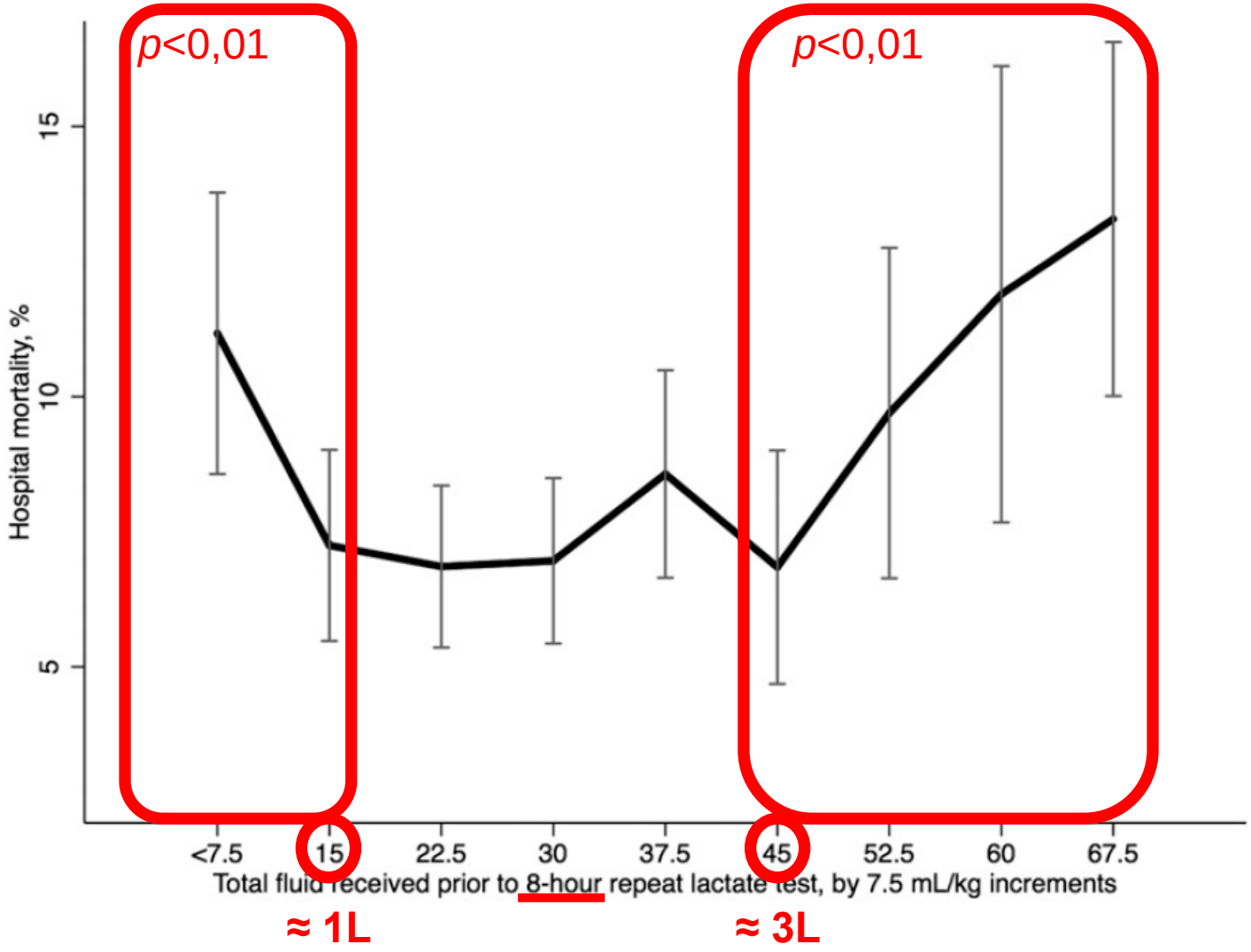
… des cristalloïdes « *normotoniq. balancés* » …

Hammo
NEJ
META

ancet
RCT

D'emblée selon le prix ?
Chlorémie < 110 mmol/L ?
Volume SSI < 4L ?

Un peu de modération …



Fluid Volume, Lactate Values, and Mortality in Sepsis Patients with Intermediate Lactate Values

Liu et al. 2013 Ann Am Tho Soc

Etude rétrospective multicentrique
21 Hôpitaux – Californie (USA)
9190 patients admis aux urgences
2010-2012

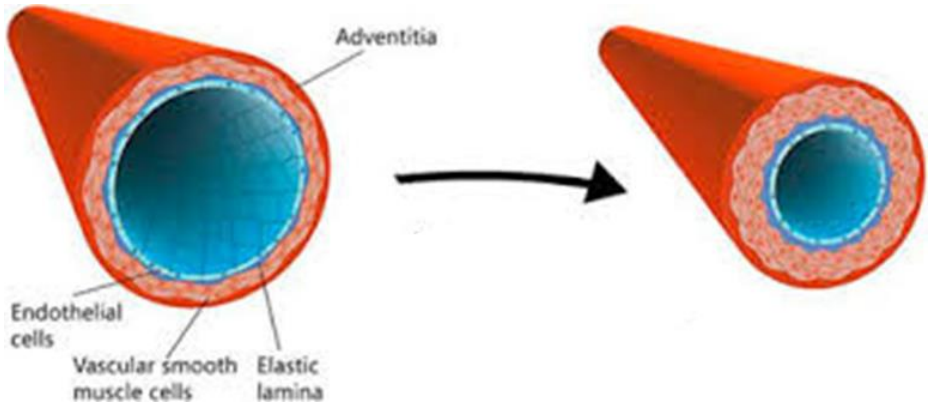
Sepsis +
Lactatémie 2 à 4 mmol/L
…

Quel vasoconstricteur en première intention ?

37 For adults with septic shock, we **recommend** using norepinephrine as the first-line agent over other vasopressors.

HIGH	Dopamine
MODERATE	Vasopressin
LOW	Epinephrine
LOW	Selepressin
VERY LOW	Angiotensin 2

Evans L et al. 2021 ICM
SSC Guideline 2021



Les vasoconstricteurs …

VERY LOW

44 For adults with septic shock, we **suggest** starting vasopressors peripherally to restore mean arterial pressure rather than delaying initiation until a central venous access is secured. VVP proximale … < 6 heures …

MODERATE

38 For adults with septic shock on norepinephrine with inadequate mean arterial pressure levels, we **suggest** adding vasopressin instead of escalating the dose of norepinephrine.

LOW

39 For adults with septic shock and inadequate mean arterial pressure levels despite norepinephrine and vasopressin, we **suggest** adding epinephrine.

VERY LOW

43 For adults with septic shock, we **suggest** invasive monitoring of arterial blood pressure over non-invasive monitoring, as soon as practical and if resources are available.

Evans L et al. 2021 ICM - ***SSC Guideline 2021***

Les vasoconstricteurs

Fondamentaux

La NAD => Améliore le pronostic !

Jamais vraiment démontré …

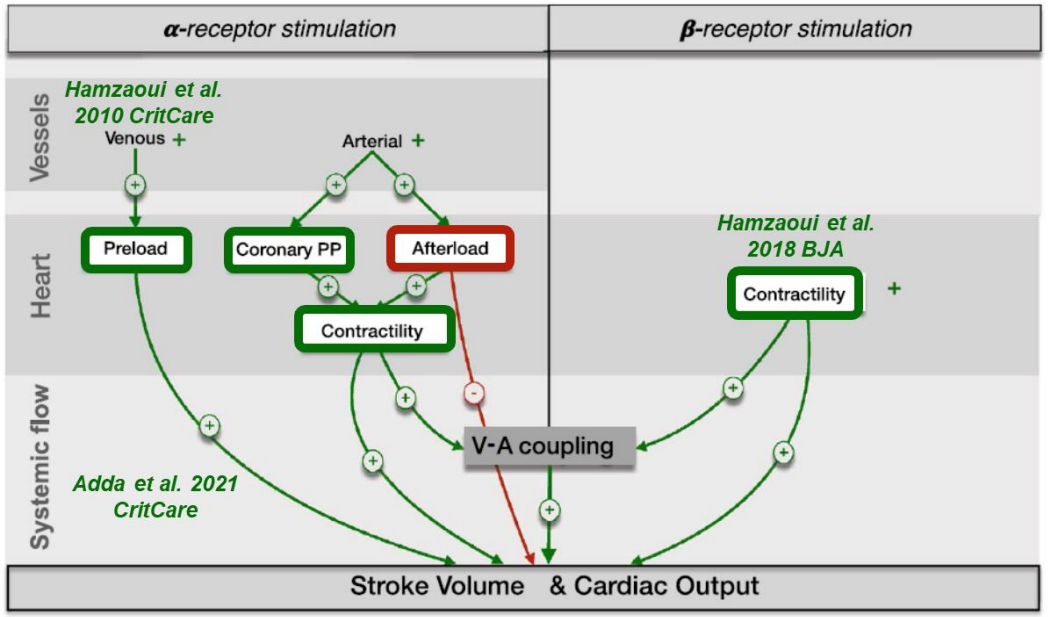
Permpikul et al. 2019 AJRCCM
CENSER

Bai et al. 2014 Crit Care

Indication => Hypotension artérielle …

Scheeren et al. 2019 AIC

Permpikul et al. 2019 AJRCCM
CENSER



G Hernandez, Teboul JL, Bakker J
*2019 ICM - **REVIEW***

Les vasoconstricteurs

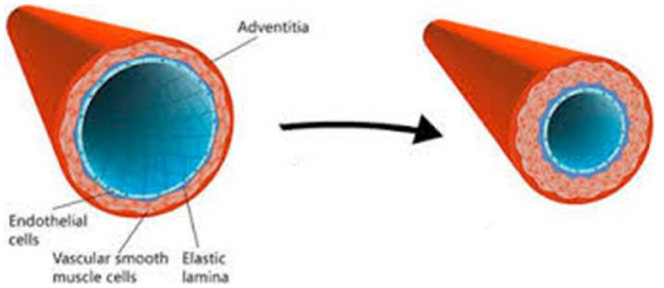
Fondamentaux

La **dopamine** et la **terlipressine** font moins bien que la NAD !

(-) *De Backer et al. 2010*
NEJM ***SOAP-II***

(--) *Liu V et al. 2018*
ICM ***China***

(--) *Avni et al. 2015*
PLOS 1



L'**adrénaline** ne fait pas mieux que NAD ou NAD+Dobu …

Annane et al. 2007
Lancet - ***CATS*** (N-)

Myburgh et al. 2008
ICM - ***CAT*** (N-)

Les vasoconstricteurs

Incertitudes

L'**AVP**, la **Selepressin** ou l'**ATII** ne font pas mieux … pour l'instant ?

(-) Russel et al. 2008
NEJM ***VASST***

(-) Gordon et al. 2016
JAMA ***VANISH***

(-) Hajjar et al. 2019
CCM ***VANCS II***

(-) Laterre et al. 2019
JAMA ***SEPSIS-ACT***

Khanna et al. 2017
NEJM ***ATHOS-3***

Tumlin et al 2018 CCM
Post-hoc ATHOS-3 (+)

(+) McIntyre et al. 2018
JAMA – ***META-ANALYSIS***

(-+) Nagendran et al. 2019
ICM – ***META-ANALYSIS***

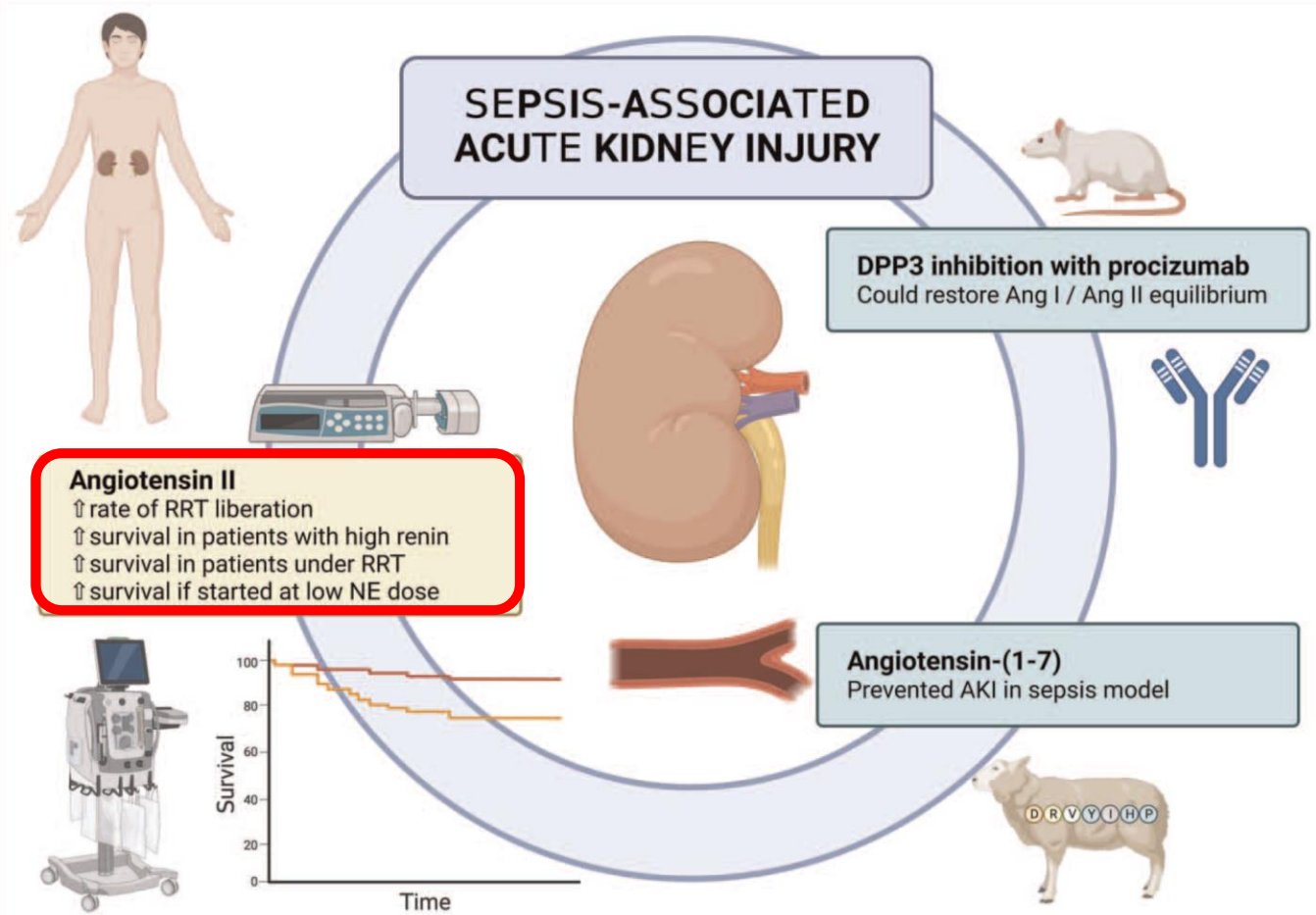
Vasoconstricteur pur !

Chocs hyperkinétiques ?

Monitorage hémodynamique +++

Les vasoconstricteurs

The role of renin-angiotensin system in sepsis-associated acute kidney injury: mechanisms and therapeutic implications



20 ng/Kg/min **puis**
1,25 à 80 ng/Kg/min **3H puis**
1,25 à 40 ng/Kg/min …
Prix …
Remboursement …
AMM choc vasoplégique réfractaire …

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HAS
HAUTE AUTORITÉ DE SANTÉ

SMR modéré
ASMR 5 (absence)

Garcia B. et al. 2023
Current Opinion in Crit Care

Quand débuter le(s) vasoconstricteur(s) ?

Fondamentaux

Immédiatement en cas d'échec du remplissage vasculaire initial !

Bai et al. 2014
Crit Care
Obs-retro-mono

Vite après la fin des 30mL/Kg de RV

Ospina-Tascon et al. 2020 Crit Care
Obs-pros

<1h Initiation RV

Hongxiang et al. 2020
Crit Care
META-ANALYSE
2RCT+3OBS
n=929 Sepsis

Scheeren et al. 2019 AIC
AUDIT experts

Incertitudes

Dès l'initiation d'un remplissage vasculaire ?

Permpikul et al. 2019
AJRCCM ***CENSER***

Elbouhy et al.
2019 Arch Med Res
101 patients
RCT

Early Use of Norepinephrine in Septic Shock Resuscitation (CENSER) : A Randomized Trial

Permpikul et al.
2019 AJRCCM

MAP ≥ 65 mmHg
+
Diurèse ≥ 0,5mL/Kg/h pendant 2h
OU
↘ Lactatémie ≥ 10%

Outcome	Early Norepinephrine (N=155)	Standard Treatment (N=155)	Odds Ratio or Relative Risk (95%CI)	P Value
Primary outcome, No. (%)			Odds ratio	
Achieved target mABP + tissue perfusion goal by 6 hours	118 (76.1)	75 (48.4)	3.4 (2.09–5.53)	<0.001
-Achieved target mABP + urine output + lactate clearance > 10% by 6 hours	48 (31.0)	27 (17.4)	2.13 (1.24-3.64)	0.005
-A by				0.04
- cl				0.3
Secondary outcomes				
Mortality at 28 days, No. (%)	24 (15.5)	34 (21.9)	0.79 (0.53–1.11)	0.15
Hospital mortality, No. (%)	35 (22.6)	38 (24.5)	0.95 (0.72–1.24)	0.69
Time from initial treatment to achieving target mABP + tissue perfusion goal, median (IQR), h:min	4:45 (3:30–5:56)	6:02 (4:20–9:18)		<0.001

RV ≈ 12 mL/Kg (800mL) avant NAD

Essai Randomisé
Contrôlé
Monocentrique
Thaïlande
310 patients

***Sepsis* + PAM<65 mmHg**
2013 - 2017

NAD 0,05 µg/Kg/min
≈ 0,25 mg/h
=> 8mg/500mL G5%

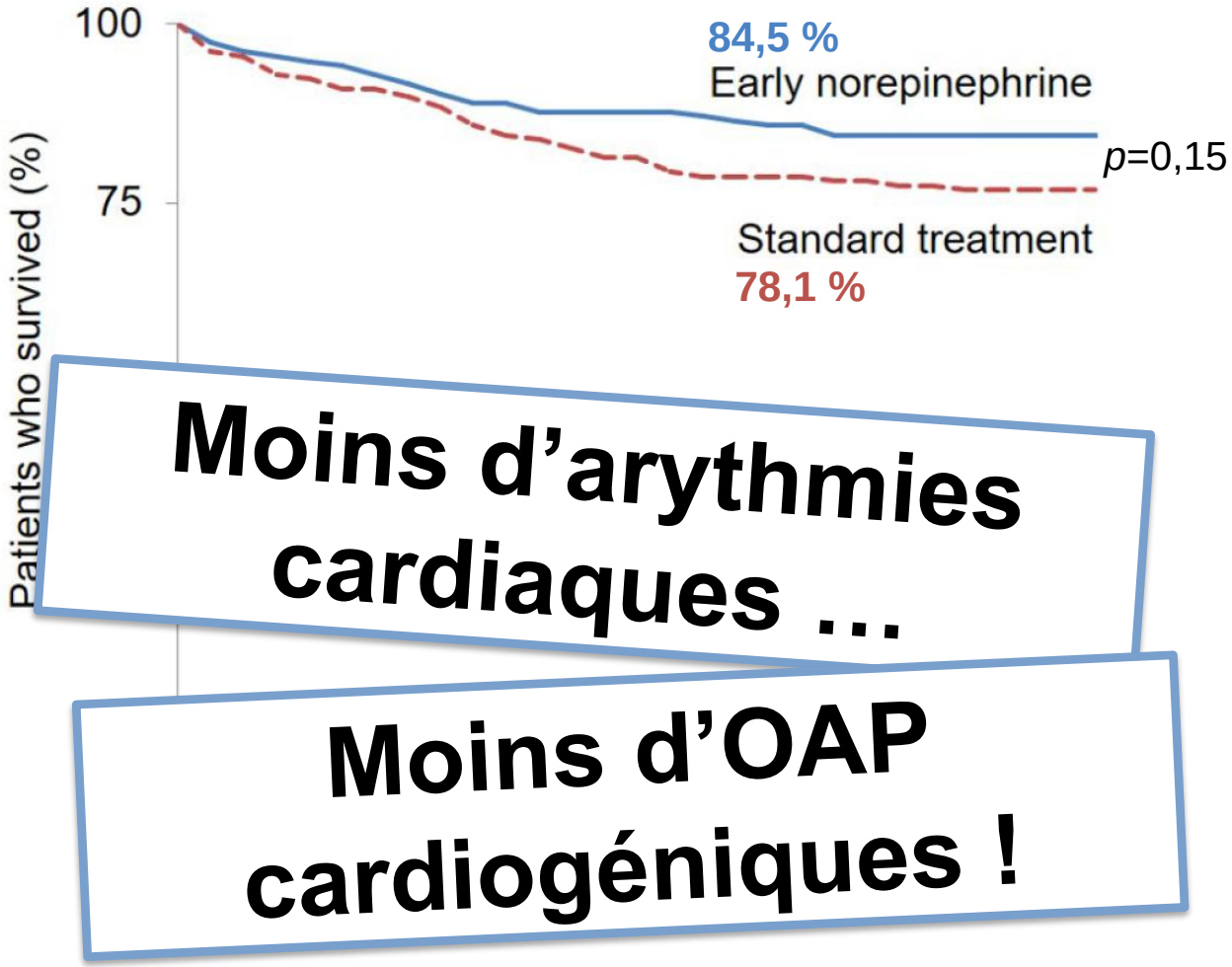
versus

Placebo

Pendant 24h

Early Use of Norepinephrine in Septic Shock Resuscitation (CENSER) : A Randomized Trial

Permpikul et al.
2019 AJRCCM



Moins d'arythmies cardiaques …

Moins d'OAP cardiogéniques !

Essai Randomisé
Contrôlé
Monocentrique
Thaïlande
310 patients

***Sepsis* + PAM<65 mmHg**
2013 - 2017

NAD 0,05 µg/Kg/min
≈ 0,25 mg/h
=> 4mg/250mL G5%

versus

Placebo

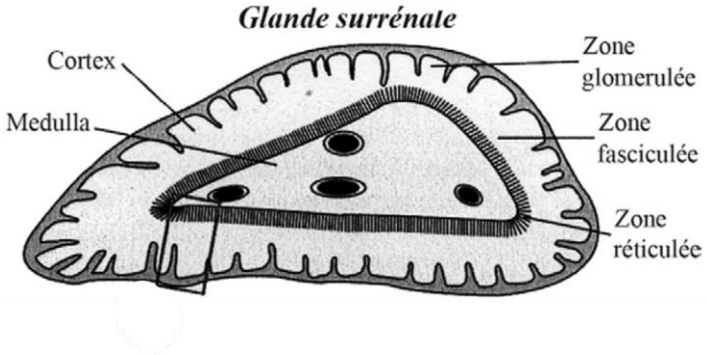
Pendant 24h

La corticothérapie « faible doses »

Evans L et al. 2021 ICM
SSC Guideline 2021

MODERATE

58 For adults with septic shock and an ongoing requirement for vasopressor therapy we **suggest** using IV corticosteroids.



Kloeckner M., Annane D. et al. 2007 Ann Endoc
REVIEW

La corticothérapie diminue la durée du choc !

Annane et al. 2018 NEJM (+)
APROCCHSS

Evans et al. 2021 ICM - ***SSC-GUIDELINES META-ANALYSIS*** (N+)

Venkatesh et al. 2018 NEJM (N+)
ADRENAL

Pirracchio R., Annane D. et al. 2023 NEJMevidence (N+)
Patient-level META-ANALYSIS

La corticothérapie diminue la mortalité ?

La corticothérapie « faible doses »

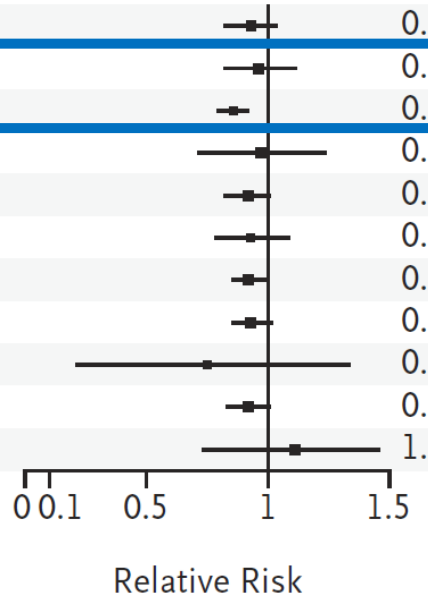
Patient-Level Meta-Analysis of Low-Dose Hydrocortisone in Adults with Septic Shock

17 RCT - 7882 patients

Mortalité à J90
7 RCT - 5929 patients

A

Treatment	Subgroup	Total No. of Patients (treatment+ control) (%)	No. Treated (%)	No. of Deaths in Treated (%)	No. Placebo (%)	No. of Deaths in Placebo (%)	Relative Risk (CI)
Overall		5929 (100)*	2966 (100)	1026 (36)	2963 (100)	1069 (37)	0.93 (0.82–1.04)
Hydrocortisone	Without fludrocortisone	4389 (74)	2202 (74)	665 (31)	2187 (74)	656 (31)	0.96 (0.82–1.12)
	With fludrocortisone	1540 (26)	764 (26)	361 (47)	776 (26)	413 (53)	0.86 (0.79–0.92)
Taper	Taper	657 (11)	329 (11)	135 (51)	328 (11)	127 (49)	0.97 (0.71–1.24)
	No taper	5272 (89)	2637 (89)	891 (34)	2635 (89)	942 (36)	0.92 (0.82–1.01)
Continuous	Continous	3844 (65)	1922 (65)	538 (29)	1922 (65)	552 (30)	0.93 (0.78–1.09)
	Bolus	2085 (35)	1044 (35)	488 (48)	1041 (35)	517 (51)	0.92 (0.85–1.00)
Steroid duration	Fixed	5771 (97)	2888 (97)	999 (35)	2883 (97)	1043 (37)	0.93 (0.85–1.02)
	Shock reversal	158 (3)	78 (3)	27 (60)	80 (3)	26 (63)	0.75 (0.21–1.34)
Steroid initiation	<24 h	5723 (97)	2865 (97)	982 (35)	2858 (97)	10,255 (37)	0.92 (0.83–1.01)
	>24 h	176 (3)	85 (3)	40 (56)	91 (3)	39 (50)	1.11 (0.73–1.46)

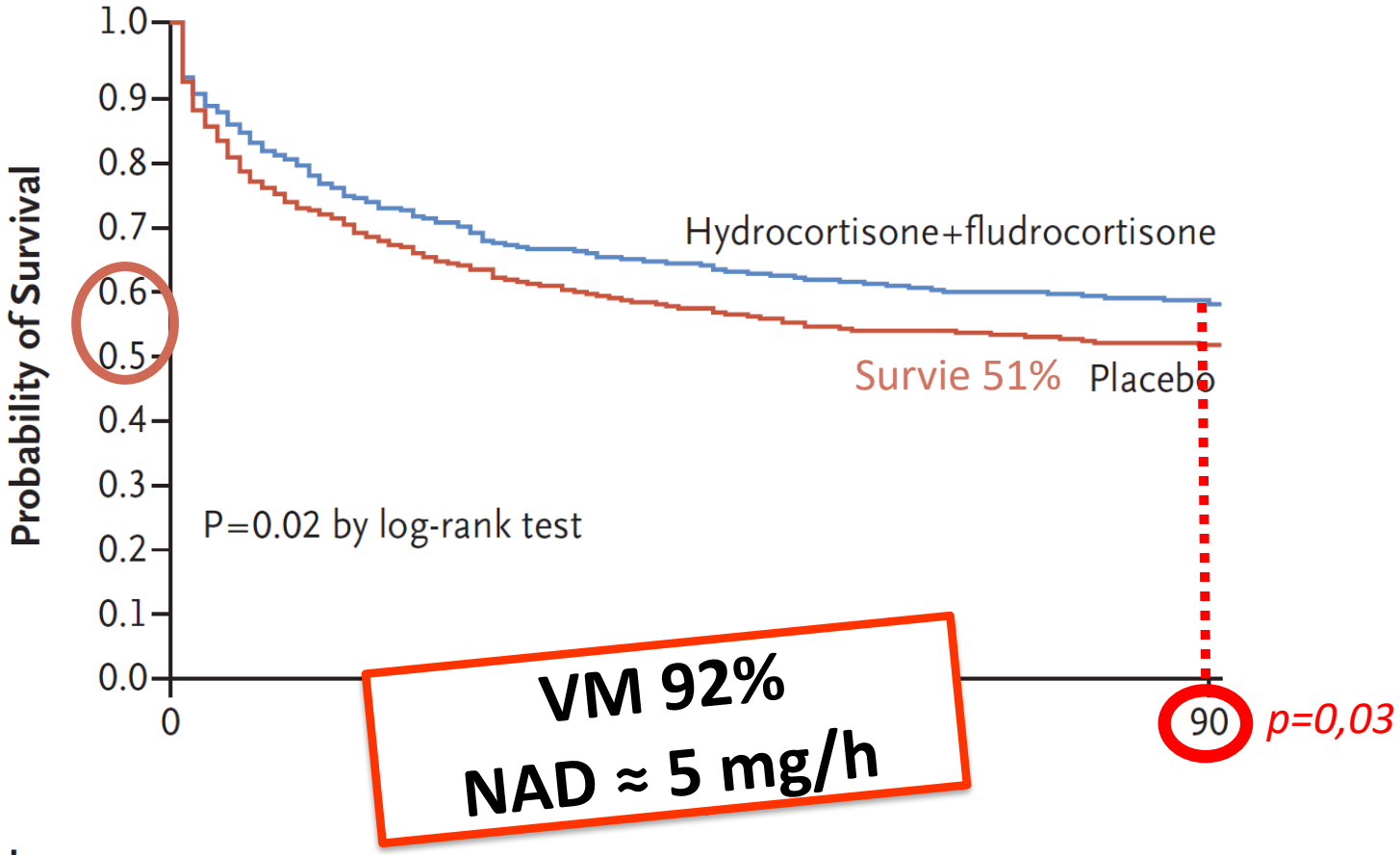


Pirracchio R., Annane D. et al. 2023 NEJMevidence

Patient-level META-ANALYSIS

La corticothérapie « faible doses »

Bolus **HSHC+Fludro** versus **Placebo** pendant 7 jours



VM 92%
NAD ≈ 5 mg/h

No. at Risk				
Hydrocortisone+ fludrocortisone	614	405	372	353
Placebo	627	381	333	319

Essai contrôlé randomisé
Double aveugle
Multicentrique

1241 patients septiques
Entre H6 et H24

Vasoconstricteur IV > 6H
Et > 1mg/H
pour une PAM > 65 mmHg

SOFA ≥ ¾ pour ≥ 2 organes

Annane et al. 2018 NEJM
APROCCHSS

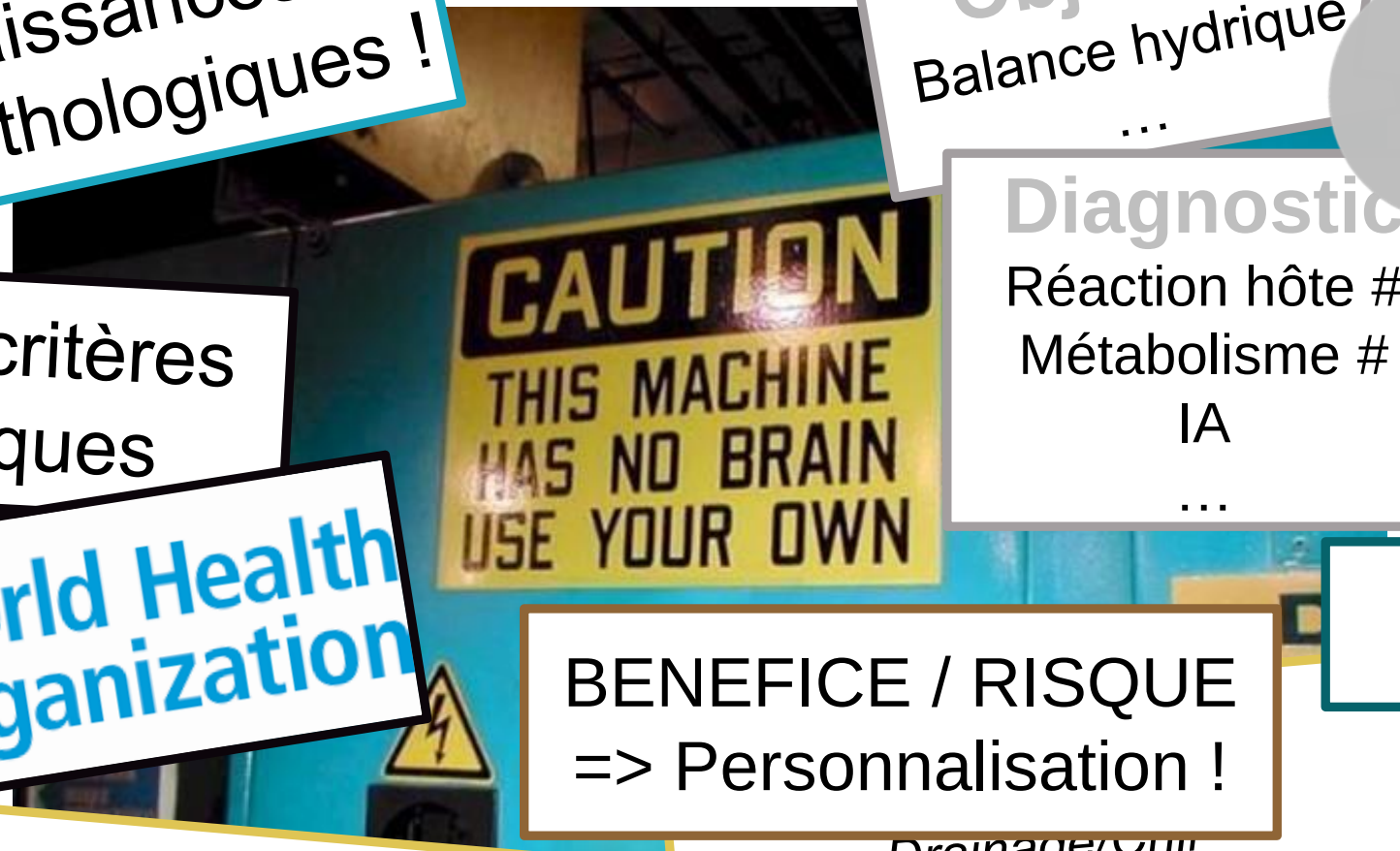
CONCLUSION

Connaissances physiopathologiques !

Nouveaux critères diagnostiques

World Health Organization

Des recommandations internationales !



Objectifs
Balance hydrique
…

Traitements
β- IV
Anti-infectieux
…

?

Diagnostic
Réaction hôte #
Métabolisme #
IA
…

Monitorage
Dosage ABT
Débit cardiaque
…

BENEFICE / RISQUE
=> Personnalisation !

> H6
Corticoïdes ?

Drainage/Chir
Perfusion tissulaire
Remplissage
Vasoconstricteurs
…

MODERATE

Annane et al. 2018 NEJM
APROCCHSS

Annane et al. 2002 JAMA
RCT-HSHC-FC