Choc septique
Quoi de neuf en 2024 ?

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PARIS

ALGER 2024

INTRODUCTION

REMPLISSAGE VASCULAIRE

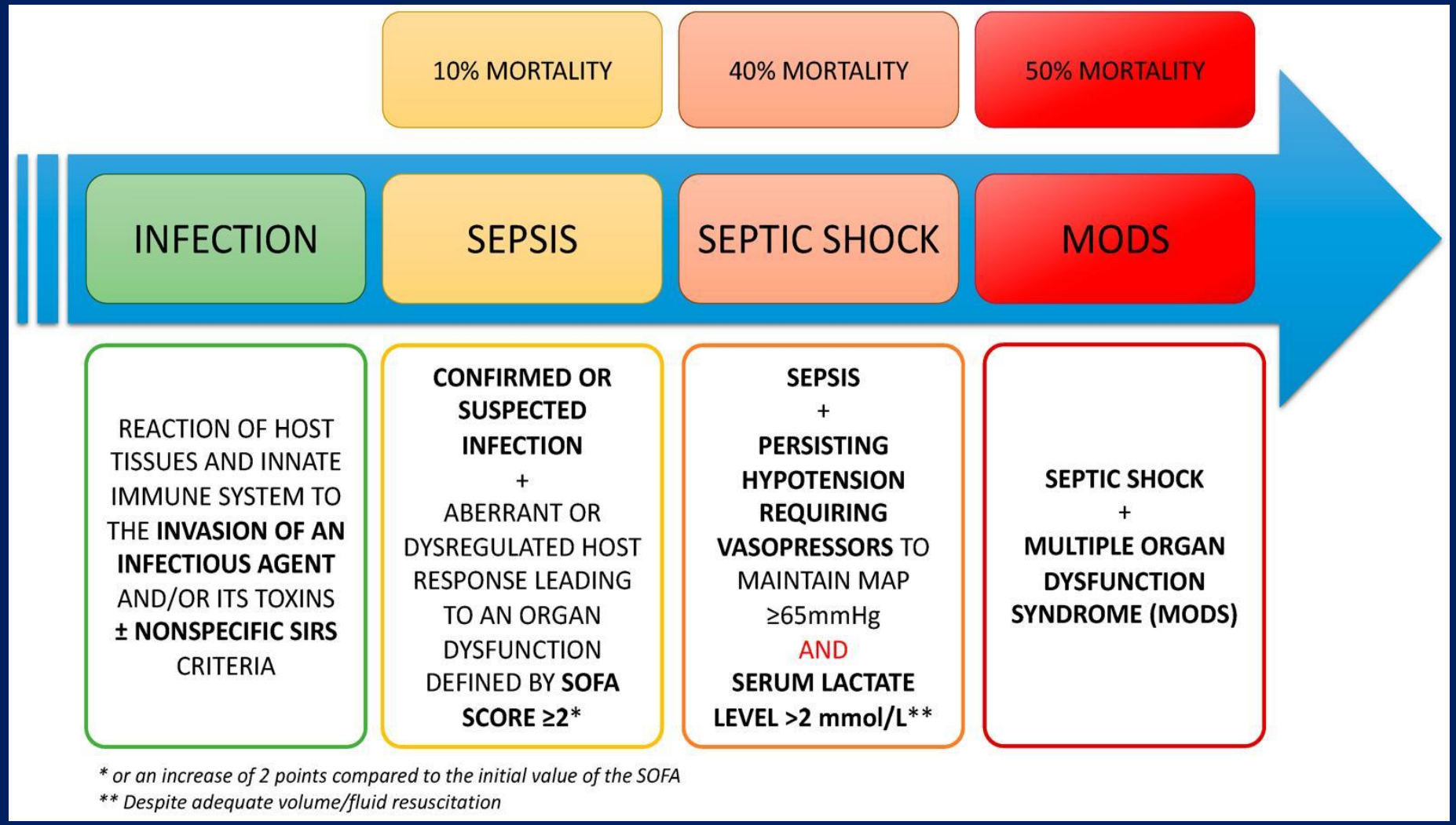
NOUVEAUX VASOPRESSEURS

CHOC SEPTIQUE REFRACTAIRE

PRONOSTIC DU CHOC SEPTIQUE

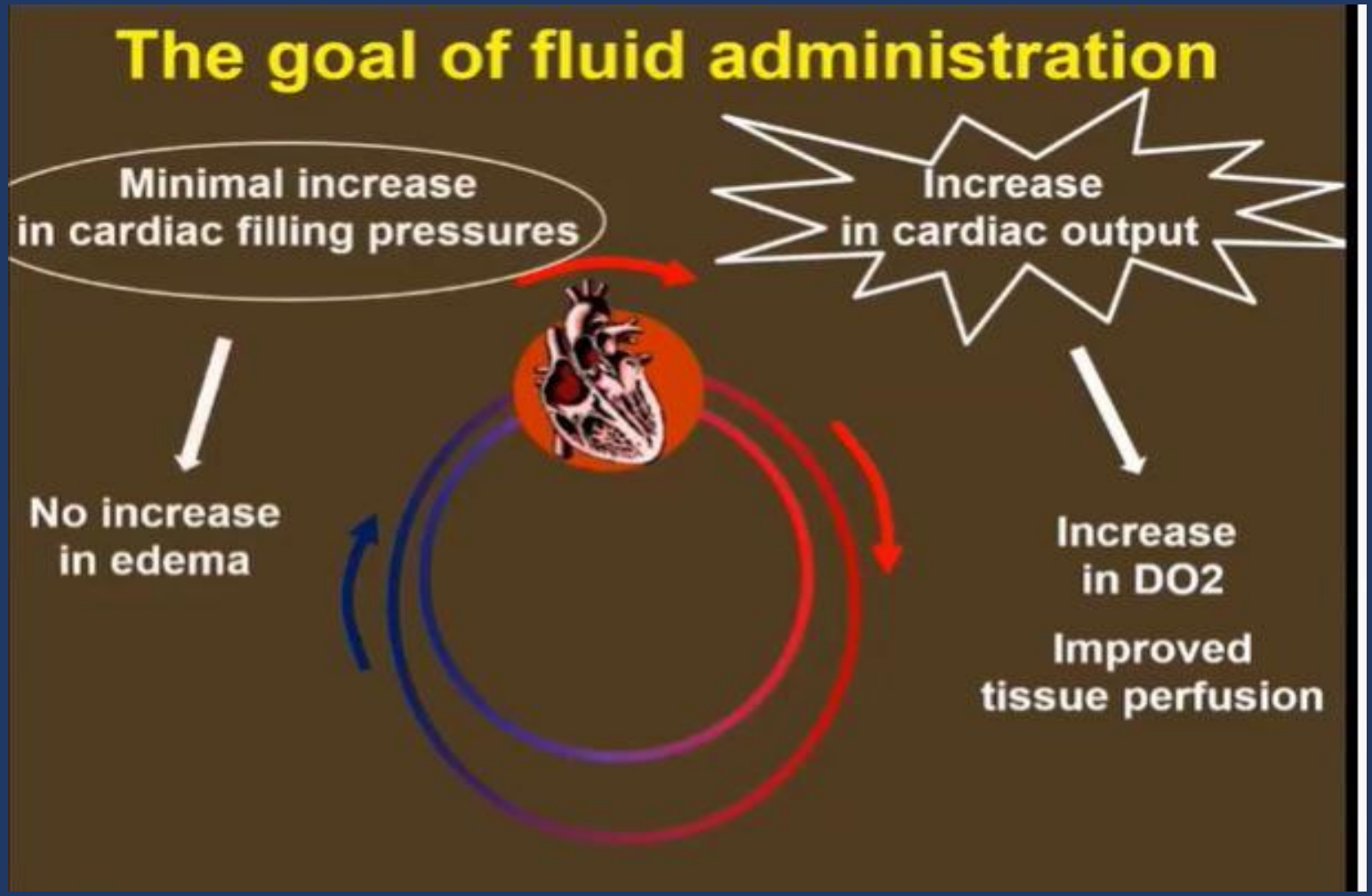
MONITORAGE LACTATES, MOTTLING SCORE ,DSI,CRT

NOUVELLE DEFINITION DU SEPSIS



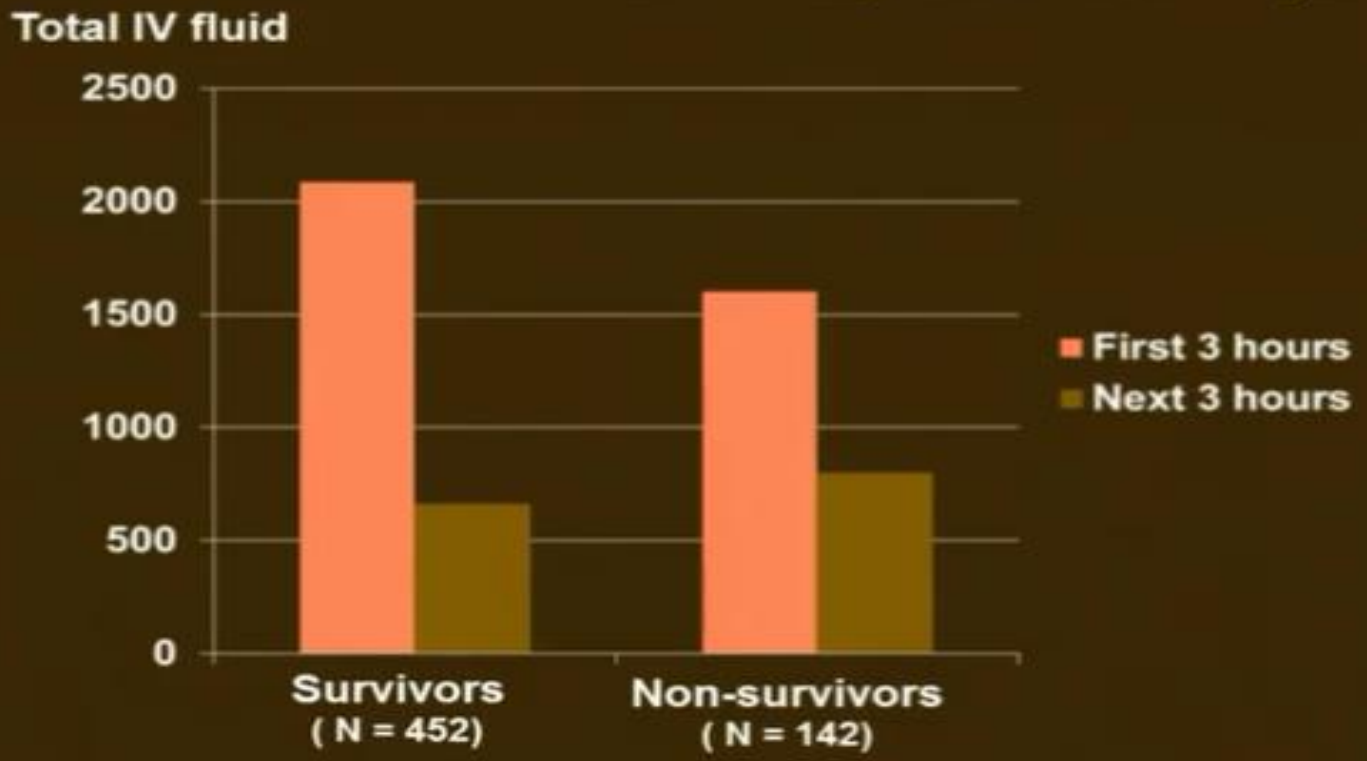
MORTALITE SELON LA GRAVITE

JAMA 2016


The goal of fluid administration
Minimal increase
in cardiac filling pressures
Increase
in cardiac output
No increase
in edema
Increase
in DO2
Improved
tissue perfusion

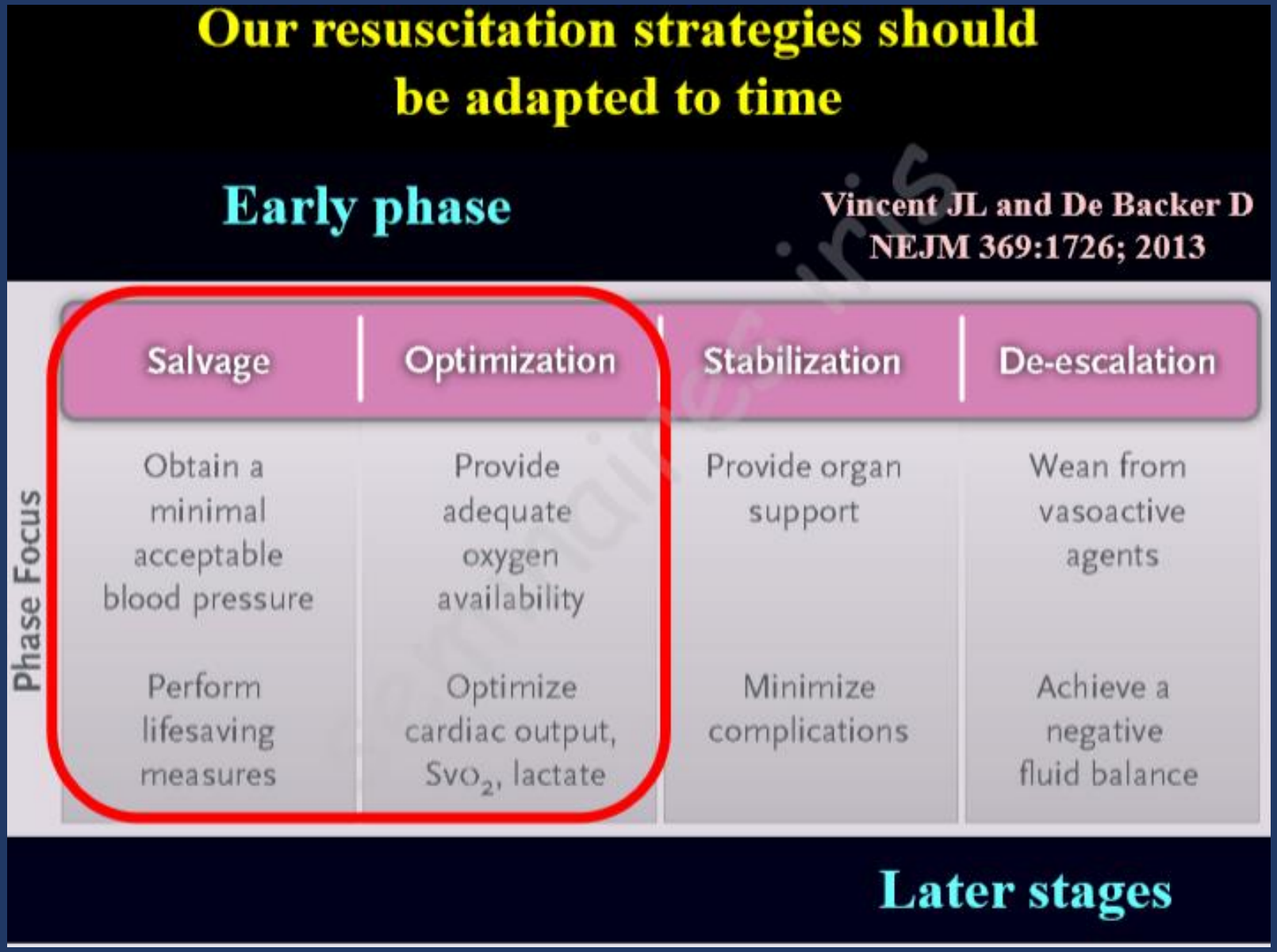
Reduced mortality with increased fluid administration in the first 3 hours of sepsis resuscitation

Lee et al, Chest 146: 908, 2014

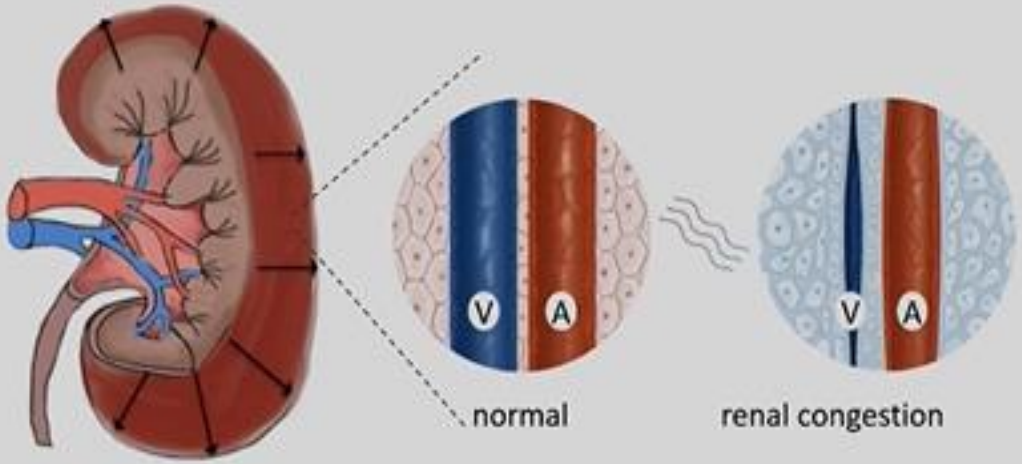


OR 0.34 (0.15-0.75) p<0.01

SOSD


Our resuscitation strategies should be adapted to time
Early phase
Vincent JL and De Backer D
NEJM 369:1726; 2013
Phase Focus
Salvage
Optimization
Stabilization
De-escalation
Obtain a minimal acceptable blood pressure
Provide adequate oxygen availability
Provide organ support
Wean from vasoactive agents
Perform lifesaving measures
Optimize cardiac output, Svo2, lactate
Minimize complications
Achieve a negative fluid balance
Later stages

hypervolaemia
R heart failure → venous pressure ↑



intra-renal congestion

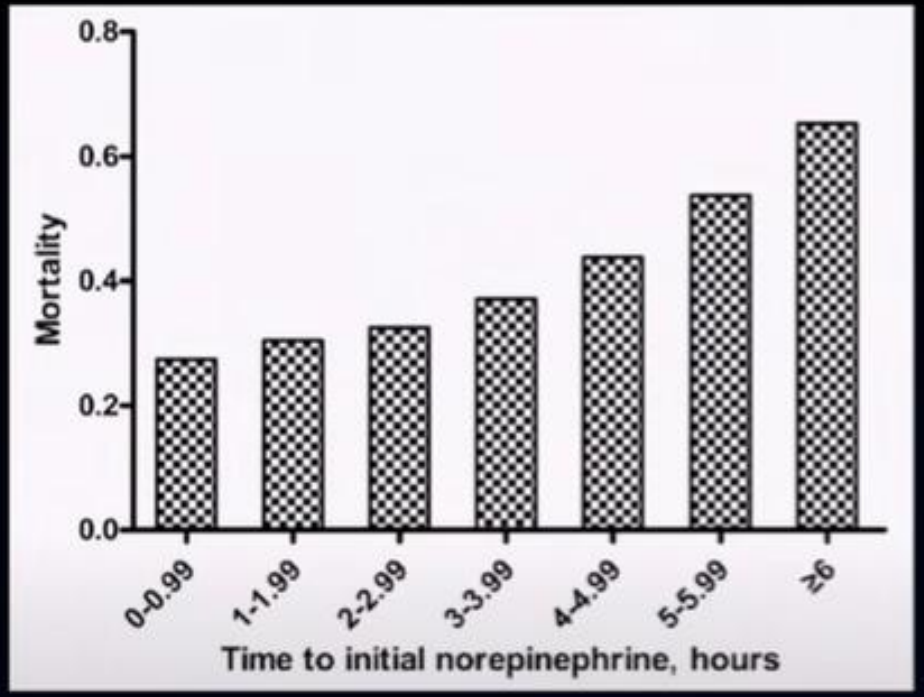
↑ intra-renal hydrostatic pressure

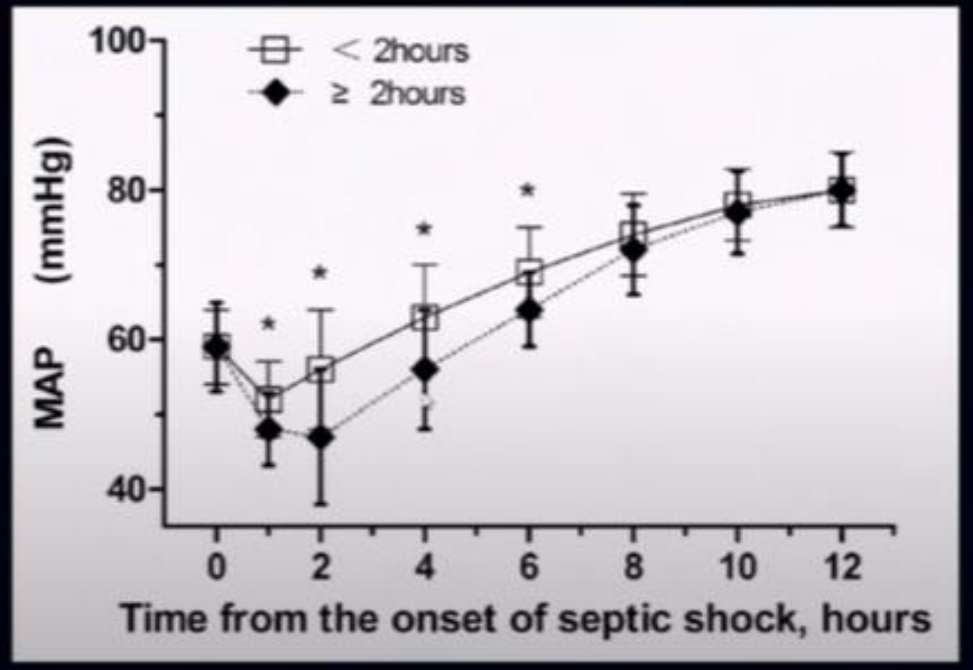
↑ intratubular pressure

development / progression of AKI

Duration of hypotension before initiation of vasopressor agents is associated with poor outcome

Bai X et al
Crit Care 2014





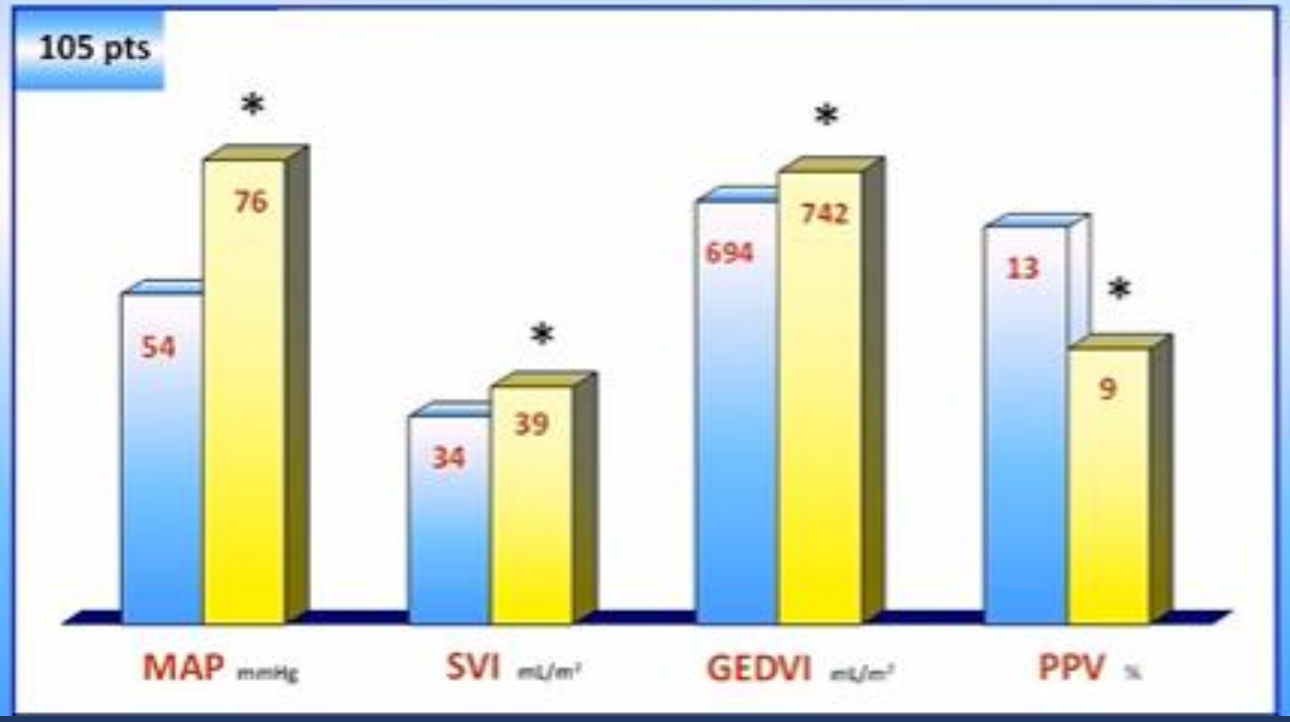
213 pts with septic shock

DELAI D'ADMINISTRATION DES VASOPRESSEURS ET MORTALITE

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



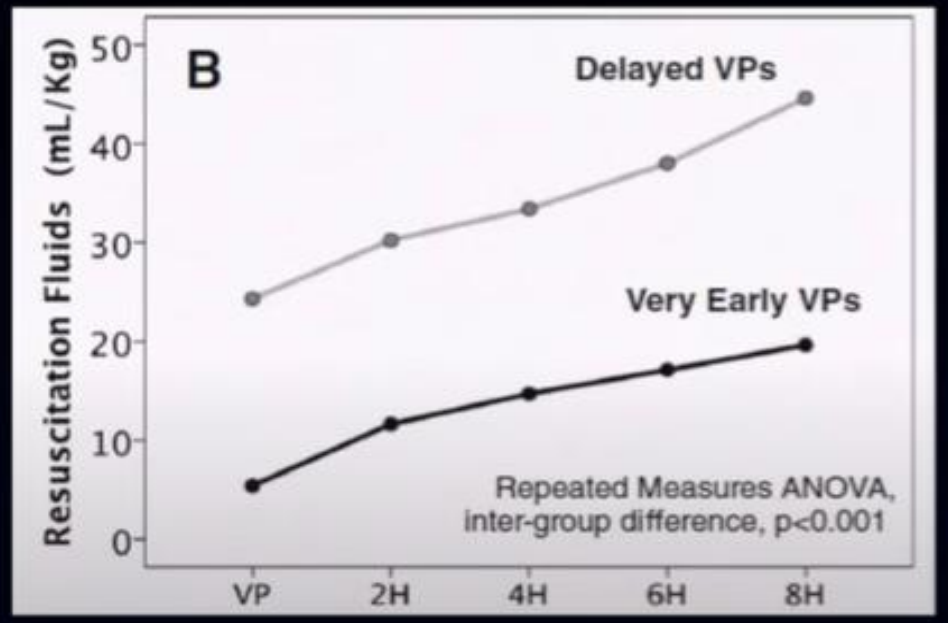
NORADRENALINE ADMINISTREE PRECOCEMENT AUGMENTE LA PRECHARGE ET LE DEBIT CARDIAQUE

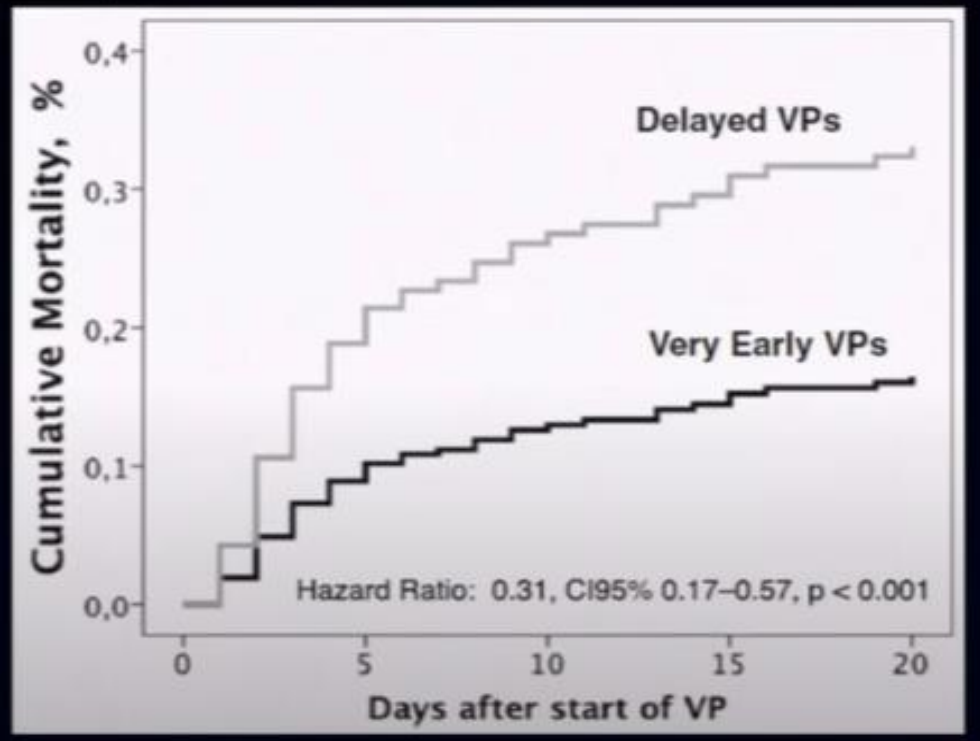
RESEARCH Open Access

Effects of very early start of norepinephrine in patients with septic shock: a propensity score-based analysis

Gustavo A. Ospina-Tascón[1,2*], Glenn Hernandez[3], Ingrid Alvarez[1], Luis E. Calderón-Tapia[1], Ramiro Manzano-Nunez[1], Alvaro I. Sánchez-Ortiz[1], Egardo Quiñones[1], Juan E. Ruiz-Yucuma[1], José L. Aldana[1,2], Jean-Louis Teboul[4], Alexandre Biasi Cavalcanti[5], Daniel De Backer[6] and Jan Bakker[3,7,8,9]

Ospina-Tascon et al
Crit Care 2020

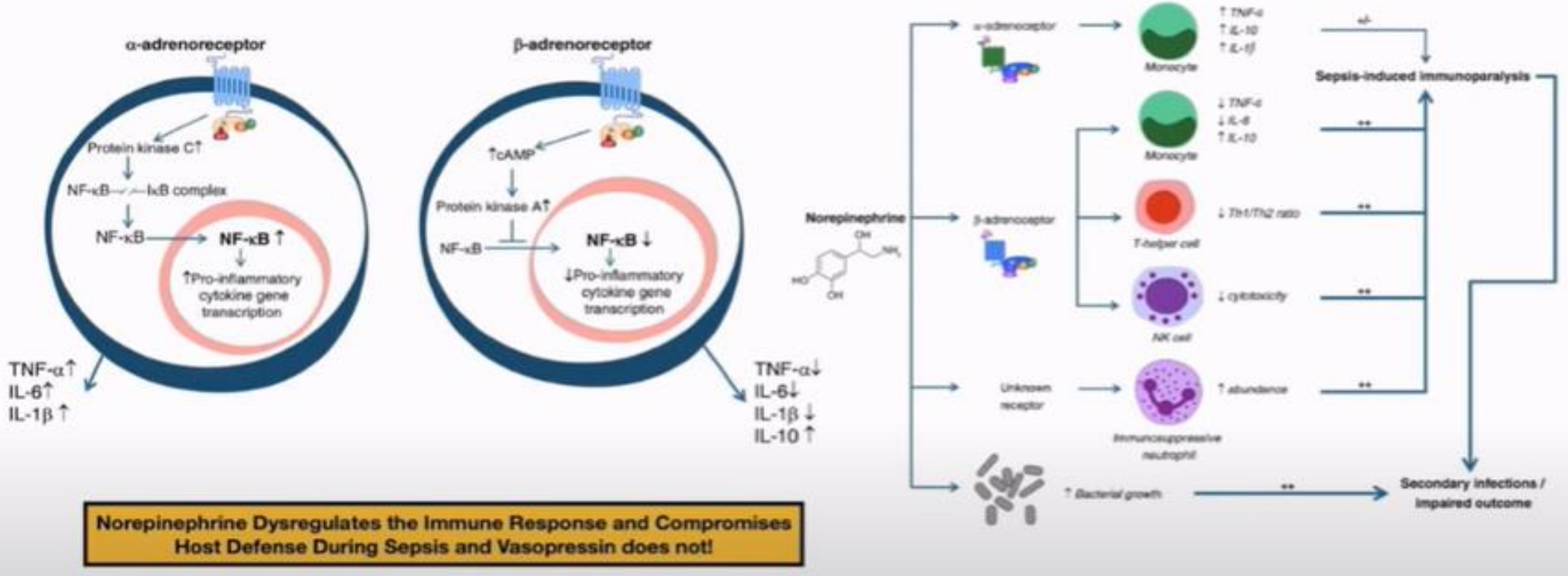




N=337

Noradrénaline précoce: Diminution du remplissage et de la mortalité

Norephrine dysregulates the immune system and vasopressin does not



Norepinephrine Dysregulates the Immune Response and Compromises Host Defense During Sepsis and Vasopressin does not!

Stolk RF. Am J Resp Crit Care Med 2016;194:550-558
Stolk R. Am J Resp Crit Care Med 2020

10

Norepinephrine attenuated the production of proinflammatory mediators and reactive oxygen species and augmented anti-inflammatory IL-10 production both *in vitro* and in LPS-challenged mice.

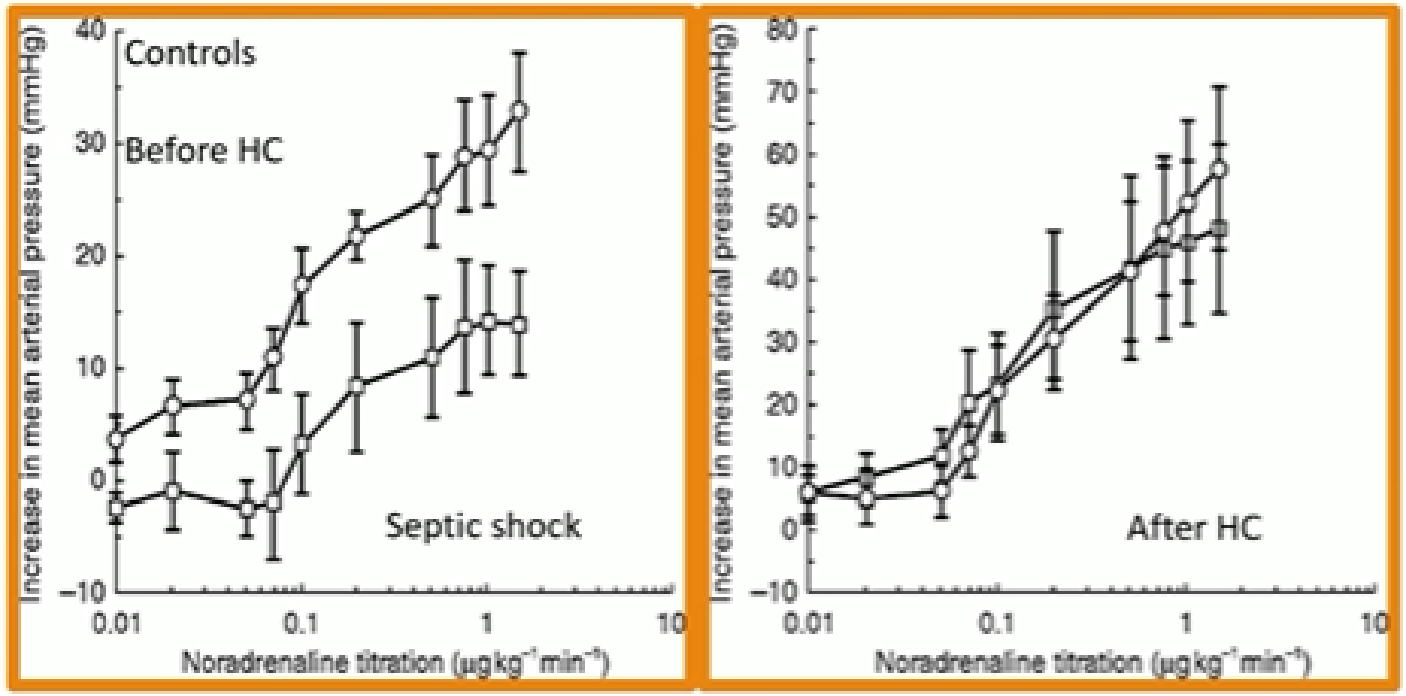
CHOC REFRACTAIRE

Définition choc réfractaire

persistance d’ une hypotension artérielle et d’ une hypoperfusion tissulaire malgré une posologie de noradrénaline supérieure à 0,25mcg/kg/min

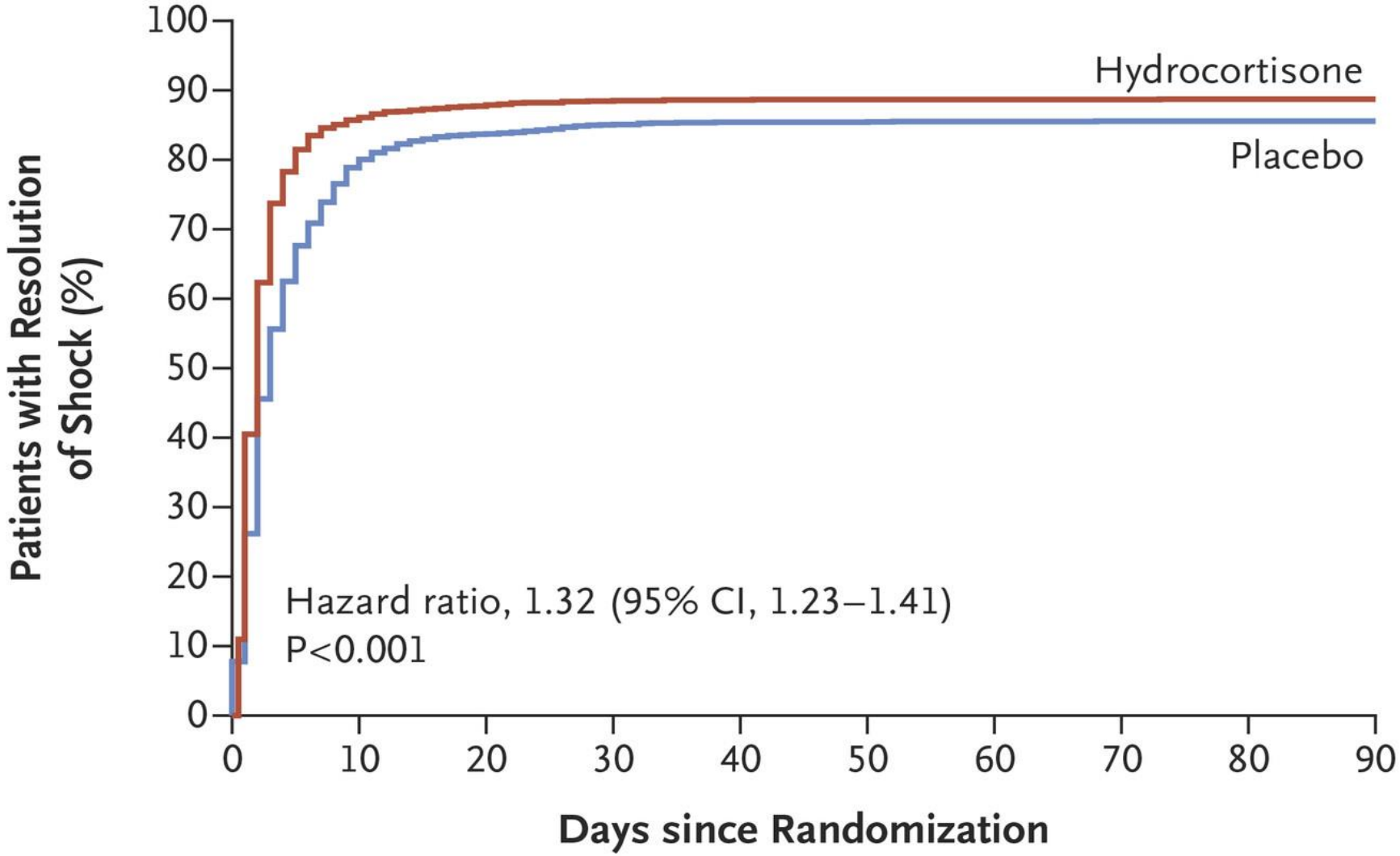
Hydrocortisone dans le choc septique réfractaire

Hydrocortisone restores sensitivity to catecholamines



Annane, BJCP 1998

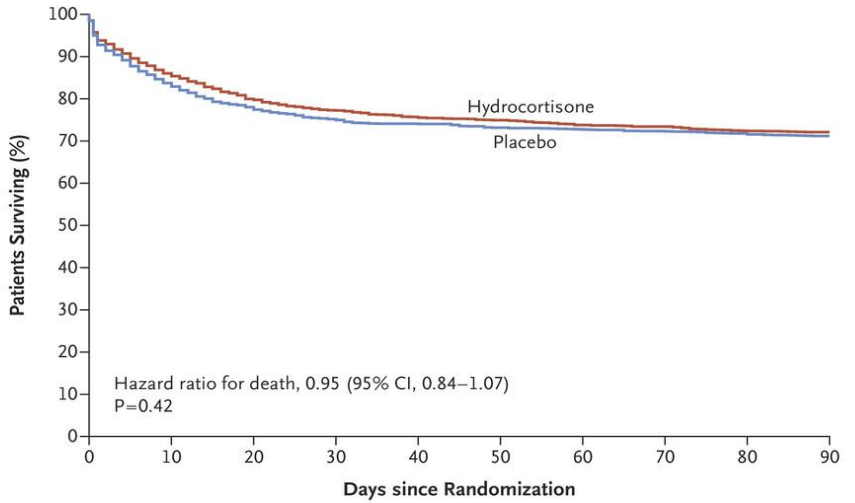
Augmentation de l, expression des alpha récepteurs et diminution du NO endothélial



No. at Risk

Hydrocortisone	1843	104	34	9	6	3	3	2	1	0
Placebo	1854	213	53	19	8	6	4	0	0	0

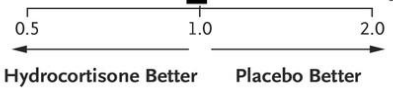
A Survival



No. at Risk										
Hydrocortisone	1832	1591	1481	1418	1388	1374	1356	1348	1328	1321
Placebo	1826	1546	1433	1376	1354	1337	1330	1322	1312	1300

B Subgroup Analysis of Death at 90 Days

Subgroup	Hydrocortisone	Placebo	Odds Ratio (95% CI)	P Value for Interaction
	no. of patients with event/total no. of patients (%)			
Sex				0.53
Male	312/1106 (28.2)	336/1122 (29.9)	0.92 (0.76–1.10)	
Female	199/726 (27.4)	190/704 (27.0)	1.01 (0.80–1.28)	
Admission type				0.73
Surgical	125/568 (22.0)	138/580 (23.8)	0.91 (0.69–1.21)	
Medical	386/1264 (30.5)	388/1245 (31.2)	0.97 (0.81–1.15)	
Catecholamine dose				0.25
≤15 μg/min	224/968 (23.1)	228/995 (22.9)	1.02 (0.82–1.26)	
>15 μg/min	281/849 (33.1)	291/805 (36.1)	0.86 (0.70–1.05)	
Site of sepsis				0.63
Pulmonary	243/799 (30.4)	250/828 (30.2)	0.99 (0.80–1.23)	
Other	268/1033 (25.9)	276/998 (27.7)	0.92 (0.76–1.12)	
APACHE II score				0.17
≥25	326/840 (38.8)	297/785 (37.8)	1.01 (0.83–1.24)	
<25	184/990 (18.6)	229/1039 (22.0)	0.82 (0.66–1.02)	
Time from shock onset to randomization				0.08
<6 hr	110/352 (31.2)	96/344 (27.9)	1.16 (0.83–1.61)	
6 to <12 hr	127/511 (24.9)	153/486 (31.5)	0.71 (0.54–0.94)	
12 to <18 hr	119/437 (27.2)	106/423 (25.1)	1.13 (0.83–1.54)	
≥18 hr	154/525 (29.3)	167/566 (29.5)	0.99 (0.76–1.29)	



For Practice

- Give
  - hydrocortisone (50mg q6) +
  - fludrocortisone (50µg q24)
- For
  - 7 days
  - No need to taper off
- To
  - Septic shock,
  - Sepsis + ARDS,
  - Sepsis + CAP
- Not TO
  - ACTH responders, ie delta cortisol>9µg/dl

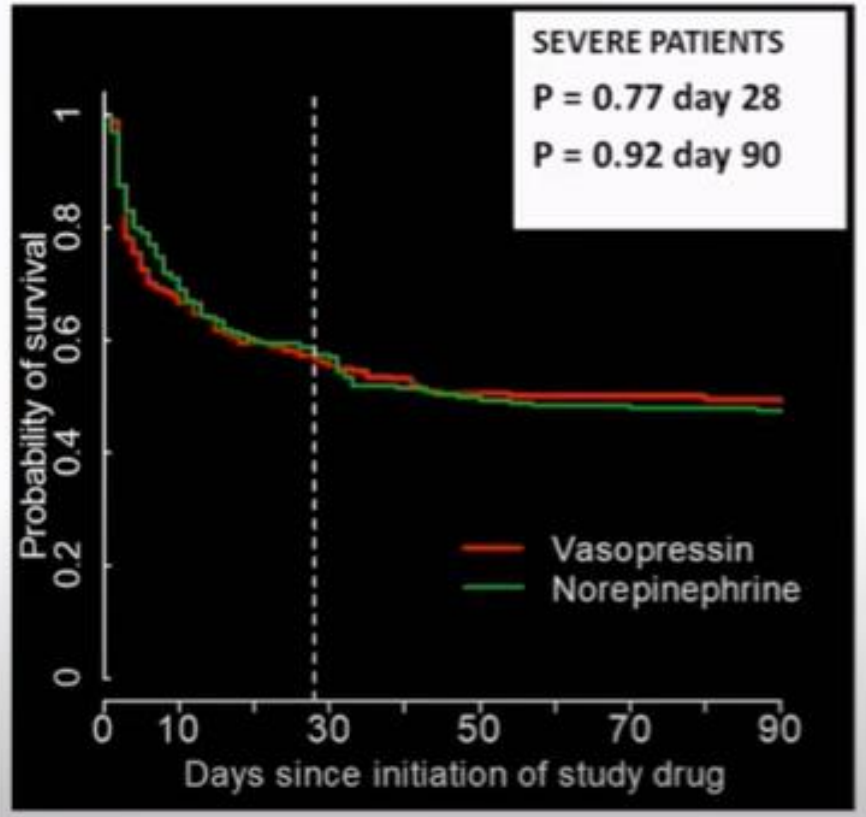
INTERET DE LA VASOPRESSINE DANS LE CHOC REFRACTAIRE

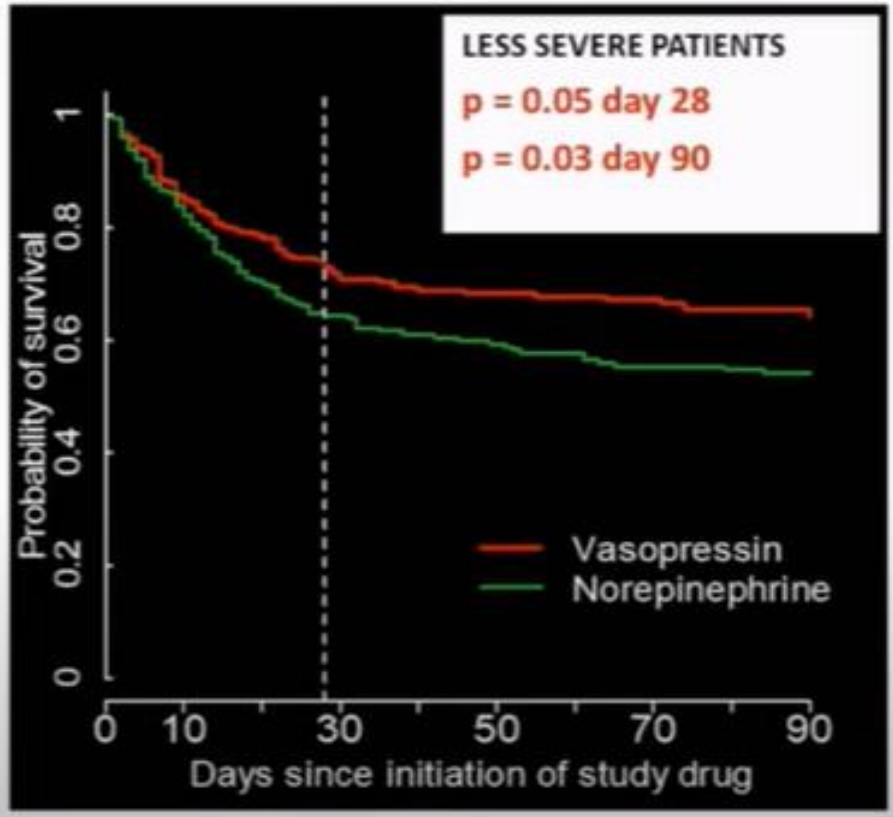
Vasopressin in (refractory) septic shock

- Treatment of hypotension when patient is (refractory) hypotensive despite NE infusion.
- Less NE requirement (< impact on immune system) & less NE-induced side-effects (Less new-onset atrial fibrillation).
- Higher vasopressin response rate and better patient outcomes, including higher survival when combined at lower norepinephrine doses, lower lactate levels and higher arterial-pH levels.
- Less need for RRT for at risk patients.

The NEW ENGLAND JOURNAL of MEDICINE

Vasopressin vs. Norepinephrine in Septic Shock: A Randomized Controlled Trial



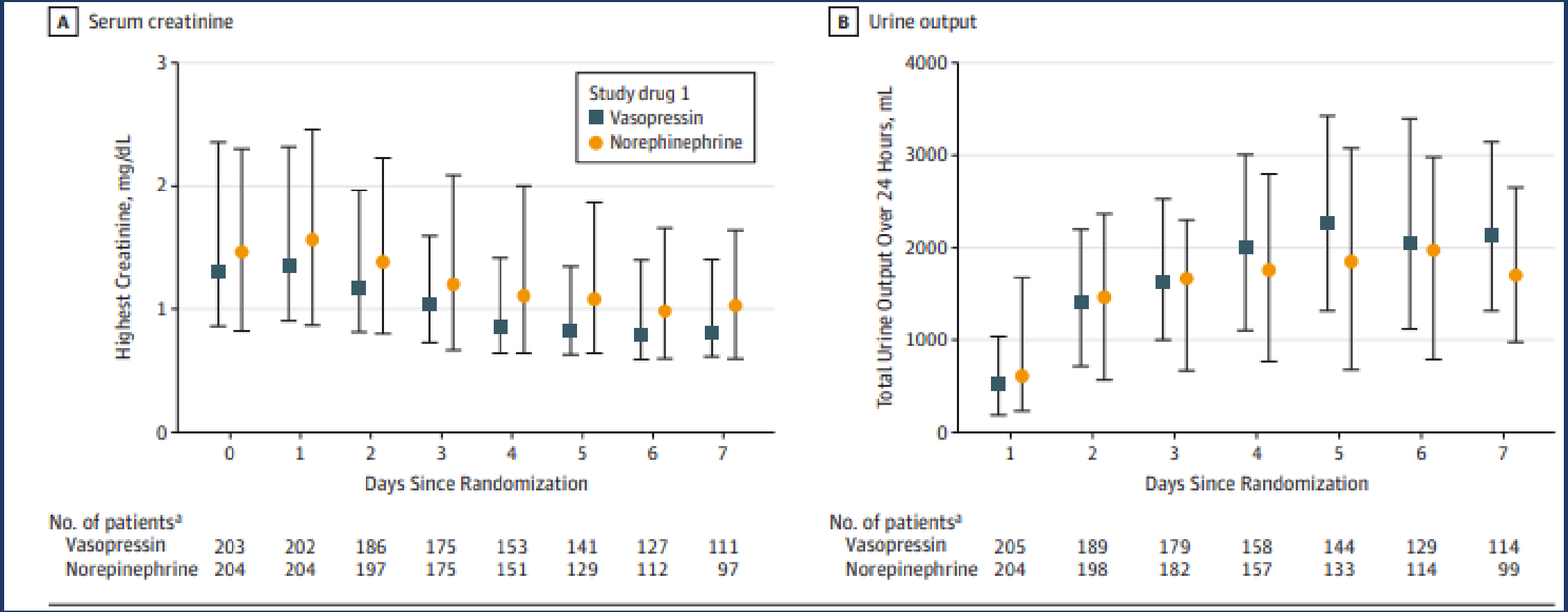


Less severe< 15mcg/mn

VASST TRIAL:VS+NAD vs NAD

Russell *et al* 2008;358:877

Gordon et al .Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock: The VANISH Randomized Clinical Trial. JAMA. 2016 Aug 2;316(5):509-18.



Pas de différence de mortalité entre les 2 groupes moins de dialyse dans le group vasopressine

The New England Journal of Medicine

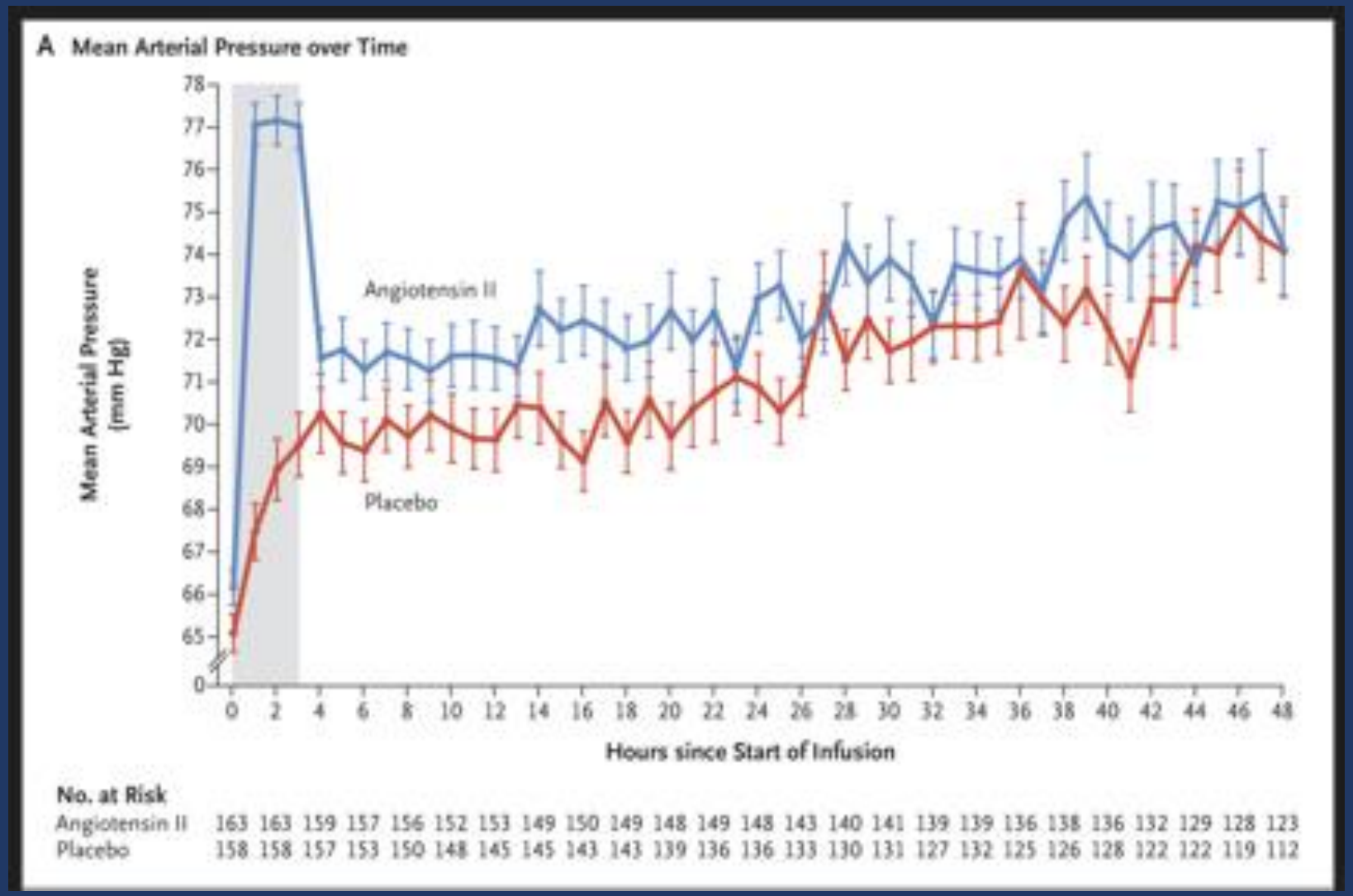
Angiotensin II for Vasodilatory Shock

KEY POINTS FROM

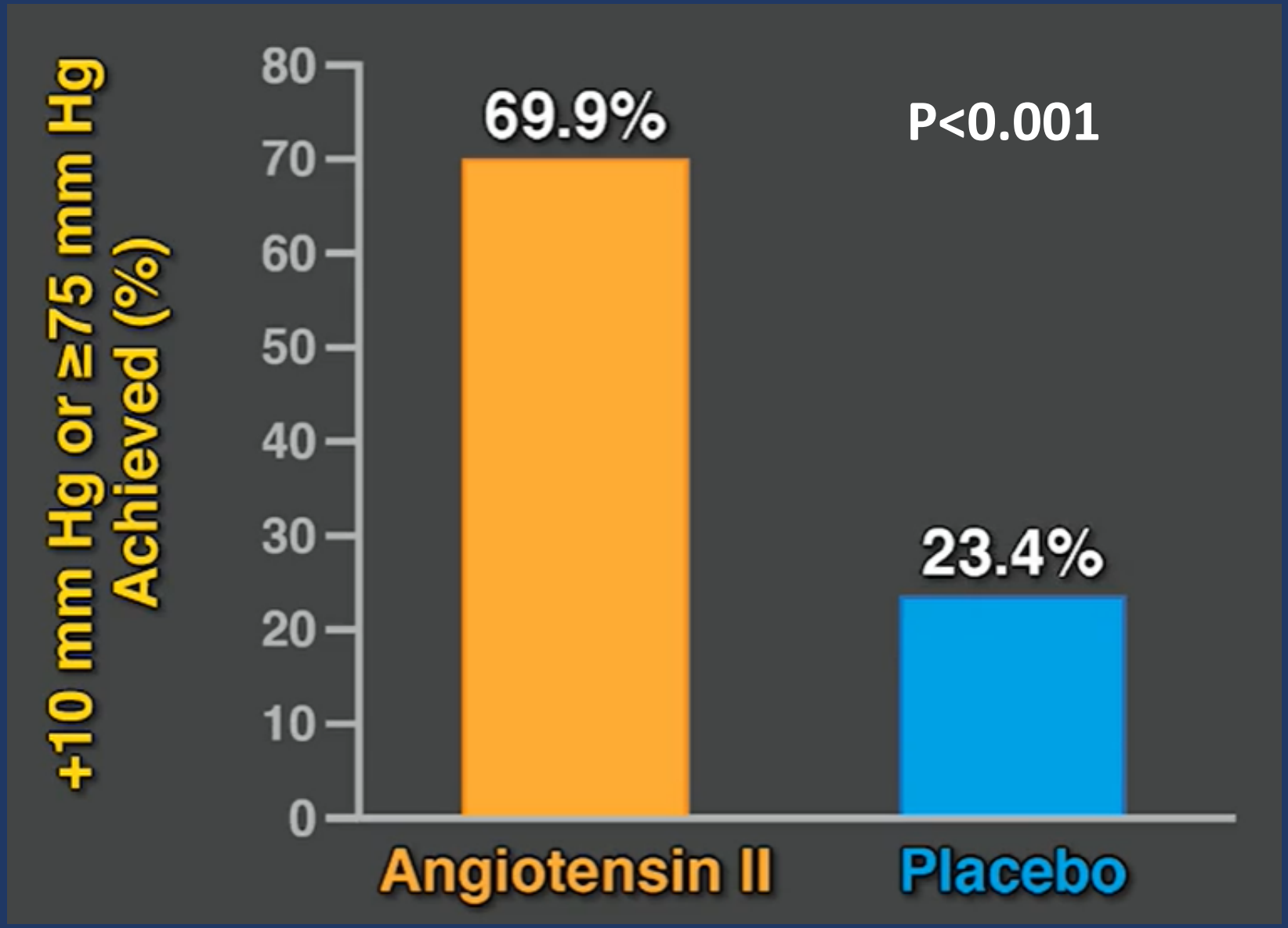
Angiotensin II for the Treatment of Vasodilatory Shock

by A. Khanna et al.

AUGUST 3, 2017


A Mean Arterial Pressure over Time
Mean Arterial Pressure (mm Hg)
78
77
76
75
74
73
72
71
70
69
68
67
66
65
0
Angiotensin II
Placebo
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48
Hours since Start of Infusion
No. at Risk
Angiotensin II 163 163 159 157 156 152 153 149 150 149 148 149 148 143 140 141 139 139 136 138 136 132 129 128 123
Placebo 158 158 157 153 150 148 145 145 143 143 139 136 136 133 130 131 127 132 125 126 128 122 122 119 112

ATHOS 3 TRIAL



Therapeutic effects of CytoSorb in septic shock

Critical Care

RESEARCH Open Access

Hemoadsorption by CytoSorb in septic patients: a case series

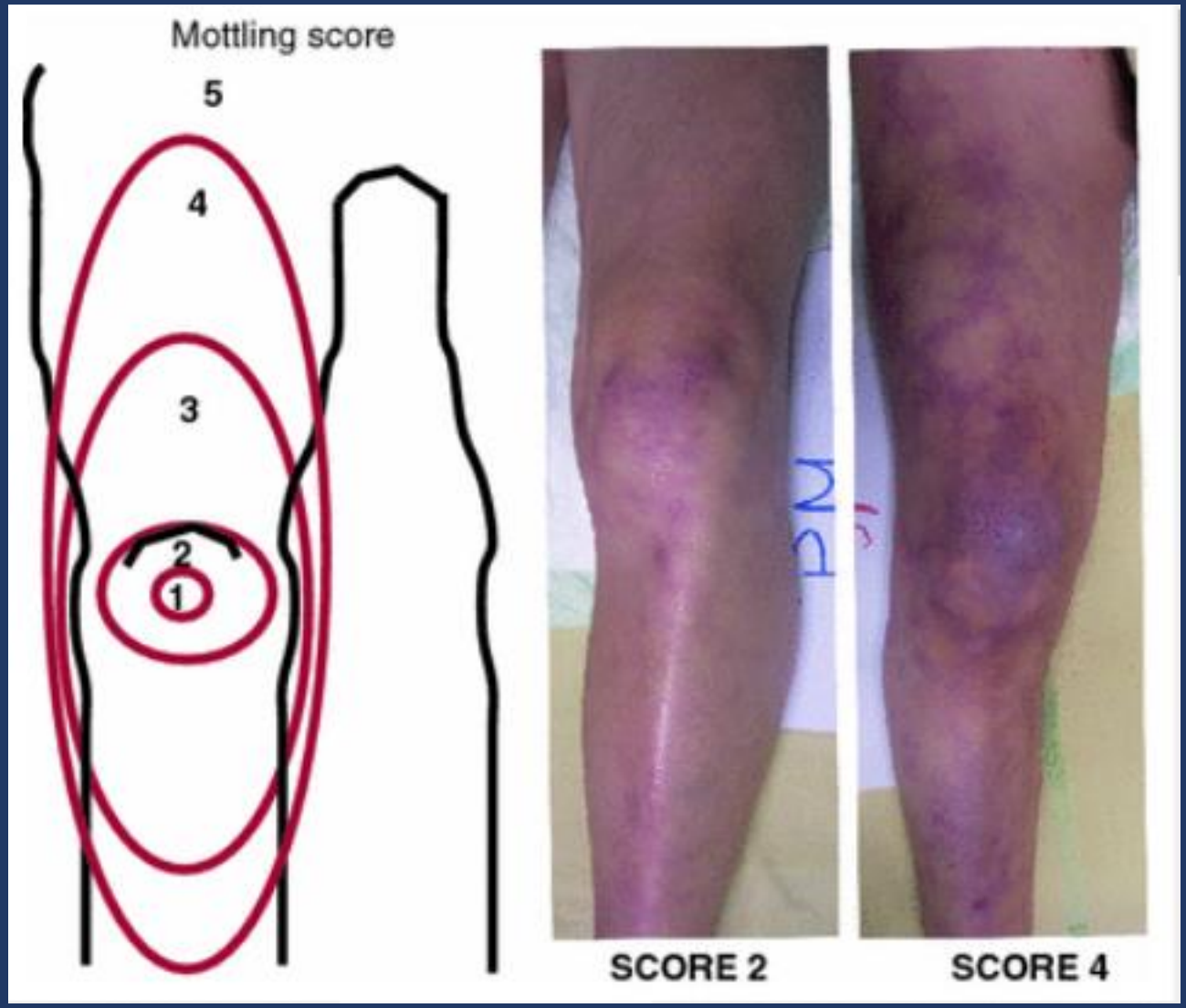
Klaus Kogelmann[*], Dominik Jarczak[2], Morten Scheller[1] and Matthias Drüner[1]

- 26 consecutive patients fulfilled the inclusion criteria (post-surgical; 13, pneumonia; 13)
- Both vasopressor and lactate levels showed a sustained reduction even beyond 72 hrs after the last CytoSorb treatment
- SAPS II decreased by 18.1% and SOFA Score decreased by 4.1%
- **Actual mortality was lower than the mortality predicted by APACHE II.** These favorable effects seem to be more pronounced in patients where therapy started within 24 hours after the septic shock

EFFET FAVORABLE SI DEBUTE DANS LES 24H SUIVANT LE CHOC SEPTIQUE

MARQUEURS PRONOSTIC DU CHOC SEPTIQUE

MOTTLING SCORE : indicateur de perfusion tissulaire et valeur pronostique



G Dumas et al,Mottling score is a strong predictor of 14- day mortality in septic patients whatever vasopressor doses and other tissue perfusion parameters ***Crit Care 2019***

MOTTLING SCORE AT H-6

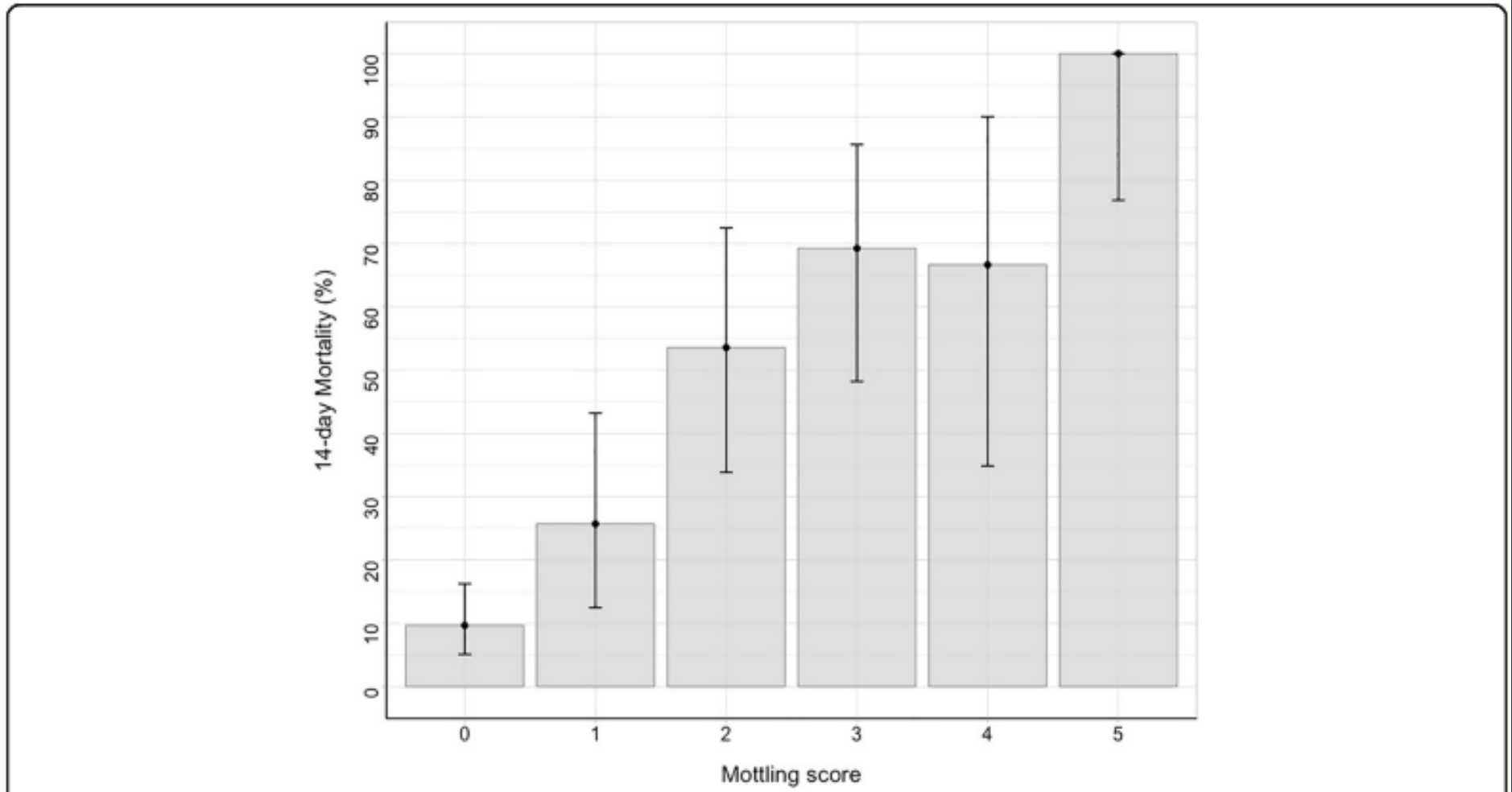


Fig. 1 14-day mortality according to mottling score value at H-6. Error-bars represent 95% confidence interval

G Dumas et al,Mottling score is a strong predictor of 14- day mortality in septic patients whatever vasopressor doses and other tissue perfusion parameters ***Crit Care 2019***

JAMA Network

QUESTION Does a resuscitation strategy targeting normalization of capillary refill time, compared with targeting serum lactate levels, reduce mortality in patients with septic shock?

CONCLUSION This randomized clinical trial of adults with septic shock found that use of a peripheral perfusion-targeted resuscitation strategy, compared with targeting serum lactate, did not significantly reduce mortality.

POPULATION

198 Men 226 Women

Adults in the ICU with septic shock

Mean age: 63 years

LOCATIONS

28 ICUs in 5 countries in South America

INTERVENTION

424 Patients randomized

212

Peripheral perfusion group

Resuscitation protocol of normalizing capillary refill time (measured in seconds)

212

Lactate group

Resuscitation protocol of normalizing or decreasing lactate levels (>20% per 2 hours)

PRIMARY OUTCOME

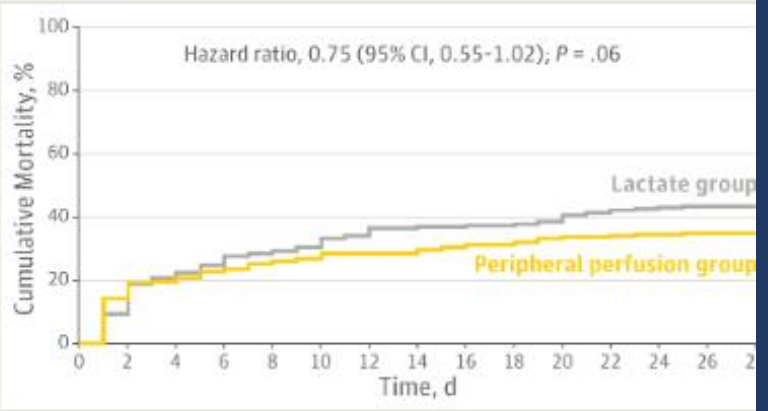
All-cause mortality at 28 days

FINDINGS

All-cause mortality at 28 days

Peripheral perfusion group 34.9% (74 patients died)

Lactate group 43.4% (92 patients die

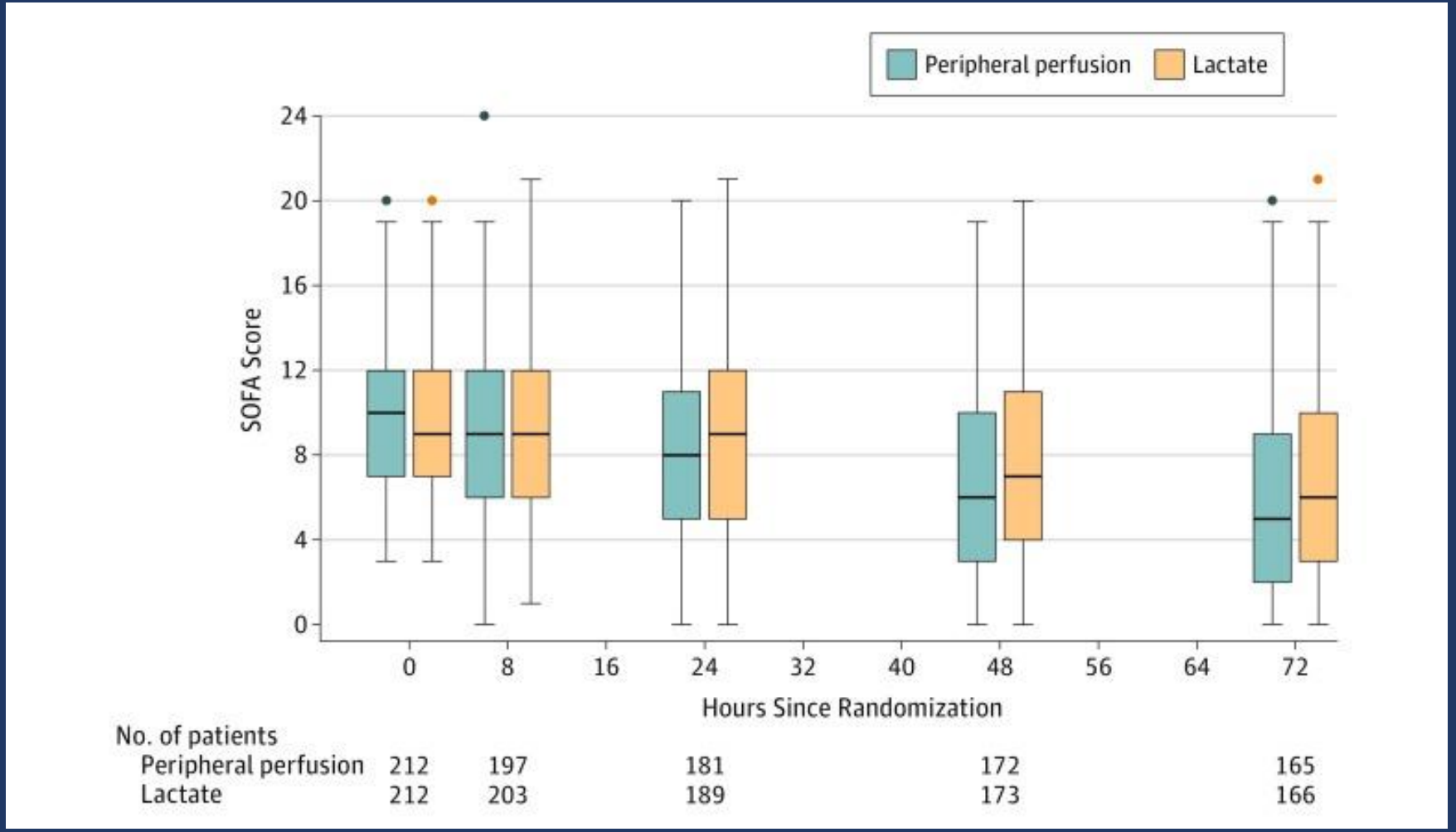


No significant risk difference between groups:

-8.5% (95% CI, -18.2% to 1.2%),

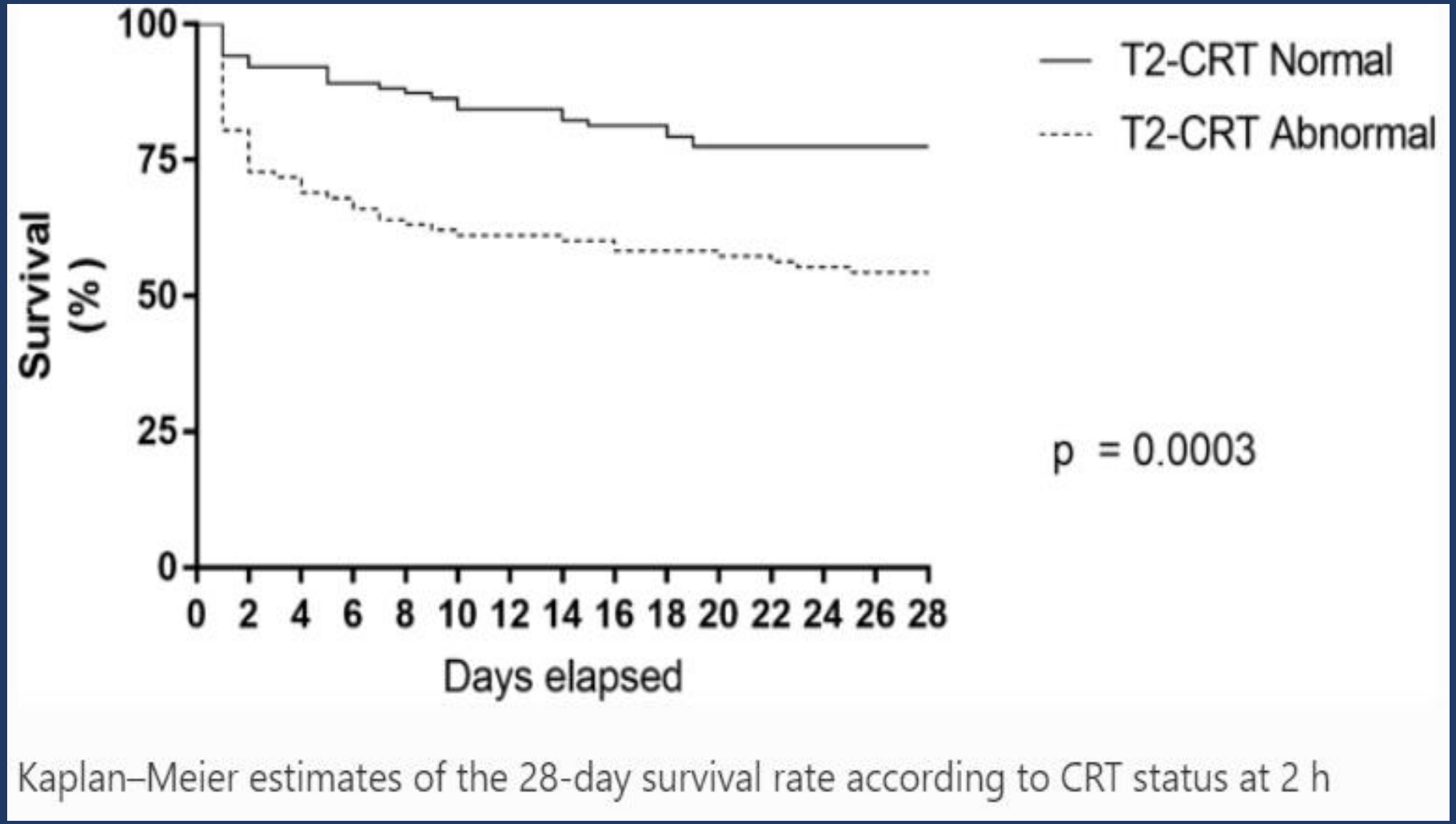
Hernandez et al Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28-Day Mortality Among Patients With Septic Shock: The ANDROMEDA-SHOCK Randomized Clinical Trial. JAMA. 2019

ANDROMEDA SHOCK TRIAL



No differences in global mortality but beneficial effects on SOFA score at 72h.
Lower 28 day mortality in the subgroup of patients with less severe organ dyfunction at baseline

CAPILLARY REFILL TIME : OUTIL EFFICACE ETMARQUEUR PRONOSTIC

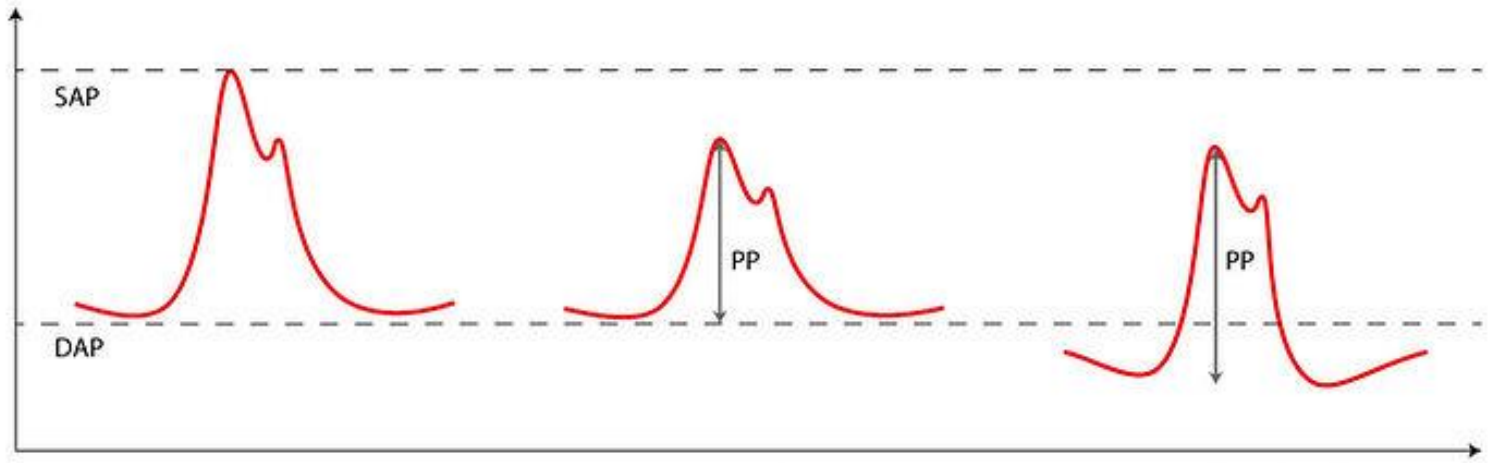


Kaplan–Meier estimates of the 28-day survival rate according to CRT status at 2 h

Hernandez et al 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. JAMA. 2019

DIASTOLIC SHOCK INDEX DSI = HR/DAP

Arterial Blood Pressure



DSI = HR / DAP

SAP: Systolic Arterial Pressure
DAP: Diastolic Arterial Pressure
PP: Pulse Pressure
HR: Heart Rate
DSI: Diastolic Shock Index

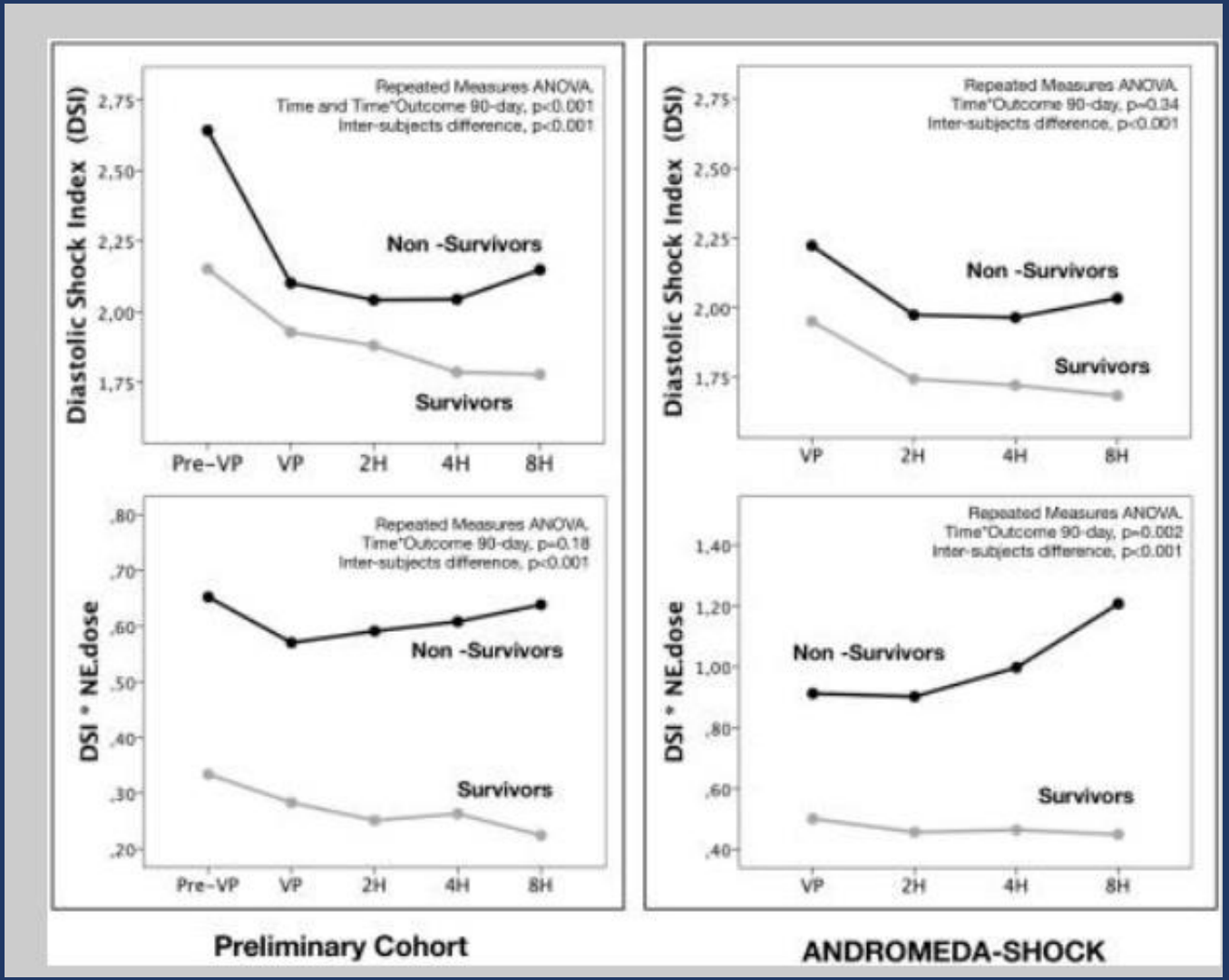
AVANTAGES DU DIASTOLIC SHOCK INDEX

Facilité de calcul

Outil dynamique

Prédictif de la gravité du choc septique et guide la prise en charge

DIASTOLIC SHOCK INDEX



DSI and DSI*NE.dose at 8 h showed again similar performances than SOFA score and lactate values, while mean arterial pressure, diastolic arterial pressures and the systolic shock index depicted a poor performance to predict mortality at day-90

TAKE HOME MESSAGES

REMPLISSAGE VASCULAIRE ADEQUAT ET PERSONNALISE

CHOC REFRACTAIRE : VASOPRESSINE ET SI BESOIN ANGIOTENSIN II

EVALUATION DE L'HEMOADSORPTION DE CYTOKINES

INTERET DU MONITORAGE DES Lactates , SvCo2 , PvaCo2 gap ,MOTTLING SCORE, CRT ,DSI