Sepsis/Choc septique
Cas clinique interactif

Enseignement national DES Maladies Infectieuses

28 mars 2023

P.E. Charles

Médecine Intensive Réanimation – CHU DIJON

pierre-emmanuel.charles@chu-dijon.fr

M. M., 73 ans, se présente aux urgences pour difficultés respiratoires

- Antécédents:
  - Diabète de type 2
  - HTA
  - Insuffisance rénale chronique (néphroangiosclérose: créatininémie habituelle à 150 umol/L)

- Traitements habituels:
  - Amlodipine
  - Furosemide
  - Repaglinide

L’histoire commence 5 jours plus tôt…

- Dysurie, constipation inhabituelle, vomissements, « mal au dos »…
- Apparition secondaire d’un essoufflement
- *Température non prise*
- A la prise en charge au SAU:
  - Fc = 100 bpm
  - TA = 120/67 mmHg
  - FR = 33/min
  - T°=38.6°C
  - SpO2 = 93% sous 2 L/min aux lunettes

Examen clinique initial…

- CGS 15
- Dyspnée et polypnée: ne finit pas ses phrases
- Pas de marbrure, allongement du temps de recoloration cutané
- Abdomen souple et sensible
- Globe vésical (bladderScan: 700 mL)
- Champs pulmonaires libres

Q1: comment décrire et prendre en charge le patient selon les recommandations ?

A. Il existe un sepsis
B. Il existe un syndrome de réponse inflammatoire systémique donc un sepsis
C. Le patient présente une suspicion d'infection sans signe de gravité
D. Un remplissage vasculaire doit être débuté sans délai car le patient est tachycarde
E. Une antibiothérapie doit être débutée sans délai après prélèvement des hémocultures et d'un ECBU

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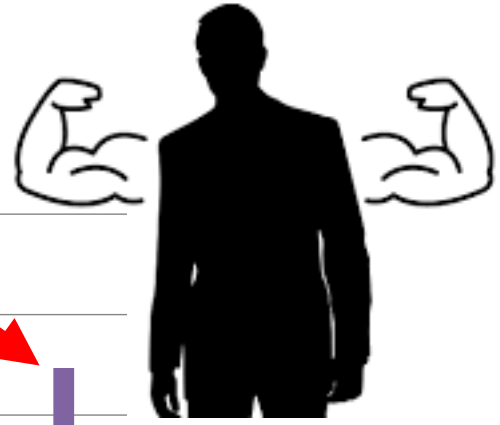
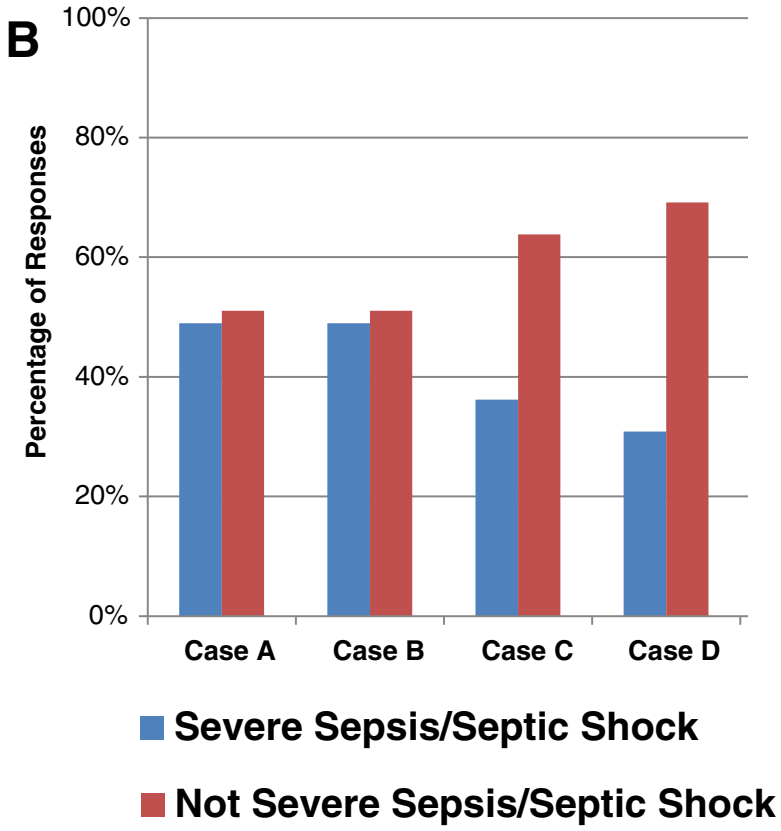
Diagnosing sepsis is subjective and highly variable: a survey of intensivists using case vignettes





Rhee *et al*. Crit Care 2018

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

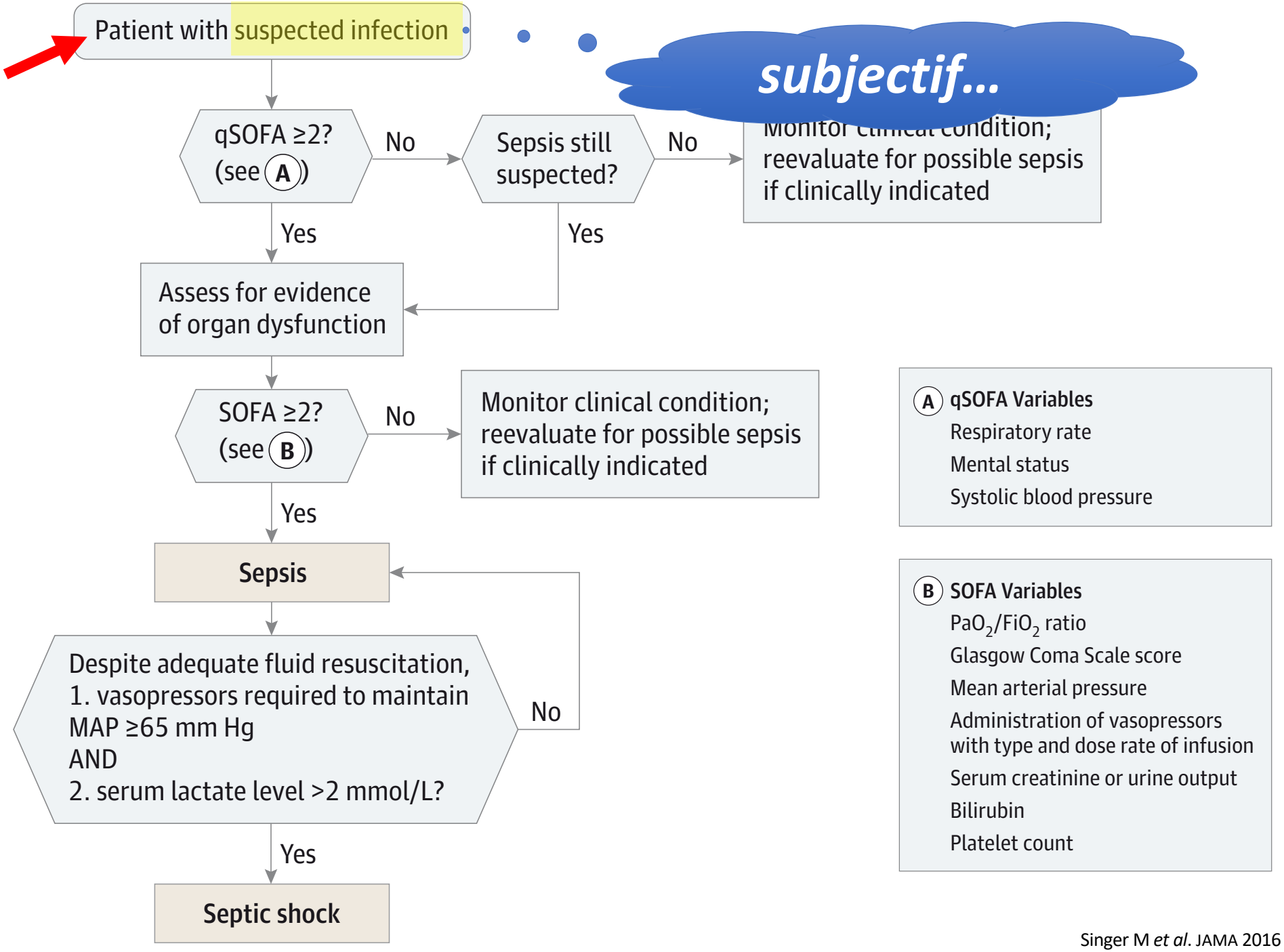
Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥22/min

Altered mentation

Systolic blood pressure ≤100 mm Hg

Singer M *et al*. JAMA 2016

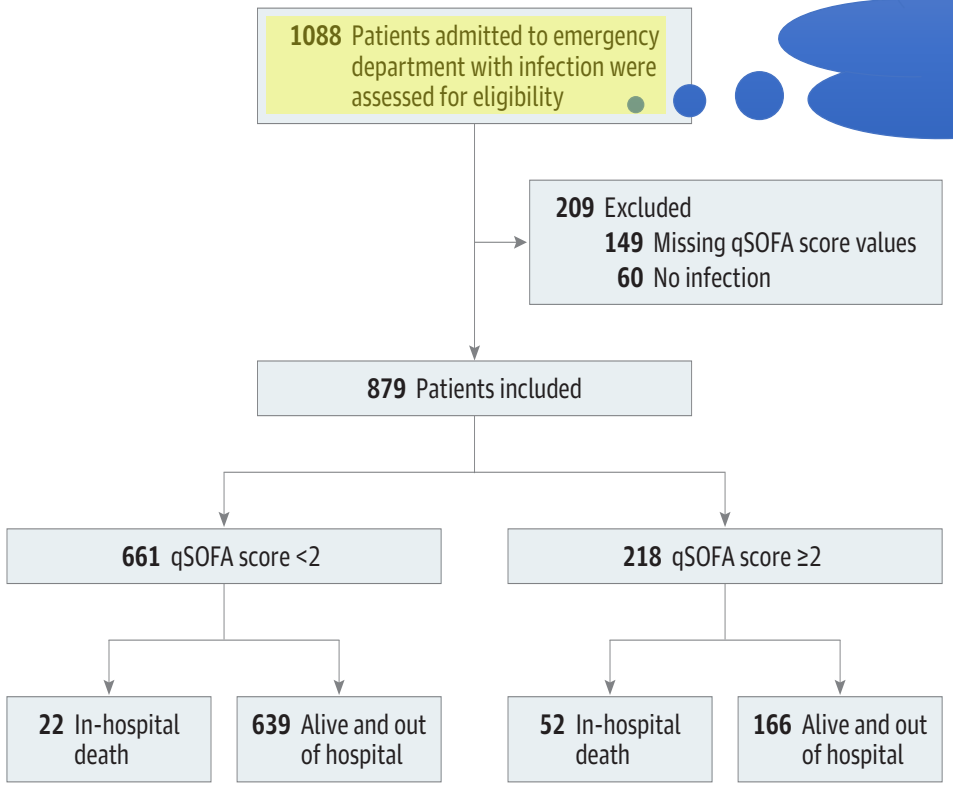


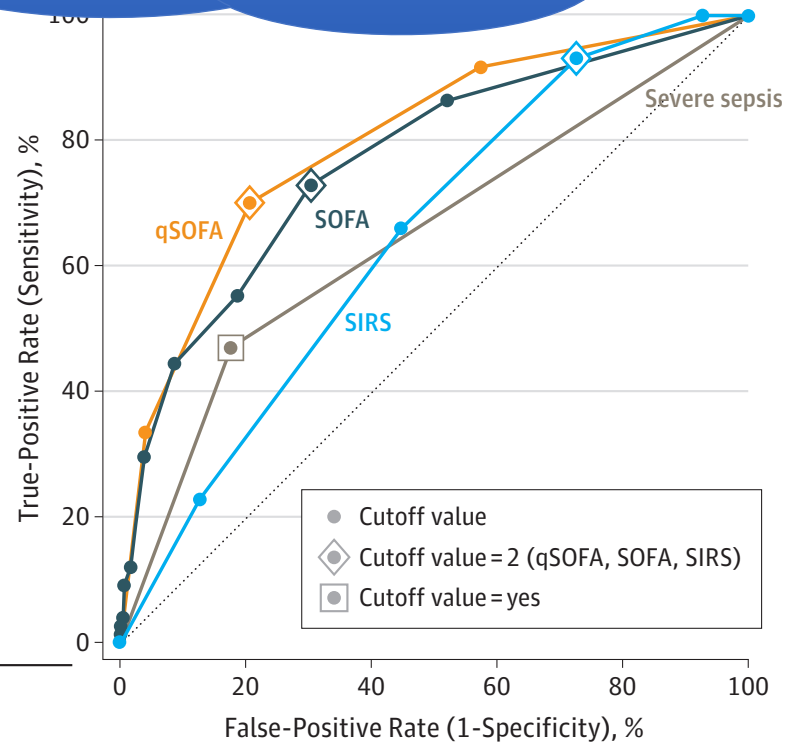
Singer M *et al*. JAMA 2016

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Prognostic Accuracy of Sepsis-3 Criteria for In-Hospital Mortality Among Patients With Suspected Infection Presenting to the Emergency Department

Diagnostic rétrospectif de l'infection …

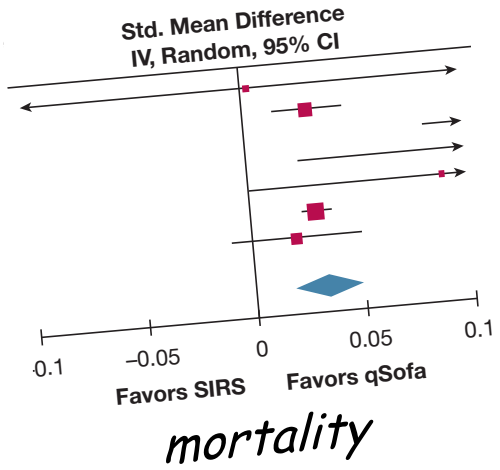


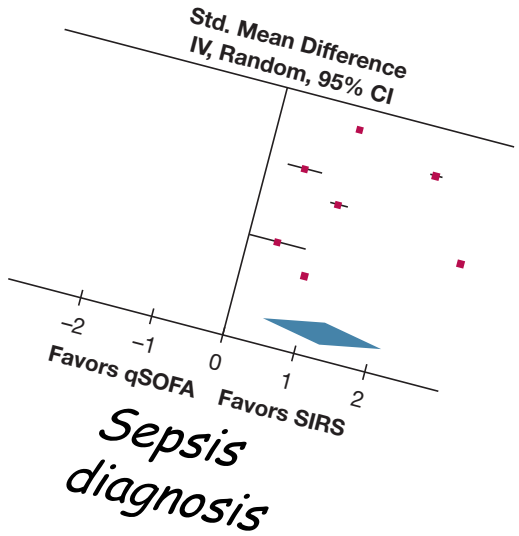


Freund *et al*. JAMA 2017

A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality

A Systematic Review and Meta-Analysis





Sensibilité qSOFA…

Recommendation
2. We **recommend against** using qSOFA compared with SIRS, NEWS, or MEWS as a single screening tool for sepsis or septic shock.
Strong recommendation, moderate-quality evidence.

Evans L *et al*. Crit Care Med 2021

Serafim R *et al*. Chest 2018

Le premier bilan biologique vous parvient…

- Hb = 13.4 g/dL
- GB = 1600/mm3
  - PNN = 780/mm^3
  - PNB = 0 /mm^3
  - PNE = 0 /mm^3
  - Lc = 360/mm^3
  - Monocytes = 100/mm^3
- Plaquettes = 133,000/mm^3

Na = 139 Meq/L

K = 4.3 Meq/L

Cl = 104 Meq/L

HCO3 = 18 Meq/L

Glycémie = 12.5 mmol/L

Urée = 27 mmol/L

Créatininémie = 403 micromol/L

Des **gaz du sang** et une **RP** sont également réalisés…

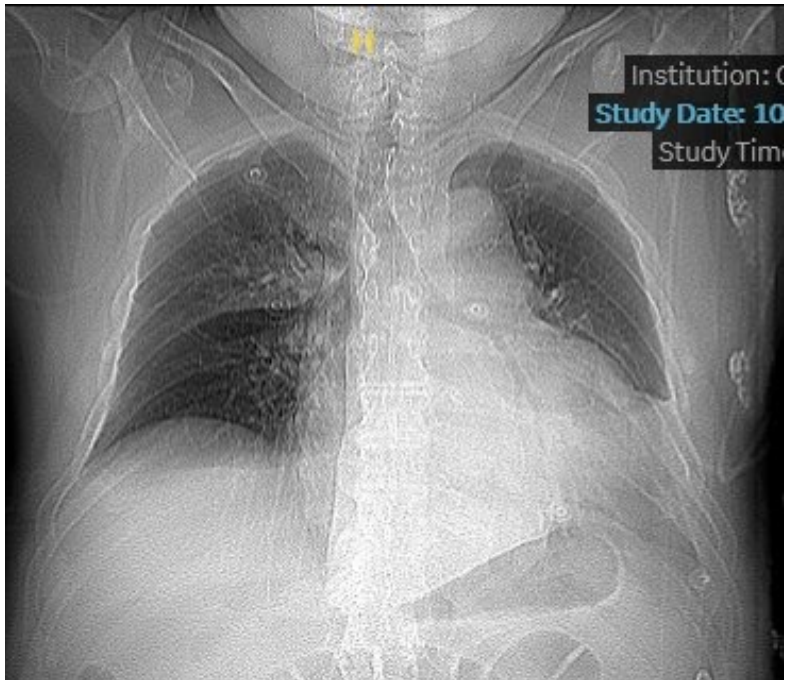
pH= 7.44

PaO2 = 61 mmHg

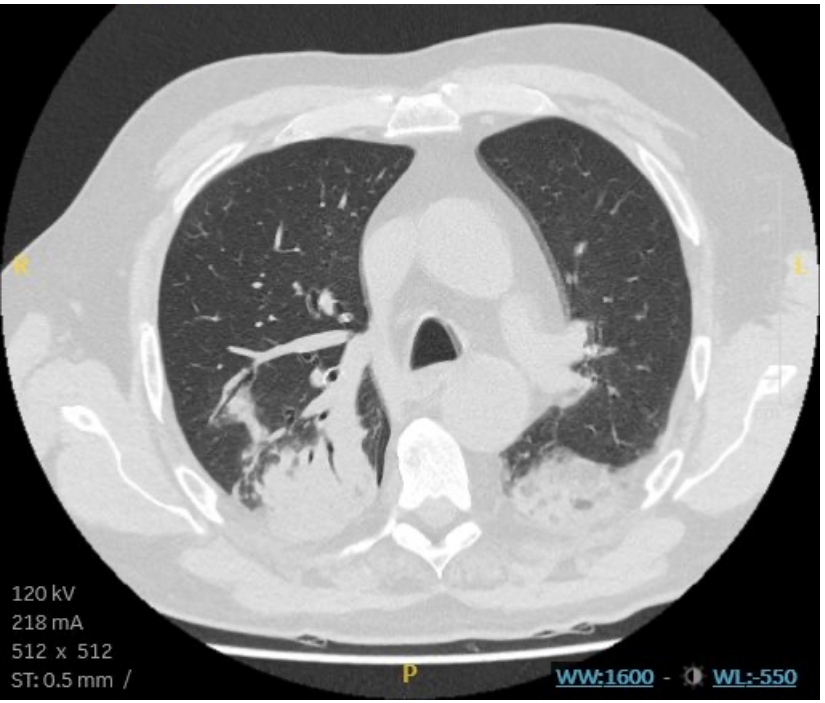
PaCO2 = 23 mmHg

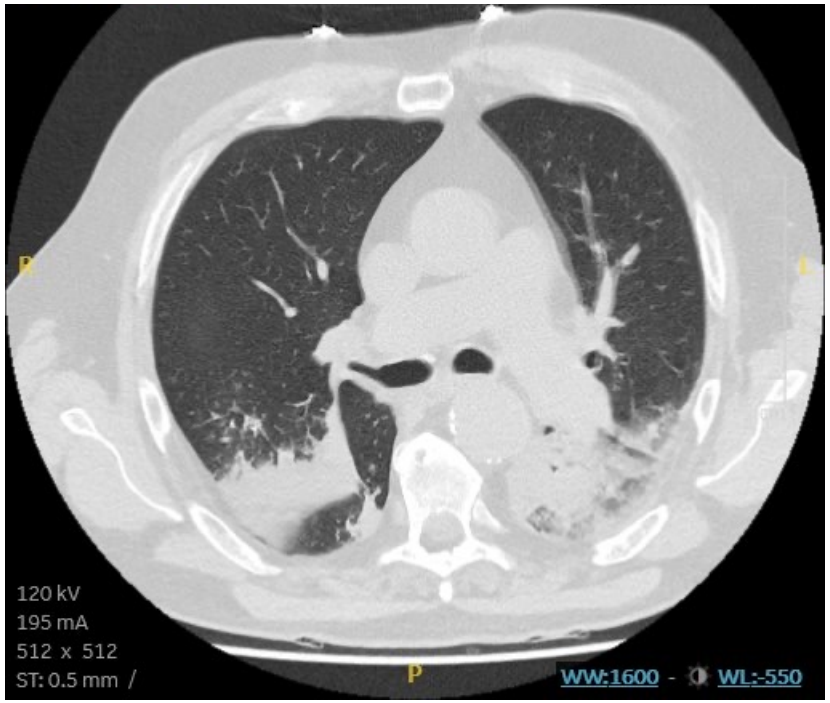
HCO3 = 17 Meq/L

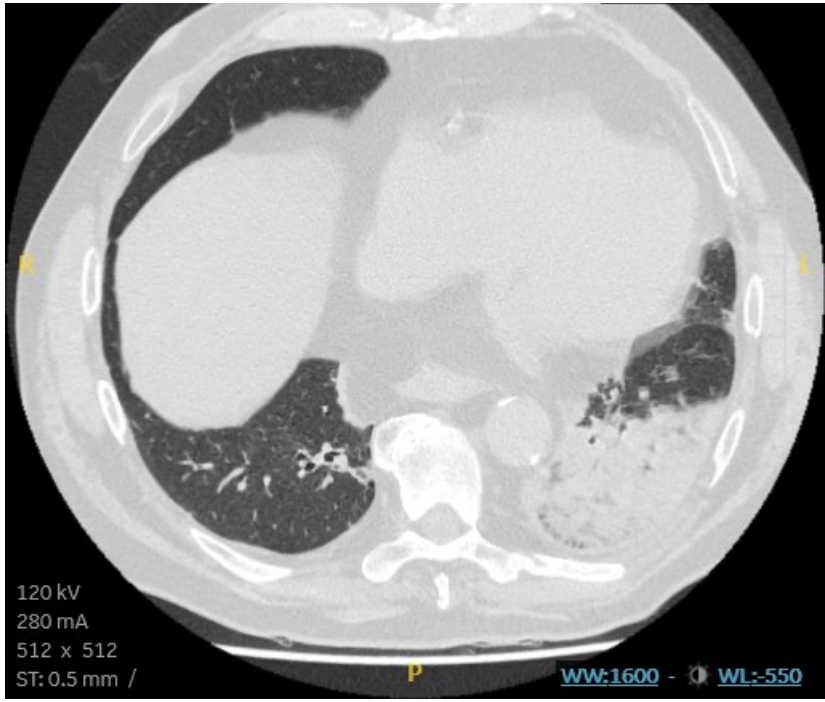
SpO2 = 92%



Ainsi qu’un **scanner thoracique**…







Q2. Avec ces nouveaux éléments, allez vous revoir votre jugement concernant la gravité du patient?

A. Oui car il existe des critères de gravité selon vous
B. Oui car il existe des critères de sepsis selon les recommandations
C. Non car il n’existe pas d’élément de gravité selon vous
D. Oui car il existe une neutropénie
E. Non car l’insuffisance rénale est fonctionnelle

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Score **SOFA**

System	Score 0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

6 points

Q3. Vous considérez désormais que le patient présente un sepsis. Qu’allez vous doser en urgence? (QROC)

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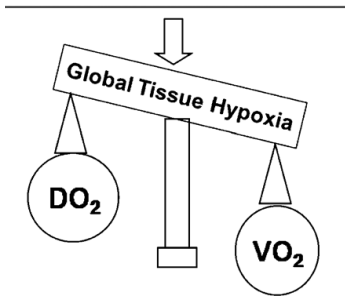
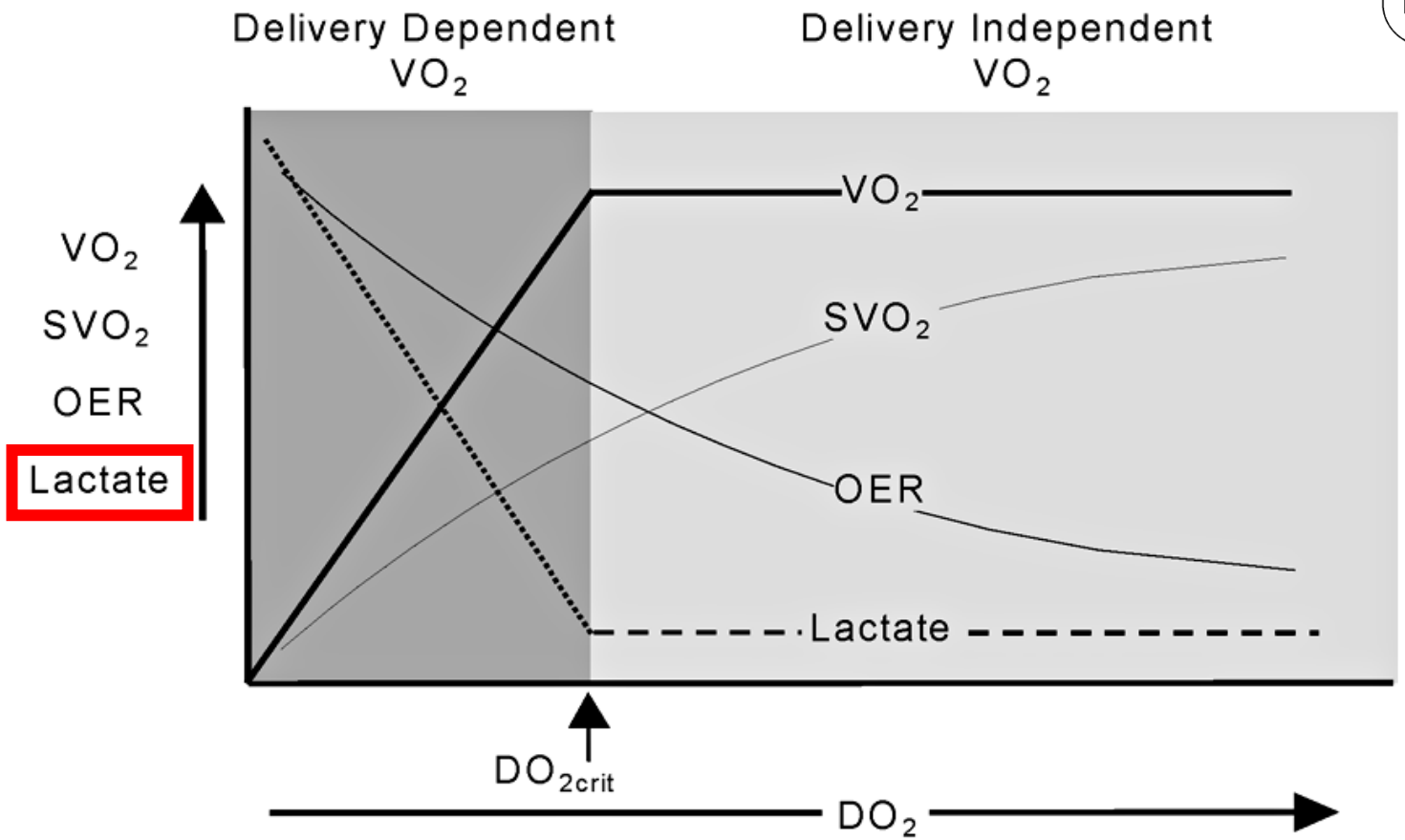
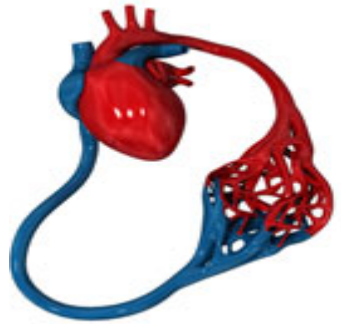
- Lactate (artériel ou veineux)

Insuffisance circulatoire aiguë: *inadéquation* VO_2/DO_2

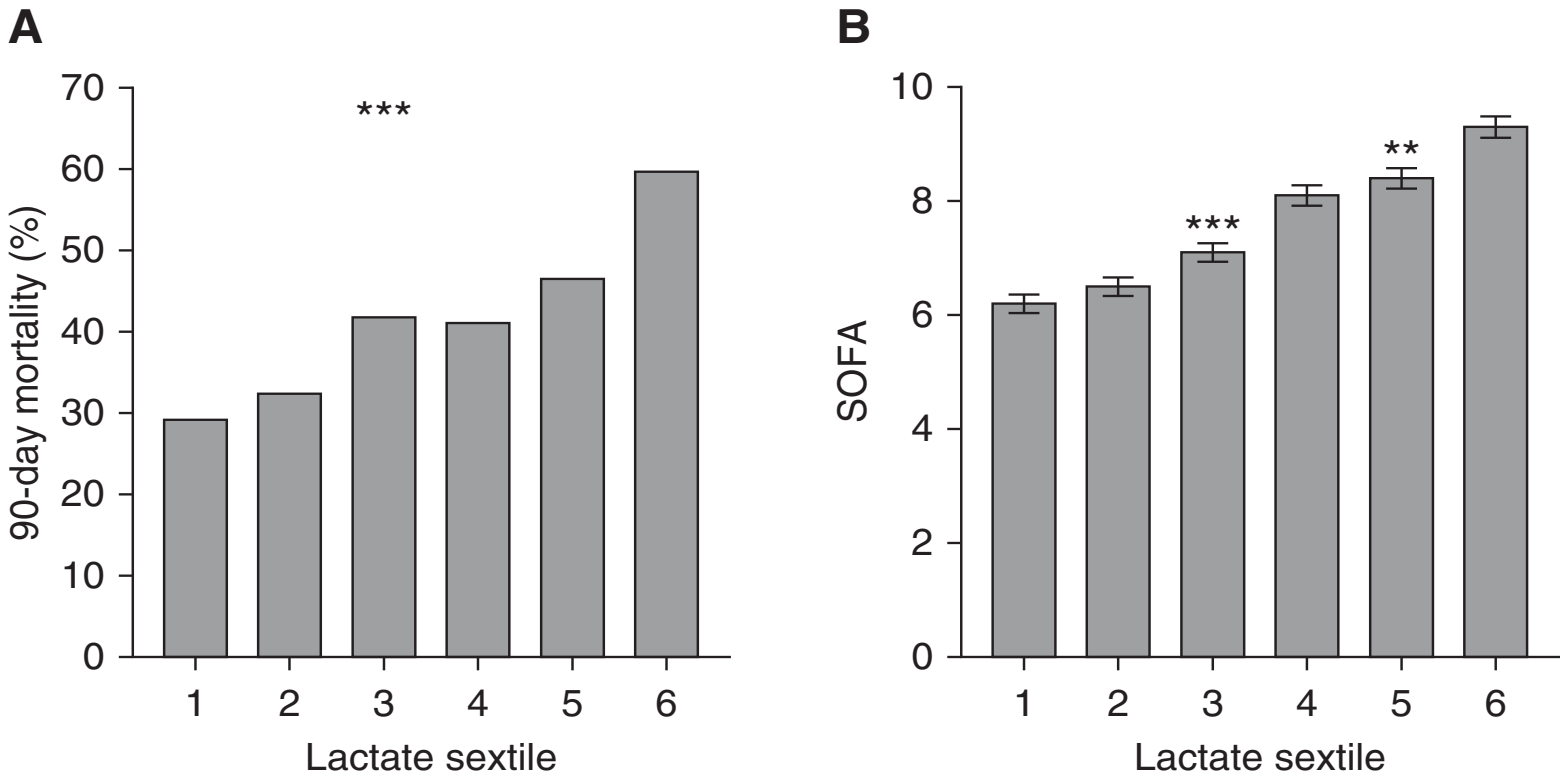




$DO_2 = Hb \times 1.36 \times SaO_2 \times Qc$



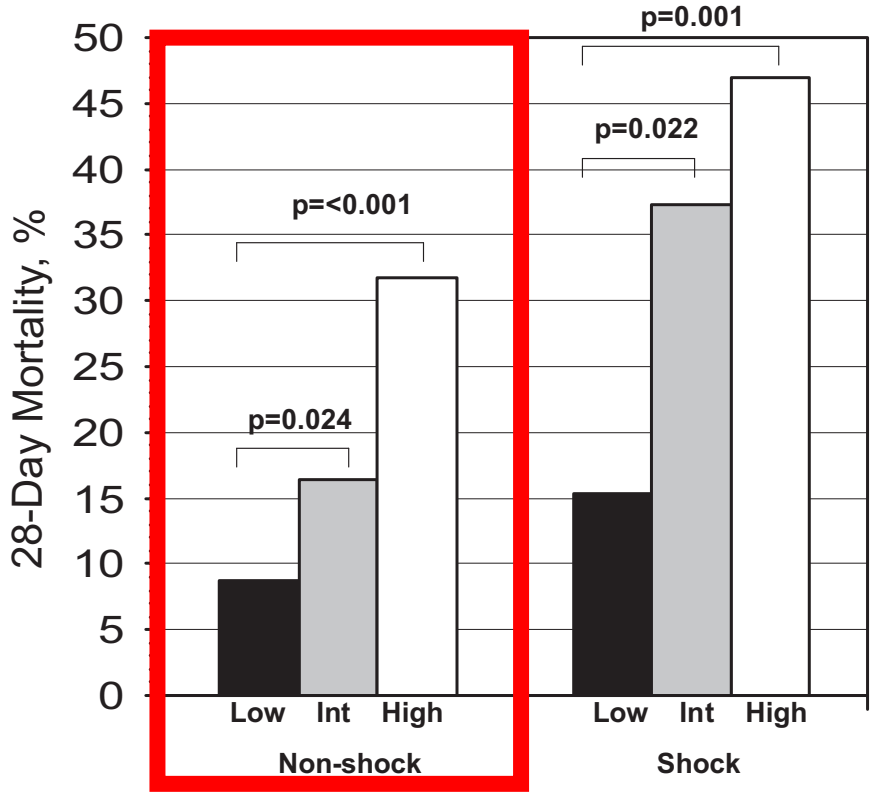
Hyperlactatémie et **sévérité** clinique



Gattinoni *et al*. Am J Respir Crit Care Med 2019

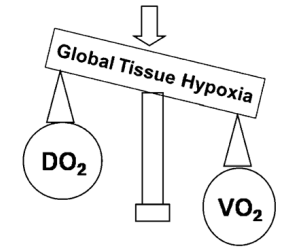
Lactate elevation …risk stratification

Même si tension conservée!!!



Mikkelsen M *et al*. Crit Care Med 2009

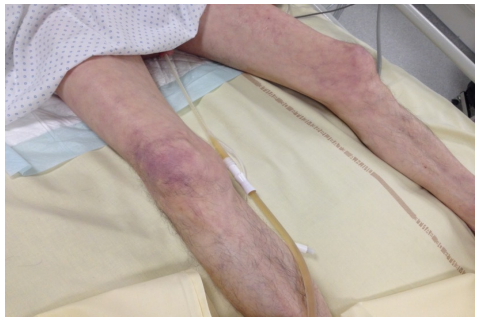
Evaluation hémodynamique



MACROCIRCULATION

- Pression artérielle
- Fréquence cardiaque
- Débit cardiaque
- *Pression veineuse centrale*

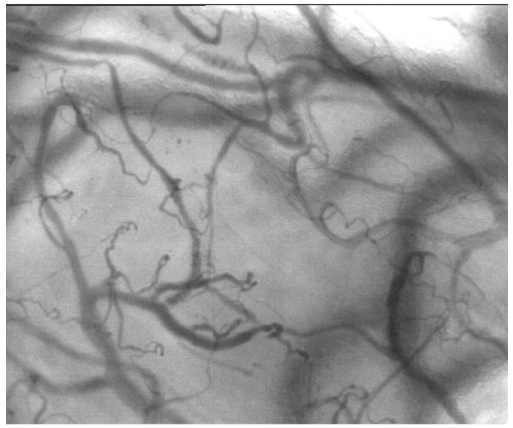
PERFUSION TISSULAIRE MICROCIRCULATION

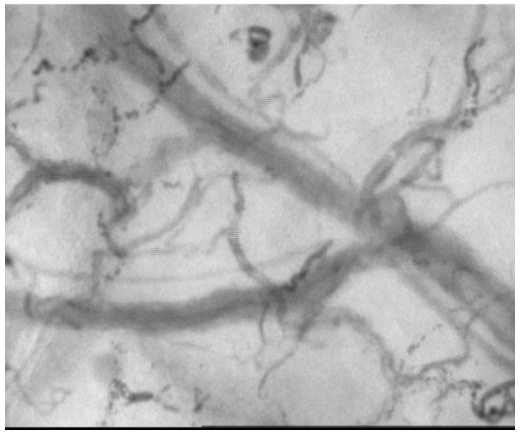


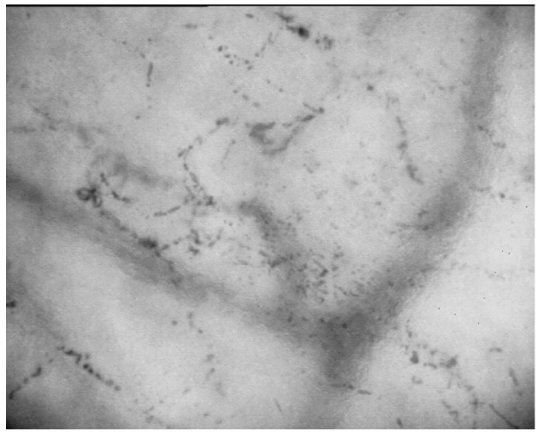
- Téguments
- Diurèse
- **Lactate**
- *$SvcO_2$*

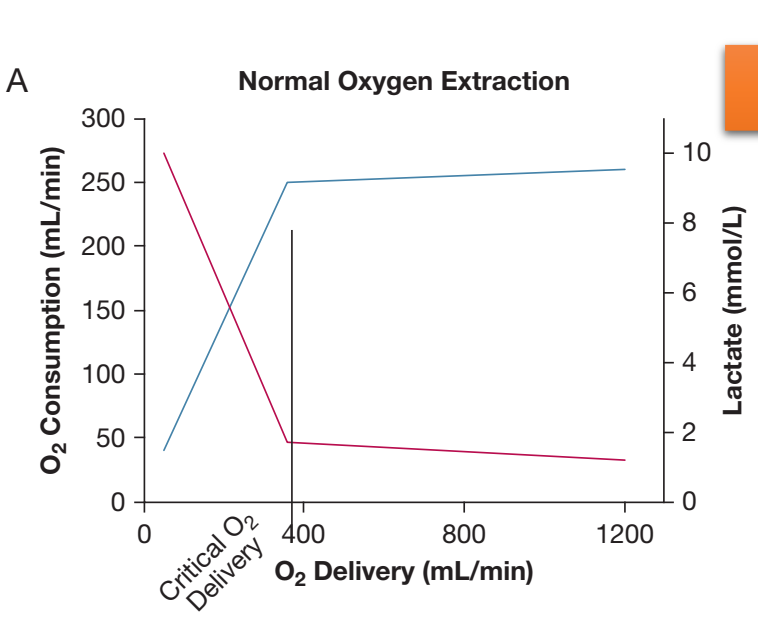
Discordances et manque de cohérence dans le sepsis…

Baisse **extraction** O_2…

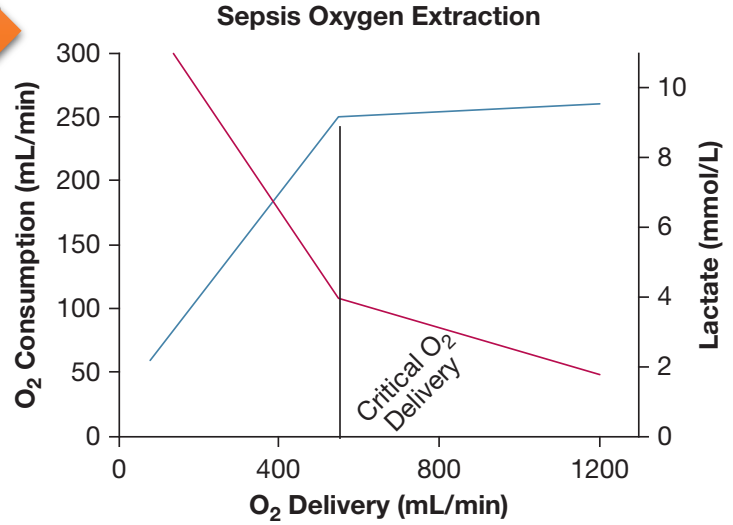




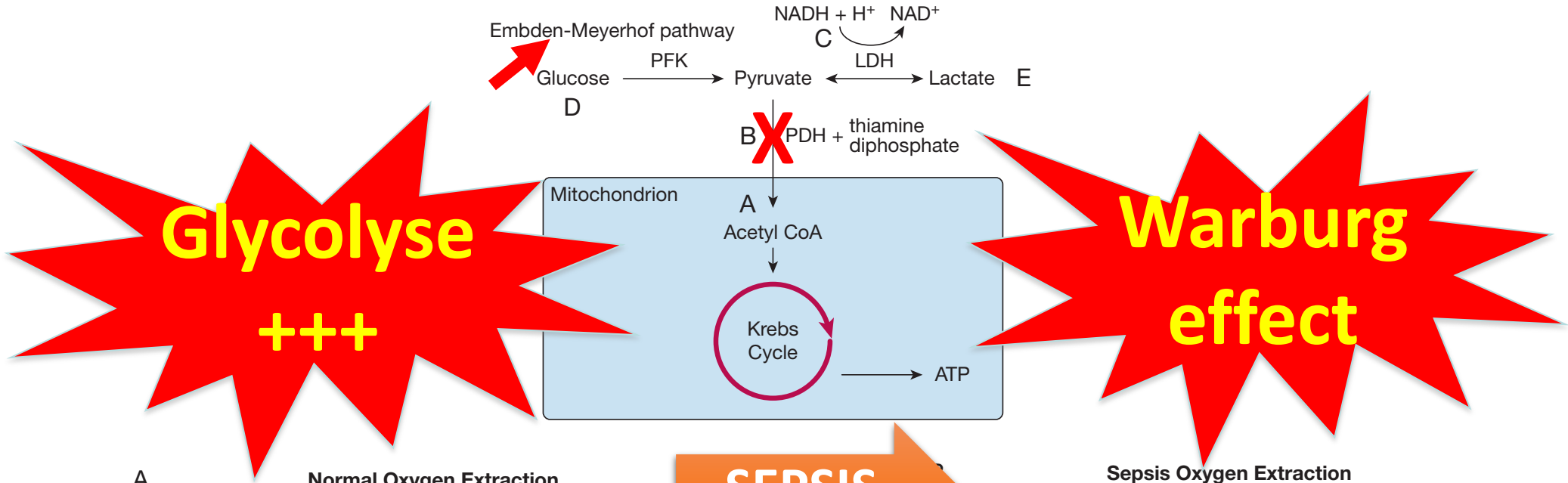


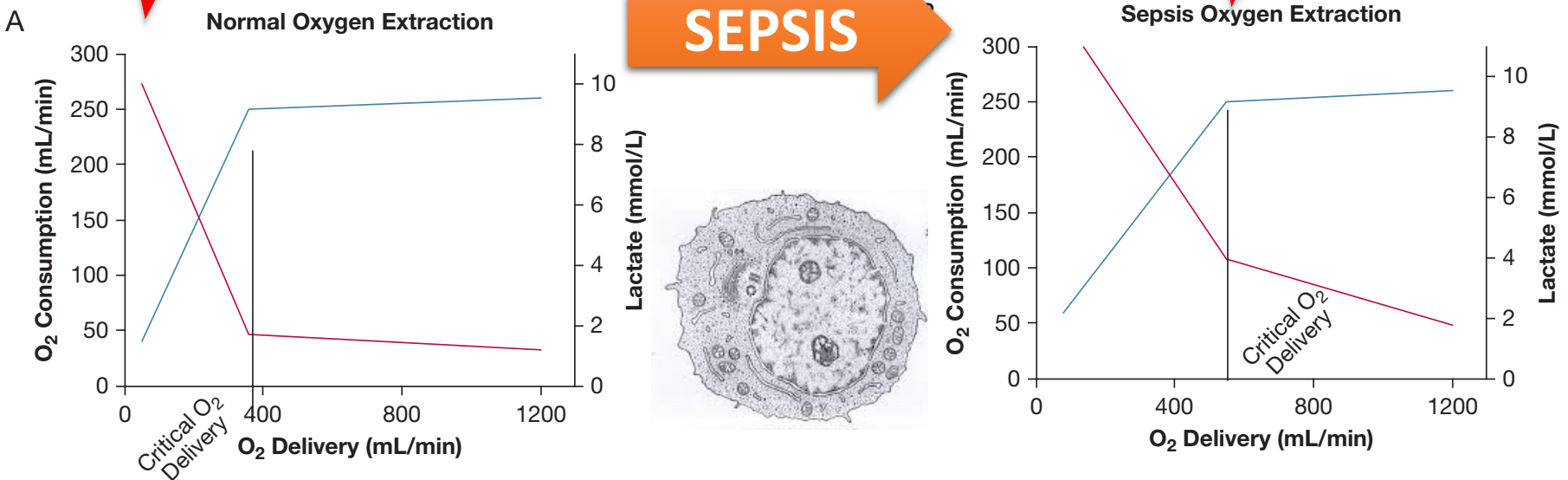


SEPSIS



Baisse **extraction** O_2...





Q4. La lactatémie est à 5.5 mmol/L. Quelle(s) doit(vent) désormais être votre(vos) priorité(s) dans l'heure?

A. Drainage des urines
B. Antibiothérapie adaptée
C. Remplissage vasculaire par soluté colloïde
D. Remplissage vasculaire par soluté cristalloïde
E. Mise sous noradrénaline

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SPECIAL EDITORIAL

The Surviving Sepsis Campaign Bundle: 2018 update

- Measure lactate level. Remeasure if initial lactate is >2 mmol/L.
- Obtain blood cultures prior to administration of antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of 30ml/kg crystalloid for hypotension or lactate ≥4 mmol/L.
- Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥65 mm Hg.

**"Time zero" or "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 anr elements of sepsis (formerly severe sepsis) or septic shock ascerta.*

Fig. 1 Hour-1 Surviving Sepsis Campaign Bundle of Care

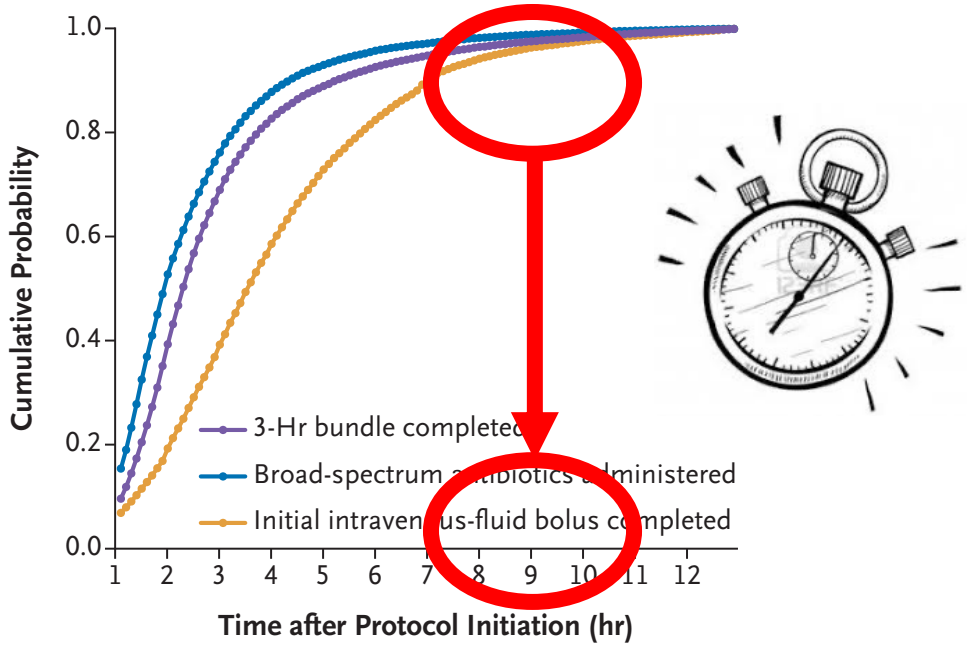
Dans l'heure!!!

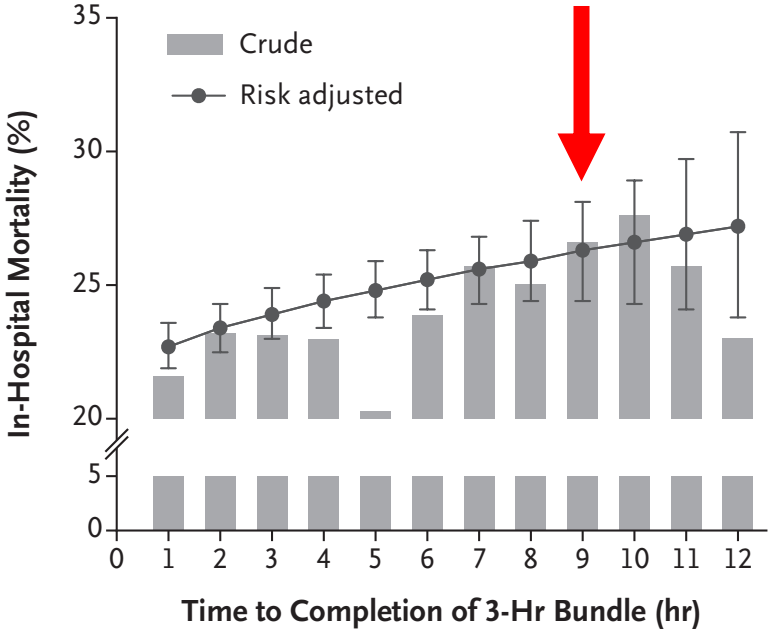
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

3-Hrs Bundle:
- **Broad spectrum ATB**
- **Blood culture collection**
- **Lactate measurement**

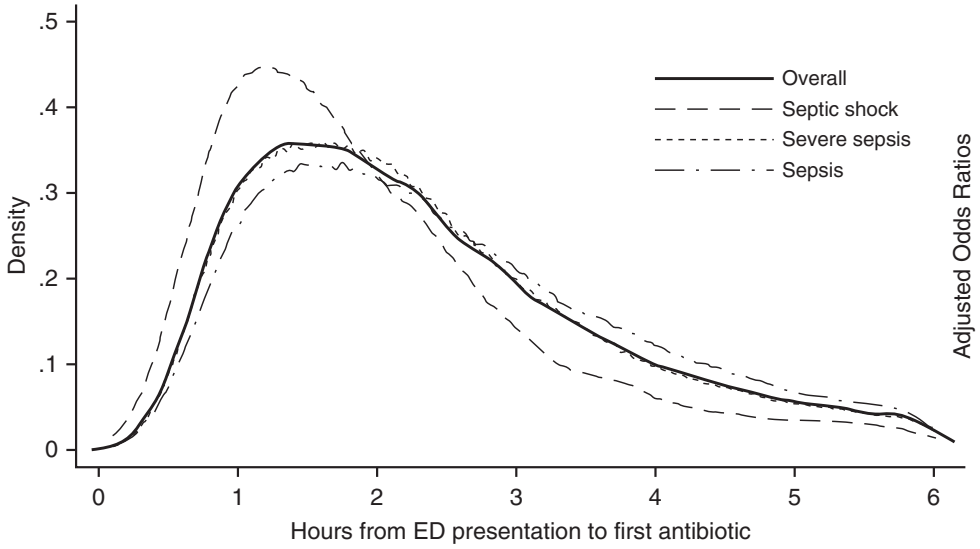


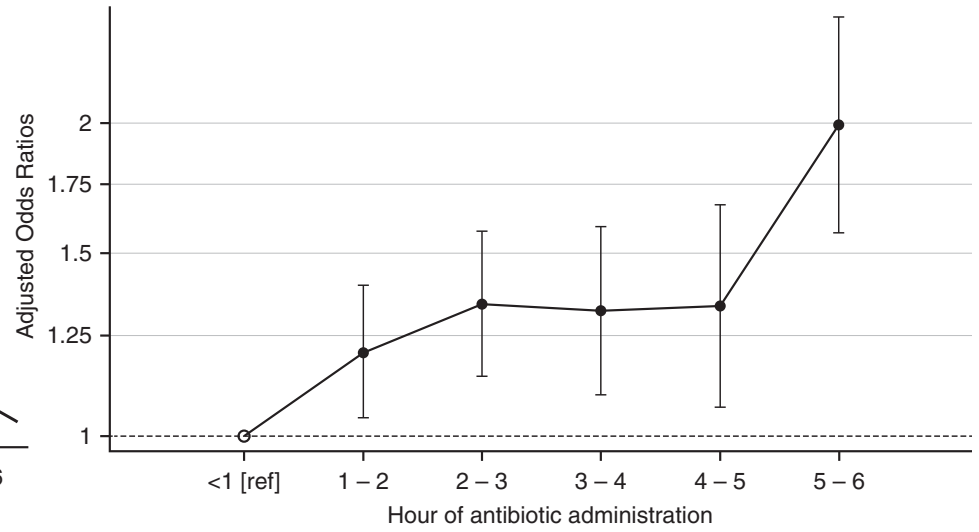


Seymour *et al*. N Eng J Med 2017

ORIGINAL ARTICLE

The Timing of Early Antibiotics and Hospital Mortality in Sepsis





Model	Odds Ratio for Hospital Mortality, per Elapsed Hour until Antibiotic Administration	95% CI	*P* Value
Unadjusted	0.89	0.86–0.91	<0.001
+ Sepsis severity strata	0.96	0.93–0.99	0.013
+ Severity of illness	1.08	1.04–1.12	<0.001
+ Demographics	1.09	1.05–1.13	<0.001
Fully adjusted model, in each subgroup			
Sepsis only	1.09	1.00–1.19	0.046
Severe sepsis only	1.07	1.01–1.24	0.014
Septic shock only	1.14	1.06–1.23	0.001

Liu VX *et al* Am J Respir Crit Care Med 2017

Q5. Le(s)quel(s) des solutés suivants allez vous utiliser du coup?

A. Sérum physiologique
B. Sérum hypersalé
C. Ringer lactate
D. Isofundine®
E. Glucosé à 5%

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Quel soluté **cristalloïde**?

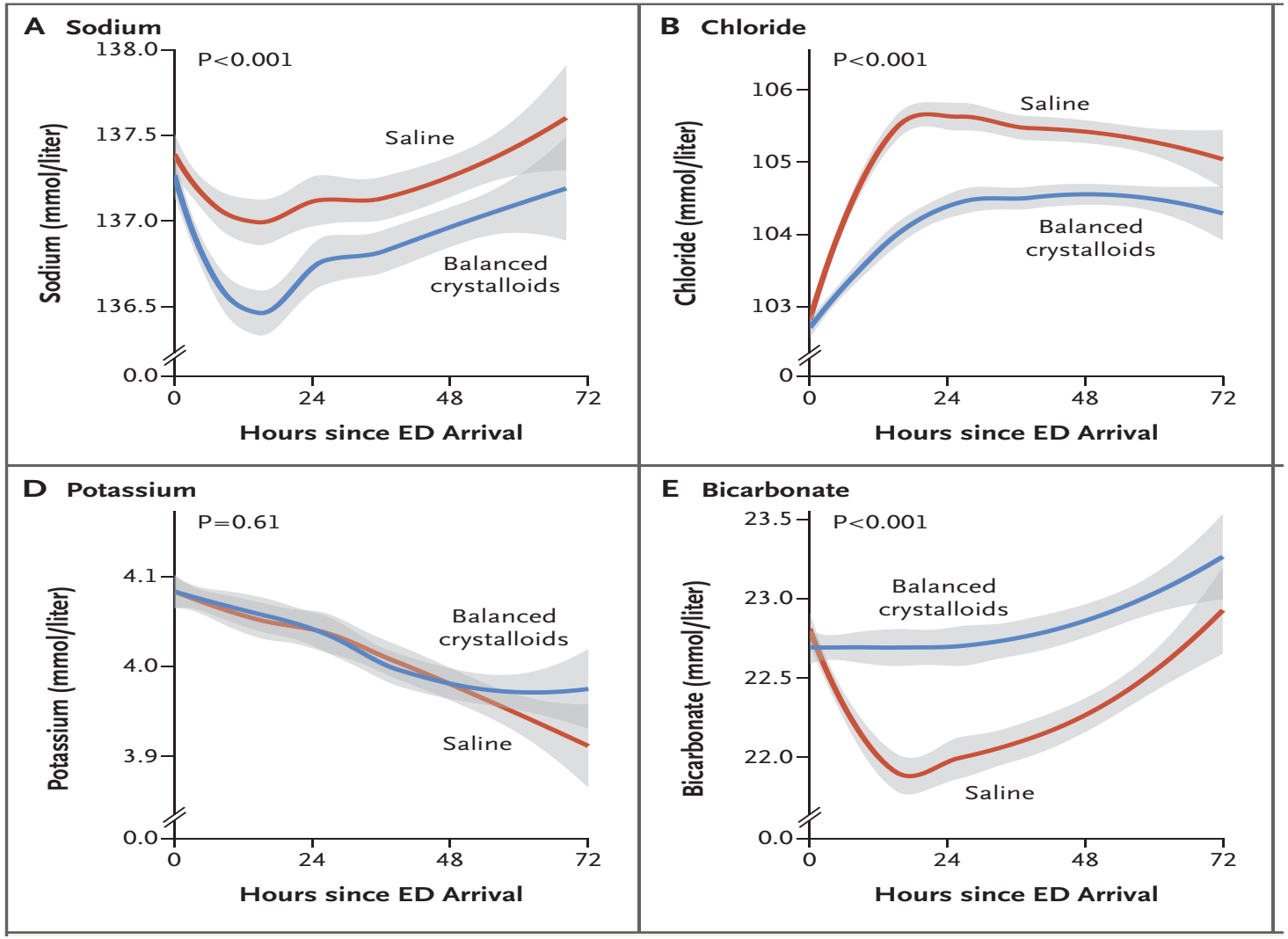
Le « physio » n'est pas physio!

Variable	Human plasma	Crystalloids		
		0.9% saline	Compounded sodium lactate	Balanced salt solution
Trade name		Normal saline	Hartmann's or Ringer's lactate	PlasmaLyte
Colloid source				
Osmolarity (mmol litre^{-1})	291	308	280.6	294
Sodium (mmol litre^{-1})	135–145	154	131	140
Potassium (mmol litre^{-1})	4.5–5.0		5.4	5.0
Calcium (mmol litre^{-1})	2.2–2.6		2.0	
Magnesium (mmol litre^{-1})	0.8–1.0			3.0
Chloride (mmol litre^{-1})	94–111	154	111	98

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Noncritically Ill Adults



Self WH et al New Eng J Med 2018

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Sepsis
A Secondary Analysis of the SMART Clinical Trial

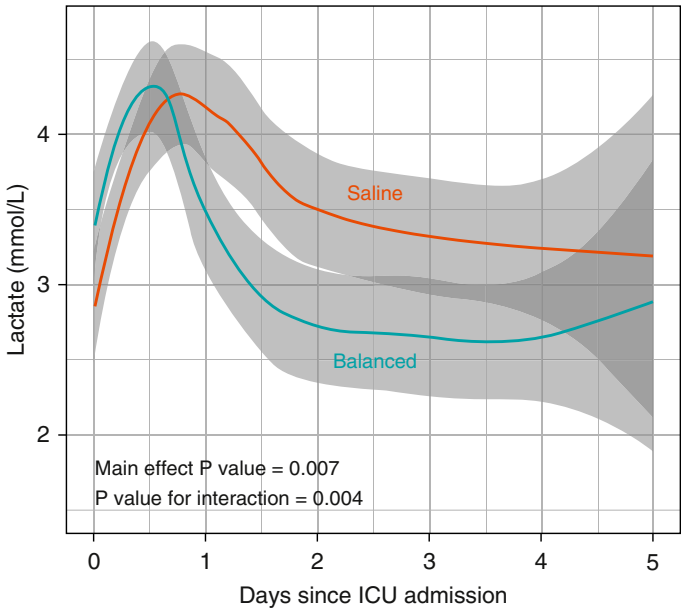
Clearance lactate plus rapide

Outcome*	*n*	Balanced Crystalloids (*n* = 824)	Saline (*n* = 817)	Adjusted OR (95% CI)†
Primary outcome				
30-d in-hospital mortality, *n* (%)	1,641	217 (26.3)	255 (31.2)	0.74 (0.59 to 0.93)
Additional renal outcomes§				
Major adverse kidney event within 30 d, *n* (%)‖	1,641	292 (35.4)	328 (40.1)	0.78 (0.63 to 0.97)

Recommendations

32. For adults with sepsis or septic shock, we **recommend** using crystalloids as first-line fluid for resuscitation.
Strong recommendation, moderate quality of evidence.

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



Evans L *et al*. Crit Care Med 2021
Brown *et al* Am J Respir Crit Care Med 2020

Vous prenez le temps de réexaminer le patient…

Q6. Quel volume de remplissage allez vous administrer durant les premières heures?

A. 30 mL/kg de solutés puis arrêt
B. Selon l’évolution du lactate
C. Selon des critères de précharge-dépendance
D. Selon l’augmentation de la pression artérielle
E. Selon l’évolution du temps de recoloration cutané

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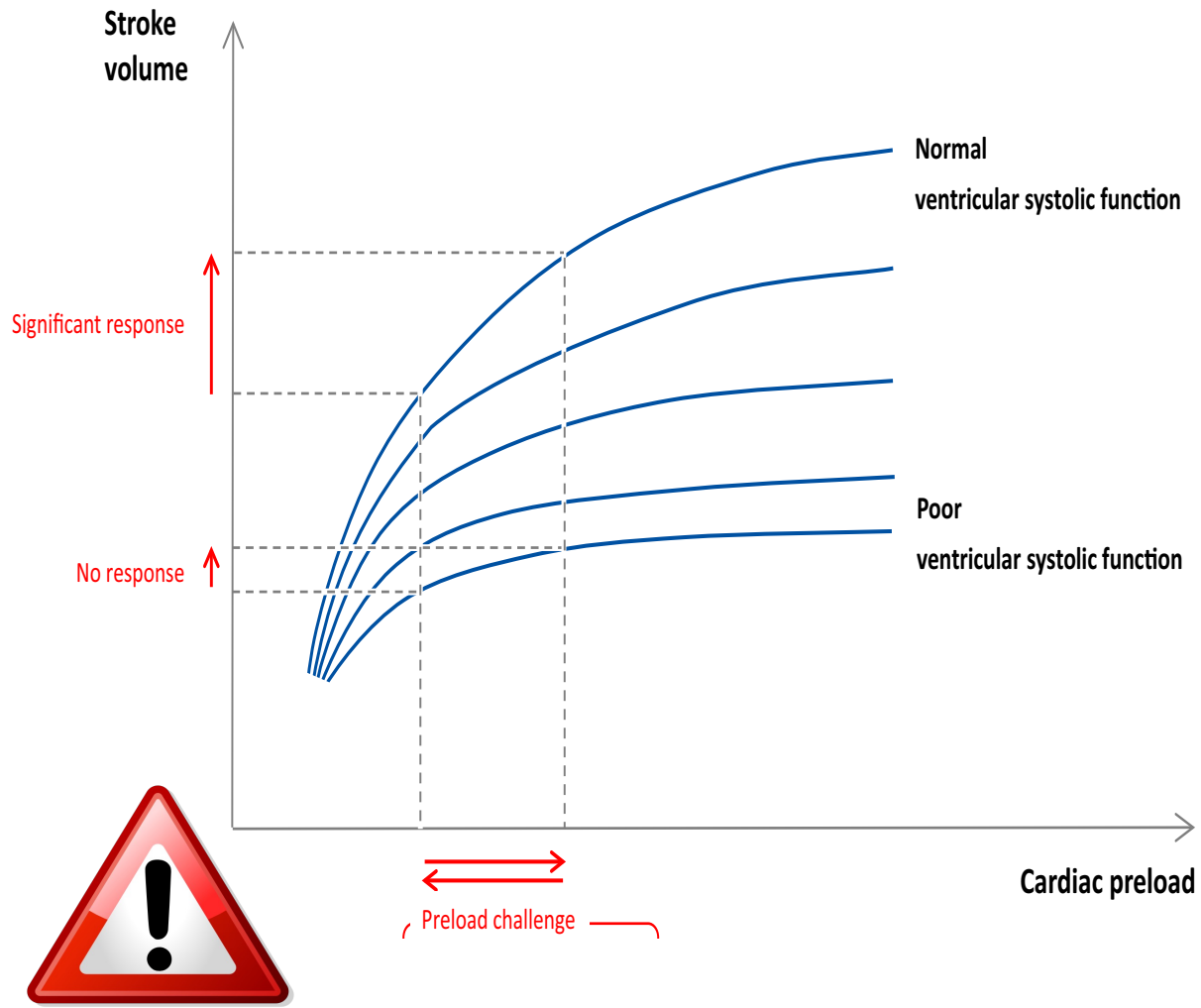
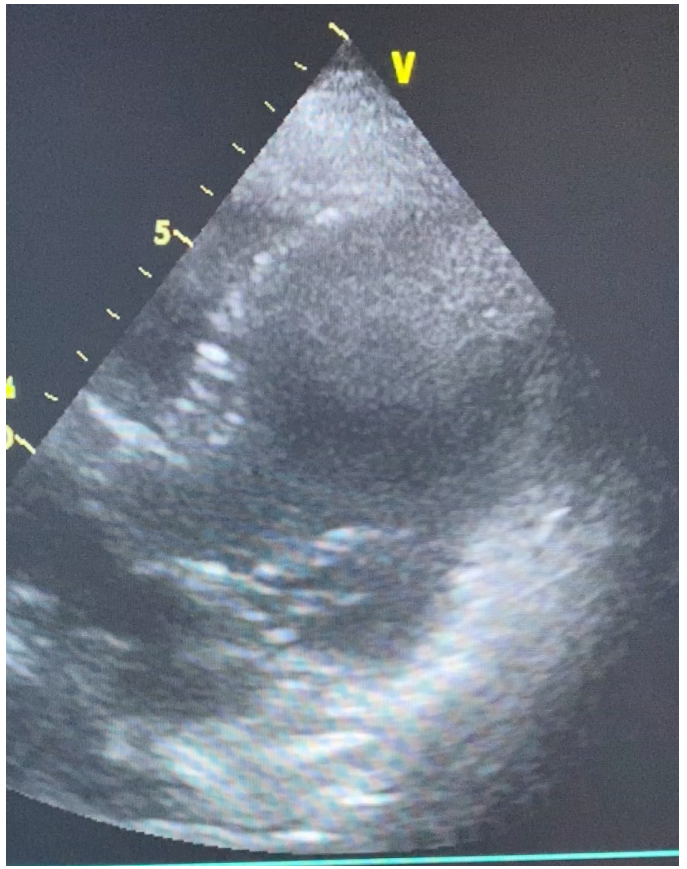
Amélioration DO_2: ***Précharge*-dépendance?**





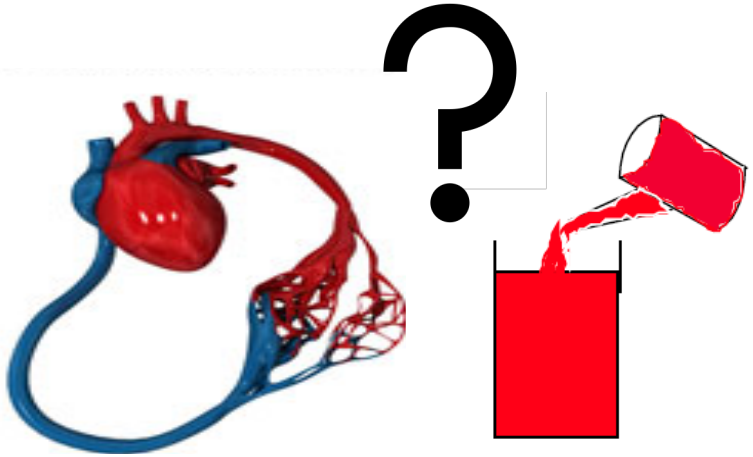
Is there acute circulatory failure?
- Low blood pressure or cardiac output?
- Signs of tissue hypoperfusion?

NO

YES

Is hypovolemia obvious ?
- Obvious fluid loss?
- Initial phase of septic shock?

NO



Method	Threshold	Main limitations
Pulse pressure/stroke volume variations [22]	12%	Cannot be used in case of spontaneous breathing, cardiac arrhythmias, low tidal volume/ lung compliance
Inferior vena cava diameter variations [44]	12%	Cannot be used in case of spontaneous breathing, low tidal volume/lung compliance
Superior vena caval diameter variations [44]	36%*	Requires performing transesophageal Doppler
Passive leg raising [55]	10%	Cannot be used in case of spontaneous breathing, low tidal volume/lung compliance
End-expiratory occlusion test [75]	5%	Requires a direct measurement of cardiac output
"Mini"-fluid challenge (100 mL) [84]	6%**	Cannot be used in non-intubated patients
"Conventional" fluid challenge (500 mL) [81]	15%	Cannot be used in patients who interrupt a 15-s respiratory hold
		Requires a precise technique for measuring cardiac output
		Requires a direct measurement of cardiac output
		Induces fluid overload if repeated

Passive leg raising test

End-expiratory occlusion test

End-expiratory

"Mini" fluid challenge

"Mini" fluid challenge

YES

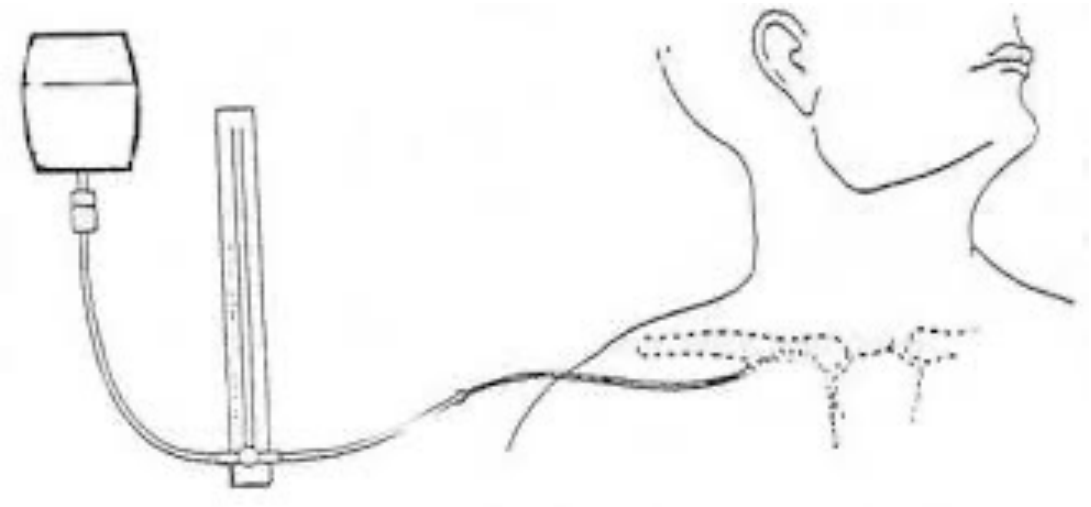
NO

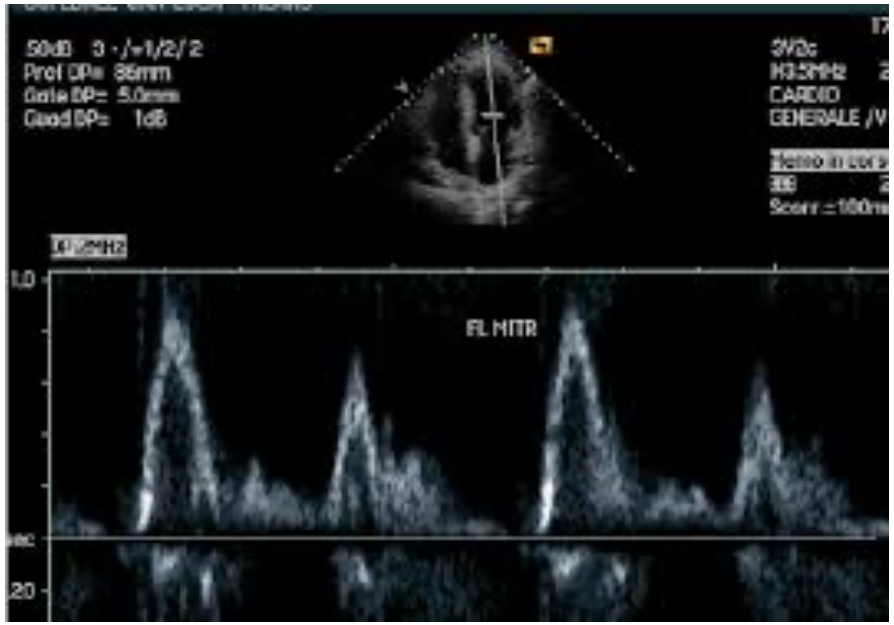
Consider volume expansion
(depending on the risk of fluid overload)

Do not
consider volume expansion

Monnet X *et al*. Ann Intensive Care 2016

Indicateurs **statiques**

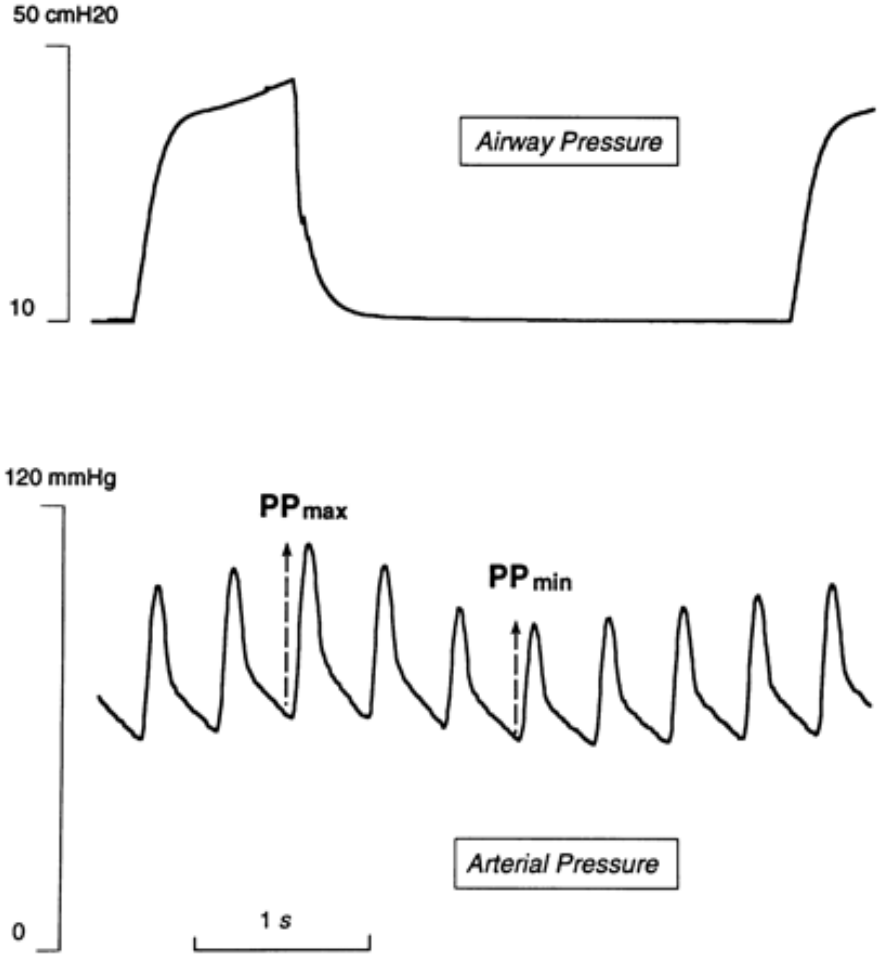




Pression Veineuse Centrale

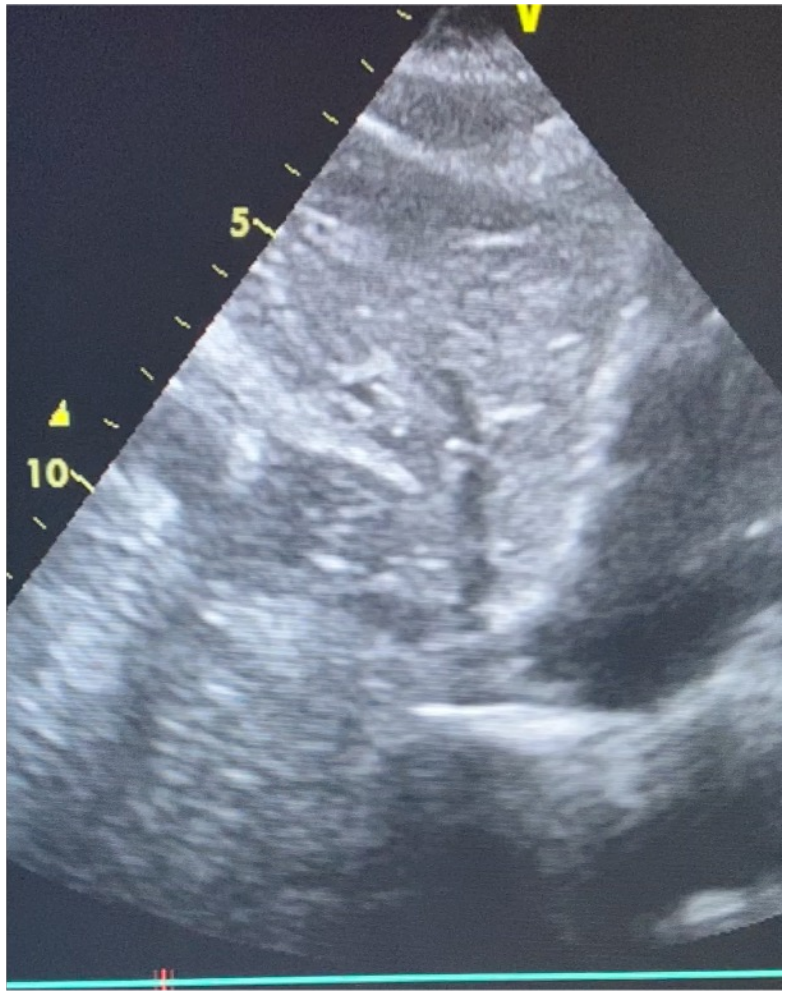
Pressions de remplissage

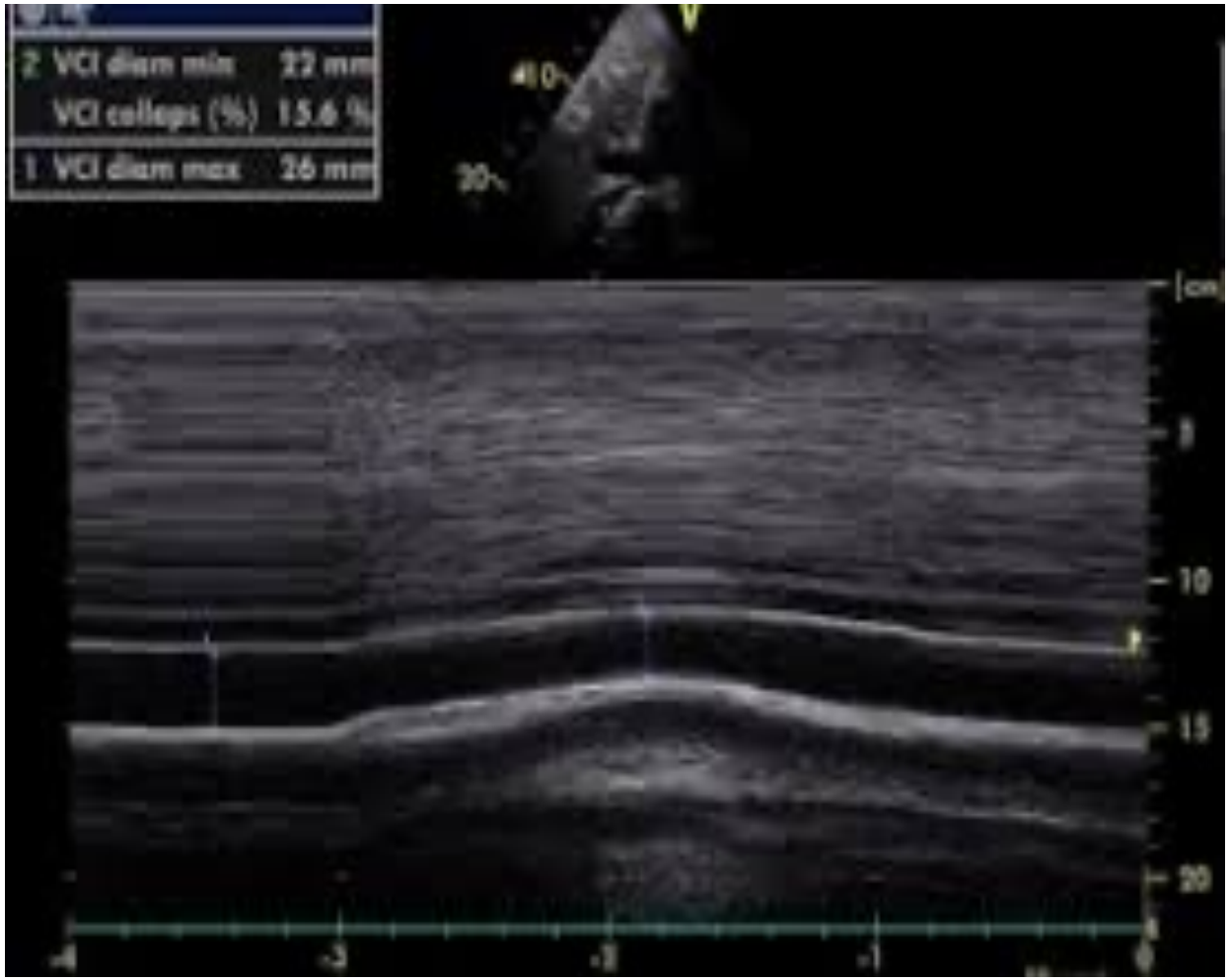
Indicateurs **dynamiques**



Variations Pression Pulsée

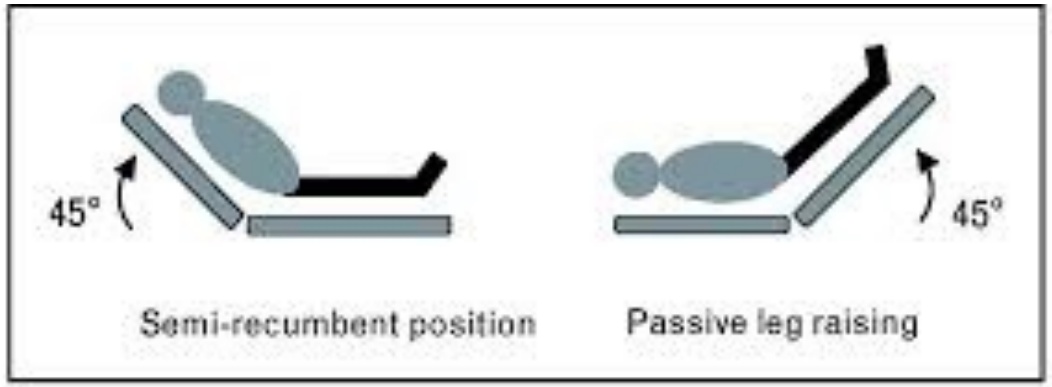
Indicateurs **dynamiques**





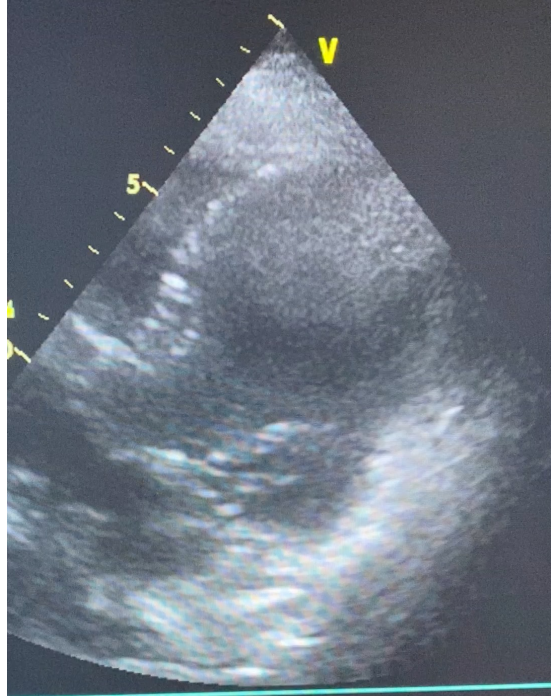
Variations Respiratoires VCI (ou VCS)

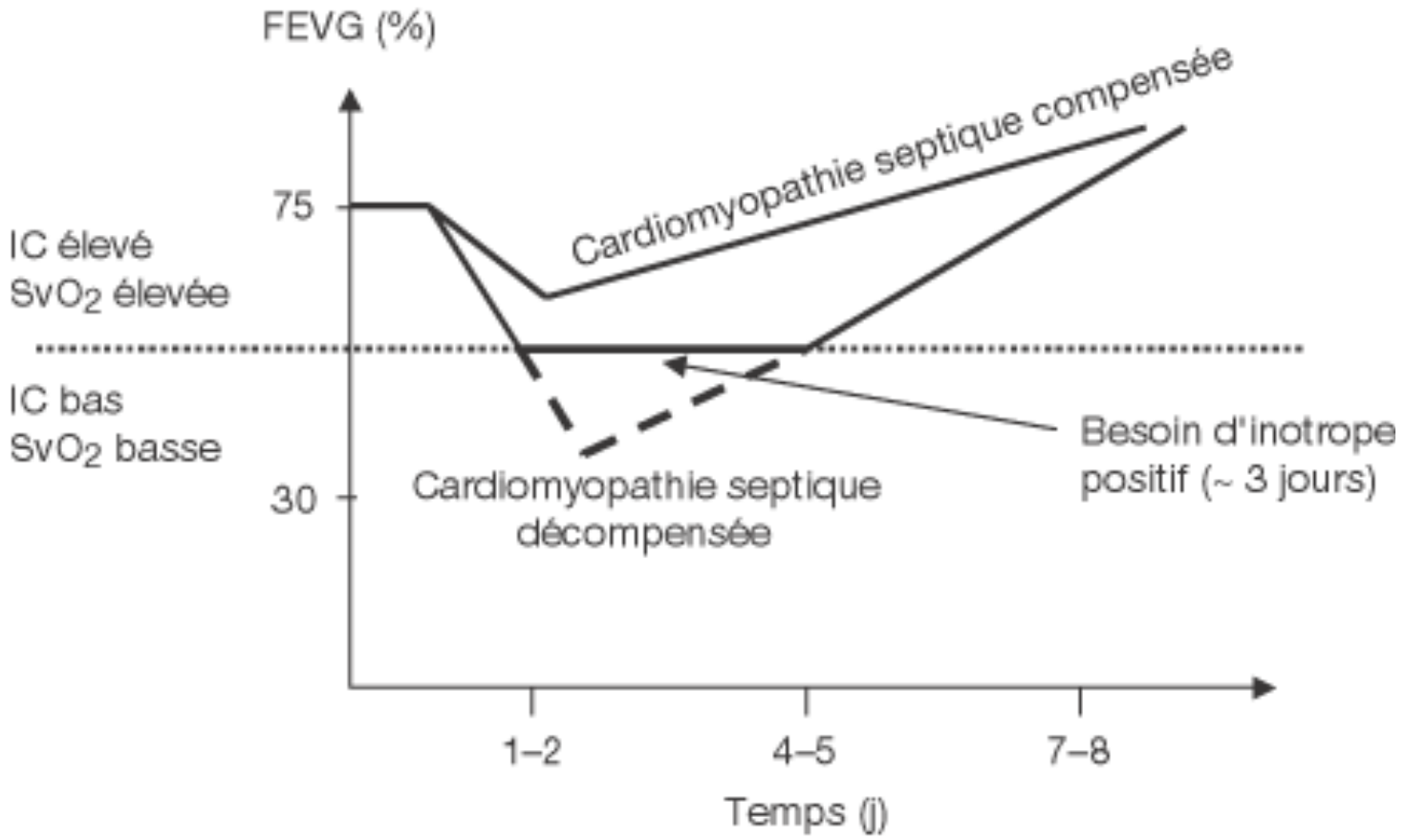
Prédire la précharge-dépendance: levé de jambes passif

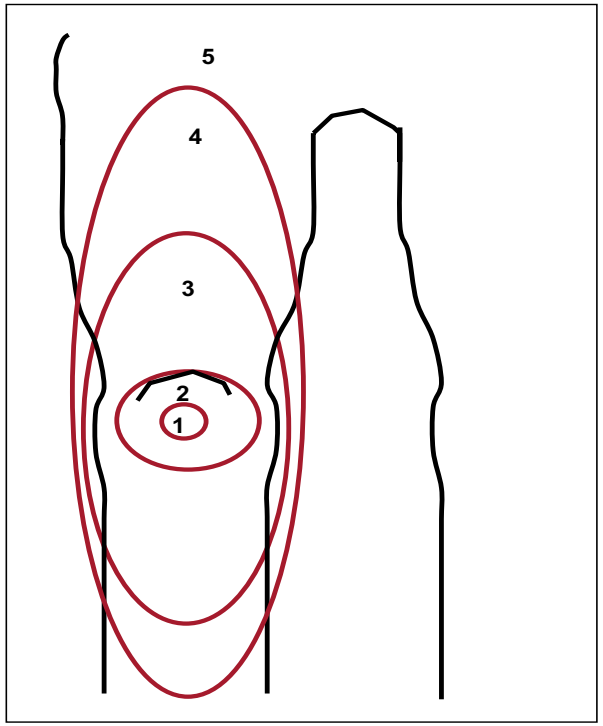


« auto-remplissage »
 # 250 mL

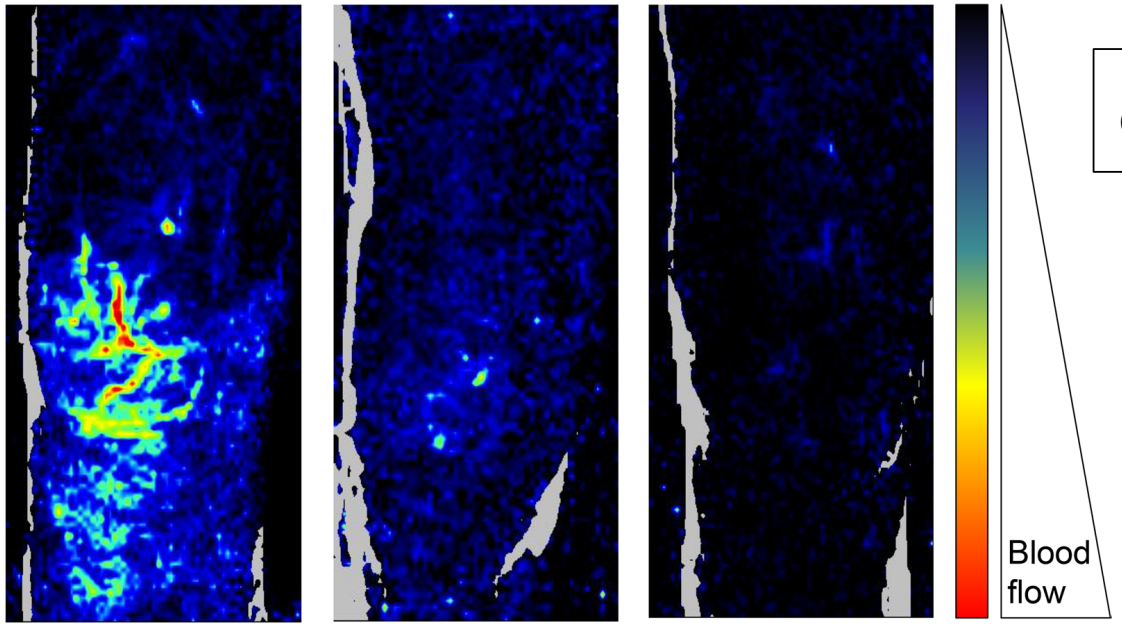
Défaillance myocardique
au cours du choc septique



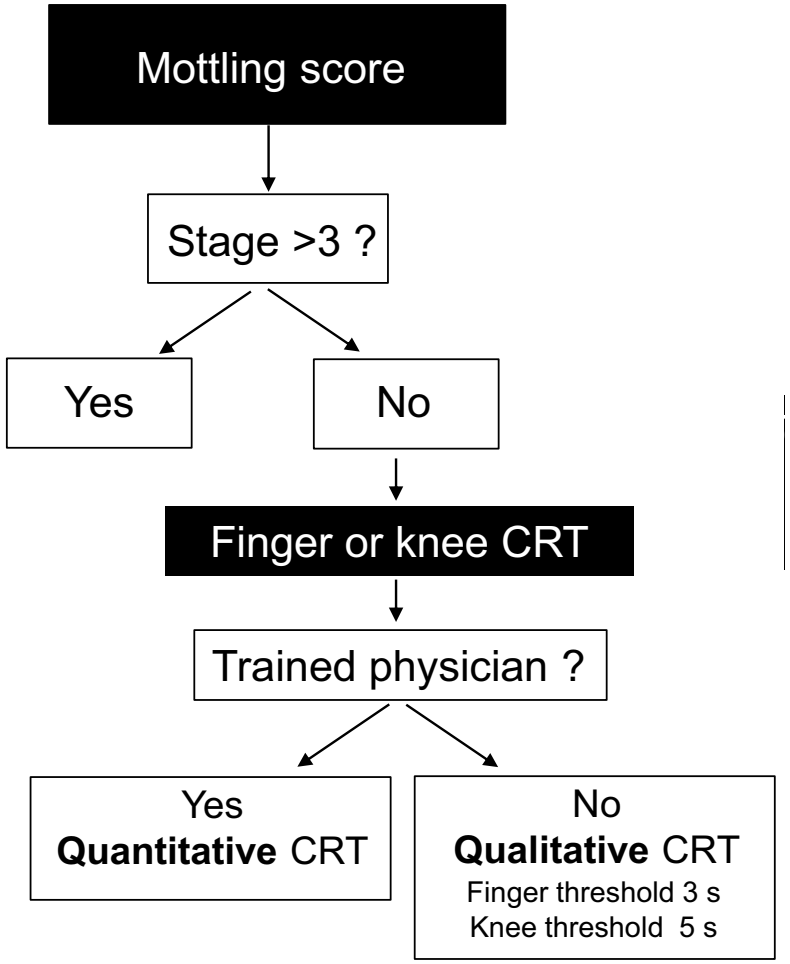





STAGE 4



Stage 0 Stage 3 Stage 5



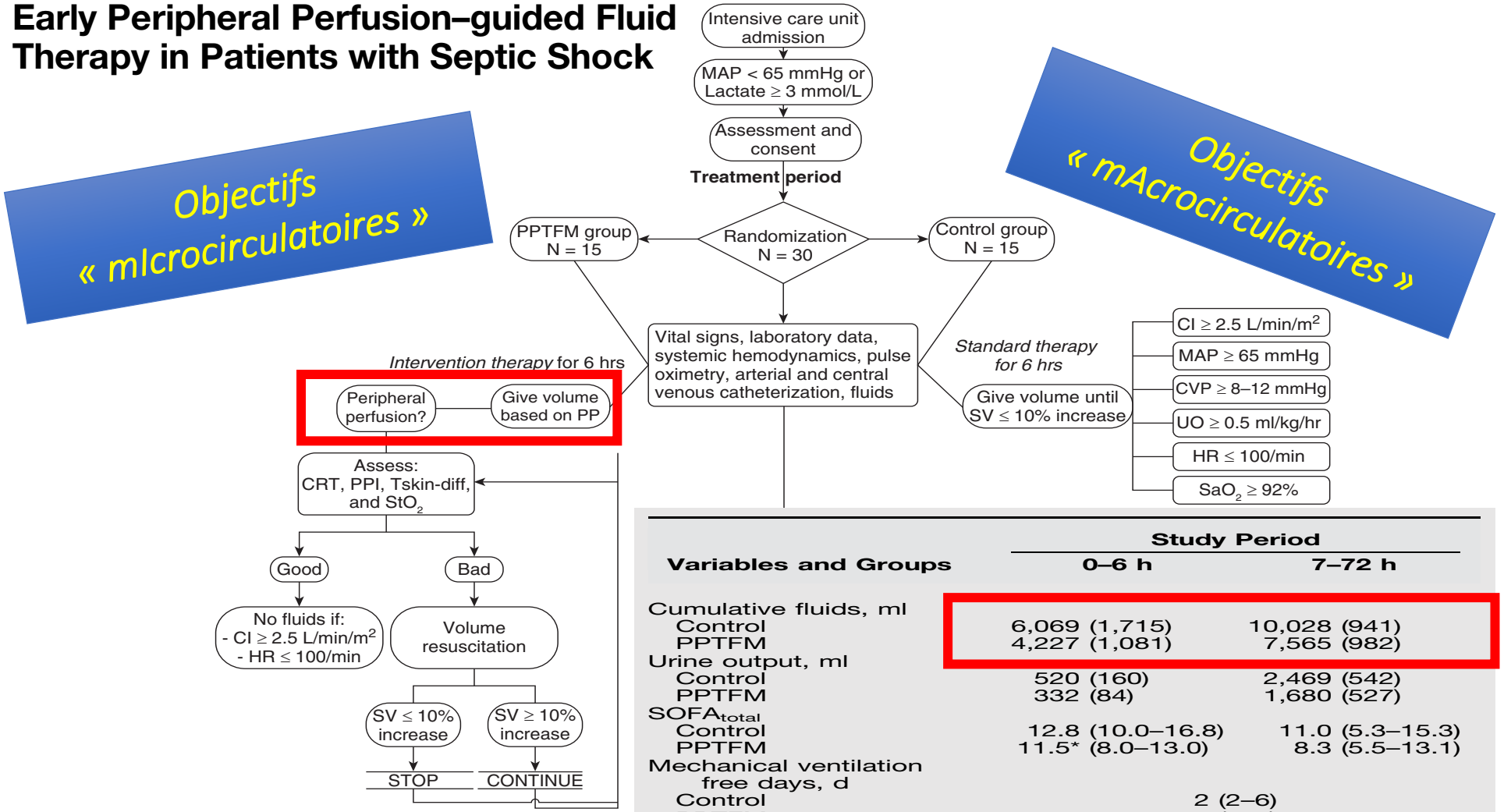
Guidage du remplissage?

Ait-Houfella X *et al*. Ann Intensive Care 2019

Early Peripheral Perfusion–guided Fluid Therapy in Patients with Septic Shock

Objectifs « mIcrocirculatoires »

Objectifs « mAcrocirculatoires »



Variables and Groups	Study Period 0–6 h	Study Period 7–72 h
Cumulative fluids, ml		
Control	6,069 (1,715)	10,028 (941)
PPTFM	4,227 (1,081)	7,565 (982)
Urine output, ml		
Control	520 (160)	2,469 (542)
PPTFM	332 (84)	1,680 (527)
$SOFA_{total}$		
Control	12.8 (10.0–16.8)	11.0 (5.3–15.3)
PPTFM	11.5* (8.0–13.0)	8.3 (5.5–13.1)
Mechanical ventilation free days, d		
Control	2 (2–6)	
PPTFM	2 (1–5)	
Intensive care unit mortality, n (%)		
Control	6 (40)	
PPTFM	7 (47)	
Intensive care unit stay, d		
Control	8 (3–8)	
PPTFM	10 (2–10)	
Hospital stay, d		
Control	43 (8–45)	
PPTFM	16 (5– 28)*	

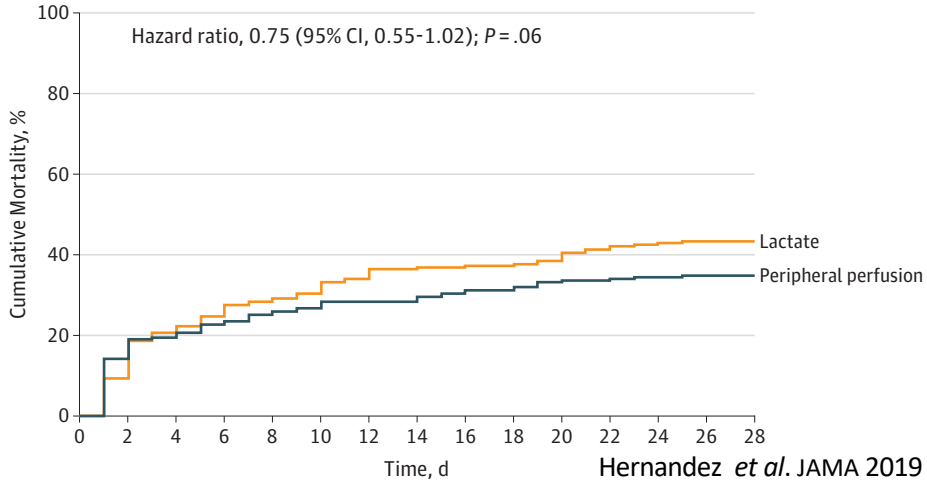
Van Genderen *et al*. Am J Respir Crit Care Med 2015

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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

Outcome	Peripheral Perfusion-Targeted Resuscitation (n = 212)	Lactate Level-Targeted Resuscitation (n = 212)	Unadjusted Absolute Difference (95% CI)	Adjusted Relative Measure (95% CI)	*P* Value
SOFA at 72 h, No.[d]	165	166			.045
Mean (SD)	5.6 (4.3)	6.6 (4.7)	−1.00 (−1.97 to −0.02)		
ICU length of stay, mean (SD), d[e]	9.1 (9.8)	9.0 (9.6)	0.1 (−1.7 to 2.0)		.91
Hospital length of stay, mean (SD), d[f]	22.9 (28.8)	18.3 (19.0)	4.6 (0.0 to 9.1)		.05
Amount of resuscitation fluids within the first 8 h, No.	206	209			
Mean (SD), mL	2359 (1344)	2767 (1749)	−408 (−705 to −110)		.01



Hernandez *et al*. JAMA 2019

Recommendations

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

Best practice statement.

Quand?

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

Weak recommendation, low-quality evidence.

Combien?

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

Weak recommendation, very low-quality evidence.

Remarks:

Dynamic parameters include response to a passive leg raise or a fluid bolus, using stroke volume (SV), stroke volume variation (SVV), pulse pressure variation (PPV), or echocardiography, where available.

Guidage?

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.

Weak recommendation, low-quality evidence.

Remarks:

During acute resuscitation, serum lactate level should be interpreted considering the clinical context and other causes of elevated lactate.

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

Weak recommendation, low-quality evidence.

Soluté?

Recommendations

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

Strong recommendation, moderate quality of evidence.

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

Weak recommendation, low quality of evidence.

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

Weak recommendation, moderate quality of evidence.

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

Strong recommendation, high quality of evidence.

Evans L *et al*. Crit Care Med 2021

Q7. Parmi les propositions suivantes, la(les)quelle(s) de ces antibiothérapies empiriques vous paraît(aissent)-elle(s) appropriée(s)?

A. Amoxicilline-Acide clavulanique
B. Céfotaxime
C. Imipénème
D. Céfotaxime + Amikacine
E. Céfotaxime + Amikacine+ Métronidazole

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Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Broad-spectrum is tantalizing!

D. ANTIMICROBIAL THERAPY

1. **We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and within 1 h for both sepsis and septic shock (strong recommendation, moderate quality of evidence; grade applies to both conditions).**

In addition, the clinician must assess risk factors for infection with multidrug-resistant pathogens including prolonged hospital/chronic facility stay, recent antimicrobial use, prior hospitalization, and prior colonization or infection with multidrug-resistant organisms. The occurrence of more severe illness (e.g., septic shock) may be intrinsically associated with a higher probability of resistant isolates due to selection in failure to respond to earlier antimicrobials.

Rhodes *et al*. Intensive Care Med 2016

Intensive Care Med (2015) 41:1181–1196
DOI 10.1007/s00134-015-3853-7

Cédric Bretonnière
Marc Leone
Christophe Milési
Bernard Allaouchiche
Laurence Armand-Lefevre
Olivier Baldesi
Lila Bouadma
Dominique Decré
Samy Figueiredo
Rémy Gauzit
Benoît Guery
Nicolas Joram
Boris Jung
Sigismond Lasocki
Alain Lepape
Fabrice Lesage
Olivier Pajot
François Philippart
Bertrand Souweine
Pierre Tattevin
Jean-François Timsit
Renaud Vialet
Jean Ralph Zahar
Benoît Misset
Jean-Pierre Bedos

Strategies to reduce curative … in intensive care …

Carbapenems should be avoided except…

In terms of empirical antimicrobial treatment, … hospital-acquired severe bacterial infection is suspected, we recommend not prescribing carbapenem solely on the basis of the nosocomial nature of the infection, but rather considering the presence of at least two of the following criteria:

- Previous treatment with a third-generation cephalosporin, fluoroquinolones (including a single dose) or a piperacillin–tazobactam combination in the last 3 months,
- Carriage of extended-spectrum β-lactamase-producing *Enterobacteriaceae* or of ceftazidime-resistant *P. aeruginosa*, determined within the last 3 months, whatever the sampling site,
- Hospitalization during the last 12 months,
- Patient living in a nursing facility or in a long-term care facility for elderly and carrying an indwelling catheter and/or a gastrostomy tube,
- Ongoing epidemic episode of multidrug-resistant bacteria in the healthcare institution for which the only treatment option is carbapenem

PNA grave

Traitement probabiliste

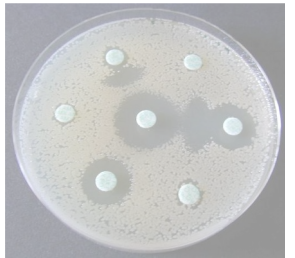
- C3G IV (céfotaxime ou ceftriaxone) + amikacine

- si allergie :
  - aztréonam + amikacine

- si antécédent de BLSE (IU ou colonisation urinaire < 6 mois)
  - carbapénème (imipénème, méropénème) + amikacine
  - en cas d'allergie aux carbapénèmes : aztréonam + amikacine

- si choc septique, ET présence d'au moins un facteur de risque d'EBLSE*
  - carbapénème (imipénème, méropénème) + amikacine
  - en cas d'allergie aux carbapénèmes : aztréonam + amikacine

* Facteurs de risque d'EBLSE : colonisation urinaire ou IU à EBLSE < 6 mois, antibiothérapie par pénicilline+inhibiteur, céphalosporine de 2ème ou 3ème génération, ou fluoroquinolone< 6 mois, voyage récent en zone d'endémie d'EBLSE, hospitalisation < 3 mois, vie en long-séjour

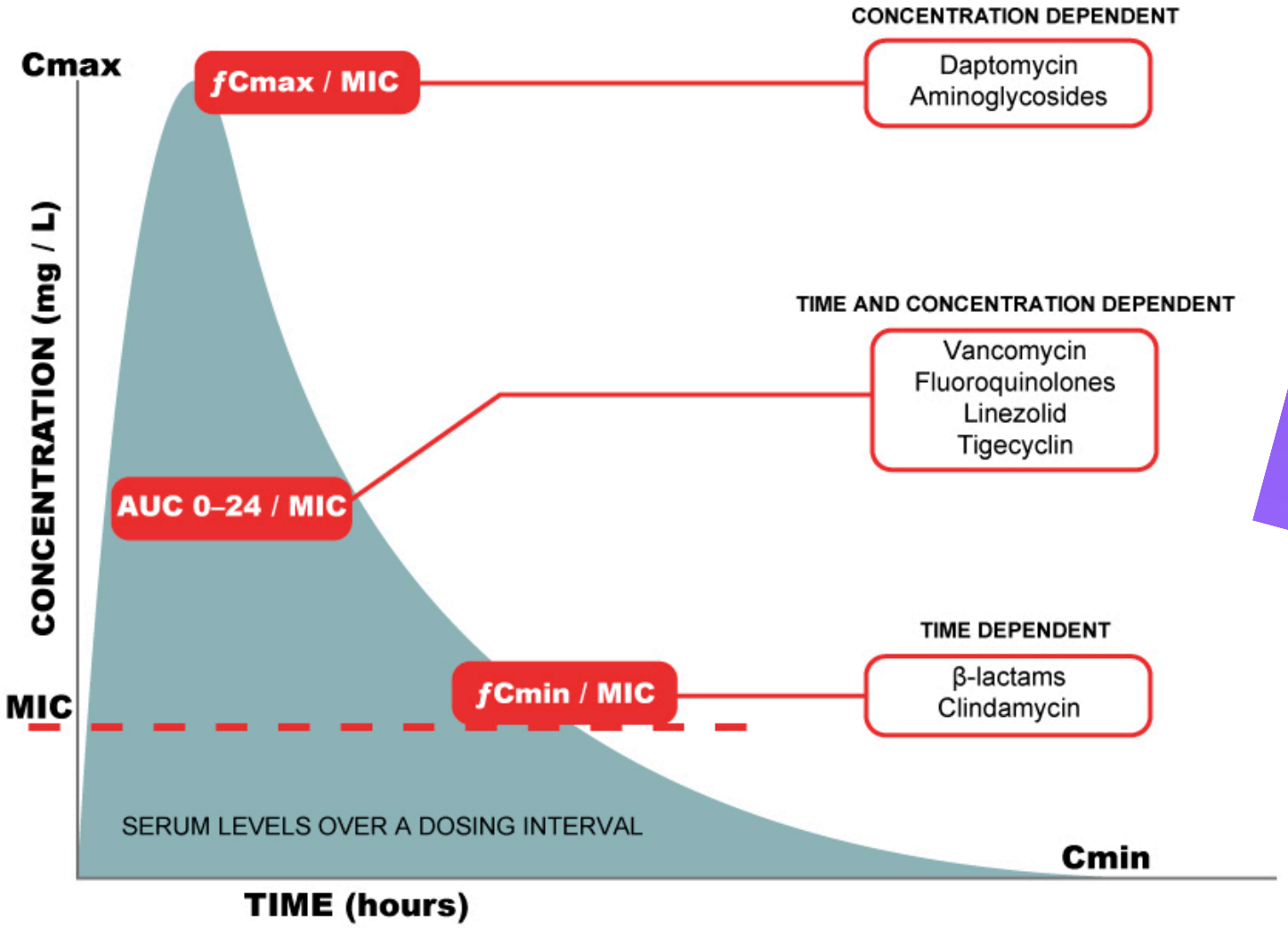


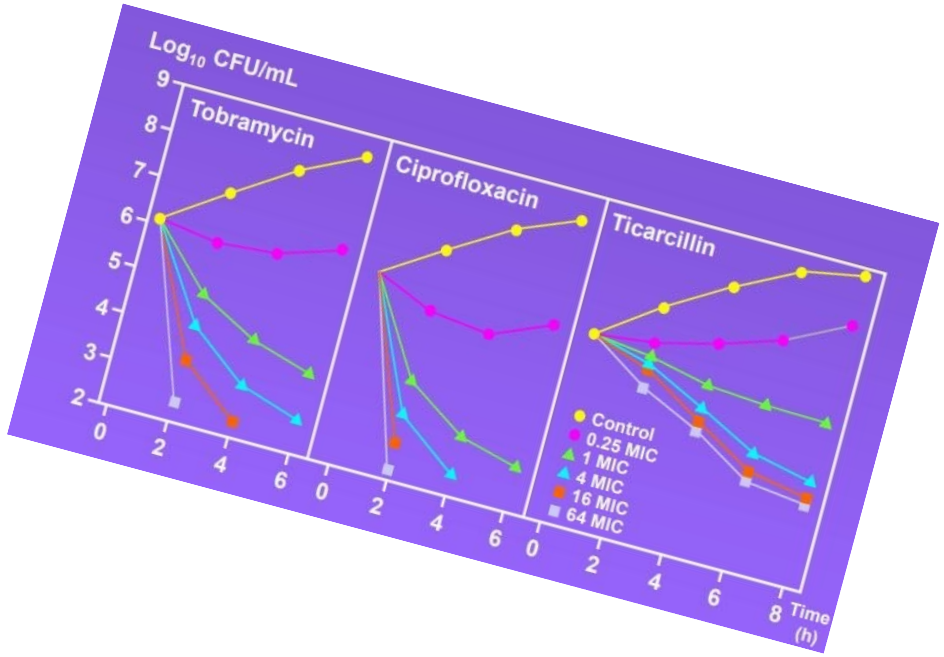
Optimisation des doses!

Long-established antibiotics		
Piperacillin/tazobactam	4.5 g every 6 h CI	BSI, HAP, VAP, UTI, cIAI
Ceftazidime	6 g every 24 h CI	BSI, HAP, VAP, UTI
Cefepime	2 g every 8 h or CI	BSI, HAP, VAP, UTI
Aztreonam	1 g (2 g) every 8 h	BSI, HAP, VAP, UTI, SSTI
Imipenem/cilastatin	500 mg (1 g) every 6 h	BSI, HAP, VAP, UTI, cIAI
Meropenem	1 g (2 g) every 8 h or CI	BSI, HAP, VAP, UTI, cIAI
Tigecycline	100–200 mg loading those, then 50–100 mg every 12 h	cIAI
"Old"antibiotics		
Gentamicin	7 mg/kg/day every 24 h	In combination for BSI, UTI, c HAP, cIAI, VAP
Amikacin	25–30 mg/kg/day every 24 h	In combination for BSI, UTI,VA HAP, VAP
Colistin	9 MU loading dose, 4.5 MU every 8–12 h	In combination for BSI, UTI, HAP, VAP
Fosfomycin	4–6 g every 6 h CI	In combination for BSI, UTI, HAP, VAP
Vancomycin	15–30 mg/kg loading dose, 30–60 mg/kg every 12 h, 6 h or CI	BSI, HAP, VAP
Linezolid	600 mg every 12 h	BSI, HAP, VAP, SSTI

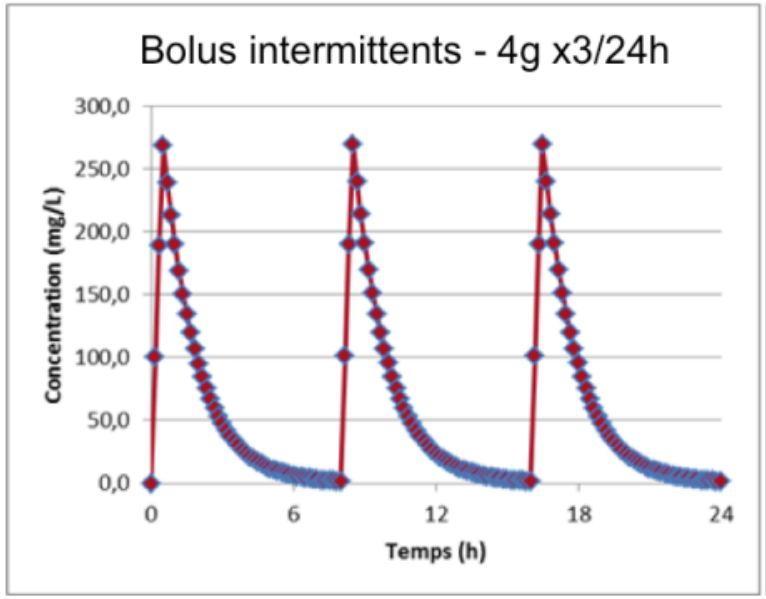
Timsit *et al*. Intensive Care Med 2019

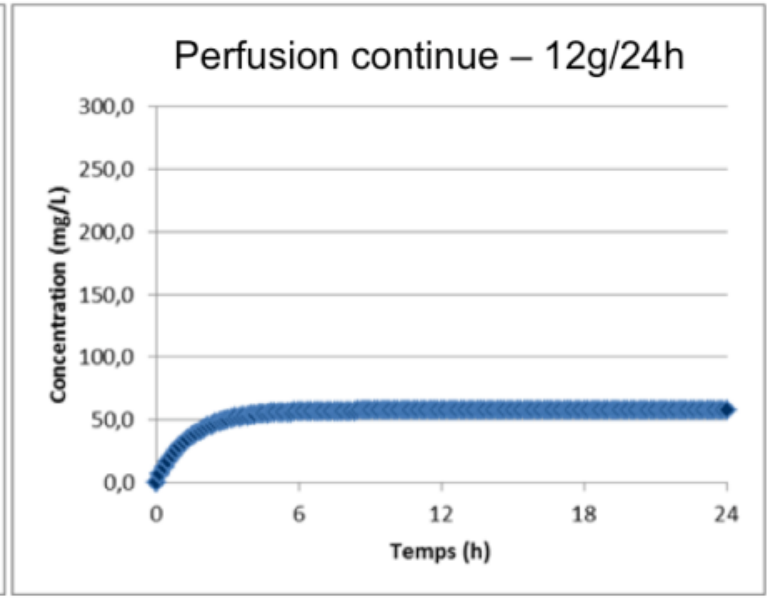
Objectifs PK/PD… concentrations *vs*. bactéricidie

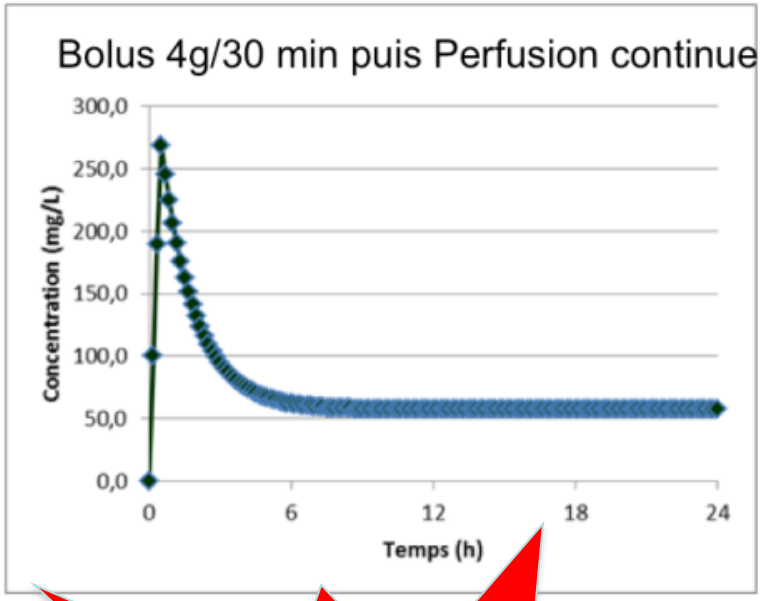


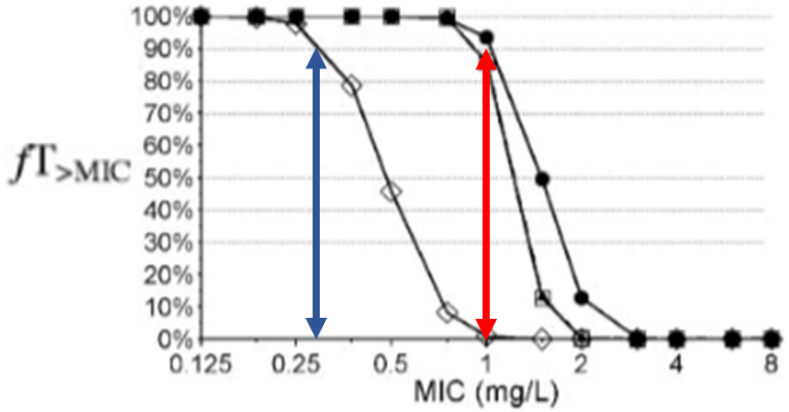


Exemple des Beta-lactamines… (TAZO)



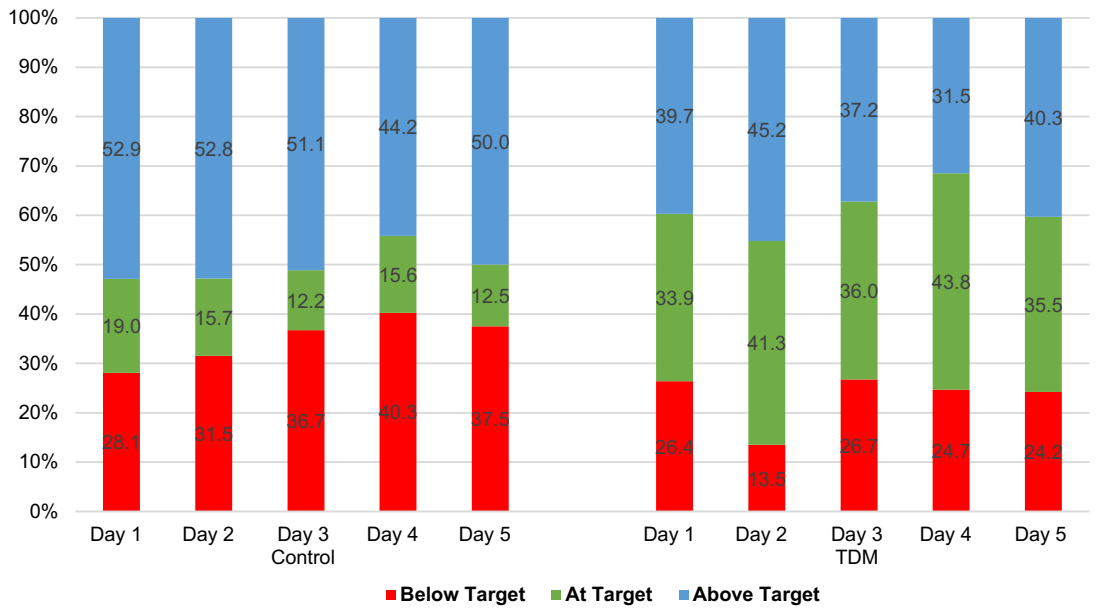






objectifs PK/PD!

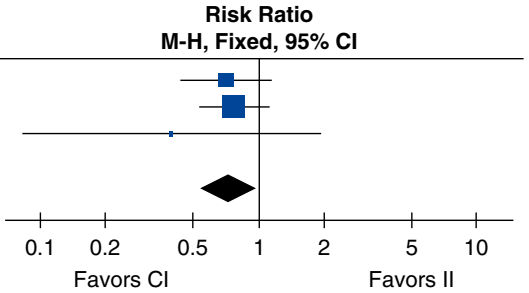
Exemple des Beta-lactamines…



Impact clinique!

Study or Subgroup	CI Events	CI Total	II Events	II Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abdul-Aziz 2016	20	70	28	70	33.3%	0.71 [0.45, 1.14]
Dulhunty 2015	39	212	52	220	60.7%	0.78 [0.54, 1.13]
Dulhunty 2013	2	30	5	30	5.9%	0.40 [0.08, 1.90]
Total (95% CI)		**312**		**320**	**100.0%**	**0.73 [0.55, 0.98]**
Total events	61		85			

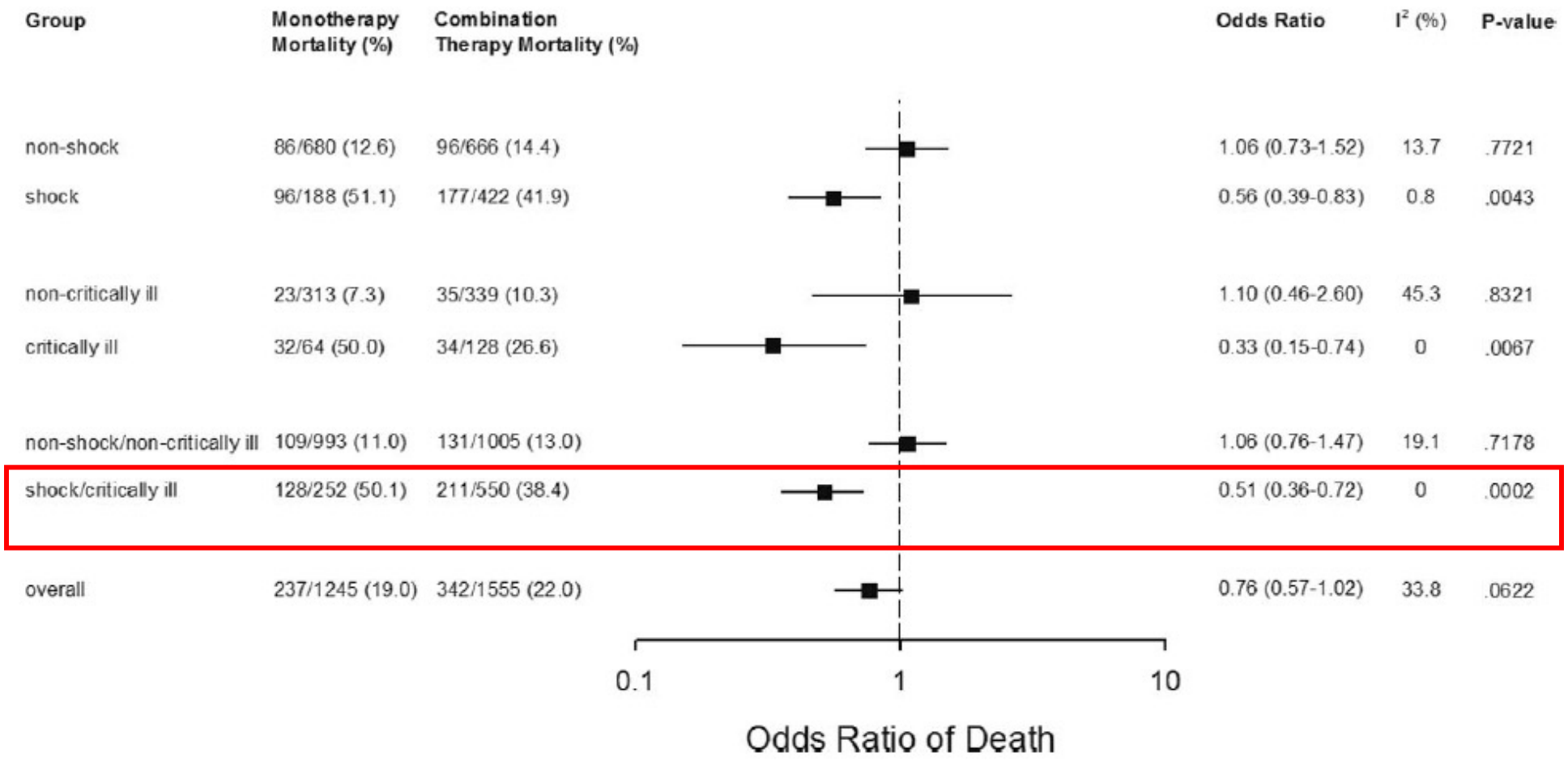
Heterogeneity: $Chi^2 = 0.69$, df = 2 (P = 0.71); $I^2 = 0\%$
Test for overall effect: Z = 2.11 (P = 0.03)



Hagel S *et al*. Intensive Care Med 2022

Roberts JA *et al*. Am J Respir Crit Care Med 2016

Bithérapie?



Kumar *et al*. Crit Care Med 2010

Q8. Malgré le remplissage, la pression artérielle a chuté à 72/41 mmHg. Quelle est votre attitude thérapeutique à présent?

A. Mise sous noradrénaline sur VVP avec un objectif de PAM à 65 mmHg
B. Mise sous terlipressine
C. Mise sous noradrénaline sur VVP avec un objectif de PAM à 75 mmHg
D. Mise sous noradrénaline sur VVC avec un objectif de PAM à 75 mmHg
E. Mise sous noradrénaline sur VVC avec un objectif de PAM à 65 mmHg

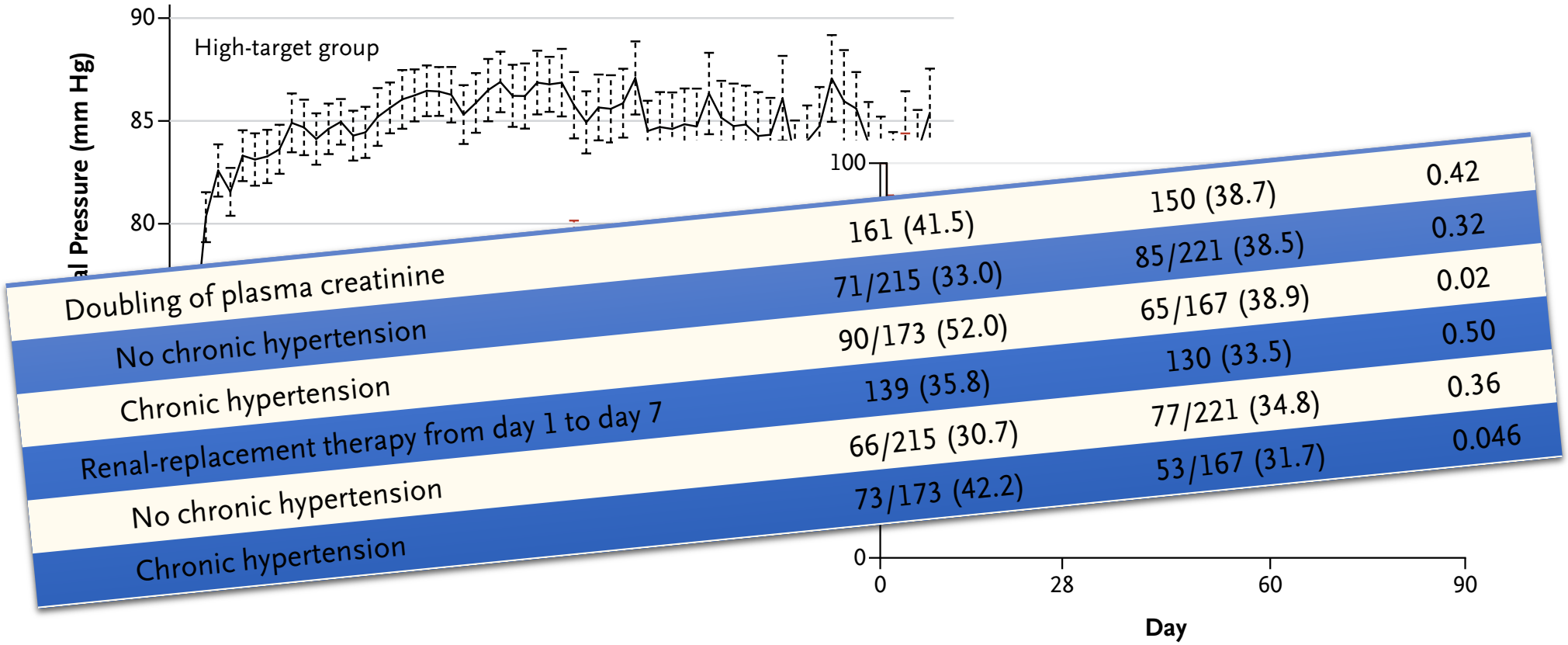
Q8. Malgré le remplissage, la pression artérielle a chuté à 72/41 mmHg. Quelle est votre attitude thérapeutique à présent?

A. Mise sous noradrénaline sur VVP avec un objectif de PAM à 65 mmHg
B. Mise sous terlipressine
C. Mise sous noradrénaline sur VVP avec un objectif de PAM à 75 mmHg
D. Mise sous noradrénaline sur VVC avec un objectif de PAM à 75 mmHg
E. Mise sous noradrénaline sur VVC avec un objectif de PAM à 65 mmHg

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 24, 2014 VOL. 370 NO. 17

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



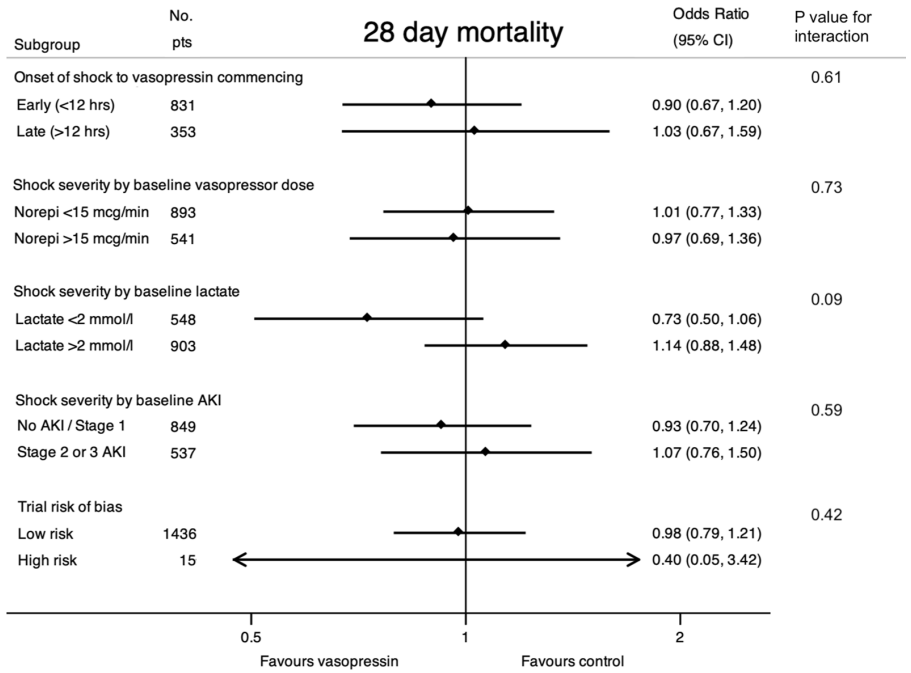
Doubling of plasma creatinine	161 (41.5)	150 (38.7)	0.42
No chronic hypertension	71/215 (33.0)	85/221 (38.5)	0.32
Chronic hypertension	90/173 (52.0)	65/167 (38.9)	0.02
Renal-replacement therapy from day 1 to day 7	139 (35.8)	130 (33.5)	0.50
No chronic hypertension	66/215 (30.7)	77/221 (34.8)	0.36
Chronic hypertension	73/173 (42.2)	53/167 (31.7)	0.046

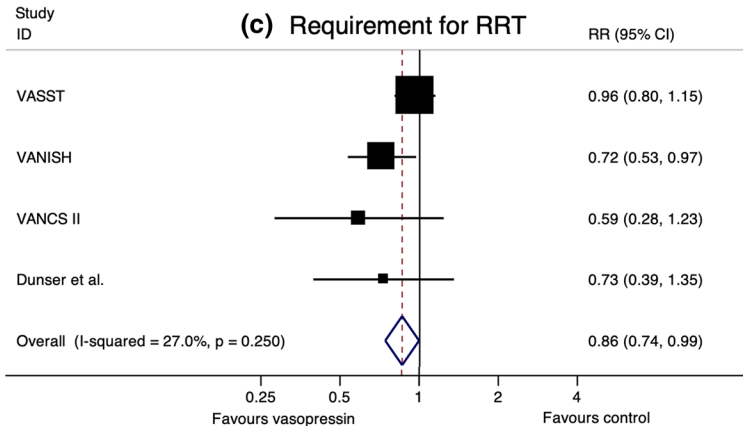
No. at Risk

Low target	379	256	233	225
High target	375	249	227	219

Asfar et al N Eng J Med 2014

Vasopressin in septic shock: an individual patient data meta-analysis of randomised controlled trials





Outcome	Vasopressin	Norepinephrine	ARD[a] (95% CI)
Serious adverse events, no./total (%)	124/735 (16.9)	120/718 (16.7)	0.2 (− 3.7 to 4.0)
Digital ischaemia	21/735 (2.9)	8/718 (1.1)	1.7 (0.3–3.2)
Mesenteric ischaemia[b]	14/727 (1.9)	18/711 (2.5)	− 0.6 (− 2.1 to 0.9)
Acute coronary syndrome	18/735 (2.5)	17/718 (2.4)	0.1 (− 1.5 to 1.7)
Arrhythmia	39/735 (5.3)	58/718 (8.1)	− 2.8 (− 0.2 to − 5.3)

Quand dégainer la **noradré** plus tôt???

Problem	Effect	Setting	Potential benefit of early start of vasopressors
Time of hypotension and outcomes	Prolonged hypotension is related with worse clinical outcomes	Clinical	Shortening time of hypotension
Low preload / low myocardial contractility	Decreased cardiac output	Clinical/experimental	Mobilization of blood volume from the non-stressed to the stressed circulatory compartment Increasing myocardial contractility Optimization of ventriculo-arterial coupling
Low diastolic pressure	Altered myocardial perfusion	Clinical	Severe hypotension derived from serious vasodilation is unlikely to be reversed by simple fluid administration
Low microcirculatory driving pressure	Altered convective microcirculatory blood flow	Clinical	Correcting hypotension improves microcirculatory blood flow Nevertheless, increasing vasopressor dose can derange microcirculatory blood flow when baseline microcirculation is already corrected
Altered splanchnic flow	Decreased splanchnic perfusion	Experimental	Early combination of fluids and vasopressors might be superior at restoring mesenteric blood flow and tissue oxygenation compared to fluid resuscitation alone Nevertheless, isolated use of vasopressors might worsen splanchnic flow
Using a pre-defined fixed volume of resuscitation fluids	Paradoxical increase in vasopressor requirements	Experimental	A very early vasopressor start might decrease subsequent need for fluid therapy

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Prise en charge
du patient septique aux urgences

- **Remplissage** du patient septique démarre le plus souvent aux **urgences**
- **Simultanément avec** l'antibiothérapie
- La **précocité** impacte fortement sur le **devenir** des patients (préserver les *organes vulnérables*)
- **Objectifs**: clinique (**TRC**), **lactate**, $SvcO_2$
- Choix du soluté: **cristalloïdes** (sol. balancées+++)
- Introduction « *rapide* » de la **noradrénaline**