QUELLES CIBLES HEMODYNAMIQUES AU COURS DU CHOC SEPTIQUE ?

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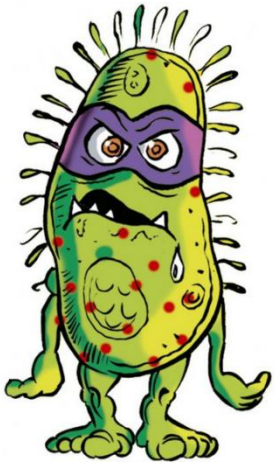
Tuteur : R. FAVORY

DESC de Réanimation – Rouen – 18/12/2014

Choc septique



- Etat infectieux grave
- Réponse inflammatoire systémique de l'hôte
- Dysfonctions d'organes
- Défaillance circulatoire aigüe généralisée
  - Ne répondant pas au remplissage vasculaire
  - Nécessitant un support vasopresseur
- Utilisation inadéquate de l'oxygène par les cellules → dysoxie cellulaire

- Pronostic vital engagé
- **URGENCE THERAPEUTIQUE**

Choc septique

- Choc **distributif**
- **Hypotension artérielle systémique**
- Signes d'**hypoperfusion :**
  - Cutanés : marbrures
  - Rénaux : diurèse < 0,5 ml/kg/h
  - Neurologiques : obnubilation, confusion
- **Hyperlactatémie :** métabolisme cellulaire de l'oxygène anormal

Table 1. Diagnostic Criteria for Sepsis, Severe Sepsis, and Septic Shock.*

Sepsis (documented or suspected infection plus ≥1 of the following)†

General variables
- Fever (core temperature, >38.3°C)
- Hypothermia (core temperature, <36°C)
- Elevated heart rate (>90 beats per min or >2 SD above the upper limit of the normal range for age)
- Tachypnea
- Altered mental status
- Substantial edema or positive fluid balance (>20 ml/kg of body weight over a 24-hr period)
- Hyperglycemia (plasma glucose, >120 mg/dl [6.7 mmol/liter]) in the absence of diabetes

Inflammatory variables
- Leukocytosis (white-cell count, >12,000/mm^3)
- Leukopenia (white-cell count, <4000/mm^3)
- Normal white-cell count with >10% immature forms
- Elevated plasma C-reactive protein (>2 SD above the upper limit of the normal range)
- Elevated plasma procalcitonin (>2 SD above the upper limit of the normal range)

Hemodynamic variables
- Arterial hypotension (systolic pressure, <90 mm Hg; mean arterial pressure, <70 mm Hg; or decrease in systolic pressure of >40 mm Hg in adults or to >2 SD below the lower limit of the normal range for age)
- Elevated mixed venous oxygen saturation (>70%)‡
- Elevated cardiac index (>3.5 liters/min/square meter of body-surface area)§

Organ-dysfunction variables
- Arterial hypoxemia (ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, <300)
- Acute oliguria (urine output, <0.5 ml/kg/hr or 45 ml/hr for at least 2 hr)
- Increase in creatinine level of >0.5 mg/dl (>44 μmol/liter)
- Coagulation abnormalities (international normalized ratio, >1.5; or activated partial-thromboplastin time, >60 sec)
- Paralytic ileus (absence of bowel sounds)
- Thrombocytopenia (platelet count, <100,000/mm^3)
- Hyperbilirubinemia (plasma total bilirubin, >4 mg/dl [68 μmol/liter])

Tissue-perfusion variables
- Hyperlactatemia (lactate, >1 mmol/liter)
- Decreased capillary refill or mottling

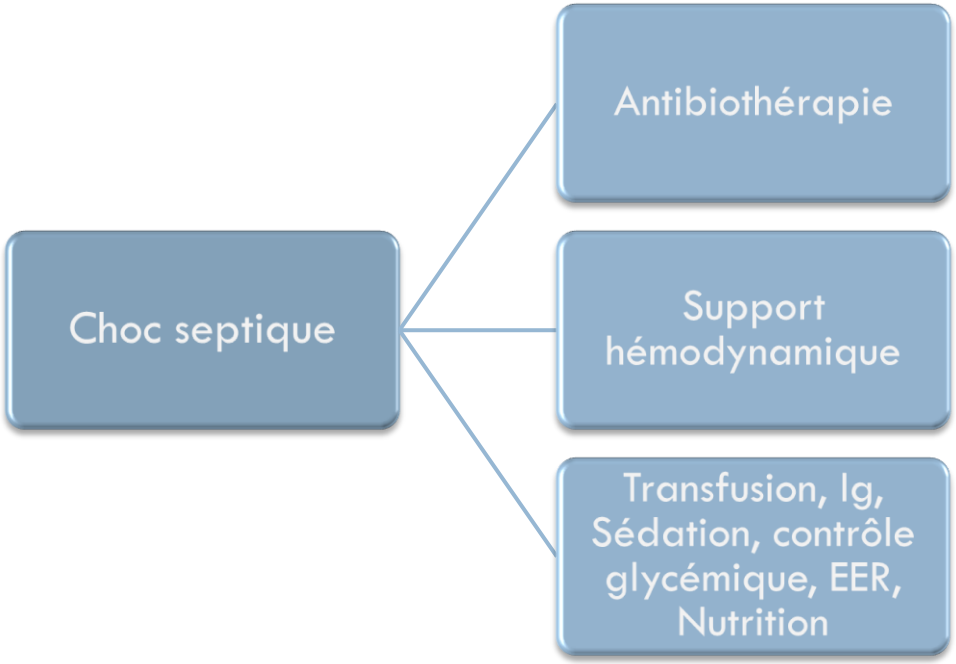
Severe sepsis (sepsis plus organ dysfunction)

Septic shock (sepsis plus either hypotension [refractory to intravenous fluids] or hyperlactatemia)¶

Angus D. et al. NEJM 2013. 369,9 : 840 - 851

Surviving sepsis campaign

- Plusieurs millions / an dans le monde
- Mortalité 80% → 20-30%



Intensive Care Med (2013) 39:165–228
DOI 10.1007/s00134-012-2769-8

GUIDELINES

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Djillali Annane
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Gordon D. Rubenfeld
Steven Webb
Richard J. Beale
Jean-Louis Vincent
Rui Moreno
The Surviving Sepsis Campaign Guidelines Committee including The Pediatric Subgroup*

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

SURVIVING SEPSIS CAMPAIGN CARE BUNDLES

TO BE COMPLETED WITHIN 3 HOURS:
1) Measure lactate level
2) Obtain blood cultures prior to administration of antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L

TO BE COMPLETED WITHIN 6 HOURS:
5) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥ 4 mmol/L (36 mg/dL):
- Measure central venous pressure (CVP)*
- Measure central venous oxygen saturation ($ScvO_2$)*
7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg, $ScvO_2$ of ≥ 70%, and normalization of lactate.

Dellinger et al. Intensive Care Med 2013, 39 : 165 - 228

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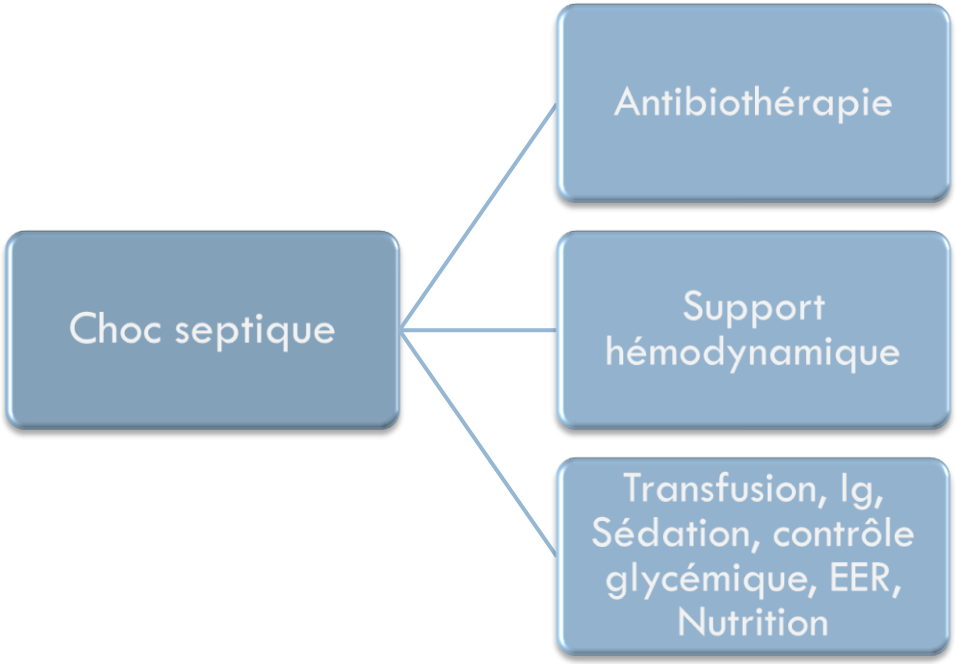

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Surviving Sepsis Campaign: association between performance metrics and outcomes in a 7.5-year study

Dellinger et al. Intensive Care Med 2013, 39 : 165 - 228

Surviving sepsis campaign

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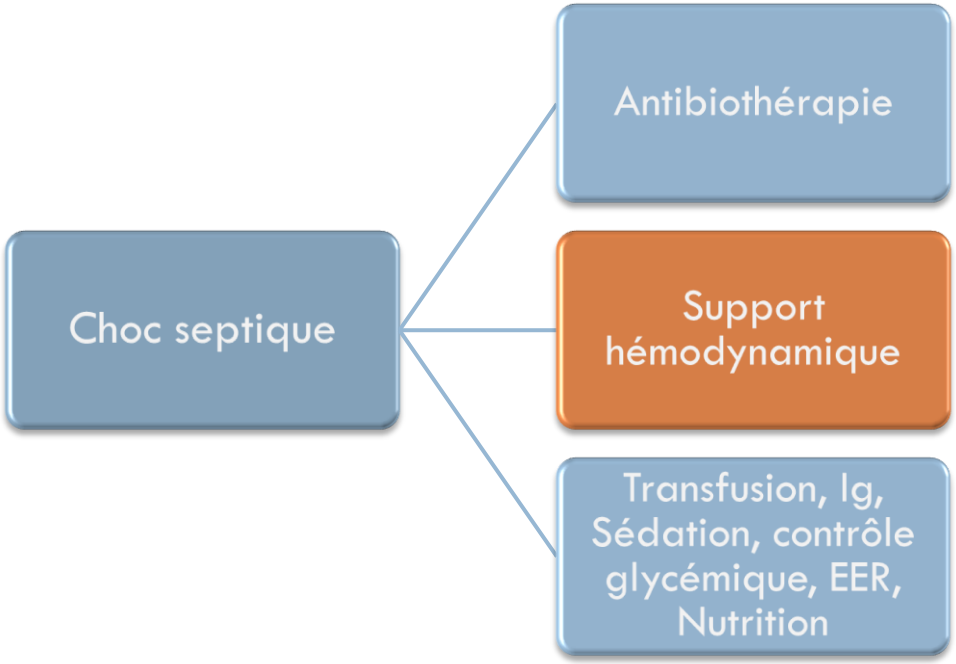

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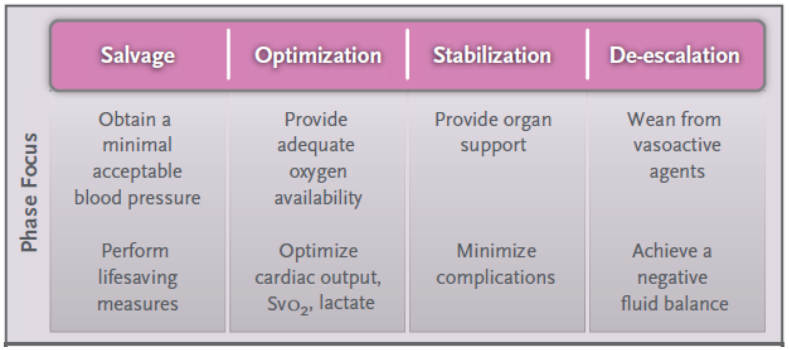
Dellinger et al. Intensive Care Med 2013, 39 : 165 - 228

Cible initiale

- Dans les 6h :
  - **PVC 8-12 mmHg**
  - **PAM ≥ 65 mmHg**
  - **Diurèse ≥ 0,5 ml/kg/h**
  - **ScvO2 ≥ 70%**

  } *(grade 1C)*

  - Normalisation **lactatémie** *(grade 2C)*
- Support hémodynamique ⇔ prévenir les dysfonctions d'organes
  - Cathéter artériel (monitorage / prise de sang)
  - Cathéter veineux central (perfusion / vasopresseurs)



VIP rule :
Ventilate (O2)
Infuse (remplissage vasculaire)
Pump (vasopresseurs)

Vincent JL. NEJM 2013. 369,18 : 1726 - 1734

Les moyens

- Remplissage vasculaire
  - **Cristalloïdes** en 1ère intention *(grade 1B)*
  - Minimum 30 ml/kg
  - Fluid challenge
  - Monitorer

- Amines vasopressives
  - **Noradrénaline** *(grade 1B)*

RESEARCH Open Access

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*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 4, 2010 VOL. 362 NO. 9

Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D., Didier Chochrad, M.D., Cesar Aldecoa, M.D., Alexandre Brasseur, M.D., Pierre Defrance, M.D., Philippe Gottignies, M.D., and Jean-Louis Vincent, M.D., Ph.D., for the SOAP II Investigators*

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).
3. Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).
4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).
5. Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (e.g., change in pulse pressure, stroke volume variation) or static (eg, arterial pressure, heart rate) variables (UG).

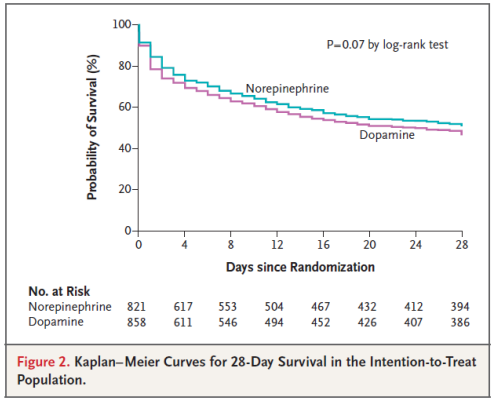
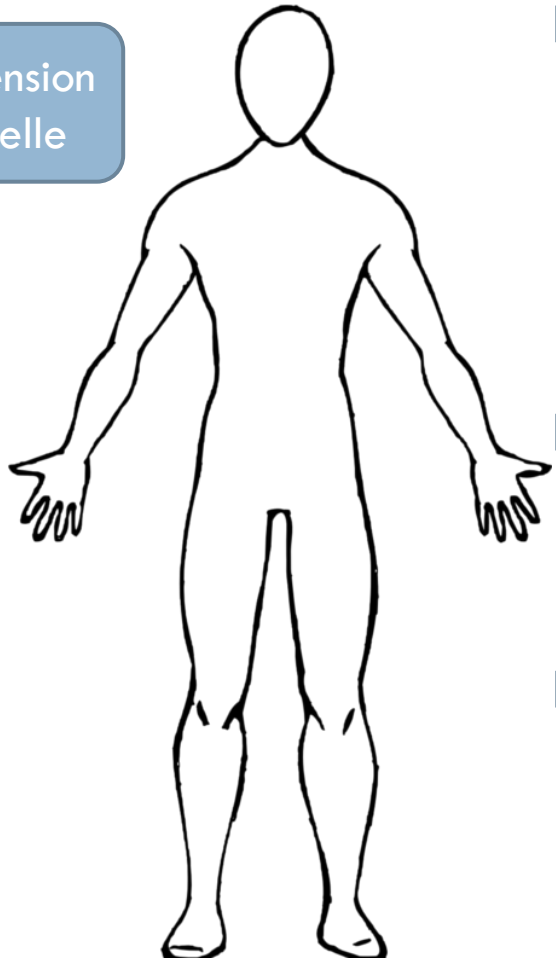


Figure 2. Kaplan–Meier Curves for 28-Day Survival in the Intention-to-Treat Population.

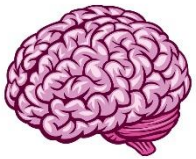
Dellinger et al. Intensive Care Med 2013, 39 : 165 - 228

Clinique

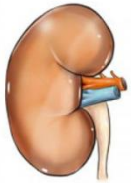
Hypotension artérielle



Encéphalopathie ?



Oligurie ?



Marbrures ?

Marbrures

Intensive Care Med (2011) 37:801–807
DOI 10.1007/s00134-011-2163-y

ORIGINAL

H. Ait-Oufella
S. Lemoinne
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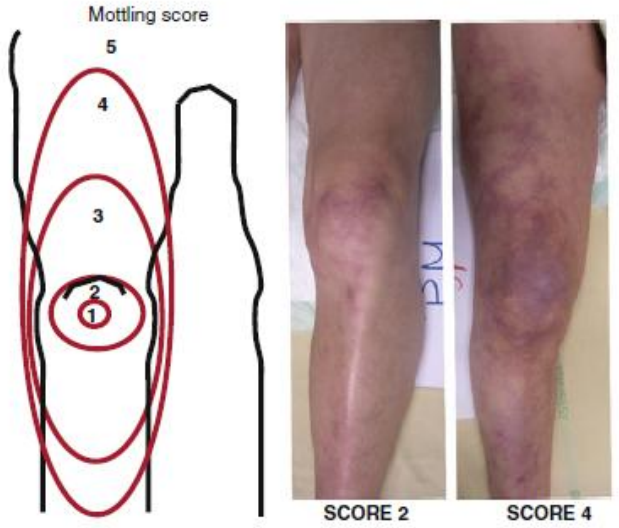
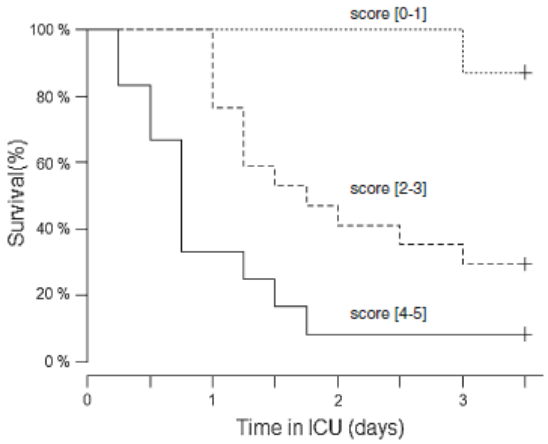
D. Margetis
B. Guidet
E. Maury
G. Offenstadt

Mottling score predicts survival in septic shock

- Rôle crucial de la microcirculation
- Etude prospective observationnelle
- Corrélation entre marbrures et survie
- « **Mottling score** » de 0 à 5
  - Association mottling score / mortalité à J14 :
    - Score 0–1 OR 1
    - Score 2–3 OR 16, 95% CI (4–81)
    - Score 4–5 OR 74, 95% CI (11–1,568), p < 0.0001
  - Plus le score est élevé, plus tôt les patients meurent (p < 0,0001)
  - ↓ pendant réanimation : meilleur pronostic (77 vs 12%, p = 0,0005)





Ait Oufella H. et al. Intensive Care Med 2011. 37 : 801 - 807

Diurèse

Nephrol Dial Transplant (2008) 23: 904–909
doi: 10.1093/ndt/gfm610
Advance Access publication 7 December 2007

Original Article

Acute renal failure in patients with severe sepsis and septic shock—a significant independent risk factor for mortality: results from the German Prevalence Study

- ↓ diurèse fréquente dans le choc septique
- ↓ pression perfusion rénale
- Hypovolémie : remplissage vasculaire → limiter l'altération de la fonction rénale

- Etude prospective, 401 patients
- ARF :
  - créatinine 2N ou diurèse < 0,5 ml/kg/h
  - ↑ **significative de mortalité** dans le groupe ARF (67,3% vs 42,8 % p < 0,0001)
  - ARF facteur indépendant de mortalité (OR 2,11 IC 95% 1,27-3,52)

ARF in patients with severe sepsis/septic shock

Table 3. Clinical outcome parameters in patients with and without ARF

	With ARF ($n = 166$)	Without ARF ($n = 224$)	P-value
In-hospital mortality (%)	67.3[a]	42.8[b]	<0.0001
ICU mortality (%)	64.6[c]	39.5[d]	<0.0001
Median (IQR) APACHE II score (points)	22 (17–28)	16 (11–22)	<0.0001
Median (IQR) Non-renal APACHE II score (points)	18 (13–23)	15 (10–21)	0.0002
Median (IQR) SOFA score (points)	10 (7–13)	7 (5–9)	<0.0001
Median (IQR) Renal SOFA score (points)	2 (1–4)	0 (0–1)	<0.0001
Median (IQR) Non-renal SOFA score (points)	8 (5–11)	7 (4–8)	0.0023

Legrand M. Understanding urine output in critically ill patients. Annals of intensive care. 2011, 1 : 13

Encéphalopathie septique

- Dysfonction cérébrale résultant de la réponse inflammatoire à une infection sans infection directe du SNC
- Fréquent et grave, ↑ **morbi-mortalité**
- **Altération vigilance et conscience :** delirium, coma
- Réversible ? (altérations cognitives au décours du sepsis)
- Physiopathologie mal connue
  - Altération de la BHE
  - Troubles microcirculatoires
  - Hypoperfusion et ischémie cérébrale

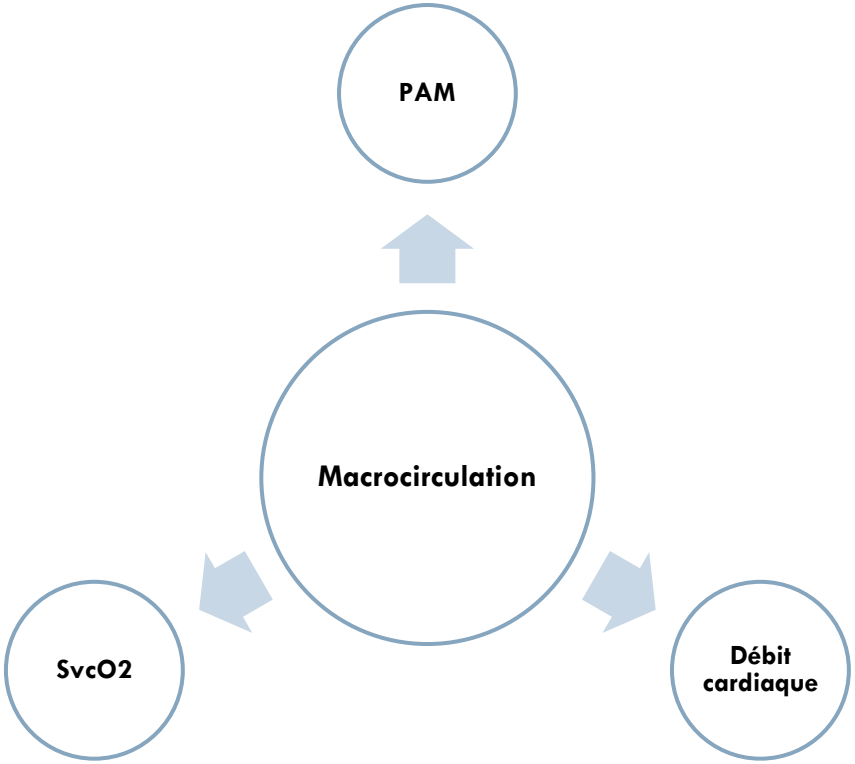
- Evaluation sous sédation ?

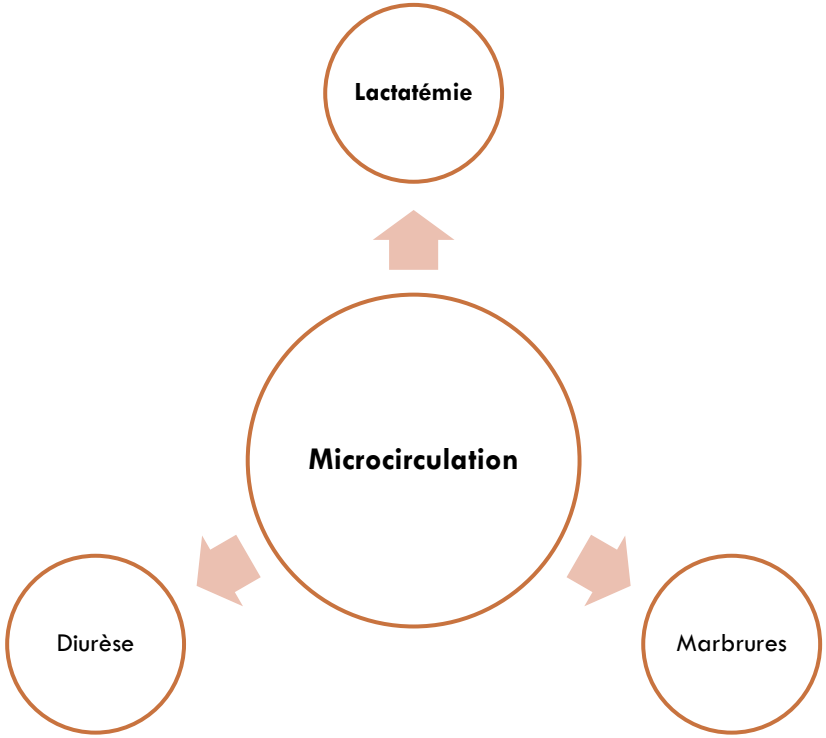
A.Checinski et al. L'encéphalopathie liée au sepsis et ses diagnostics différentiels. SRLF 2010

Cibles

- **Marbrures** : score / évolution
- Maintenir **perfusion rénale**
  - Diurèse > 0,5 ml/kg/h
- Maintenir **perfusion cérébrale**

Macro / Micro


PAM
Macrocirculation
SvcO2
Débit cardiaque


Lactatémie
Microcirculation
Diurèse
Marbrures

Evaluer la perfusion tissulaire

- Near-Infrared-Spectroscopy (**NIRS**) : mesure oxygénation tissulaire (StO2)
- Orthogonal polarization spectral (**OPS**)
- Sidestream dark field (**SDF**)
  - Measure of vessel density
  - 2 indices of vascular perfusion
  - Flow heterogeneity index
- Recherche

Research

Open Access

How to evaluate the microcirculation: report of a round table conference

Daniel De Backer[1], Steven Hollenberg[2], Christiaan Boerma[3,4], Peter Goedhart[4], Gustavo Büchele[1], Gustavo Ospina-Tascon[1], Iwan Dobbe[4] and Can Ince[4]

The ideal analysis report

Component of report	Measure (if applicable)	Details (if applicable)
Vessel density	Total vessel density	
	Perfused vessel density (PVD)	All (n/mm)[a] Small vessels (n/mm)[a]
Perfusion indices	Proportion of perfused vessels (PPV [%])	All Large vessels Small vessels
	Microvascular flow index (MFI)	All Large vessels Small vessels
Heterogeneity index (%)		

De Backer et al. Critical Care 2007, 11 : R101

PAM

- Surviving sepsis campaign
- **PAM ≥ 65 mmHg ?**

PAM

- Niveau PAM cible ?
- Analyse post hoc :
  - Pas d'augmentation de survie pour PAM ≥ 70 mmHg
  - ↑ PAM > 70 mmHg en ↑ amines pourrait ↑ mortalité
  - Futures études : PAM acceptable la plus basse ?

Research Open Access

Association of arterial blood pressure and vasopressor load with septic shock mortality: a post hoc analysis of a multicenter trial

Martin W Dünser[1], Esko Ruokonen[2], Ville Pettilä[3], Hanno Ulmer[4], Christian Torgersen[5], Christian A Schmittinger[5], Stephan Jakob[1] and Jukka Takala[1]

Dünser et al. Critical Care 2009, 13:R181

- Etude prospective randomisée
  - Effets de l'augmentation de la PAM sur fonction rénale
  - De 65 à 85 mmHg
  - Pas d'amélioration de la fonction rénale

Increasing mean arterial pressure in patients with septic shock: Effects on oxygen variables and renal function*

Aurélie Bourgoin, MD; Marc Leone, MD; Anne Delmas, MD; Franck Garnier, MD; Jacques Albanèse, MD; Claude Martin, MD, FCCM

Bourgoin et al. Critical care Med 2005, 33 : 780 - 786

Intensive Care Med (2014) 40:1795–1815
DOI 10.1007/s00134-014-3525-z
CONFERENCE REPORTS AND EXPERT PANEL

PAM

Maurizio Cecconi
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Christoph Hofer
Roman Jaeschke
Alexandre Mebazaa
Michael R. Pinsky
Jean Louis Teboul
Jean Louis Vincent
Andrew Rhodes

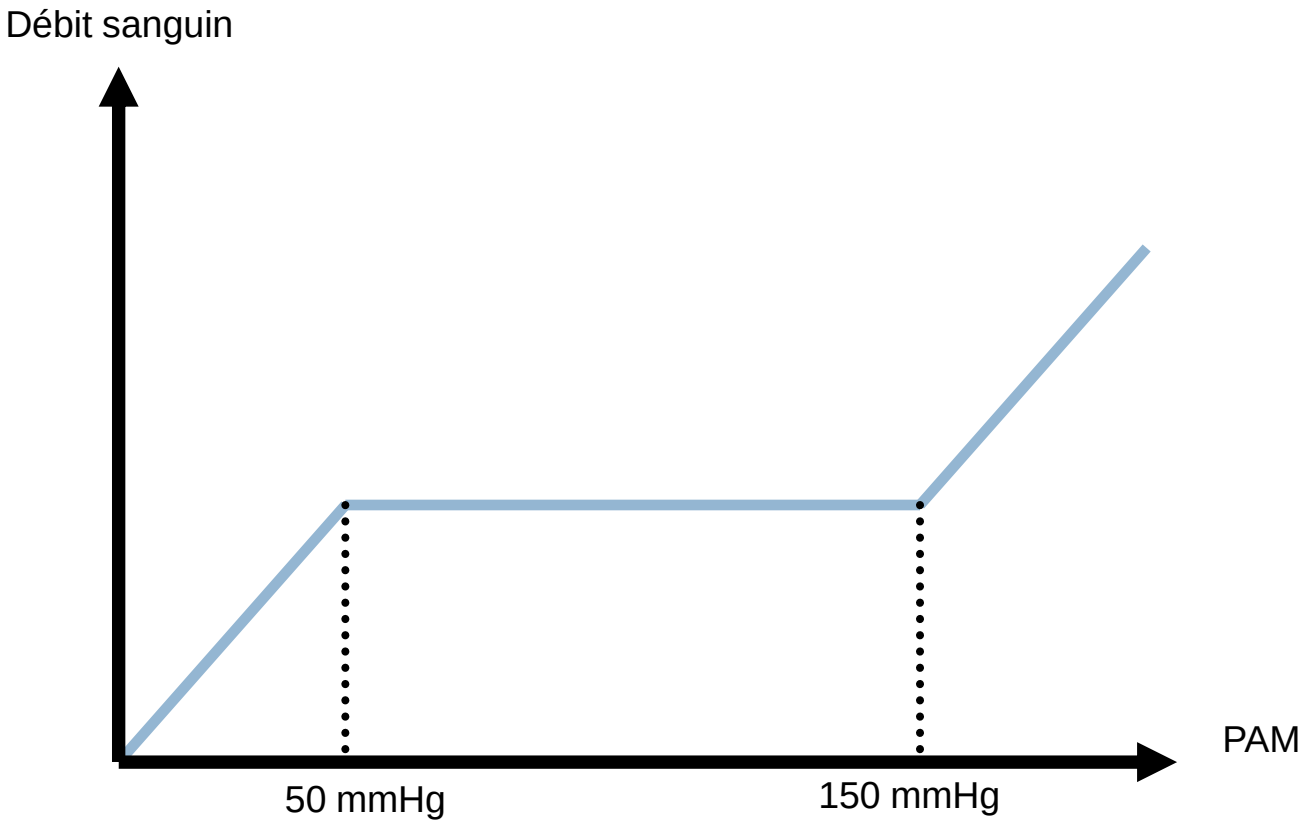
Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine

- Variations interindividuelles
- Variations dans le temps
- Entre 65 mmHg et 75 mmHg → **INDIVIDUALISE**
- Cible plus élevée pour patients avec HTA (↓ risque d'insuffisance rénale ?)

21.	We recommend individualizing the target blood pressure during shock resuscitation	Level 1; QoE moderate (B)	Recommendation
22.	We recommend to initially target a MAP of ≥65 mmHg	Level 1; QoE low (C)	Recommendation
23.	We suggest to tolerate a lower level of blood pressure in patients with uncontrolled bleeding (i.e. in patients with trauma) without severe head injury	Level 2; QoE low(C)	Recommendation
24.	We suggest a higher MAP in septic patients with history of hypertension and in patients that show clinical improvement with higher blood pressure	Level 2; QoE moderate (B)	Recommendation

Cecconi et al. Intensive Care Med 2014, 40 : 1795 - 1815

Autorégulation



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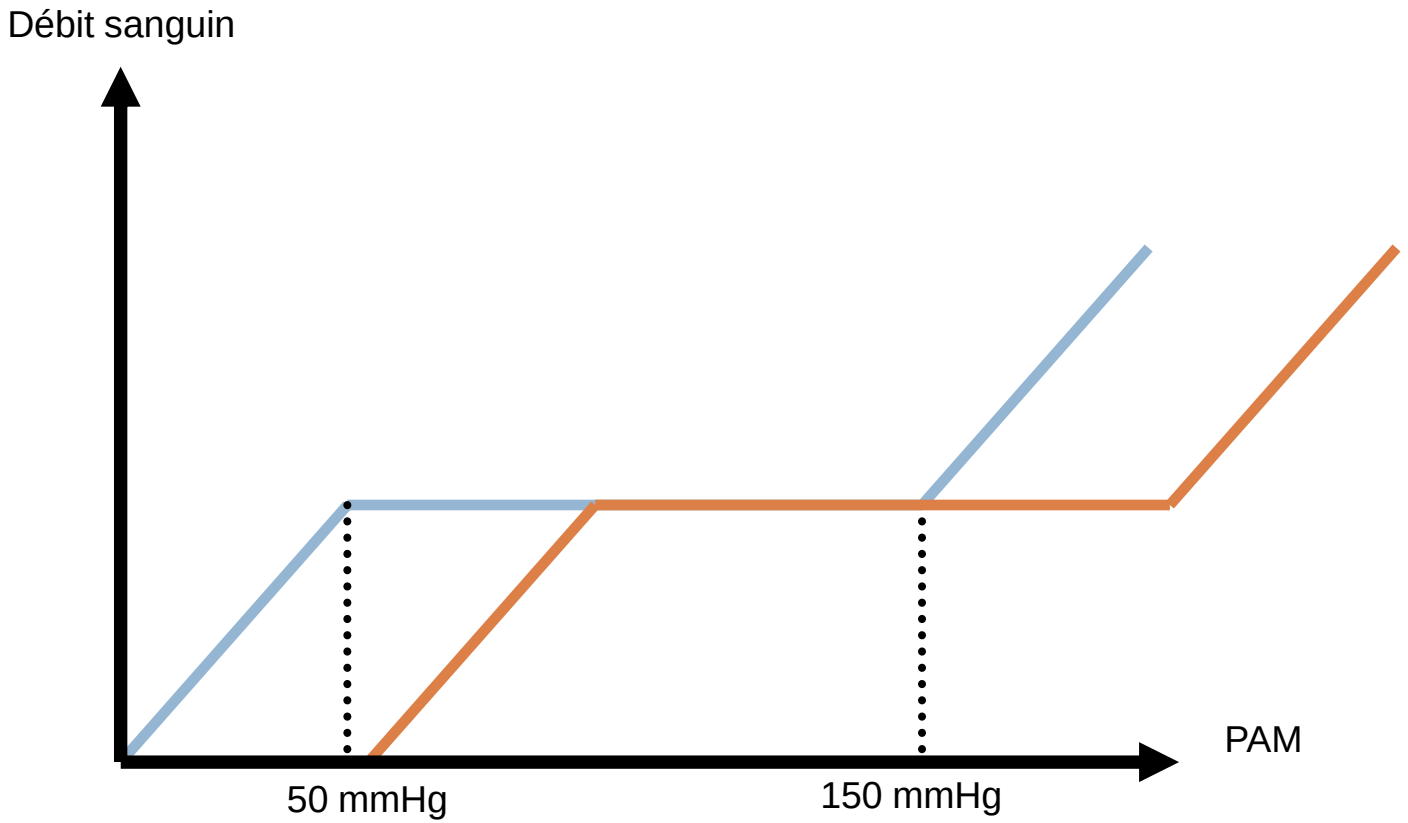
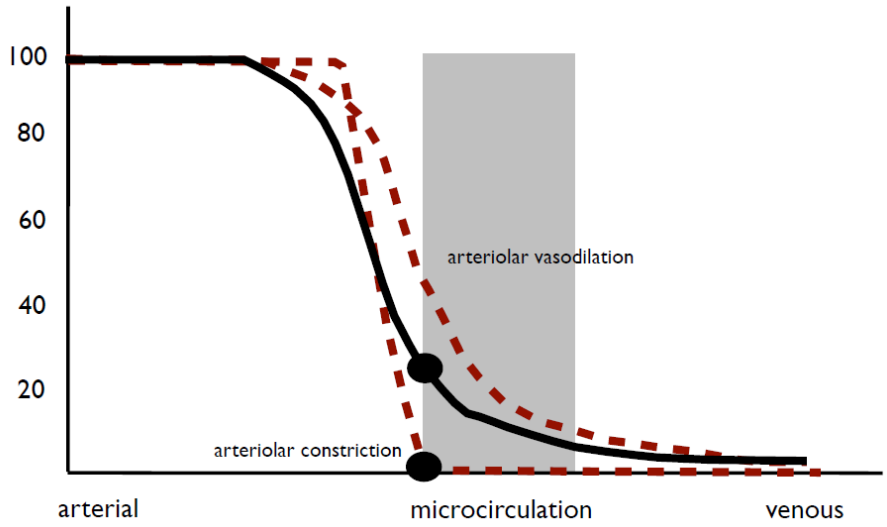


Bénéfice / risque

- Objectif de PAM
- Retentissement sur microcirculation



PAM > 75 mmHg ?

- Etudes prospectives randomisées sur choc septique
- PAM > 65 mmHg souvent observées : entre 75 et 95 mmHg dans les 24h

The New England Journal of Medicine

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*

VARIABLE AND TREATMENT GROUP	BASE LINE (0 hr)	HOURS AFTER START OF THERAPY		
		6	0–6†	7–72‡
Heart rate (beats/min)				
Standard therapy	114±27	105±25	108±23	99±18
EGDT	117±31	103±19	105±19	96±18
P value	0.45	0.12	0.25	0.04
Central venous pressure (mm Hg)				
Standard therapy	6.1±7.7	11.8±6.8	10.5±6.8	11.6±6.1
EGDT	5.3±9.3	13.8±4.4	11.7±5.1	11.9±5.6
P value	0.57	0.007	0.22	0.68
Mean arterial pressure (mm Hg)				
Standard therapy	76±24	81±18	81±16	80±15
EGDT	74±27	95±19	88±16	87±15
P value	0.60	<0.001	<0.001	<0.001

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 28, 2008 VOL. 358 NO. 9

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

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Hemodynamic variables			
Systolic blood pressure — mm Hg	110±17	108±17	0.10
Mean arterial pressure — mm Hg	73±10	72±9	0.23
Arterial pH	7.31±0.1	7.32±0.1	0.71
Serum lactate level — mmol/liter	3.5±3.0	3.5±3.2	0.96

Intensive Care Med (2009) 35:1225–1233
DOI 10.1007/s00134-009-1427-2

ORIGINAL

PAM > 75 mmHg ?

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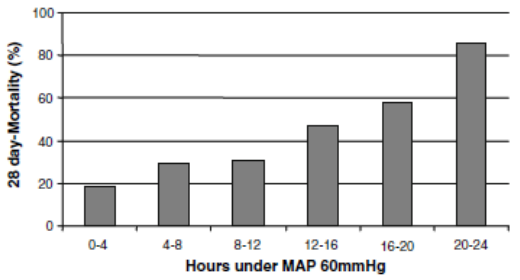
Arterial blood pressure during early sepsis and outcome

- Cohorte rétrospective, n = 274
- Analyse pression artérielle dans les premières 24h
- PAM > 60 mmHg (60 – 65 – 70 – 75 mmHg)
- Pas de différence de mortalité à J28
- Intérêt d'une PAM plus élevée pour maintenir la fonction rénale ?

Table 3 Association between different arterial blood pressure levels and 28-day-mortality adjusted for disease severity

	n^a	Mean ± SD[b]	AUC ROC	Sens (%)	Spec (%)	PPV (%)	NPV (%)	*P* value
SAP								
HTI of ABP drops < 95 mmHg SAP	246	308 ± 604	0.743	93.4	29	77.4	62.9	0.06
HTI of ABP drops < 90 mmHg SAP	235	212 ± 542	0.737	94.4	26.3	77	64.5	0.12
HTI of ABP drops < 85 mmHg SAP	217	143 ± 489	0.734	93.4	25	76	59.4	0.22
HTI of ABP drops < 80 mmHg SAP	189	96 ± 444	0.731	94.4	26.3	77	64.5	0.4
HTI of ABP drops < 75 mmHg SAP	159	67 ± 406	0.731	94.4	26.3	77	64.5	0.63
HTI of ABP drops < 70 mmHg SAP	124	50 ± 373	0.731	94.4	26.3	77	64.5	0.84
HTI of ABP drops < 65 mmHg SAP	77	38 ± 343	0.731	94.4	26.3	77	64.5	0.99
MAP								
HTI of ABP drops < 75 mmHg MAP	261	475 ± 388	0.775	93.4	42.1	80.7	71.1	<0.001**
HTI of ABP drops < 70 mmHg MAP	252	297 ± 303	0.777	94.9	40.8	80.6	75.6	<0.001**
HTI of ABP drops < 65 mmHg MAP	245	162 ± 217	0.778	95.9	39.5	80.4	79	<0.001**
HTI of ABP drops < 60 mmHg MAP	220	74 ± 141	0.779	95.4	39.5	80.3	76.9	<0.001**
HTI of ABP drops < 55 mmHg MAP	177	30 ± 86	0.764	94.9	32.9	78.6	71.4	0.001**
HTI of ABP drops < 50 mmHg MAP	135	11 ± 49	0.757	94.9	26.3	77	66.7	0.02
HTI of ABP drops < 45 mmHg MAP	85	5 ± 28	0.751	94.4	29	77.5	66.7	0.05
HTI of ABP drops < targeted MAP	159	56 ± 113	0.769	95.4	37.3	78.1	80	0.001*
MPP								
HTI of ABP drops < 60 mmHg MPP	210	398 ± 432	0.788	92.4	42.9	74.4	71.4	<0.001**
HTI of ABP drops < 55 mmHg MPP	200	252 ± 343	0.791	92.4	41.4	78	70.7	<0.001**
HTI of ABP drops < 50 mmHg MPP	177	147 ± 254	0.793	92.4	40	77.5	70	<0.001**
HTI of ABP drops < 45 mmHg MPP	159	77 ± 175	0.797	92.4	40	77.5	70	<0.001**
HTI of ABP drops < 40 mmHg MPP	128	38 ± 111	0.793	93	38.6	77.3	71.1	0.001**
HTI of ABP drops < 35 mmHg MPP	90	17 ± 63	0.792	93.6	38.6	77.4	73	0.01
HTI of ABP drops < 30 mmHg MPP	60	7 ± 31	0.782	90.5	37.1	76.3	63.4	0.02



Dünser et al. Intensive Care Med 2009. 35 : 1225 - 1233

SEPSISPAM

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

- Essai multicentrique randomisé
- n = 776
- 2 groupes :
  - « high target group » : 80 – 85 mmHg
  - « low target group » : 65 – 70 mmHg

- Pas de différence significative sur mortalité
  - à J 28 : 36,5 % vs 34 % (p = 0,57)
  - à J 90 : 43,7 % vs 42,3 % (p = 0,74)

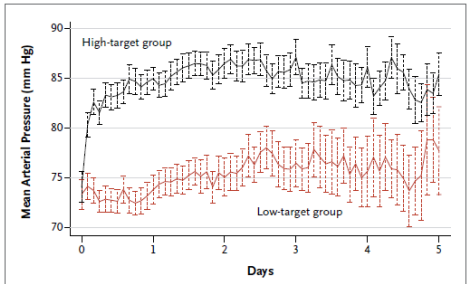


Figure 2. Mean Arterial Pressure during the 5-Day Study Period.
Mean arterial pressures were significantly lower in the low-target group than in the high-target group during the 5 protocol-specified days (P=0.02 by repeated-measures regression analysis), although the values exceeded the target values of 80 to 85 mm Hg in the high-target group and 65 to 70 mm Hg in the low-target group. The I bars represent 95% confidence intervals.

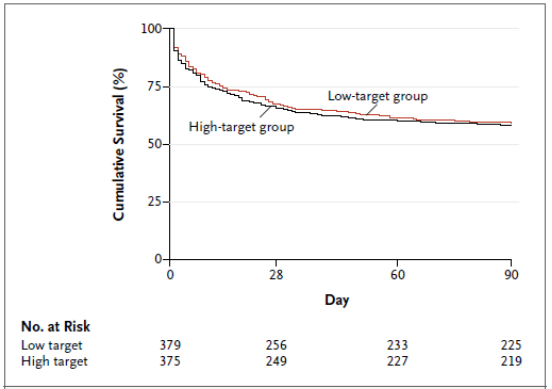


Figure 3. Kaplan–Meier Curves for Cumulative Survival.
Data for the survival analysis, which was performed in the intention-to treat population, were censored at 90 days. There was no significant difference in survival between the high-target group and the low-target group (P=0.57 at 28 days; P=0.74 at 90 days).

Asfar P. et al. NEJM 2014. 370 : 1583 - 1593

Débit cardiaque

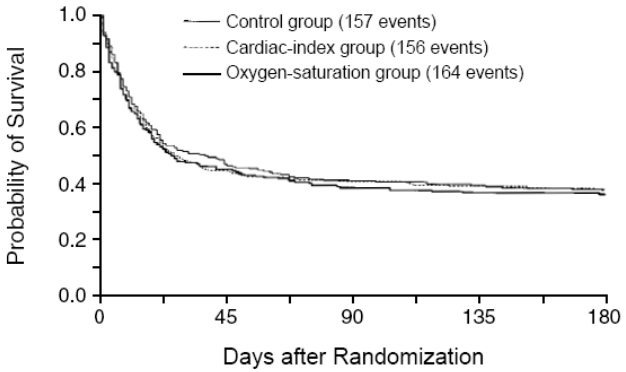
The New England
Journal of Medicine

Volume 333 OCTOBER 19, 1995 Number 16

A TRIAL OF GOAL-ORIENTED HEMODYNAMIC THERAPY IN CRITICALLY ILL PATIENTS

LUCIANO GATTINONI, M.D., LUCA BRAZZI, M.D., PAOLO PELOSI, M.D., ROBERTO LATINI, M.D., GIANNI TOGNONI, M.D., ANTONIO PESENTI, M.D., AND ROBERTO FUMAGALLI, M.D., FOR THE SvO_2 COLLABORATIVE GROUP*

- Adapté …
- Monitoring fonction cardiaque
  - Poser un **diagnostic** : mécanisme du choc
  - Guider la **thérapeutique**
  - **Evaluer** la réponse au traitement



- Etude prospective randomisée :
  - Groupe cardiac-index vs. SvO2 vs. contrôle
  - Thérapeutiques hémodynamiques visant un débit cardiaque supra normal
  - Pas de différence de mortalité (48,4 % vs. 48,6% vs 52,1% p = 0,638)

Gattinoni et al. NEJM 1995. 333, 16 : 1025 - 1032

Monitorer

- Variations respiratoires / Delta PP
- Test lever de jambes
- Fluid challenge
- Echographie cardiaque
- PiCCo
- Swan - Ganz

Vincent et al. Critical Care 2011, 15:229
http://ccforum.com/content/15/4/229

CRITICAL CARE

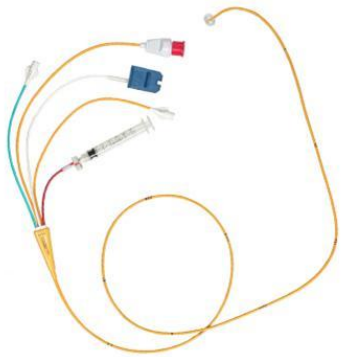
REVIEW

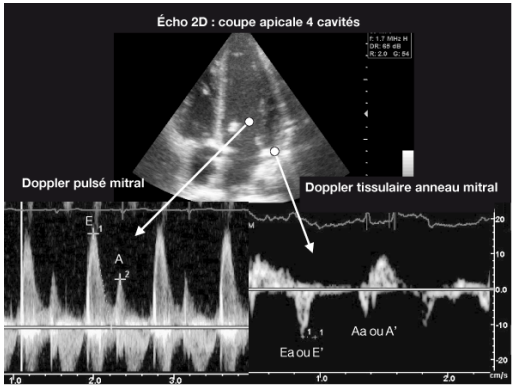
Clinical review: Update on hemodynamic monitoring - a consensus of 16

Jean-Louis Vincent[1*], Andrew Rhodes[2], Azriel Perel[3], Greg S Martin[4], Giorgio Della Rocca[5], Benoit Vallet[6], Michael R Pinsky[7], Christoph K Hofer[8], Jean-Louis Teboul[9], Willem-Pieter de Boode[10], Sabino Scolletta[11], Antoine Vieillard-Baron[12], Daniel De Backer[1], Keith R Walley[13], Marco Maggiorini[14] and Mervyn Singer[15]

Monitoring cardiac function and cardiac output

- Echocardiography can be used for the sequential evaluation of cardiac function in shock *Statement of fact*.
- We do not recommend the routine use of the pulmonary artery catheter for patients in shock. *Recommendation*. Level 1; QoE high (A).
- We suggest PAC in patients with refractory shock and RV dysfunction. *Recommendation*. Level 2; QoE low (C).
- We suggest the use of transpulmonary thermodilution or PAC in patients with severe shock especially in the case of associated acute respiratory distress syndrome. *Recommendation*. Level 2; QoE low (C).
- We recommend that less invasive devices are used, instead of more invasive devices, only when they have been validated in the context of patients with shock. *Best practice*.





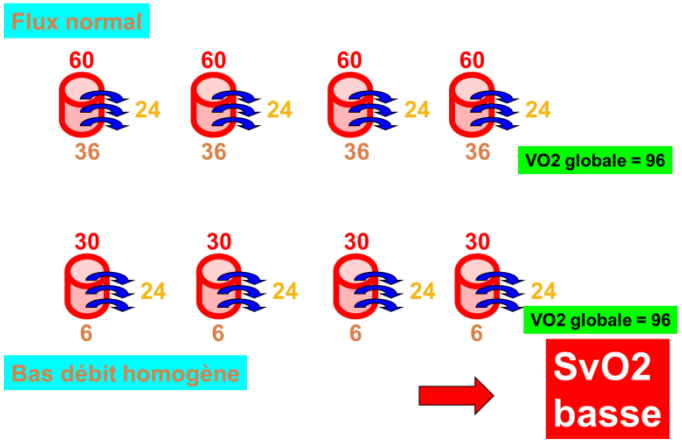
Cecconi et al. Intensive Care Med 2014, 40 : 1795 - 1815

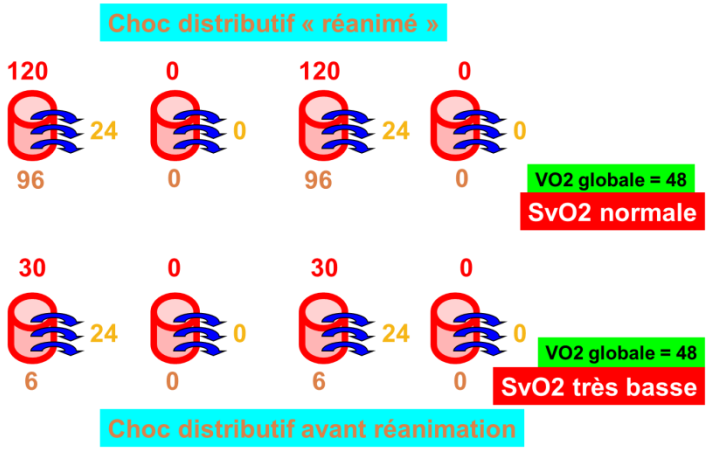
ScvO2

- Corrélation SvO2 (sang veineux mêlé)
- Balance entre transport (TaO2) et consommation en O2 par tissus (VO2)
- Norme : SvO2 = 70 à 75 %

SvO2 = SaO2 – [VO2 / (Débit cardiaque x Hb x 1,34)]
SvO2 = 1 – EO2

- ScvO2 basse dans le choc septique : inadéquation du transport en O2





Favory R. Dysfonction hépato-splanchnique. DURP

Limites ScvO2

- Valeur élevée de ScvO2 : usage limité dans contexte de sepsis
- Ne permet pas de discriminer si le transport en O2 est adéquat
- **pCO2 gap :**
  - Différence artério-veineuse en CO2
  - Peut identifier les patients « under-resuscitated »
  - Valeur > 6 mmHg ⇔ flux sanguin tissulaire insuffisant quand ScvO2 > 70%

Intensive Care Med (2008) 34:2218–2225
DOI 10.1007/s00134-008-1199-0

ORIGINAL

Fabrice Vallée
Benoit Vallet
Olivier Mathe
Jacqueline Parraguette
Arnaud Mari
Stein Silva
Kamran Samii
Olivier Fourcade
Michèle Genestal

Central venous-to-arterial carbon dioxide difference: an additional target for goal-directed therapy in septic shock?

Intensive Care Med (2013) 39:1653–1655
DOI 10.1007/s00134-013-2998-5

EDITORIAL

B. Vallet
M. R. Pinsky
M. Cecconi

Resuscitation of patients with septic shock: please "mind the gap"!

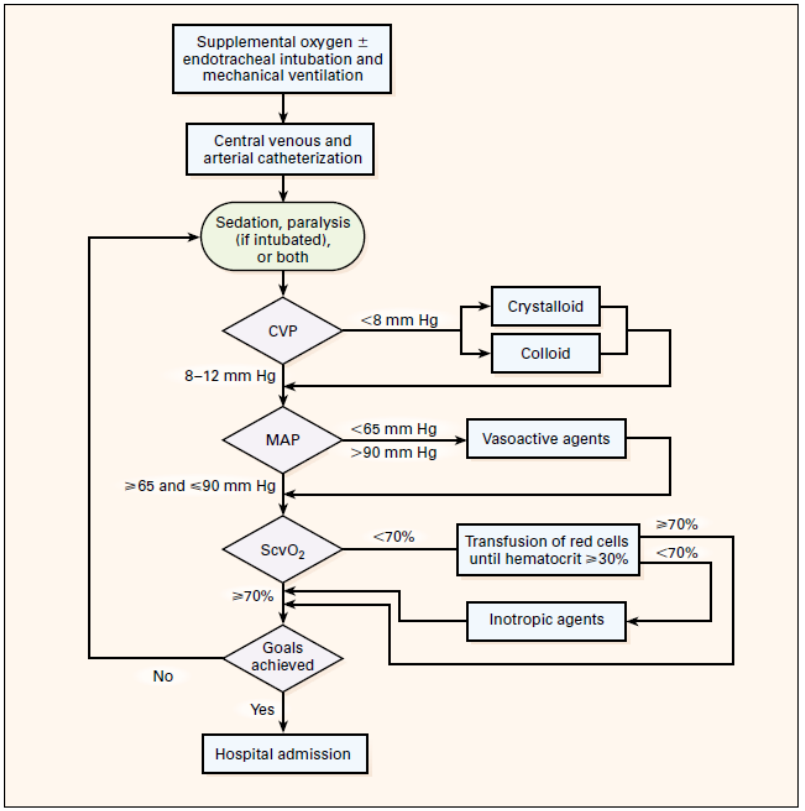
EGDT

The New England Journal of Medicine

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*

- EGDT vs « standard therapy »
- Avant admission en soins intensifs
- n = 263
- ↓ **mortalité** (p = 0,009) :
  - EGDT 30,5 %
  - Contrôle 46,5 %
- EGDT : ↑ significative de ScvO2 (70,4 vs 65,3)
- ↑ ScvO2 > 70% était associé à une meilleure issue
- (ScvO2 moyennes de base : 48 et 49%)



Rivers E. et al. NEJM 2001. 345,19 : 1368 - 1377

ProCESS

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MAY 1, 2014 VOL. 370 NO. 18

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

The ProCESS Investigators*

- Etude multicentrique
- 1341 patients

- Pas de différence significative
  - Mortalité à J90
  - Mortalité à 1an
  - Suppléance d'organe

Table 2. Outcomes.*

Outcome	Protocol-based EGDT (N=439)	Protocol-based Standard Therapy (N=446)	Usual Care (N=456)	P Value†
Death — no./total no. (%)				
In-hospital death by 60 days: primary outcome	92/439 (21.0)	81/446 (18.2)	86/456 (18.9)	0.83‡
Death by 90 days	129/405 (31.9)	128/415 (30.8)	139/412 (33.7)	0.66
New organ failure in the first week — no./total no. (%)				
Cardiovascular	269/439 (61.3)	284/446 (63.7)	256/456 (56.1)	0.06
Respiratory	165/434 (38.0)	161/441 (36.5)	146/451 (32.4)	0.19
Renal	12/382 (3.1)	24/399 (6.0)	11/397 (2.8)	0.04
Duration of organ support — days§				
Cardiovascular	2.6±1.6	2.4±1.5	2.5±1.6	0.52
Respiratory	6.4±8.4	7.7±10.4	6.9±8.2	0.41
Renal	7.1±10.8	8.5±12	8.8±13.7	0.92
Use of hospital resources				
Admission to intensive care unit — no. (%)	401 (91.3)	381 (85.4)	393 (86.2)	0.01
Stay in intensive care unit among admitted patients — days	5.1±6.3	5.1±7.1	4.7±5.8	0.63
Stay in hospital — days	11.1±10	12.3±12.1	11.3±10.9	0.25
Discharge status at 60 days — no. (%)				
Not discharged	3 (0.7)	8 (1.8)	2 (0.4)	0.82
Discharged to a long-term acute care facility	16 (3.6)	22 (4.9)	22 (4.8)	
Discharge to another acute care hospital	8 (1.8)	2 (0.4)	5 (1.1)	
Discharged to nursing home	71 (16.2)	93 (20.9)	88 (19.3)	
Discharged home	236 (53.8)	227 (50.9)	235 (51.5)	
Other or unknown	13 (3.0)	13 (2.9)	18 (3.9)	
Serious adverse events — no. (%)¶	23 (5.2)	22 (4.9)	37 (8.1)	0.32

The ProCESS investigators. NEJM 2014. 370,18 : 1683 - 1693

ARISE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

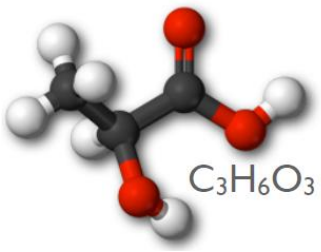
- 1600 patients
- EGDT vs « usual care »
- Pas de différence significative :
  - Mortalité à J90
  - Suppléance d'organe
  - Durée de séjour

Table 2. Study Outcomes.

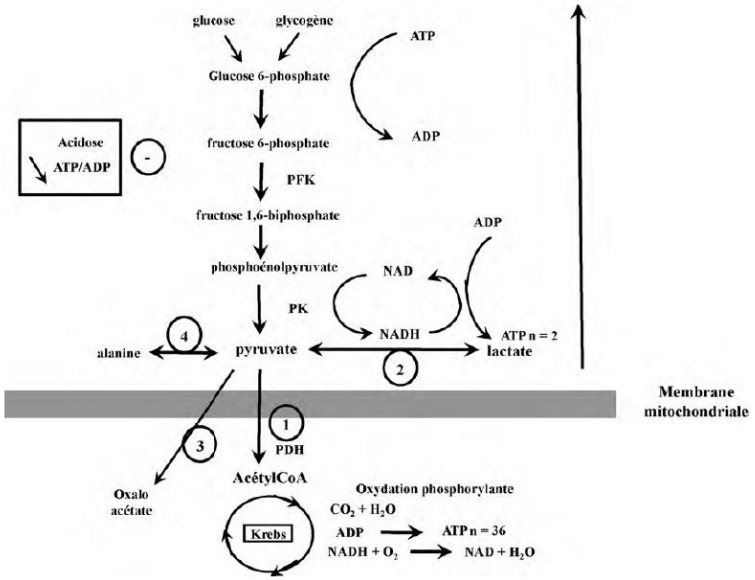
Variable	EGDT (N = 793)	Usual Care (N = 798)	Relative Risk (95% CI)	Risk Difference (95% CI)*	P Value
				percentage points	
Primary outcome: death by day 90 — no./total no. (%)	147/792 (18.6)	150/796 (18.8)	0.98 (0.80 to 1.21)	−0.3 (−4.1 to 3.6)	0.90
Secondary outcomes					
Median duration of stay (IQR)†					
Emergency department — hr	1.4 (0.5–2.7)	2.0 (1.0–3.8)			<0.001
ICU — days	2.8 (1.4–5.1)	2.8 (1.5–5.7)			0.81
Hospital — days	8.2 (4.9–16.7)	8.5 (4.9–16.5)			0.89
Use and duration of organ support‡					
Invasive mechanical ventilation — no./total no. (%)	238/793 (30.0)	251/798 (31.5)	0.95 (0.82 to 1.11)	−1.4 (−6.0 to 3.1)	0.52
Median duration of invasive mechanical ventilation (IQR) — hr	62.2 (23.5–181.8)	65.5 (23.0–157.9)			0.28
Vasopressor support — no./total no. (%)	605/793 (76.3)	525/798 (65.8)	1.16 (1.09 to 1.24)	10.5 (6.1 to 14.9)	<0.001
Median duration of vasopressor support (IQR) — hr	29.4 (12.9–61.0)	34.2 (14.0–67.0)			0.24
Renal-replacement therapy — no./total no. (%)	106/793 (13.4)	108/798 (13.5)	0.99 (0.77 to 1.27)	−0.2 (−3.5 to 3.2)	0.94
Median duration of renal-replacement therapy (IQR) — hr§	57.8 (25.3–175.0)	85.9 (29.3–182.9)			0.40
Tertiary outcomes — no./total no. (%)					
Death by day 28	117/792 (14.8)	127/797 (15.9)	0.93 (0.73 to 1.17)	−1.2 (−4.7 to 2.4)	0.53
Death by the time of discharge from ICU	79/725 (10.9)	85/661 (12.9)	0.85 (0.64 to 1.13)	−2.0 (−5.4 to 1.5)	0.28
Death by the time of discharge from hospital¶	115/793 (14.5)	125/797 (15.7)	0.92 (0.73 to 1.17)	−1.2 (−4.7 to 2.3)	0.53

The ARISE investigators. NEJM 2014. 371, 16 : 1496 - 1506

Lactate



- L-Lactate
- Substrat issu de la glycolyse
- Pyruvate + NADH + H^+ ⇔ Lactate + NAD
- Accumulation :
  - excès de production
  - défaut de clairance
- Concentration plasmatique < 2 mmol/L
- Demi-vie brève < 10 min
- Source d'énergie

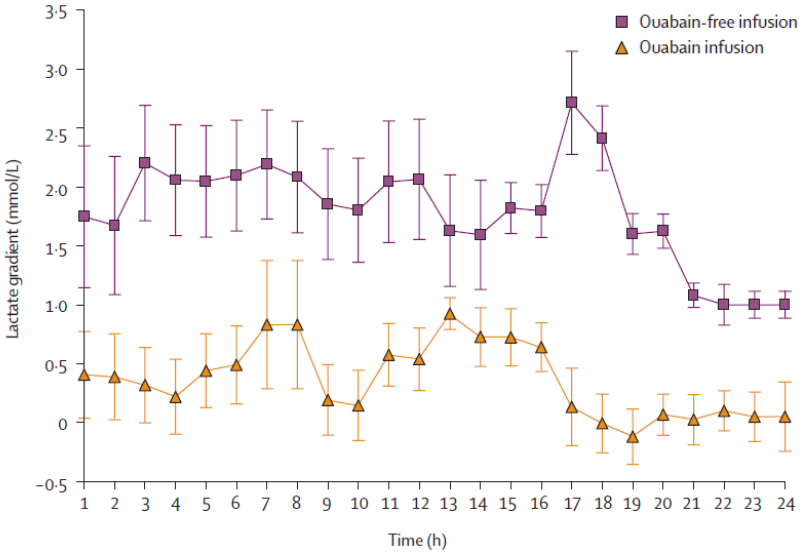


Orban JC. Réanimation 2010, 19 : 384 - 392

Relation between muscle Na^+K^+ ATPase activity and raised lactate concentrations in septic shock: a prospective study

Bruno Levy, Sébastien Gibot, Patricia Franck, Aurélie Cravoisy, Pierre-Edouard Bollaert

- Hyperlactatémie ⇔ preuve de l'hypoxie tissulaire
- Muscle squelettique : source de formation de lactate par glycolyse aérobie et stimulation Na/K ATPase
  - In vivo microdialysis : ↓ lactate musculaire par inhibition Na/K ATPase
  - Ouabaïne = inhibiteur pompe Na/K ATPase
  - n = 14, patients en choc septique
  - Ouabaïne ↓ production de lactate et pyruvate (p = 0,0001)

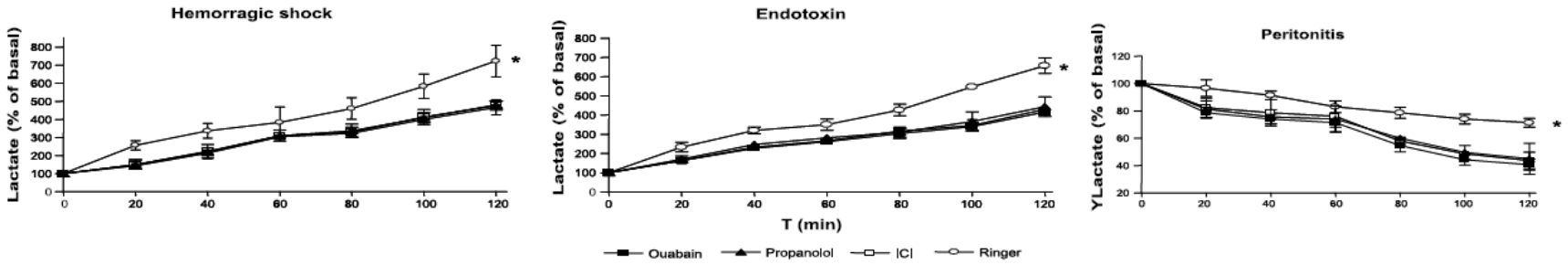


INCREASED AEROBIC GLYCOLYSIS THROUGH BETA-2 STIMULATION IS A COMMON MECHANISM INVOLVED IN LACTATE FORMATION DURING SHOCK STATES

Bruno Levy, Olivier Desebbe, Chantal Montemont, and Sebastien Gibot
Groupe CHOC, Contrat AVENIR INSERM 2006, Faculté de Médecine, Nancy Université, Vandoeuvre les Nancy, France

Shock 2008;30(4);417–421

- <u>Stimulation ß2 :</u> ↑ **glycolyse aérobie** et ↑ **production lactate**
- Etude chez le rat, 3 modèles de chocs
  - Production de lactate par le muscle au cours de l'état de choc
  - Liée à une stimulation ß2 adrénergique
- Ouabaïne → lactate musculaire ↓
- ↑ de la lactatémie due à une ↑ **d'activité de la pompe Na/K ATPase** ⇔ indépendante de l'hypoxie tissulaire



Levy B. et al. Shock 2008, 30 (4) : 417 - 421

Fluid Resuscitation of Adults With Severe Falciparum Malaria: Effects on Acid-Base Status, Renal Function, and Extravascular Lung Water*

Josh P. Hanson, MBBS[1]; Sophia W.K. Lam, MBBS[1]; Sanjib Mohanty, MD[2]; Shamshul Alam, MD[3]; Rajyabardhan Pattnaik, MBBS[2]; Kishore C. Mahanta, MD[2]; Mahatab Uddin Hasan, MD[3]; Prakaykaew Charunwatthana, MD[1]; Saroj K. Mishra, MD[2]; Nicholas P.J. Day, MD[1,4]; Nicholas J. White, MD[1,4]; Arjen M. Dondorp, MD[1,4]

- Plasmodium Falciparum
- Expansion volémique monitorée par PICCO
- Peu de ↓ de la lactatémie
  - Acidose lactique → séquestration des érythrocytes parasités dans la circulation
  - Et non de l'hypovolémie !
- Peu d'effets du remplissage vasculaire
- Attention risque d'œdème pulmonaire

- Augmentation mortalité à J28
- Bolus albumine vs. SSI vs. pas de bolus
- Prévalence paludisme 57 à 59 %

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Mortality after Fluid Bolus in African Children with Severe Infection

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Review Article

Blood lactate monitoring in critically ill patients: A systematic health technology assessment*

Tim C. Jansen, MD; Jasper van Bommel, MD, PhD; Jan Bakker, MD, PhD

Crit Care Med 2009 Vol. 37, No. 10

- Bases de données, Pubmed
- CCL : The use of blood lactate monitoring has a place in risk-stratification in critically ill patients, but it is unknown whether the routine use of lactate as a resuscitation endpoint improves outcome.
  This warrants randomized controlled studies on the efficacy of lactate-directed therapy.

Table 1. Eight-question format for performing a systematic health technology assessment

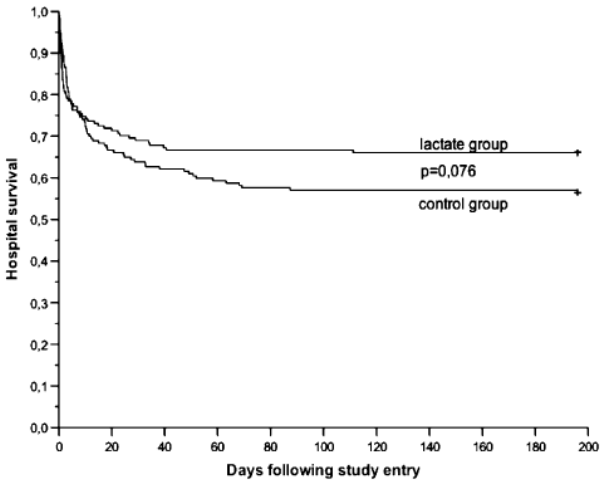
I.	Does lactate measurement perform well in a laboratory setting?
II.	Does lactate monitoring provide important information in a number of clinical situations?
III.	Is there a relationship between lactate levels and metabolic acidosis?
IV.	Does lactate monitoring increase workers' confidence?
V.	Does lactate measurement alter therapeutic decisions?
VI.	Does lactate monitoring result in benefit to the patients?
VII.	Can you expect a similar benefit in your own setting?
VIII.	Are the expected benefits worth the extra costs?

Early Lactate-Guided Therapy in Intensive Care Unit Patients

A Multicenter, Open-Label, Randomized Controlled Trial

Tim C. Jansen[1], Jasper van Bommel[1], F. Jeanette Schoonderbeek[3], Steven J. Sleeswijk Visser[4], Johan M. van der Klooster[5], Alex P. Lima[1], Sten P. Willemsen[2], and Jan Bakker[1], for the LACTATE study group*

- Lactate guided therapy
- Patients admis en ICU, lactatémie > 3 mEq/L
  - Groupe lactate : ↓ lactate de 20% par 2h pendant les 8 premières heures
- Objectif principal : mortalité hospitalière
- ↓ **significative de mortalité** dans le groupe lactate :
  - HR 0,61 [IC 95% : 0,43-0,87], p= 0,006
- Intérêt du monitorage du lactate ?



Jansen et al. AJRCCM 2010. 182 : 752 - 761

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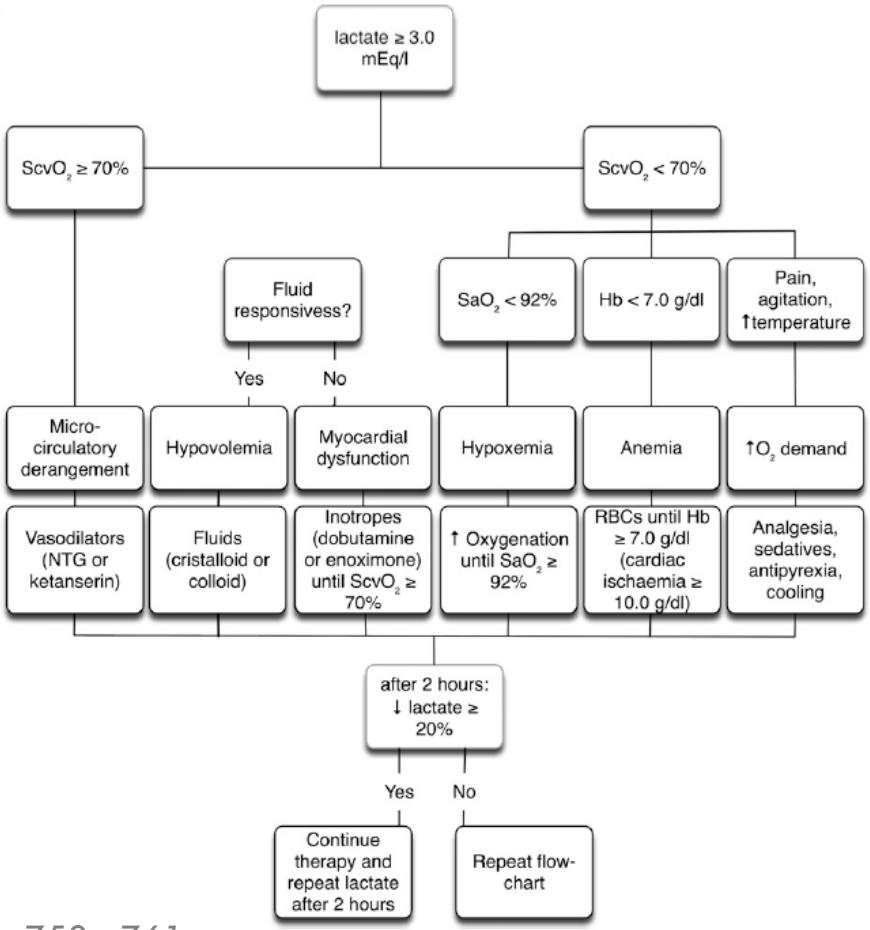

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Lactate vs ScvO2

Lactate Clearance vs Central Venous Oxygen Saturation as Goals of Early Sepsis Therapy

Alan E. Jones, MD

- Etude de non-infériorité
- Essai randomisé multicentrique
- n = 300
- PVC + PAM + ScvO2 / lactate
- **Pas de différence significative** de mortalité :
  - ScvO2 group : 23 %
  - Lactate clearance group : 17 %

Table 5. Hospital Mortality and Length of Stay

Variable	Lactate Clearance Group (n = 150)	$ScvO_2$ Group (n = 150)	Proportion Difference (95% Confidence Interval)	*P* Value[b]
In-hospital mortality, No. (%)[a]				
Intent to treat	25 (17)	34 (23)	6 (–3 to 15)	
Per protocol	25 (17)	33 (22)	5 (–3 to 14)	
Length of stay, mean (SD), d				
ICU	5.9 (8.46)	5.6 (7.39)		.75
Hospital	11.4 (10.89)	12.1 (11.68)		.60
Hospital complications				
Ventilator-free days, mean (SD)	9.3 (10.31)	9.9 (11.09)		.67
Multiple organ failure, No. (%)	37 (25)	33 (22)		.68
Care withdrawn, No. (%)	14 (9)	23 (15)		.15

Jones A. et al. JAMA 2010. 303 : 739 - 746

Lactate to guide therapy ?

- Diminution significative (20% par 2h) de la lactatémie
- Réduction mortalité hospitalière
- Diminution des dysfonctions d'organe

- Monitorer le lactate !

- Lactate // ScvO2

Et en résumé …

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- Pression artérielle moyenne > 65 mmHg et < 75 mmHg
  … mais **adaptée** à chaque patient et dans le temps !
- **Individualisation** pour un patient donné
- **ScvO2 > 70%** ??
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- **Lactate** : ↓ de 20% par 2h, mesures itératives
- Controverse Rivers / nouvelles études : probablement pas antinomiques

- Avenir : marbrures ? pression artérielle plus basse ? FC ??

Merci de votre attention