

Quelle PAM dans le sepsis?

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DESC Réa

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65

Merci!

Au programme

- × Dernières définitions du sepsis
- × Hypotension: Ami ou Ennemi?
- × Hypotension et rein
- × Hypotension et microcirculation
- × Les années Rivers et la Goal directed therapy

Du nouveau en 2016

- × Dernière mise à jour depuis 2003
- × Nécessité d'une nouvelle définition car connaissance plus approfondie sur les mécanismes et littérature vaste
- × Plus orienté vers les dysfonctions d'organes

JAMA. 2016 Feb 23;315(8):801-10. doi: 10.1001/jama.2016.0287.

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

Singer M¹, Deutschman CS², Seymour CW³, Shankar-Hari M⁴, Annane D⁵, Bauer M⁶, Bellomo R⁷, Bernard GR⁸, Chiche JD⁹, Coopersmith CM¹⁰, Hotchkiss RS¹¹, Levy MM¹², Marshall JC¹³, Martin GS¹⁴, Opal SM¹², Rubenfeld GD¹⁵, van der Poll T¹⁶, Vincent JL¹⁷, Angus DC¹⁸.

Définition « ancienne »

Box 1. SIRS (Systemic Inflammatory Response Syndrome)

Two or more of:

Temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$

Heart rate $>90/\text{min}$

Respiratory rate $>20/\text{min}$ or $\text{PaCO}_2 <32 \text{ mm Hg}$ (4.3 kPa)

White blood cell count $>12\,000/\text{mm}^3$ or $<4000/\text{mm}^3$
or $>10\%$ immature bands

From Bone et al.⁹

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Définition du sepsis

Table 2. Terminology and *International Classification of Diseases* Coding

Current Guidelines and Terminology	Sepsis	Septic Shock
1991 and 2001 consensus terminology ^{9,10}	Severe sepsis Sepsis-induced hypoperfusion	Septic shock ¹³
2015 Definition	Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection	Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality
2015 Clinical criteria	Suspected or documented infection and an acute increase of ≥ 2 SOFA points (a proxy for organ dysfunction)	Sepsis ^a and vasopressor therapy needed to elevate MAP ≥ 65 mm Hg and lactate > 2 mmol/L (18 mg/dL) despite adequate fluid resuscitation ¹³

Box 3. New Terms and Definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥ 2 points consequent to the infection.
 - The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
 - A SOFA score ≥ 2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.

Du SOFA au qSOFA

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score*

Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥ 22 /min

Altered mentation

Systolic blood pressure ≤ 100 mm Hg

Glasgow Coma Scale score ^c	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL ($\mu\text{mol/L}$)	<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

Hypotension dans le sepsis (1)

- × Insuffisance circulatoire secondaire à une hypovolémie
- × Hyperperméabilité vasculaire ou vasoplégie
- × État hyperkinétique avec débit cardiaque conservé ou élevé malgré une dysfonction myocardique
- × Résistance relative aux catecholamines

L'hypotension dans le sepsis (2)

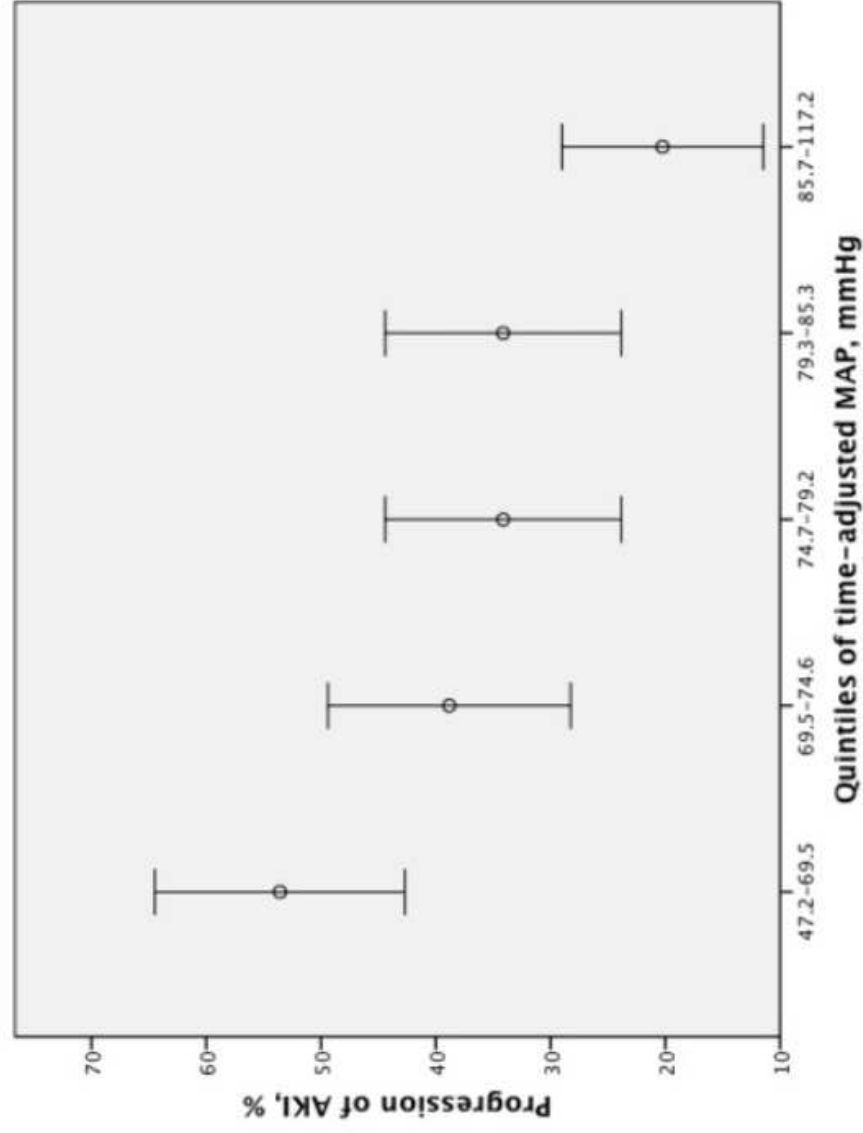
- × Patients hypertendus chroniques ont une courbe d'autorégulation déviée vers la droite
- × Le rein aurait-il besoin d'une PAM supérieure que les autres organes?

Crit Care. 2013 Dec 13;17(6):R295. doi: 10.1186/cc13161.

Hemodynamic variables and progression of acute kidney injury in critically ill patients with severe sepsis: data from the prospective observational FINNAKI study.

Poukkanen M, Wilkman E, Vaara ST, Pettilä V, Kaukonen KM, Korhonen AM, Jusaro A, Hovilehto S, Inkinen O, Laru-Sompa R, Hautamäki R, Kuitunen A, Karlsson S; FINNAKI Study Group.

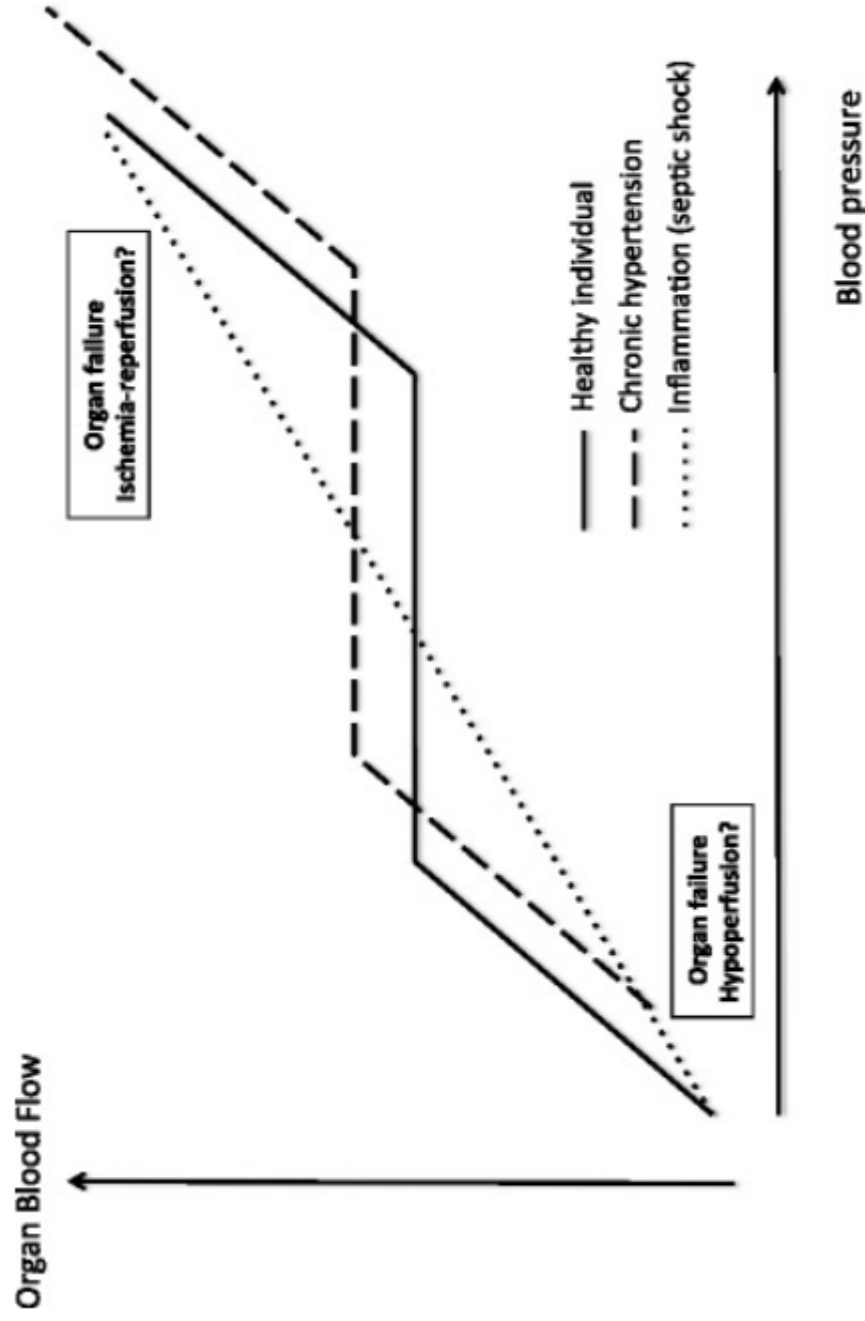
Figure 2



Crit Care. 2015 Mar 10;19:101. doi: 10.1186/s13054-015-0794-z.

Optimizing mean arterial pressure in septic shock: a critical reappraisal of the literature.

Leone M¹, Asfar P², Radermacher P³, Vincent JL⁴, Martin C⁵.

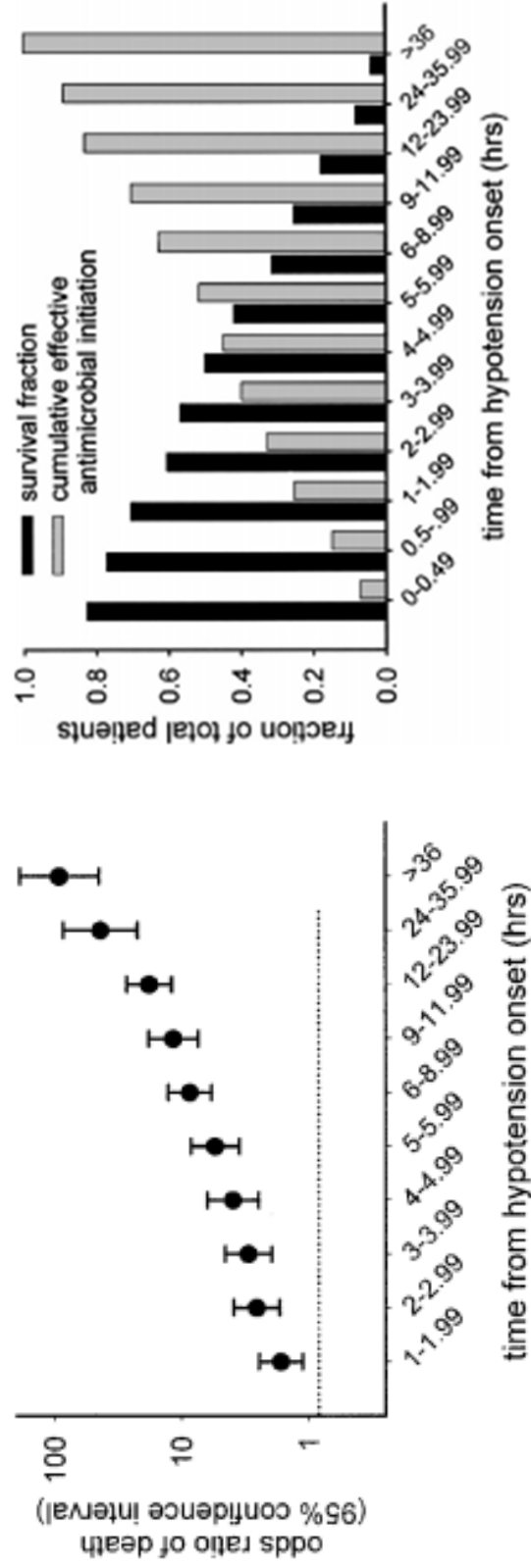


Papier important



Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc



Effet d'une PAM >65 sur la microcirculation

Crit Care. 2011;15(5):R222. doi: 10.1186/cc10462. Epub 2011 Sep 21.

Effects of changes in arterial pressure on organ perfusion during septic shock.

Thooft A¹, Favory R, Salgado DR, Taccone FS, Donadello K, De Backer D, Creteur J, Vincent JL.

Crit Care Med. 2009 Jun;37(6):1961-6. doi: 10.1097/CCM.0b013e3181a00a1c.

The effect of increasing doses of norepinephrine on tissue oxygenation and microvascular flow in patients with septic shock.

Jhanji S¹, Stirling S, Patel N, Hinds CJ, Pearse RM.

Crit Care. 2009;13(3):R92. doi: 10.1186/cc7922. Epub 2009 Jun 17.

Increasing arterial blood pressure with norepinephrine does not improve microcirculatory blood flow: a prospective study.

Dubin A¹, Pozo MO, Casabella CA, Pálizas F Jr, Murias G, Moseinco MC, Kanoore Edul VS, Pálizas F, Estenssoro E, Ince C.

Crit Care. 2015 Mar 30;19:130. doi: 10.1186/s13054-015-0866-0.

A high mean arterial pressure target is associated with improved microcirculation in septic shock patients with previous hypertension: a prospective open label study.

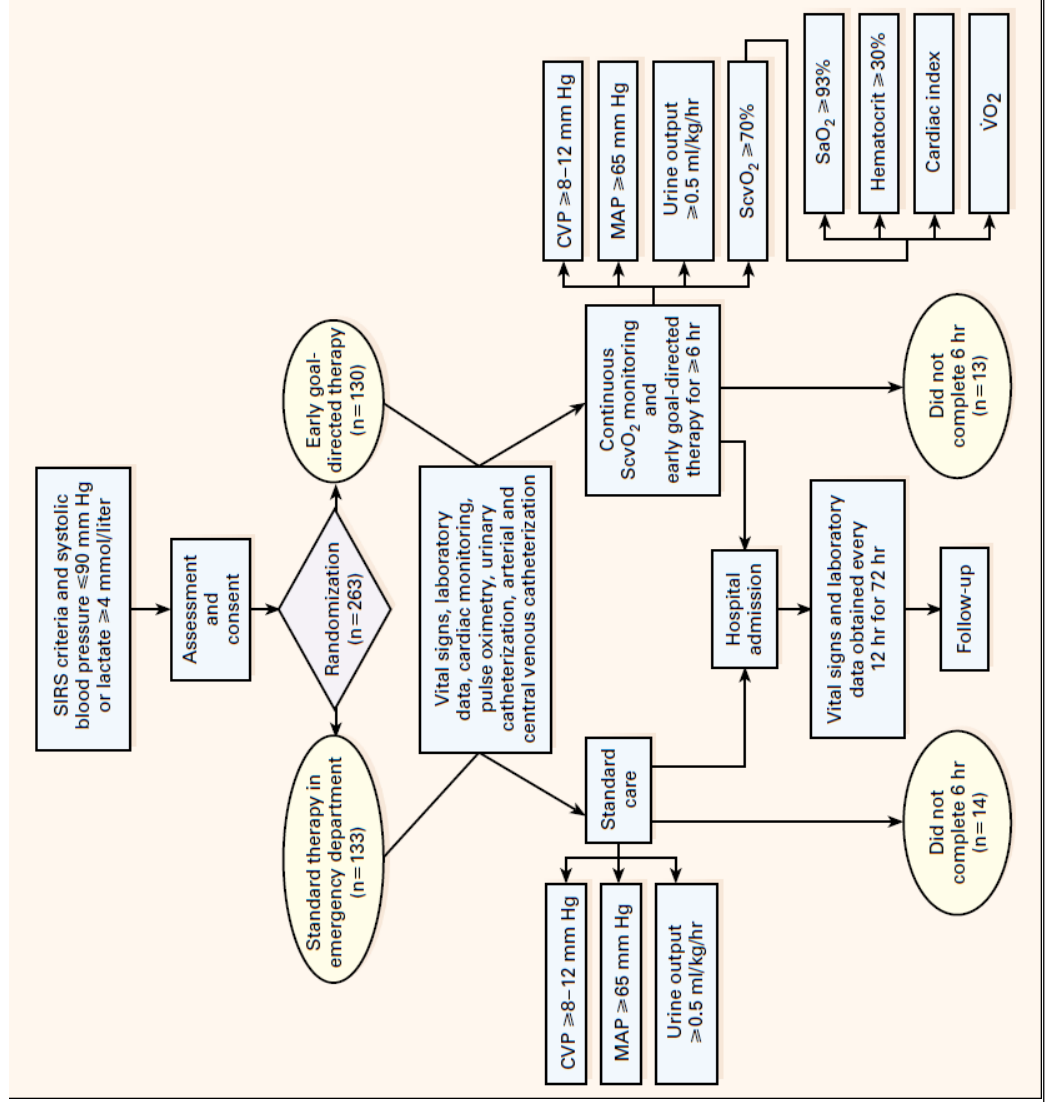
Xu JY¹, Ma SQ², Pan C³, He HL⁴, Cai SX⁵, Hu SL⁶, Liu AR⁷, Liu L⁸, Huang YZ⁹, Guo FM¹⁰, Yang Y¹¹, Qiu HB¹².

Papier important



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*



Papier important



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

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 (ScvO₂)*
- 7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥ 8 mm Hg, ScvO₂ of $\geq 70\%$, and normalization of lactate.

Papier important



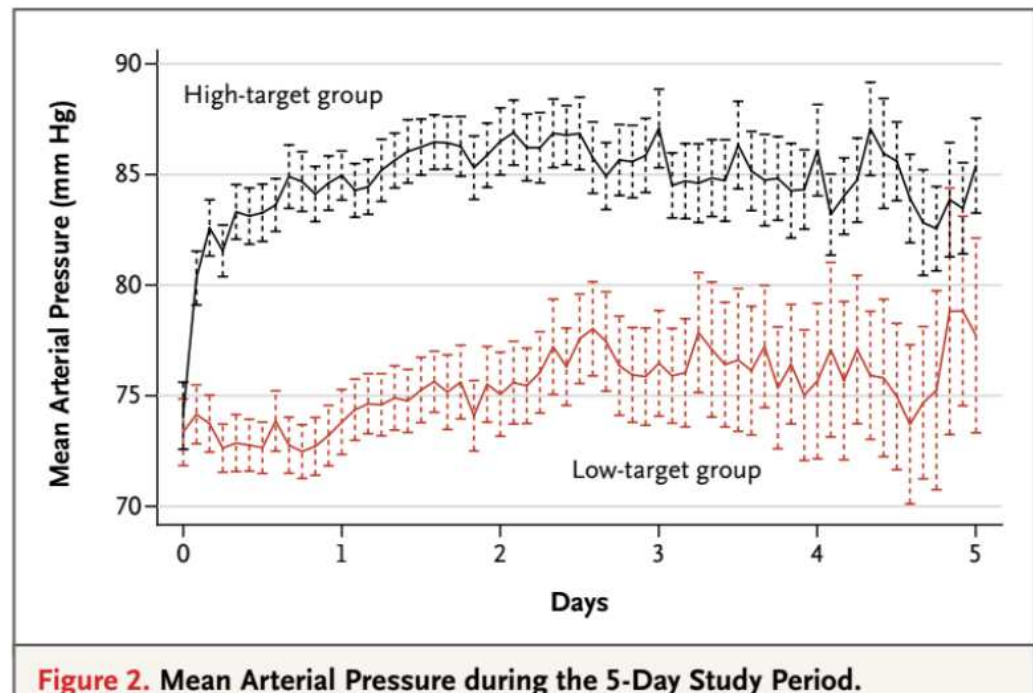
High versus Low Blood-Pressure Target in Patients with Septic Shock

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

Critères d'inclusion

- × Choc septique (nécessité de noradrénaline à plus de 0,1mcg/kg/min)
- × Dans les 6 heures suivant le début des amines
- × Après remplissage adéquat (30ml/kg de sérum physiologique)
- × Choc septique défini comme SIRS + dysfonction d'organe

- ✗ Chaque patient est randomisé au High MAP target ou Low MAP target group
- ✗ 65-70 mm Hg vs. 80-85 mm Hg pendant 5 jours ou jusqu'à l'arrêt de la Noradrénaline
- ✗ Baisse de la PAM à 65 mm Hg si évènement indésirable grave



Résultats

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

Variable	Low-Target Group (N=388)	High-Target Group (N=388)	P Value
Cumulative fluid intake from day 1 to day 5 — liters	10.0 (5.8–14.0)	10.5 (5.5–14.0)	0.89
Cumulative urine output from day 1 to day 5 — liters	6.7 (2.9–10.7)	6.9 (2.4–10.7)	0.87
Cumulative fluid balance from day 1 to day 5 — liters	2.8 (0.0–6.2)	2.4 (0.0–6.0)	0.74
Median dose of norepinephrine (IQR) — $\mu\text{g}/\text{kg}/\text{min}$			
Day 1	0.45 (0.17–1.21)	0.58 (0.26–1.80)	<0.001
Day 2	0.16 (0.03–0.48)	0.38 (0.14–0.90)	<0.001
Day 3	0.02 (0.00–0.16)	0.14 (0.01–0.50)	<0.001
Day 4	0.00 (0.00–0.05)	0.03 (0.00–0.22)	<0.001
Day 5	0.00 (0.00–0.03)	0.01 (0.00–0.15)	<0.001
Duration of catecholamine infusion — days	3.7 \pm 3.2	4.7 \pm 3.7	<0.001
Primary outcome: death at day 28 — no. (%)*	132 (34.0)	142 (36.6)	0.57
Secondary outcomes — no./total no. (%)			
Death at day 90 [†]	164 (42.3)	170 (43.8)	0.74
Survival at day 28 without organ support [‡]	241 (62.1)	235 (60.6)	0.66
Doubling of plasma creatinine	161 (41.5)	150 (38.7)	0.42
No chronic hypertension	71/215 (33.0)	85/221 (38.5)	0.32
Chronic hypertension	90/173 (52.0)	65/167 (38.9)	0.02
Renal-replacement therapy from day 1 to day 7	139 (35.8)	130 (33.5)	0.50
No chronic hypertension	66/215 (30.7)	77/221 (34.8)	0.36
Chronic hypertension	73/173 (42.2)	53/167 (31.7)	0.046
Serious adverse events — no. (%)			
Any	69 (17.8)	74 (19.1)	0.64
Acute myocardial infarction [§]	2 (0.5)	7 (1.8)	0.18
Atrial fibrillation	11 (2.8)	26 (6.7)	0.02
Ventricular fibrillation or tachycardia	15 (3.9)	22 (5.7)	0.24
Digital ischemia	9 (2.3)	10 (2.6)	0.82
Mesenteric ischemia	9 (2.3)	9 (2.3)	1.00
Bleeding	42 (10.8)	31 (8.0)	0.22

Is There a Good MAP for Septic Shock?

James A. Russell, M.D.

Table 1. Comparison of Norepinephrine Control Groups and Intervention Groups in Randomized, Controlled Trials of Vasoactive Agents in Shock.*

Trial	Mean Arterial Pressure (MAP)		Norepinephrine Infusion Rate			Fluid Balance		Renal- Replacement Therapy	Death at 28 Days	
	Target	Actual, Day 0	Actual, Day 1	Day 0	Day 1	Day 2	Day 0			Day 1
	mm Hg	mm Hg	mm Hg	µg/kg/min			ml		%	
Asfar et al. ^{4,†}										
Low-target group										
All patients	65 to 70	74	74	0.35	0.45	0.16	1603	1016	2,800	35.8
Patients with chronic hypertension	65 to 70									42.2
High-target group										
All patients	80 to 85	74	84	0.40	0.58	0.38	1595	1106	2,400	33.5
Patients with chronic hypertension	80 to 85									31.7
Annane et al. ^{6,‡}	70	70	80	0.94	1.09	0.65	1586	172	-2,767	24.8
De Backer et al. ⁷	MD	58	76	0.54	0.82	0.68	2100	1700	8,300	17.0§
Myburgh et al. ^{8,¶}	MD	70	73	0.26	0.17	0.07	2232	1782	5,712	22.1
Rivers et al. ^{9,}	65	76	81	NA	NA	NA	3500	NA	10,602**	NA
Russell et al. ¹⁰	65 to 75	72	73	0.28	0.20	0.08	1500	2500	11,000	43.6

La PAM mais pas que...

- × Prise en charge du sepsis dans le cadre d'un bundle of care regroupant les autres critères :
 - × objectif d'hémoglobine
 - × objectif de diurèse
 - × Pression veineuse centrale
 - × mesure de lactatémie et SvO₂
 - × antibiothérapie précoce +/- corticoïdes

En conclusion

- × L'hypotension tue
- × La PAM minimale est de 65 mm Hg
- × Pas ou peu d'effets bénéfiques sur la microcirculation d'une PAM >65
- × Une PAM plus élevée serait « néphroprotectrice »
- × Faites des objectifs de PAM sur mesure
- × Attention aux effets délétères d'une PAM trop élevée

Merci ! (cette fois ci c'est vraiment fini)