

Manejo do choque séptico

Como adaptar o SSCG ao paciente
cirrótico?

Rodolpho Pedro

Intensivista da UTI da Gastroenterologia do HCFMUSP

Paciente masculino, 57 anos

- Cirrose VHC
- Admitido junto ao PS por piora da encefalopatia

- EH II
- PAM 55
- Ar ambiente, SatO₂ 97%
- Ascite moderada, BT 6,5 mg/dl
- Cr 2,7 mg/dl
- Hb 12, Leuco 33 mil
- Lactato 65 mg/dl

Volume? Droga? Alvos?

Sepse? Choque Séptico?



Definição

February 23, 2016

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

Mervyn Singer, MD, FRCP¹; Clifford S. Deutschman, MD, MS²; Christopher Warren Seymour, MD, MSc³; et al

» [Author Affiliations](#) | [Article Information](#)

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

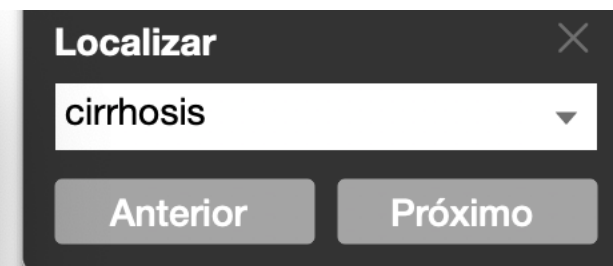
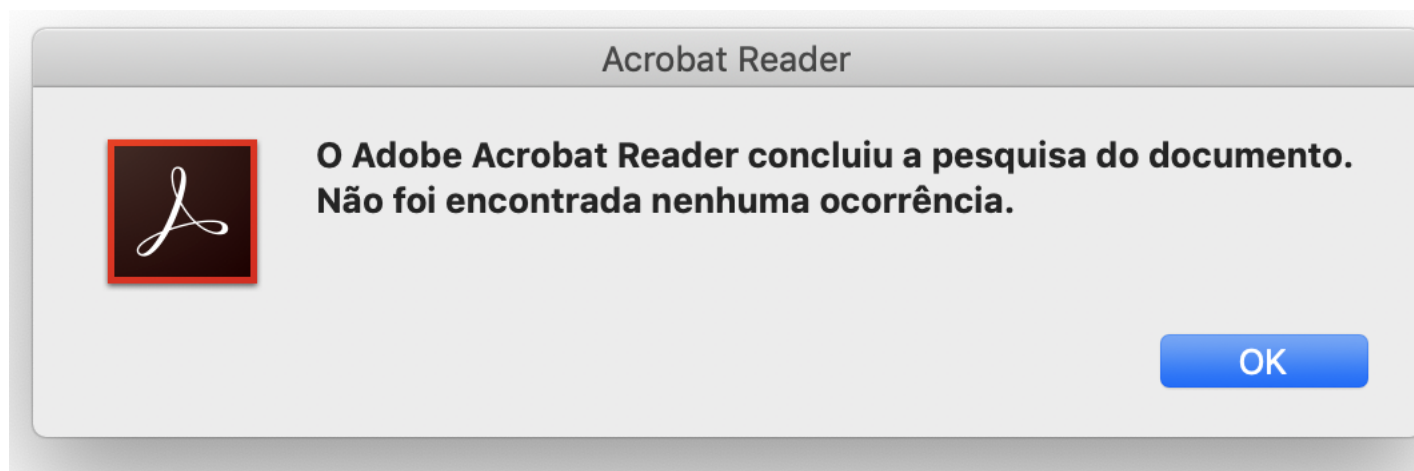
Sepse

Disfunção Orgânica ameaçadora à vida causada por uma resposta desmedida à infecção. (Δ Sofa ≥ 2)

Choque Séptico

Sepse + **Vasopressor** + **Lactato $\geq 18\text{mg/dl}$** apesar de volume adequado

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



Consenso?

Petition to retire the surviving sepsis campaign guidelines

May 2, 2018 by Josh Farkas — 23 Comments

Why IDSA Did Not Support the Surviving Sepsis Campaign

July 1, 2018

By **Dean L. Winslow, MD, FACP, FIDSA**

The Surviving Sepsis Campaign: A Rush to Judgment

Daniel J. Pallin, MD, MPH and Rory Spiegel, MD

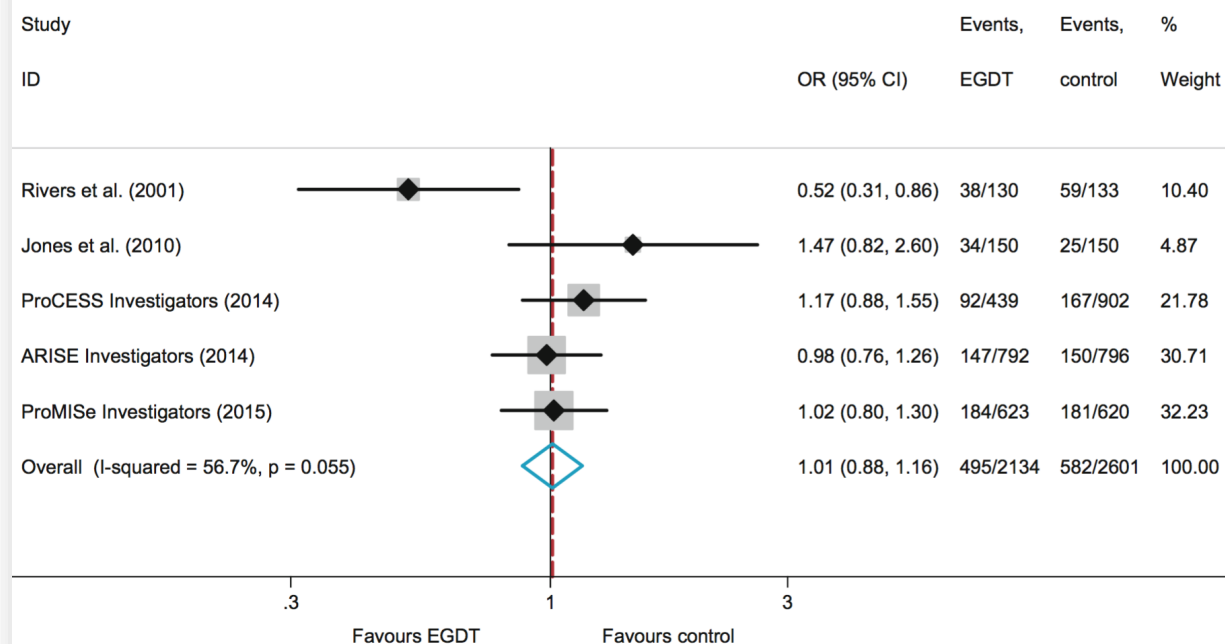
A new 1-hour sepsis care bundle was ill conceived and may have unintended negative consequences.

The “New” Surviving Sepsis guidelines: The good, the bad and the ugly!

Metas 2012

- a) CVP 8–12 mm Hg
- b) MAP \geq 65 mm Hg
- c) Débito Urinário \geq 0.5 mL/kg/hr
- d) Scvo2 \geq 70%.

A Primary mortality outcome of each study



Metas 2016

Bundle 1 Hora

- **1- Medir Lactato**
- 2- Coleta de culturas
- 3- Antibióticos
- **4- Expansão Volêmica para PAM > 65mmHg**
- **5- Vasopressores para PAM > 65mmHg**

Lactato

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

Serum lactate is not a direct measure of tissue perfusion (31).
Increases in the serum lactate level may represent tissue
hypoxia, accelerated aerobic glycolysis driven by excess beta-
adrenergic stimulation, or other causes (e.g., liver failure).

Regardless of the source, increased lactate levels are associated
with worse outcomes (32).

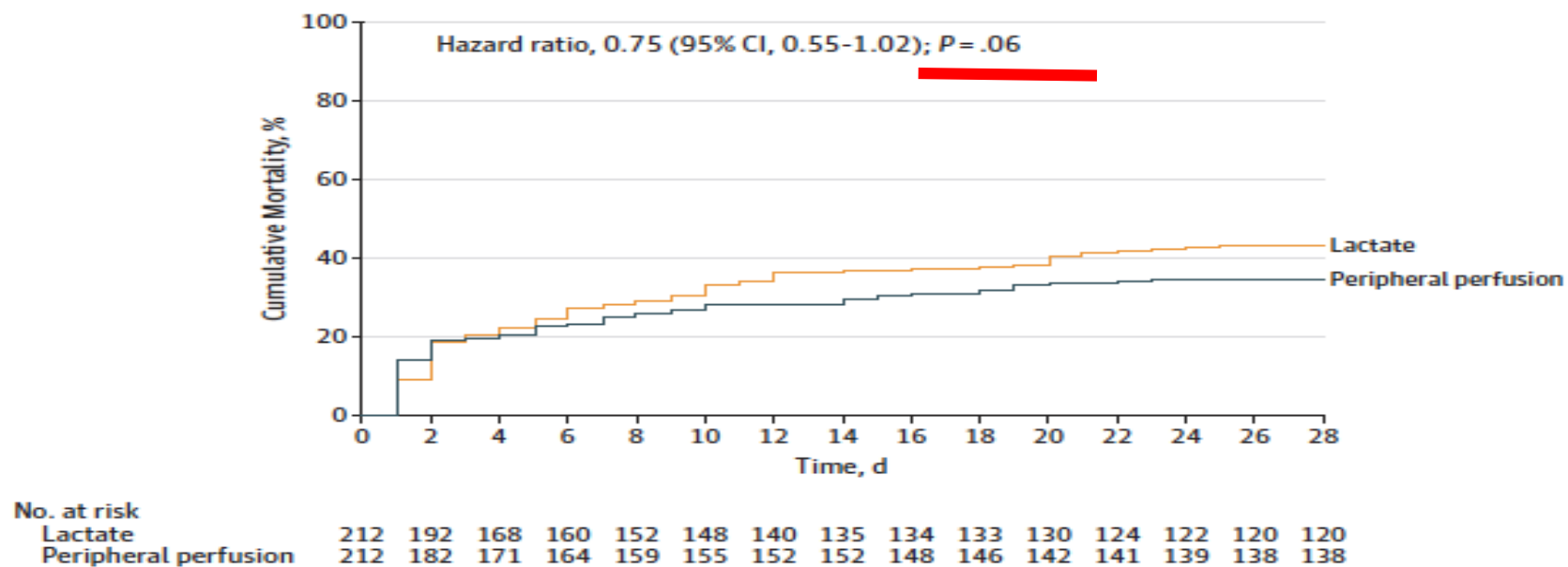
Lactato x TEC

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 **JAMA. 2019;**

Figure 2. Kaplan-Meier Estimates of Cumulative Mortality Within 28 Days Among Patients Treated With Peripheral Perfusion-Targeted Resuscitation vs Lactate Level-Targeted Resuscitation



Perfusão Periférica X Cirrose

Journal of Hepatology 2015

Exploration of skin perfusion in cirrhotic patients with septic shock

Arnaud Galbois^{1,2,3,*}, Naïke Bigé^{1,2}, Claire Pichereau^{1,2}, Pierre-Yves Boëlle^{2,4,5}, Jean-Luc Baudel¹,
Simon Bourcier^{1,2}, Eric Maury^{1,2,5}, Bertrand Guidet^{1,2,5}, Hafid Ait-Oufella^{1,2,6}

perfusion is higher in the patient with cirrhosis.

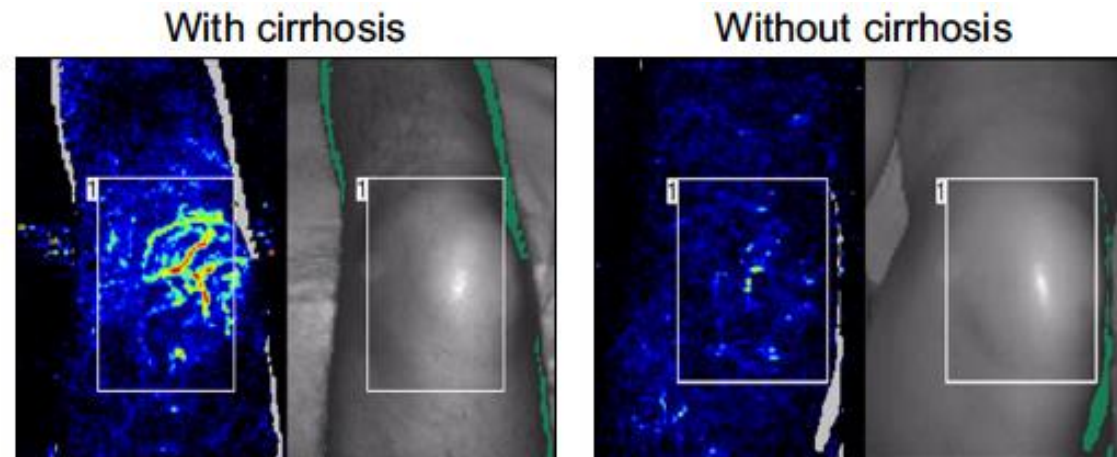


Fig. 4. Laser-Doppler exploration of skin perfusion in the knee area of patients without mottling. Comparison between 8 patients with cirrhosis and 8 patients without: * $p < 0.01$. Bottom: example of laser-Doppler imaging in the knee

skin perfusion was longer preserved in patients with cirrhosis;



Exploration of skin perfusion in cirrhotic patients with septic shock

Arnaud Galbois^{1,2,3,*}, Naïke Bigé^{1,2}, Claire Pichereau^{1,2}, Pierre-Yves Boëlle^{2,4,5}, Jean-Luc Baudel¹,
Simon Bourcier^{1,2}, Eric Maury^{1,2,5}, Bertrand Guidet^{1,2,5}, Hafid Ait-Oufella^{1,2,6}

Table 2. Hemodynamic parameters at H6 in patients with liver cirrhosis according to their survival status at day 14: univariate analysis.

Parameters:	OR (95% CI)	p value
MAP (mmHg)		
≥65	1	
<65	2.1 (0.4-11.8)	0.46
Heart rate (beats/min)		
>100	1	
≤100	3.0 (0.7-12.2)	0.17
Central venous pressure (mmHg)		
≥8	1	
<8	1.2 (0.1-13.1)	1
Cardiac output (L/min)		
≥5.5	1	
<5.5	1.3 (0.3-5.2)	1
Urinary output (ml/kg/h)		
≥0.5	1	
<0.5	3.8 (0.8-15.9)	0.09

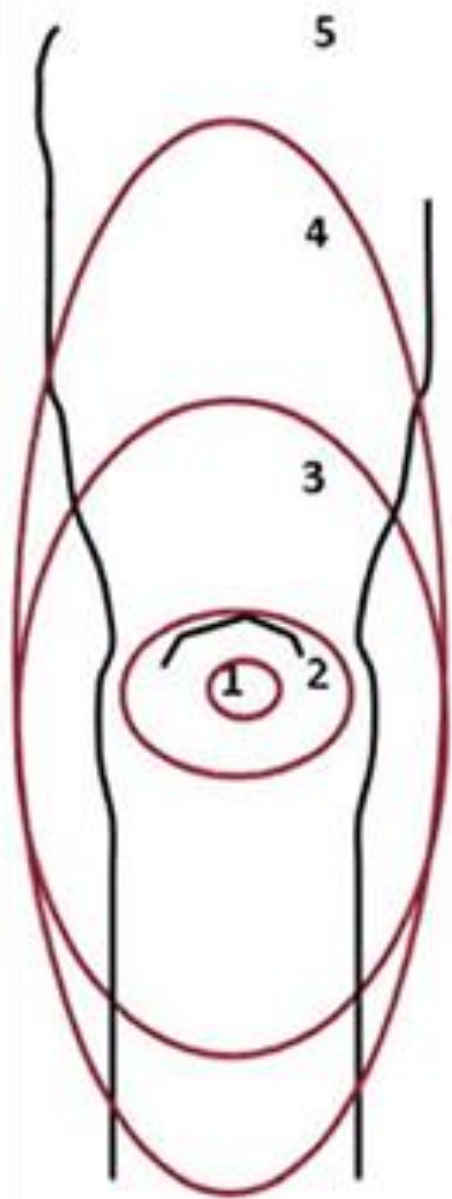
Macrocirculação

Arterial lactate (mmol/L)

<5	1	
≥5	5.2 (1.2-23.3)	0.04
Lactate clearance (%)		
>0	1	
≤0	8.0 (1.8-35.8)	0.009
ScvO ₂ (%)		
≥70	1	
<70	15.0 (0.8-280.7)	0.08
Mottling score		
≤1	1	
>1	42.4 (2.3-785.9)	0.0001

MAP, mean arterial pressure; ScvO₂, central venous oxygen saturation.

Microcirculação



Mottling score



Stage 2



Stage 3



Stage 5

Perfusão Periférica X Cirrose

Exploration of skin perfusion in cirrhotic patients with septic shock

Arnaud Galbois^{1,2,3,*}, Naïke Bigé^{1,2}, Claire Pichereau^{1,2}, Pierre-Yves Boëlle^{2,4,5}, Jean-Luc Baudel¹,
Simon Bourcier^{1,2}, Eric Maury^{1,2,5}, Bertrand Guidet^{1,2,5}, Hafid Ait-Oufella^{1,2,6}

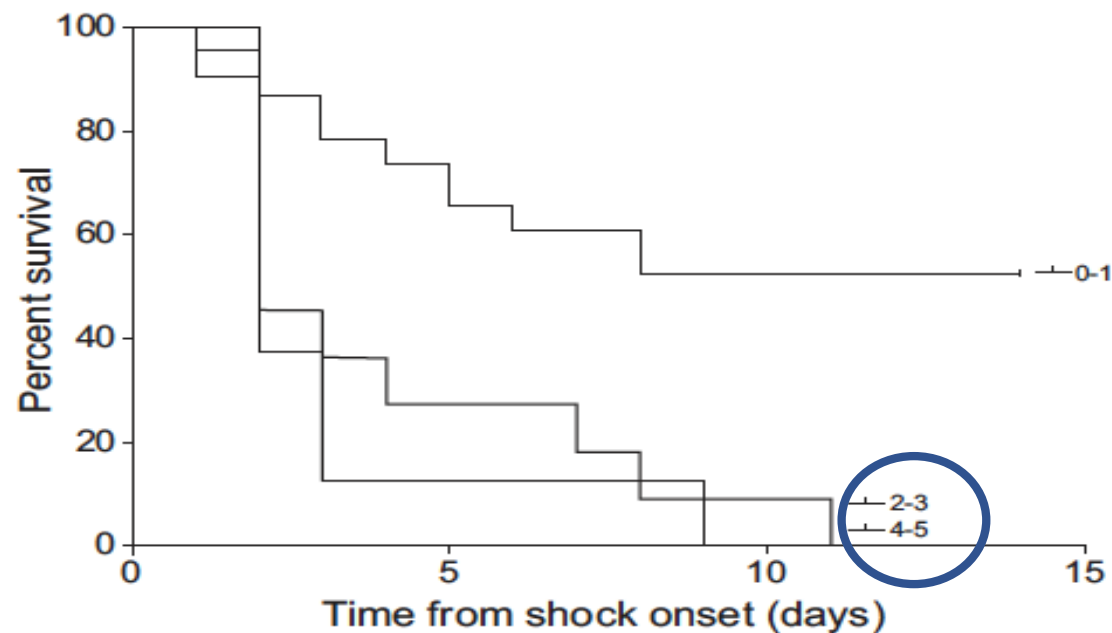


Fig. 1. Kaplan Meier survival estimates according to the H6 mottling score. All the patients with mottling score >1 died (log-rank test = 0.19 for comparison between score = 2–3 and score = 4–5). The probability of survival was higher for patients with mottling score = 0–1 (log-rank test <0.001).



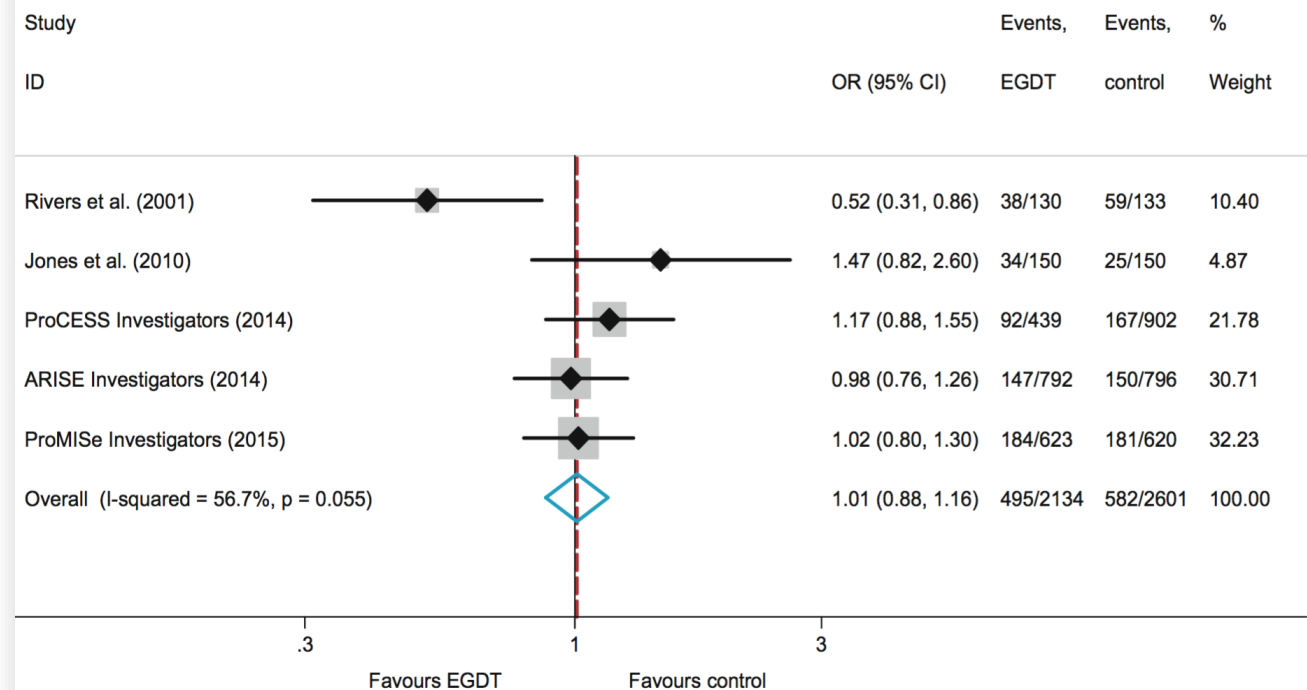
Expansão Volêmica

2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hours (strong recommendation, low quality of evidence).

Expansão Volêmica

- 45 kg >> 1350ml/3h
- 70 Kg >> 2100ml/3h
- 100 kg >> 3000ml/3h
- Oligúria? Hipervolemia?

A Primary mortality outcome of each study



Volume

JAMA | The Rational Clinical Examination

Will This Hemodynamically Unstable Patient Respond to a Bolus of Intravenous Fluids?

Peter Bentzer, MD, PhD; Donald E. Griesdale, MD, MPH; John Boyd, MD; Kelly MacLean, MD; Demetrios Sirounis, MD; Najib T. Ayas, MD, MPH

The summary prevalence of fluid responsiveness was 50% (95% CI, 42%-56%).

Predicting stroke volume and arterial pressure fluid responsiveness in live cirrhosis patients using dynamic preload variables

A prospective study of diagnostic accuracy

Eur J Anaesthesiol 2016; **34**:1–8

Chun-Yu Wu, Ya-Jung Cheng, Ying-Ju Liu, Tsung-Ta Wu, Chiang-Ting Chien and Kuang-Cheng Chan, on behalf of the NTUH Center of Microcirculation Medical Research (NCMMR)

Table 2 Changes in haemodynamic parameters before and after fluid loading in stroke volume fluid responders and non-responders

37%	SV responders (n = 23)		SV non-responders (n = 39)	
	Before	After	Before	After

Table 3 Changes in haemodynamic parameters before and after fluid loading in mean arterial pressure fluid responders and non-responders

25,8%	Arterial pressure responders (n = 16)		Arterial pressure non-responders (n = 46)	
	Before	After	Before	After

Cirrose
X
Volume



- Qual Fluido?

2. We recommend crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock (strong recommendation, moderate quality of evidence).

Qual Fluido?

Albumina 4%
X
Salina

ORIGINAL ARTICLE

N Engl J Med 2004;350:2247-56.

A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

The SAFE Study Investigators*

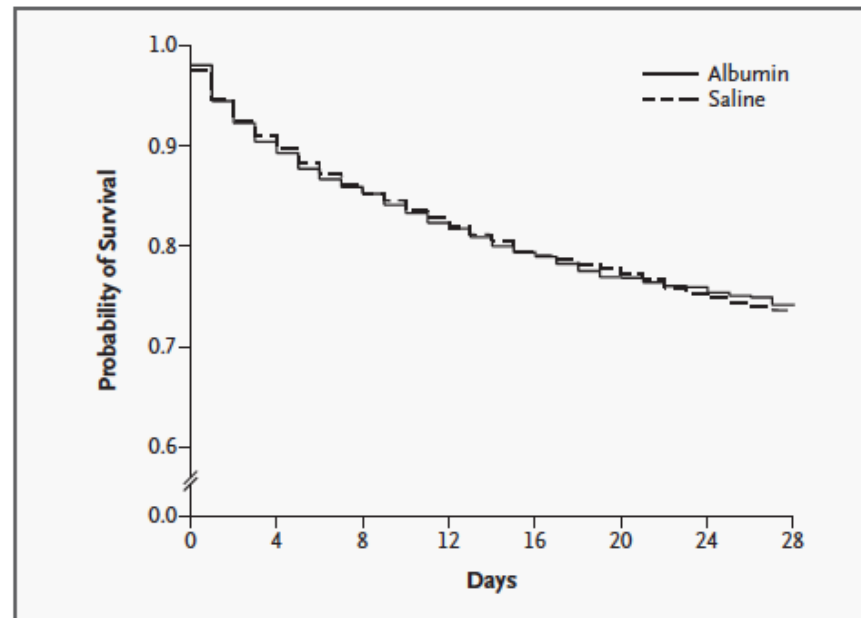


Figure 1. Kaplan-Meier Estimates of the Probability of Survival.

P=0.96 for the comparison between patients assigned to receive albumin and those assigned to receive saline.

6997 patients

ORIGINAL ARTICLE

N ENGL J MED 370;15 NEJM.ORG APRIL 10, 2014

Albumin Replacement in Patients with Severe Sepsis or Septic Shock

ALBIOS Study Investigators*

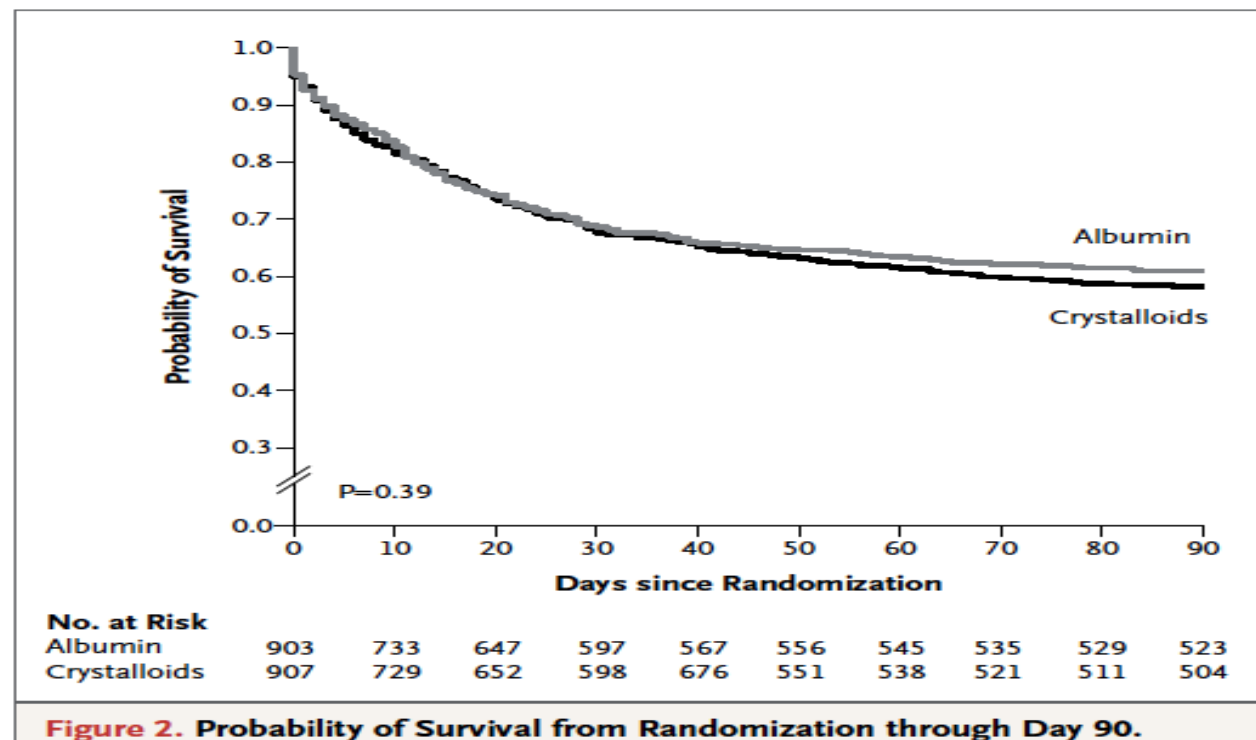
1818 patients

• Qual Fluido?

Cristalóide

X

Albumina 20%
+ Cristalóides



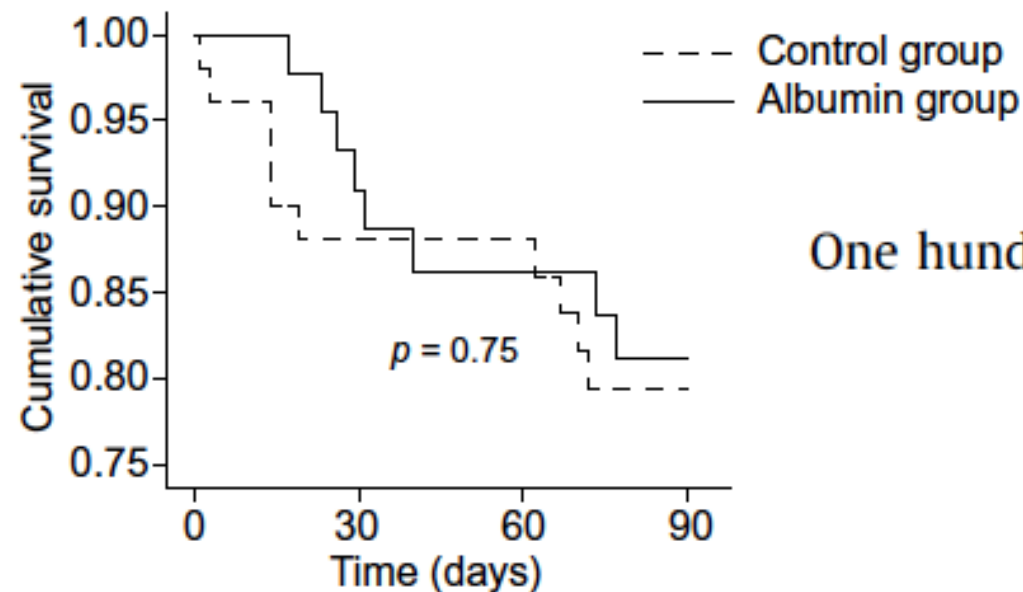
Journal of Hepatology 2012

Albumin for bacterial infections other than spontaneous bacterial peritonitis in cirrhosis. A randomized, controlled study[☆]

Mónica Guevara^{1,2,3,4,†}, Carlos Terra^{1,2,3,4,†}, André Nazar^{1,2,3,4}, Elsa Solà^{1,2,3,4}, Javier Fernández^{1,2,3}, Marco Pavesi^{1,2,3}, Vicente Arroyo^{1,2,3}, Pere Ginès^{1,2,3,4,*}

Cirrótico

Qual Fluido ?

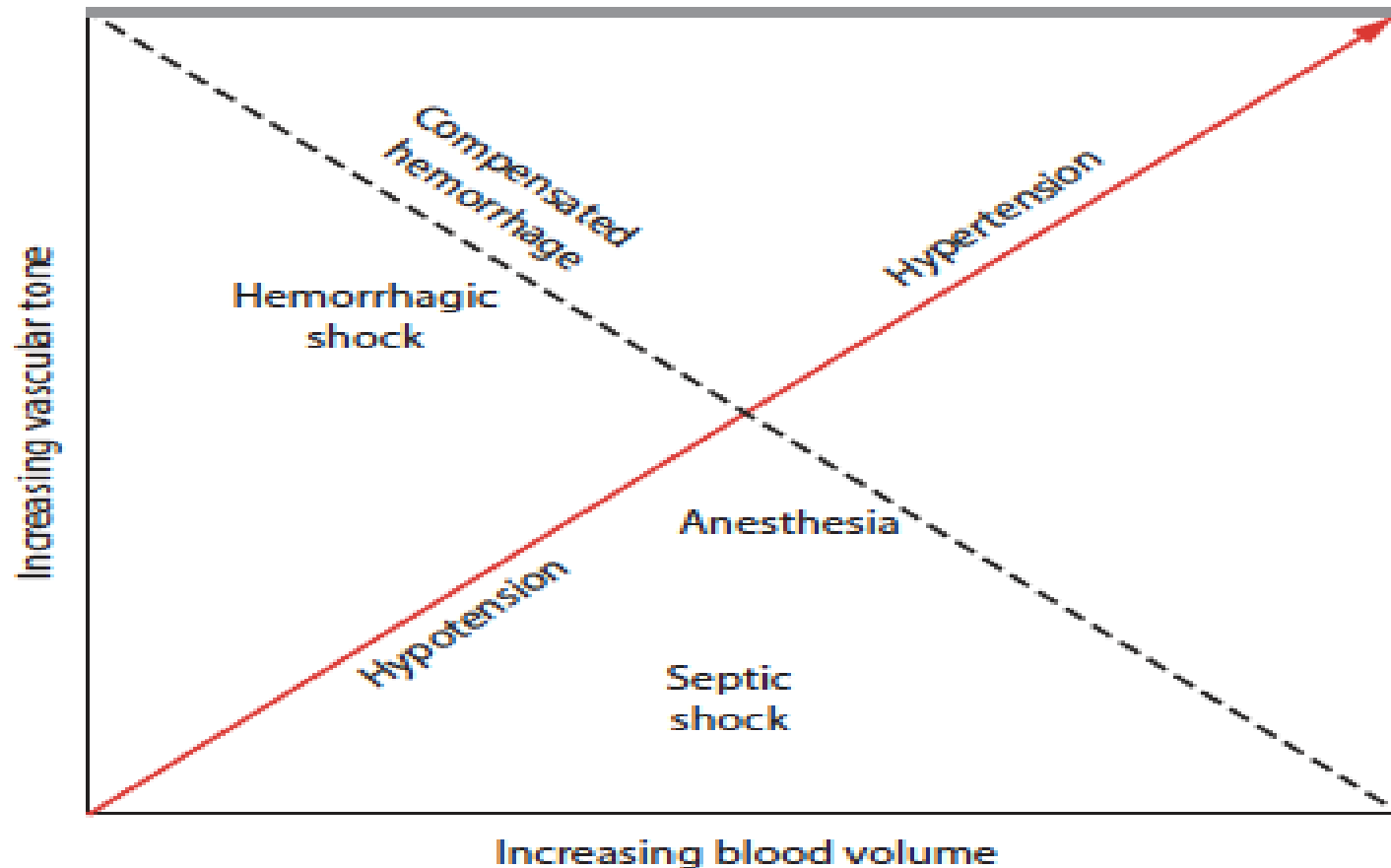


One hundred and ten patients

calculated to detect a difference of 30% in the survival rate of patients treated and not treated with albumin (75% vs. 45%, respectively) [12,19], with a type I error of 0.05 and an 80% power.

Changing paradigms in surgical resuscitation

Yvette Fouche, MD; Robert Sikorski, MD; Richard P. Dutton, MD, MBA





1. We recommend **norepinephrine** as the first-choice vasopressor (strong recommendation, moderate quality of evidence).

Vasopressores

2. We suggest **adding either vasopressin** (up to 0.03 U/min) (weak recommendation, moderate quality of evidence) **or epinephrine** (weak recommendation, low quality of evidence) to norepinephrine with the intent of raising MAP to target, or adding vasopressin (up to 0.03 U/min) (weak recommendation, moderate quality of evidence) to decrease norepinephrine dosage.

Vasopressores

X

Cirrose

Vasopressin deficiency and vasodilatory state in end-stage liver disease
J Cardiothorac Vasc Anesth. 2011

Gebhard Wagener, MD^{1,#}, Galina Kovalevskaya, PhD², Moury Minhaz, BS¹, Fallon Mattis, MD¹, Jean C. Emond, MD³, and Donald W. Landry, MD, PhD⁴

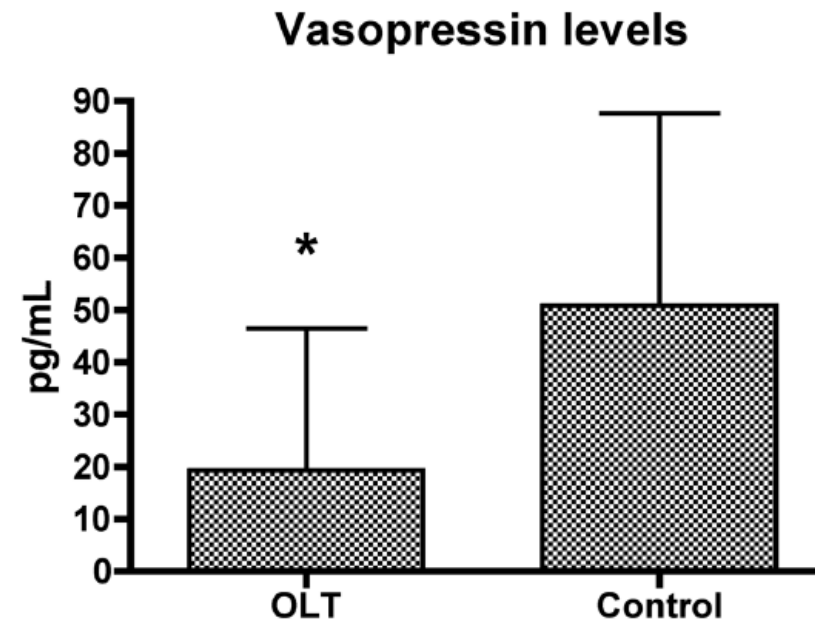


Figure 1.
Baseline vasopressin levels in patients with liver disease undergoing liver transplantations

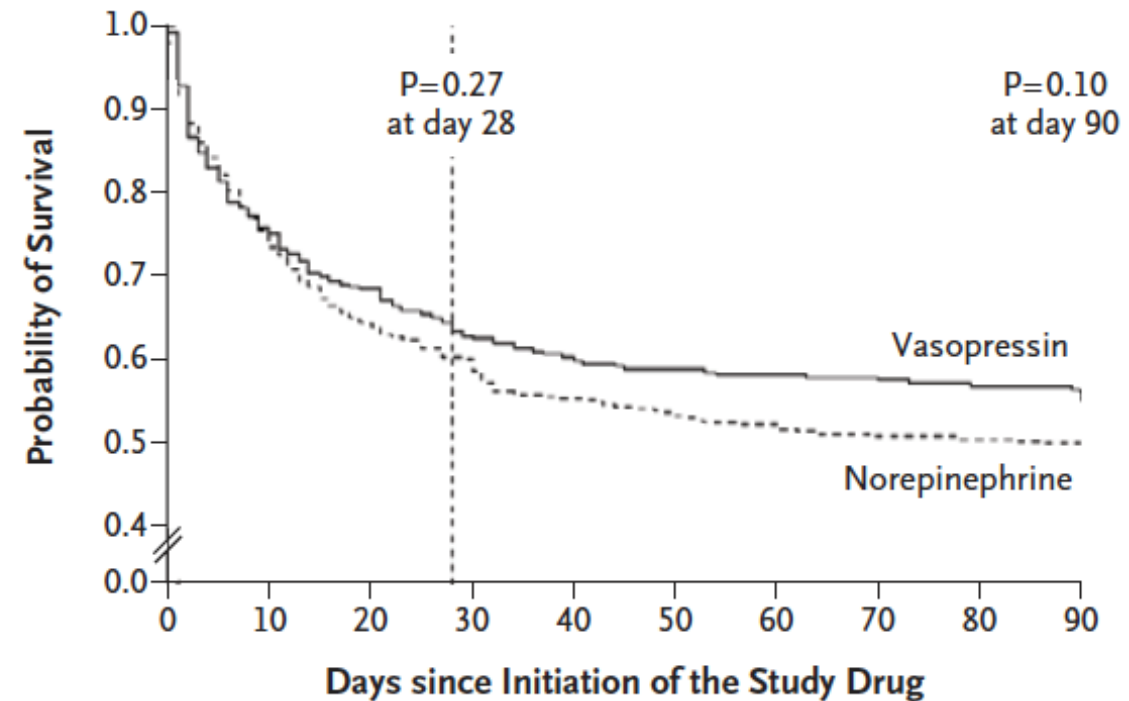
The **NEW ENGLAND**
JOURNAL of MEDICINE

Vaso x Nora

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock VASST Investigators*

FEBRUARY 28, 2008

vasopressin levels were measured, the levels were extremely low at baseline (median, 3.2 pmol per



Vasopressores

Quando?

Predicting stroke volume and arterial pressure fluid responsiveness in liver cirrhosis patients using dynamic preload variables

A prospective study of diagnostic accuracy

Chun-Yu Wu, Ya-Jung Cheng, Ying-Ju Liu, Tsung-Ta Wu, Chiang-Ting Chien and Kuang-Cheng Chan, on behalf of the NTUH Center of Microcirculation Medical Research (NCMMR)

Eur J Anaesthesiol 2016; **34**:1–8

74% permanecem hipotensos após prova
volêmica!

Vasopressor Precoce !



- Alvo de PAM

6. We recommend an initial target mean arterial pressure (MAP) of 65 mm Hg in patients with septic shock requiring vasopressors (strong recommendation, moderate quality of evidence).

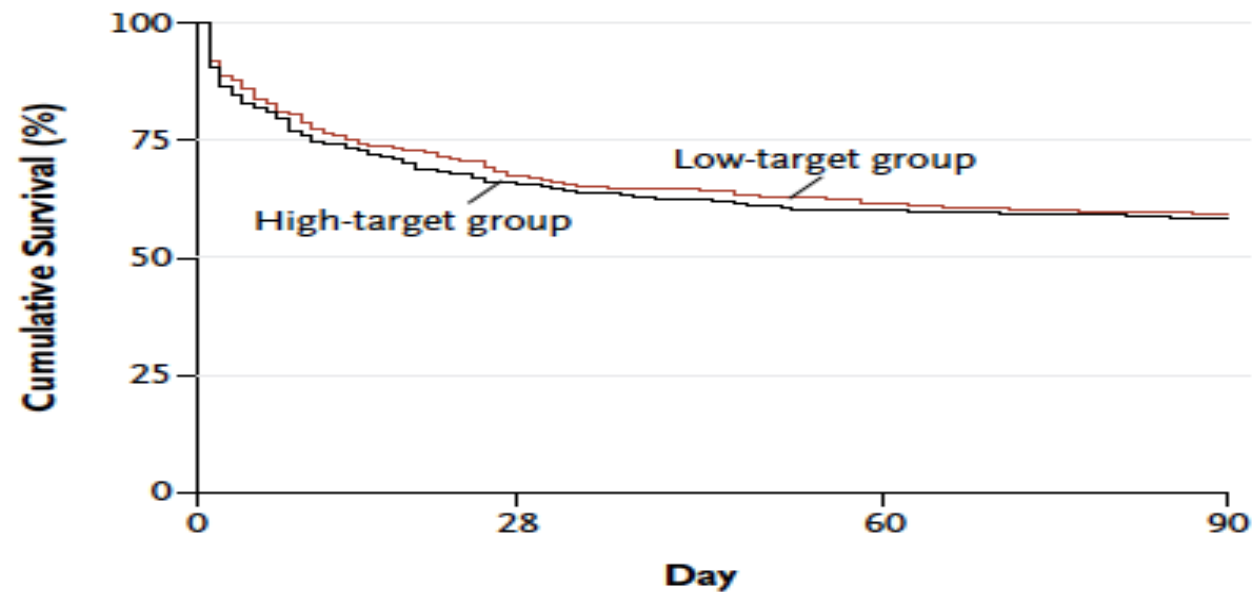
The **NEW ENGLAND**
JOURNAL of MEDICINE

APRIL 24, 2014

Alvo de PAM

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

SEPSISPAM Investigators*



No. at Risk
 Low target
 High target

379
 375

256
 249

233
 227

225
 219

80 to 85 mm Hg

65 to 70 mm Hg

The NEW ENGLAND
JOURNAL *of* MEDICINE

APRIL 24, 2014

Alvo de PAM

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

SEPSISPAM Investigators*

80 to 85 mm Hg

65 to 70 mm Hg

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

Corticoide ??

H. CORTICOSTEROIDS

1. We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vaso-pressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg per day (weak recommendation, low quality of evidence).



Anca Trifan, Professor, Series Editor

Update on adrenal insufficiency in patients with liver cirrhosis

Anca Trifan, Stefan Chiriac, Carol Stanciu

Corticoide

X

Cirroze

Table 1 Prevalence of adrenal insufficiency in critically ill patients with liver cirrhosis

Ref.	No. of patients (type of cirrhosis)	Diagnosis and definition of AI	Prevalence of AI
Harry <i>et al</i> ^[14]	20 (ALF/CLD)	SD-SST: Peak cortisol < 500 nmol/L ¹	69%
Marik <i>et al</i> ^[12]	340 (ALF: 24) (CLD: 146) (recent LT: 119) (remote LT: 51)	LD-SST: Peak cortisol < 552 nmol/L or random cortisol level < 414 nmol/L in non-stressed patients or random cortisol level < 552 nmol/L in stressed patients	72% 33% 66% 92% 61%
Tsai <i>et al</i> ^[8]	101 (cirrhosis+ severe sepsis)	SD-SST: Baseline cortisol < 414 nmol/L or delta cortisol < 250 nmol/L if baseline cortisol between 414 and 938 nmol/L	51%
Fernandez <i>et al</i> ^[13]	25 (cirrhosis + septic shock)	SD-SST: Baseline cortisol < 414 nmol/L or delta cortisol < 250 nmol/L if baseline cortisol between 414 and 966 nmol/L	68%
Thierry <i>et al</i> ^[64]	14 (cirrhosis + septic shock)	SD-SST: Baseline cortisol < 414 nmol/L; delta cortisol < 250 nmol/L	77%
du Cheyron <i>et al</i> ^[65]	50 (critically ill cirrhosis)	SD-SST: Baseline cortisol < 414 nmol/L; delta cortisol < 250 nmol/L if baseline cortisol between 414 and 938 nmol/L	82%
Vasu <i>et al</i> ^[86]	24 (critically ill cirrhotics)	SD-SST: Definition of AI was not reported	62%
Arabi <i>et al</i> ^[29]	75 (cirrhosis + septic shock)	SD-SST: Delta cortisol < 250 nmol/L	76%
Mohamed <i>et al</i> ^[85]	15 (cirrhosis+septic shock)	SD-SST: Definition of AI was not reported	87%
Thevenot <i>et al</i> ^[74]	30 (cirrhosis + sepsis)	SD-SST: Peak serum total cortisol < 510 nmol/L	10%
Acevedo <i>et al</i> ^[89]	166 (decompensated cirrhosis)	SD-SST: Delta cortisol < 250 nmol/L	26%
Graupera <i>et al</i> ^[20]	37 (severe acute bleeding)	SD-SST: Baseline cortisol < 414 nmol/L and/or delta cortisol < 250 nmol/L	38%
Triantos <i>et al</i> ^[16]	20 (cirrhosis with variceal bleeding)	SD-SST: Baseline cortisol < 276 nmol/L or delta cortisol < 250 nmol/L LD-SST: Peak serum cortisol < 690 nmol/L or a delta cortisol < 250 nmol/L	30% 60%
El Damarawy <i>et al</i> ^[66]	45 (cirrhosis with septic shock or HRS, cirrhosis without septic shock or HRS)	SD-SST: Baseline cortisol < 414 nmol/L or delta cortisol < 250 nmol/L in patients with baseline cortisol < 966 nmol/L	73%



Corticoide

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JANUARY 10, 2008

VOL. 358 NO. 2

Hydrocortisone Therapy for Patients with Septic Shock

Charles L. Sprung, M.D., Djillali Annane, M.D., Ph.D., Didier Keh, M.D., Rui Moreno, M.D., Ph.D.,
Mervyn Singer, M.D., F.R.C.P., Klaus Freivogel, Ph.D., Yoram G. Weiss, M.D., Julie Benbenishty, R.N.,
Armin Kalenka, M.D., Helmuth Forst, M.D., Ph.D., Pierre-Francois Laterre, M.D., Konrad Reinhart, M.D.,
Brian H. Cuthbertson, M.D., Didier Payen, M.D., Ph.D., and Josef Briegel, M.D., Ph.D., for the CORTICUS Study Group*

499 patients

did not improve survival

although hydrocortisone hastened reversal of shock

Corticoide

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

MARCH 1, 2018

VOL. 378 NO. 9

Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhandari, Y. Arabi, R. Bellomo, L. Billot, M. Correa, P. Glass,
M. Harward, C. Joyce, Q. Li, C. McArthur, A. Perner, A. Rhodes, K. Thompson, S. Webb, and J. Myburgh,
for the ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group*

3658 patients

did not result in lower 90-day mortality than placebo.

hydrocortisone had faster resolution of shock



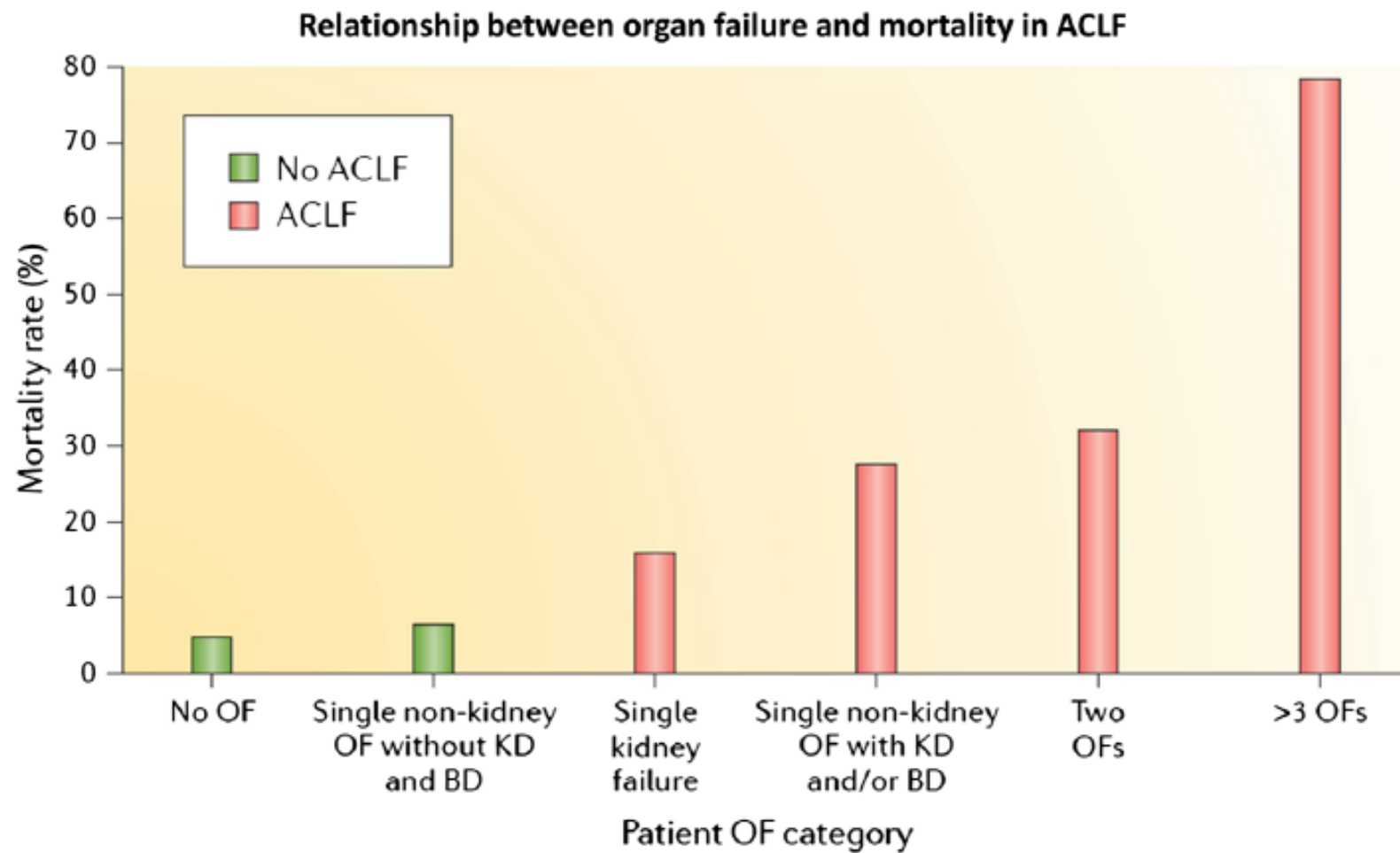
Prognóstico

U. SETTING GOALS OF CARE

1. We recommend that goals of care and prognosis be discussed with patients and families (BPS).
2. We recommend that goals of care be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate (strong recommendation, moderate quality of evidence).
3. We suggest that goals of care be addressed as early as feasible, but no later than within 72 hours of ICU admission (weak recommendation, low quality of evidence).



Prognóstico



Paciente masculino, 57 anos

- Cirrose VHC
- Admitido junto ao PS por piora da encefalopatia

- EH II
- PAM 55
- Ar ambiente, SatO₂ 97%
- Ascite moderada, BT 6,5 mg/dl
- Cr 2,7 mg/dl
- Hb 12, Leuco 33 mil
- Lactato 65 mg/dl

Volume? Droga? Alvos?

Sepse? Choque Séptico?



Mensagem final

- Individualizar Expansão Volêmica
- Lactato x Perfusão
- Vasopressor precoce!
- Culturas + ATB
- Corticoide
- Prognóstico + Diálogo!



Obrigado!