IV JORNADA D'ACTUALITZACIÓ

GRUP D'UNITATS DE CURES AGUDES CARDIOLÒGIQUES

22 de novembre de 2019

DIAGNÒSTIC I TRACTAMENT DE LA SÈPSIA

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Àrea de Vigilancia Intensiva

Hospital Clínic de Barcelona

SOCIETAT CATALANA DE CARDIOLOGIA

L'Acadèmia

FUNDACIÓ ACADÈMIA DE CIÈNCIES MÈDIQUES I DE LA SALUT DE CATALUNYA I DE BALEARS

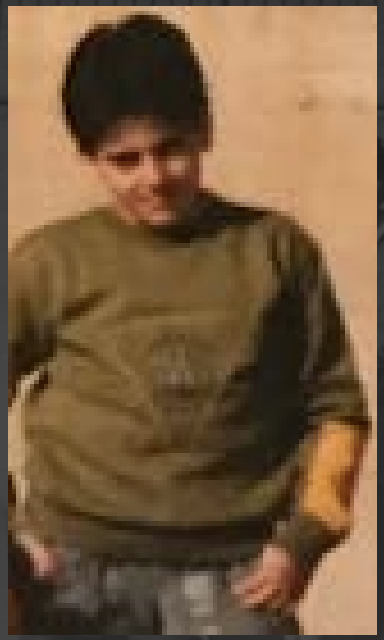
DISCLOSURES

- Honoraria for scientific collaboration (Pfizer, MSD, Gilead).
- Advisory Board (Alexion, Jansen).

- Dangerous friendships

DISCLOSURES

DISCLOSURES



AGENDA

- Definitions
- Relevance of sepsis in the cardiology setting
- Diagnosis
- Treatment

DEFINITION I (1992)

accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis

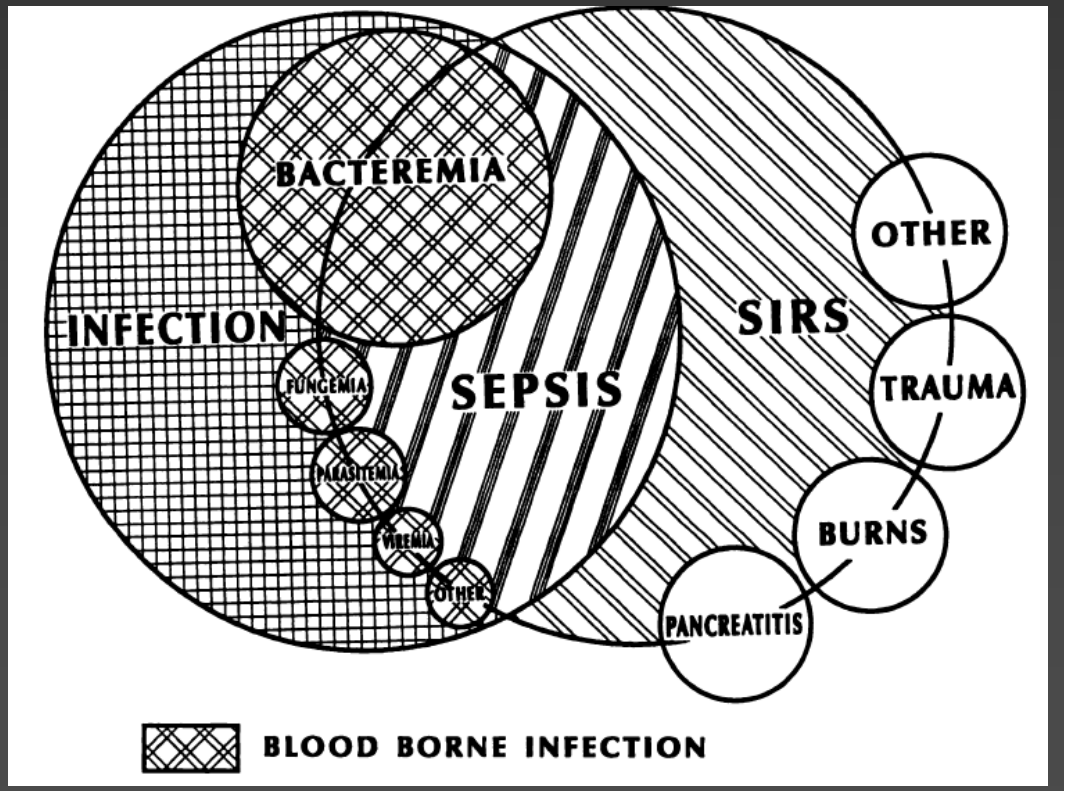


Table 1—*Definitions*

Infection = microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms.

Bacteremia = the presence of viable bacteria in the blood.

Systemic inflammatory response syndrome (SIRS) = the systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions: (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or $PaCO_2$ <32 mm Hg; and (4) white blood cell count >12,000/cu mm, <4,000/cu mm, or >10% immature (band) forms

Sepsis = the systemic response to infection, manifested by two or more of the following conditions as a result of infection: (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or $PaCO_2$ <32 mm Hg; and white blood cell count >12,000/cu mm, <4,000/cu mm, or >10% immature (band) forms.

Severe sepsis = sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status.

Septic shock = sepsis-induced with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients who are receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured.

Sepsis-induced hypotension = a systolic blood pressure <90 mm Hg or a reduction of ≥40 mm Hg from baseline in the absence of other causes for hypotension.

Multiple organ dysfunction syndrome (MODS) = presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.

Bone RC, Chest 1992

DEFINITION II (2001)

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference

Criterios diagnósticos de sepsis (Conferencia Consenso 2001)	
Infección (documentada o sospechada) y alguno de los siguientes	
Variables generales	
Fiebre (Tª central >38,3ºC)	Hipotermia (Tª central <36ºC)
FC >90 lpm o >2DS de valor normal	Taquipnea
Alteración del sensorio	Edema significativo o balance positivo (>20 ml/kg en 24h)
Hiperglucemia (>120 mg/dl) sin DM	
Variables inflamatorias	
Leucocitosis (>12000 /µl) o >10% bandas	Leucopenia (<4000 /µl)
PCR > 2DS valor normal	Procalcitonina >2DS valor normal
Variables hemodinámicas	
Hipotensión arterial (PAS <90 mmHg, PAM < 70 mmHg, o ↓ PAS >40 mmHg o 2 DS valor normal)	SvO2 >70%
	IC > 3,5 L/min/m^2
Variables de disfunción orgánica	
Hipoxemia (PaO2/FiO2 < 300)	Oliguria aguda (<0,5 ml/Kg/h) o ↑Cr >0,5 mg/dL
INR >1,5 o TTPA >60 segundos	Íleo
Plaquetas <100.000/µl	Bilirrubina total >4 mg/dL
Variables de perfusión tisular	
Lactato > 1 mmol/L	↓ Relleno capilar o livideces

Modificado de Levy MM, Crit Care Med 2003

DEFINITION III (2016): SEPSIS

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

Sepsis: Life-threatening organ dysfunction (defined as ↑△SOFA ≥ 2) caused by a dysregulated host response to infection.

Singer M, JAMA 2016

SOFA (SEQUENTIAL (SEPSIS-RELATED) ORGAN FAILURE ASSESSMENT)

Puntuación de disfunción o fallo orgánico en la sepsis (escala SOFA: Sequential Organ Failure Assessment)

Puntuación	0	1	2	3	4
Respiratorio (PaO_2/FiO_2)	≥400	<400	<300	<200	<100
				–con soporte respiratorio–	
Coagulación (Plaquetas × 10^9/L)	≥150	<150	<100	<50	<20
Hepático (Bilirrubina (mg/dL))	<1,2	1,2-1,9	2-5,9	6-11,9	>12
Hemodinámico (PAM (mmHg), aminas (µg/kg/min))	PAM ≥ 70	PAM < 70	DA < 5 o DBT (cualquier dosis)[a]	DA 5,1-15 o Adr ≤ 0,1 o NA ≤ 0,1[a]	DA > 15 o Adr > 0,1 o NA > 0,1[a]
Neurológico (CGS)	15	13-14	10-12	6-9	<6
Renal (Cr (mg/dL) o diuresis (mL/día))	<1,2	1,2-1,9	2,0-3,4	3,5-4,9 o <500	>5 o <200

[a] Catecolaminas administradas durante al menos 1 h. Adr: adrenalina; CGS: Escala de coma de Glasgow; Cr: creatinina; DA: dopamina; DBT: dobutamina; NA: noradrenalina; PAM: presión arterial media.

Modificat de Vincent JL, et al. Intensive Care Med 1996

DEFINITION III (2016): SEPTIC SHOCK

Sepsis +

+ hypotension requiring vasopressor to maintain Mean Arterial Pressure (MAP) ≥ 65 mmHg +

+ lactate > 18 mg/dL (2 mmol/L) in the absence of hypovolemia

Singer M, JAMA 2016

RELEVANCE IN THE CARDIOLOGY SETTING

- Patients with CHF (almost 1/4) die from sepsis
- Patients with AHF (some) die from sepsis
- Patients with CS are at increased risk of sepsis and it increases mortality
- There are patients with sepsis admitted to the CCCU
- Patients with infections develop more cardiovascular events

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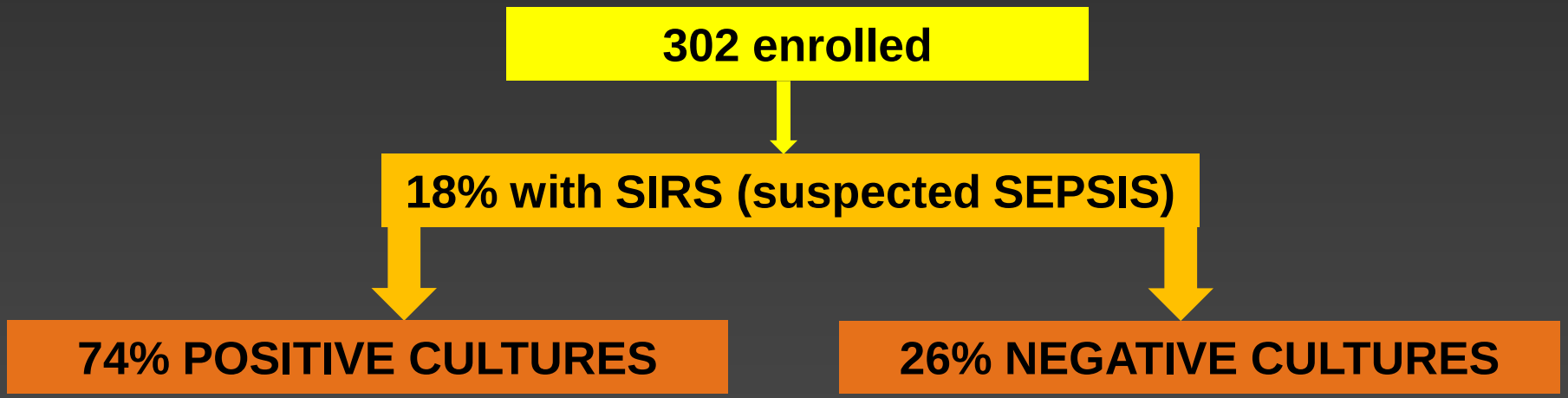
RELEVANCE IN THE CARDIOLOGY SETTING

SHOCK Trial (Cardiogenic Shock complicating AMI)



Kohsaka S, Arch Intern Med 2005

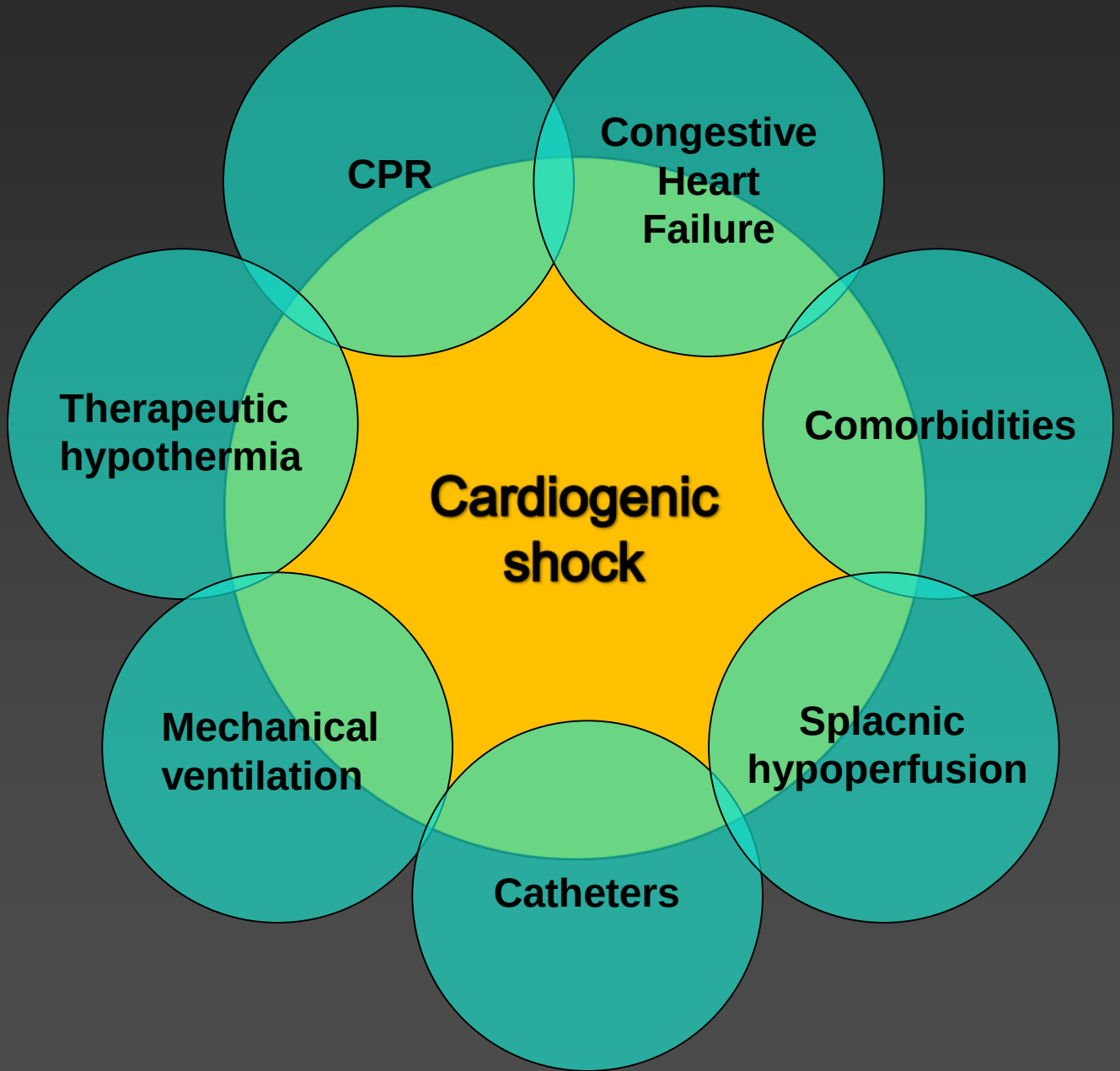
RELEVANCE IN THE CARDIOLOGY SETTING

SHOCK Trial (Cardiogenic Shock complicating AMI)

Organism	Source of infection				
	Lung (67.5%)	Catheter (42.5%)	UTI (12.5%)	Surgical site (10%)	Other sources (5%)
S. aureus	32%	41%	38%	14%	50%
GN rods	36%	27%	24%	43%	50%
Other organisms	32%	32%	38%	43%	0%

Kohsaka S, Am J Cardiol 2007

RELEVANCE IN THE CARDIOLOGY SETTING



P. Castro 2019

DIAGNOSIS

- Syndromic, source and etiologic (cultures)

- Syndromic: Life-threatening **organ dysfunction** (defined as ↑△SOFA ≥ 2) caused by a **dysregulated host response** to **infection**.

- When the organ dysfunction is caused by an infection?

DIAGNOSIS. SEPSIS VS NON-INFECTIOUS SIRS

The New England
Journal of Medicine

Volume 235 SEPTEMBER 12, 1946 Number 11

ACUTE MYOCARDIAL INFARCTION

A Study of 100 Consecutive Cases

WILLIAM N. CHAMBERS, M.D.*

Chambers WN, NEJM 1946

DIAGNOSIS. SEPSIS VS NON-INFECTIOUS SIRS

Pulse and Temperature

On admission the average pulse in the fatal cases was 115; rapid pulse usually persisted until death. The average rectal temperature for this group was 101.7°F.*, and the temperature remained elevated until death. In only 1 fatal case was there no evidence of tachycardia, and fever was present in all fatal cases.

The pulse in the surviving patients averaged 100 and remained rapid for an average of eight days; the temperature, which was slightly over 100°F.** on admission, usually fell to normal on the ninth or tenth day — one or two days after the pulse returned to normal.

*38.7ºC; **37.7ºC

Chambers WN, NEJM 1946

DIAGNOSIS. SEPSIS VS NON-INFECTIOUS SIRS

Prospective, 192 AMI patients

The temperature course in acute myocardial infarction

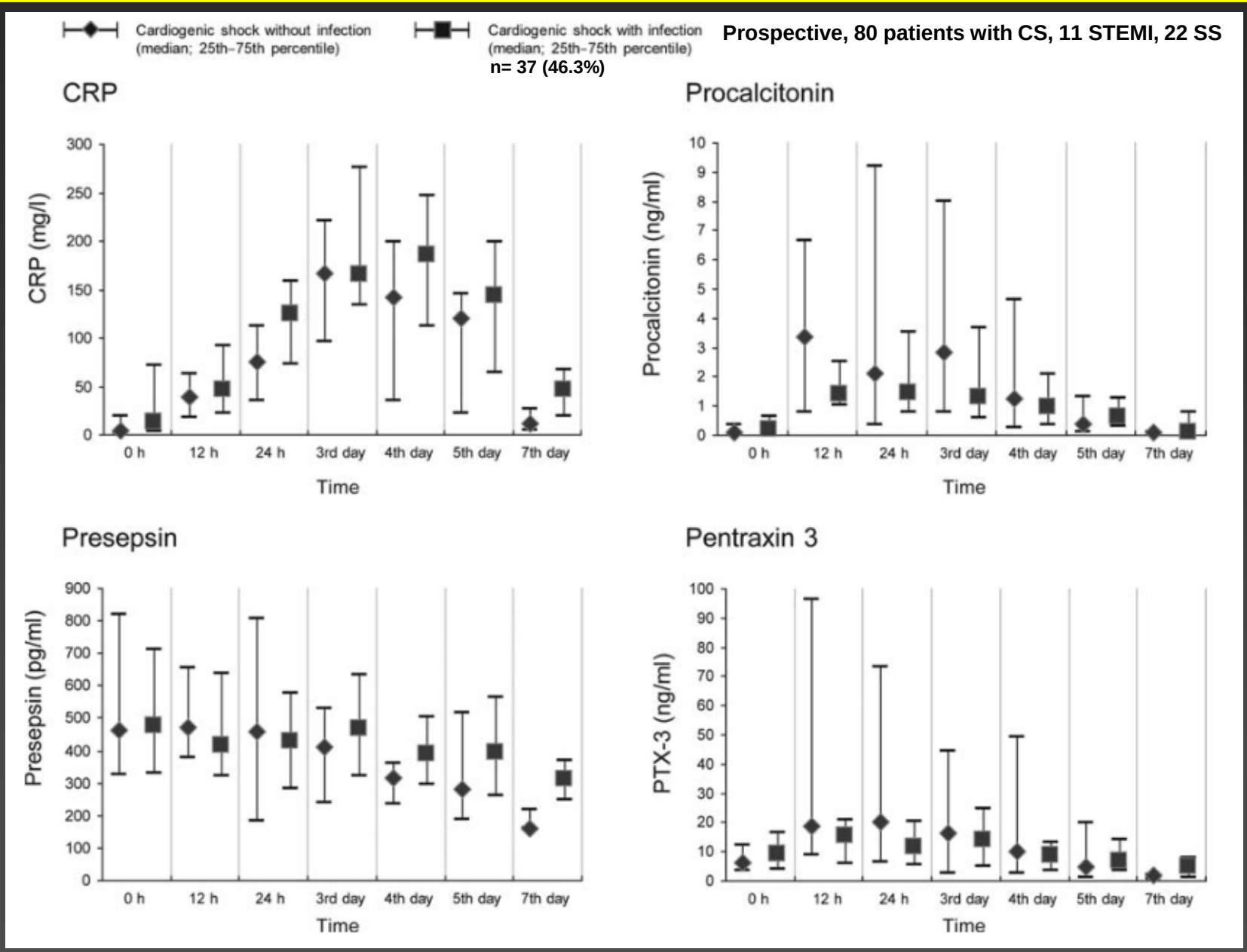
Diagnosed or suspected cause of fever besides AMI	**13%** *No.*	*Temperature course "atypical" for AMI* No.*
Urinary tract infections	11	3
Upper respiratory infections	2	0
Pneumonias	3	3
Operation/wound infections	5	4
Septicemia(?) + pulmonary emboli	1	1
Tuberculosis (treatment)	1	1
Fever of unknown cause	2	1

Rectal T[a] (any of them):

- >38.2º first morning
- Maximum before day 2
- Maximum after day 5
- >39º
- Increases >0.6ºC after day 5

Löfmark R, Am Heart J 1977

DIAGNOSIS. BIOMARKERS



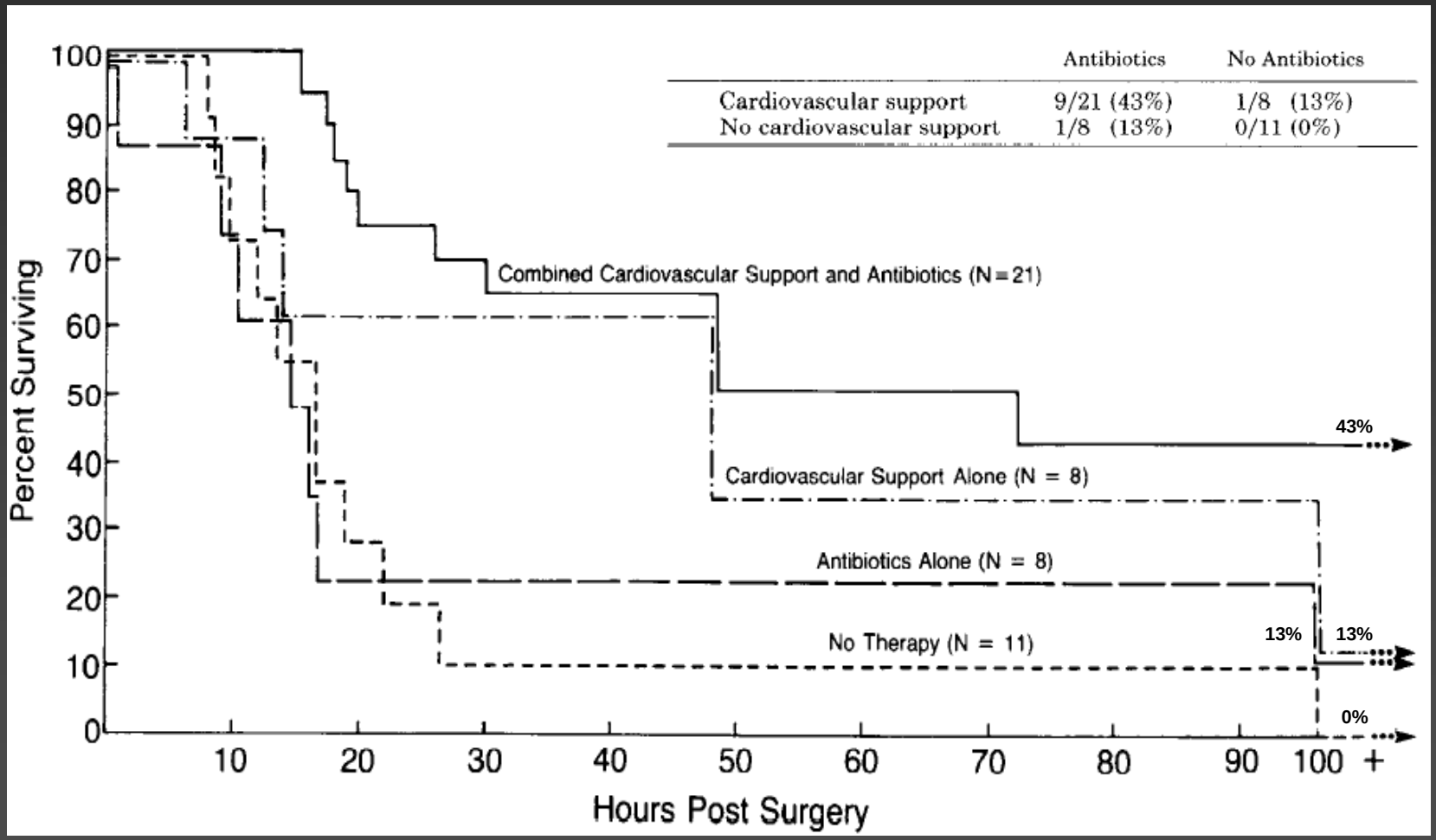
Parenica J, Shock 2017

INITIAL TREATMENT. WHAT?

- Etiologic treatment
  - Antibiotic treatment
  - Source control
- Supportive treatment (to restore perfusion)
  - Fluids
  - Vasopressors

INITIAL TREATMENT. WHAT?

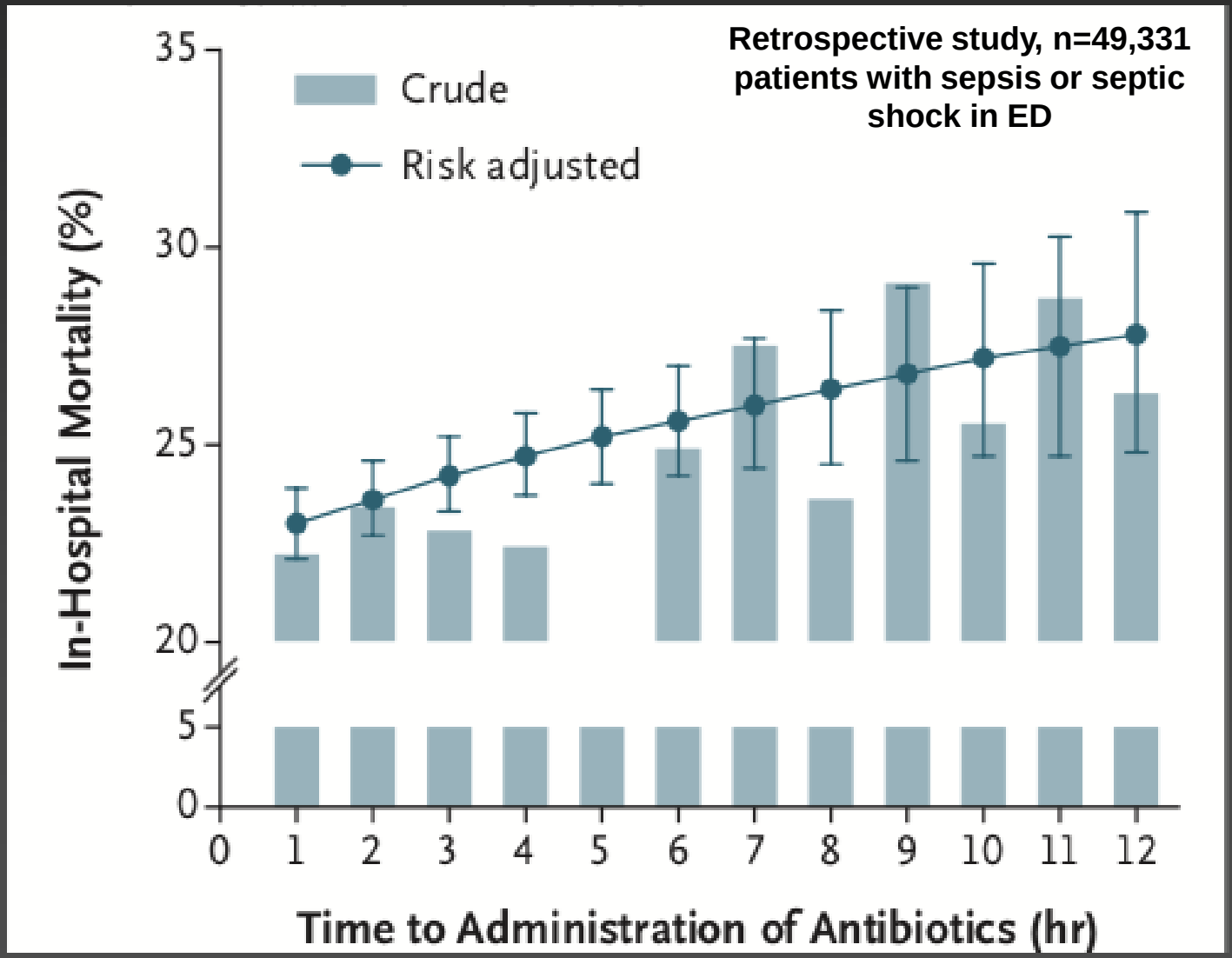
Initial resuscitation (fluids ± vasopressors) is “as” important as antibiotic treatment



Natanson C, Am J Physiol 1990

ANTIBIOTIC. WHEN?

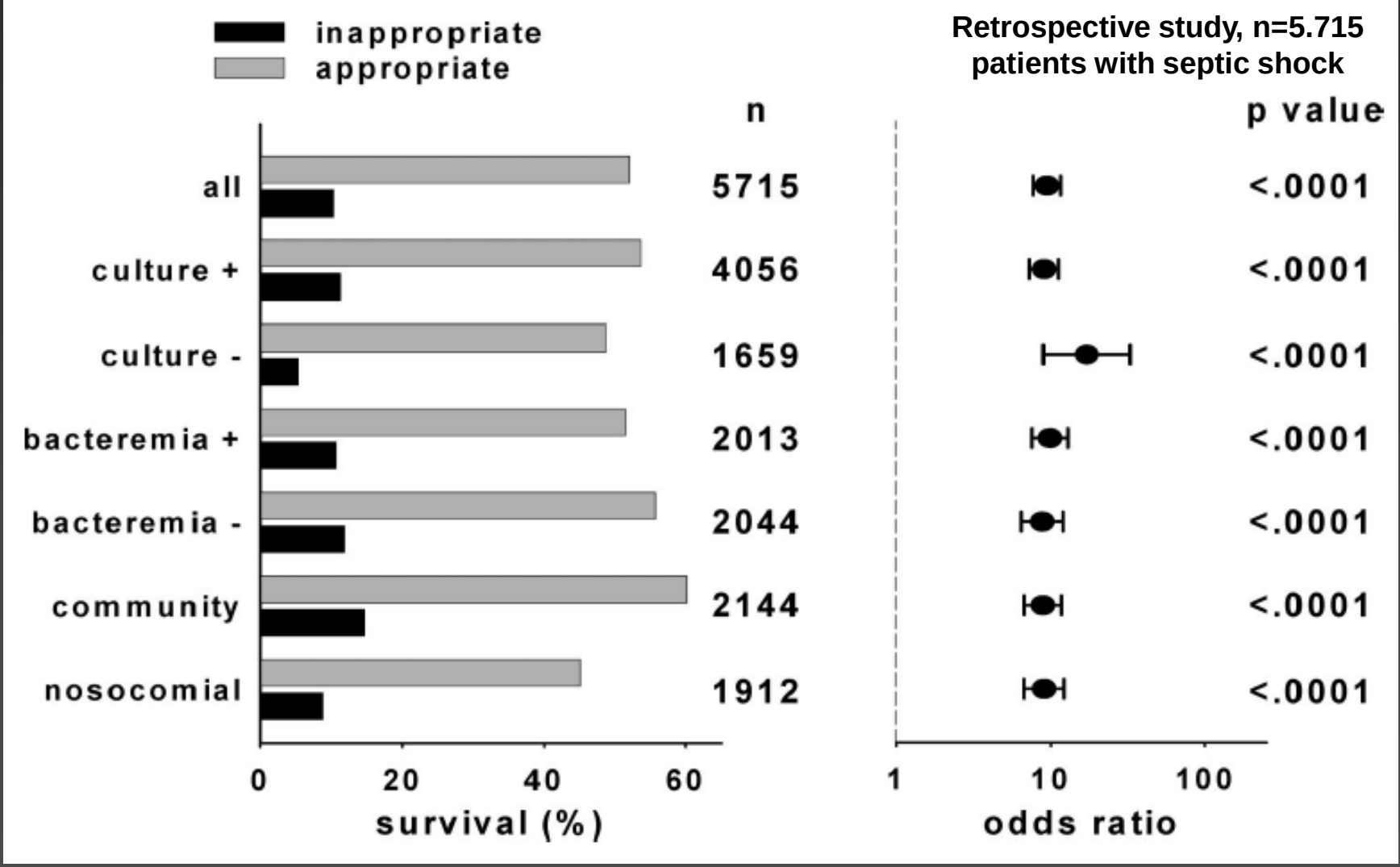
EARLY. As soon as possible (first hour → empiric)



Seymour CW, NEJM 2017

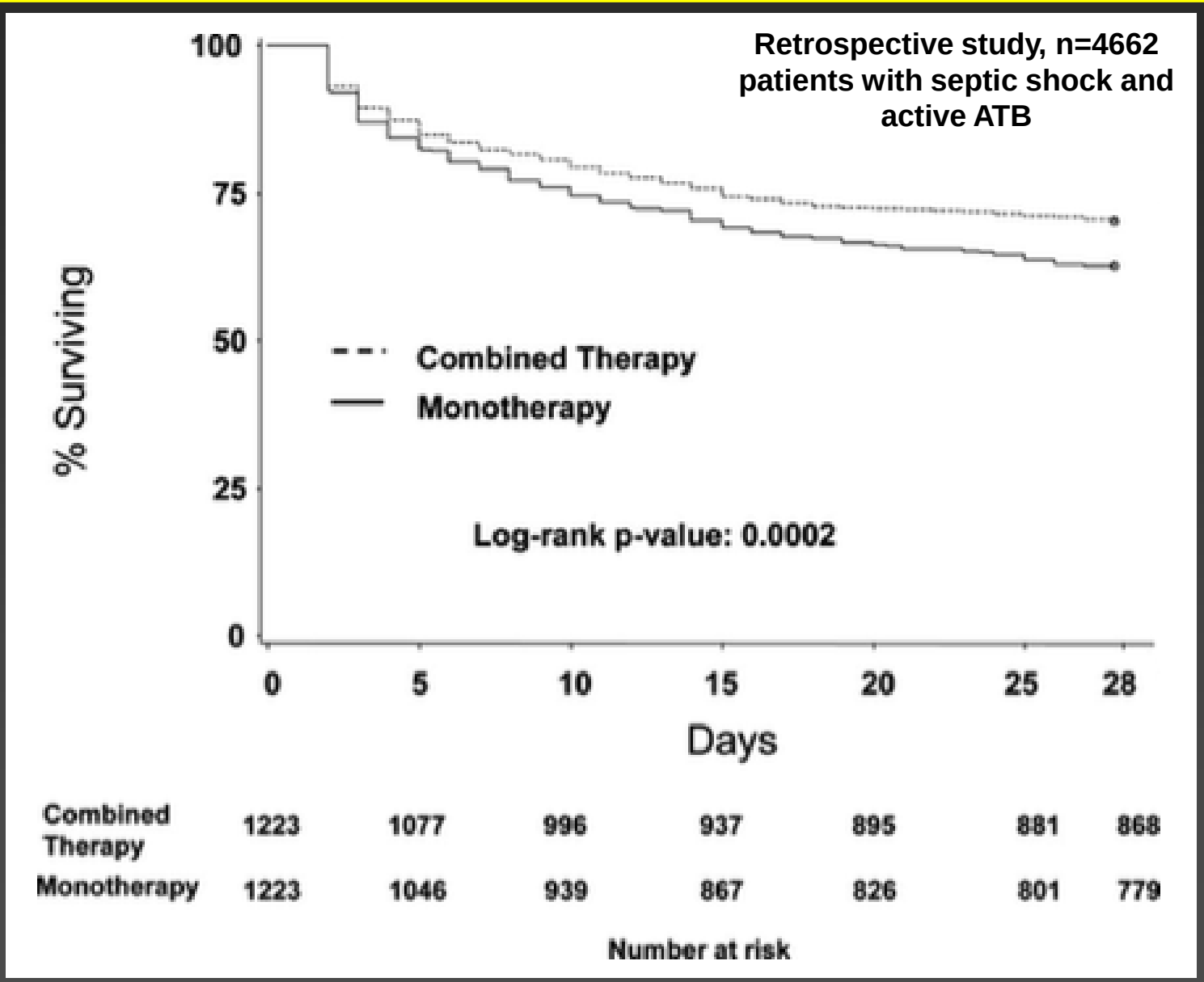
ANTIBIOTIC. WHICH?

APPROPRIATE. Covering “100%” most probable pathogens



Kumar A, Chest 2009

ANTIBIOTIC. COMBINATION TREATMENT



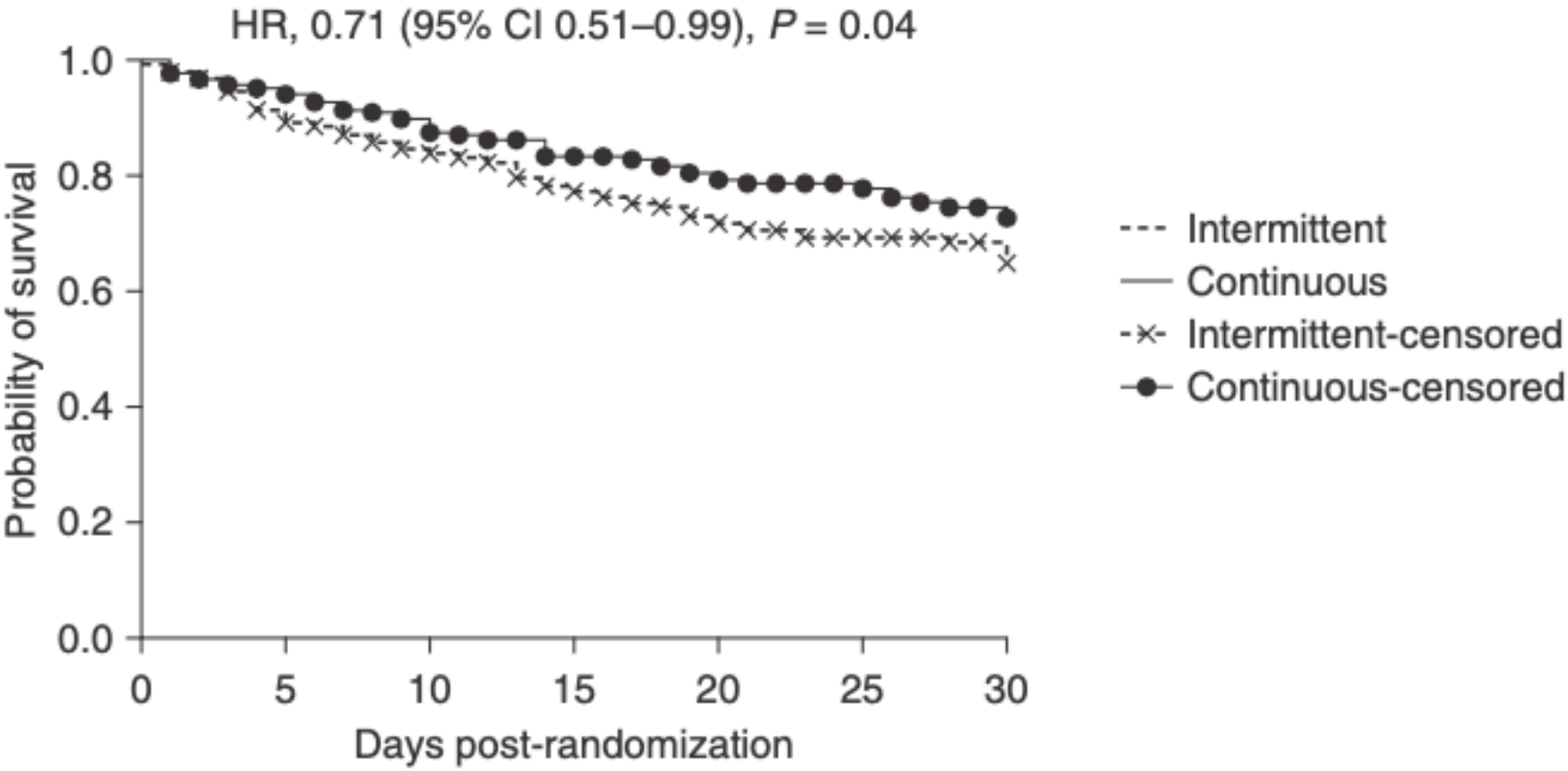
Kumar A, Crit Care Med 2010

ANTIBIOTIC. HOW?

- Optimize its effect:
  - Intravenous
  - Use all available catheters
  - “Fast administration” antibiotics first
  - High doses
  - Consider pharmacokinetics / pharmacodynamics characteristics (including tissue penetration)

ANTIBIOTIC. HOW?. INTERMITTENT VS CONTINOUS

Individual patient meta-analysis



Roberts JA, Am J Respir Crit Care Med 2016

SOURCE CONTROL

- Critical in several situations (intestinal perforation, intraabdominal abscess, cholangitis, cholecystitis, empyema, obstructive pyelonephritis…)

- It may include:
  - Infected devices and foreign bodies removal (catheter, pacemaker, prosthetic valves...)
  - Infected fluids (empyema) or abscess drainage
  - Tissue debridement and resection

SOURCE CONTROL

Prospective observational, n=1011 patients with severe sepsis or septic shock admitted to ICU; n=422 with intervention to source control

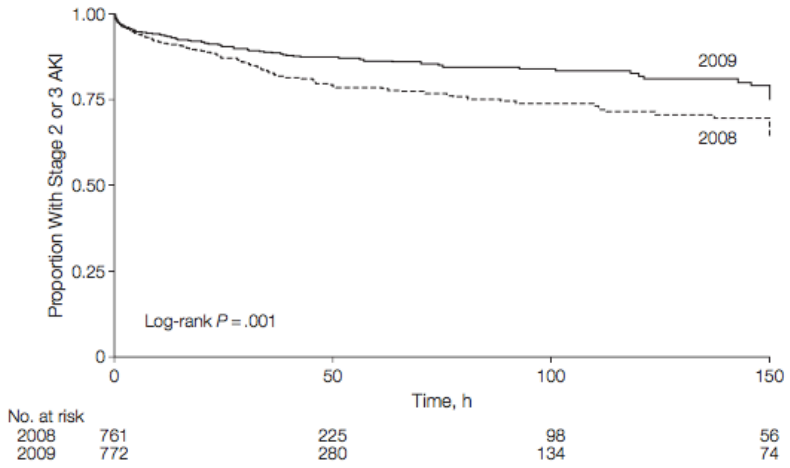
	Time to source control (hours)		
	Survivors	**Nonsurvivors**	**p**
28 d-survival	2 (-0,5 to 10.1)	5.7 (0.4 to 18)	0.004
ICU survival	2 (-0.6 to 9.1)	6 (0.5 to 19.9)	<0.001
Hospital survival	2 (-0.5 to 9.3)	5.5 (0.4 to 18.9)	0.001

Source control >6h→ ↑ mortality (30.3 vs 40.9%)

Bloos F, Crit Care 2014

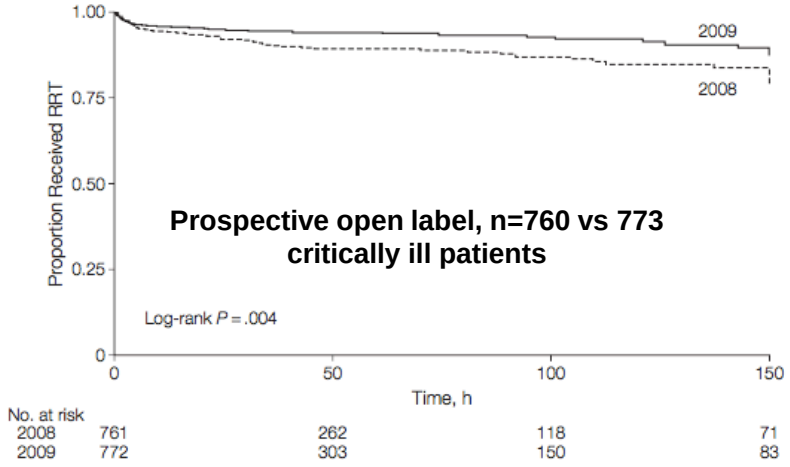
FLUIDS. WHICH?. SALINE VS BUFFERED CRYSTALLOID

Figure 1. Development of Stage 2 or 3 Acute Kidney Injury (AKI) While in the Intensive Care Unit (ICU)



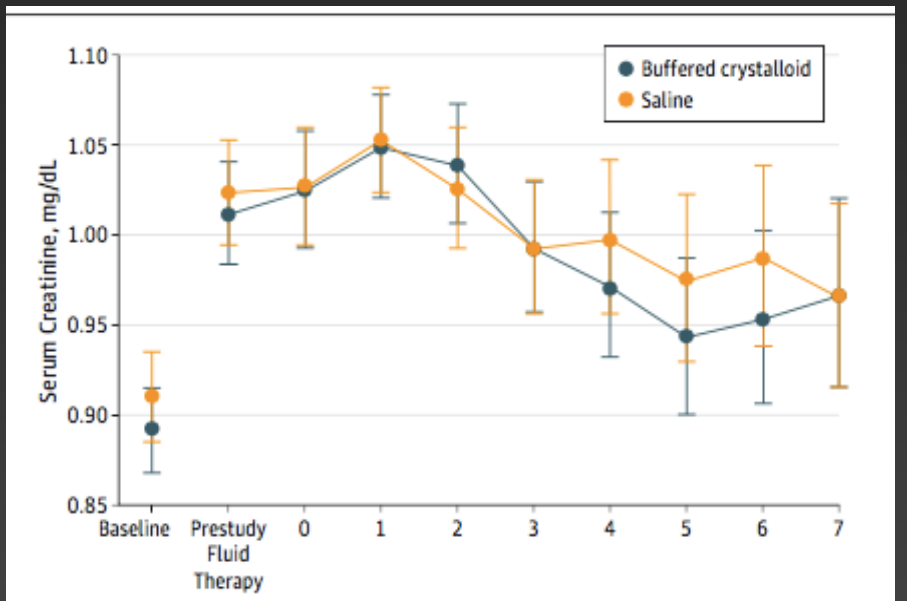
Stage 2 or 3 defined according to the Kidney Disease: Improving Global Outcomes clinical practice guideline.

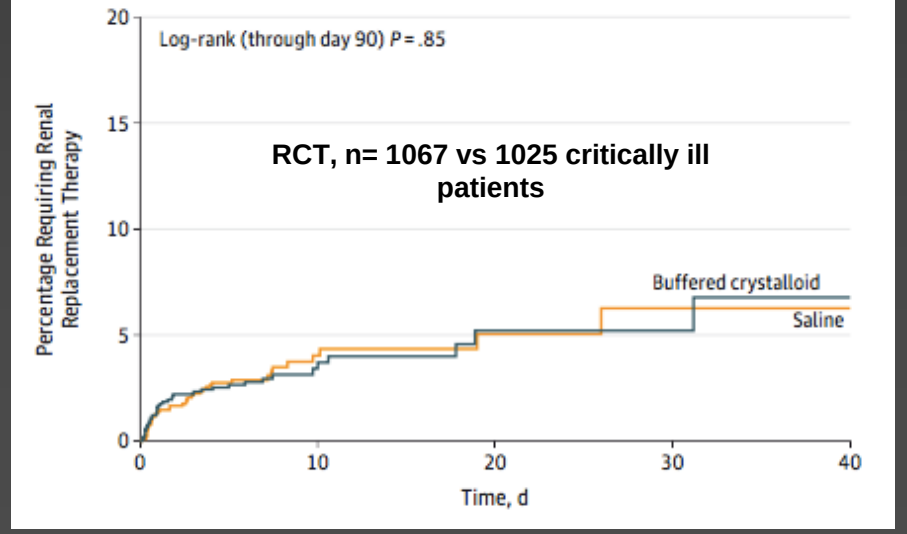
Figure 2. Renal Replacement Therapy (RRT) in the Intensive Care Unit (ICU)



Prospective open label, n=760 vs 773 critically ill patients

Yunos NM, JAMA 2014





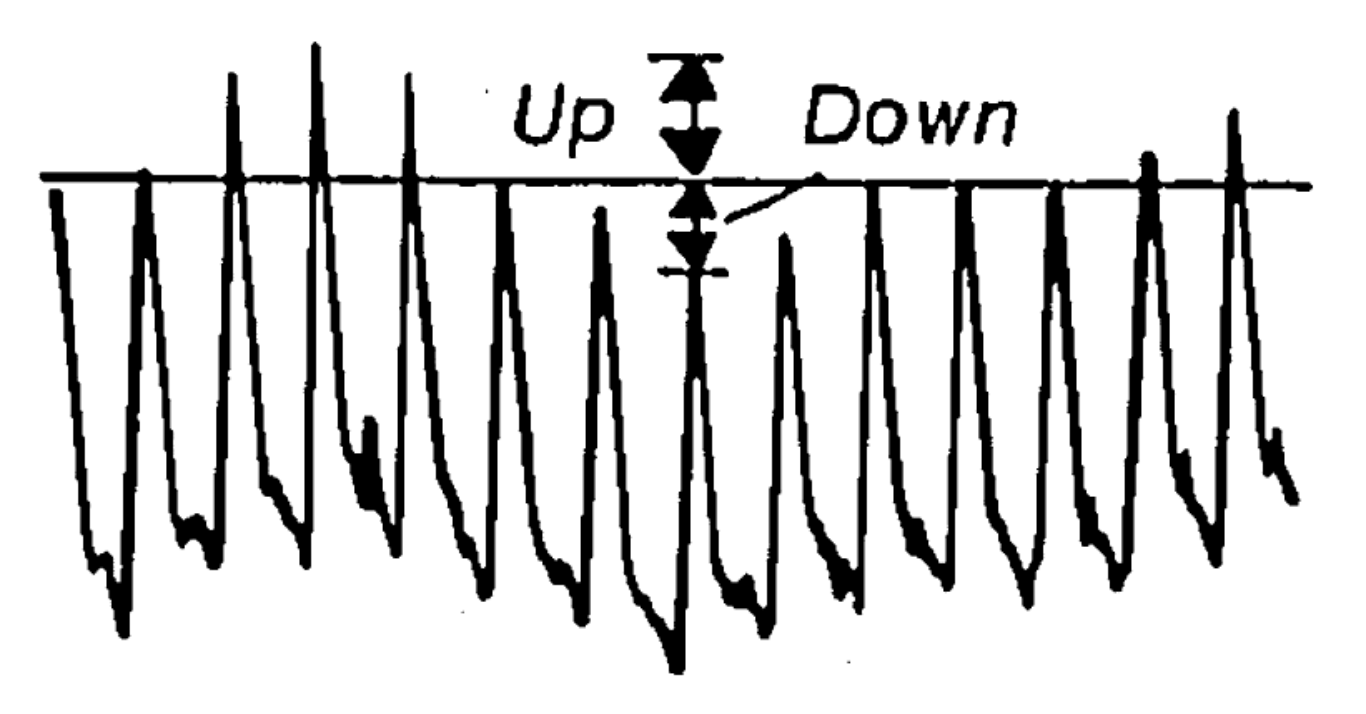
RCT, n= 1067 vs 1025 critically ill patients

Young P, JAMA 2015

FLUIDS: HOW MUCH?

- It depends: "It has to be needed, it has to work and it has not to do harm”
- Usually, septic patient is hypovolemic (real and/or relative) → cardiac output is low or insufficiently normal
- Fluid resuscitation has to increase perfusion (by increasing cardiac output increasing preload): fluid responsiveness
- Fluid resuscitation does not have to cause overload and adverse events

FLUIDS: HOW MUCH?. DYNAMIC PRELOAD AND FLUID RESPONSIVENESS



- It considers influence of ventilation on venous return.
- It is useful in ventilated patients, with tidal volume >8 mL/Kg, synchronic with the ventilator and in sinus rhythm.

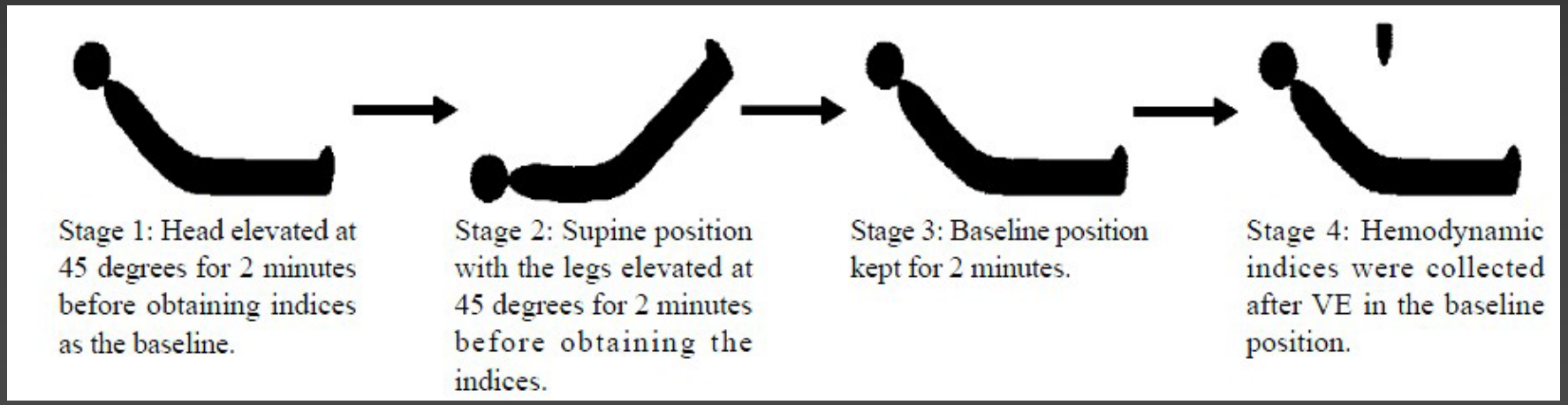
Perel A, Intensive Care Med 2014

FLUIDS. HOW?. FLUID CHALLENGE

If there are doubts about a shock patient will respond to fluid resuscitation, it is advisable a “mini-fluid challenge”: administer in short period of time 100 mL of crystalloid.

FLUIDS. HOW?. FLUID CHALLENGE

Alternative: *Passive leg raising test*



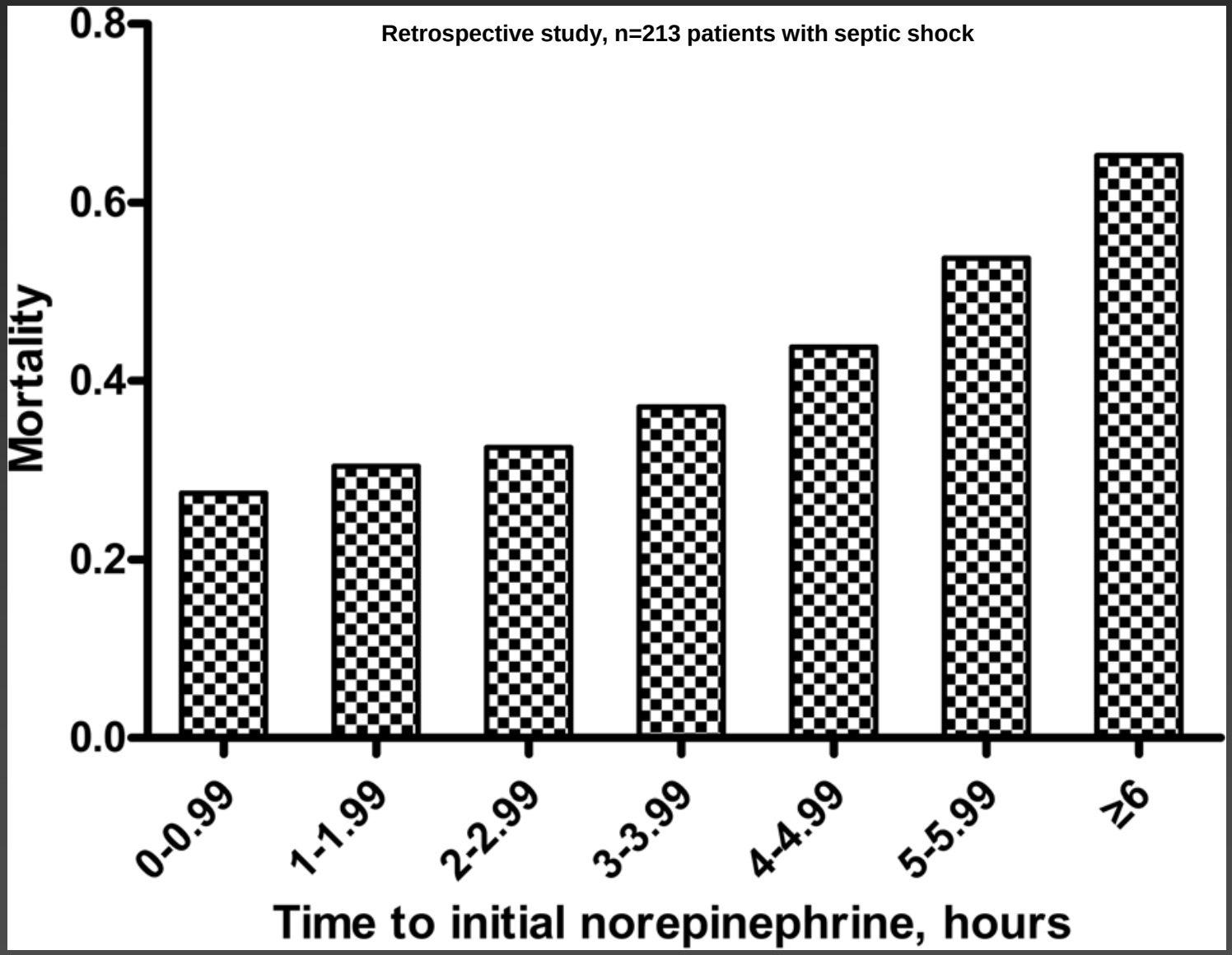
Stage 1: Head elevated at 45 degrees for 2 minutes before obtaining indices as the baseline.

Stage 2: Supine position with the legs elevated at 45 degrees for 2 minutes before obtaining the indices.

Stage 3: Baseline position kept for 2 minutes.

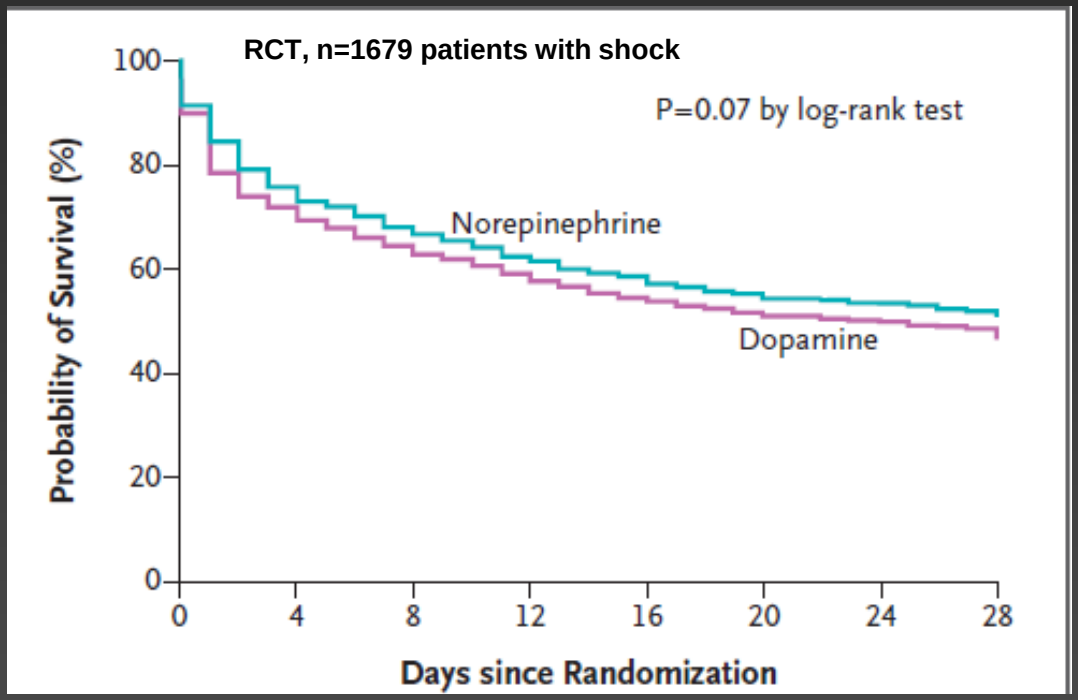
Stage 4: Hemodynamic indices were collected after VE in the baseline position.

VASOPRESSORS. WHEN?

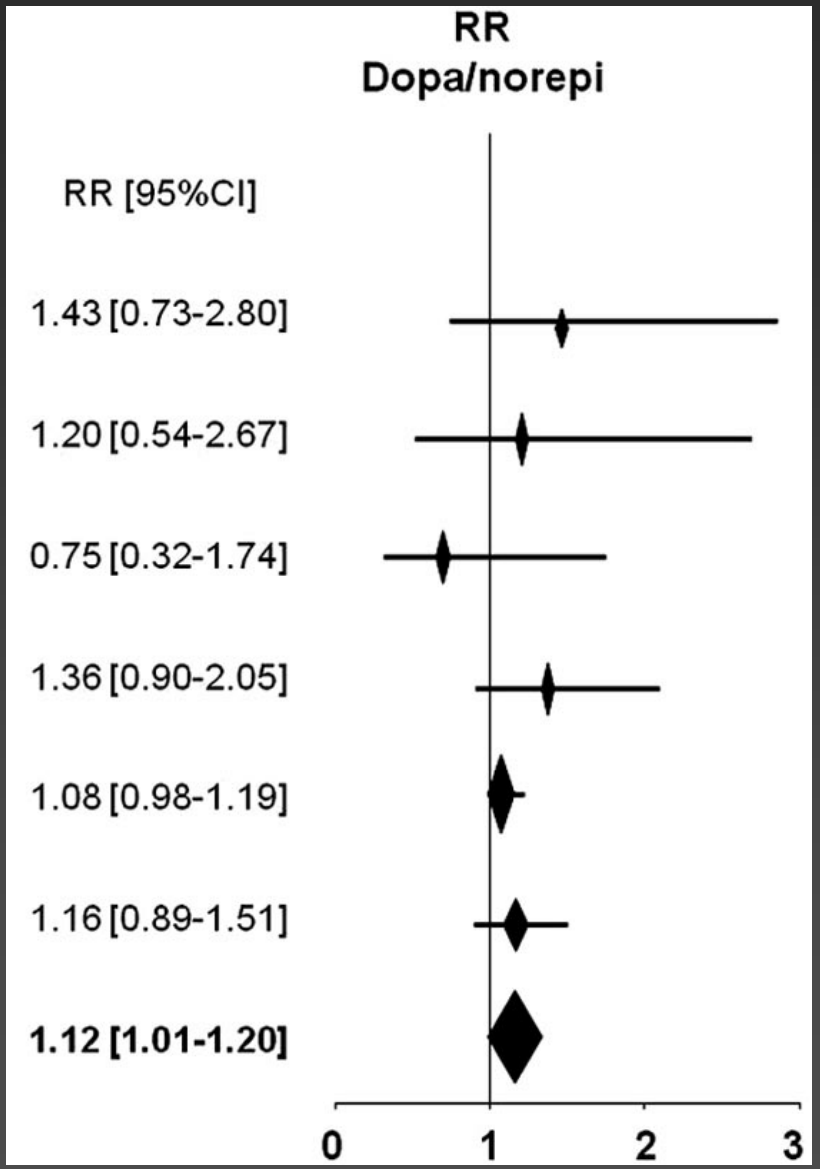


Bai X, Crit Care 2014

VASOPRESSORS. WHICH?

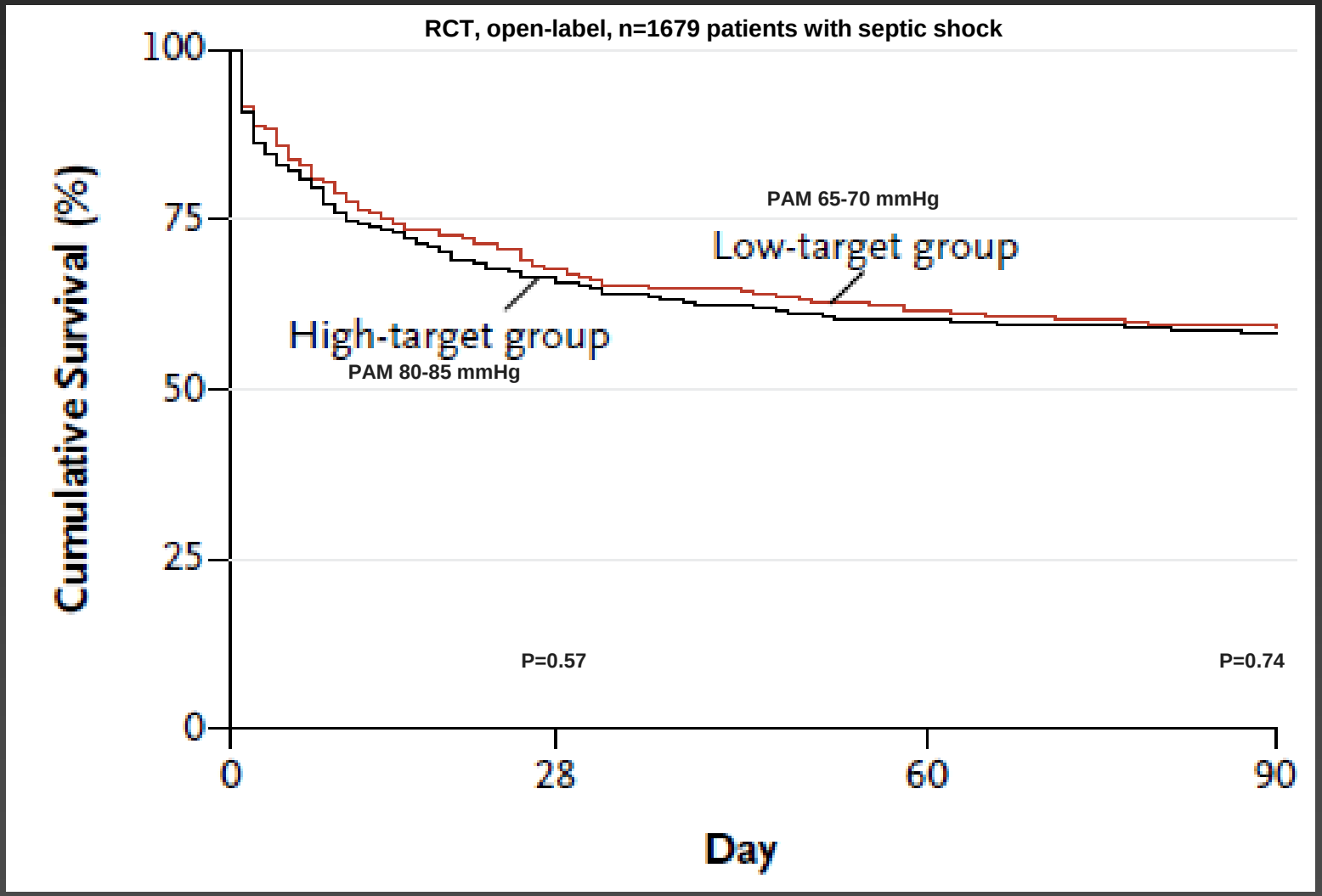


De Backer D, NEJM 2010



De Backer D, Crit Care Med 2012

VASOPRESSORS. HOW MUCH?

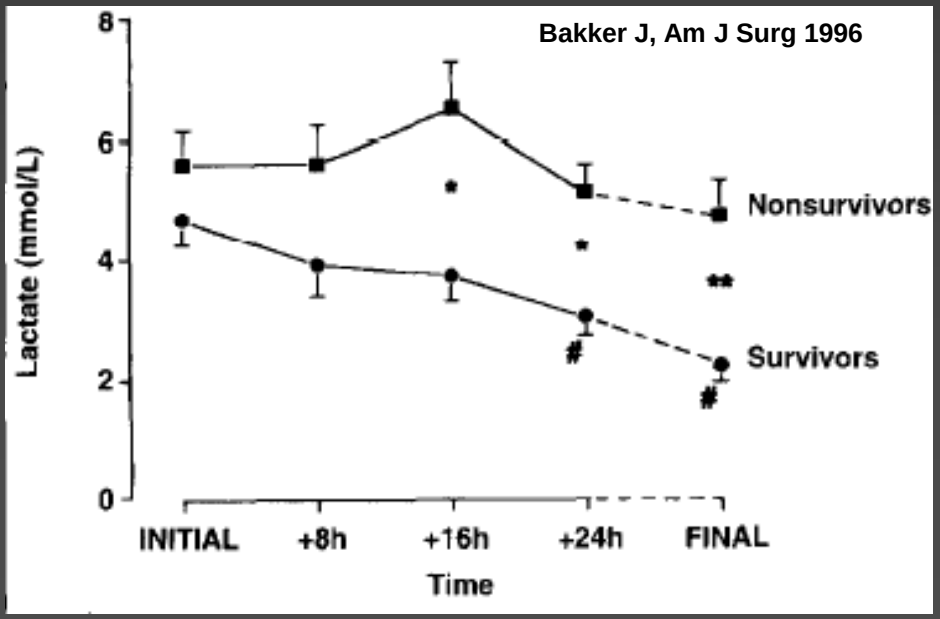


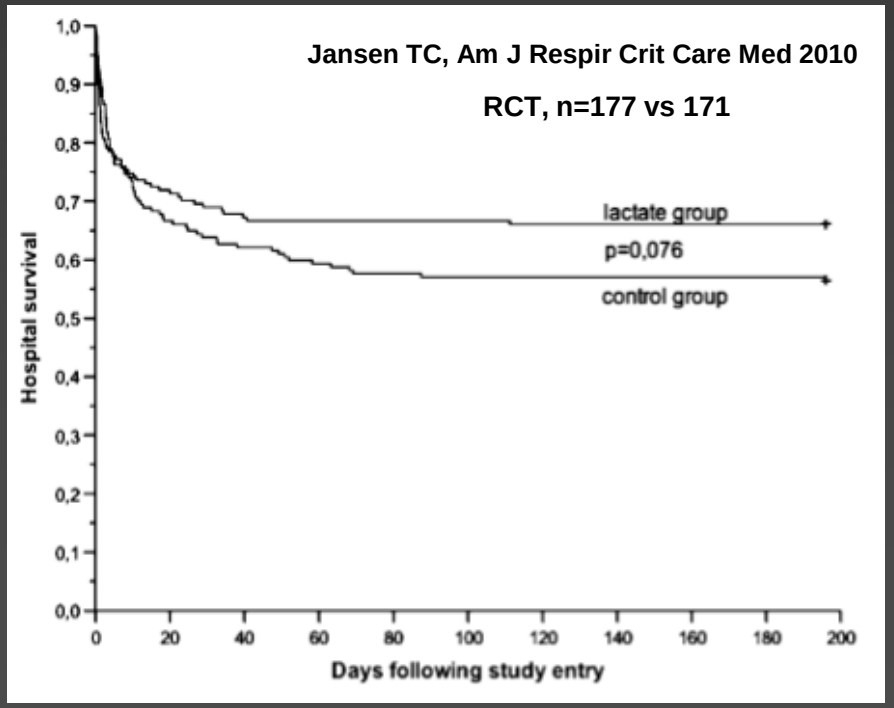
Patients with chronic hypertension presented more renal failure in the group of lower MAP

Asfar P, NEJM 2014

INITIAL RESUSCITATION: REASSESSMENT

In case of shock frequent reassessment is needed: arterial pressure (invasive better), hypoperfusion signs (urine output, level of consciousness) and biomarkers (lactate reduction)





Jones AE, JAMA 2010; Antonelli M, Intensive Care Med 2007

CONCLUSIONS

- Sepsis (and septic shock) are serious problems, also in the cardiology setting.
- In the initial treatment, resuscitation is as important as antibiotic.
- Antibiotic has to be early, appropriate, combined and high doses.
- Sources has to be addressed and controlled when possible.
- Fluid resuscitation has to be early, in challenges and with regular crystalloids.
- If there is no rapid response to fluids, begin with noradrenaline early.
- Reassess response

DISCLOSURES