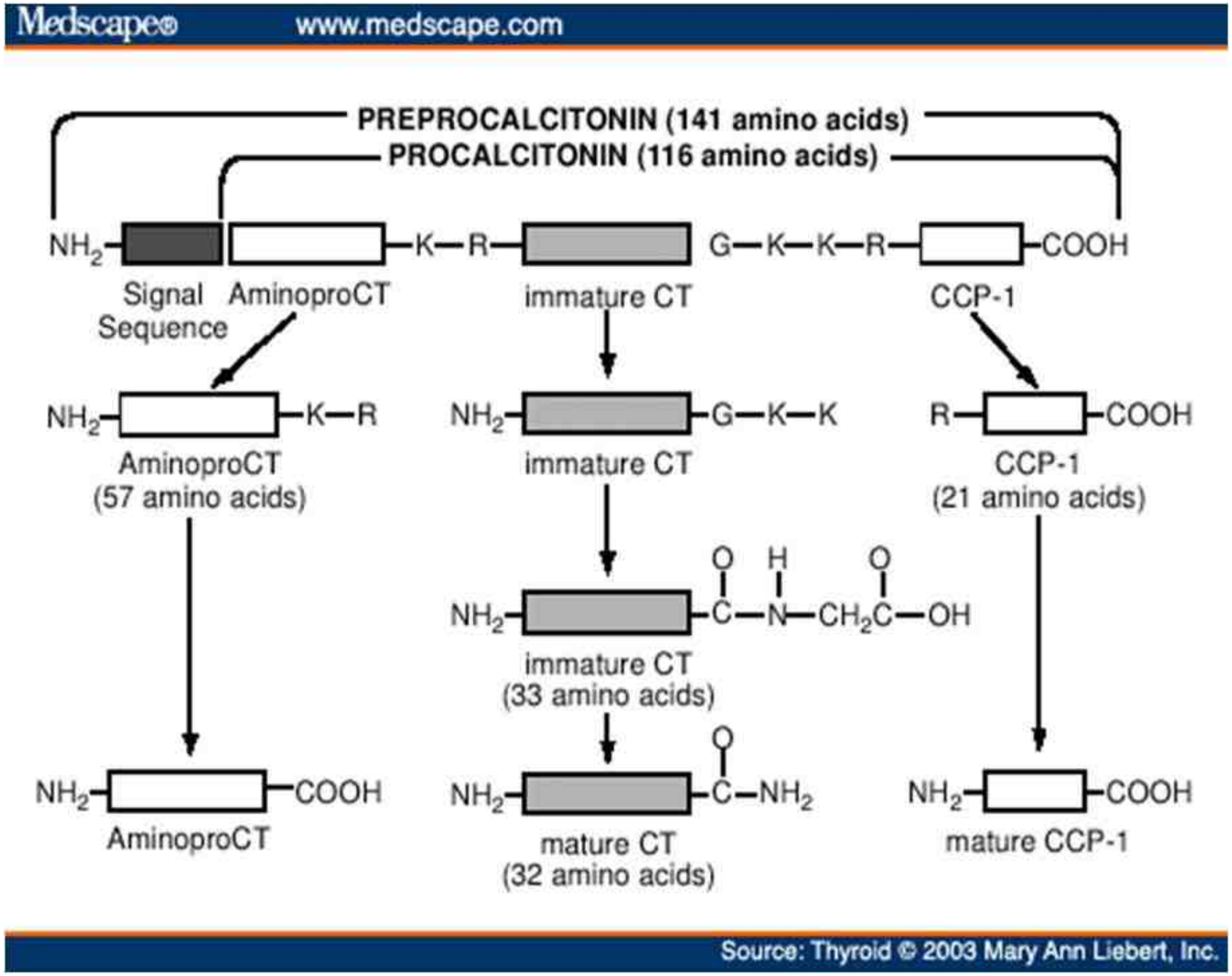
CARACT
2010
Pisa 17-19 Novembre

LA PROCALCITONINA

G.Paternoster
Terapia Intensiva e Anestesia Cardiovascolare
Ospedale San Carlo
Potenza

LA PROCALCITONINA (PCT)


Medscape®
www.medscape.com
PREPROCALCITONIN (141 amino acids)
PROCALCITONIN (116 amino acids)
NH2
Signal Sequence
AminoproCT
K—R
immature CT
G—K—K—R
CCP-1
COOH
NH2
K—R
AminoproCT (57 amino acids)
NH2
G—K—K
immature CT
R
COOH
CCP-1 (21 amino acids)
NH2
C—N—CH2C—OH
O H O
immature CT (33 amino acids)
NH2
COOH
AminoproCT
NH2
C—NH2
O
mature CT (32 amino acids)
NH2
COOH
mature CCP-1

Source: Thyroid © 2003 Mary Ann Liebert, Inc.

LA PROCALCITONINA (PCT)

E' il pro-ormone della calcitonina composta da 116 amminoacidi

Nell'individuo sano è prodotta dalle cellule C della tiroide

Altre sedi di produzione

Macrofagi

Monociti

Fegato

ELIMINAZIONE

- Degradazione per proteolisi
- Escrezione renale 20%

PCT intatta nel filtrato durante CVVH e nel dialisato durante CVVHDF.

PCT NELLA PRATICA CLINICA

- PCT nella diagnosi differenziale tra SIRS E SEPSI
- PCT nel periodo Postoperatorio
- PCT durante Shock Cardiogeno
- PCT per guidare l'Antibiotico Terapia

PCT nella diagnosi differenziale tra SIRS E SEPSI

PCT NELLA DIAGNOSI DI SIRS E SEPSI

SIRS

risposta infiammatoria sistemica caratterizzata da due o più delle seguenti condizioni

- *Temperatura > 38°C o < 36°C*
- *FC > 90 bmp*
- *FR > 20 atti/min o PaCO2 < 32 mmHg*
- *GB > 12000/mm3 o < 4000/mm3 o > 10% di forme immature*

SEPSI

risposta sistemica dell'organismo all'infezione. Manifestata da due o più condizioni cliniche:

- *Temperatura > 38°C o < 36°C*
- *FC > 90 bmp*
- *FR > 20 atti/min o PaCO2 < 32 mmHg*
- *GB > 12000/mm3 o < 4000/mm3 o > 10% di forme immature*

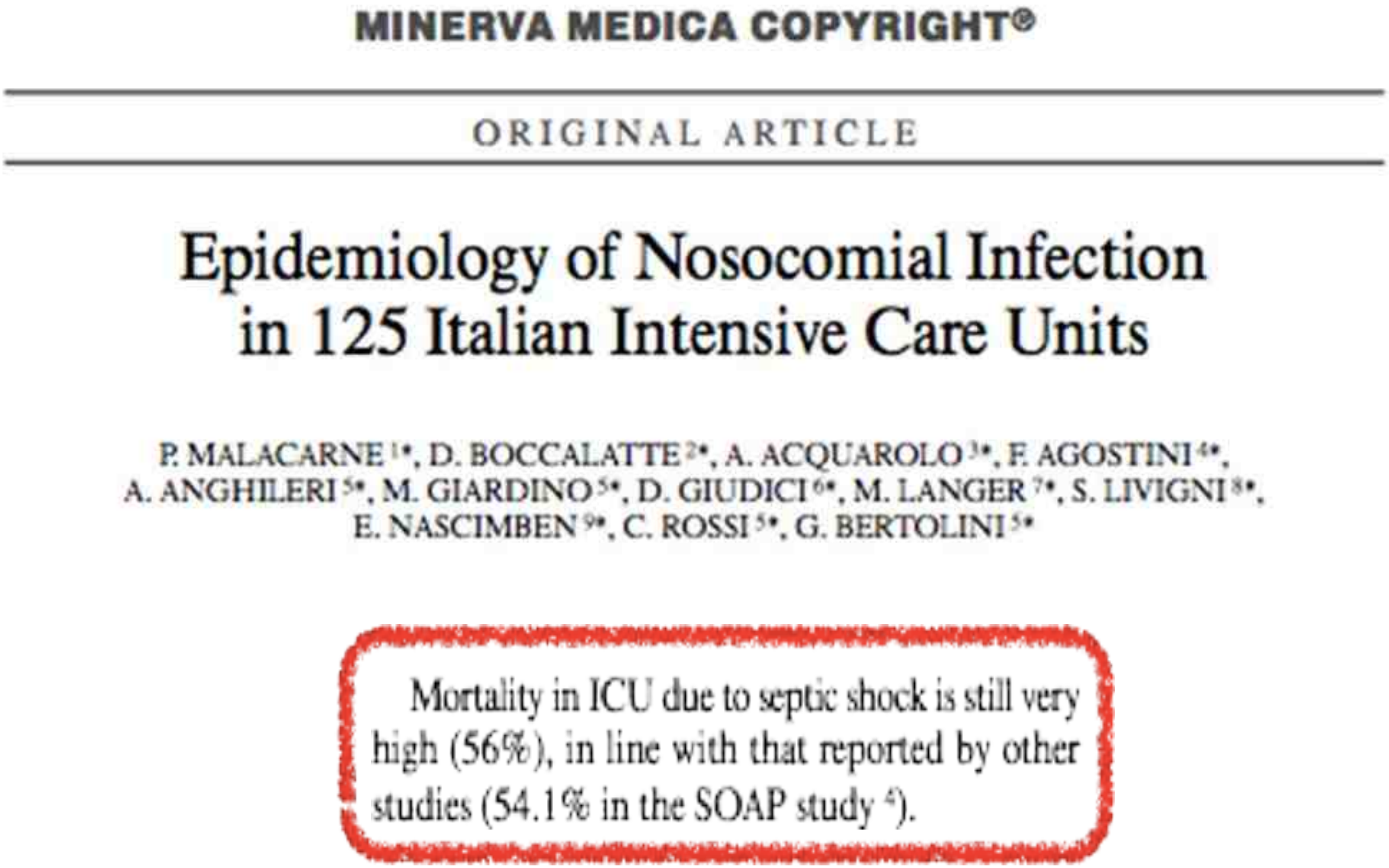
PCT NELLA DIAGNOSI DI SIRS E SEPSI

JAMA

International Study of the Prevalence
and Outcomes of Infection
in Intensive Care Units

Vincent JL. JAMA 302:2323 (2009)

PCT NELLA DIAGNOSI DI SIRS E SEPSI



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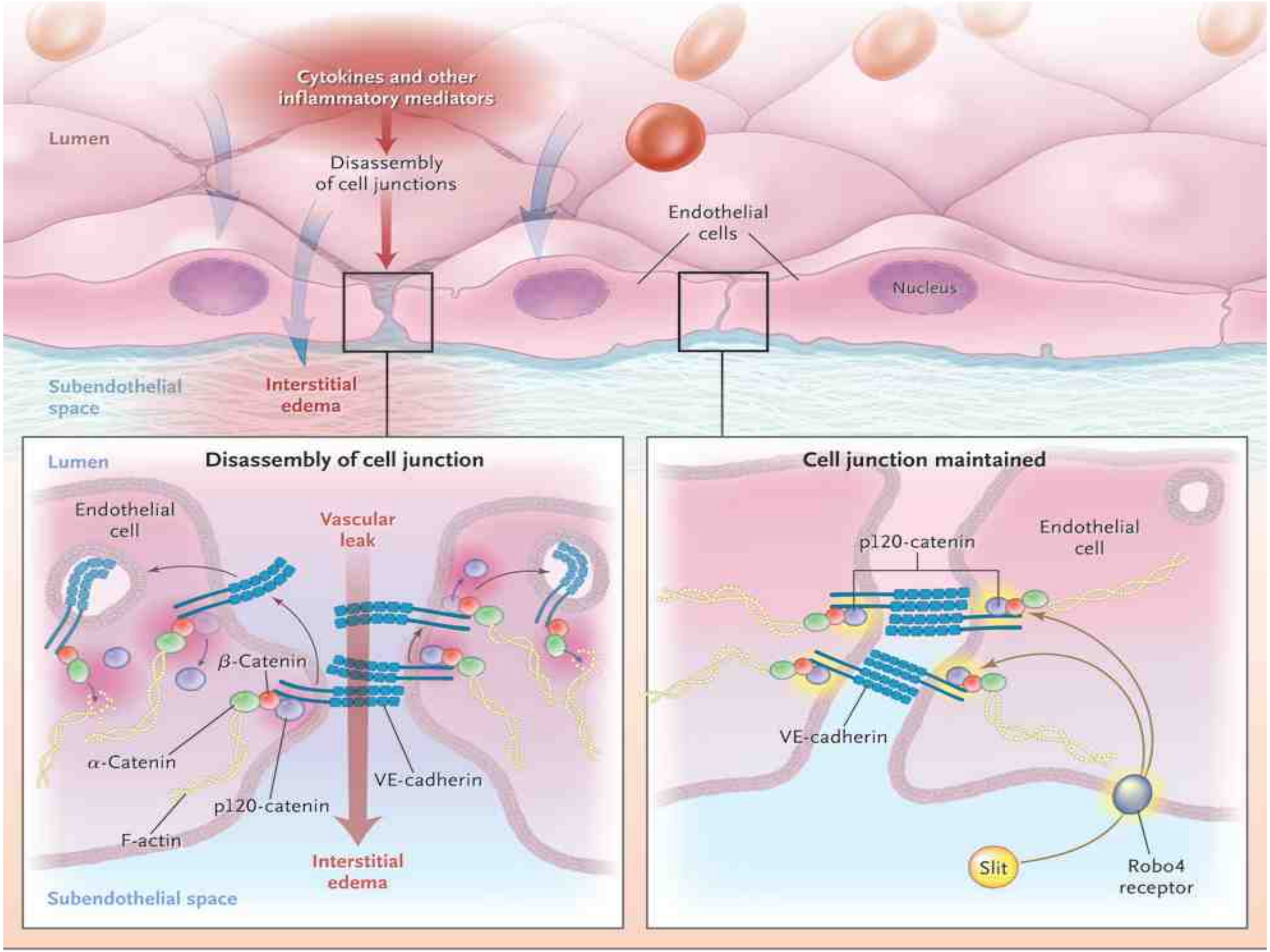
ORIGINAL ARTICLE

Epidemiology of Nosocomial Infection in 125 Italian Intensive Care Units

P. MALACARNE[1*], D. BOCCALATTE[2*], A. ACQUAROLO[3*], F. AGOSTINI[4*],
A. ANGHILERI[5*], M. GIARDINO[5*], D. GIUDICI[6*], M. LANGER[7*], S. LIVIGNI[8*],
E. NASCIMBEN[9*], C. ROSSI[5*], G. BERTOLINI[5*]

Mortality in ICU due to septic shock is still very high (56%), in line with that reported by other studies (54.1% in the SOAP study[4]).


Lumen
Cytokines and other inflammatory mediators
Disassembly of cell junctions
Endothelial cells
Nucleus
Subendothelial space
Interstitial edema
Lumen
Disassembly of cell junction
Endothelial cell
Vascular leak
β-Catenin
α-Catenin
p120-catenin
F-actin
VE-cadherin
Interstitial edema
Subendothelial space
Cell junction maintained
p120-catenin
Endothelial cell
VE-cadherin
Slit
Robo4 receptor

Warren L.Lee The New England Journal of Medicine August 12 2010

PCT NELLA DIAGNOSI DI SIRS E SEPSI

In corso di:

infezioni batteriche gravi

sepsi

shock settico

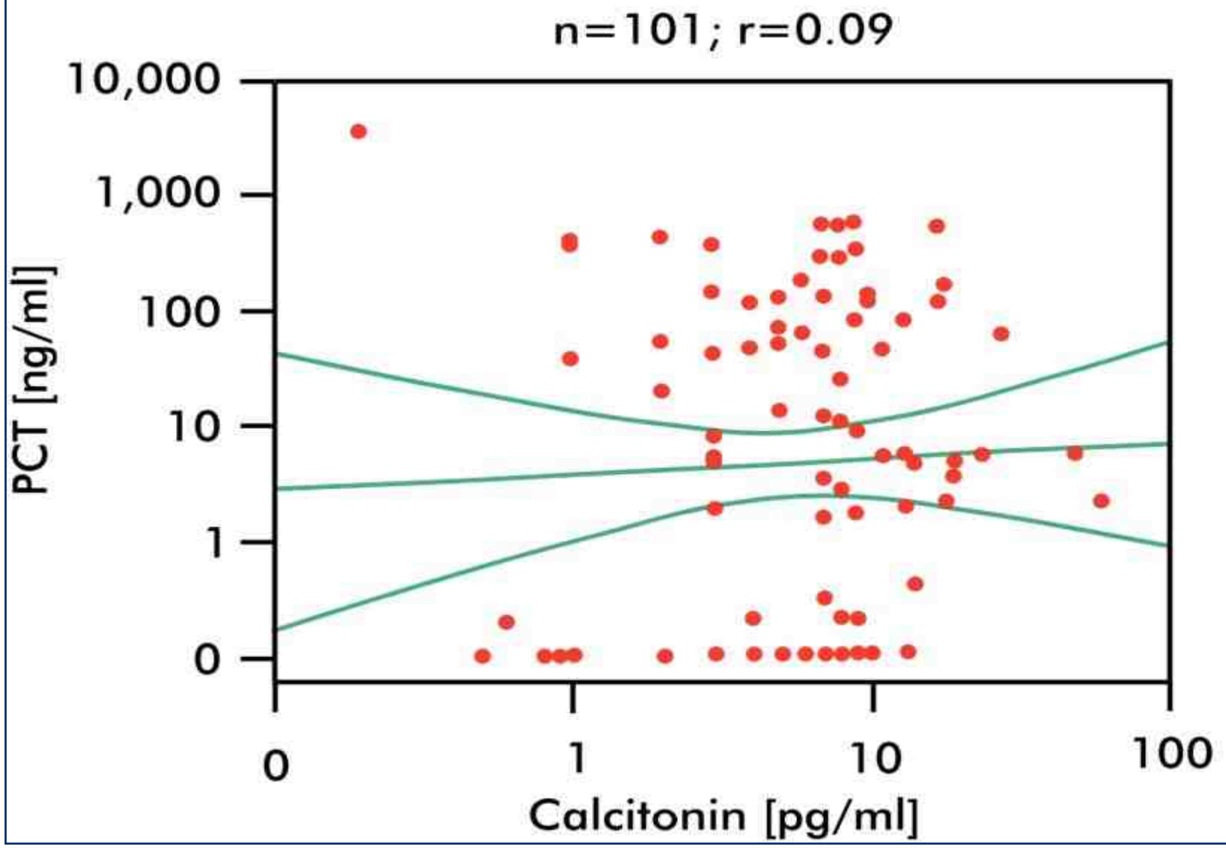
MODS

sono state ritrovate nel sangue alte concentrazioni di precursori della calcitonina senza che vi sia un aumento dei livelli di calcitonina

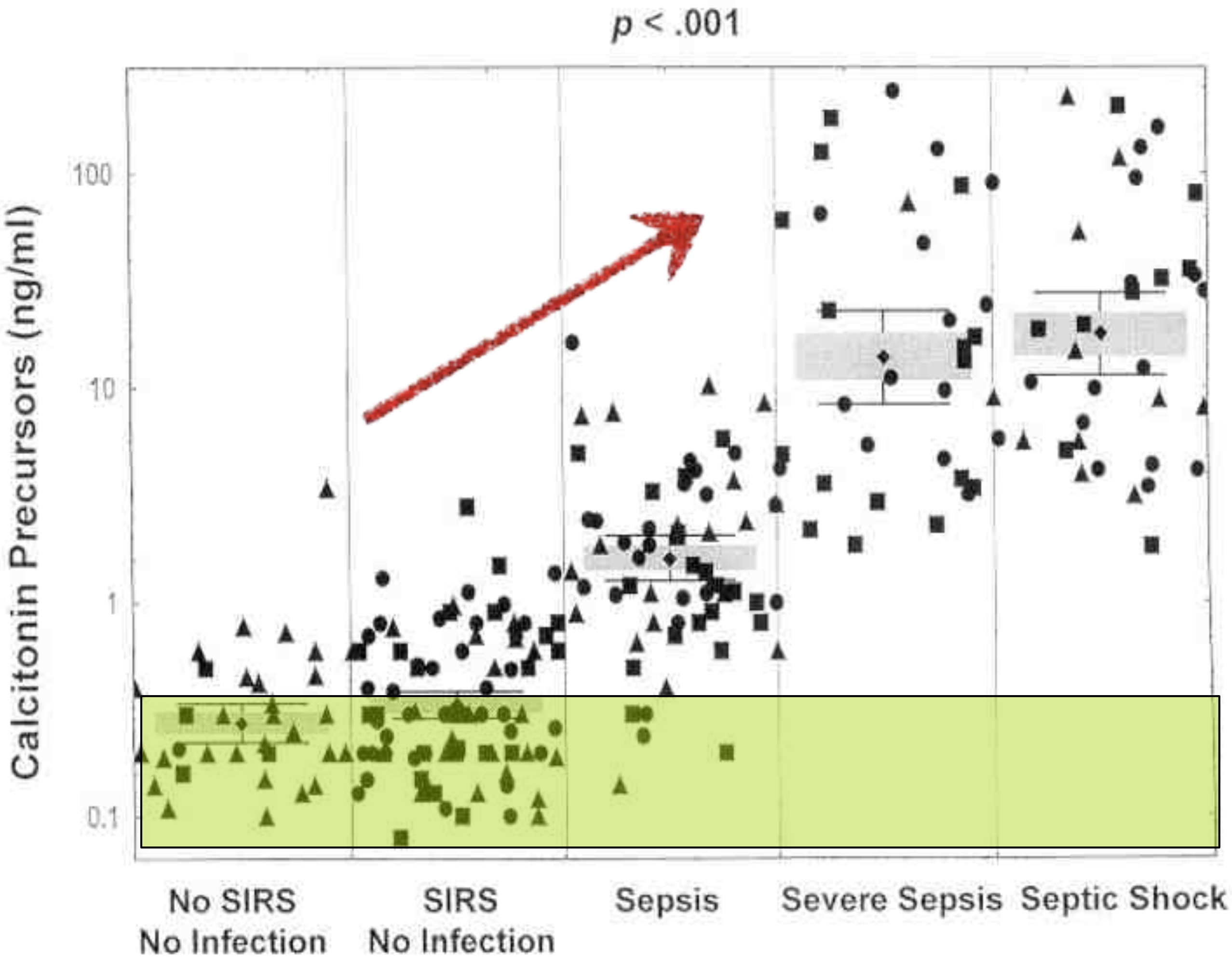
Whang et. J.Clin Endocrin Metab 1998;83:3296-3301

PCT NELLA DIAGNOSI DI SIRS E SEPSI

Correlation PCT vs Calcitonin
in normal subjects and septic patients



PCT NELLA DIAGNOSI DI SIRS E SEPSI

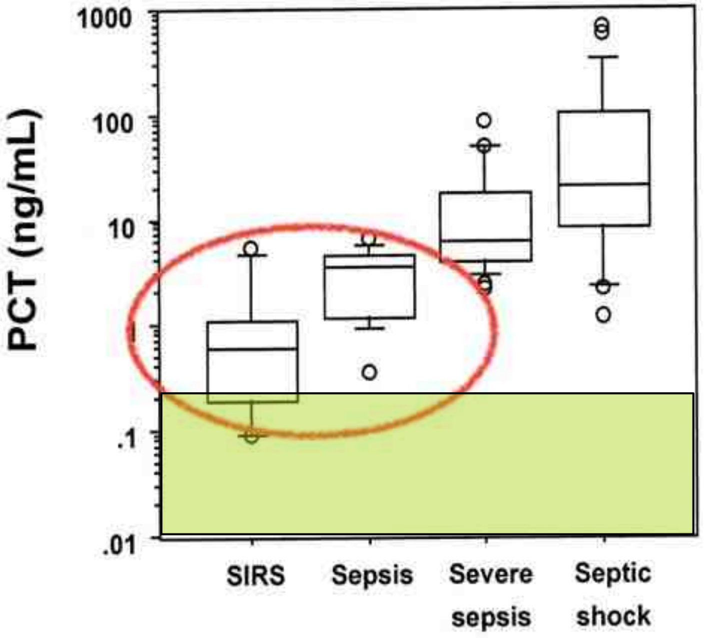


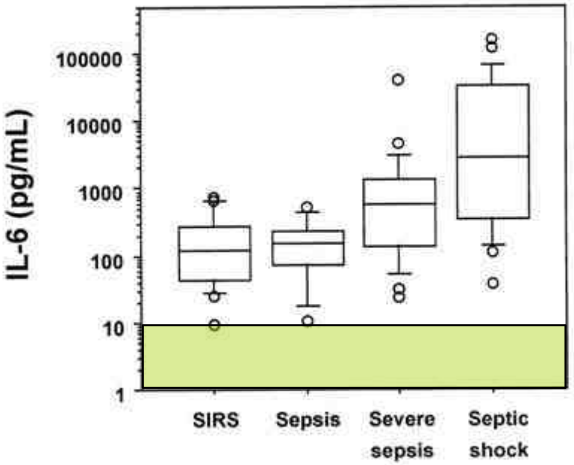
Muller et al Crit Care Med (2000) 28:977

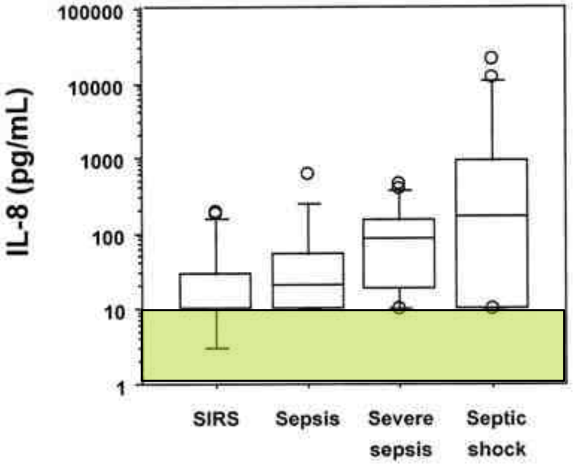
PCT NELLA DIAGNOSI DI SIRS E SEPSI

PCT vs CITOCHINE

Medical and surgical ICU patients with SIRS and suspected infection (n=78)





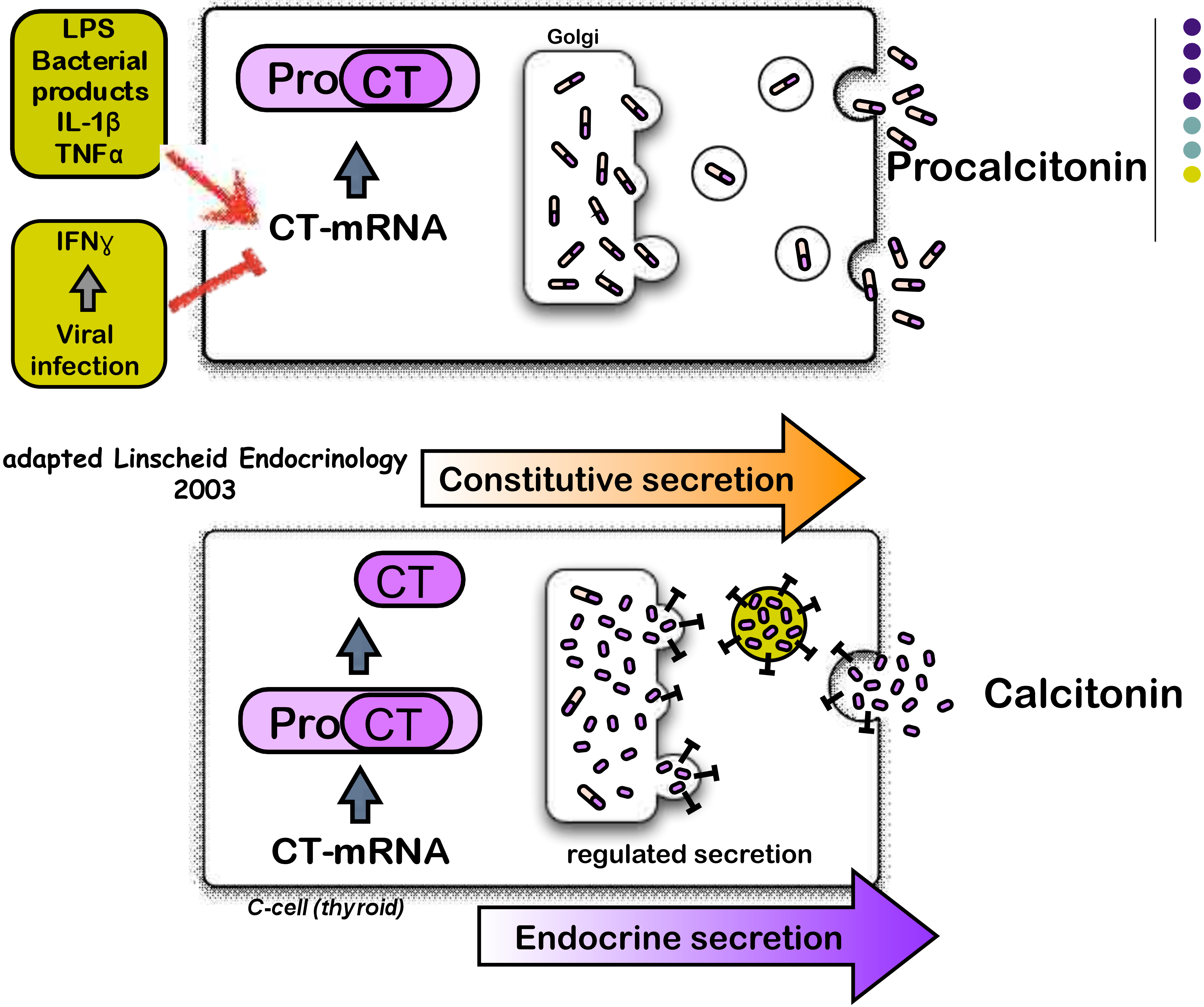


Harbarth Am J Respir Crit Care Med 2001;164:396-402

PCT NELLA DIAGNOSI DI SIRS E SEPSI

In presenza di **citochine ed endotossina** la degradazione della PCT viene **bloccata** e si ritrova nel plasma con i suoi frammenti

Whang et. J.Clin Endocrin Metab 1998;83:3296-3301



LPS
Bacterial products
IL-1β
TNFα

IFNɣ

Viral infection

Pro CT

CT-mRNA

Golgi

Procalcitonin

adapted Linscheid Endocrinology 2003

Constitutive secretion

CT

Pro CT

CT-mRNA

regulated secretion

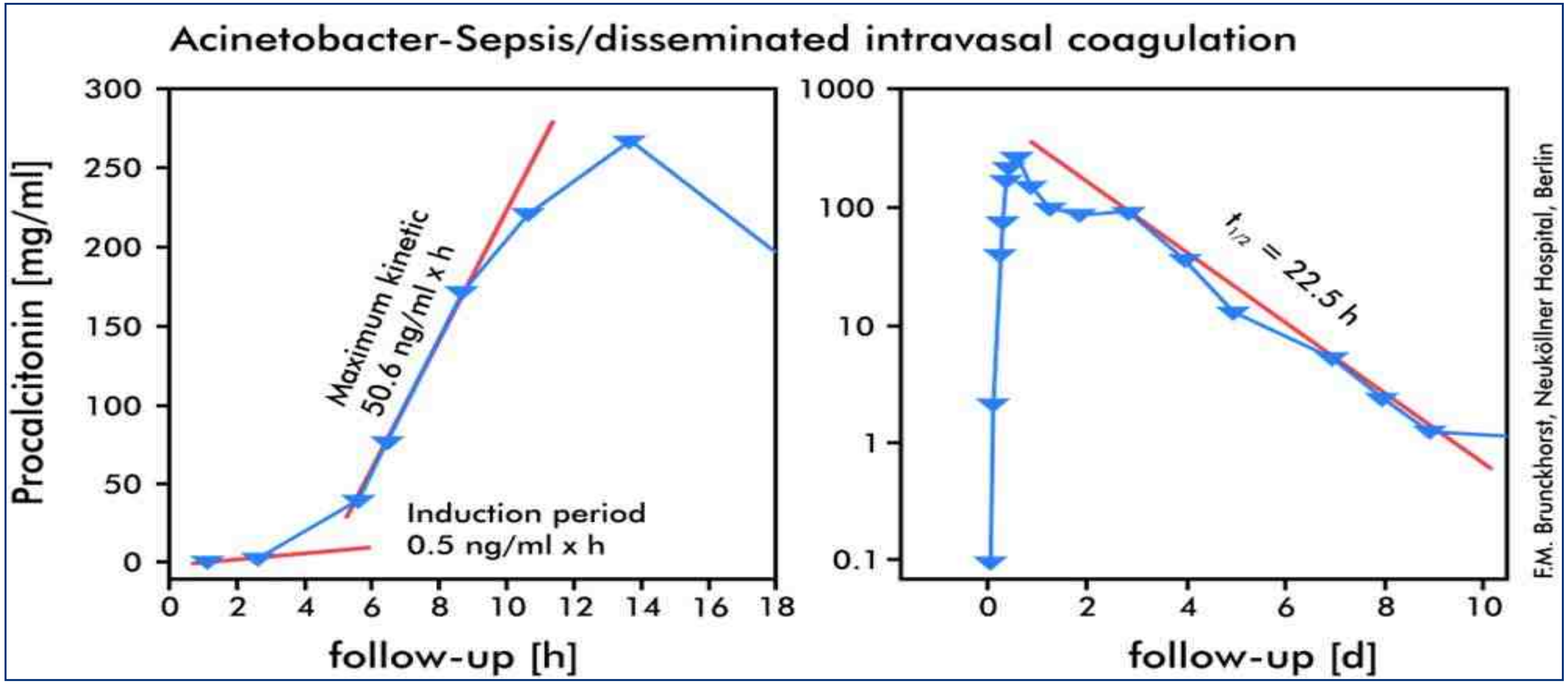
Calcitonin

C-cell (thyroid)

Endocrine secretion

PCT NELLA DIAGNOSI DI SIRS E SEPSI

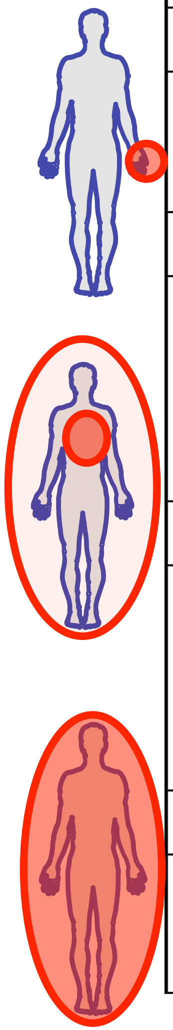
CINETICA ED EMIVITA



A 76 year old woman with peripheral artery disease
Received deproteinized hemodialysate of calf blood (out-patient “questionable procedure”) found to have severe contamination with Acinetobacter Baumanii

Brunkhorst, Intensive Care Med 24:888-892 (1998)

PROCALCITONINA RANGE DI RIFERIMENTO



<table>
<tr><th colspan="2">Normal Values (healthy individuals) <0.05 ng/ml</th></tr>
<tr><td>Healthy individuals (age ≥ 4 days of life); for neonates aged 0-72 hrs, special reference ranges are used</td><td>Normal range for PCT (95% CI). No systemic inflammatory reaction</td></tr>
<tr><th colspan="2">PCT <0.5 ng/ml</th></tr>
<tr><td>Measurable but low PCT response</td><td>Low or no significant systemic inflammatory reaction. Local inflammation and local infection are possible</td></tr>
<tr><th colspan="2">PCT 0.5 to 2.0 ng/ml</th></tr>
<tr><td>Significant by moderate systemic inflammatory reaction. Infection is possible but there are various conditions also known to induce PCT (severe trauma, major surgery, cardiogenic shock)</td><td>Sepsis should be assumed and sepsis-specific treatment should be initiated, as long as there is no exclusion of diagnosis of sepsis or infection. If infection found: positive diagnosis of sepsis. Futher PCT measurements recommended (6-24 hrs)</td></tr>
<tr><th colspan="2">PCT ≥2-10 ng/ml</th></tr>
<tr><td>Severe systemic inflammatory reaction, most likely due to infection (sepsis) provided no other causes known</td><td>Diagnosis of sepsis, severe sepsis or septic shock most likely. High risk of the development of organ dysfunction. If persistently high levels (>4 days): reconsider treatment of sepsis. Possibly unfavorable prognosis. Daily measuring of PCT recommended</td></tr>
<tr><th colspan="2">PCT ≥ 10 ng/ml</th></tr>
<tr><td>Marked systemic inflammatory reaction, almost exclusively as a result of severe bacterial sepsis or septic shock</td><td>Frequently associated with organ dysfunction. High risk of fatal outcome. Daily measurement of PCT level to monitor treatment success</td></tr>
</table>

Adapted from Meisner, Procalcitonin- Biochemistry and Clinical Diagnosis (book), 2010

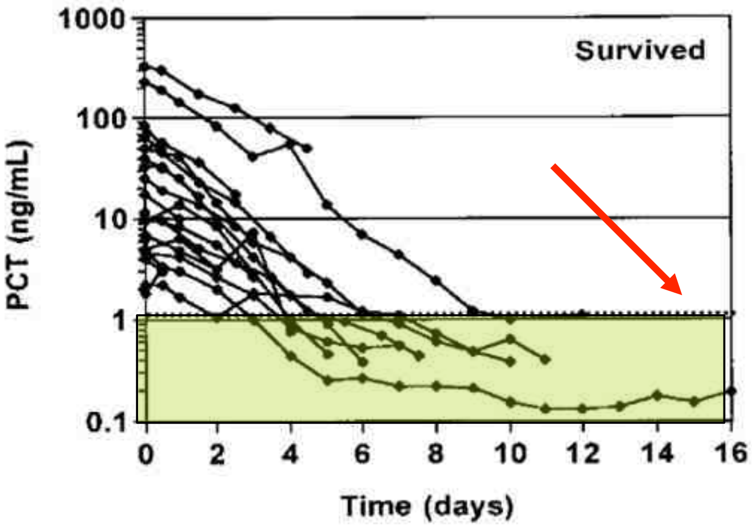
PCT SENSITIVITY SPECIFICTY

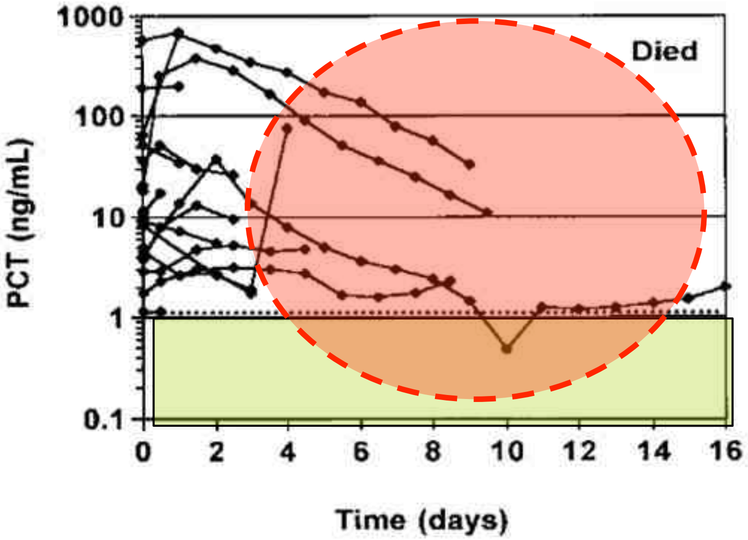
CUT OFF ng/ml	SENS %	SPEC %	n.di pz
0.8	68	48	208
0.6	68	62	190
2	96	86	185
1.11	79	85	150
1	94	64	119
2	91	89	108
1	89	94	101
2	65	70	95
1.3	73	83	85
1.1	97	78	78
1	95	54	75

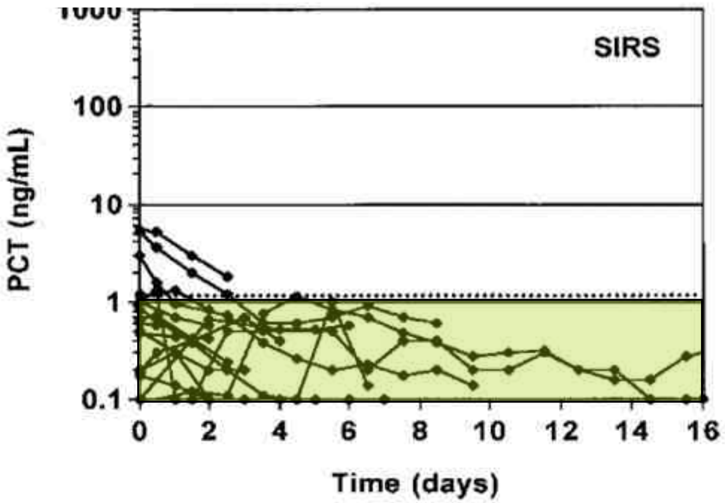
Adapted from Meisner, Procalcitonin- Biochemistry and Clinical Diagnosis (book), 2010

PCT NELLA DIAGNOSI DI SIRS E SEPSI

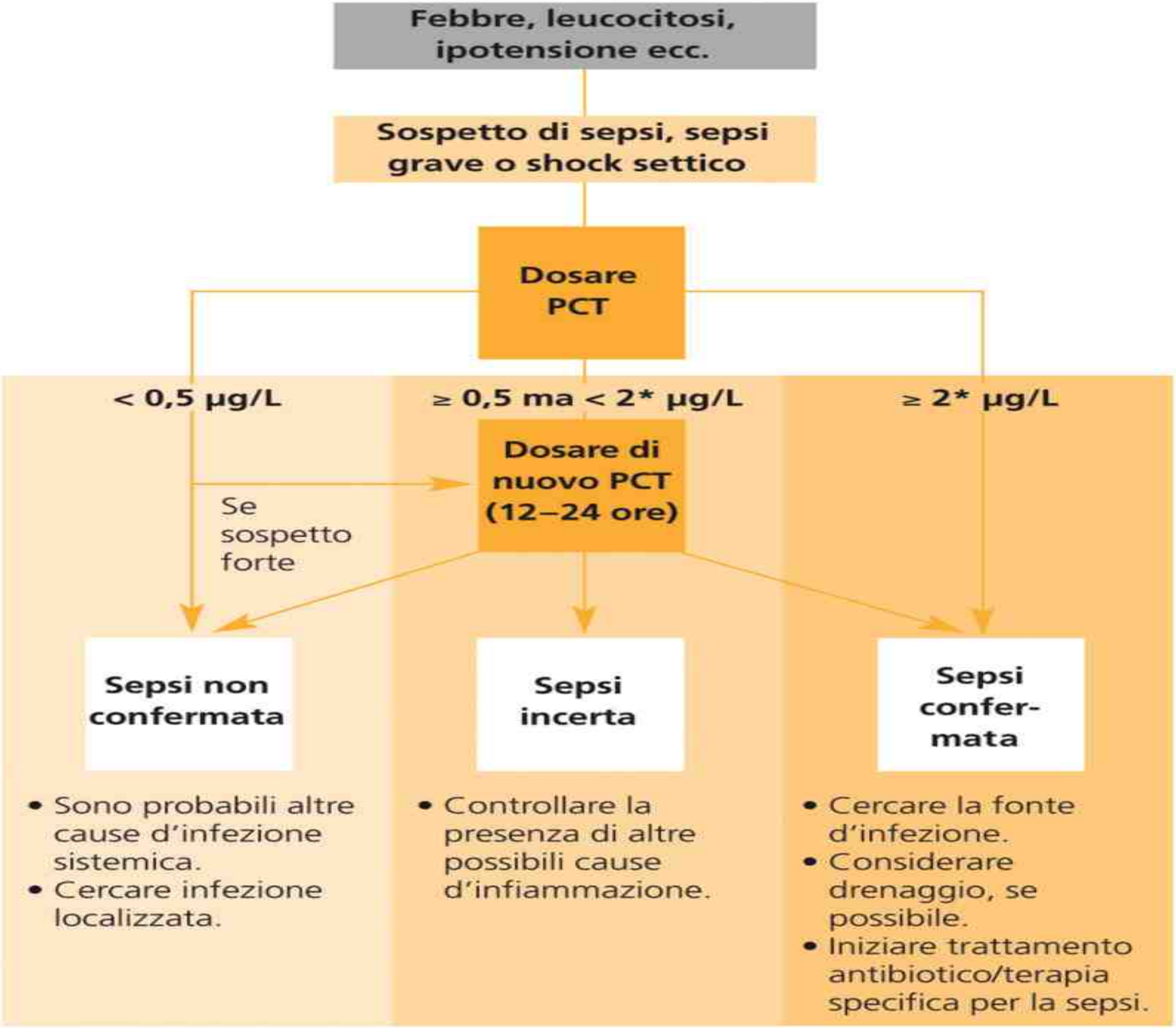
VALORE PROGNOSTICO DELLA PCT







Harbarth Am J Respir Crit Care Med (2001),



Febbre, leucocitosi, ipotensione ecc.

Sospetto di sepsi, sepsi grave o shock settico

Dosare PCT

< 0,5 μg/L

Se sospetto forte

≥ 0,5 ma < 2* μg/L

Dosare di nuovo PCT (12–24 ore)

≥ 2* μg/L

Sepsi non confermata

- Sono probabili altre cause d'infezione sistemica.
- Cercare infezione localizzata.

Sepsi incerta

- Controllare la presenza di altre possibili cause d'infiammazione.

Sepsi confermata

- Cercare la fonte d'infezione.
- Considerare drenaggio, se possibile.
- Iniziare trattamento antibiotico/terapia specifica per la sepsi.

Adapted from Meisner, Procalcitonin- Biochemistry and Clinical Diagnosis (book), 2010

PCT NELLA DIAGNOSI DI SIRS E SEPSI

LA PCT AUMENTA ANCHE:

Dopo chirurgia	up to 7 ng/ml
Politrauma	approx 5 ng/ml
Shock Cardiogeno	up to 10 ng/ml
Neonati	up to 20 ng/ml day 2
Medications (OKT3)	up to 50 ng/ml
Ustioni	around 2 ng/ml
Circolazione Extracorporea	2 – 100 ng/ml
Alcuni tumori	up to 50 ng/ml
Cirrosi Epatica	up to 4 ng/ml
Emodialisi	approx 1 ng/ml
Syndrome di Goodpasture	approx 34 ng/ml
Alzheimer e Demenza	up to 0,6 ng/ml in

PCT NELLA PRATICA CLINICA

- PCT nella diagnosi differenziale tra SIRS E SEPSI
- PCT nel periodo Postoperatorio
- PCT durante Shock Cardiogeno
- PCT per guidare l'Antibiotico Terapia

PCT nel periodo Postoperatorio e durante Shock Cardiogeno

PCT NEL PERIODO POSTOPERATORIO

"STRESS RESPONSE" DURANTE CARDIOCHIRURGIA

Sia la chirurgia off-pump che quella on-Pump causano SIRS per:

attivazione del complemento

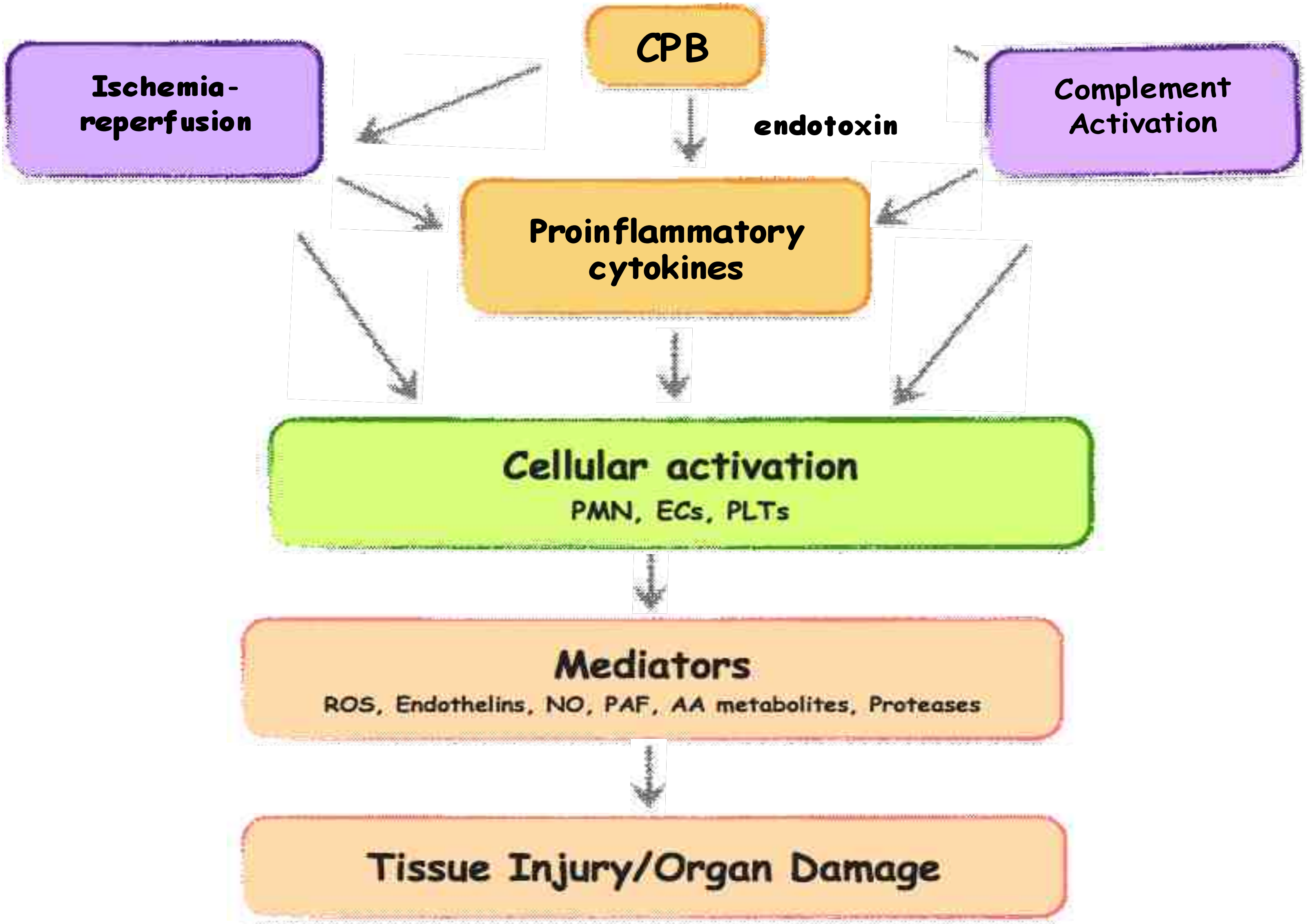
IL1β

IL6

IL8

TNF -α

PCT NEL PERIODO POSTOPERATORIO



CPB

Ischemia-reperfusion

endotoxin

Complement Activation

Proinflammatory cytokines

Cellular activation

PMN, ECs, PLTs

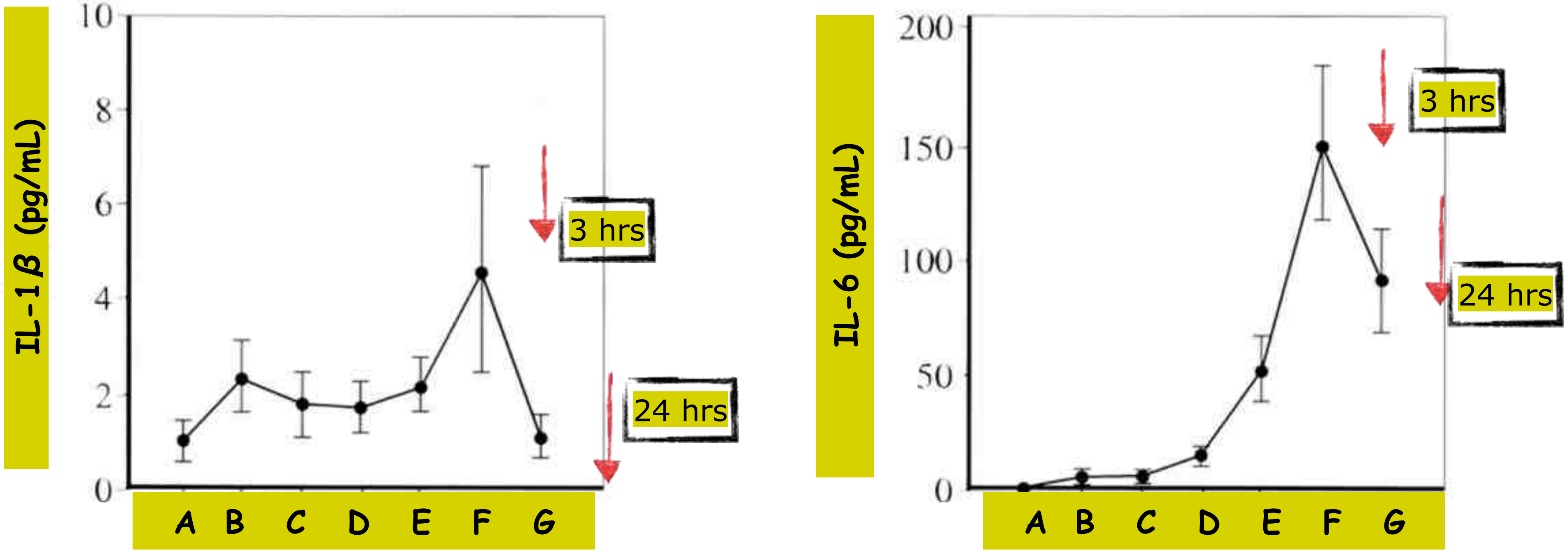
Mediators

ROS, Endothelins, NO, PAF, AA metabolites, Proteases

Tissue Injury/Organ Damage

adapted from Wan et al Chest 1997

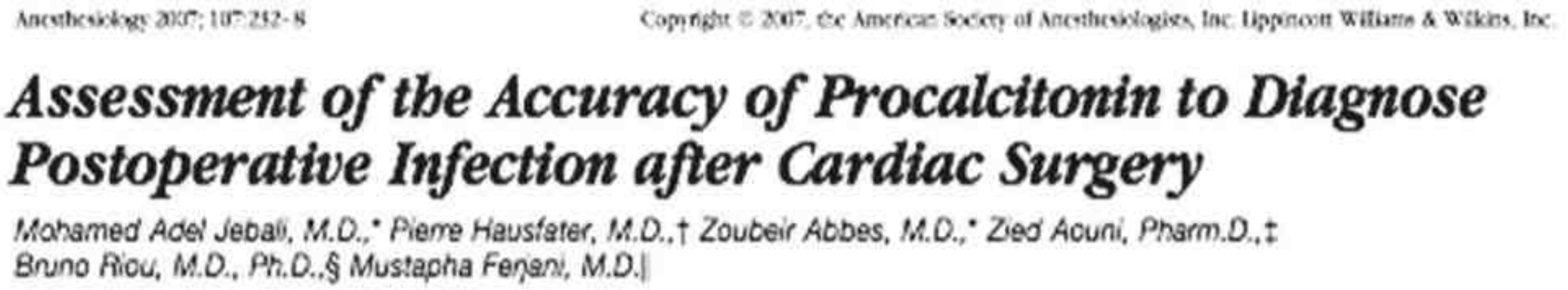
PCT NEL PERIODO POSTOPERATORIO



A, induction of anesthesia
B, 5 minutes after heparin
C, 10 minutes after starting CPB
D, end of CPB
E, 20 minutes after protamine
F, 3 hours after CPB
G, 24 hours after CPB.

In: Cohn LH, Edmunds LH Jr, eds. Cardiac Surgery in the Adult. New York: McGraw-Hill, 2003:349360. Menasche P, Edmunds LH Jr. Extracorporeal Circulation: The Inflammatory Response.

PCT NEL PERIODO POSTOPERATORIO


Anesthesiology 2007; 107:232–8

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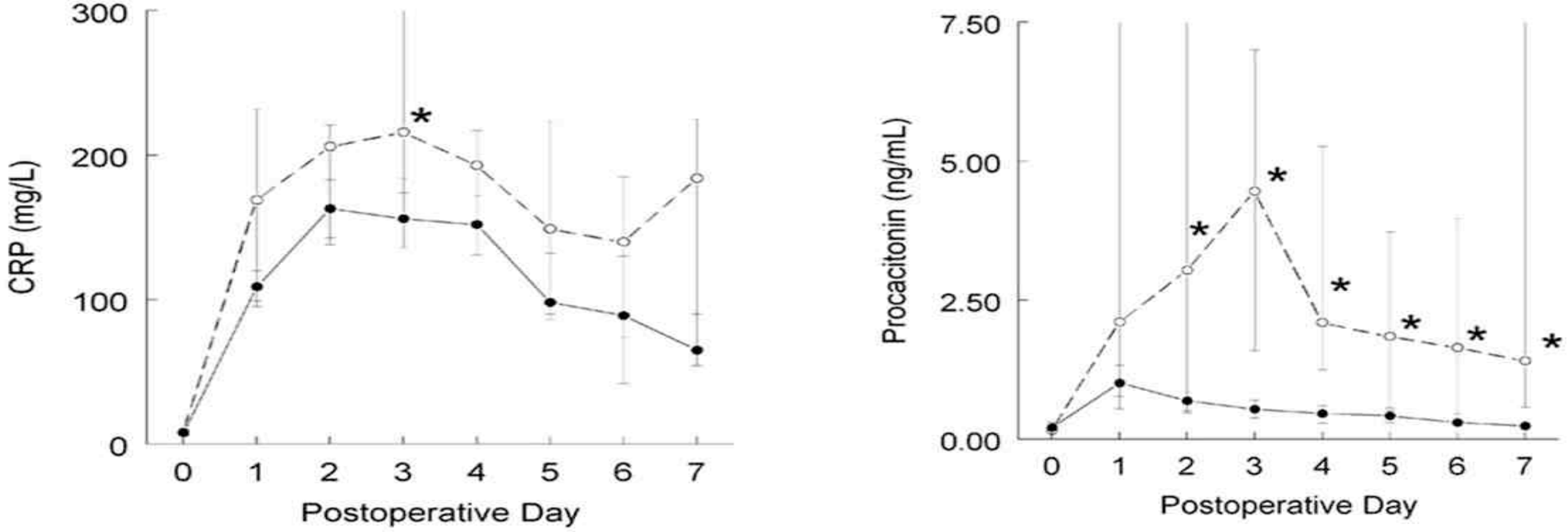
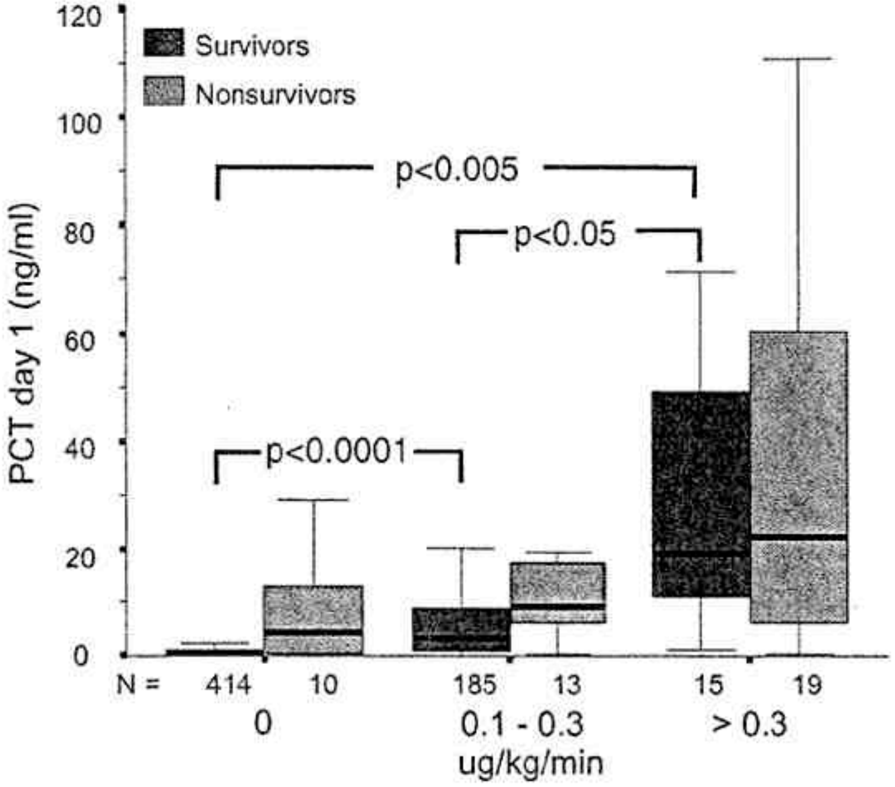
Assessment of the Accuracy of Procalcitonin to Diagnose Postoperative Infection after Cardiac Surgery

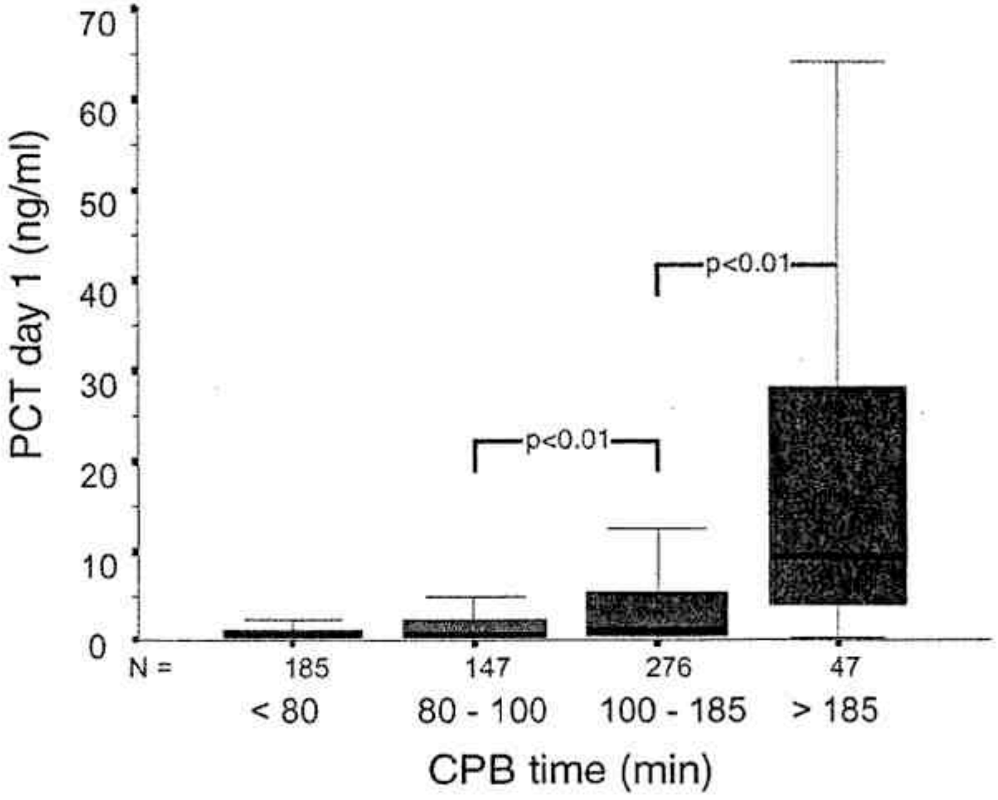
Mohamed Adel Jebali, M.D., Pierre Hausfater, M.D.,† Zoubeir Abbes, M.D.,* Zied Aouni, Pharm.D.,‡*
Bruno Riou, M.D., Ph.D.,§ Mustapha Ferjani, M.D.‖



Jebali Anesthesiology 107:232 (2007)

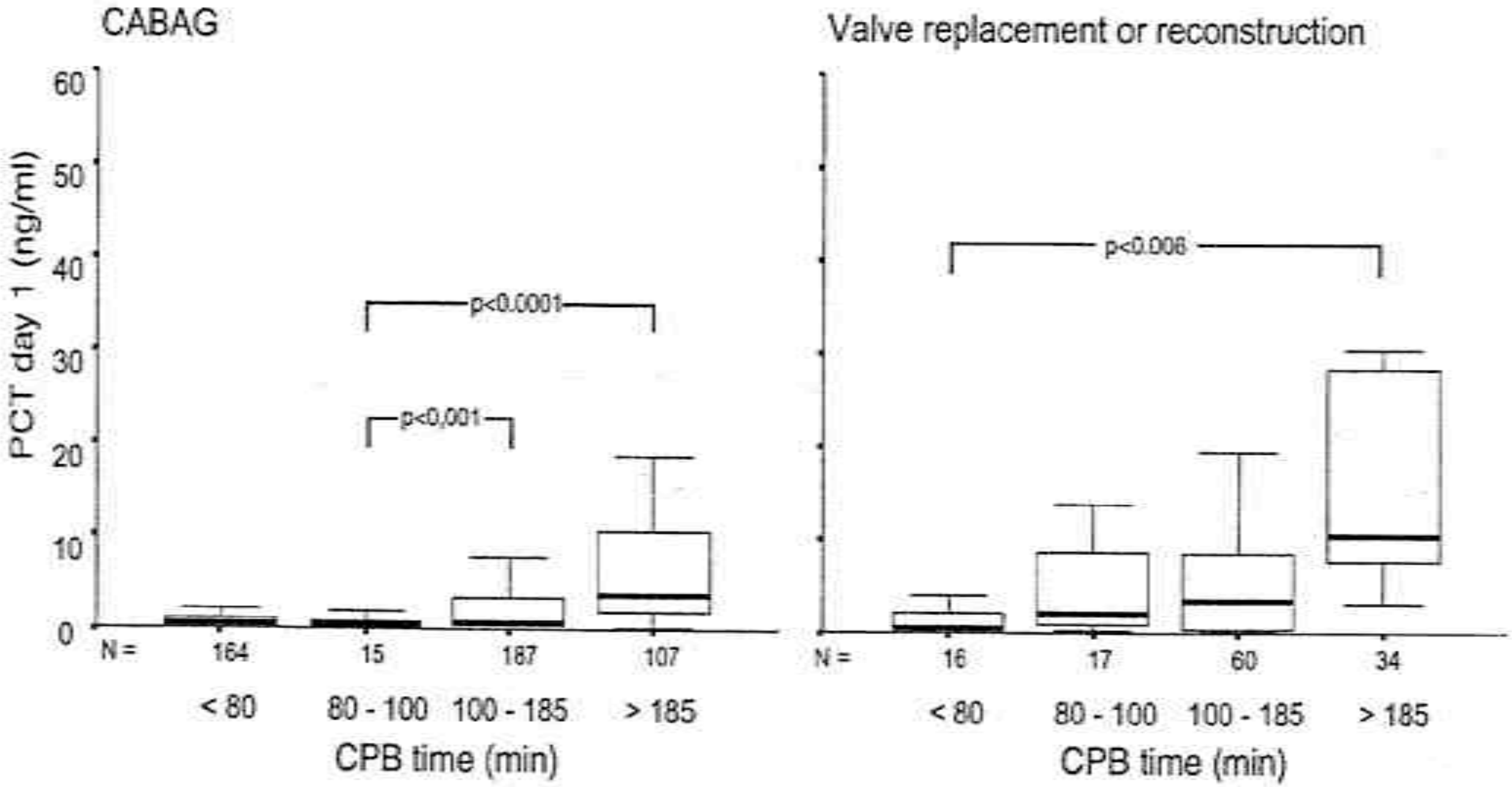
PCT NEL PERIODO POSTOPERATORIO





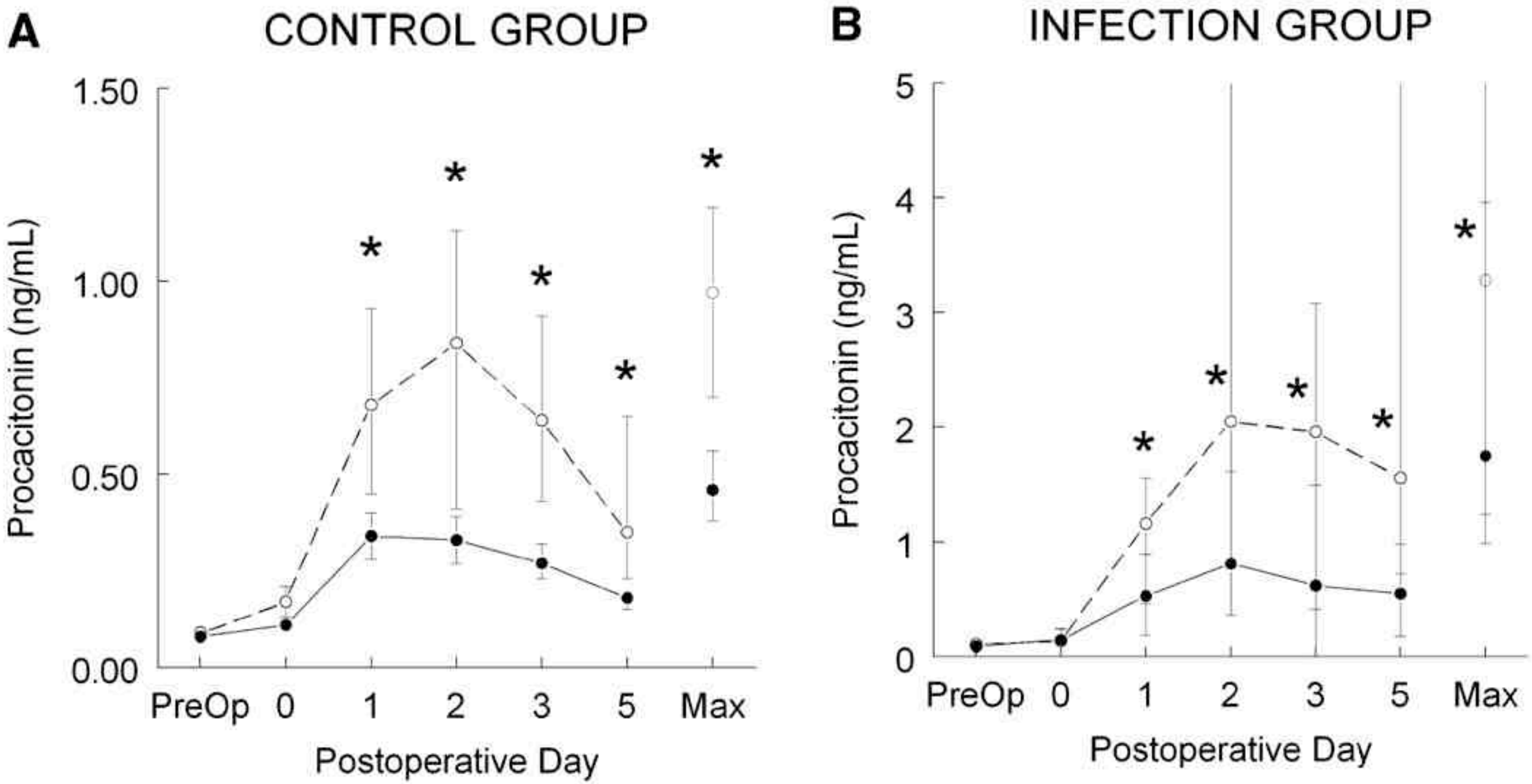
Loebe Intensive Care Med 26 Suppl 2:S193 (2000)

PCT NEL PERIODO POSTOPERATORIO



Loebe Intensive Care Med 26 Suppl 2:S193 (2000)

PCT NEL PERIODO POSTOPERATORIO



Amour Crit Care Med 36:1147 (2008)

PCT NELLA PRATICA CLINICA

- PCT nella diagnosi differenziale tra SIRS E SEPSI
- PCT nel periodo Postoperatorio
- PCT durante Shock Cardiogeno
- PCT per guidare l'Antibiotico Terapia

PCT DURANTE SHOCK CARDIOGENO

Nello Shock Cardiogeno le concentrazioni di PCT sono basse all'inizio 1.8 ± 4.9 ng/ml rispetto allo shock settico primario 89.5 ± 133ng/ml

Inte J cardiol 1999

PCT DURANTE SHOCK CARDIOGENO

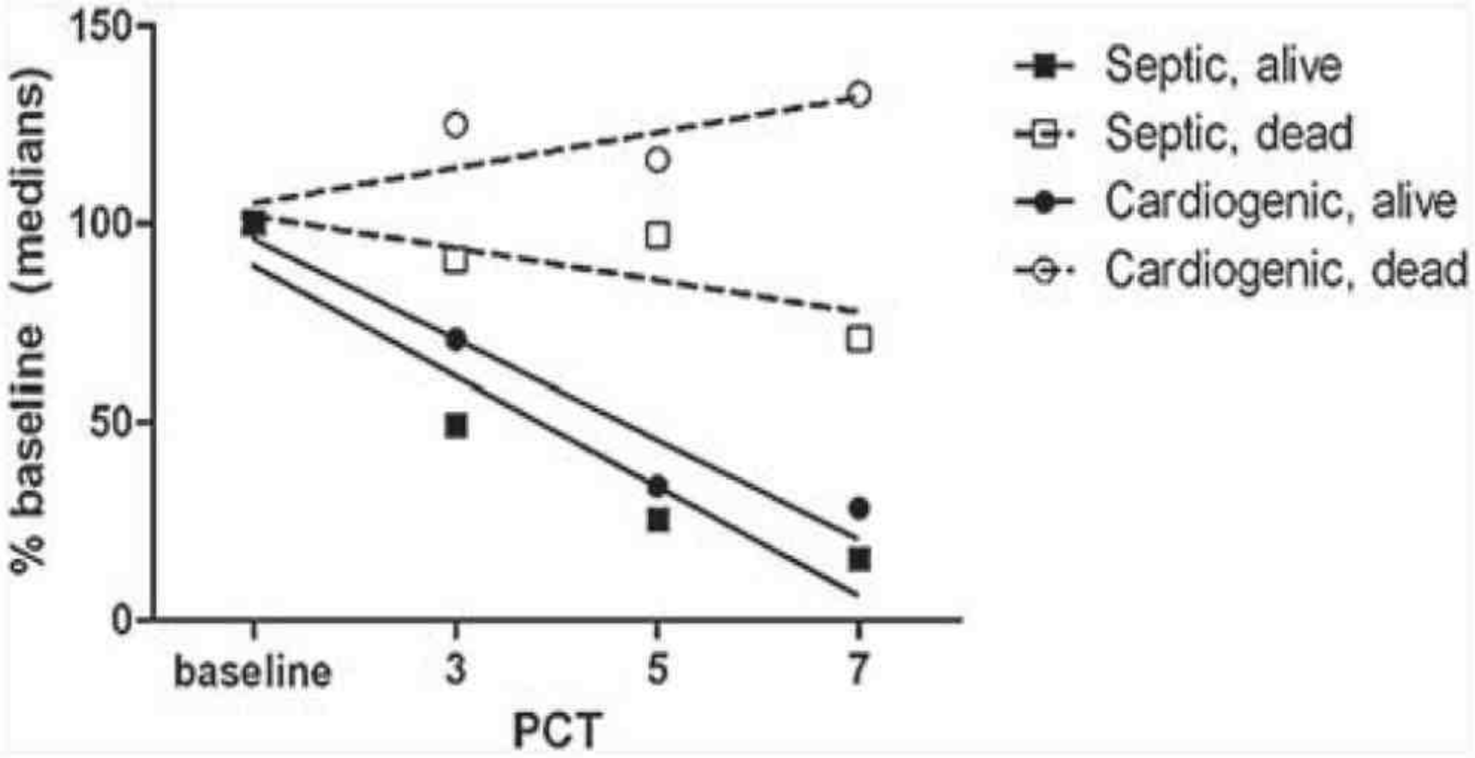


Figure 1. The behavior of PCT levels in the first week both in septic shock (squares) and in cardiogenic shock (circles). Survived patients: continuous lines. Dead patients: dotted lines.

Picariello Acute Card Care : (2010)

PCT DURANTE SHOCK CARDIOGENO

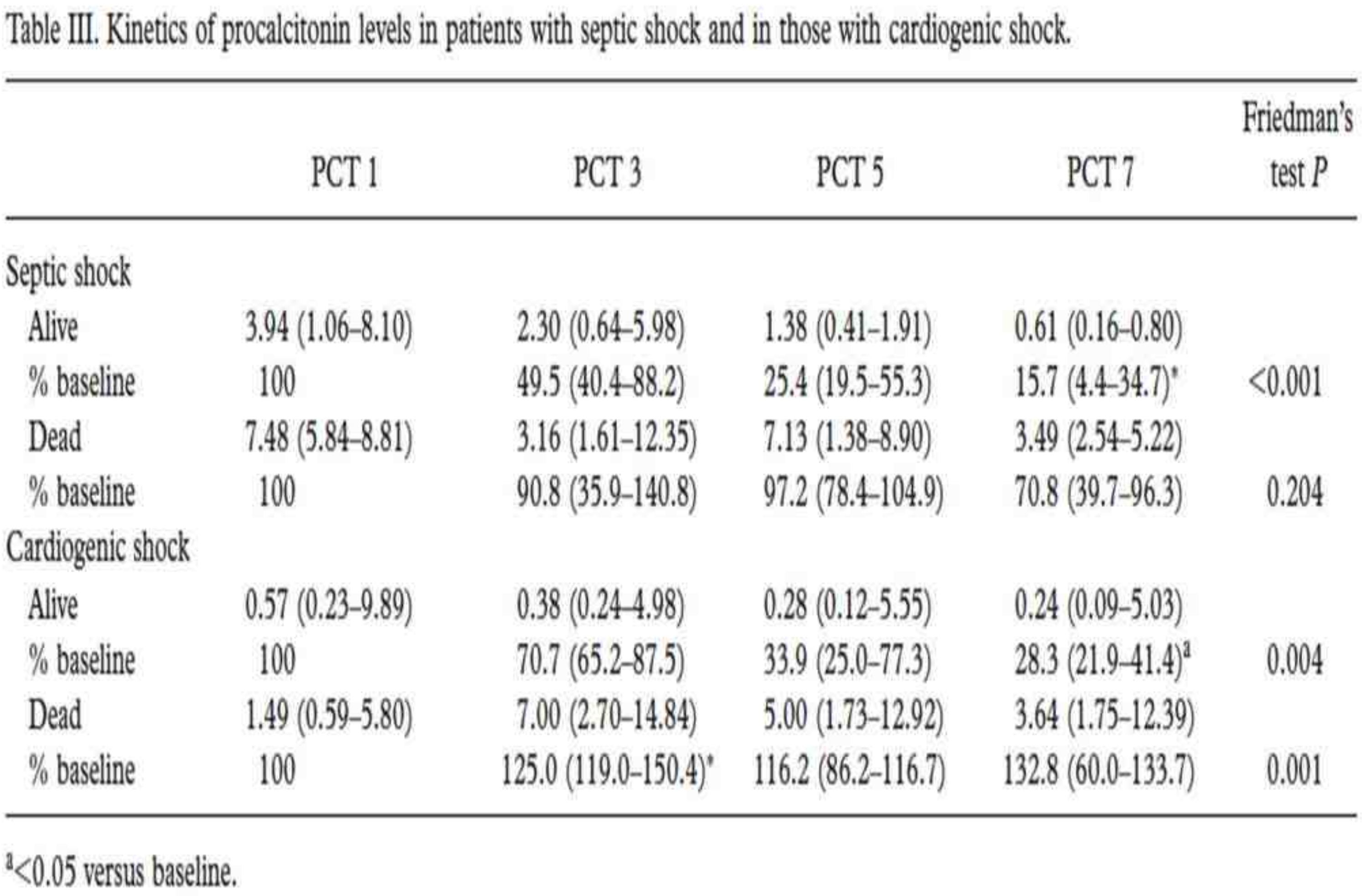


Table III. Kinetics of procalcitonin levels in patients with septic shock and in those with cardiogenic shock.

	PCT 1	PCT 3	PCT 5	PCT 7	Friedman's test *P*
Septic shock					
Alive	3.94 (1.06–8.10)	2.30 (0.64–5.98)	1.38 (0.41–1.91)	0.61 (0.16–0.80)	
% baseline	100	49.5 (40.4–88.2)	25.4 (19.5–55.3)	15.7 (4.4–34.7)[a]	<0.001
Dead	7.48 (5.84–8.81)	3.16 (1.61–12.35)	7.13 (1.38–8.90)	3.49 (2.54–5.22)	
% baseline	100	90.8 (35.9–140.8)	97.2 (78.4–104.9)	70.8 (39.7–96.3)	0.204
Cardiogenic shock					
Alive	0.57 (0.23–9.89)	0.38 (0.24–4.98)	0.28 (0.12–5.55)	0.24 (0.09–5.03)	
% baseline	100	70.7 (65.2–87.5)	33.9 (25.0–77.3)	28.3 (21.9–41.4)[a]	0.004
Dead	1.49 (0.59–5.80)	7.00 (2.70–14.84)	5.00 (1.73–12.92)	3.64 (1.75–12.39)	
% baseline	100	125.0 (119.0–150.4)[a]	116.2 (86.2–116.7)	132.8 (60.0–133.7)	0.001

[a]<0.05 versus baseline.

Picariello Acute Card Care : (2010)

PCT DURANTE SHOCK CARDIOGENO

ATTENZIONE

Alle prime 48 ore…

Shock cardiogeno

Insufficienza renale

Amine,IABP,CEC

Tipo di Chirurgia

PCT NELLA PRATICA CLINICA

- PCT nella diagnosi differenziale tra SIRS E SEPSI
- PCT nel periodo Postoperatorio
- PCT durante Shock Cardiogeno
- PCT per guidare l'Antibiotico Terapia

PCT per guidare
l'Antibiotico Terapia

PCT PER GUIDARE L'ANTIBIOTICO TERAPIA

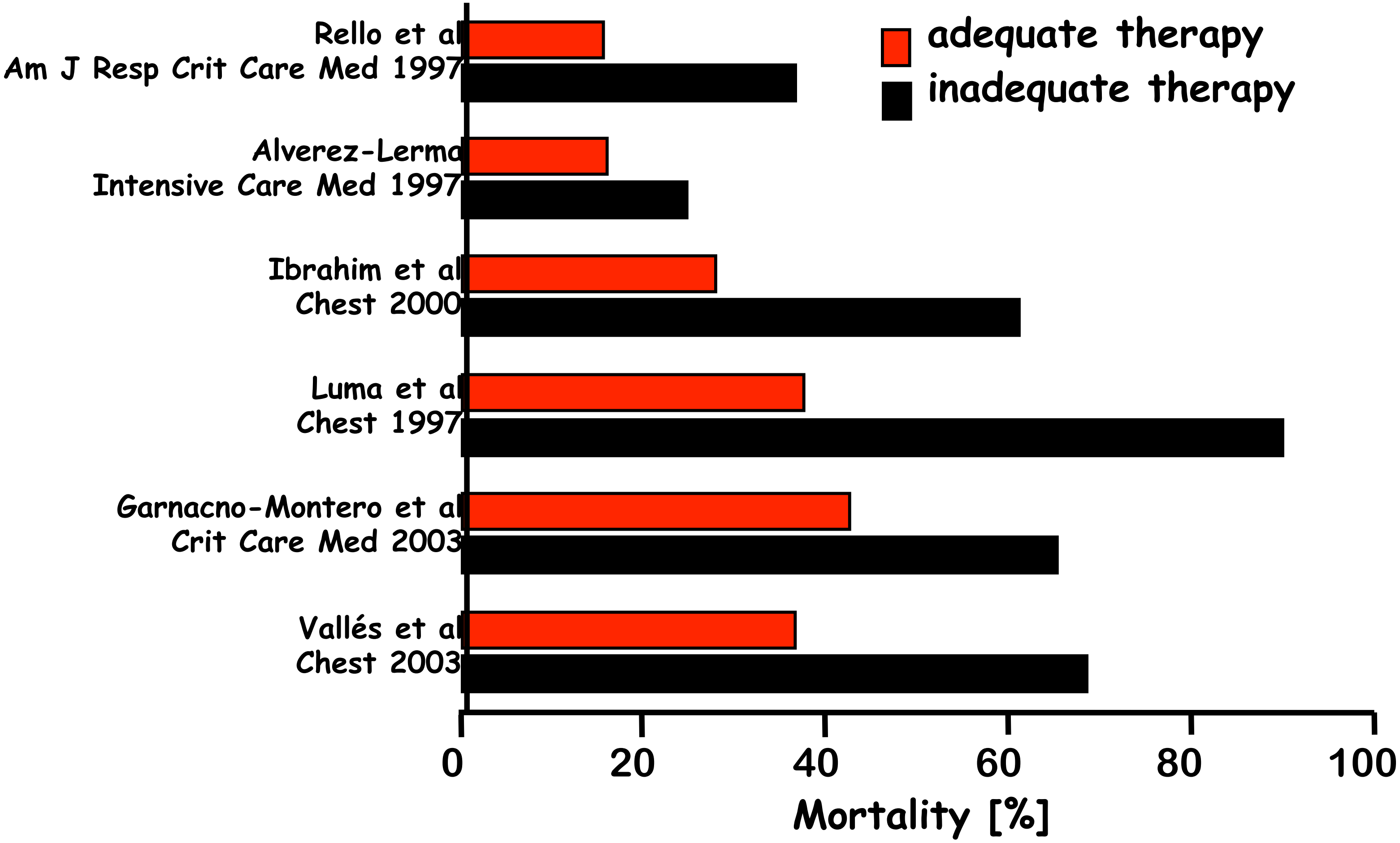
MASSIMA EFFICACIA

RIDURRE LE RESISTENZE

- DIAGNOSI RAPIDA E CORRETTA
- UTILIZZO DEGLI ANTIBIOTICI QUANDO SERVONO
- POSSIBILITA' DI SCALARE GLI ANTIBIOTICI
- TERAPIA DI BREVE DURATA

PCT PER GUIDARE L'ANTIBIOTICO TERAPIA

APPROPRIATEZZA DELLA TERAPIA ANTIBIOTICA



PCT PER GUIDARE L'ANTIBIOTICO TERAPIA

OBIETTIVO

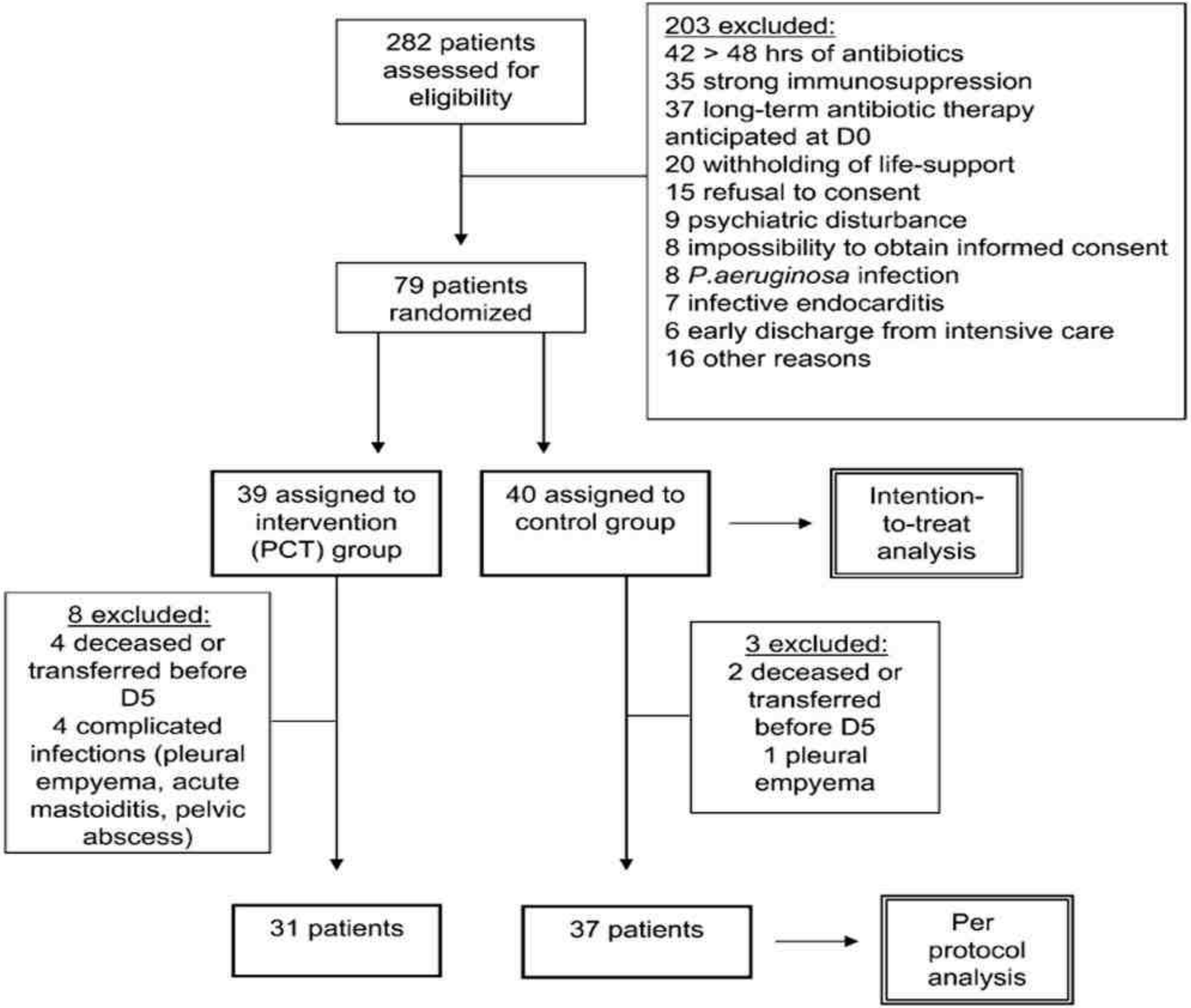
UN ALGORITMO BASATO SULLA MISURAZIONE SERIATA DELLA PCT POTREBBE

RIDURRE LA DURATA DELLA TERAPIA ANTOBIOTICA SENZA AUMENTARE GLI EFFETTI AVVERSI

RIDURRE LA DEGNEZA IN ICU

RIDURRE LA DEGENZA IN OSPEDALE

Nobre V et al. Am J Respir Crit Care Med 2008; 117: 498-505



282 patients assessed for eligibility

203 excluded:
42 > 48 hrs of antibiotics
35 strong immunosuppression
37 long-term antibiotic therapy anticipated at D0
20 withholding of life-support
15 refusal to consent
9 psychiatric disturbance
8 impossibility to obtain informed consent
8 *P.aeruginosa* infection
7 infective endocarditis
6 early discharge from intensive care
16 other reasons

79 patients randomized

39 assigned to intervention (PCT) group

40 assigned to control group

Intention-to-treat analysis

8 excluded:
4 deceased or transferred before D5
4 complicated infections (pleural empyema, acute mastoiditis, pelvic abscess)

3 excluded:
2 deceased or transferred before D5
1 pleural empyema

31 patients

37 patients

Per protocol analysis

Nobre V et al; 2008

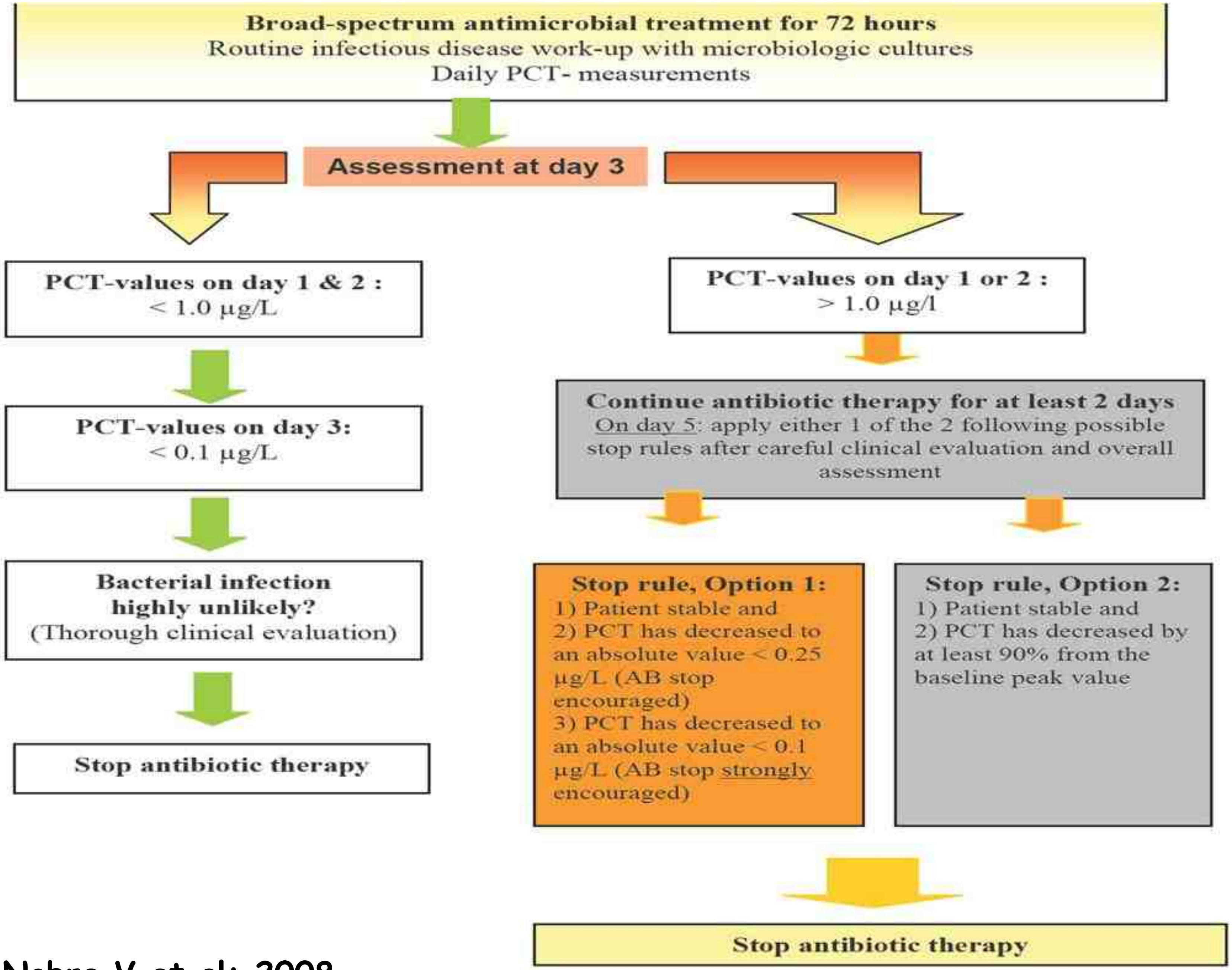
BASELINE CHARACTERISTICS OF THE PATIENTS (PER-PROTOCOL ANALYSIS)

Characteristic	Control Group ($n = 37$)	Procalcitonin Group ($n = 31$)	P Value
Age, yr, mean ± SD	66.9 ± 13.8	64.0 ± 12.3	0.36
Female sex, n (%)	12 (32.4)	10 (32.3)	0.80
Baseline organ failure, n (%)			
Acidosis	20 (54.1)	14 (45.2)	0.62
ARDS D0	6 (16.2)	7 (22.6)	0.72
Coma D0	4 (10.8)	5 (16.1)	0.38
Dialysis D0	4 (10.8)	5 (16.1)	0.38
Heart failure D0	2 (5.4)	2 (6.5)	0.62
Respiratory failure D0	28 (75.7)	23 (74.2)	0.88
Shock D0	20 (54.1)	14 (45.2)	0.62
Renal failure D0	5 (13.5)	1 (3.2)	0.14
Comorbidities, n (%)			
Neoplasia	5 (13.5)	12.9	0.61
Immunosuppression	1 (2.7)	1 (3.2)	0.70
Cardiopathy	17 (45.5)	11 (35.5)	0.85
COPD	7 (18.9)	12 (38.7)	0.12
ID diabetes mellitus	2 (5.4)	0	0.29
Non-ID diabetes mellitus	6 (16.2)	12.9	0.48
Chronic renal failure	6 (16.2)	2 (6.5)	0.19
Peripheral vascular disease	1 (2.7)	1 (3.2)	0.70
Chronic hepatopathy	5 (13.5)	5 (16.1)	0.51
Baseline characteristics of sepsis			
Pulmonary sepsis, n (%)	25 (67.6)	22 (71.0)	0.96
Abdominal sepsis, n (%)	6 (16.2)	2 (6.5)	0.27
Urinary sepsis, n (%)	5 (13.5)	5 (16.1)	0.96
Other sepsis, n (%)	1 (2.7)	2 (6.5)	0.58
Septic shock, n (%)	16 (43.2)	48.4	0.85
SAPS 3, points (mean ± SD)	70.1 ± 13.1	68.5 ± 12.1	0.60
SOFA, points (mean ± SD)	6.6 ± 3.0	6.4 ± 3.3	0.74
Laboratory			
Positive blood culture, n (%)	11 (29.7)	11 (35.5)	0.80
Baseline procalcitonin µg/L, median (range)	5.4 (0.1–354)	7.3 (0.1–93)	0.76
Procalcitonin < 1 µg/L, n (%)	6 (16.2)	7 (22.5)	0.72
Adjuvant therapy for sepsis, n (%)			
Ventilatory support	30 (81.1)	26 (83.9)	0.50
Vasopressors and/or inotropes	23 (62.2)	16 (51.6)	0.52

Definition of abbreviations: ARDS = acute respiratory distress syndrome; COPD = chronic obstructive pulmonary disease; D0 = Day 0; ID = insulin-dependent; SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment.

Nobre V et al2008

ALGORITMO DI TRATTAMENTO



Broad-spectrum antimicrobial treatment for 72 hours
Routine infectious disease work-up with microbiologic cultures
Daily PCT- measurements

Assessment at day 3

PCT-values on day 1 & 2 :
< 1.0 µg/L

PCT-values on day 3:
< 0.1 µg/L

Bacterial infection highly unlikely?
(Thorough clinical evaluation)

Stop antibiotic therapy

PCT-values on day 1 or 2 :
> 1.0 µg/l

Continue antibiotic therapy for at least 2 days
On day 5: apply either 1 of the 2 following possible stop rules after careful clinical evaluation and overall assessment

Stop rule, Option 1:
1) Patient stable and
2) PCT has decreased to an absolute value < 0.25 µg/L (AB stop encouraged)
3) PCT has decreased to an absolute value < 0.1 µg/L (AB stop strongly encouraged)

Stop rule, Option 2:
1) Patient stable and
2) PCT has decreased by at least 90% from the baseline peak value

Stop antibiotic therapy

Nobre V et al; 2008

PCT PER GUIDARE L'ANTIBIOTICO TERAPIA

ENDOPOINTS PRIMARI

DURATA DELL'ANTIBIOTICO TERAPIA

GIORNI DI ESPOSISZIONE AGLI ANTIBIOTICI

GIORNI LIBERI DA ANTIBIOTICI

Nobre V et al; 2008

PCT PER GUIDARE L'ANTIBIOTICO TERAPIA

ENDPOINTS SECONDARI

MORTALITA' 28 gg.

MORTALITA' OSPEDALIERA

DEGENZA IN ICU E IN OSPEDALE

Nobre V et al; 2008

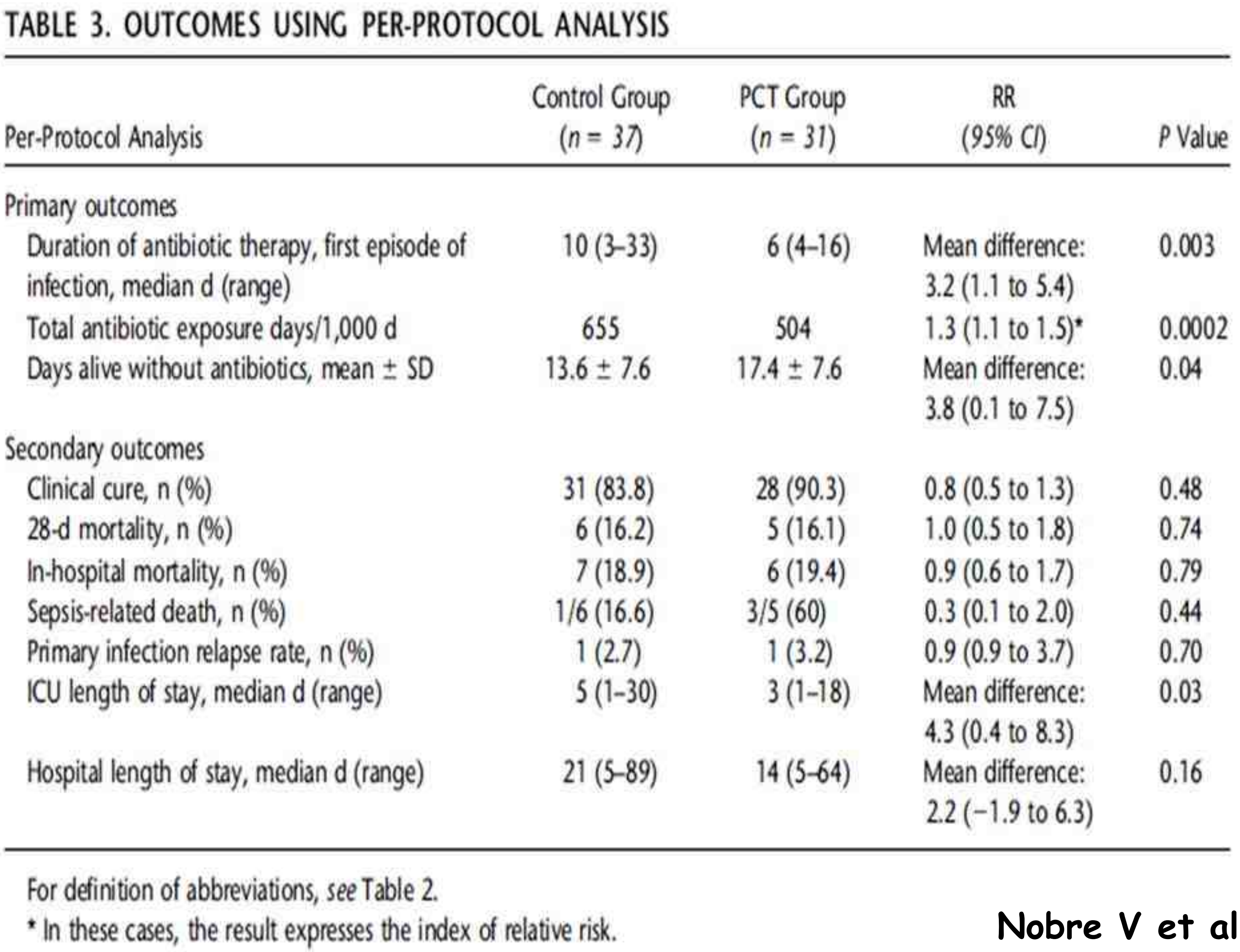


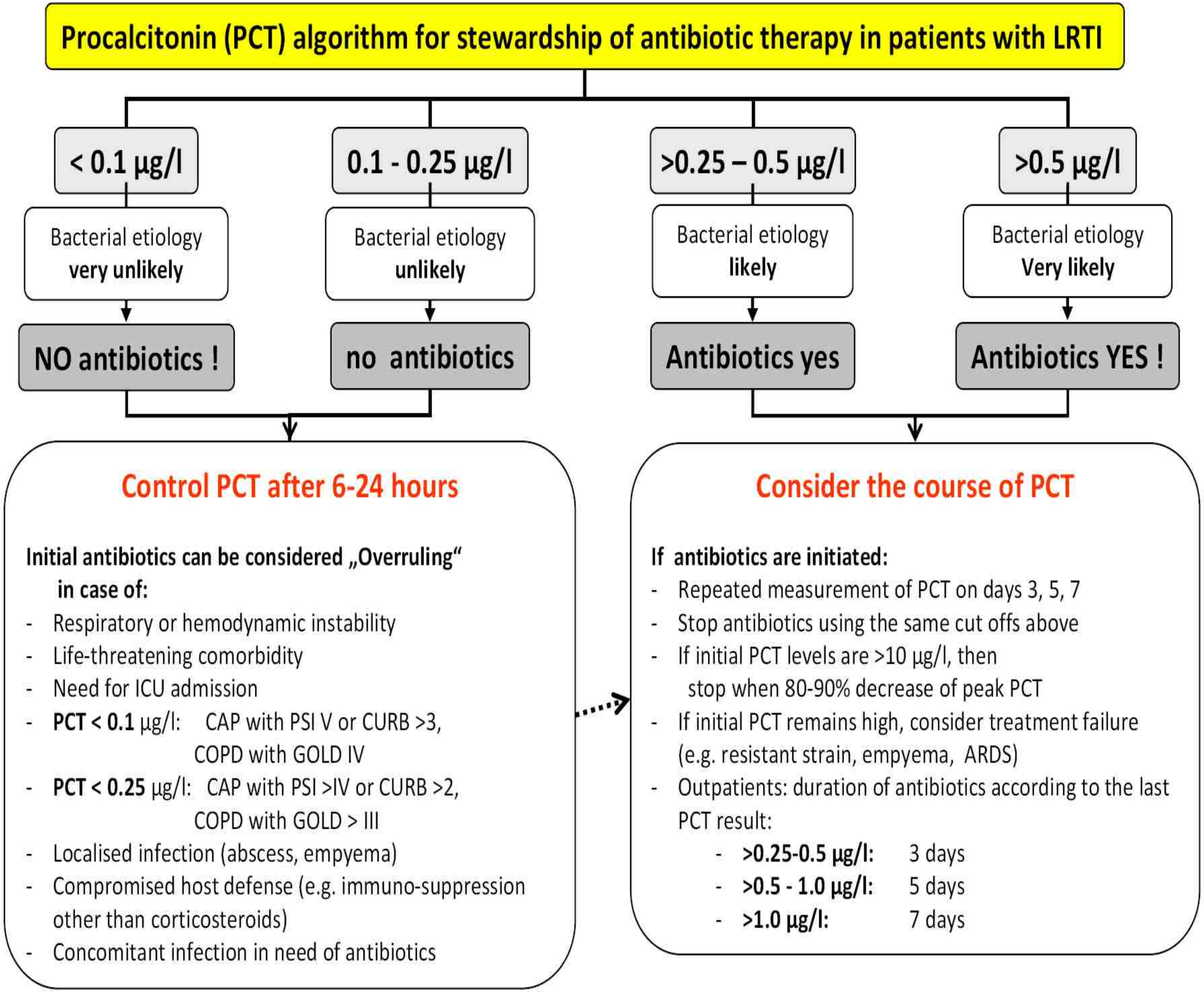
TABLE 3. OUTCOMES USING PER-PROTOCOL ANALYSIS

Per-Protocol Analysis	Control Group (*n* = 37)	PCT Group (*n* = 31)	RR (95% *CI*)	*P* Value
Primary outcomes				
Duration of antibiotic therapy, first episode of infection, median d (range)	10 (3–33)	6 (4–16)	Mean difference: 3.2 (1.1 to 5.4)	0.003
Total antibiotic exposure days/1,000 d	655	504	1.3 (1.1 to 1.5)*	0.0002
Days alive without antibiotics, mean ± SD	13.6 ± 7.6	17.4 ± 7.6	Mean difference: 3.8 (0.1 to 7.5)	0.04
Secondary outcomes				
Clinical cure, n (%)	31 (83.8)	28 (90.3)	0.8 (0.5 to 1.3)	0.48
28-d mortality, n (%)	6 (16.2)	5 (16.1)	1.0 (0.5 to 1.8)	0.74
In-hospital mortality, n (%)	7 (18.9)	6 (19.4)	0.9 (0.6 to 1.7)	0.79
Sepsis-related death, n (%)	1/6 (16.6)	3/5 (60)	0.3 (0.1 to 2.0)	0.44
Primary infection relapse rate, n (%)	1 (2.7)	1 (3.2)	0.9 (0.9 to 3.7)	0.70
ICU length of stay, median d (range)	5 (1–30)	3 (1–18)	Mean difference: 4.3 (0.4 to 8.3)	0.03
Hospital length of stay, median d (range)	21 (5–89)	14 (5–64)	Mean difference: 2.2 (−1.9 to 6.3)	0.16

For definition of abbreviations, *see* Table 2.

* In these cases, the result expresses the index of relative risk.

Nobre V et al; 2008



Procalcitonin (PCT) algorithm for stewardship of antibiotic therapy in patients with LRTI

< 0.1 µg/l	0.1 - 0.25 µg/l	>0.25 – 0.5 µg/l	>0.5 µg/l
Bacterial etiology **very unlikely**	Bacterial etiology **unlikely**	Bacterial etiology **likely**	Bacterial etiology **Very likely**
NO antibiotics !	**no antibiotics**	**Antibiotics yes**	**Antibiotics YES !**

Control PCT after 6-24 hours

Initial antibiotics can be considered „Overruling“ in case of:

- Respiratory or hemodynamic instability
- Life-threatening comorbidity
- Need for ICU admission
- **PCT < 0.1** µg/l: CAP with PSI V or CURB >3,
  COPD with GOLD IV
- **PCT < 0.25** µg/l: CAP with PSI >IV or CURB >2,
  COPD with GOLD > III
- Localised infection (abscess, empyema)
- Compromised host defense (e.g. immuno-suppression other than corticosteroids)
- Concomitant infection in need of antibiotics

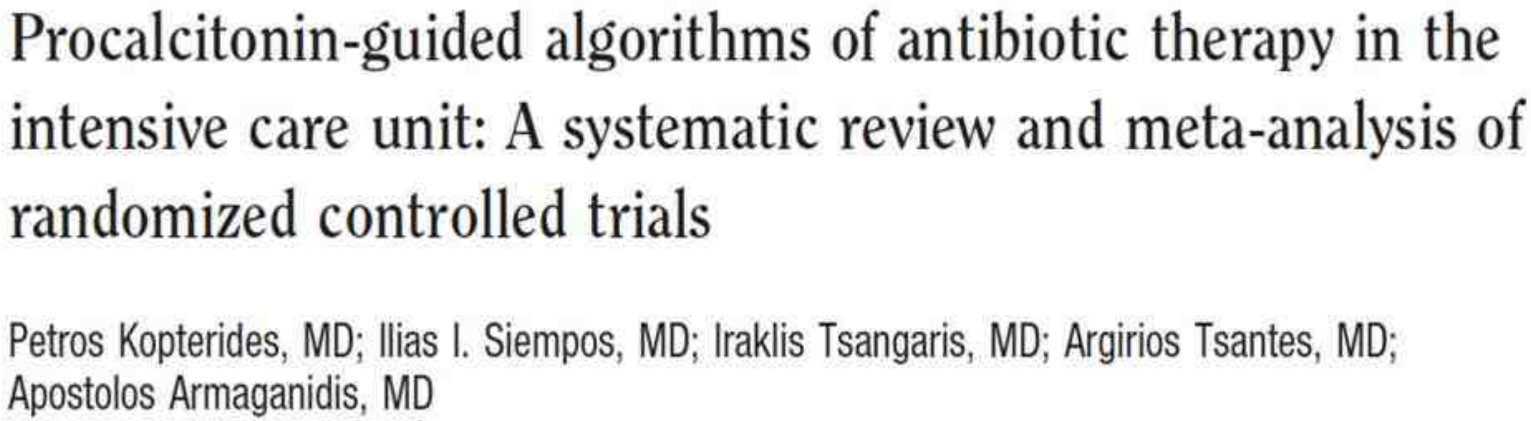
Consider the course of PCT

If antibiotics are initiated:

- Repeated measurement of PCT on days 3, 5, 7
- Stop antibiotics using the same cut offs above
- If initial PCT levels are >10 µg/l, then stop when 80-90% decrease of peak PCT
- If initial PCT remains high, consider treatment failure (e.g. resistant strain, empyema, ARDS)
- Outpatients: duration of antibiotics according to the last PCT result:

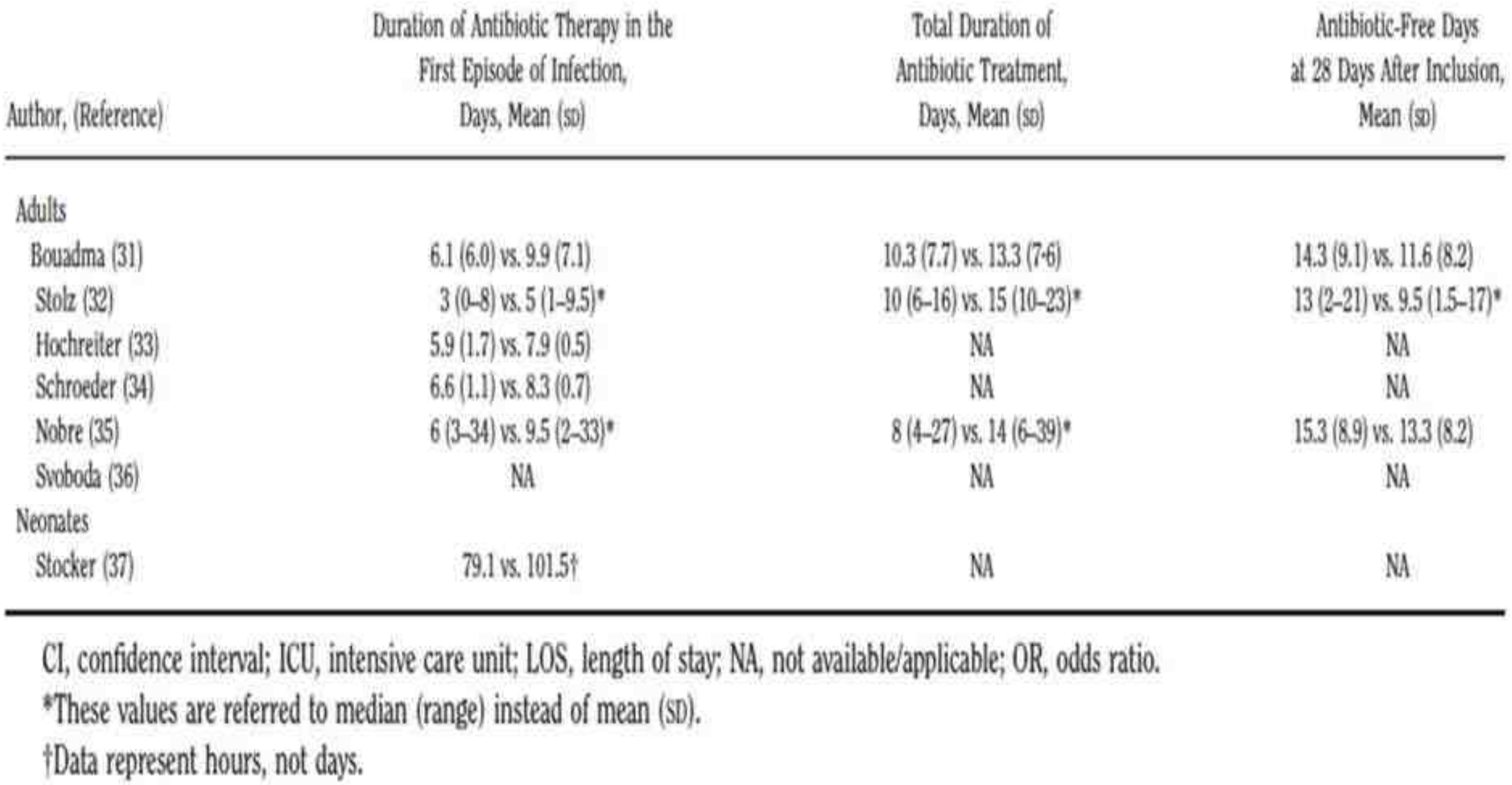
>0.25-0.5 µg/l:	3 days
>0.5 - 1.0 µg/l:	5 days
>1.0 µg/l:	7 days

Schütz et al., JAMA.2009;302(10):1059-66



Procalcitonin-guided algorithms of antibiotic therapy in the intensive care unit: A systematic review and meta-analysis of randomized controlled trials

Petros Kopterides, MD; Ilias I. Siempos, MD; Iraklis Tsangaris, MD; Argirios Tsantes, MD; Apostolos Armaganidis, MD



Author, (Reference)	Duration of Antibiotic Therapy in the First Episode of Infection, Days, Mean (SD)	Total Duration of Antibiotic Treatment, Days, Mean (SD)	Antibiotic-Free Days at 28 Days After Inclusion, Mean (SD)
Adults			
Bouadma (31)	6.1 (6.0) vs. 9.9 (7.1)	10.3 (7.7) vs. 13.3 (7·6)	14.3 (9.1) vs. 11.6 (8.2)
Stolz (32)	3 (0–8) vs. 5 (1–9.5)*	10 (6–16) vs. 15 (10–23)*	13 (2–21) vs. 9.5 (1.5–17)*
Hochreiter (33)	5.9 (1.7) vs. 7.9 (0.5)	NA	NA
Schroeder (34)	6.6 (1.1) vs. 8.3 (0.7)	NA	NA
Nobre (35)	6 (3–34) vs. 9.5 (2–33)*	8 (4–27) vs. 14 (6–39)*	15.3 (8.9) vs. 13.3 (8.2)
Svoboda (36)	NA	NA	NA
Neonates			
Stocker (37)	79.1 vs. 101.5†	NA	NA

CI, confidence interval; ICU, intensive care unit; LOS, length of stay; NA, not available/applicable; OR, odds ratio.

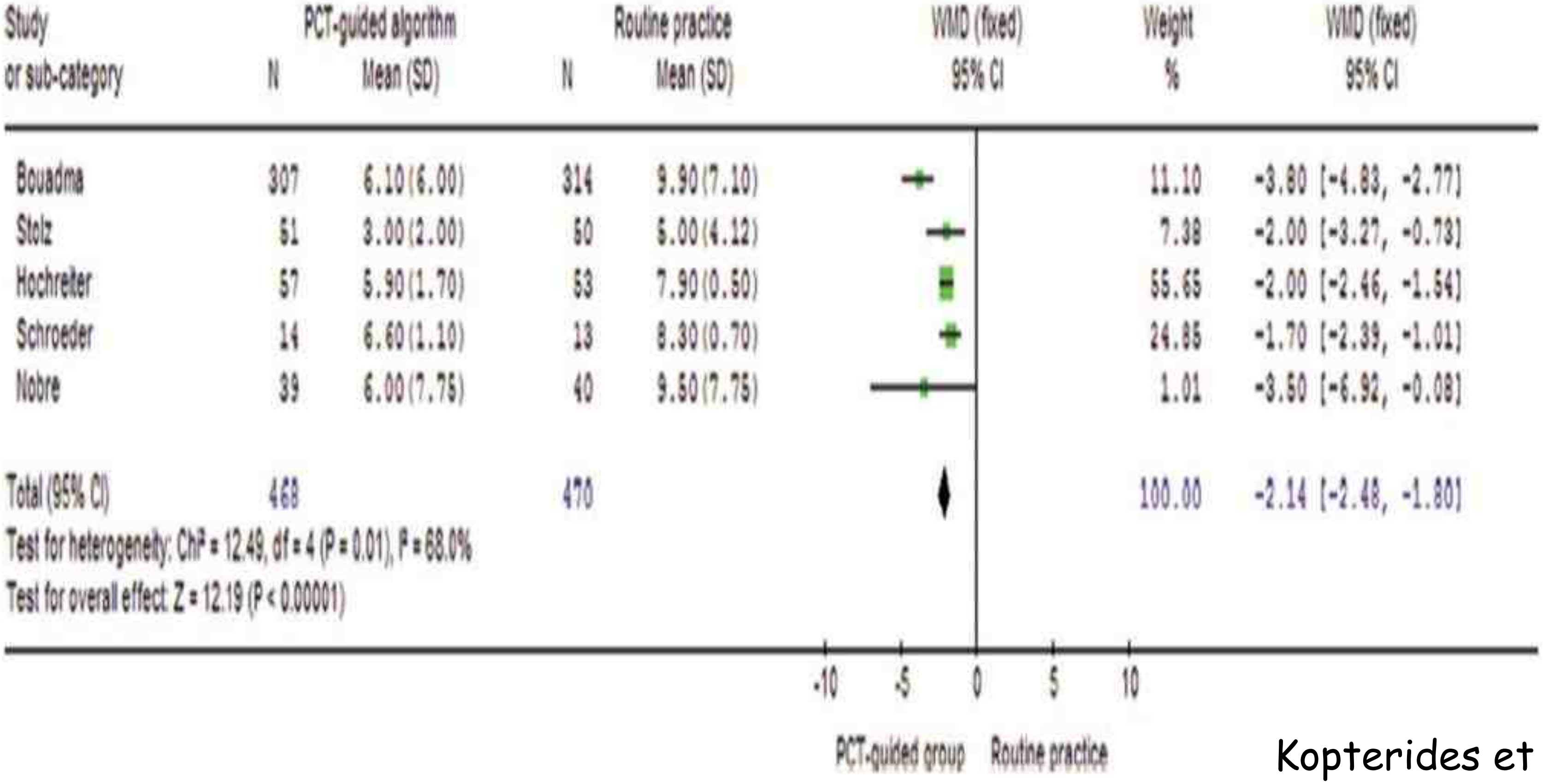
*These values are referred to median (range) instead of mean (SD).

†Data represent hours, not days.

Kopterides et al. Crit Care Med; 2010;38(11):2229-41.

PCT PER GUIDARE L'ANTIBIOTICO TERAPIA

GIORNI DI TERAPIA ANTIBIOTICA



Study or sub-category	PCT-guided algorithm N	 Mean (SD)	Routine practice N	 Mean (SD)	Weight %	WMD (fixed) 95% CI
Bouadma	307	6.10 (6.00)	314	9.90 (7.10)	11.10	-3.80 [-4.83, -2.77]
Stolz	51	3.00 (2.00)	50	5.00 (4.12)	7.38	-2.00 [-3.27, -0.73]
Hochreiter	57	5.90 (1.70)	53	7.90 (0.50)	55.65	-2.00 [-2.46, -1.54]
Schroeder	14	6.60 (1.10)	13	8.30 (0.70)	24.85	-1.70 [-2.39, -1.01]
Nobre	39	6.00 (7.75)	40	9.50 (7.75)	1.01	-3.50 [-6.92, -0.08]
Total (95% CI)	468		470		100.00	-2.14 [-2.48, -1.80]

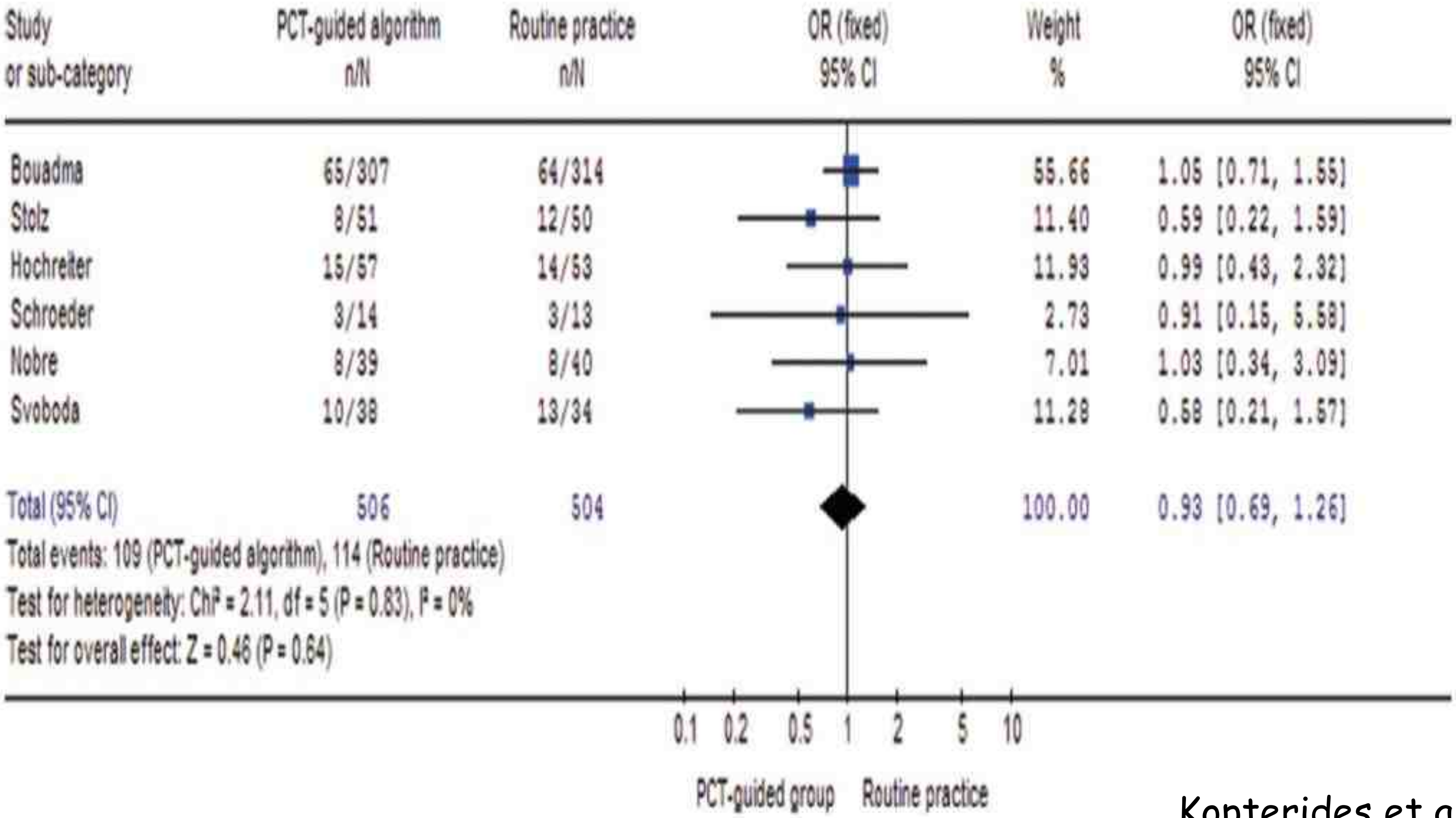
Test for heterogeneity: $Chi^2 = 12.49$, df = 4 ($P = 0.01$), $I^2 = 68.0\%$

Test for overall effect: $Z = 12.19$ ($P < 0.00001$)

Kopterides et al; 2010

PCT PER GUIDARE L'ANTIBIOTICO TERAPIA

MORTALITA' 28 GIORNI



Study or sub-category	PCT-guided algorithm n/N	Routine practice n/N	Weight %	OR (fixed) 95% CI
Bouadma	65/307	64/314	55.66	1.05 [0.71, 1.55]
Stolz	8/51	12/50	11.40	0.59 [0.22, 1.59]
Hochreiter	15/57	14/53	11.93	0.99 [0.43, 2.32]
Schroeder	3/14	3/13	2.73	0.91 [0.15, 5.58]
Nobre	8/39	8/40	7.01	1.03 [0.34, 3.09]
Svoboda	10/38	13/34	11.28	0.58 [0.21, 1.57]
Total (95% CI)	506	504	100.00	0.93 [0.69, 1.26]

Total events: 109 (PCT-guided algorithm), 114 (Routine practice)

Test for heterogeneity: Chi^2 = 2.11, df = 5 (P = 0.83), I^2 = 0%

Test for overall effect: Z = 0.46 (P = 0.64)

OR (fixed)
95% CI
0.1
0.2
0.5
1
2
5
10
PCT-guided group
Routine practice

Kopterides et al; 2010

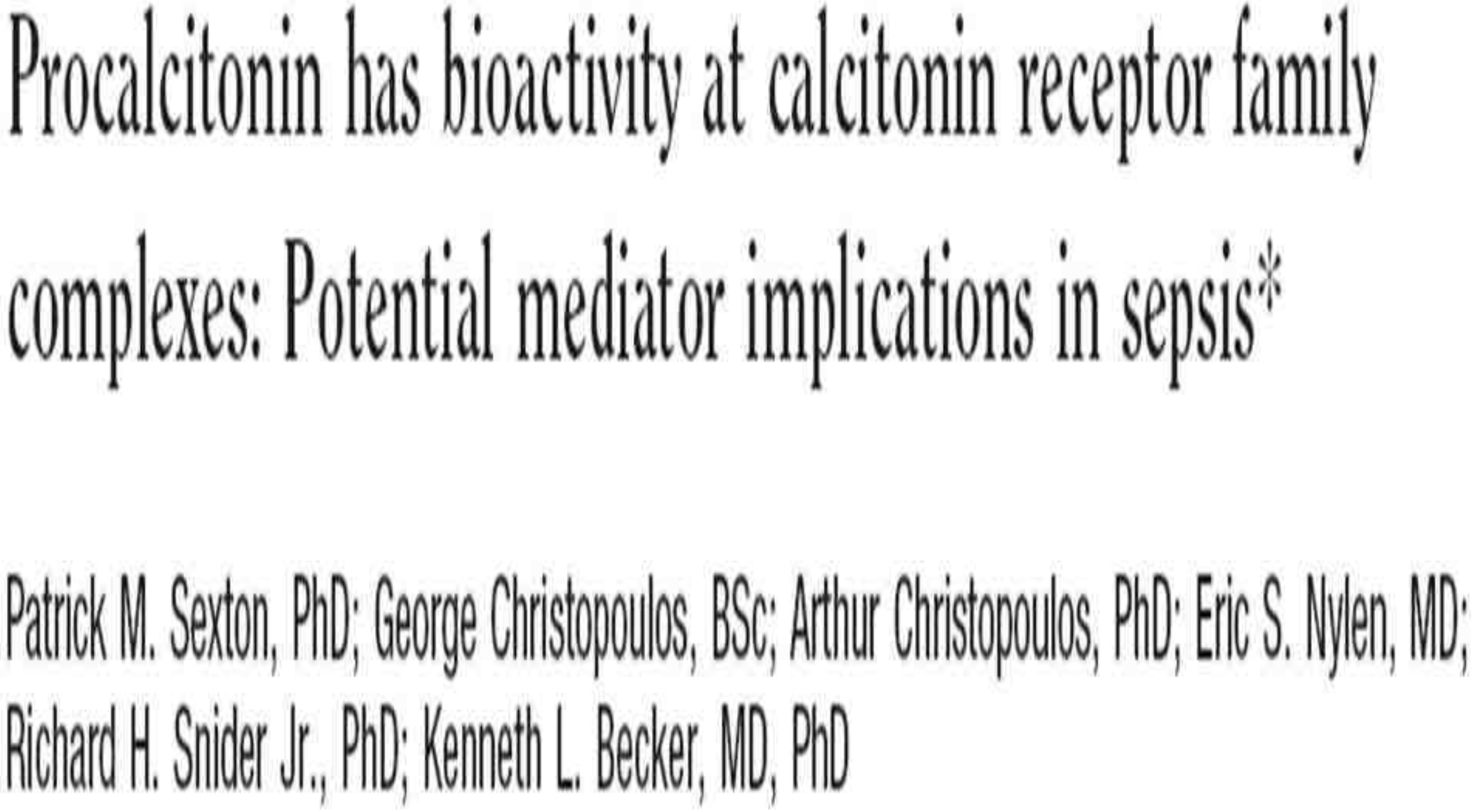
CONCLUSIONI

- ✓ LA PCT E' UTILE NELLA DIAGNOSI DIFFERENZIALE TRA SIRS E SEPSI
- ✓ ATTENZIONE AL PAZIENTE POSTOPERATO
- ✓ ATTENZIONE ALLO SHOCK CARDIOGENO
- ✓ E'UTILE NEL GIUDARE L'ANTIBIOTICO TERAPIA

CONCLUSIONI

- ✓ NO UNA SINGOLA MISUARZIONE SEGUIRE IL TREND
- ✓ ASSOCIARLA AGLI ALTRI PARAMETRI ED ALLA SITUAZIONE CLINICA
- ✓ RICORDIAMOCI DELLE ALTRE CONDIZIONI CLINICHE IN CUI AUMENTA

PCT BIOMARKER O TOSSINA?



Procalcitonin has bioactivity at calcitonin receptor family complexes: Potential mediator implications in sepsis*

Patrick M. Sexton, PhD; George Christopoulos, BSc; Arthur Christopoulos, PhD; Eric S. Nylen, MD; Richard H. Snider Jr., PhD; Kenneth L. Becker, MD, PhD

Sexton Crit Care Med 36:1637 (2008)

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