SEMI
LA VISIÓN GLOBAL DE LA PERSONA ENFERMA

FEMI

XXXI Congreso Nacional de la Sociedad Española de Medicina Interna

OVIEDO
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Auditorio-Palacio de Congresos
"Príncipe Felipe"

II Congreso Ibérico de Medicina Interna

VII Congreso de la Sociedad Asturiana de Medicina Interna

IMPACTO DEL DETERIORO RENAL EN PACIENTES INFECTADOS POR COCOS GRAMPOSITIVOS

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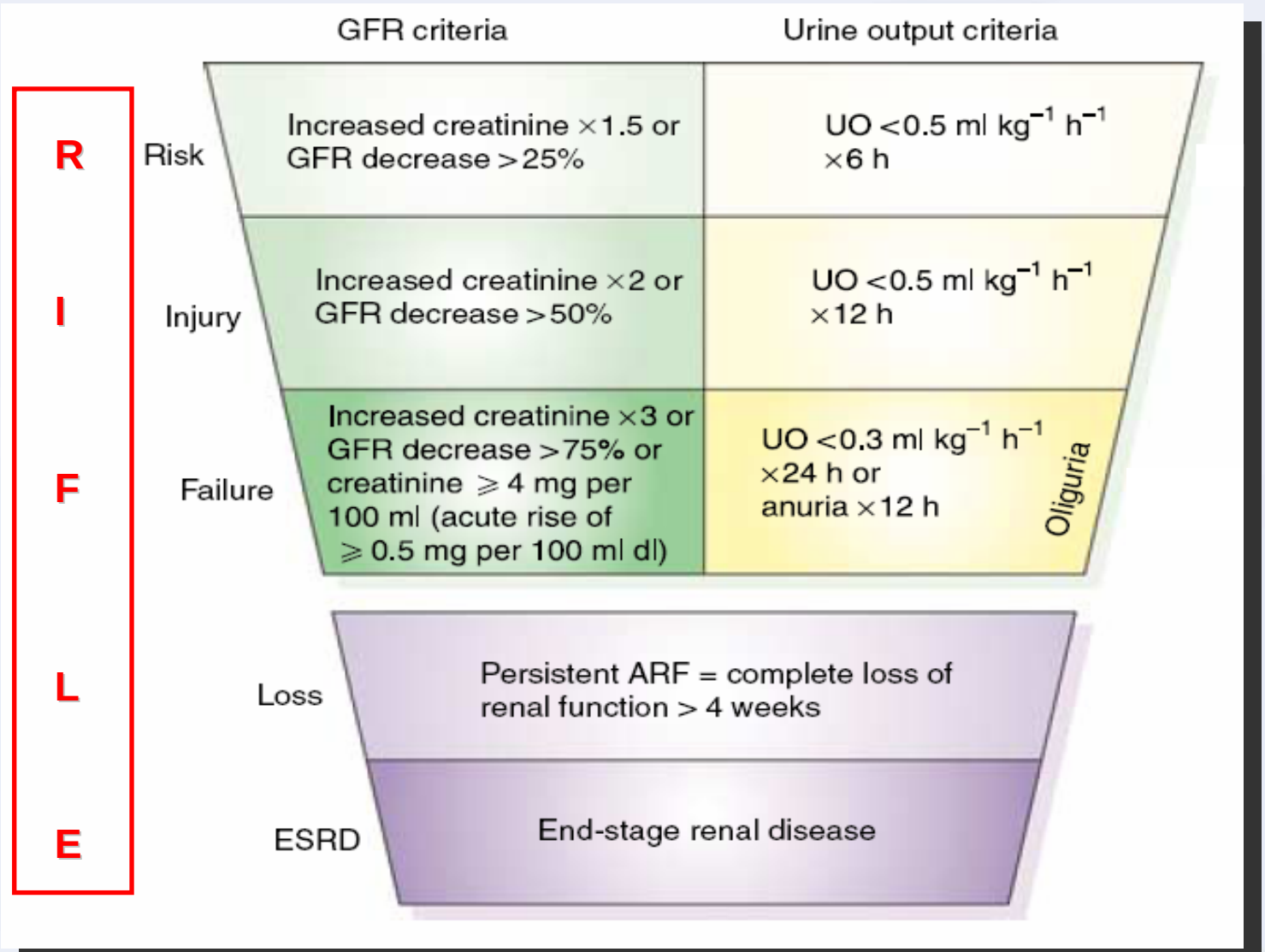
IMPACTO DEL DETERIORO RENAL (…)

DEFINICIÓN DE DAÑO RENAL AGUDO: ESCALA RIFLE



Critical Care 2004, **8**:R204-R212

ESCALA RIFLE PREDICE MORTALIDAD INTRAHOSPITALARIA

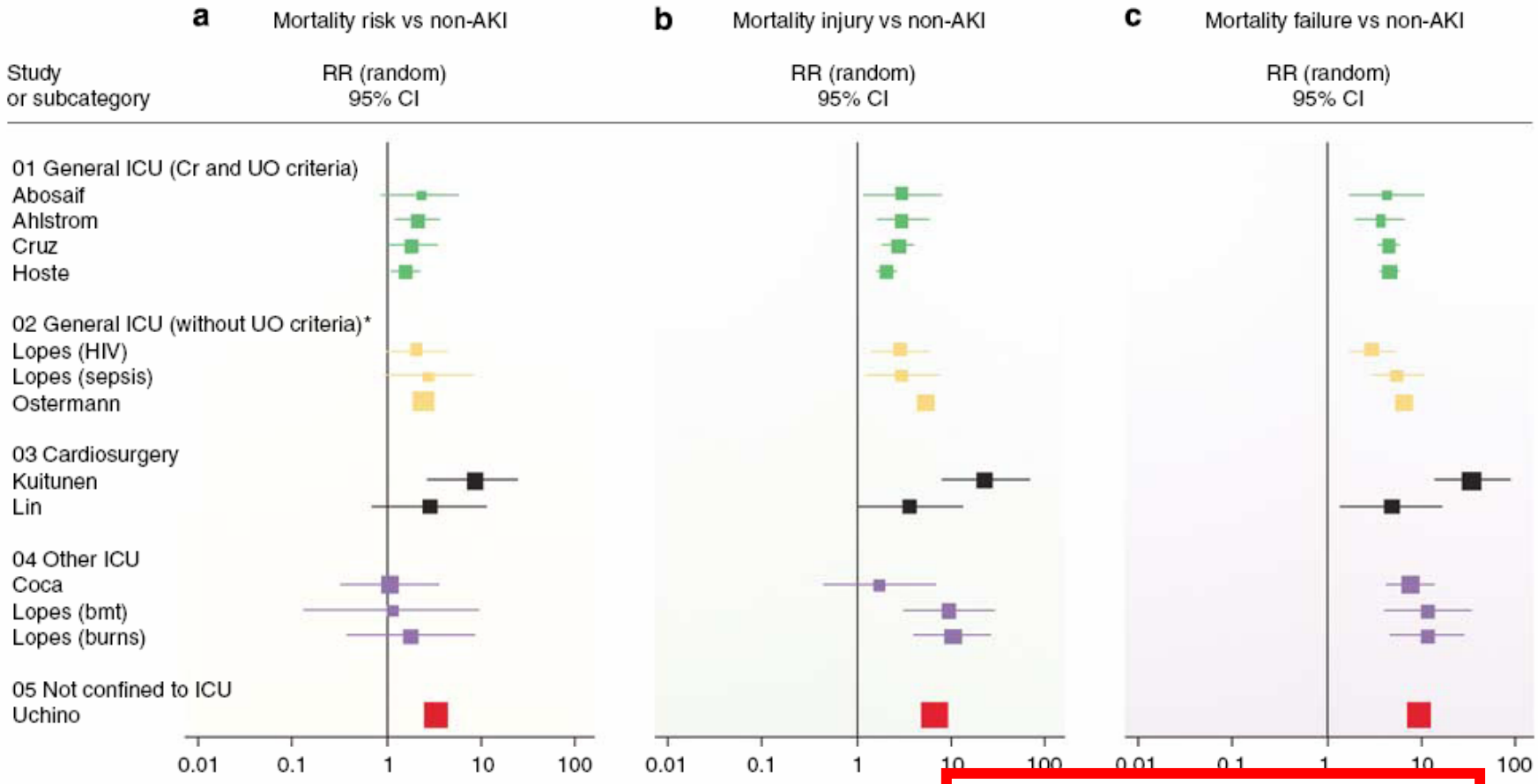
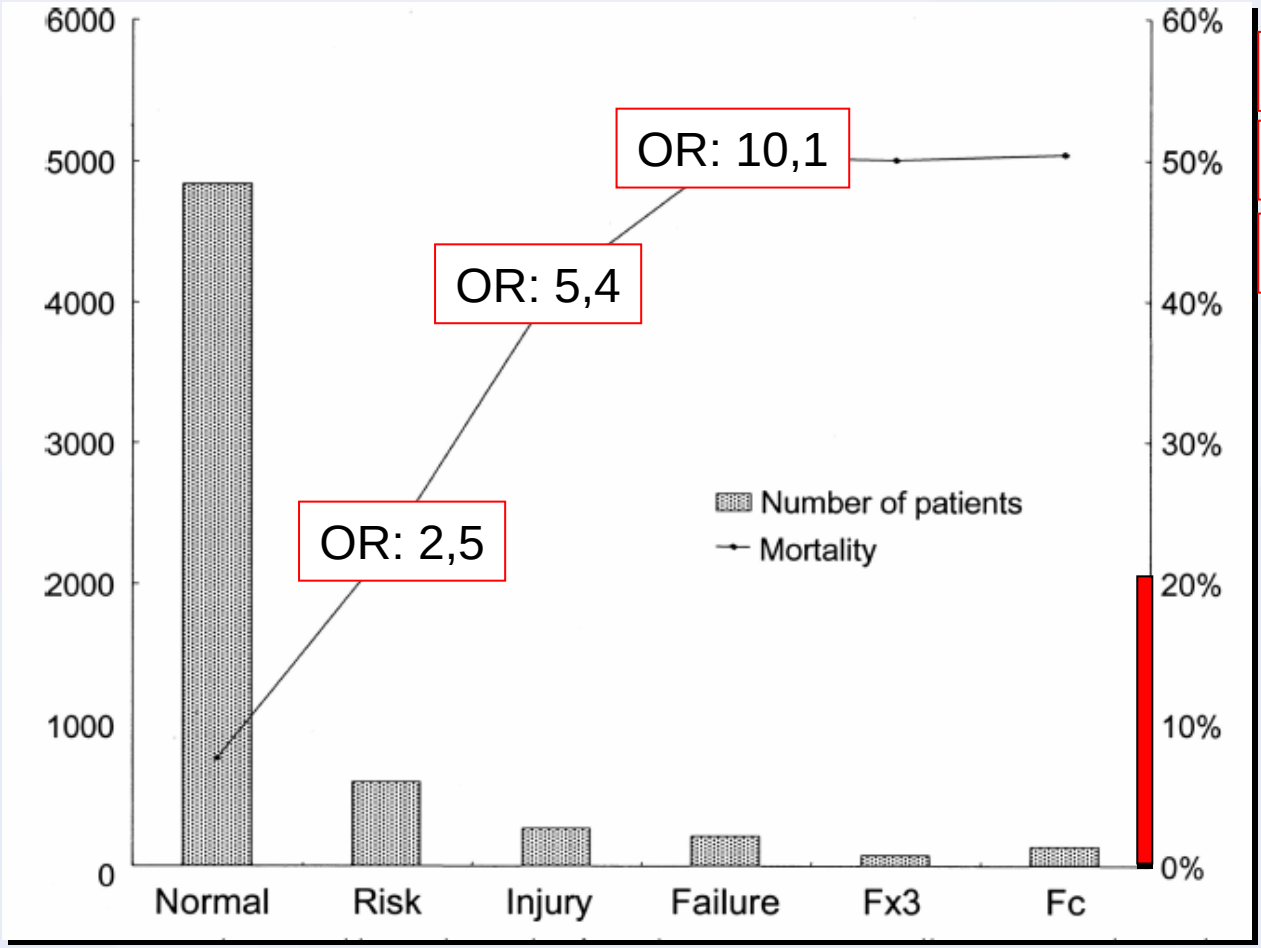


Figure 2 | Forest plot showing RR for death with respect to non-AKI patients.[3–15] (**a**) Risk (RR = 2.40; 58 073 participants included in meta-analysis), (**b**) Injury (RR = 4.15; 55 351 participants included in meta-analysis), and (**c**) Failure (RR = 6.37; 55 758 participants included in meta-analysis). Cr, creatinine; UO, urine output. See Table 2 for details.

Kidney International (2008) **73,** 538–546;

ESCALA RIFLE PREDICE MORTALIDAD INTRAHOSPITALARIA



R: 2,5(2,15-2,98)

I: 5,4(4,54-6,47)

F: 10,1(8,32-12,32)

prevalencia acumulada próxima al 20%

Crit Care Med 2006 Vol. 34, No. 7

ESCALA RIFLE PREDICE INGRESOS PROLONGADOS

Characteristic	All	R	I	F	*P*
n	474	105	233	136	
In-hospital mortality (*n* [%])	155 (33)	28 (27)	71 (30)	56 (41)	0.035
90 d mortality (*n* [%])	196 (41)	37 (35)	94 (40)	65 (48)	0.132
6-mo mortality (*n* [%])	236 (50)	48 (46)	112 (48)	76 (56)	0.224
Full renal recovery (*n* [%])	321 (68)	75 (71)	176 (75)	70 (51)	<0.001
RRT required (*n* [%])	37 (8)	1 (1)	7 (3)	29 (21)	<0.001
Referred to nephrologist (*n* [%])	119 (25)	15 (14)	41 (18)	63 (46)	<0.001
RRT received among referred (*n* [%])	36 (30)	1 (7)	7 (17)	28 (44)	0.001
RRT received among not referred (*n* [%])	1 (0.3)	0 (0)	0 (0)	1 (1)	0.206
Hospital stay (d; median [IQR])	17.0 (9.0 to 33.0)	13.0 (7.5 to 28.0)	18.5 (9.0 to 33.0)	18.5 (9.0 to 40.8)	0.047
Hospital stay (d; median [IQR])[a]	19.0 (10.0 to 33.0)	12.5 (7.3 to 26.8)	19.0 (12.0 to 34.0)	24.5 (13.3 to 45.5)	0.001

[a]Excluding those who died during admission.

J Am Soc Nephrol 18: 1292–1298, 2007.

FRA PREDICE INCREMENTO DE COSTES

Table 3. LOS and costs associated with selected changes in SCr[a]

Criterion	Mean Unadjusted Increase in Total Cost ($)	Mean Adjusted (Marginal) Increase in Total Cost ($)
↑ SCr ≥ 0.3 mg/dl	$ 8,902	$ 4,886
↑ SCr ≥ 0.5 mg/dl	$12,656	$ 7,499
↑ SCr ≥ 1.0 mg/dl	$21,475	$13,200
↑ SCr ≥ 2.0 mg/dl	[illegible]	[illegible]
↑ SCr by 25%	$ 7,469	$ 3,721
↑ SCr by 50%	$10,125	$ 5,510
↑ SCr by 100%	$15,192	$ 8,999
↑ SCr by 50% to a minimum peak of 2.0 mg/dl	$19,517	$11,719
↑ SCr ≥ 0.5 mg/dl with baseline SCr < 2.0 mg/dl or ↑ SCr ≥ 1.0 mg/dl with baseline SCr ≥ 2.0 and < 5.0 mg/dl	$13,451	$ 7,982

[a] n = 2892, 1236, 351, 105, 4060, 1967, 714, 352, and 1160 for respective AKI criteria from denominator sample n = 9205. Results are relative to those without the change indicated. Multivariable analyses were adjusted for age, gender, DRG weight, and ICD-9-CM categories of cardiovascular, respiratory, malignant, and infectious diseases.

J Am Soc Nephrol 16: 3365–3370, 2005.

¿HAY MANERA DE PREDECIR EL DESARROLLO DE FRA? ANTECEDENTES PERSONALES (1)

TABLE 4. **Odds Ratios for AKI of Selected Variables**[a,b]

Variable	Mantel-Haenszel summary OR (95% CI)	*P* value[c]
Sex (male vs female)	0.9 (0.6-1.3)	.50
Race (nonwhite vs white)	1.2 (0.8-1.9)	.30
Comorbidities ≥2	3.5 (2.4-5.1)	<.001
CKD	3.9 (2.7-5.6)	<.001
≥1 Nephrotoxic medications[d]	1.7 (1.2-2.4)	.007
Volume depletion[e]	2.7 (1.8-3.9)	<.001

[d] These include angiotensin II receptor antagonists, aminoglycosides, nonsteroidal anti-inflammatory drugs, and intravenous contrast agents.

***Mayo Clin Proc*. 2009;84(5):410-416**

¿HAY MANERA DE PREDECIR EL DESARROLLO DE FRA? ANTECEDENTES PERSONALES (2)

Table 2
Characteristics of patients according to departments.

Department (*n* patients)	Women (%)	Age X + SD	Serum creatinine X + SD	eGFR stages 3–5 (%)
Internal Medicine (4429)	48.8	66.7 ± 19.5	1.15 ± 0.74	35.2
Cardiology (1249)	38.8	65.9 ± 14.7	1.22 ± 0.85	36.7
Neurology (675)	40.9	63.9 ± 16.8	1.06 ± 0.54	26.2
Pulmonary Medicine (827)	35.0	62.7 ± 17.2	1.03 ± 0.65	21.8
Gastroenterology (926)	46.5	60.1 ± 19.0	1.04 ± 0.73	21.0
Endocrinology (350)	58.3	59.1 ± 18.9	1.10 ± 0.69	28.9
Hematology (376)	50.5	55.0 ± 18.6	0.95 ± 0.66	15.4
Surgery (836)	45.2	62.8 ± 17.3	1.09 ± 0.84	20.8
Oncology (594)	47.6	60.9 ± 14.3	1.05 ± 0.87	18.2
Critical Care (677)	40.3	61.1 ± 16.5	1.14 ± 0.81	27.6
Urology (216)	32.4	63.2 ± 17.4	1.50 ± 1.87	31.9
Orthopedic Surgery (425)	63.3	65.9 ± 18.6	1.10 ± 0.82	29.2
Gynecology (343)	100.0	62.9 ± 14.9	1.06 ± 0.83	27.4

European Journal of Internal Medicine 21 (2010) 327–332

¿HAY MANERA DE PREDECIR EL DESARROLLO DE FRA? MOTIVOS DE INGRESO

Sepsis was a precipitating factor in 47% of patients.

J Am Soc Nephrol 18: 1292–1298, 2007.

Septic shock was the most common contributing factor to ARF. The frequency in which it was a contributing factor to the development of ARF was around 50% in all centers.

JAMA. 2005;294:813-818

The most common precipitating factor was sepsis, at least partly causative in 69% of cases.

Q J Med 2002; **95**:579–583

¿Y QUÉ HAY QUE HACER?

- Assess airway intubation for high-risk patients
- Assess breathing
  - Administer oxygen
  - Maintain tidal volume of 6 ml/kg of IBW if mechanical ventilation needed
- Assess circulation (follow protocol of Rivers et al.[2])
  - Fluids, vasopressors, inotropes, transfusion
  - MAP >65 mm Hg
  - CVP 8–12 mm Hg
  - Hematocrit >30%
  - $ScvO_2$ >70%

- Start drug therapy
  - Broad-spectrum antibiotics
  - Consider APC if
    - APACHE II score ≥25
    - Failure of ≥2 organs
  - Consider hydrocortisone

- Control the source of sepsis
  - Abscess, empyema
  - Cholecystitis, cholangitis
  - Urinary obstruction
  - Peritonitis, bowel infarct
  - Necrotizing fasciitis
  - Gas gangrene

N Engl J Med 2006;355:1699-713.

(…)
PACIENTES INFECTADOS POR COCOS GRAMPOSITIVOS

¿QUÉ ALTERNATIVAS HAY?

- **PENICILINAS**
- **VANCOMICINA**
- **TIGECICLINA**
- **LINEZOLID**
- **DAPTOMICINA**

PENICILINAS

- Limitado por el perfil de sensibilidades:
  - SARM
  - Staph. coagulasa negativos
  - Enterococos
- En general poco nefrotóxicas.

VANCOMICINA (1): ¿es eficaz?

Table 5. Factors independently associated with mortality in a logistic regression model of patients with episodes of methicillin-resistant *Staphylococcus aureus* bacteremia.

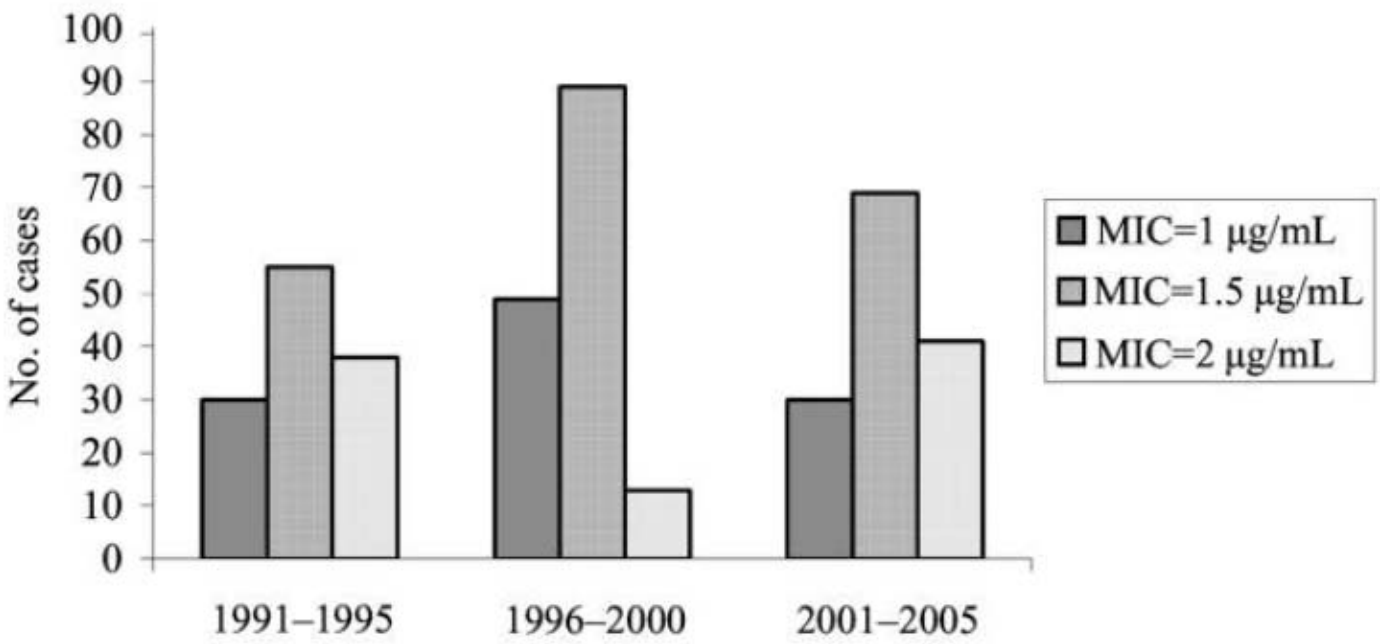
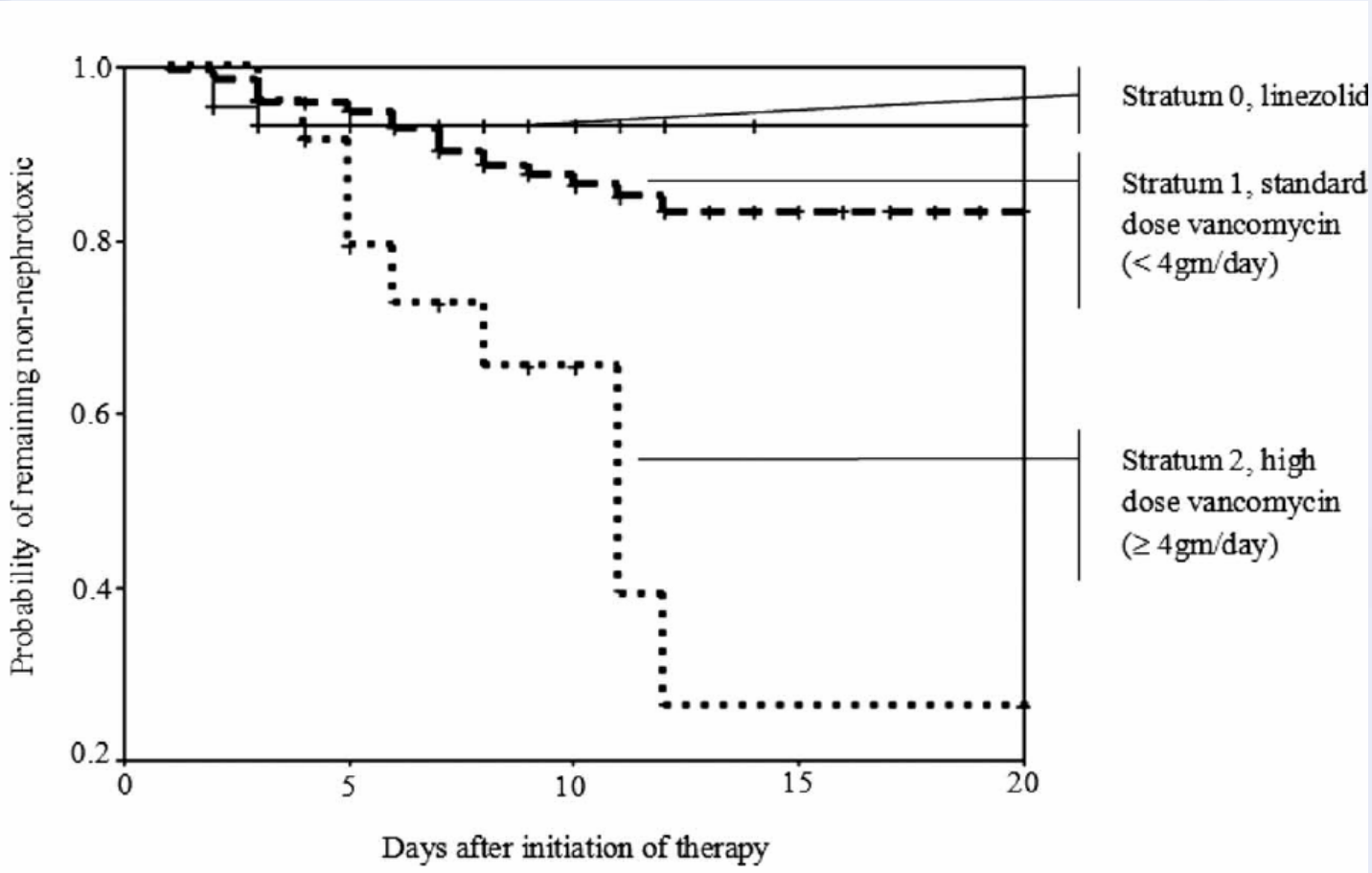


Figure 1. Number of cases of bacteremia stratified by the vancomycin MIC of the infecting strain and the study period.

Clinical Infectious Diseases 2008; 46:193–200

VANCOMICINA (2): ¿es segura?



Dosis elevadas de vancomicina se asocian con mayor frecuencia a nefrotoxicidad asociada al tratamiento: Van≥ 4 g/dia, 34,6%; Van< 4 g/dia, 10,9%.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2008, p. 1330–1336

VANCOMICINA (3): ¿es segura?

Table 3 | Studies evaluating the nephrotoxicity of higher vancomycin doses

	No. of patients	Design	Definition nephrotoxicity	% With nephrotoxicity: Total	Trough <15	Trough ⩾15	Independent risk factor for nephrotoxicity
Hidayat *et al.*[12]	95	Prospective cohort study Adult patients with MRSA	↑ creat of 0.5 mg/dl or	11.6	0	17.4	Concurrent nephrotoxic agents High trough levels
Jeffres *et al.*[17]							
Ingram *et al.*[18]							
Lodise *et al.*[13,19]							
Lodise *et al.*[3]	166	Retrospective study, vanco >48 h	↑ creat of 0.5 mg/dl or ⩾50% of baseline	12.7	10.1	25.9	Empiric trough value ICU stay
Hutschala *et al.*[21]	149	Retrospective cohort of ICU patients after open-heart surgery; continuous infusion (CI) versus intermittent administration (IA)	↑ creat of ⩾0.3 mg/dl or ⩾50% of baseline, or ↓ in urinary output to <0.5 ml/kg per h for >6 h	29.5 overall 27.7% in CI 36.7% in IA			NA

Nefrotoxicidad 6,3%<7 días, 21,1% 8-14 días, 30%>14 días

Mortalidad: 45 vs. 15% Estancia: 44,8 vs 28,7 días

Desarrollo más lento de nefrotoxicidad, aunque la prevalencia última es idéntica y relacionada con una exposición al fármaco acumulada

Ingram PR et al. Int J Antimicrob Agents. 2009;34(6):570-4.

Kidney International (2010) **77,** 760–764

TIGECICLINA: ¿es eficaz?

FDA Drug Safety Communication: Increased risk of death with Tygacil (tigecycline) compared to other antibiotics used to treat similar infections

Safety Announcement
Additional Information for Healthcare Professionals
Data Summary

Safety Announcement

[09-01-2010] The U.S. Food and Drug Administration (FDA) is reminding healthcare professionals of an increased mortality risk associated with the use of the intravenous antibacterial Tygacil (tigecycline) compared to that of other drugs used to treat a variety of serious infections. The increased risk was determined using a pooled analysis of clinical trials. The cause of the excess death in these trials is often uncertain, but it is likely that most deaths in patients with these severe infections were related to progression of the infection.

The increased risk was seen most clearly in patients treated for hospital-acquired pneumonia, especially ventilator-associated pneumonia, but was also seen in patients with complicated skin and skin structure infections, complicated intra-abdominal infections and diabetic foot infections. Tygacil is not approved for the treatment of hospital-acquired pneumonia (including ventilator-associated pneumonia) or diabetic foot infection. Tygacil is approved by FDA for the treatment of complicated skin and skin structure infections, complicated intra-abdominal infections, and community acquired pneumonia.

LINEZOLID (1): ¿es eficaz?

Primary Efficacy Endpoint: Per Protocol (PP) at End of Study (EOS)

	Linezolid n (%)	Vancomycin n (%)	P-Value	95% CI
Subjects	165 (100)	174 (100)		
Success/Cure	95 (57.6)	81 (46.6)	0.042	0.5%, 21.6%
Failure	70 (42.4)	93 (53.4)		
Unknown*	7	2		

IDSA-Vancouver 2010

LINEZOLID (2): ¿es seguro?

Adverse Events* of Interest
All Causality: ITT

Adverse Event	Linezolid n=597 n (%)	Vancomycin n=587 n (%)
Anemia	30 (5.2)	42 (7.2)
Renal failure/azotemia	23 (3.8)	42 (7.2)
Cardiac arrest	11 (1.8)	13 (2.2)
Thrombocytopenia	8 (1.3)	13 (2.2)
Pancreatitis	5 (0.8)	1 (0.2)
Polyneuropathy	2 (0.3)	0
Neutropenia	2 (0.3)	1 (0.2)
Pancytopenia	2 (0.3)	1 (0.2)
Acute myocardial infarction	0	2 (0.3)
Paresthesia	0	1 (0.2)

*Investigator reported Events to study safety database

IDSA-Vancouver 2010

LINEZOLID (3) : ¿es seguro?

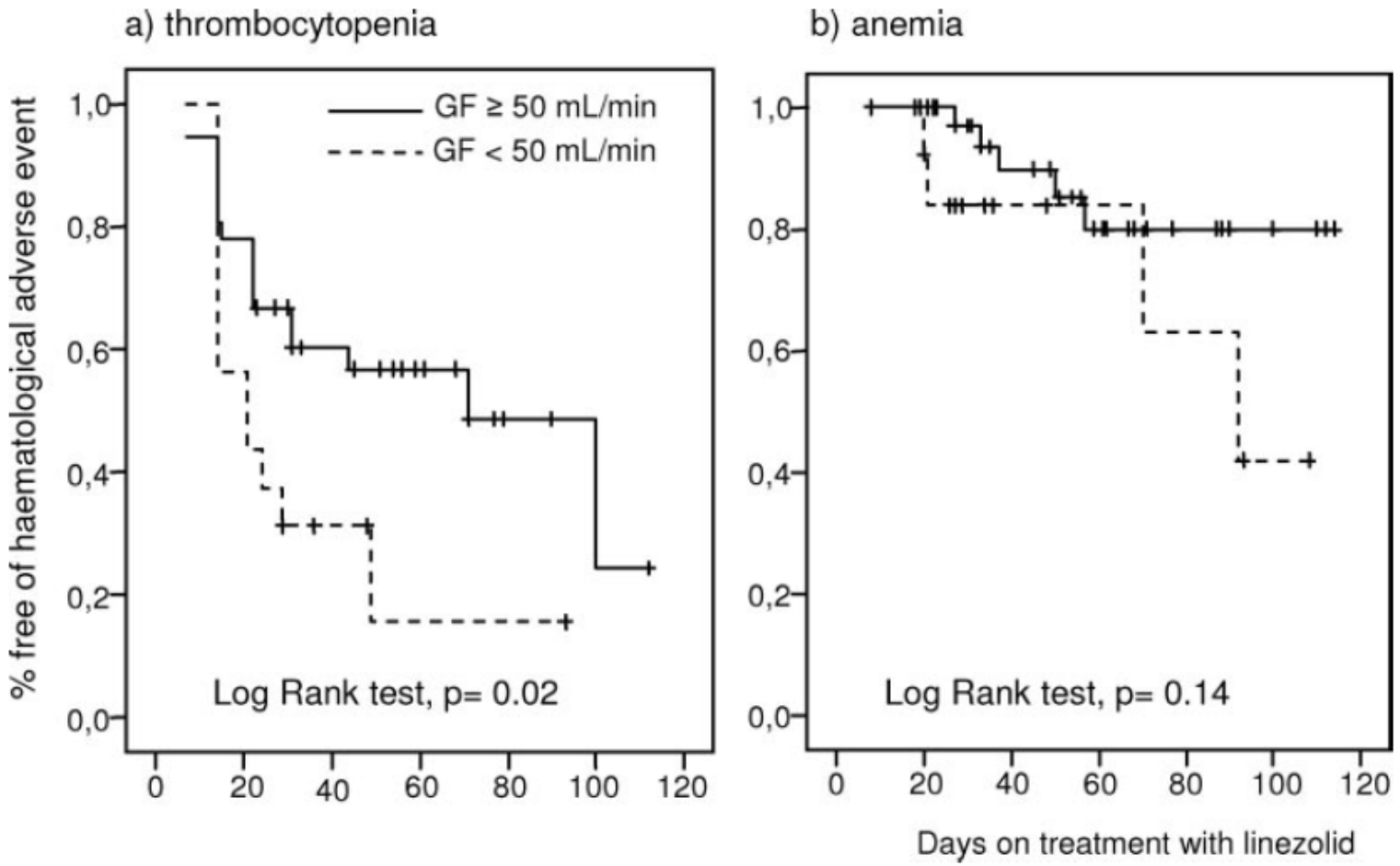
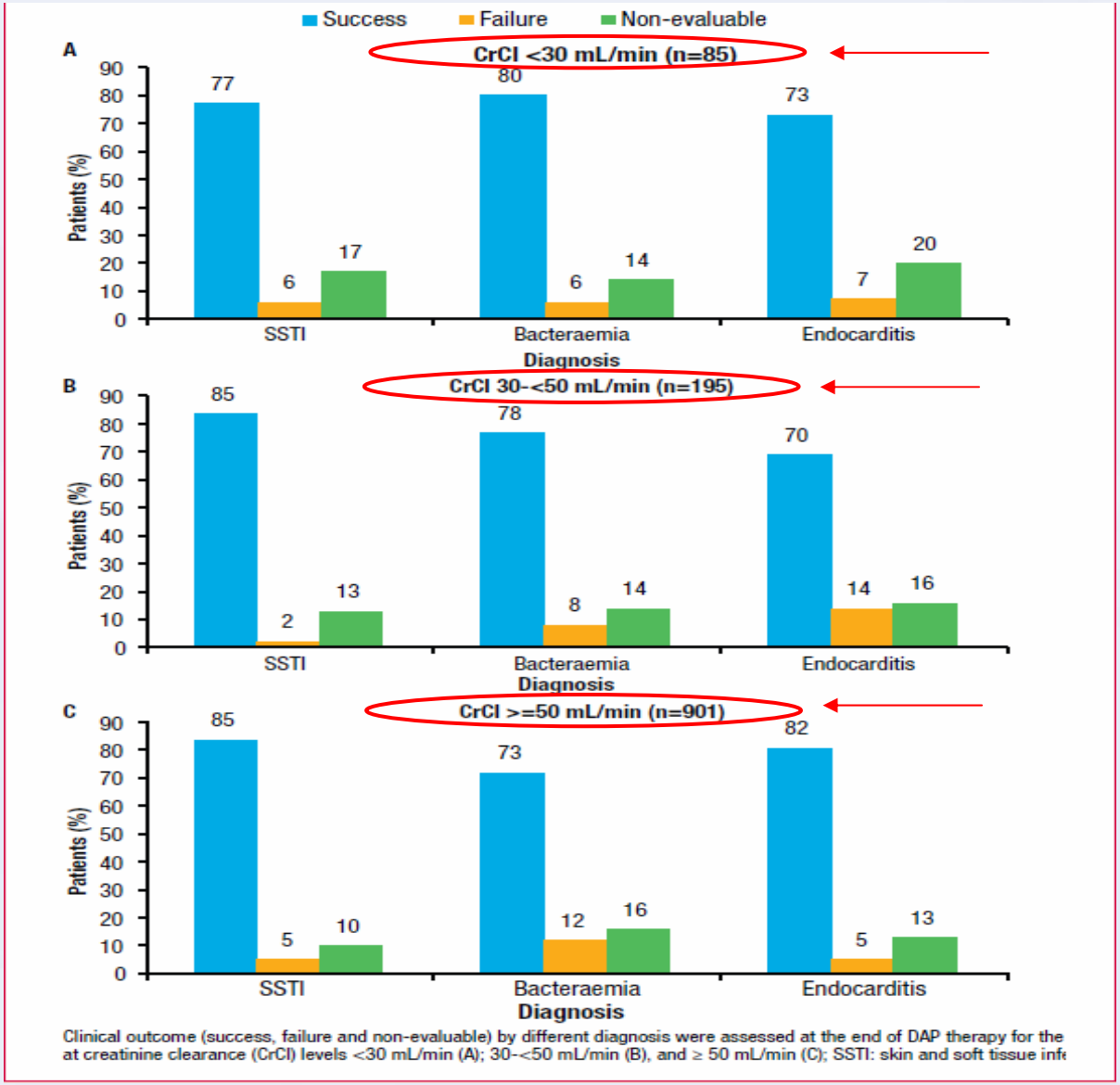


FIG. 3. Cumulative probability of hematological adverse events according to GFR.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2007, p. 2559–2563 Vol. 51, No. 7

DAPTOMICINA (1): ¿es eficaz?

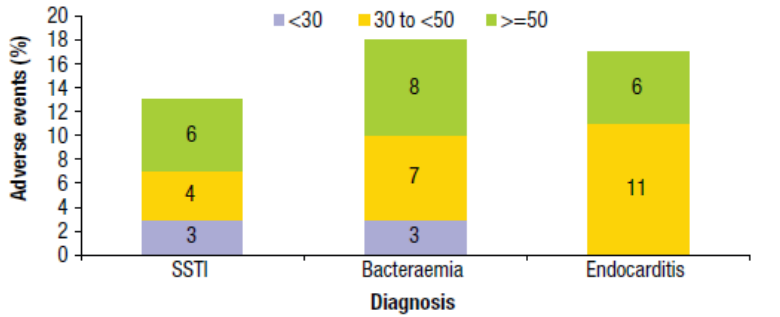


Clinical outcome (success, failure and non-evaluable) by different diagnosis were assessed at the end of DAP therapy for the at creatinine clearance (CrCl) levels <30 mL/min (A); 30-<50 mL/min (B), and ≥ 50 mL/min (C); SSTI: skin and soft tissue infe

Safety and effectiveness of daptomycin in patients with renal insufficiency not requiring renal replacement therapy

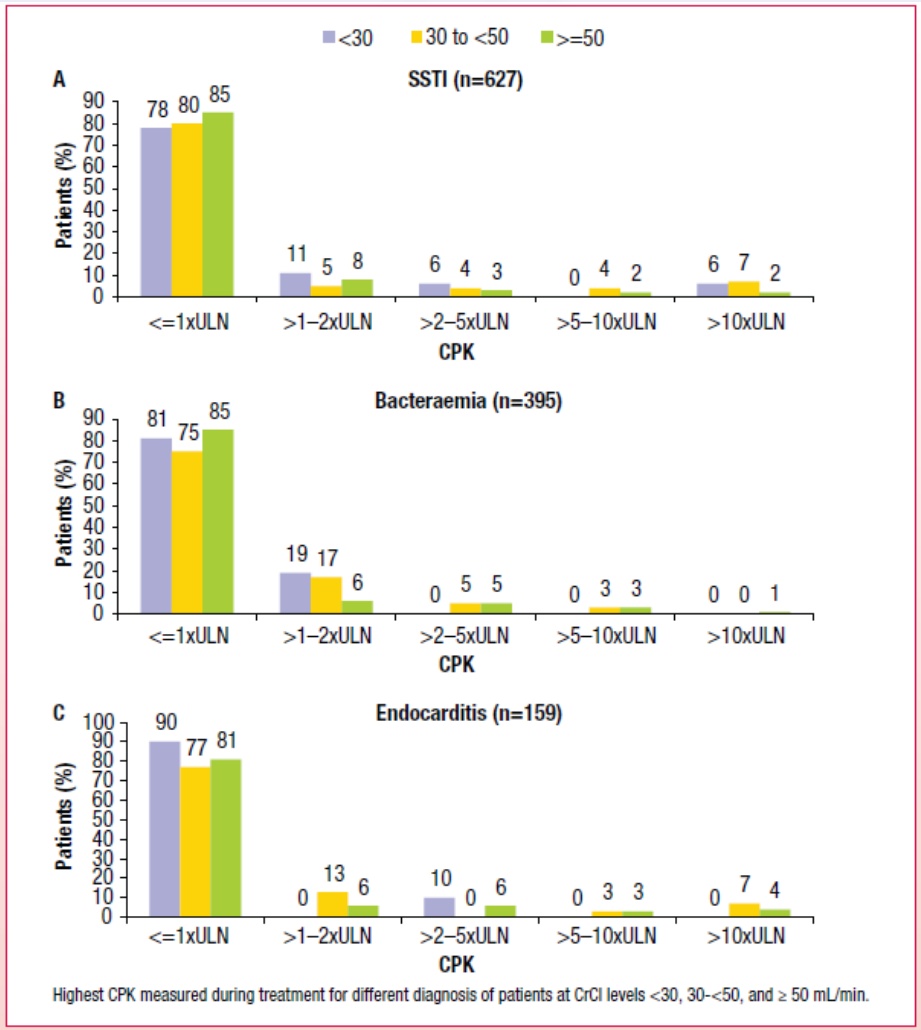
Gonzalez-Ruiz A[1], Lamp KC[2], Lin M-Y[2] and Chaves RL[3]

DAPTOMICINA (2): ¿es segura?



Adverse events (AEs) reported with different diagnosis for the patients at CrCl levels <30, 30-<50, and ≥ 50 mL/min.

Figure 3. Adverse events related to study medication



Highest CPK measured during treatment for different diagnosis of patients at CrCl levels <30, 30-<50, and ≥ 50 mL/min.

Figure 2. Serum creatine phosphokinase (CPK) during DAP therapy

Safety and effectiveness of daptomycin in patients with renal insufficiency not requiring renal replacement therapy

Gonzalez-Ruiz A[1], Lamp KC[2], Lin M-Y[2] and Chaves RL[3]

[1]Darent Valley Hospital, Microbiology Department, Kent, UK; [2]Cubist Pharmaceuticals, Lexington, MA, US; [3]Novartis Pharma AG, Basel, Switzerland

DAPTOMICINA (3) ¿y cuando se asocia a otros nefrotóxicos?

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 1990, p. 139–147 Vol. 34, No. 1
0066-4804/90/010139-09$02.00/0

Effects of Daptomycin and Vancomycin on Tobramycin Nephrotoxicity in Rats

DENIS BEAUCHAMP,* MICHEL PELLERIN, PIERRETTE GOURDE, MARTINE PETTIGREW, AND MICHEL G. BERGERON

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 1994, p. 1027–1035 Vol. 38, No. 5
0066-4804/94/$04.00+0

Attenuation by Daptomycin of Gentamicin-Induced Experimental Nephrotoxicity

NATHALIE THIBAULT, LOUIS GRENIER, MARIE SIMARD, MICHEL G. BERGERON, AND DENIS BEAUCHAMP*

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 1994, p. 742–749 Vol. 38, No. 4
0066-4804/94/$04.00+0

Daptomycin May Attenuate Experimental Tobramycin Nephrotoxicity by Electrostatic Complexation to Tobramycin

MICHÈLE COUTURE,[1] MARIE SIMARD,[1] PIERRETTE GOURDE,[1] CÉLINE LESSARD,[1] KOMAL GURNANI,[2] LESHENG LIN,[1] DANIELLE CARRIER,[2] MICHEL G. BERGERON,[1] AND DENIS BEAUCHAMP[1]*

CONCLUSIONES

1- El deterioro agudo de la función renal se asocia con:
- Aumento de la mortalidad intrahospitalaria
- Ingresos prolongados
- Incremento significativo de costes

2- El deterioro renal agudo se produce fundamentalmente:
- En el contexto de la sepsis
- En pacientes pluripatológicos
- Cuando existe enfermedad renal previa
- Cuando se asocian otros fármacos nefrotóxicos

3- En el contexto del deterioro de la función renal, una elección individualizada del tratamiento podría tener implicaciones en el pronóstico :
- Bacteriemia, endocarditis, celulitis complicada: DAPTOMICINA
- Neumonía: LINEZOLID (no indicado en bacteriemia)
- PENICILINAS: para secuenciar siempre según antibiograma
- TIGECICLINA: 3º lugar. Infecciones polimicrobianas.