Practical Management of HAP/VAP

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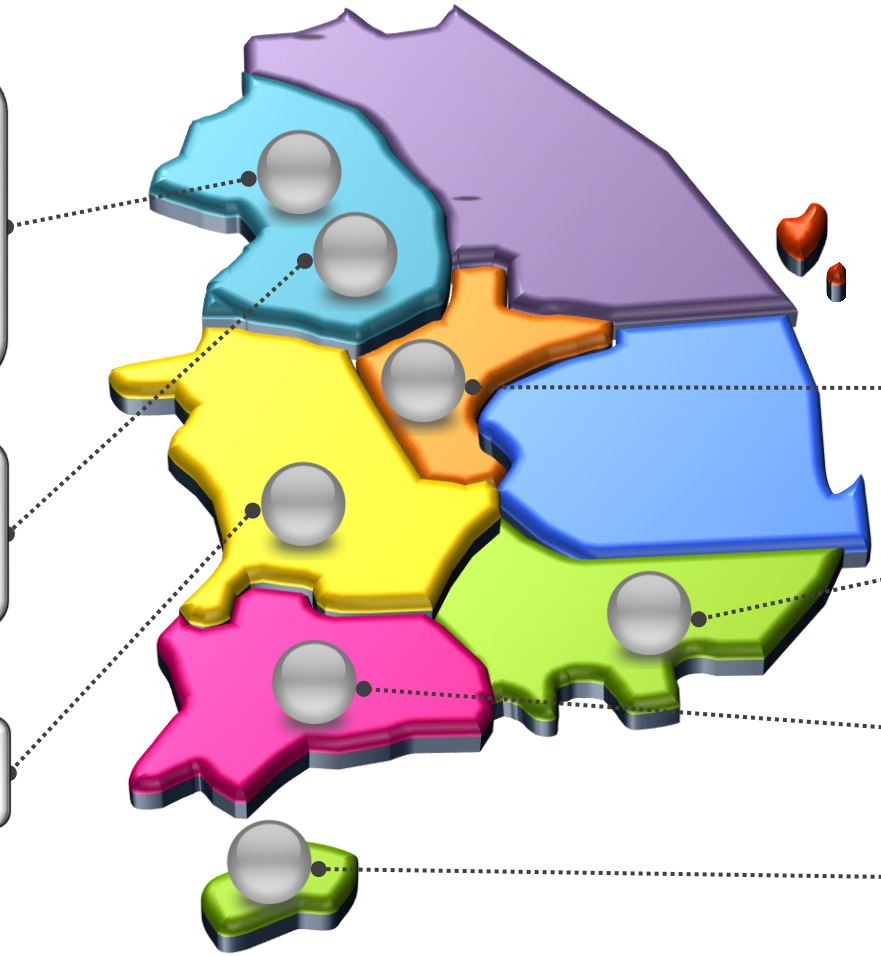
Korean HAP/VAP Study

Multicenter Retrospective Cohort, Koran HAP/VAP Study Group



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Study Population

- All consecutive adult patients who admitted to the 13 participating hospitals during a six-month (July 1 through Deccember 31, 2019) period were screened for eligibility.
- Diagnosis of HAP/VAP with IDSA/ATS diagnostic criteria
  - New lung infiltrate plus clinical evidence that the infiltrate is of an infectious origin, which include
    - New onset of fever
    - Purulent sputum
    - Leukocytosis
    - Decline in oxygenation
  - HAP is defined as a pneumonia not incubating at the time of hospital admission and occurring 48 hours or more after admission.
  - VAP is defined as a pneumonia occurring >48 hours after endotracheal intubation.

Clin Infect Dis 2016;63(5):e61

Prevalence of HAP/VAP

2019.07.01 ~ 2019.12.31
206,372 adult patients hospitalized

Diagnosed with HAP/VAP
n = 526 (2.54/1000patients)

Diagnosed at GW (72.1%)

Diagnosed during ICU stay (27.9%)

Hospital mortality: 28.1%

KATRDIC 2020

Baseline Characteristics

Variables	No. of patients or Median (IQR)
Age, year	71.0 (62.0–79.0)
Sex, male	360 (68.4)
Reason for admission Medical Diagnostic work up Medical disease treatment Surgical Elective operation Emergency operation Other reasons than operation	 303 (57.6) 52 (9.9) 106 (20.2) 52 (9.9) 13 (2.5)
Charlson comorbidity index	5.0 (3.0–6.0)
Clinical frailty scale	5.0 (3.0–7.0)
Risk for aspiration Impaired swallowing Impaired consciousness Increased change of gastric contents reaching the lung Impaired cough reflex	333 (63.3) 223 171 202 156

Microorganism Isolated (n=211, 40.1%)

Microorganism	No. of patients
Gram-positive pathogens	
Staphylococcus aureus	24
Streptococcus pneumonia	7
Enterococcus faecium	5
Nonstaphylococcus aureus Staphylococcus species	4
Others*	5
Gram-negative pathogens	
Acinetobacter baumannii	68
Pseudomonas aeruginosa	36
Klebsiella pneumoniae	35
Escherichia coli	11
Sternotrophomonas maltophilia	11
Enterobacter cloacae	10
Serratia marcescens	5
Proteus species	4
Klebsiella aerogenes	3
Moraxella catarrhalis	2
Burkholderia cephacia	2
Citrobacter species	2
Others**	2

*Others included one *Streptococcus pyogenes*, one *Streptococcus mitis*, one *Streptococcus agalactiae*, one *Streptococcus angiosus*, and one *Listeria monocytogenes*.

**Others included one *Klebsiella oxytoca* and one *Raoultella planticola*.

Clinical Findings

Variables	No. of patients or Median (IQR)
Initial empirical antibiotics	
Extended-spectrum penicillin/beta-lactamase inhibitor	312 (59.3)
Respiratory fluoroquinolone	169 (32.1)
3rd cephalosporin	53 (10.1)
Cefepime	35 (6.7)
Aminoglycoside	13 (2.5)
Glycopeptide	79 (15.0)
Carbapenem	107 (20.3)
Colistin	8 (1.5)
Marcrolide	5 (1.0)
Others	44 (8.4)
More than two drugs	249 (47.3)
Adjunctive corticosteroid treatment	91 (17.3)
Classification of infection	
Microbiologically documented	213 (40.3)
Clinically documented	297 (56.2)
Possible infection	18 (3.4)
Inappropriate antibiotic treatment (n = 211)	102 (48.3)
Occurrence of MDR pathogen (n=211)	138 (70.4)
Staphylococcus aureus	67
Enterococcus spp.	30
Enterobacteriaceae	27
Pseudomonas aeruginosa	19
Acinetobacter spp.	4
Duration of antibiotic treatment, day	13.0 (7.0–24.0)

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Outcomes of HAP/VAP

Variables	No. of patients or Median (IQR)
Clinical response Clinical cure Clinical Failure Recurrence	 344 (65.4) 171 (32.5) 11 (2.1)
Microbiological response (n=211) Microbiological eradication Colonization Microbiological failure Microbiological recurrence	 106 (57.9) 23 (12.6) 50 (27.3) 4 (2.2)
Additional ICU admission	107 (28.2)
Hospital mortality	28.1%
Hospital length of stay, day	30 [18–53]
Discharge destination (n=378) Home Transfer Step-down referral Step-up referral	 205 (54.2) 173 (45.8) 158 15
Limitation of life-sustaining treatment at any time	157 (29.8)

Summary of Korean HAP/VAP Study

- The prevalence of HAP/VAP in adult patients hospitalized during a six-month period in Korea was 2.54/1000 hospitalized patients.
- Overall in-hospital mortality was 28.1% in adult patients with HAP/VAP in Korea.
- Patients with HAP/VAP from tertiary hospitals in Korea were elderly, had a risk of aspiration, and were often referred to step-down centers.

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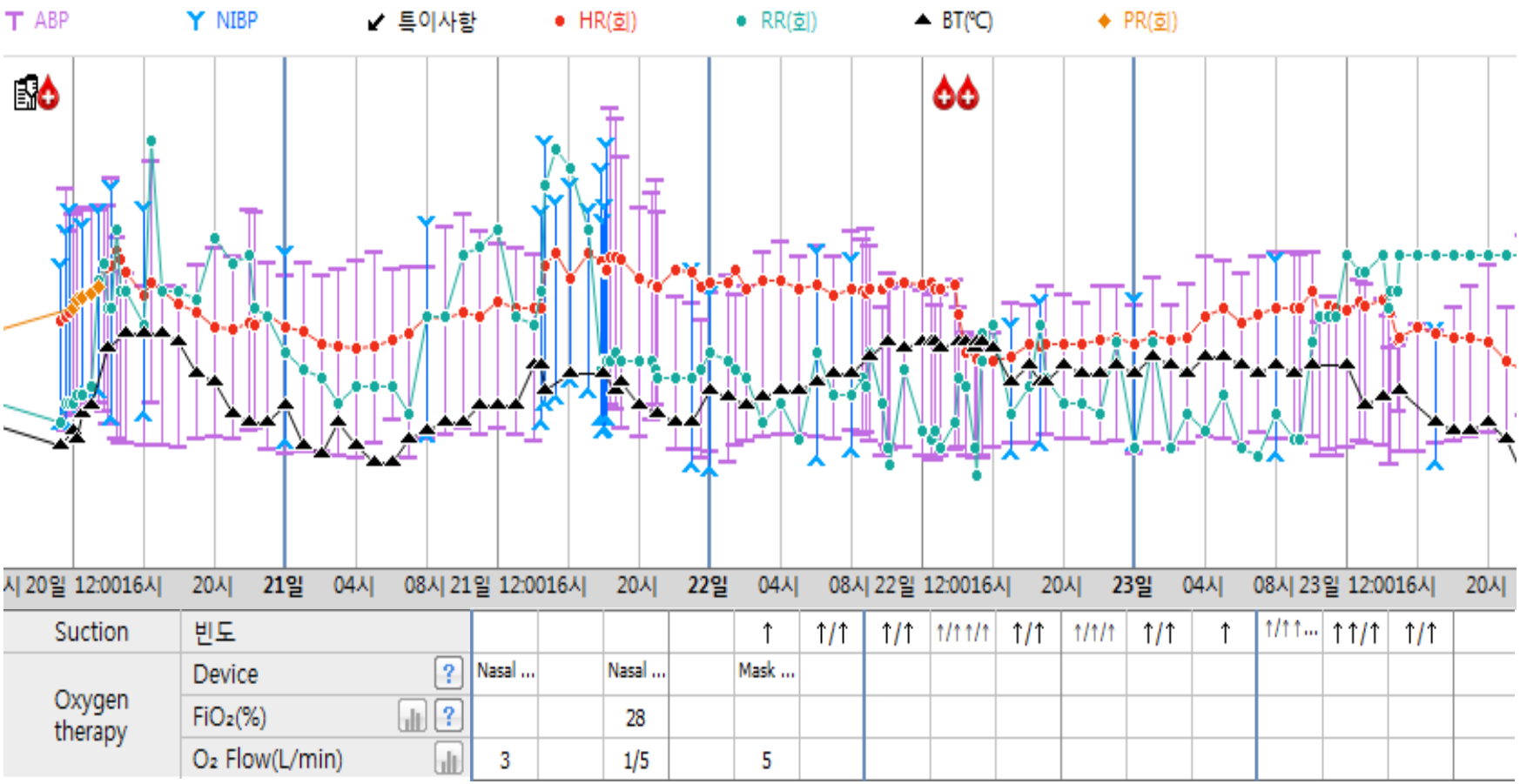
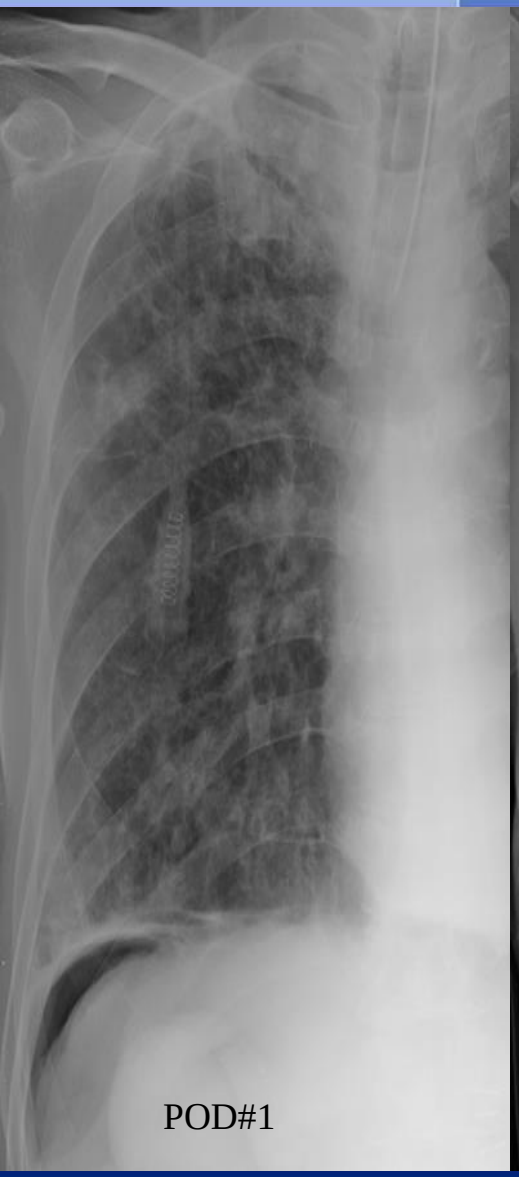
66 Male with AGC

Radical STG with Billroth I Anastomosis



66 Male with AGC

Progression of New Lung Infiltrates



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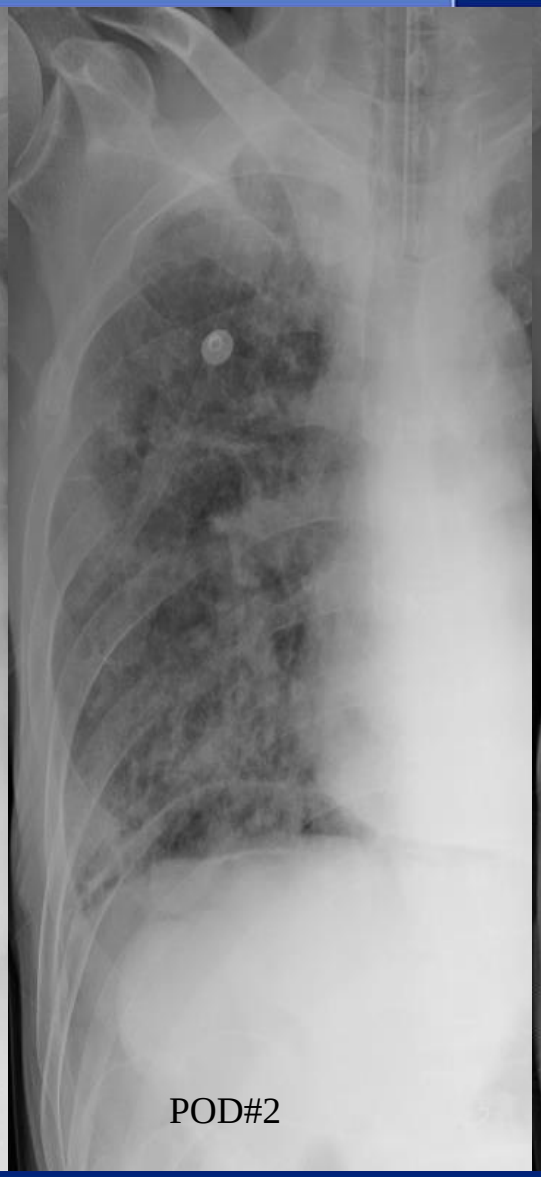

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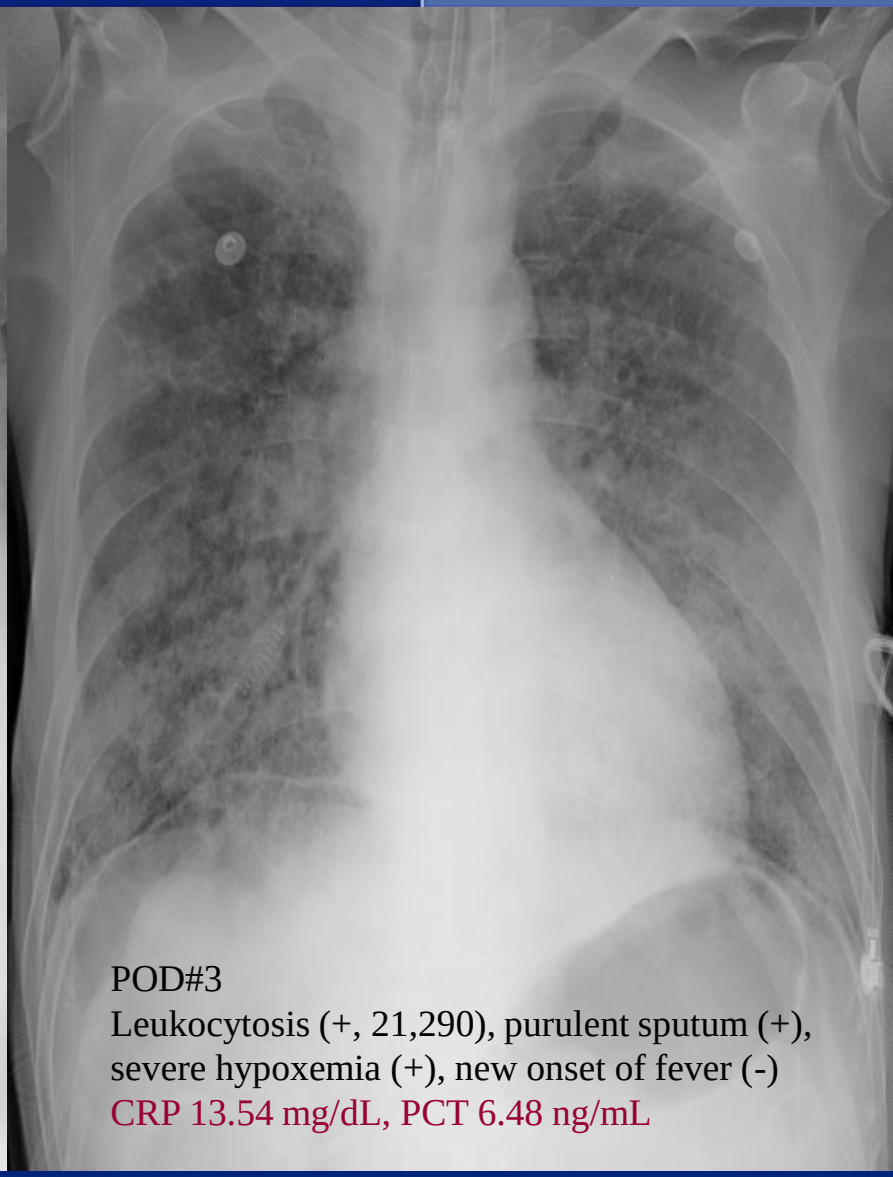


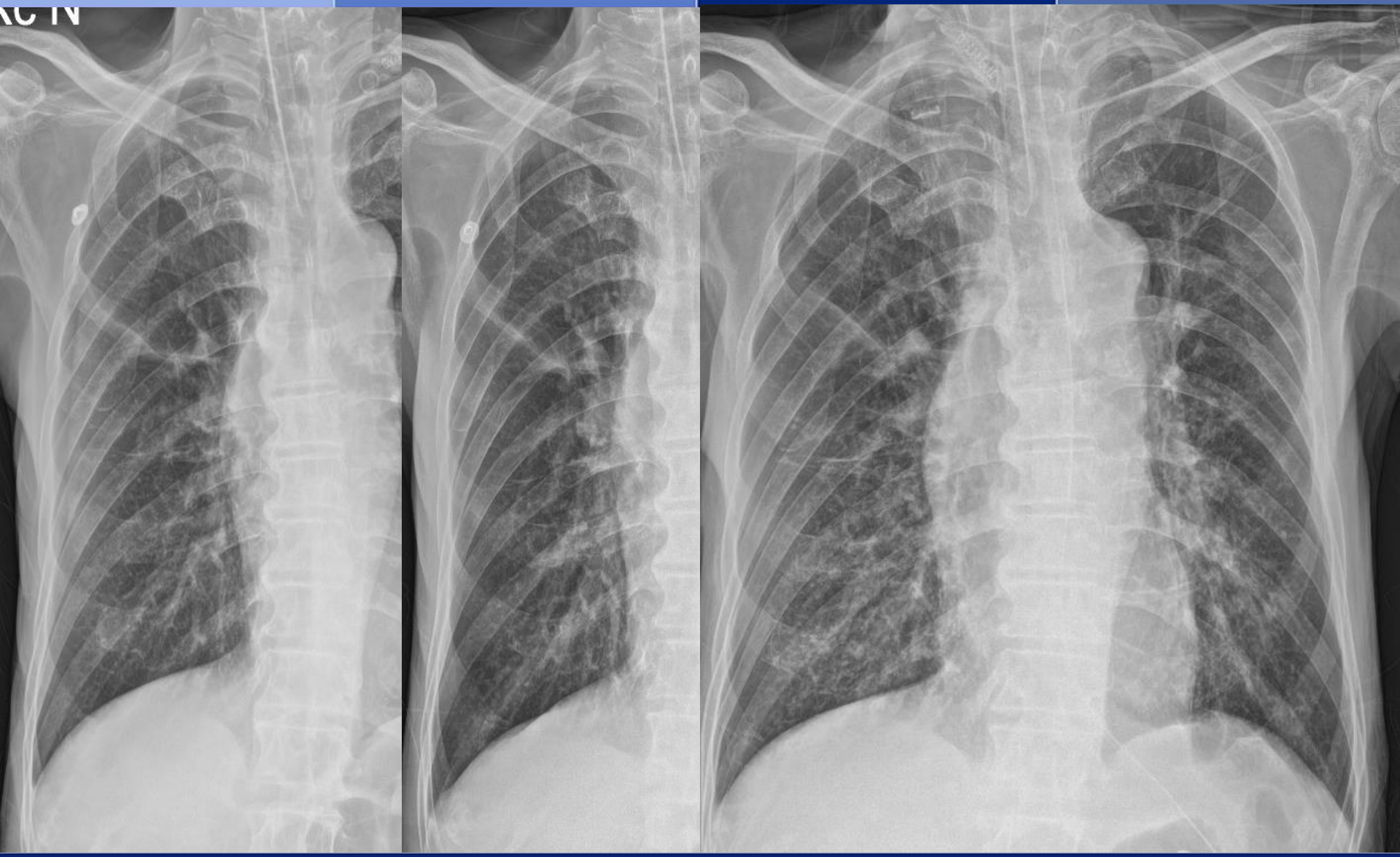
POD#3
Leukocytosis (+, 21,290), purulent sputum (+), severe hypoxemia (+), new onset of fever (-)
CRP 13.54 mg/dL, PCT 6.48 ng/mL

Sensitivity & Specificity of Clinical Variables
In Diagnosis of VAP

Finding and Source	Gold Standard	Sensitivity, %	Specificity, %	LR (95% CI) Positive	LR (95% CI) Negative
Fever					
Independent					
Chastre et al,[39] 1984	Histology alone	67	65	1.9 (0.84-4.3)	0.51 (0.16-1.7)
Torres et al,[41] 1994	Histology alone	56	58	1.3 (0.61-2.9)	0.76 (0.38-1.5)
Fàbregas et al,[45] 1999	Histology and culture	46	42	0.79 (0.37-1.7)	1.3 (0.56-3.0)
Summary				1.2 (0.76-1.9)	0.86 (0.54-4.1)
Abnormal WBC count					
Independent					
Chastre et al,[39] 1984	Histology alone	50	45	0.91 (0.37-2.2)	1.1 (0.44-2.8)
Fàbregas et al,[45] 1999	Histology and culture	77	58	1.8 (0.89-3.8)	0.40 (0.13-1.2)
Summary				1.3 (0.76-2.4)	0.74 (0.34-1.6)
Sputum purulence, macroscopic					
Independent					
Torres et al,[41] 1994	Histology alone	83	33	1.3 (0.80-2.0)	0.50 (0.14-1.8)
Fàbregas et al,[45] 1999	Histology and culture	69	42	1.2 (0.65-2.2)	0.74 (0.26-2.1)
Summary				1.3 (0.88-1.8)	0.63 (0.28-1.4)
Crepitation on auscultation					
Nonindependent					
Petersen et al,[10] 1999	Histology alone	73	40	1.2 (0.75-2.0)	0.68 (0.27-1.7)
Hypoxemia					
Nonindependent					
Petersen et al,[10] 1999	Histology alone	64	40	1.1 (0.63-1.8)	0.91 (0.40-2.1)
New infiltrate on radiograph					
Independent					
Chastre et al,[39] 1984	Histology alone	100	75	3.5 (1.7-7.5)	0.10 (0.01-1.4)
Torres et al,[41] 1994	Histology alone	78	42	1.3 (0.78-2.3)	0.53 (0.18-1.6)
Fàbregas et al,[45] 1999	Histology and culture	92	33	1.4 (0.88-2.2)	0.24 (0.03-1.8)
Summary				1.7 (1.1-2.5)	0.35 (0.14-0.87)

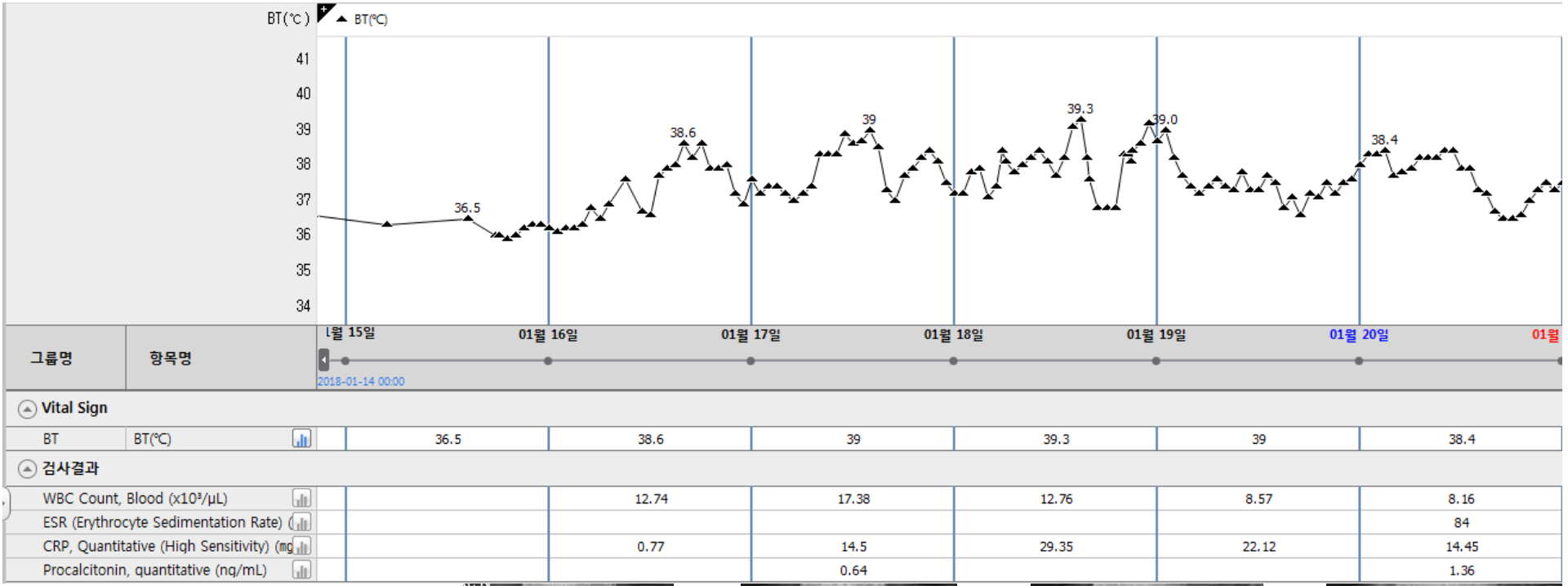
JAMA 2007;297:1583

67 YO Male on MV for Respiratory Failure

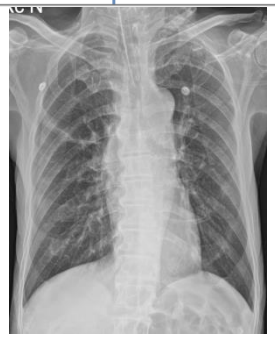


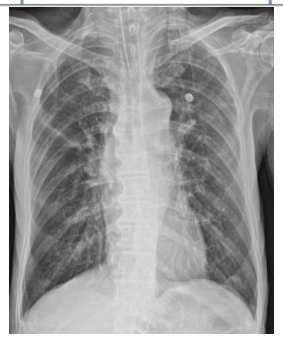
Delayed Diagnosis of VAP

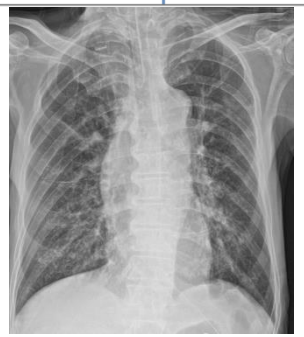
Slow Progression on CXR

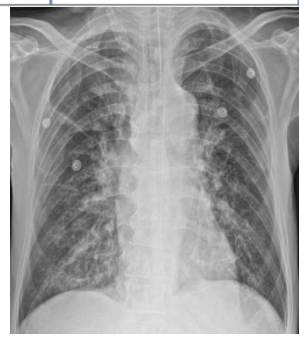


그룹명	항목명						
Vital Sign							
BT	BT(℃)	36.5	38.6	39	39.3	39	38.4
검사결과							
	WBC Count, Blood (x10³/μL)		12.74	17.38	12.76	8.57	8.16
	ESR (Erythrocyte Sedimentation Rate) (						84
	CRP, Quantitative (High Sensitivity) (mg		0.77	14.5	29.35	22.12	14.45
	Procalcitonin, quantitative (ng/mL)			0.64			1.36

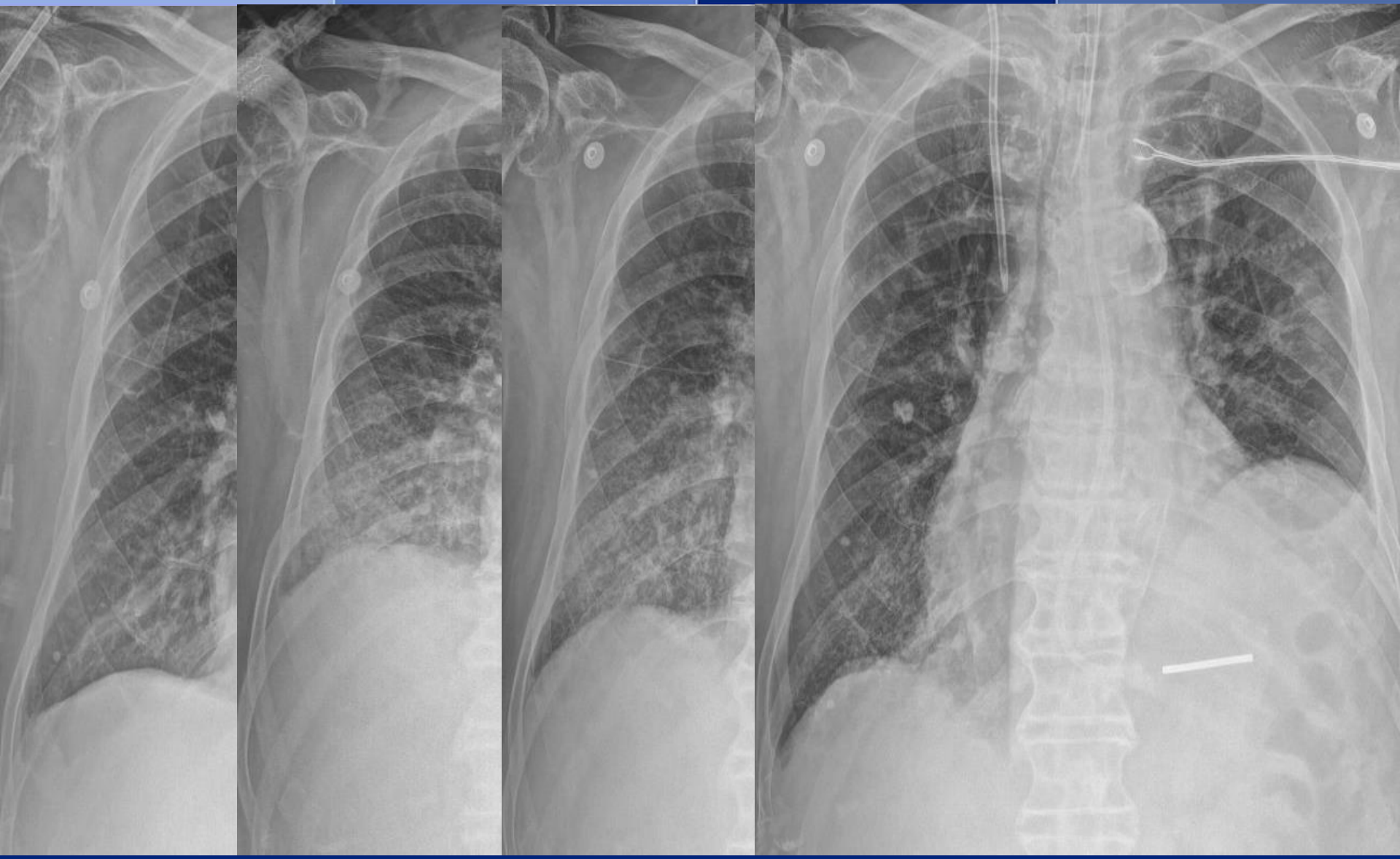








88 YO Male with AE of COPD



Difficulty in Clinical Diagnosis of HAP/VAP

- Prospective observation with suspected VAP (n = 84)
  - New & persistent infiltration on CXR & purulent tracheal aspirates
  - Clinical/histologic/microbiologic diagnosis

Have pneumonia		Not have pneumonia	
Definite	Probable	Definite	Probable
17 (20%)	10 (12%)	34 (41%)	23 (27%)

- Evaluation of clinical diagnosis ▶ not permit the accurate diagnosis

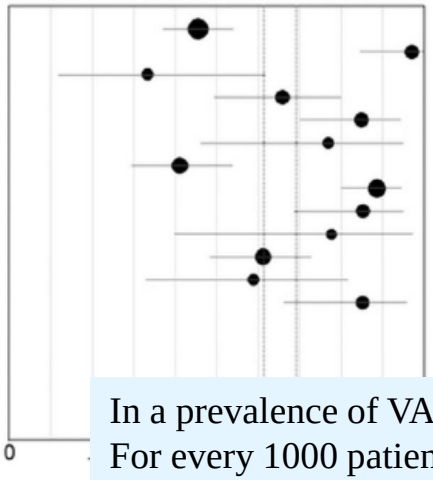
Predictions	Percentage of Accurate Prediction		
	All patients (n = 84)	Patients Who Had Pneumonia (n = 27)	Patients Who Did Not Have Pneumonia (n = 57)
All predictions	77	62	84
Predictions of			
Senior consultants (n = 110)	77	57	84
Staff physicians (n = 186)	72	56	81
Residents (n = 112)	78	70	81
Predictions			
Of best predictor	82	72	86
Of worst predictor	71	50	83
When decision was unanimous (n = 49)	90	79	94

Chest 1993;103:547

Diagnostic Accuracy of CPIS

Systematic Review and Meta-analysis

A



First Author	Year	Sensitivity	95% CI
Tejerina	2010	0.45	0.37–0.54
Pelosi	2008	0.97	0.85–1.00
Pham	2007	0.33	0.12–0.62
Veinstein	2006	0.66	0.49–0.80
Fartoukh	2003	0.85	0.70–0.94
Fábregas	1999	0.77	0.46–0.95
Carolina	2004	0.41	0.29–0.54
Luyt	2004	0.89	0.80–0.94
Jung	2010	0.85	0.69–0.95
Ramirez	2008	0.78	0.40–0.97
Croce	2006	0.61	0.49–0.73
Luyt	2008	0.59	0.33–0.82
Flanagan	2000	0.85	0.66–0.96

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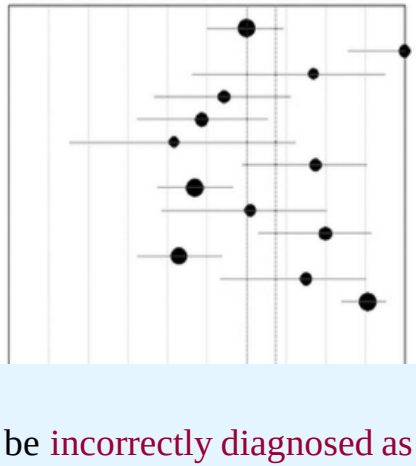
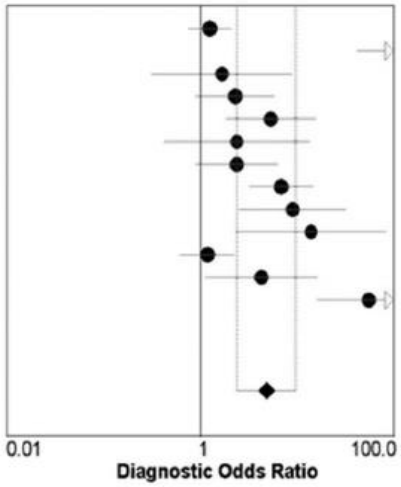


First Author	Year	Specificity	95% CI
Tejerina	2010	0.60	0.50–0.69
Pelosi	2008	1.00	0.86–1.00
Pham	2007	0.77	0.46–0.95
Veinstein	2006	0.54	0.37–0.71
Fartoukh	2003	0.49	0.32–0.65
Fábregas	1999	0.42	0.15–0.72
Carolina	2004	0.77	0.59–0.90
Luyt	2004	0.49	0.37–0.57
Jung	2010	0.61	0.39–0.80
Ramirez	2008	0.80	0.63–0.92
Croce	2006	0.43	0.33–0.54
Luyt	2008	0.75	0.53–0.90
Flanagan	2000	0.91	0.84–0.95

In a prevalence of VAP of 48%,
For every 1000 patients tested, 168 patients (16.8%) will be incorrectly diagnosed as not having HAP/VAP and 187 patients (18.7%) will be incorrectly diagnosed as having VAP

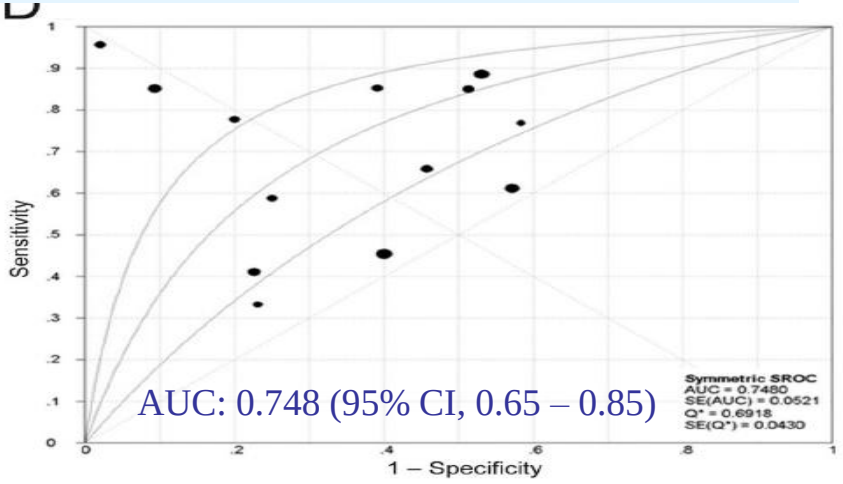
C



Tejerina	2010	1.25	0.76–2.07
Pelosi	2008	1,094.33	42.74–28,019.31
Pham	2007	1.67	0.31–8.93
Veinstein	2006	2.29	0.91–5.79
Fartoukh	2003	5.38	1.84–15.71
Fábregas	1999	2.38	0.42–13.39
Carolina	2004	2.40	0.91–6.33
Luyt	2004	6.89	3.24–14.66
Jung	2010	9.02	2.54–31.99
Ramirez	2008	14.00	2.37–82.72
Croce	2006	1.18	0.62–2.25
Luyt	2008	4.29	1.13–16.31
Flanagan	2000	55.93	16.35–191.33

Random Effects Model
Pooled Diagnostic Odds Ratio = 4.85 (2.42 to 9.71)
Cochran-Q = 67.85; df = 12 (P < .001)
Inconsistency (I^2) = 82.3%
Tau^2 - 1.2020

D



AUC: 0.748 (95% CI, 0.65 – 0.85)

Respir Care 2011;56:1087

Biomarkers for Dx of HAP/VAP

Results from Meta-analysis

Serum Procalcitonin				
Sensitivity	Specificity	PLR	NLR	Diagnostic OR
67% (53%–79%)	83% (43%–97%)	3.9 (9–17.5)	0.4 (.25–.62)	10 (2–59)
AUC: 0.76 (95% CI, .72–.79)				

In a prevalence of HAP/VAP of 50%,
For every 1000 patients with suspected HAP/VAP who are evaluated with serum PCT plus clinical criteria, 165 patients (16.5%) would be incorrectly diagnosed as not having HAP/VAP and 85 patients (8.5%) will be incorrectly diagnosed as having HAP/VAP.

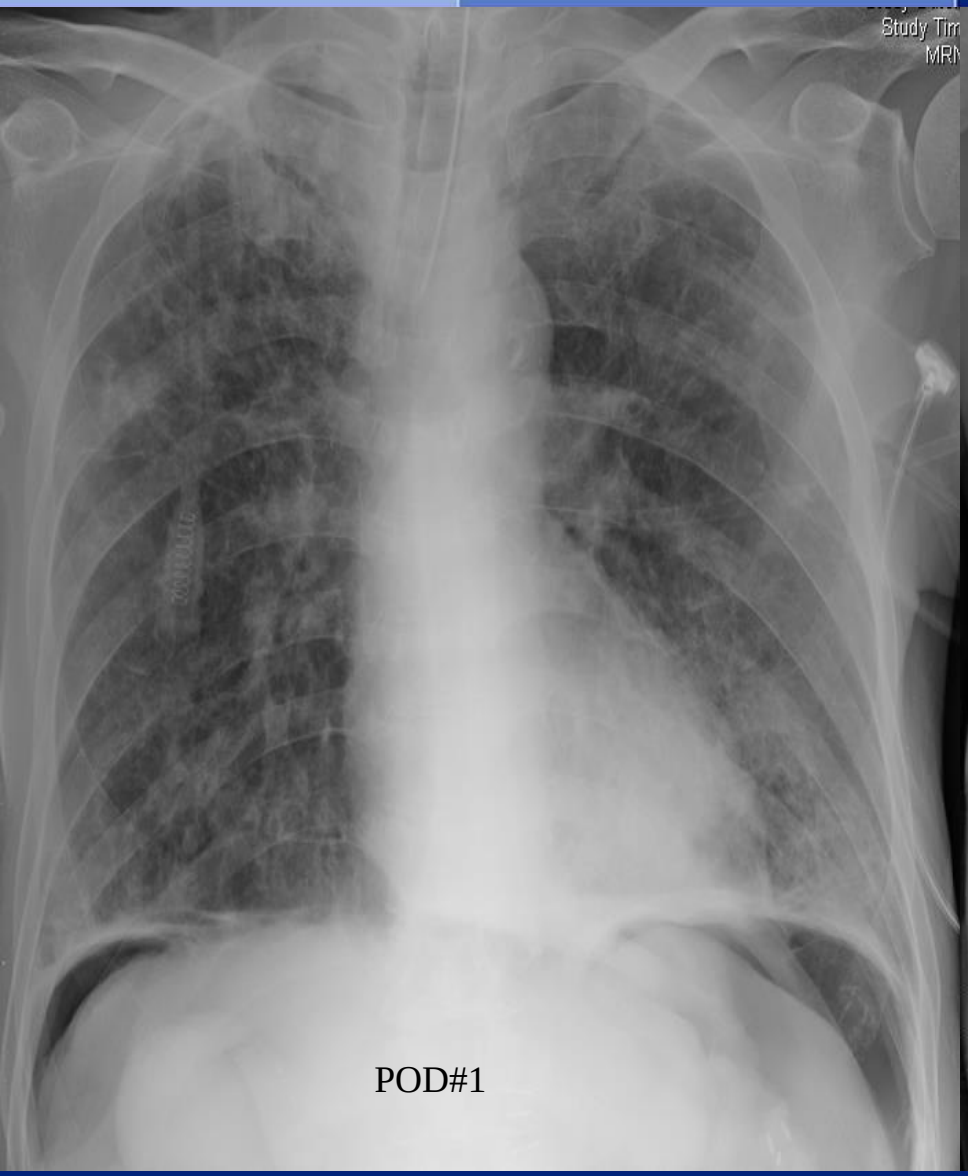
BAL fluid sTREM-1				
Sensitivity	Specificity	PLR	NLR	Diagnostic OR
84% (63%–94%)	49% (18%–81%)	1.6 (.8%–3.3)	0.33 (.12–0.93)	5 (1–24),
AUC: 0.78 (95% CI, .75–.82)				

In a prevalence of HAP/VAP of 50%,
For every 1000 patients tested, 80 patients (8%) will be incorrectly diagnosed as not having HAP/VAP and 255 patients (25.5%) will be incorrectly diagnosed as having HAP/VAP.

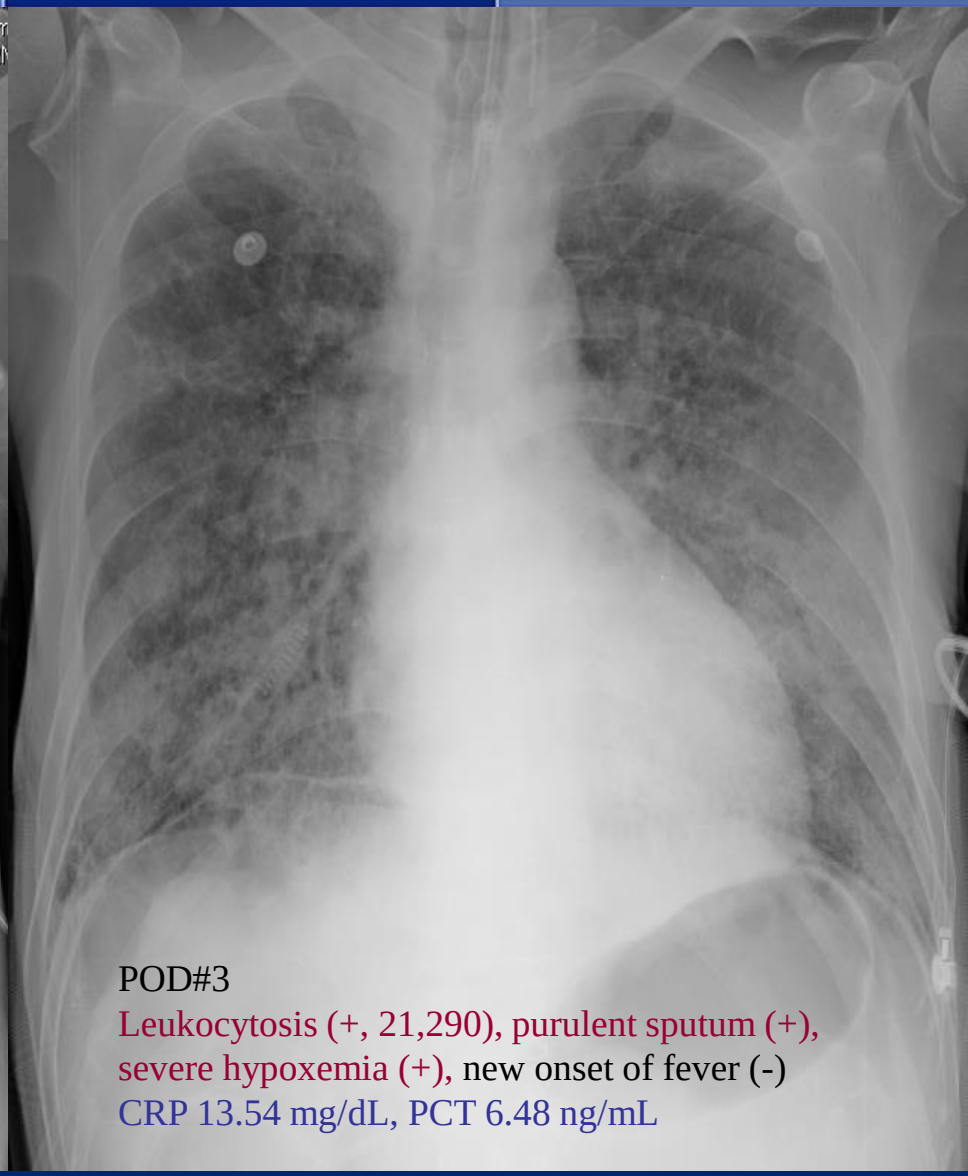
▶ For patients with suspected HAP/VAP, the guideline recommends using clinical criteria alone, rather than using serum PCT or BAL fluid sTREM-1 plus clinical criteria, to decide whether or not to initiate antibiotic therapy (strong recommendation, moderate-quality evidence).

Clin Infect Dis 2016;63(5):e61

66 Male with AGC
Diagnosis of HAP/VAP



POD#1



POD#3
Leukocytosis (+, 21,290), purulent sputum (+),
severe hypoxemia (+), new onset of fever (-)
CRP 13.54 mg/dL, PCT 6.48 ng/mL

Classification of HAP/VAP by Time of Onset
Early vs. Late

- Rationale of prior classification
  - Upper airway colonization was an independent predictor of subsequent tracheobronchial colonization
  - Colonization patterns in the upper and lower airways changed within the first 3–4 days from a community-like to a typical nosocomial pattern

Early onset	**Late onset**
Within < 5 days	After ≥ 5 days
• Antibiotic sensitive bacteria - *Streptococcus pneumoniae* - *Haemophilus influenzae* - *Staphylococcus aureus* • Better prognosis	• Multidrug-resistant (MDR) pathogens - *P. aeruginosa* - *Acinetobacter* species - MRSA • Associated with increased mortality and morbidity

Am J Respir Crit Care Med 2002;165:867

Early- and Late-Onset Pneumonia
Is This Still a Useful Classification?

TABLE 3. Isolates per 100 pneumonia cases for the most frequent microorganisms, together with the order of frequency of the four most frequent pathogens[a]

Pathogen	No. of isolates per 100 pneumonia cases (order of frequency)					
	"Early-onset" pneumonia			"Late-onset" pneumonia		
	1–4 days	1–5 days	1–7 days	>4th day	>5th day	>7th day
S. aureus	25.7 (1st)	26.8 (1st)	26.9 (1st)	23.7 (1st)	23.0 (1st)	21.0 (1st)
MSSA	21.4	22.9	22.7	16.8	13.8	14.5
MRSA	4.3	4.0	4.3	6.9	6.5	6.5
P. aeruginosa	11.6 (2nd)	11.6 (2nd)	11.9 (2nd)	17.4 (2nd)	16.1 (2nd)	19.9 (2nd)
K. pneumoniae	10.8 (3rd)	10.7 (4th)	11.1 (3rd)	11.8 (3rd)	10.6 (3rd)	12.6 (3rd)
E. coli	10.0 (4th)	10.8 (3rd)	10.6 (4th)	10.1 (4th)	8.7 (4th)	10.1 (4th)
S. pneumoniae	9.3	8.9	8.3	5.1	4.2	4.3
Enterobacter spp.	6.4	6.7	7.5	8.8	7.9	9.4
Haemophilus spp.	6.9	6.9	6.7	3.9	3.1	2.9
Acinetobacter spp.	2.6	2.6	3.2	4.8	4.5	5.5
S. maltophilia	1.3	1.3	1.4	3.1	3.0	3.8

[a] From KISS, 1997 to 2004.

Thus, the predictabilities of the occurrence of pathogens were similar for the earlier (1997-to-2004) and later (2005-to- 2006) time frames. This classification is no longer helpful for empirical antibiotic therapy, since the pathogens are the same for both groups.

Antimicrob Agents Chemother 2009; 53: 2714

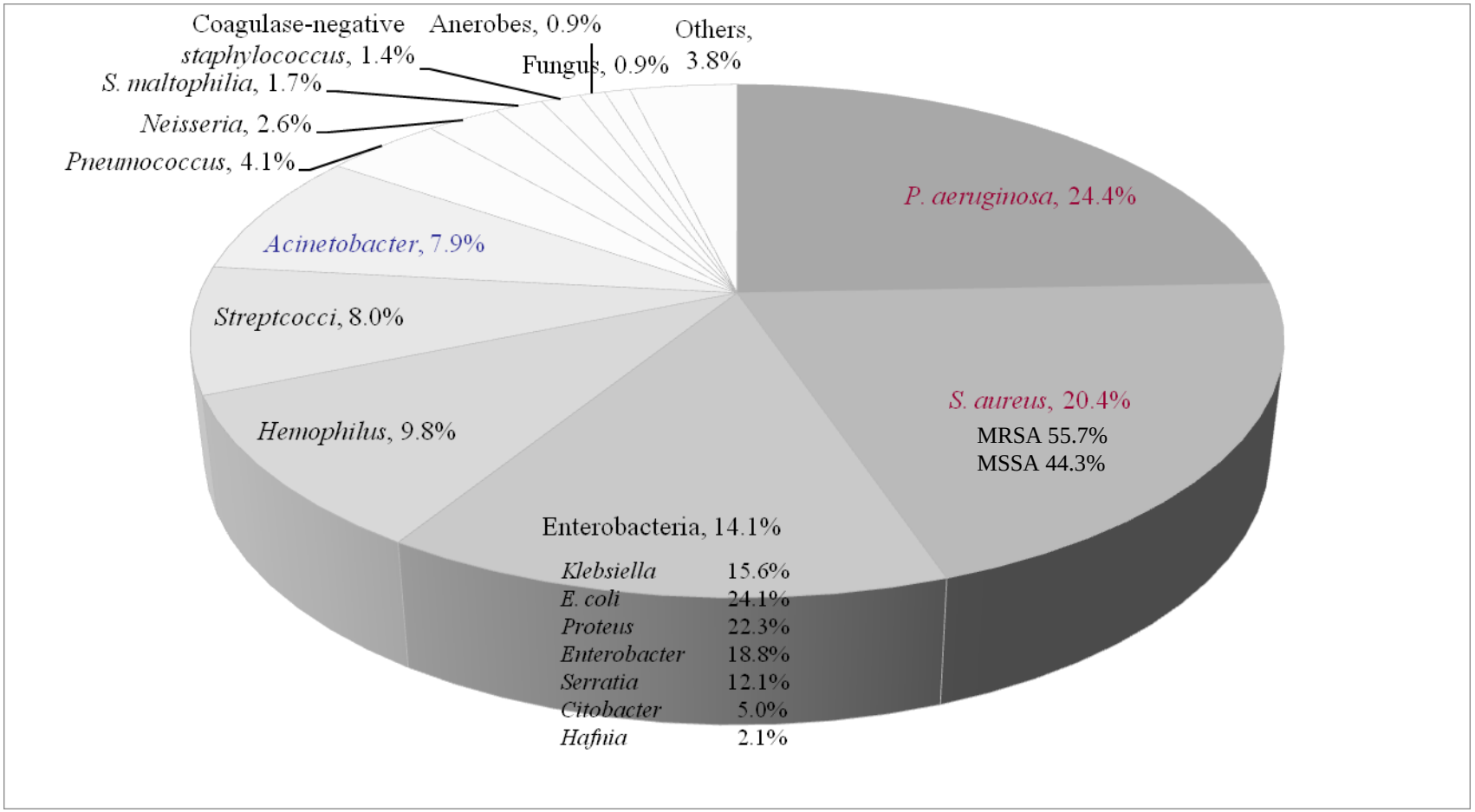
Risk Factors for MDR Pathogens
ATS/IDSA, 2016

Risk factors for MDR VAP
Prior intravenous antibiotic use within 90 d Septic shock at time of VAP ARDS preceding VAP Five or more days of hospitalization prior to the occurrence of VAP Acute renal replacement therapy prior to VAP onset
Risk factors for MDR HAP
Prior intravenous antibiotic use within 90 d
Risk factors for MRSA VAP/HAP
Prior intravenous antibiotic use within 90 d
Risk factors for MDR Pseudomonas VAP/HAP
Prior intravenous antibiotic use within 90 d
Factors **not** associated with MDR risk
Re-intubation Immunosuppression Chronic respiratory failure Tracheostomy Diabetes Recent use of corticosteroids

Clin Infect Dis 2016;63(5):e61

Microbiologic Epidemiology of VAP

Data from 24 Studies in US



Am J Respir Crit Care Med 2002;165:867

Microbiologic Epidemiology of VAP

National Healthcare Safety Network (NHSN), U.S., 2009-2010

Pathogen	Frequency	Antimicrobial Resistance Rates
Staphylococcus aureus	24.1%	Methicillin / oxacillin resistant – 48%
Pseudomonas aeruginosa	16.6%	Ciprofloxacin / levofloxacin resistant – 33% Imipenem / meropenem resistant – 30% Cefepime / ceftazidime resistant – 28% Piperacillin-tazobactam resistant – 19% Aminoglycoside resistant – 11% Resistant to ≥3 of the above classes – 18%
Klebsiella species	10.1%	Cefepime / ceftazidime / cefotaxime resistant – 24% Imipenem / meropenem resistant – 11% Resistant to ≥3 classes – 13%
Enterobacter species	8.6%	Cefepime / ceftazidime / ceftriaxone resistant – 30% Imipenem / meropenem resistant – 4% Resistant to ≥3 classes – 1%
Acinetobacter baumannii	6.6%	Imipenem / meropenem resistant – 61% Resistant to ≥3 classes – 63%
Escherichia coli	5.9%	Ciprofloxacin / levofloxacin resistant – 35% Cefepime / ceftazidime / ceftriaxone resistant – 16% Imipenem / meropenem resistant – 4% Resistant to ≥3 classes – 3%

Infect Control Hosp Epidemiol 2013;34:1

Differences in Causative Pathogens

Pathogen	Percentage of cases			
	United States (n = 2585)		All regions (n = 7496)	
	HABP	VABP	HABP	VABP
Staphylococcus aureus	36.5[a]	31.9[a]	26.6[a]	19.5[a]
Pseudomonas aeruginosa	19.0[a]	21.4[a]	22.4[a]	26.6[a]
Enterobacter species	8.6	8.8	7.5	7.0
Klebsiella species	8.0	6.6	10.5	10.2
Serratia species	5.5	6.5	4.1	4.1
Acinetobacter species	4.4	5.3	8.3[a]	14.3[a]
Top 6 species	80.4	80.5	79.4	81.7
Pathogens causing CABP[b]	3.3	6.6	2.6	4.1

Clin Infect Dis 2010; 51(suppl 1):S81

Microbiologic Epidemiology of VAP in Asia

Asian HAP Working Group, 2008

	India	Thailand	Malaysia	China	Korea	Taiwan
Acinetobacter spp	38%	30%	23%	16%	26%	20%
P. aeruginosa	20%	18%	18%	18%	18%	21%
MRSA	5%	8%	12%	16%	34%	18%
Klebsiella spp	23%	7%	6%	14%	9%	9%
E. coli	-	-	-	6%	-	4%
Enterobacteriaceae	-	-	-	8%	-	3%
S. maltophilia	2%	-	11%	-	6%	3%

Am J Infect Control 2008;36:S83

Microbiologic Epidemiology of VAP in SMC
MICU, 2017.01

접수일자	보고일자	검사코드	검사명	검체명	미생물명
2017-01-01 13:50:48	2017-01-03 10:12:48	BL4020	Gram Stain/Culture	(Endo)Tracheal Aspir	Acinetobacter baumannii complex (CRGNB)
2017-01-03 11:24:00	2017-01-06 11:02:50	BL4020	Gram Stain/Culture	(Endo)Tracheal Aspir	Staphylococcus aureus (MRSA)
2017-01-06 22:10:53	2017-01-10 11:52:35	BL4020	Gram Stain/Culture	(Endo)Tracheal Aspir	Acinetobacter baumannii complex (CRGNB)
2017-01-08 00:20:04	2017-01-10 11:58:22	BL4020	Gram Stain/Culture	(Endo)Tracheal Aspir	Stenotrophomonas maltophilia
2017-01-08 18:57:24	2017-01-11 11:08:04	BL4020	Gram Stain/Culture	(Endo)Tracheal Aspir	Pseudomonas aeruginosa
2017-01-16 11:32:36	2017-01-18 11:43:07	BL4020	Gram Stain/Culture	(Endo)Tracheal Aspir	Serratia marcescens
2017-01-19 10:13:24	2017-01-21 10:27:46	BL4020	Gram Stain/Culture	(Endo)Tracheal Aspir	Pseudomonas aeruginosa
2017-01-24 18:25:52	2017-01-27 18:05:34	BL4020	Gram Stain/Culture	(Endo)Tracheal Aspir	Pseudomonas aeruginosa

Microbiologic Epidemiology of VAP in SMC
MICU, 2017.09~11

Pathogen for VAP	Number (%)	Drug resistance
Staphylococcus aureus	11 (24%)	MRSA
Acinetobacter baumannii	10 (22%)	CR 9 (90%)
Pseudomonas aeruginosa	8 (18%)	CR 6 (75%)
Stenotrophomonas maltophilia	7 (16%)	
Enterobacteriaceae	6 (13%)	
Others	3	

▶ Individual hospitals should determine their most appropriate antimicrobial regimens for the empiric treatment of VAP base on the hospital specific microbiologic information

Chest 2000;117:1434
Infect Control Hosp Epidemiol 2007; 28:389

Microorganism Isolated (n=211, 40.1%)
Korean HAP/VAP Study

Microorganism	No. of patients
Gram-positive pathogens	
Staphylococcus aureus	24
Streptococcus pneumonia	7
Enterococcus faecium	5
Nonstaphylococcus aureus Staphylococcus species	4
Others*	5
Gram-negative pathogens	
Acinetobacter baumannii	68
Pseudomonas aeruginosa	36
Klebsiella pneumoniae	35
Escherichia coli	11
Sternotrophomonas maltophilia	11
Enterobacter cloacae	10
Serratia marcescens	5
Proteus species	4
Klebsiella aerogenes	3
Moraxella catarrhalis	2
Burkholderia cephacia	2
Citrobacter species	2
Others**	2

*Others included one *Streptococcus pyogenes*, one *Streptococcus mitis*, one *Streptococcus agalactiae*, one *Streptococcus angiosus*, and one *Listeria monocytogenes*.
**Others included one *Klebsiella oxytoca* and one *Raoultella planticola*.

Initial Management of HAP/VAP in Practice

ATS/IDSA Guideline, 2016

Suspected HAP/VAP

- Presence of **new or progressive infiltrate**
- At least 2 of **fever, increase in WBC count**, and **purulence**

↓

Obtain lower respiratory tract specimen using noninvasive sampling for culture

- Antibiotic regimen can be adjusted on the basis of those results
- Opportunity to de-escalate antibiotic coverage based on the results

↓

Empiric treatment regimens informed by the local distribution of pathogens associated with HAP/VAP and their antimicrobial susceptibilities

Rapid Diagnostic Tests
Approved by US FDA

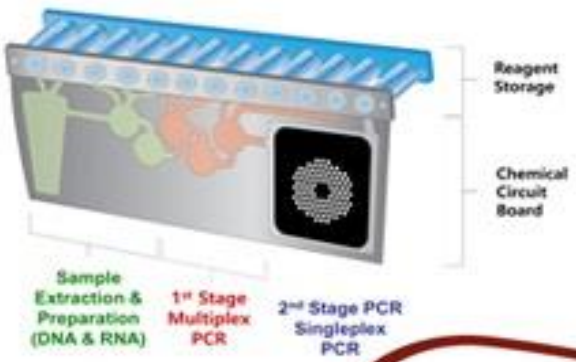




System	**FilmArray (BioMérieux)**	BD MAX (BD)	**eSensor (GenMark)**	**Verigene (Luminex)**	**NxTAG (Luminex)**	GeneXpert (Cepheid)
Method	Multiplex PCR with melt curve analysis	Real-time PCR	DNA hybridization	Microarray using nanoparticle probes	PCR with liquid phase bead array	On-demand PCR
Turnaround time	~ 1 h	~ 2 h	~ 6 hr	~ 2.5 h	< 4 hr	0.5-3 h
CLIA complexity	Moderate	Moderate	High	Moderate	High	Moderate/ waived
Panels	Resp, BC, GI, meningitis	MRSA, C. diff, GI, STD	Resp, BC	Resp, BC, GI	Resp	MRSA, CRE, VRE, C. diff

Clin Infect Dis 2016;63:1361

BioFire® FilmArray® System



FILMARRAY

+

+

Sample Prep | Amplification | Detection

Simple: Only 2 minutes of hands-on time

Easy: No precise pipetting required

Fast: Run time of about 1 hour

https://www.biomerieux-diagnostics.com/filmarray

BioFire® FilmArray® Pneumonia *plus* Panel

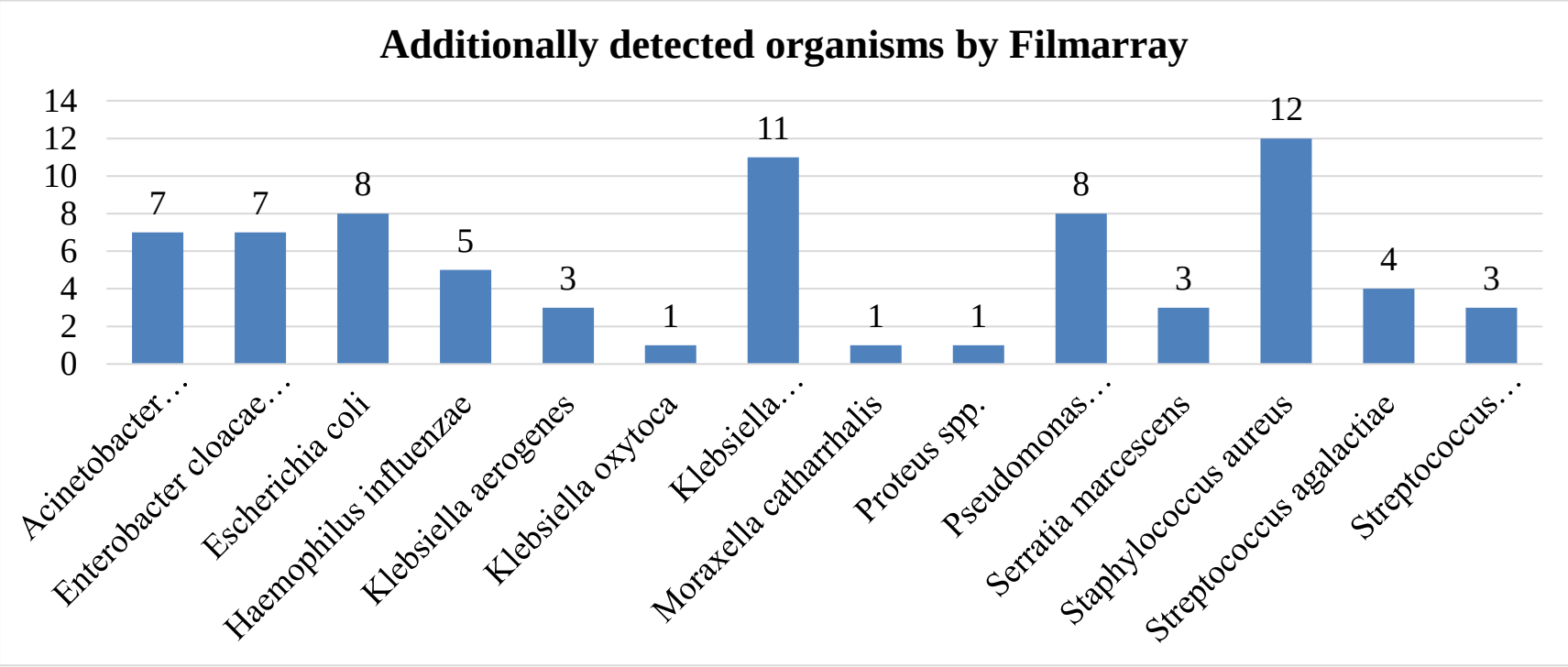
Bacteria (semi quantitative)	Antibiotic Resistance Genes	Viruses
• ***Acinetobacter calcoaceticus-baumannii* complex** • *Serratia marcescens* • *Proteus* spp. • ***Klebsiella pneumoniae* group** • ***Enterobacter aerogenes*** • ***Enterobacter cloacae*** • *Escherichia coli* • *Haemophilus influenzae* • *Moraxella catarrhalis* • ***Pseudomonas aeruginosa*** • ***Staphylococcus aureus*** • *Streptococcus pneumoniae* • *Klebsiella oxytoca* • *Streptococcus pyogenes* • *Streptococcus agalactiae* • ~~*Stenotrophomonas maltophilia*~~	**ESBL** CTX-M **Carbapenemases** KPC NDM Oxa48-like ~~Oxa23~~ ~~Oxa51~~ VIM IMP **Methicilin Resistance** mecA/mecC and MREJ	• Influenza A • Influenza B • Adenovirus • Coronavirus • Parainfluenza virus • Respiratory Syncytial virus • Human Rhinovirus/Enterovirus • Human Metapneumovirus • Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

Diagnostic Performance
SMC Experience

Evaluation of the BioFire FilmArray Pneumonia Panel for rapid detection of respiratory bacterial pathogens and antibiotic resistance genes in sputum and endotracheal aspirate specimens

In Young Yoo[a,1], Kyungmin Huh[b,c,1], Hyang Jin Shim[d], Sun Ae Yun[d], Yoo Na Chung[a], On Kyun Kang[a], Hee Jae Huh[a,*], Nam Yong Lee[a,*]

International Journal of Infectious Diseases 95 (2020) 326–331



Potential Tx Changes by FilmArray (n=46)

SMC Experience

Potential treatment changes based on FilmArray Pneumonia Panel *plus* for 46 cases of suspected pneumonia.

Treatment modification	Cases, number (%)
No modification	**23 (50.0%)**
Treatment changed	**23 (50.0%)**
Antibiotic escalation	**13 (28.3%)**
Vancomycin	3
Carbapenem	2
Agents covering CRGNB[a]	8
Antibiotic de-escalation	**10 (21.7%)**
Vancomycin	3
Meropenem	3
Piperacillin/tazobactam	2
Vancomycin and meropenem	1
Vancomycin and amikacin	1

[a] Carbapenem-resistant gram-negative bacilli.

Int J Infect Dis 2020;95:326

Multicenter Evaluation of BioFire FilmArray

French FA-PP Study

A B S T R A C T

Objectives: To evaluate performances of the rapid multiplex PCR assay BioFire FilmArray Pneumonia Panel (FA-PP) for detection of bacterial pathogens and antibiotic resistance genes in sputum, endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL) specimens.

Methods: This prospective observational study was conducted in 11 French university hospitals (July to December 2018) and assessed performance of FA-PP by comparison with routine conventional methods.

Results: A total of 515 respiratory specimens were studied, including 58 sputa, 217 ETA and 240 BAL. The FA-PP detected at least one pathogen in 384 specimens, yielding an overall positivity rate of 74.6% (384/515). Of them, 353 (68.5%) specimens were positive for typical bacteria while eight atypical bacteria and 42 resistance genes were found. While identifying most bacterial pathogens isolated by culture (374/396, 94.4%), the FA-PP detected 294 additional species in 37.7% (194/515) of specimens. The FA-PP demonstrated positive percentage agreement and negative percentage agreement values of 94.4% (95% CI 91.7%–96.5%) and 96.0% (95% CI 95.5%–96.4%), respectively, when compared with culture. Of FA-PP false-negative results, 67.6% (46/68) corresponded to bacterial species not included in the panel. At the same semi-quantification level (in DNA copies/mL for FA-PP versus in CFU/mL for culture), the concordance rate was 43.4% (142/327) for culture-positive specimens with FA-PP reporting higher semi-quantification of $\geq$1 $\log_{10}$ in 48.6% (159/327) of cases. Interestingly, 90.1% of detected bacteria with $\geq 10^6$ DNA copies/mL grew significantly in culture.

Conclusions: FA-PP is a simple and rapid molecular test that could complement routine conventional methods for improvement of diagnosis accuracy of pneumonia. **Nabil Gastli, Clin Microbiol Infect 2020;▪:1**

Clin Microbiol Infect 2021 (in press)

Unyvero LRT Panel, Curetis

FDA-cleared Unyvero uniquely and accurately detects the most clinically relevant pathogens and antibiotic resistance markers associated with pneumonia.

BACTERIA		RESISTANCE	GENES	
Acinetobacter spp.	*Moraxella catarrhalis*	Carbapenems	*kpc*	*oxa*-48
Chlamydia pneumoniae	*Morganella morganii*		*ndm*	*oxa*-58
Citrobacter freundii	*Mycoplasma pneumoniae*		*oxa*-23	*vim*
Enterobacter cloacae complex	*Proteus* spp.		*oxa*-24	
Escherichia coli	*Pseudomonas aeruginosa*	3rd Generation Cephalosporins	*ctx*-M	
Haemophilus influenzae	*Serratia marcescens*	Oxacillin/Cefoxitin	*mec*A	
Klebsiella oxytoca	*Staphylococcus aureus*	Penicillin	*tem*	
Klebsiella pneumoniae	*Stenotrophomonas maltophilia*			
Klebsiella variicola	*Streptococcus pneumoniae*			
Legionella pneumophila				

FUNGI
Pneumocystis jirovecii *

* included on the Unyvero LRT BAL panel.

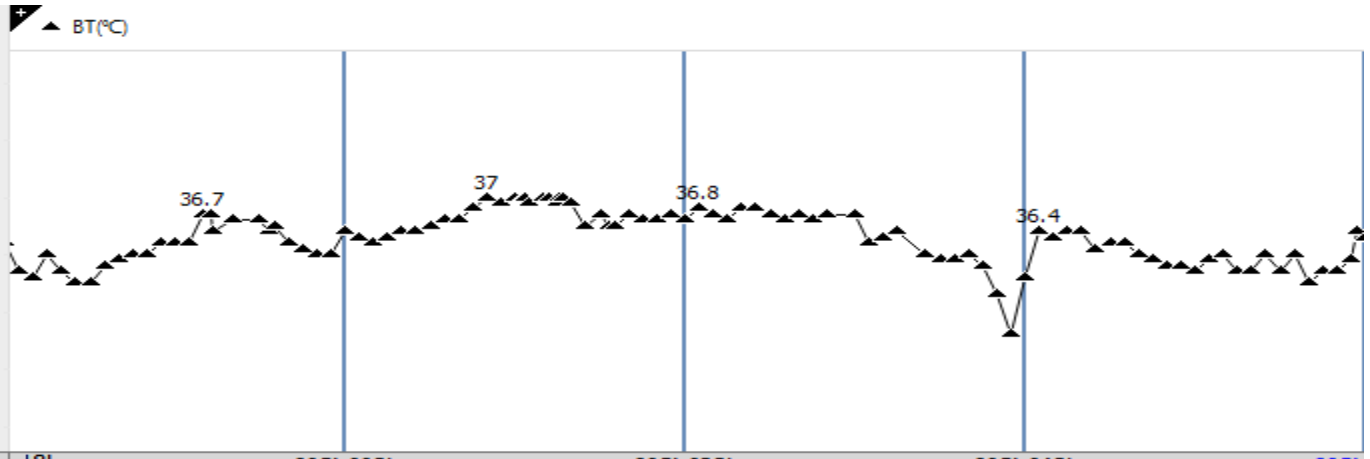
- Rapid, sample to answer direct from native specimen
- Simple and clear qualitative results based on quantitative algorithms
- Critical information for life-saving treatment decisions

Specimen Types:
- Endotracheal Aspirate
- Bronchoalveolar Lavage (including mini-BAL)

66 Male with AGC

Empiric Therapy with Cefepime 2g q 12hr

- Prior intravenous antibiotic (-)
- Septic shock (-)
- ARDS (-)
- ≥ 5 days of hospitalization (-)
- RRT (-)



그룹명	항목명				
Vital Sign					
BT	BT(℃)	36.7	37	36.8	36.4
검사결과					
WBC Count, Blood (x10³/μL)		21.29	14.38	8.89	10.61
CRP, Quantitative (High Sensitivity) (mg		13.54	11.97	13.99	16.08
Procalcitonin, quantitative (ng/mL)		6.48			
항생제					
Cefepime(g)		✓	✓	✓	✓
Vancomycin HCl(g)				✓	✓
Levofloxacin(mg)				✓	✓
Cefotetan(g)					
미생물검사					
Gram Stain and Cultur...	Nasal-MRSA	✓			
	(Endo)Tracheal Aspir		✓		
Funqus C...	(Endo)Tracheal Aspir		✓		

Dosing of Cefepime in Adults
Clinical Drug Information, Lexicomp®

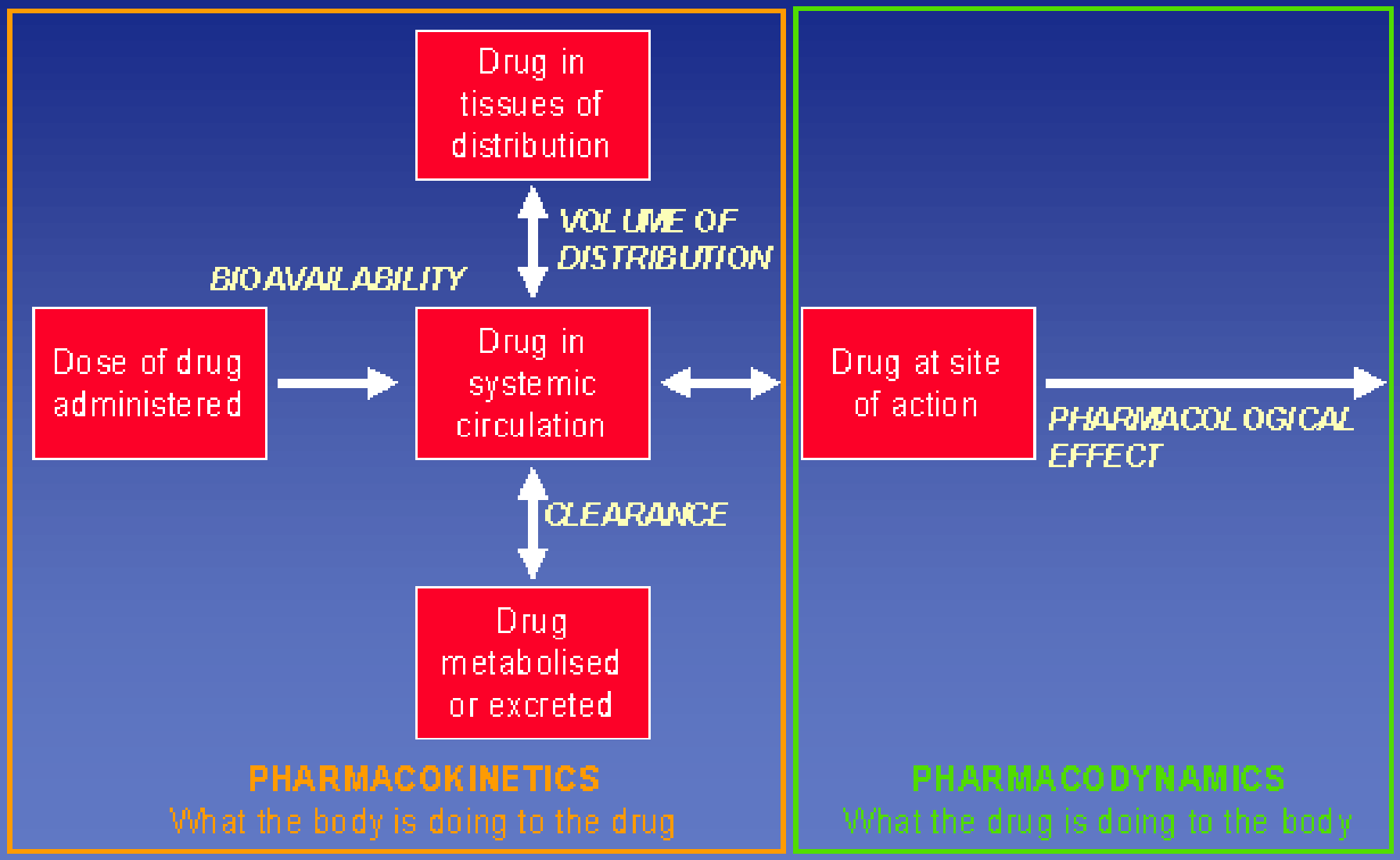
- **Pneumonia:** IV:
- *Manufacturer's labeling:*
  - Due to *P. aeruginosa:* 2 g every 8 hours for 10 days
  - Not due to *P. aeruginosa:* 1 to 2 g every 8 to 12 hours for 10 days
- *Alternate dosing:* Hospital-acquired or ventilator-associated: 2 g every 8 hours for 7 days; may consider shorter or longer duration depending on rate of clinical improvement. Administration as an extended infusion may be considered. When used as empiric therapy, use in combination with an agent active against MRSA (unless coverage of MSSA only is appropriate) with or without an additional antipseudomonal agent (dependent on patient and institution-specific risk factors) (Kalil 2016)

Initial Empiric Antibiotic Therapy for VAP

Antibiotic Dosing

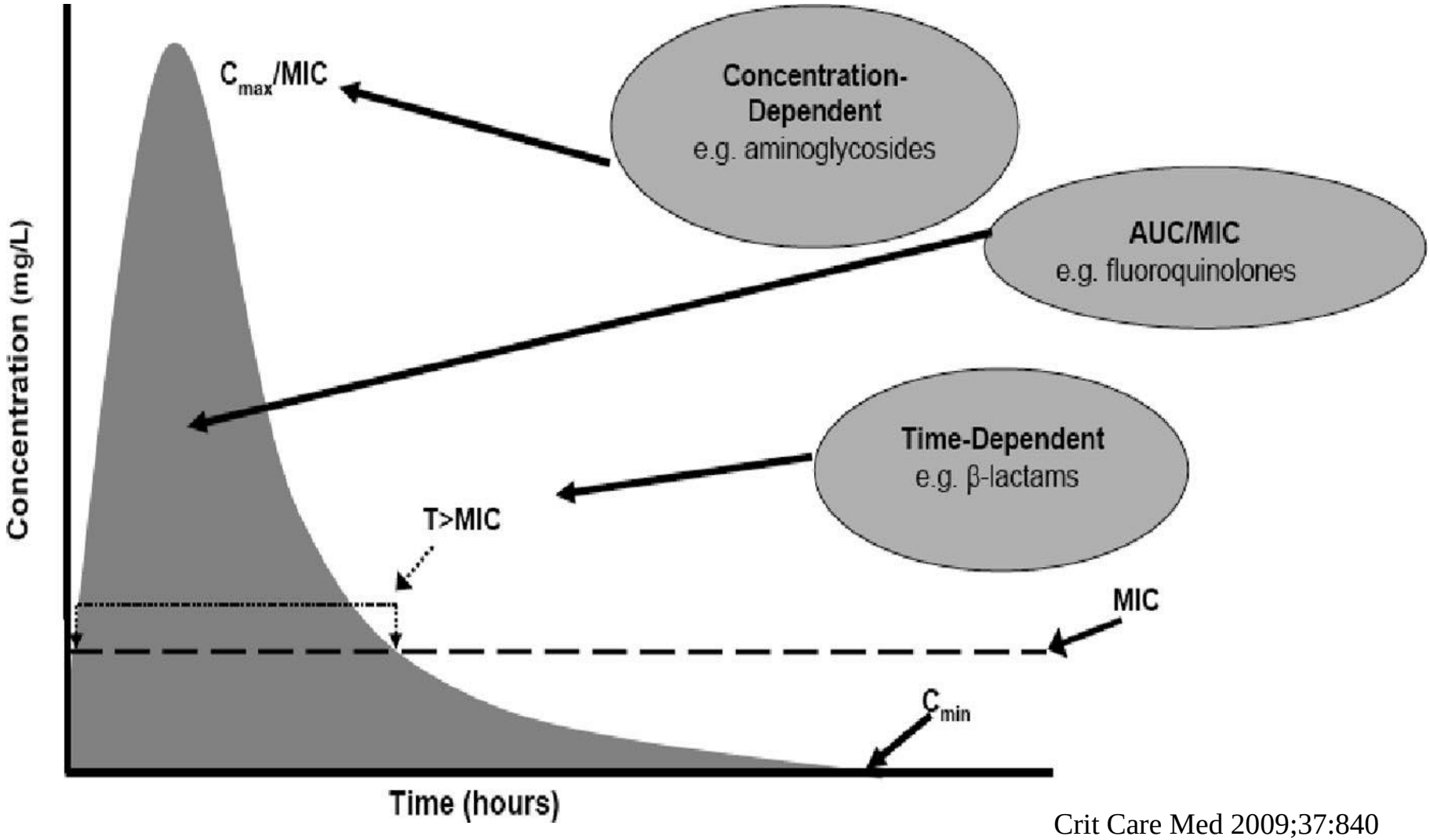
A. Gram-Positive Antibiotics With MRSA Activity	B. Gram-Negative Antibiotics With Antipseudomonal Activity: β-Lactam–Based Agents	C. Gram-Negative Antibiotics With Antipseudomonal Activity: Non-β-Lactam–Based Agents
Vancomycin 15 mg/kg IV q8–12h (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	Piperacillin-tazobactam 4.5 g IV q6h	Ciprofloxacin 400 mg IV q8h Levofloxacin 750 mg IV q24h
OR	OR	OR
Linezolid 600 mg IV q12h	Cefepime 2 g IV q8h Ceftazidime 2 g IV q8h	Amikacin 15–20 mg/kg IV q24h Gentamicin 5–7 mg/kg IV q24h Tobramycin 5–7 mg/kg IV q24h
	OR	OR
	Imipenem 500 mg IV q6h Meropenem 1 g IV q8h	Colistin 5 mg/kg IV × 1 (loading dose) followed by 2.5 mg × (1.5 × CrCl + 30) IV q12h (maintenance dose) Polymyxin B 2.5–3.0 mg/kg/d divided in 2 daily IV doses
	OR	
	Aztreonam 2 g IV q8h	
Choose one gram-positive option from column A, one gram-negative option from column B, and one gram-negative option from column C. Note that the initial doses suggested in this table may need to be modified for patients with hepatic or renal dysfunction.		

Pharmacokinetic/Pharmacodynamic Optimization



PK Alteration in Critically Ill Patients

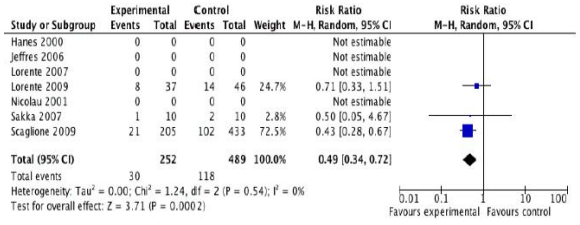
PK Profile of Antibiotics

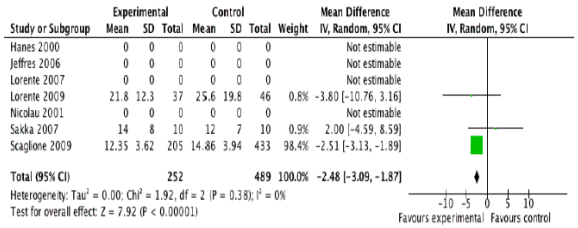


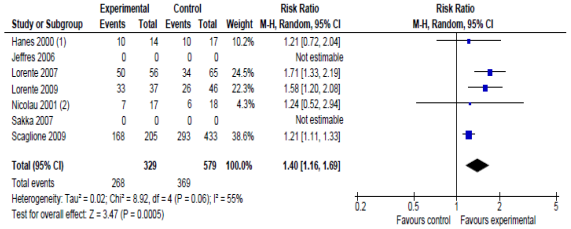
Crit Care Med 2009;37:840

Antibiotic Dosing Determined by PK/PD Data
ATS/IDSA Guideline, 2016

- PK/PD optimized dosing refers to the use of
  - Antibiotic blood concentrations
  - Extended and continuous infusions
  - Weight-based dosing







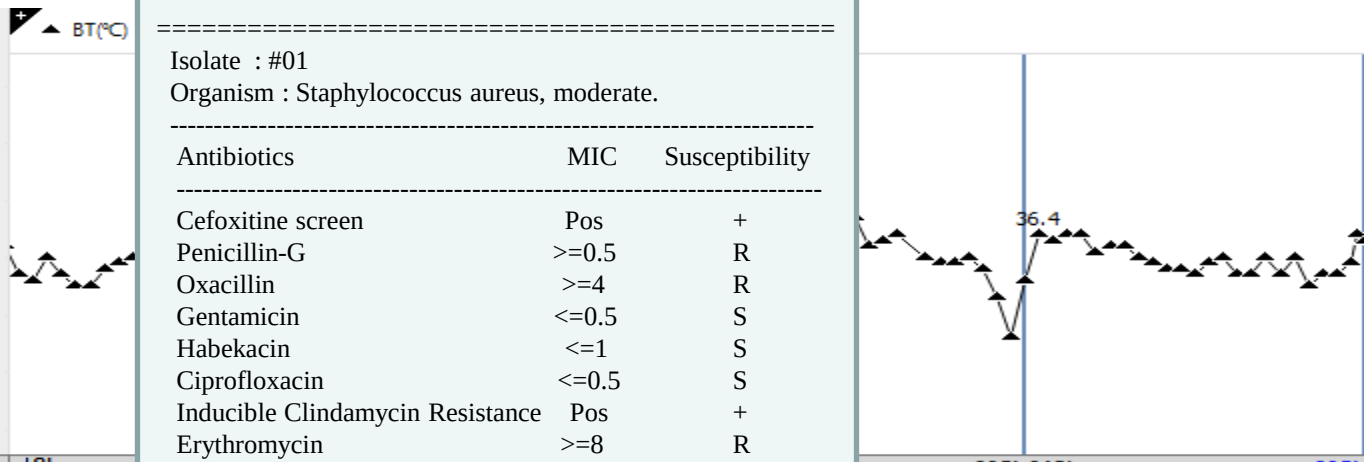
▶ Decreased mortality, decreased ICU length of stay, and increased clinical cure rate

Clin Infect Dis 2016;63(5):e61

* No published studies describing the PK/PD of piperacillin/tazobactam or polymyxins (colistin or polymyxin B) in patients with HAP/VAP are available at this time and so these drugs were not included in this recommendation.

66 Male with AGC
Isolation of MRSA

- Prior intravenous antibiotic (-)
- Septic shock (-)
- ARDS (-)
- ≥ 5 days of hospitalization (-)
- RRT (-)



그룹명	항목명			
Vital Sign				
BT	BT(℃)		.8	36.4
검사결과				
WBC Count, Blood (x10³/μL)			39	10.61
CRP, Quantitative (High Sensitivity) (mg			99	16.08
Procalcitonin, quantitative (ng/mL)				
항생제				
Cefepime(g)				
Vancomycin HCl(g)				
Levofloxacin(mg)				
Cefotetan(g)				
미생물검사				
Gram Stain and Cultur...	Nasal-MRSA			
	(Endo)Tracheal Aspir			
Fungus C...	(Endo)Tracheal Aspir			

==========

Isolate : #01

Organism : Staphylococcus aureus, moderate.

Antibiotics	MIC	Susceptibility
Cefoxitine screen	Pos	+
Penicillin-G	>=0.5	R
Oxacillin	>=4	R
Gentamicin	<=0.5	S
Habekacin	<=1	S
Ciprofloxacin	<=0.5	S
Inducible Clindamycin Resistance	Pos	+
Erythromycin	>=8	R
Telithromycin	<=0.25	S
Clindamycin	<=0.25	R
Quinupristin/Dalfopristin	<=0.25	S
Linezolid	2	S
Teicoplanin	<=0.5	S
Vancomycin	<=0.5	S
Tetracycline	<=1	S
Tigecycline	<=0.12	S
Nitrofurantoin	<=16	S
Fusidic acid	<=0.5	S
Mupirocin	<=2	S
Rifampin	<=0.5	S
Trimethoprim/Sulfa	<=10	S

==========

Vancomycin for HAP/VAP
Optimal Target Serum Concentration

- Optimal target serum concentration for complicated MRSA infection: trough serum vancomycin concentrations of 15–20 mg/L
  - Bacteremia
  - Endocarditis
  - Osteomyelitis
  - Meningitis
  - Hospital-acquired pneumonia

  ▶ Achieve an AUC/MIC of >400 for most patients if the MIC is <1 mg/L

  ▶ To achieve rapid attainment of this target concentration for seriously ill patients, a loading dose of 25–30 mg/kg (based on actual body weight) can be considered.

Am J Health-Syst Pharm 2009; 66:82

Vancomycin Loading Dose in HAP/VAP

SMC Experience

Table 2 Vancomycin dose and C_{trough} measurement between loading dose (LD) and non-LD groups

Characteristics	LD group (n=22)	Non-LD group (n=59)	P value
First dose of vancomycin			
Median dose per weight, mg/kg	24.4 (21.6–25.5)	15.2 (12.1–17.5)	<0.001
Groups by median dose per weight, mg/kg			<0.001
<15	0 (0.0)	29 (49.2)	
15–20	2 (9.1)	23 (39.0)	
20–25	14 (63.6)	7 (11.9)	
25–30	5 (22.7)	0 (0.0)	
>30	1 (4.5)	0 (0.0)	

Table 3 Proportion of pharmacokinetic target (trough concentration >15 mg/L) attainment between vancomycin loading dose (LD) and non-LD groups

Characteristics	LD group (n=22)	Non-LD group (n=59)	OR (95% CI)	P value
Time to target attainment, h	54 (24–110)	60 (24–93)	NA	0.981
Target attainment within 24 h	6 (28.6)	17 (30.9)	0.89 (0.30–2.70)	0.843
Target attainment within 48 h	10 (47.6)	22 (40.0)	1.36 (0.50–3.75)	0.547

Values are median with interquartile range or n (%). OR, odds ratio; CI, confidence interval

J Thorac Dis 2021;13(2):768

Effect of Vancomycin Loading Dose
SMC Experience

Table 5 Univariable and multivariable analyses with logistic regression model for probability of clinical cure

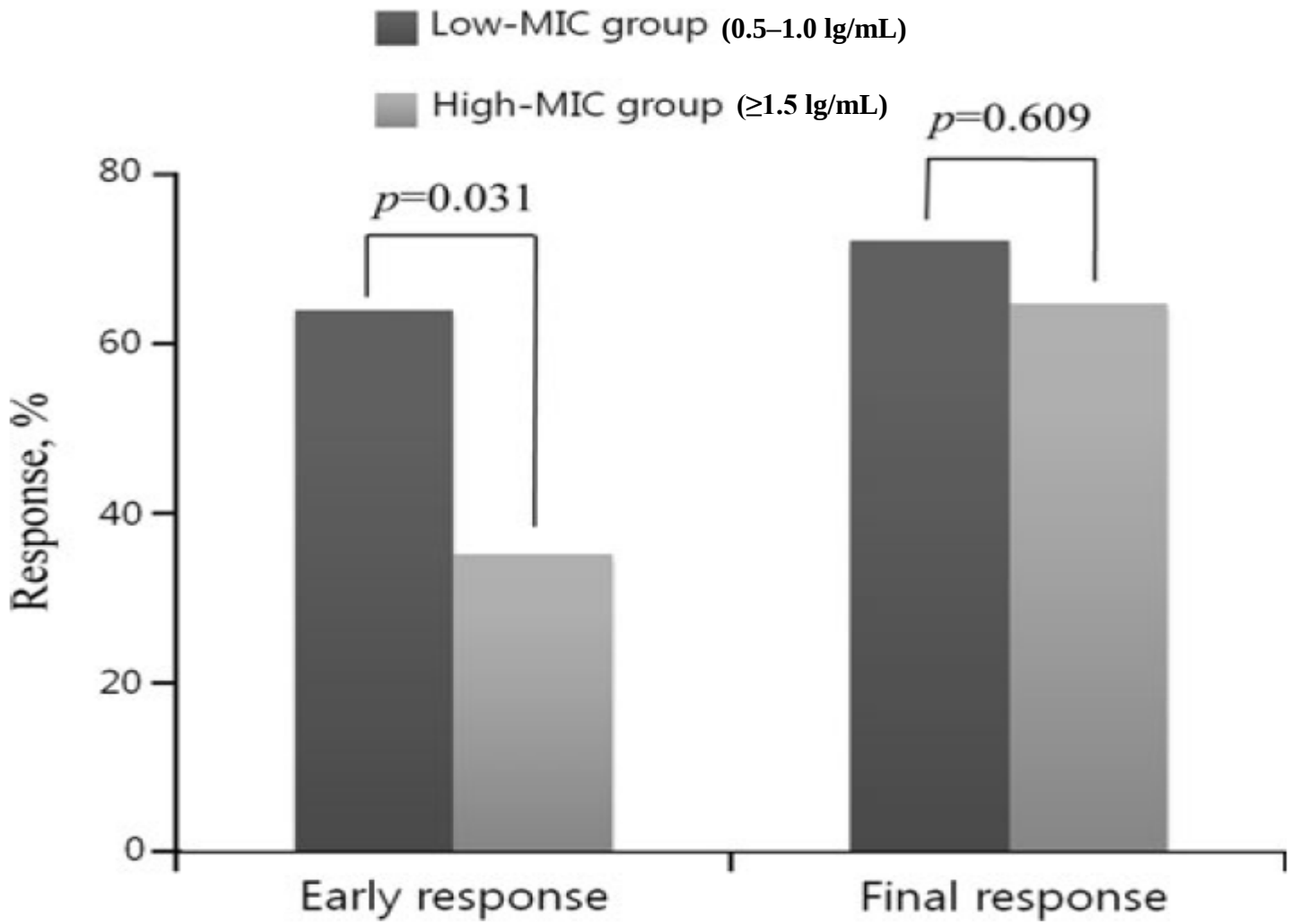
Variables	Univariable		Multivariable	
	OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Age, per year	N/A	0.486	0.97 (0.93–1.01)	0.109
Sex, female	1.20 (0.43–3.40)	0.727	1.52 (0.47–4.94)	0.484
Vancomycin LD	1.10 (0.39–3.13)	0.860	0.91 (0.27–2.99)	0.870
Target attainment in 48 h	0.83 (0.30–2.24)	0.706		
Cardiovascular disease	2.80 (0.73–10.76)	0.123	4.79 (0.99–23.17)	0.051
Mechanical ventilation	1.00 (0.87–11.54)	>0.999		
CRRT	0.33 (0.12–0.93)	0.031	0.31 (0.09–1.04)	0.058
Status of post-CPR	0.48 (0.06–3.61)	0.597		
ECMO	0.46 (0.11–2.00)	0.431		
Vancomycin MIC				
≤1	Reference		Reference	
2	0.21 (0.05–0.90)	0.054	0.19 (0.04–1.00)	0.050
Bacteremia	0.28 (0.07–1.10)	0.076	0.31 (0.07–1.40)	0.128

OR, odds ratio; CI, confidence interval; LD, loading dose; CRRT, continuous renal replacement therapy; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; MIC, minimum inhibitory concentration

J Thorac Dis 2021;13(2):768

MIC of Vancomycin and Clinical Outcome

AMC Data



Intensive Care Med 2011;37:639

Vancomycin: We Can't Get There From Here

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	AUC/MIC ratio ⩾400			Nephrotoxic event	
MIC value	0.5mg/L (%)	1.0mg/L (%)	2.0mg/L (%)	Non-ICU (%)	ICU (%)
500 mg IV Q12H	57	15	0.7	3	10
1000 mg IV Q12H	90	57	15	6	16
1500 mg IV Q12H	97	79	38	9	25
2000 mg IV Q12H	98	90	57	14	34

Clin Infect Dis 2011;52:969

New Guideline for TDM of Vancomycin, 2020

Clinical Infectious Diseases

IDSA FEATURES

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Therapeutic Monitoring of Vancomycin for Serious Methicillin-resistant *Staphylococcus aureus* Infections: A Revised Consensus Guideline and Review by the American Society of Health-system Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists

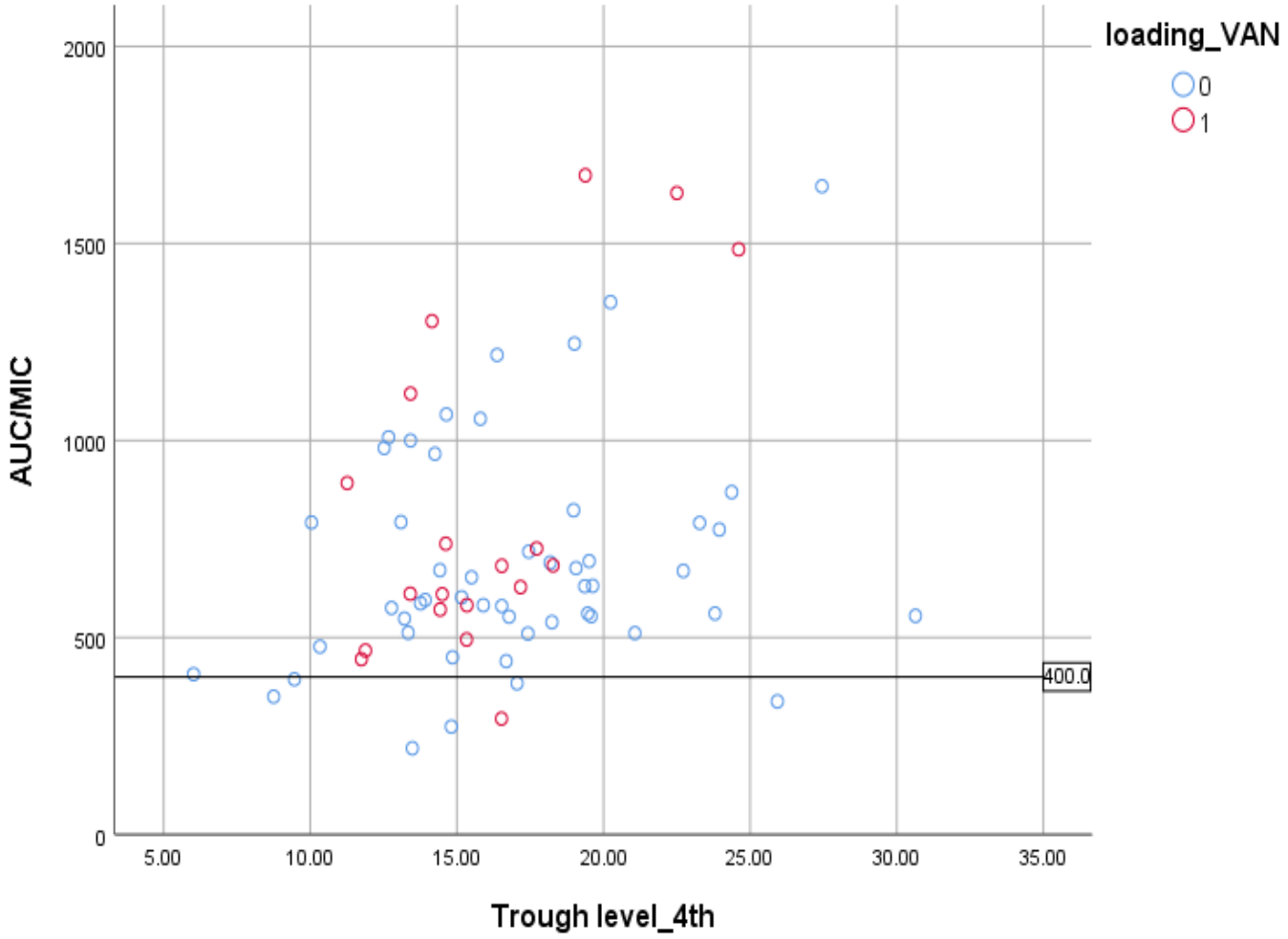
1. In patients with suspected or definitive serious MRSA infections, an individualized target of the AUC/MIC_{BMD} ratio of 400 to 600 (assuming a vancomycin MIC_{BMD} of 1 mg/L) should be advocated to achieve clinical efficacy while improving patient safety **(A-II)**.

3. Trough-only monitoring, with target between 15 and 20 mg/L, is no longer recommended based on efficacy and nephrotoxicity data in patients with serious infections due to MRSA **(A-II)**. There is insufficient evidence to provide recommendations on whether trough-only or AUC-guided vancomycin monitoring should be used among patients with noninvasive MRSA or other infections.

Clin Infect Dis 2020;71:1361

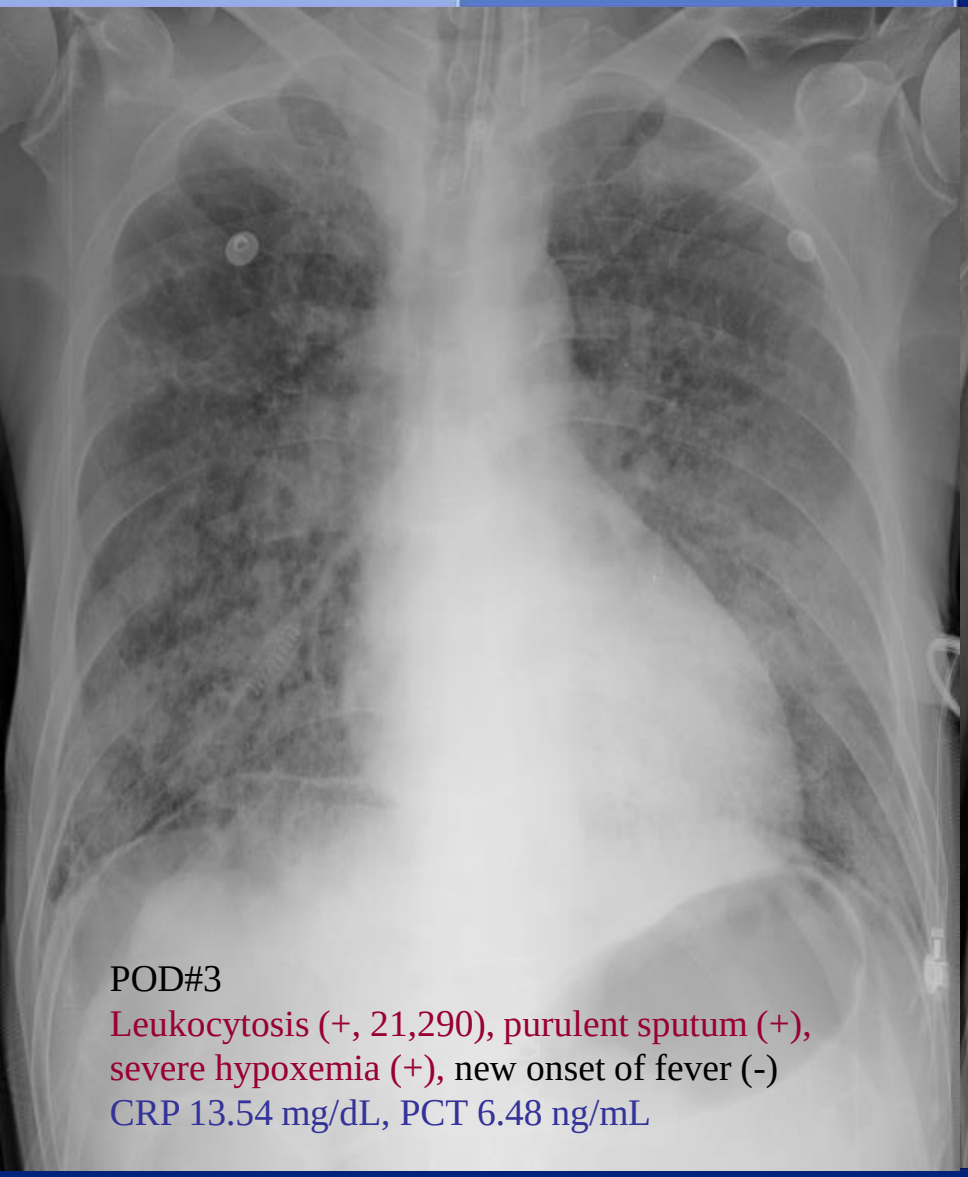
AUC/MIC Based on Trough 15–20 mg/L

SMC Experience

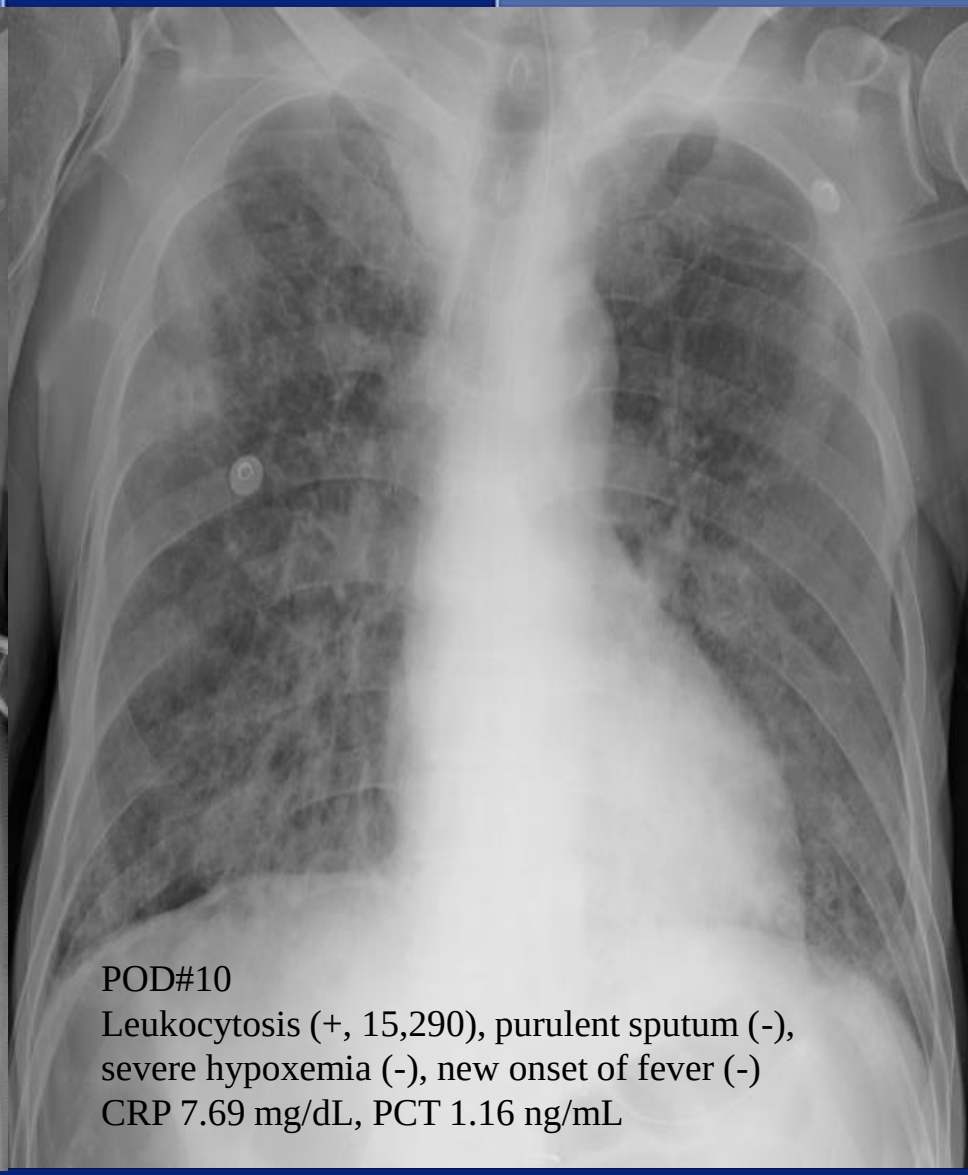


66 Male with AGC

Vancomycin for 7 days

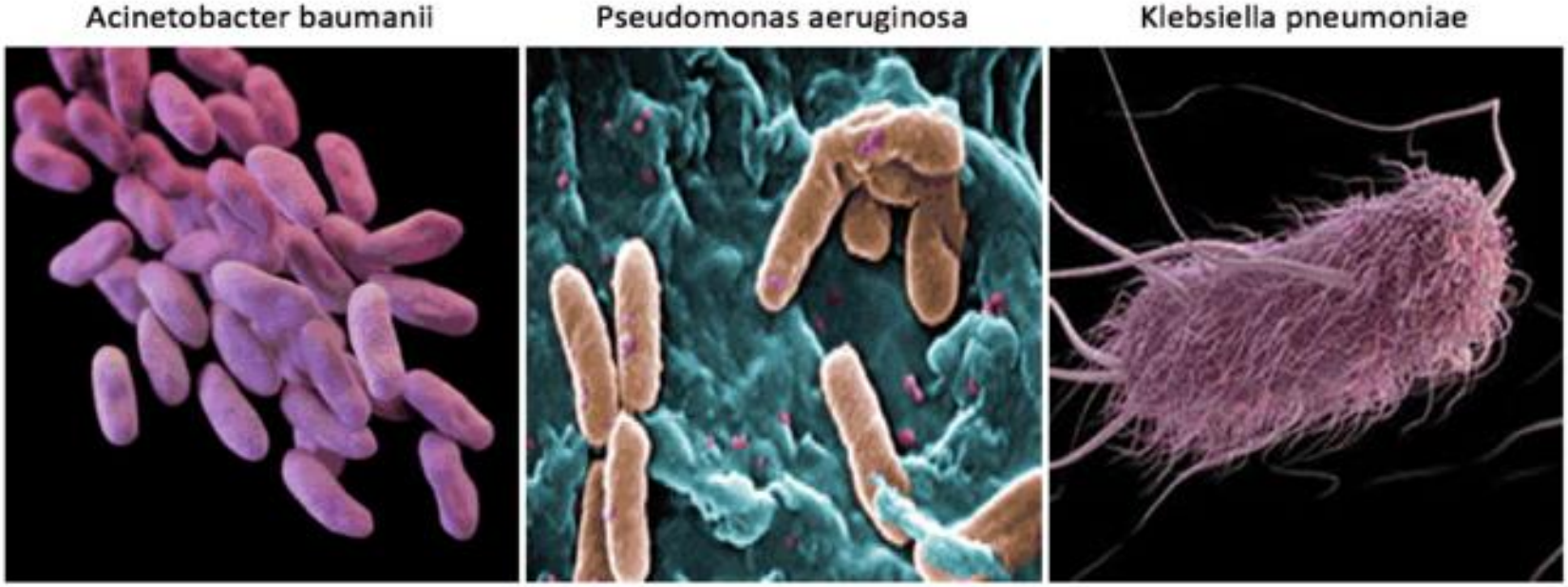


POD#3
Leukocytosis (+, 21,290), purulent sputum (+),
severe hypoxemia (+), new onset of fever (-)
CRP 13.54 mg/dL, PCT 6.48 ng/mL



POD#10
Leukocytosis (+, 15,290), purulent sputum (-),
severe hypoxemia (-), new onset of fever (-)
CRP 7.69 mg/dL, PCT 1.16 ng/mL

Carbapenem Resistant GNB



The key elements that define the threat of carbapenem-resistant gram-negative pathogens

- Increasing incidence of these pathogens worldwide since the turn of the century
- Lack of safe and efficacious agents for treatment once the efficacy of carbapenems is lost due to resistance
- High mortality rates associated with carbapenem-resistant gram-negative infections

Clin Infect Dis 2019;69(S7):S565

Which Antibiotic Should Be Used to Treat Patients With HAP/VAP Due to Carbapenem-Resistant Pathogens?

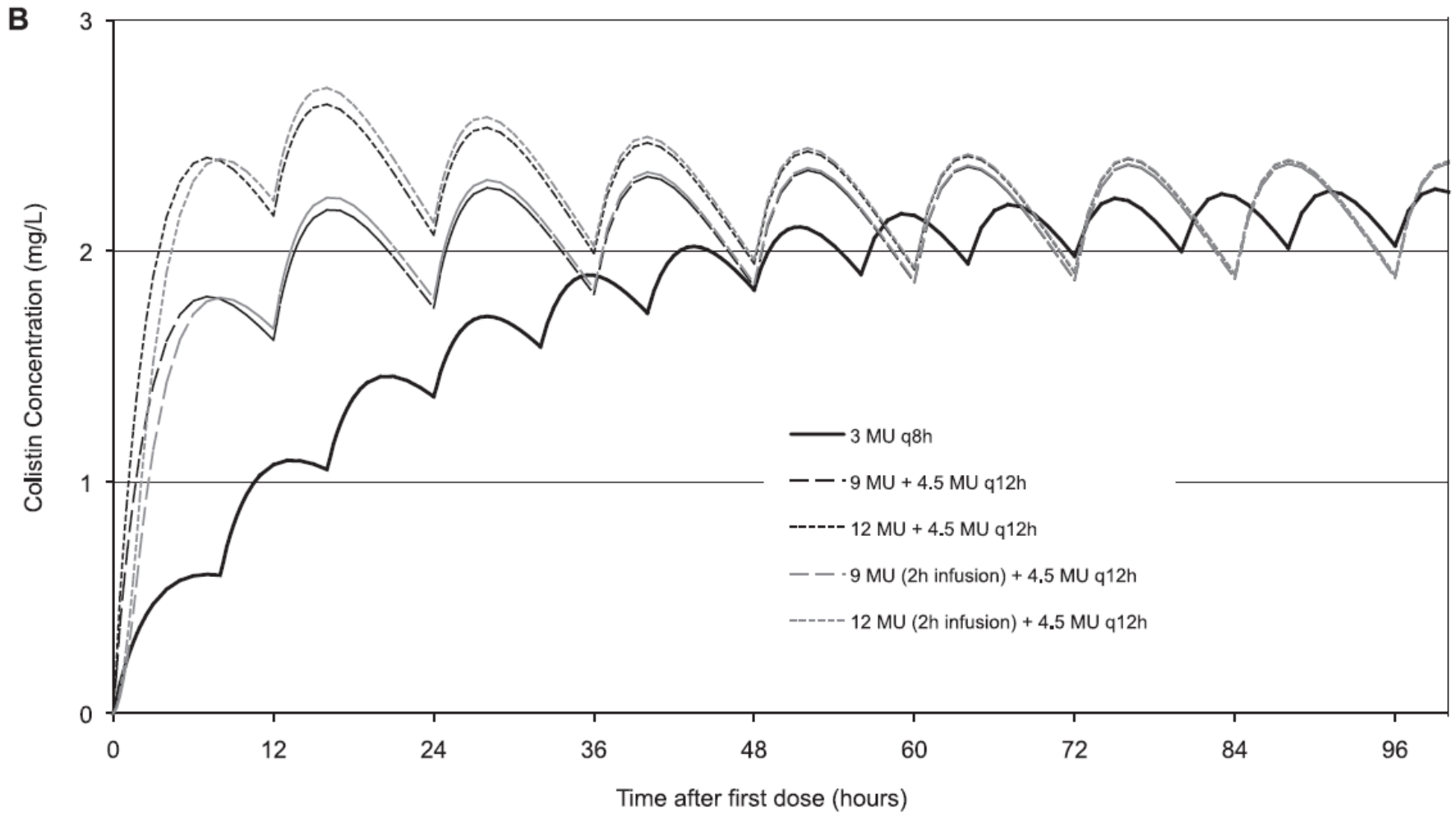
- Suggested drugs for carbapenem-resistant Gram-negative bacterial pneumonia
  - Backborn: β-Lactam
  - Accompanying drug: Fluoroquinolone
  - Alternative accompanying drug: Polymyxin or aminoglycoside
  - Other alternatives: Fosfomycin or tigecycline

Antimicrob Agents Chemother 2020;64:e02183

- IDSA/ATS Guideline, 2016
  - In patients with HAP/VAP caused by a carbapenem-resistant pathogen that is sensitive only to polymyxins, we recommend intravenous polymyxins (colistin or polymyxin B) (strong recommendation, moderate-quality evidence), and we suggest adjunctive inhaled colistin (weak recommendation, low-quality evidence).

Clin Infect Dis 2016;63(5):e61

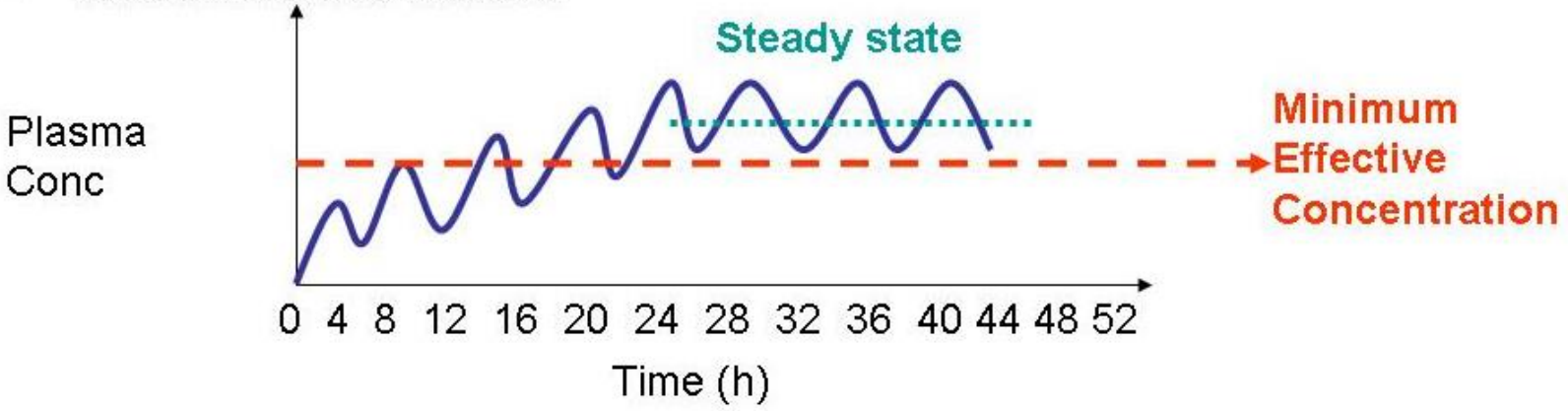
Concentrations of Colistin by Different Dosing



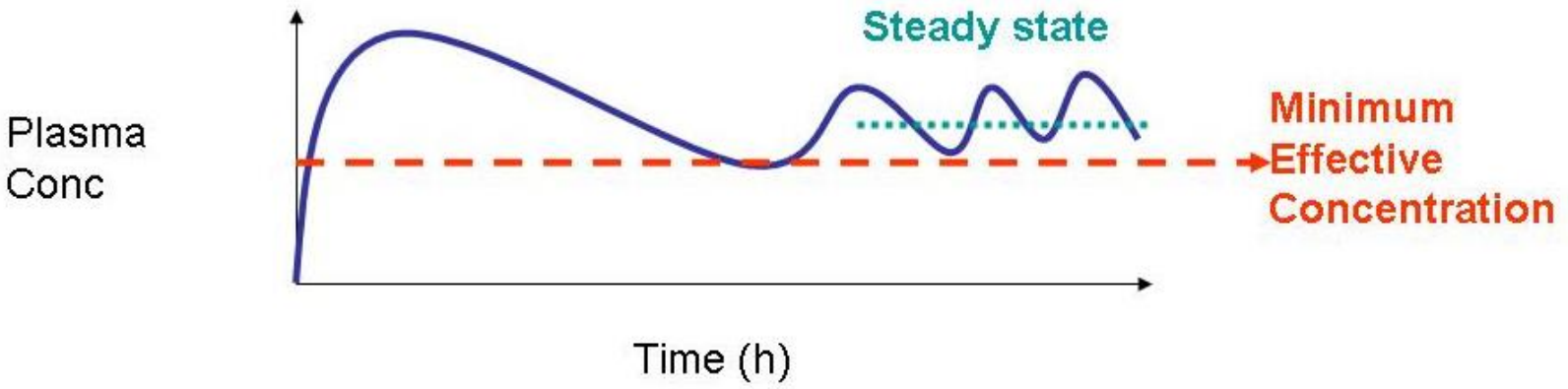
Antimicrob Agents Chemother 2009;53:3430

Loading Dose of Colistin

- Maintenance doses



- Loading dose and Maintenance doses



Clin Infect Dis 2012; 54: 1720

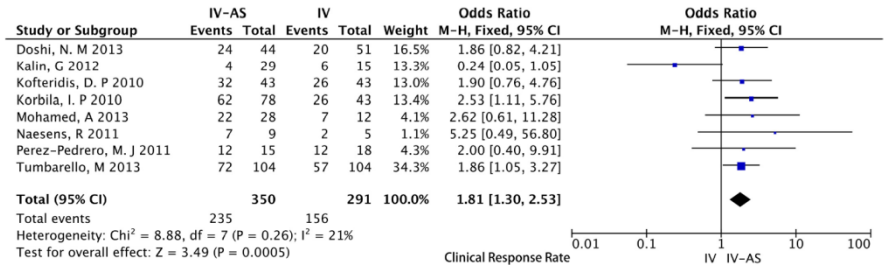
New Dosing Guidance of IV Colistin

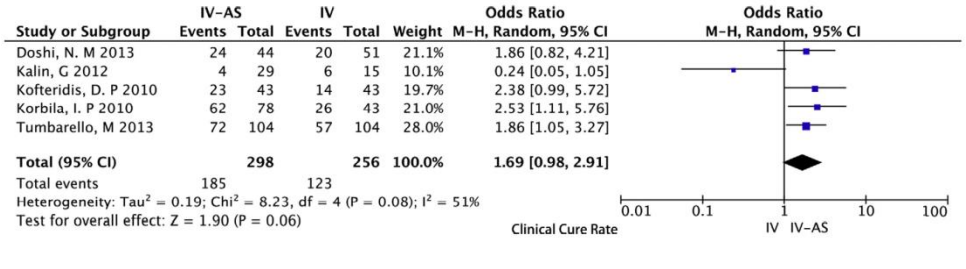
Dose	Category of Critically Ill Patient	Dosing Suggestions[a]
Loading dose	All patient categories	Equation 1: Loading dose of CBA (mg) = $C_{ss,avg}$ target (mg/L) × 2.0 × ideal body weight (kg) To achieve a $C_{ss,avg}$ of 2 mg/L in a patient with an ideal body weight of 75 kg, the loading dose would be 300 mg CBA (9 million IU), the suggested maximum loading dose. The 1st regular daily dose should be administered 12 h later.
Daily dose[b]	Not receiving RRT	Equation 2[c]: Daily dose of CBA (mg) = $C_{ss,avg}$ target (mg/L) × $10^{(0.0048 \times CrCl + 1.825)}$ See Table 3 ("look-up" table) for the daily dose to target a plasma colistin $C_{ss,avg}$ of 2 mg/L, depending on the patient's creatinine clearance.
	Receiving RRT	The baseline daily dose of colistimethate for a $C_{ss,avg}$ of 2 mg/L in a patient with creatinine clearance of 0 mL/min is 130 mg/d of CBA (3.95 million IU/d) (see Table 3)[d]; the supplement to the baseline daily dose needed during receipt of RRT is 10% of the baseline dose per 1 h of RRT.
	Intermittent hemodialysis	Nondialysis day: CBA dose of 130 mg/d (3.95 million IU/d), ie, baseline dosing for a $C_{ss,avg}$ of 2 mg/L; dialysis day supplement: add 30% or 40% to baseline daily dose after a 3- or 4-h session, respectively.[e] The dialysis session should occur toward the end of a colistimethate dosing interval, and the supplement to the baseline (nondialysis) daily dose should be administered with next regular dose, after the dialysis session has ended.
	SLED	During SLED: add 10% per 1 h of SLED replacement to baseline daily dose for a $C_{ss,avg}$ of 2 mg/L[f]; for a patient receiving a 10-h nocturnal SLED session each day and receiving colistimethate every 12 h, the dose would be (baseline CBA dose of 130 mg/d for a patient with creatinine clearance of 0 mL/min + supplemental dose comprising 10% of the baseline dose per h × 10 h); ie, for this case the CBA dose would be 260 mg/d (7.9 million IU/d). It is suggested that the SLED session begin 1–2 h after the afternoon/evening dose; in such a case, it may be most convenient and safe to administer 130 mg CBA (3.95 million IU) every 12 h.
	CRRT	During CRRT: add 10% per 1 h of CRRT to the baseline daily dose for a $C_{ss,avg}$ of 2 mg/L[g]; the suggested CBA dose is 440 mg/d (~13 million IU/d).

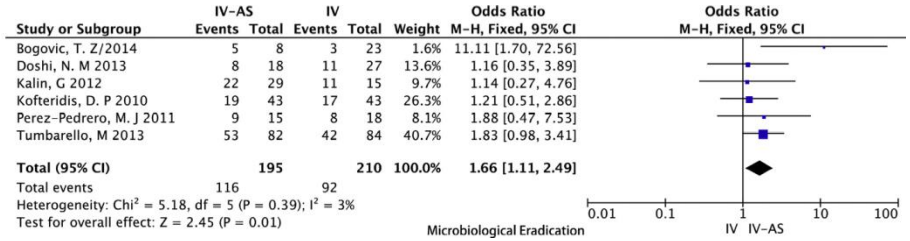
Clin Infect Dis 2017;64:565

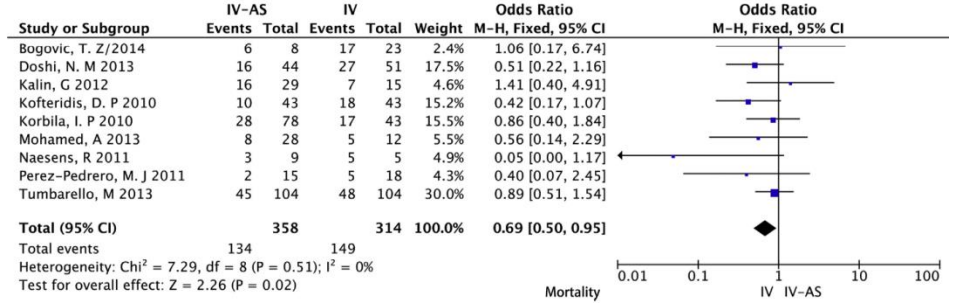
Adjunctive Inhaled Colistin

Meta-analysis









Int J Antimicrob Agents 2015;46:603

	Relative risk	95% CI
Mortality	0.84	0.63 – 1.12
Clinical cure	1.29	1.13 – 1.47
Nephrotoxicity	1.11	0.78 – 1.57

- The guidelines suggests both inhaled and systemic antibiotics, rather than systemic antibiotics alone

Clin Infect Dis 2016;63(5):e61

IV Loading and Inhaled Colistin

SMC Experience

Table 3. Clinical outcomes of 191 patients with HAP or VAP caused by CRGNB, who were treated with colistin in the ICU.

Variables	Non-LD IV ($n=70$)	LD IV ($n=86$)	AS–LD ($n=35$)	p value
Clinical response				
Clinical cure	32 (46)	36 (42)	17 (49)	0.764
Recurrence	4 (6)	10 (12)	4 (11)	0.414
Clinical failure	34 (49)	40 (47)	14 (40)	0.724
Microbiological response				
Eradication	21/67 (31)	27/81 (33)	21/35 (60)	0.010$^{\$‡}$
Recurrence	9/67 (13)	12/81 (15)	7/35 (20)	0.663
Colonization	20/67 (30)	22/81 (27)	3/35 (9)	0.047$^{\$}$
Microbiological failure	17/67 (25)	20/81 (25)	4/35 (11)	0.222
Duration of ICU stay, days	13 (8–21)	12 (8–18)	20 (10–33)	0.013$^{\$}$
Mortality				
30-day mortality	32 (46)	42 (49)	8 (23)	0.027$^{\$}$
90-day mortality	41 (59)	50 (58)	16 (46)	0.396
Nephrotoxicity	27/50 (54)	23/61 (38)	16/27 (59)	0.100
Initiation rates of RRT	8/50 (16)	5/61 (8)	6/27 (22)	0.151

AS, aerosolized; CRGNB, carbapenem-resistant gram-negative bacteria; HAP, hospital-acquired pneumonia; ICU, intensive care unit; IV, intravenous; LD, loading dose; RRT, renal replacement therapy; VAP, ventilator-associated pneumonia.
*, $, ‡indicate significant differences ($p<0.017$) between the non-LD IV group and the LD IV group, LD IV group and AS–LD group, and the non-LD IV group and the AS–LD group, respectively.

Ther Adv Respir Dis 2019;13:1753466619885529

Practical Management of HAP/VAP
Summary

- For patients with suspected HAP/VAP,
  - Diagnose with clinical criteria alone
  - Microbiologic examination with non-invasive sampling (with semi-quantitative cultures) and rapid diagnostic techniques
  - Empiric antibiotics based on the local distribution of pathogens and antimicrobial susceptibilities.
    - In case where local antimicrobial susceptibility rates are not available
      - High risk of mortality
      - MDR risk: Prior intravenous antibiotic use within 90 d

- Pharmacokinetic/Pharmacodynamic optimization of antibiotic therapy
  - Antibiotic dosing be determined using PK/PD data, rather than the manufacturer's prescribing information
    - Accurate dosing and monitoring of drug level
    - Loading dose
    - Inhaled antibiotics