

Increased mortality associated with methicillin-resistant *Staphylococcus aureus* (MRSA) infection in the ICU:

Results from the EPIC II study

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*Reference: Hakan Hanberger, Sten Walther, Marc Leone, Philip S Barie, Jordi Rello, Jeffrey Lipman, John C Marshall, Antonio Anzueto, Yasser Sakr, Peter Pickkers, Peter Felleiter, Milo Engoren, Jean-Louis Vincent on behalf of the EPIC II Group of Investigators. Increased mortality associated with methicillin-resistant *Staphylococcus aureus* (MRSA) infection in the ICU: Results from the EPIC II study. Submitted 2011.

Introduction

Controversy continues regarding whether methicillin resistance increases mortality risk in *Staphylococcus aureus* infections. We assessed the role of methicillin resistance on survival of patients in the EPIC II study cohort with *S. aureus* infection.

Methods

The EPIC II point-prevalence study of infection in critically ill patients was performed on May 8, 2007. Demographic, physiological, bacteriological and therapeutic data were collected for all adult patients in 1,265 participating intensive care units (ICUs) from 75 countries on the study day. ICU and hospital outcomes were recorded. We compared characteristics of patients with methicillin-sensitive (MSSA) and methicillin-resistant (MRSA) *S. aureus* infection. Co-morbidities, age, simplified acute physiology system (SAPS) II score, site of infection, geographical region, and MRSA/MSSA were entered into a multivariable model and adjusted odds ratios (OR)[95% CI] were calculated for ICU and hospital mortality rates.

Results

On the study day, 7,087 of the 13,796 patients (51%) were classified as infected. There were 494 patients with MRSA and 505 patients with MSSA infections. There were no significant differences between the two groups in use of mechanical ventilation or hemofiltration/hemodialysis. Cancer and chronic renal failure were more prevalent in MRSA than in MSSA patients. On the study day, 81.4% of MRSA infected patients received at least one antibiotic usually active against MRSA and 87.9% of MSSA infected patients received at least one antibiotic usually active against MSSA.

ICU mortality rates were 29.1% and 20.5%, respectively ($P<0.01$) and corresponding hospital mortality rates were 36.4% and 27.0% ($P<0.01$). Multivariable analysis of hospital mortality for MRSA infection showed an adjusted OR of 1.48 [1.05-2.10], $P=0.03$.

Conclusion

In ICU patients, MRSA infection is more common in patients with comorbid conditions, such as cancer and chronic renal failure, and is independently associated with an almost 50% higher odds of hospital death compared to MSSA infection.

Table 1. Basic characteristics of patients with methicillin-resistant (MRSA) and methicillin-sensitive (MSSA) *Staphylococcus aureus* infections in the EPIC II Study

	MRSA n = 494	MSSA n = 505	P-value
Age, median (IQR), y	63 [50-74]	62 [44-72]	0.01
Male	322 (65.3)	343 (67.9)	0.38
SAPS II, median (IQR)	37 [27-49]	37 [27-49]	0.87
SOFA, median (IQR)	6 [4-10]	7 [4-10]	0.64
Days on ICU prior to study date, median (IQR)	10 [3-22]	7 [3-14]	<0.001
Type of admission			0.08
	Surgical: Elective	60 (11.9)	
	Medical	148 (29.4)	
	Surgical: Emergency	223 (44.2)	
	Trauma	73 (14.5)	
Admission Source			<0.01
	Operating room /recovery	87 (17.3)	
	Emergency department/ambulance	168 (33.5)	
	Hospital ward	130 (25.9)	
	Other hospital	101 (20.1)	
	Other	16 (3.2)	
Reason for admission			<0.001
	Surveillance/Monitoring	37 (7.3)	
	Neurological	118 (23.4)	
	Respiratory	122 (24.2)	
	Cardiovascular	114 (22.6)	
	Renal	10 (2)	
	Digestive/Liver	30 (5.9)	
	Trauma	63 (12.5)	
	Other	11 (2.2)	
Co-morbidity			0.51
	Chronic obstructive pulmonary disease	91 (18)	
	Cancer	53 (10.5)	<0.01
	Hematologic cancer	11 (2.2)	0.96
	Insulin-dependent diabetes mellitus	66 (13.1)	0.49
	Heart failure (NYHA III-IV))	53 (10.5)	0.11
	Chronic renal failure	51 (10.1)	0.04
	HIV	2 (0.4)	0.64
	Cirrhosis	20 (4)	0.16
	Immunosuppression	20 (4)	0.34
Number of comorbidities			<0.01
	None	249 (49.3)	
	1	160 (31.7)	
	2	60 (11.9)	
	3	28 (5.5)	
	>3	8 (1.6)	
Mechanical ventilation	341 (69)	353 (70.2)	0.69
Hemofiltration/ Hemodialysis	67 (13.6)	61 (12.1)	0.5
Antibiotic treatment	475 (96.2)	485 (96)	0.79

SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; HIV, Human Immunodeficiency Virus; NYHA III-IV, New York Heart Association class III-IV. Data are given as number (%) or median (interquartile range)

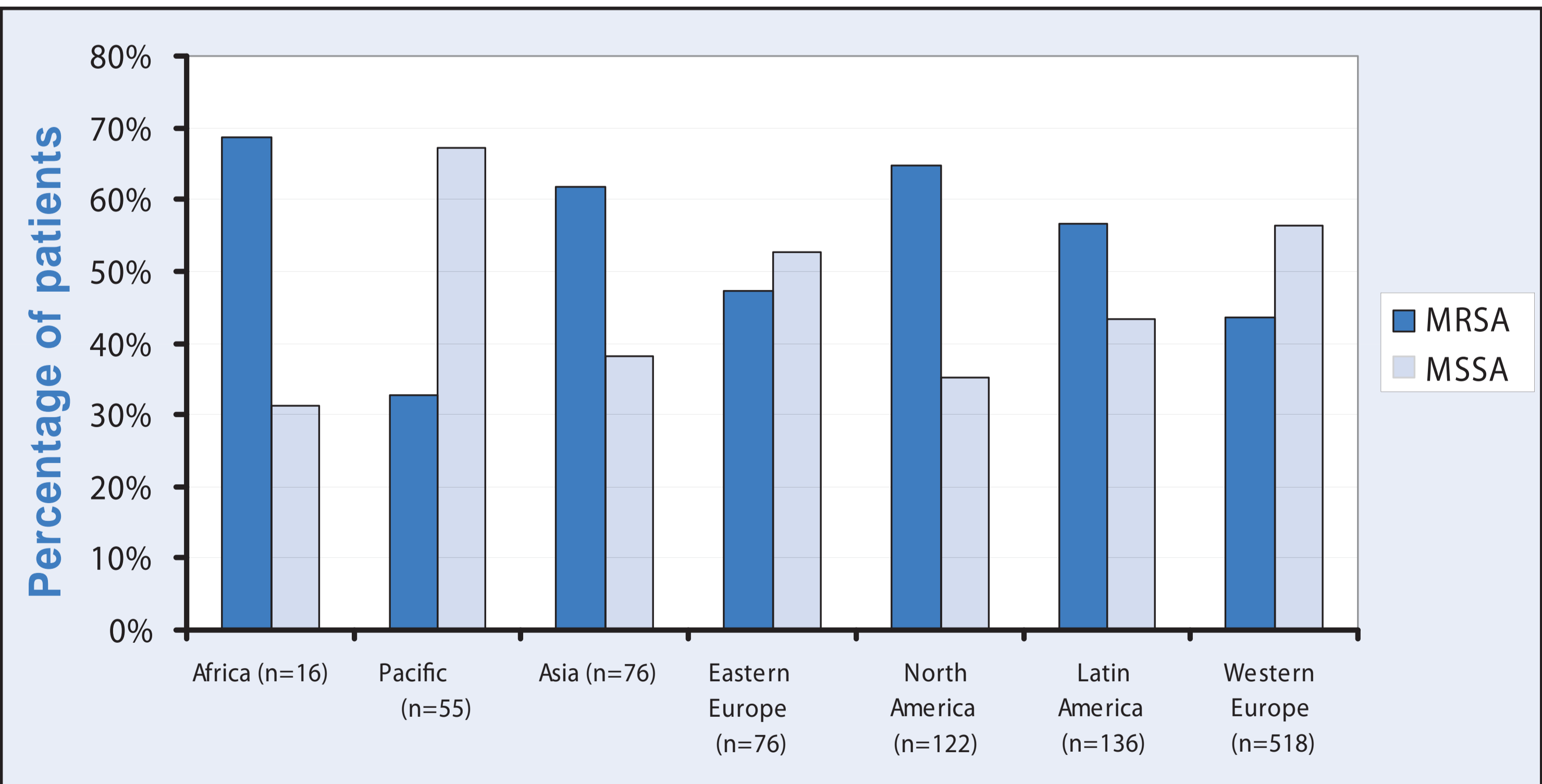


Figure 1. Percentages of infected patients with positive *Staphylococcus aureus* cultures according to their sensitivity to methicillin (resistant [MRSA] or sensitive [MSSA]) in the different geographical regions