Systemic Inflammatory Response Syndrome in Adult Patients with Nosocomial Bloodstream Infection due to *Pseudomonas aeruginosa*

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ABSTRACT

ground: *Pseudomonas aeruginosa* has the highest crude mortality among -negative pathogens causing nosocomial bloodstream infection (nBSI).

ods: We performed a historical cohort study on 57 adults with *P.aeruginosa* nBSI to define the associated systemic inflammatory response syndrome s). We examined SIRS scores 2 days prior through 14 days after the first ve blood culture. Imipenem resistant (n=15) and susceptible infections 2) were compared. Variables significant in univariate analysis were entered logistic regression model.

lts: 73.7% of BSI were caused by imipenem susceptible *P. aeruginosa*) and 26.3% by imipenem resistant *P. aeruginosa* (IRPa). Median APACHE 2) score on the day of BSI was 22. Appropriate antimicrobials were begun 24 hours in 59.6%. Septic shock occurred in 40.4% and severe sepsis in ditional 15.7%. Incidence of organ failure was as follows: respiratory 73.7%, 36.8%, hematologic 24.6%, hepatic 8.8%. Crude mortality was 45.6%. ession to septic shock was associated with death (OR 5.5, CI9 51.7-17.4, 03). There was no difference in AP2 scores on days -2, -1 and 0 between SPa and IRPa groups. Maximal SIR (severe sepsis, septic shock or death) een on day 0 for IRPa BSI vs. day 1 for ISPa. No significant difference was in the incidence of organ failure, 7-day or overall mortality between the two s. Univariate analysis revealed that AP2≥20 at BSI onset, time to priate therapy >24 hours and cardiovascular and hematologic failure were ciated with death, but age, respiratory, renal, and hepatic failure, and ion due to IRPa were not. Multivariate analysis revealed that hematologic e (OR 7.4; CI95 2.7-213.5, p=0.006), AP2≥20 at BSI onset (OR 6.0; CI95 19.9, p=0.014) and time to appropriate therapy >24 hours (OR 4.7; CI95 1.2- =0.031) independently predicted death.

lusions: In patients with *P. aeruginosa* nBSI, (1) the incidence of septic k and organ failure is high, (2) patients with IRPa BSI are not more acutely ill to infection than those with ISPa BSI, and (3) the development of tologic failure, AP2≥20 at BSI onset and the time to appropriate therapy >24 were independent predictors of death.

INTRODUCTION

domonas aeruginosa is the third most common gram-negative gen causing nosocomial bloodstream infections (BSIs), and has the st crude mortality among bacteria causing nosocomial BSI. The crude lity of *P. aeruginosa* BSI in immunocompromised patients ranges from o 33%. In a study of patients with *P. aeruginosa* pneumonia, mination of the APACHE (Acute Physiological and Chronic Health ation) II score at admission was not useful as a prognostic marker, progression of organ dysfunction after the infection due to *P. inosa* proved to be an ominous sign. There exist only a few small- studies evaluating the effect of antimicrobial resistance in hospital gens on clinical outcome. This study was conducted to explore the mmatory response, clinical course and outcome of nBSI due to *P. inosa*.

METHODS

Setting: The Virginia Commonwealth University Medical Center is a 820-bed tertiary care facility in Richmond, Virginia. The hospital houses 9 intensive care units and a burn unit; approximately 30,000 patients are admitted annually.

Study design: Historical cohort study of 57 randomly selected patients with monomicrobial *P. aeruginosa* nBSI from 1996-2003. The clinical condition of each patient was classified according to systemic inflammatory response syndrome (SIRS) criteria [SIRS, sepsis, severe sepsis or septic shock] and APACHE II scores from two days prior to positive blood culture through 14 days afterwards.

Definitions: SIRS was defined as two or more of the following: (1) temperature >38ºC or <36ºC, (2) heart rate >90 beats/minute, (3) respiratory rate >20 breaths/ minute or $PaCO_2$ <32mm HG, or (4) white blood cell count >12,000/μL or <4,000/μL or the presence of >10% immature neutrophils. Sepsis was defined as SIRS associated with *P. aeruginosa* isolated from at least one blood culture. Sepsis with the presence of hypotension or systemic manifestations of hypoperfusion constituted severe sepsis. Septic shock was defined as sepsis associated with hypotension unresponsive to intravenous fluid challenge or the need for >5μg/kg/minute of dopamine or any other vasopressor agent. Organ system failure was assessed using the criteria described by Fagon.

Statistical methods: Mean values were compared using 2 sample t tests for independent samples. Proportions were compared using a χ^2 test. All tests of significance were 2-tailed, and α was set at 0.05. Independent predictors of mortality were identified by means of stepwise logistic regression analysis, using variables found to be significant in univariate analysis.

RESULTS

Table 1: Patient characteristics and outcomes, stratified by resistance pattern of infecting organism (ISPa vs. IRPa and underlying severity of illness before infection (APACHE II score ≥ vs. < 20)

	Total (n=57)	ISPa (n=42)	IRPa (n=15)	AP2<20 (n=20)	AP2≥20 (n=37)
Mean age (years)	55	57	50	53	57
Women	40.4%	42.9%	33.0%	20.0%	51.4%
Mean LOS prior to nBSI (days)	35	23	67	22	42
Mechanical ventilation	61.4%	52.4%	86.7%	35.0%	75.7%
Hemodialysis	10.5%	7.1%	20.0%	-	16.2%
TPN	29.8%	28.6%	33.3%	35.0%	27.0%
Transfusion	17.5%	14.3%	26.7%	10.0%	21.6%
Prior antibiotics	86.0%	90.5%	73.3%	90.0%	83.8%
ICU	82.5%	81.0%	86.7%	70.0%	89.2%
Central venous line	84.2%	78.6%	100.0%	70.0%	91.9%
Neutropenia	7.0%	4.8%	13.3%	10.0%	5.4%
Imipenem resistance	26.3%			15.0%	32.4%
AP2≥20 at day 0	22	22	22		
Mean time to appropriate antimicrobial therapy (days)	1.7	1.4	3.3	1.9	1.6
Respiratory failure	73.7%	69.0%	86.7%	35.0%	94.6%
CV failure	40.4%	35.7%	53.3%	10.0%	56.8%
Renal failure	36.8%	33.3%	46.7%	20.0%	45.9%
Hematologic failure	24.6%	23.8%	26.7%	15.0%	29.7%
Liver failure	8.8%	7.1%	13.3%	5.0%	10.8%
7-day mortality	17.5%	19.0%	13.3%	-	27.0%
Overall mortality	45.6%	45.2%	46.7%	10.0%	64.9%

P<.05

Figure 1: Systemic Inflammatory response (SIRS) over time

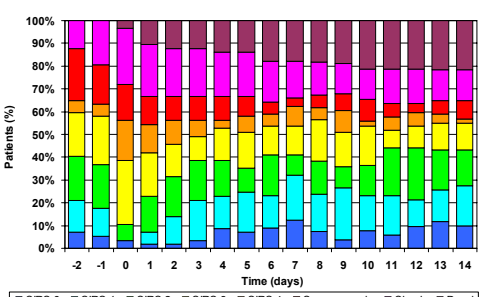
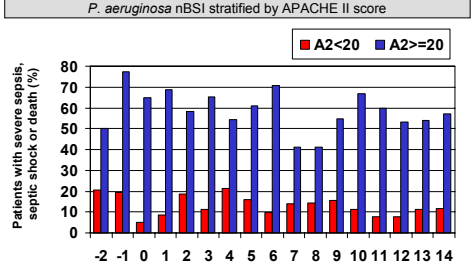


Figure 2: Severe sepsis, septic shock and death in patients with *P. aeruginosa* nBSI stratified by APACHE II score



RESULTS (continued)

Figure 3: Severe sepsis, septic shock and death in patients with *P. aeruginosa* nBSI stratified by imipenem resistance pattern

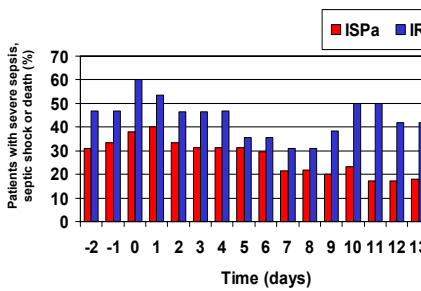


Table 2: Risk factors for death in patients with *P. aeruginosa* nosocomial bloodstream infection

	Univariate Analysis*		Multivariate A	
Risk factor	OR	*P*	OR	
Hematologic failure	12.4	0.001	7.5	
Apache II score ≥20	16.6	<0.001	6.0	
Time to appropriate therapy >24 hours	3.0	0.045	4.7	
Cardiovascular failure	5.5	0.003	1.0	

*Only significant univariate variables are shown

CONCLUSIONS

- The overall morbidity and mortality of patients with *P. aeruginosa* high.
- Patients with IRPa BSI are not more acutely ill prior to infection tha with ISPa BSI.
- When controlling for underlying severity of illness in patien *P. aeruginosa* nBSI, the hematologic failure, AP≥ 20 at BSI onset time to appropriate therapy >24 hours were independent predictors fo

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