

Online supplementary material

Impact of immunosuppression on incidence, etiology and outcome of ventilator-associated lower respiratory tract infections

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RESULTS

Main reasons for ICU admission are presented in Table S1.

Diagnostic procedure

In IC patients, the percentage of endotracheal aspirate and bronchoalveolar lavage was significantly higher in VAP than in VAT patients. In non-IC patients, although the percentage of endotracheal aspirate was significantly lower in VAP than in VAT patients; the percentage of bronchoscopy, bronchoalveolar lavage, mini bronchoalveolar lavage, and blood cultures were significantly higher in VAP than in VAT patients (Table S2).

Microorganisms

Although the percentage of patients with VA-LRTI related to MDR, *Enterobacter* spp., and MRSA was significantly higher in IC patients than in non-IC patients; the percentage of patients with VA-LRTI related to MSSA was significantly lower in IC patients than in non-IC patients (Table S3).

In the VAT subgroup, the only difference between IC patients and non-IC patients was a higher incidence of *Enterobacter* spp. in IC patients than in non-IC patients (19.2 versus 9.3%, $p=0.05$). However, in the VAP subgroup, the incidence of MRSA and *Enterobacter* spp. was significantly higher in IC patients than in non-IC patients (6.3% versus 1.3 %, $p=0.033$; 21.9% versus 10.5%, $p=0.02$; respectively); whereas MSSA incidence was significantly lower in IC patients than in non-IC patients (3.1% versus 25.6%, $p<0.001$).

Risk factors for ICU-mortality in patients with VA-LRTI by univariate analysis

At ICU admission, age, SAPS II, SOFA, immunosuppression, and admission category were significantly associated with higher ICU-mortality rate in these patients. At VA-LRTI diagnosis,

SOFA score, MDR, were associated with increased ICU-mortality. Appropriate antibiotic treatment was associated with significantly lower ICU-mortality rate (Table S4).

Table S1. Main reasons for ICU admission

	Immunosuppression		
	Yes	No	p
	n = 663	n = 2297	
Acute respiratory distress syndrome	99 (4.3)	48 (7.2)	0.01
Acute exacerbation of COPD	110 (4.8)	13 (2)	<0.001
Pneumonia	282 (12.3)	136 (20.5)	<0.001
Aspiration	40 (1.7)	9 (1.4)	0.60
Pulmonary embolism	14 (0.6)	7 (0.1)	0.29
Pleural effusion	4 (0.2)	5 (0.8)	0.03
Pneumothorax	8 (0.3)	3 (0.5)	0.72
Hemothorax	15 (0.7)	3 (0.5)	0.78
Sepsis	226 (9.8)	112 (17)	0.001
Shock	198 (8.6)	71 (11)	0.07
Agina pectoris	11 (0.5)	2 (0.3)	0.74
Abdominal aortic aneurysm	12 (0.5)	2 (0.3)	0.74
Cardiomyopathy	25 (1.1)	4 (0.6)	0.37
Congestive heart failure	84 (3.6)	12 (1.8)	0.02
Arrhythmia	30 (1.3)	4 (0,6)	0.15
Myocardial inafrcion	63 (2.7)	6 (0.9)	0.01
Rupture of esophageal varices	9 (0.4)	0 (0)	0.22
Gastrointestinal bleeding	29 (1.3)	4 (0.6)	0.21
Liver failure	30 (1.3)	4 (0.6)	0.15
Pancreatitis	34 (1.5)	2 (0.3)	0.01
Acute renal failure	32 (1.4)	13 (2)	0.28
Overdose	29 (1.3)	1 (0.2)	0.01

Seizure	56 (2.4)	15 (2,3)	0.89
Coma	232 (10.1)	44 (6.6)	0.01
Empyema	2 (0.1)	0 (0)	1.00
Stroke	110 (4.8)	11 (1.6)	<0.001
Brain aneurysm	37 (1.6)	5 (0.8)	0.13
Brain death	5 (0.2)	2 (0.3)	0.66
Transient ischemic attack	2 (0.1)	0 (0)	1,00
Traumatic brain injury	155 (6.7)	4 (0.6)	<0.001
Other	262 (11.4)	101 (15.2)	0.01

COPD, chronic obstructive pulmonary disease

Table S2. Diagnostic procedures in patients with ventilator-associated lower respiratory tract infections.

	Immunosuppression					
	Yes n = 116			No n = 573		
	VAT n = 64	VAP n = 52	p	VAT n = 268	VAP n = 305	p
Endotracheal aspirate	43 (67)	42 (81)	0.039*	235 (88)	211 (69)	<0.001*
Blind protected specimen brush	5 (8)	11 (21)	0.29	27 (10)	40 (13)	0.3
Bronchoscopy	3 (5)	11 (21)	0.085	17 (6)	45 (15)	0.001*
Bronchoalveolar lavage	4 (6)	14 (27)	0.042*	11 (4)	45 (15)	<0.001*
Mini bronchoalveolar lavage	3 (5)	5 (10)	0.73	14 (5)	40 (13)	0.001*
Blood cultures	31 (48)	45 (87)	0.25	155 (58)	230 (75)	<0.001*
Tested for <i>Streptococcus pneumoniae</i> antigen	2 (3)	6 (12)	0.29	12 (4)	10 (3)	0.46
Tested for <i>Legionella pneumophila</i> antigen	3 (5)	7 (13)	0.51	11 (4)	14 (5)	0.78

Data are numbers (%)

IC, immunocompromised; VAT, ventilator-associated tracheobronchitis; VAP, ventilator-associated pneumonia

* OR (95% CI): 2.5 (1.03-6.1); 3.17 (2.04-4.91); 0.39 (0.22-0.70); 0.3 (0.09-0.97); 0.28 (0.13-0.49); 0.37 (0.19-0.69); 0.45 (0.31-0.64); respectively

Table S3. Microorganisms in patients with ventilator-associated lower respiratory tract infections

	Immunosuppression		P
	Yes n = 116	No n = 573	
Polymicrobial	25 (22)	114 (20)	0.7
MDR	83 (72)	338 (59)	0.011*
Gram-negative bacilli	117	509	
<i>Pseudomonas aeruginosa</i>	33 (28)	135 (24)	0.26
<i>Enterobacter</i> sp.	24 (21)	57 (10)	0.001*
<i>Klebsiella</i> sp.	16 (14)	85 (15)	0.77
<i>Escherichia coli</i>	16 (14)	61 (11)	0.33
<i>Stenotrophomonas maltophilia</i>	7 (6)	24 (4)	0.38
<i>Acinetobacter baumannii</i>	7 (6)	34 (6)	0.97
<i>Serratia marcescens</i>	3 (3)	25 (4)	0.37
<i>Proteus mirabilis</i>	4 (3)	25 (4)	0.66
<i>Hemophilus influenzae</i>	5 (4)	52 (9)	0.089
<i>Citrobacter freundii</i>	2 (2)	11 (2)	0.89
Gram-positive Cocci	24	178 (31)	
<i>Streptococcus pneumoniae</i>	8 (7)	32 (6)	0.58
MSSA	10 (9)	136 (24)	<0.001*
MRSA	6 (5)	10 (2)	0.025*

Data are numbers (%)

MDR, multidrug-resistant bacteria; MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*

*OR (95% CI): 1.75 (1.13-2.71); 2.36 (1.4-4); 0.3 (0.15-0.6); 3.1 (1.1-8.62)

Table S4. Risk factors for ICU mortality in patients with ventilator-associated lower respiratory tract infection by univariate analysis.

	Survivors n = 450	Nonsurvivors n = 239	P
At ICU admission			
Age	59 (44, 71)	66 (57, 77)	<0.001
Male gender	306	157	0.54
SAPS II	45 (34, 58)	54 (42, 65)	<0.001
SOFA	7 (5, 10)	8 (6, 11)	0.002
Immunosuppression	53	63	<0.001
ARDS	36	28	0.11
Category of admission			<0.001
Medical	233	160	
Surgical	66	35	
Trauma	151	44	
At VA-LRTI diagnosis			
SOFA	6 (4, 8)	9 (6, 11)	<0.001
Appropriate antibiotic treatment	400	194	0.005*
Multidrug resistant bacteria	256	165	0.001*

Data are numbers (%) or median (interquartile range)

ICU, intensive care medicine; SAPS, simplified acute physiology score; SOFA, sequential organ failure assessment; ARDS, acute respiratory distress syndrome; VA-LRTI, ventilator-associated lower respiratory tract infection

*OR (95% CI): 0.54 (0.39-0.86), 1.72 (1.23-2.4)