

院内肺炎の耐性菌のリスク因子

名古屋大学大学院医学系研究科 呼吸器内科学

佐野 将宏 進藤 有一郎 奥村 隼也 榊原 利博
村上 靖 Nancy Thabet 長谷川 好規



COI 開示

発表者名: ©佐野 将宏 進藤 有一郎 奥村 隼也
榊原 利博 村上 靖 Nancy Thabet
長谷川 好規

演題発表内容に関連し、発表者らに開示すべき
COI 関係にある企業などはありません。

目的

院内肺炎 (HAP) や人工呼吸器関連肺炎 (VAP) は院内感染症のうちで最も頻度の多い疾患のひとつである。適切な抗菌薬治療を行い、不要な広域抗菌薬の使用を減らすために、院内肺炎や人工呼吸器関連肺炎の耐性菌 (DRPs) のリスク因子を明らかにすることは重要である。

方法

期間: 2010年3月から2016年10月

対象患者: 名古屋大学医学部附属病院 (985床) で発症した20歳以上の
全科・全病棟の院内肺炎・人工呼吸器関連肺炎患者

研究方法: 前向き観察研究

Endpoint: 耐性菌の検出

耐性菌の定義:

SBT/ABPC または CTRX に耐性

抗菌薬への感受性は一括で中央判定を行った。

統計学的解析

リスク因子の解析には単変量解析・多変量解析を用いて、オッズ比と
95%信頼区間を求めた。

$P < 0.05$ を統計学的有意水準とした。

結果

Figure 1. Patient flow

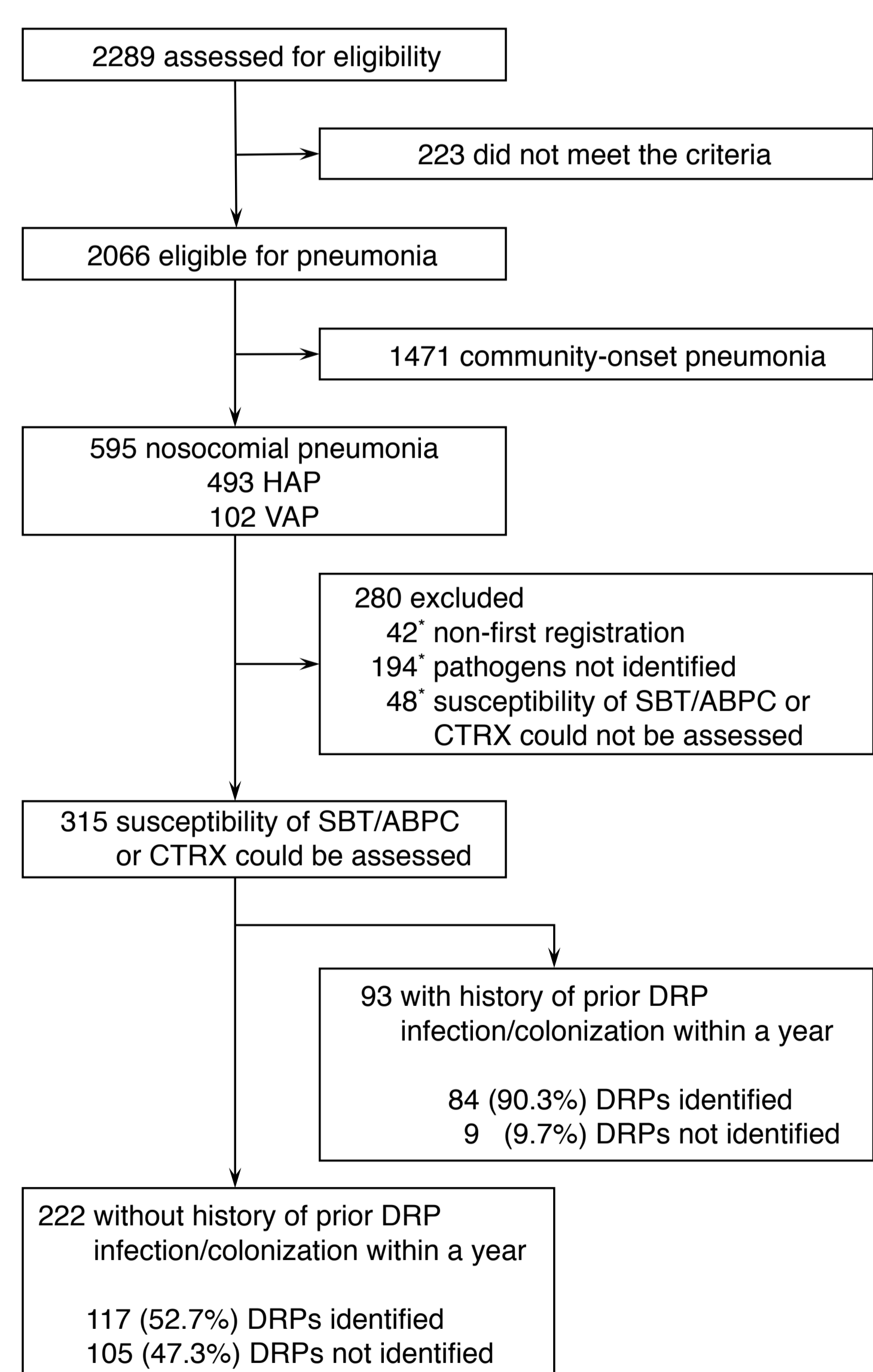
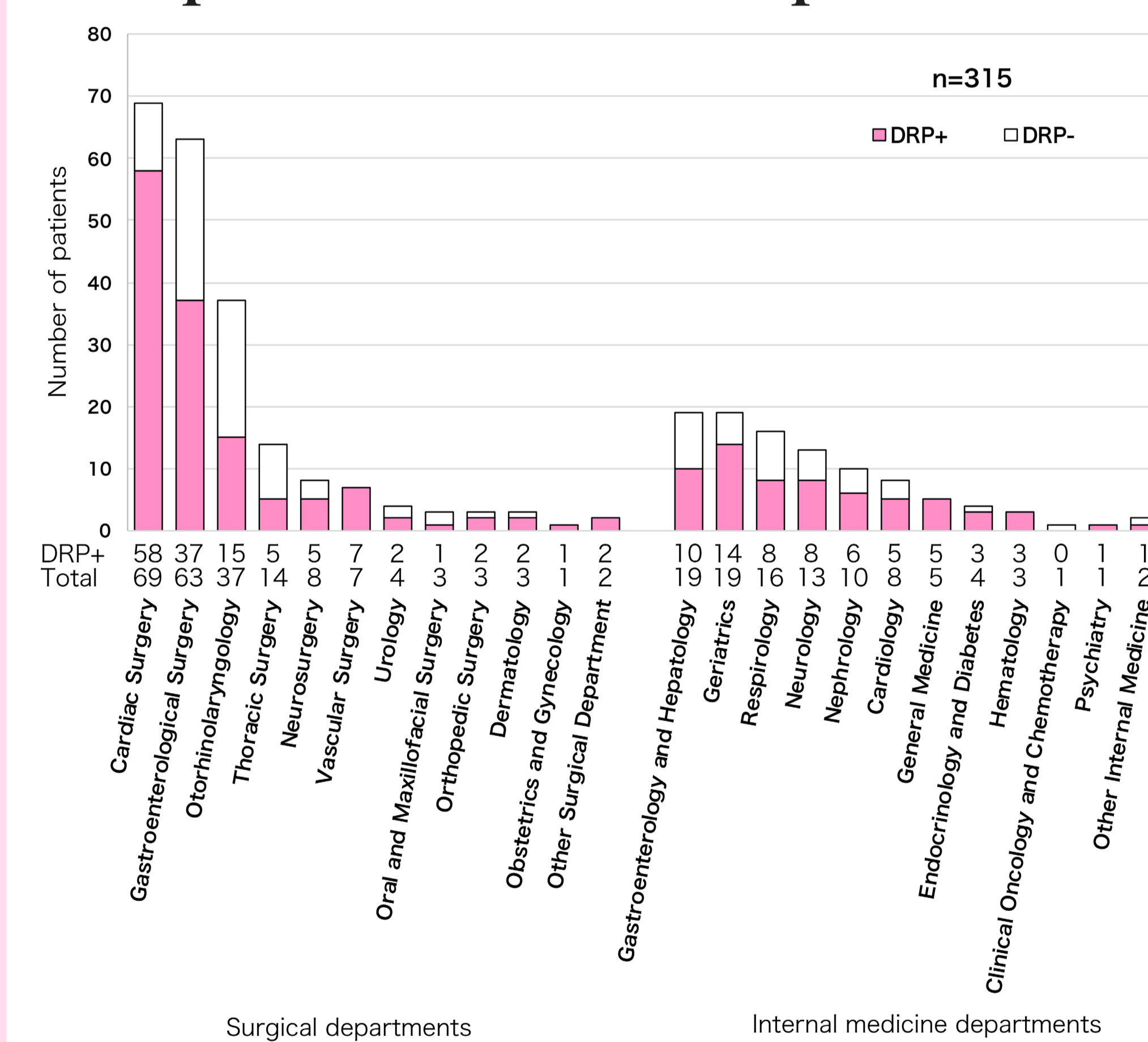


Table 2. Pathogens distributions

HAP and VAP (n = 222)	
Drug-resistant pathogens [†] , n (%)	117 (52.7)
<i>Pseudomonas aeruginosa</i> [†]	35 (15.8)
<i>Staphylococcus aureus</i> (MRSA) [†]	20 (9)
<i>Enterobacter cloacae</i>	15 (6.8)
<i>Enterococcus faecalis</i>	11 (5.0)
<i>Serratia marcescens</i>	11 (5.0)
<i>Acinetobacter</i> sp. [†]	9 (4.1)
<i>Escherichia coli</i>	9 (4.1)
ESBL+ [†]	5 (2.3)
<i>Stenotrophomonas maltophilia</i> [†]	8 (3.6)
<i>Enterobacter aerogenes</i>	5 (2.3)
<i>Klebsiella pneumoniae</i>	5 (2.3)
<i>Haemophilus influenzae</i>	3 (1.4)
<i>Klebsiella oxytoca</i>	2 (0.9)
Others	6 (2.7)
Multidrug-resistant pathogens [‡]	42 (18.9)
Non-drug-resistant pathogens [†] , n (%) 105 (47.3)	
<i>Klebsiella pneumoniae</i>	48 (21.6)
<i>Staphylococcus aureus</i>	42 (18.9)
<i>Haemophilus influenzae</i>	15 (6.8)
<i>Escherichia coli</i>	14 (6.3)
<i>Acinetobacter</i> sp. [†]	13 (5.9)
<i>Streptococcus pneumoniae</i>	11 (5.0)
<i>Enterobacter aerogenes</i>	9 (4.1)
<i>Klebsiella oxytoca</i>	9 (4.1)
<i>Branhamella catarrhalis</i>	8 (3.6)
<i>Enterobacter cloacae</i>	8 (3.6)
<i>Enterobacter sakazakii</i>	3 (1.4)
<i>Morganella morganii</i>	3 (1.4)
<i>Streptococcus agalactiae</i>	3 (1.4)
<i>Nonfermenting Gram-negative bacilli</i>	2 (0.9)
<i>Stenotrophomonas maltophilia</i> [†]	2 (0.9)
<i>Citrobacter koseri</i>	2 (0.9)
Others	4 (1.8)

Abbreviations: MRSA = methicillin-resistant *Staphylococcus aureus*; ESBL+ = extended-spectrum β -lactamase-producing;
[†]Defined as resistant to sulbactam-ampicillin or ceftriaxone.
[‡]Potentially drug-resistant pathogens.
[‡]Multidrug-resistant pathogens were defined according to the international consensus statement documented by Magiorakos, et al. Clin Microbiol Infect. 2012;18(3):268-81.

Figure 2. The number of HAP or VAP patients in each department



心臓外科・消化器外科・耳鼻咽喉科では
HAP・VAPの発症割合が高かった。
耐性菌の検出割合は外科系が64.0%に対して
内科系は63.4%であり、外科系と内科系で差は
無かった。

結論

院内肺炎・人工呼吸器関連肺炎の耐性菌のリスク因子として最も重要なものは、**過去1年以内の耐性菌検出歴**である。そして、過去1年以内の耐性菌検出歴のない患者では、**慢性腎疾患・発症時のADL寝たきり・末梢静脈ルート**の3項目の有無について考慮すべきであり、次いで**過去90日以内の抗菌薬使用歴・ $K < 3.5$ or $K \geq 5.0$ mEq/l**にも注意を払う必要がある。

Table 1. Patient characteristics

Characteristics	HAP and VAP							
	All (n = 315)	With DRPs (n = 201)	Without DRPs (n = 114)	P value	Without history of prior DRP infection/colonization (n = 222)	With DRPs (n = 117)	Without DRPs (n = 105)	P value
Age ≥ 70 yr	181 (57.5)	126 (62.7)	55 (48.2)	0.013	123 (55.4)	72 (61.5)	51 (48.6)	0.052
Male	257 (81.6)	162 (80.6)	95 (83.3)	0.547	188 (84.7)	98 (83.8)	90 (85.7)	0.687
Onset in the ICU	91 (28.9)	69 (34.3)	22 (19.3)	0.005	58 (26.1)	38 (32.5)	20 (19.0)	0.023
≥ 5 days of hospitalization prior to the occurrence of HAP/VAP	291 (92.4)	186 (92.5)	105 (92.1)	0.890	203 (91.4)	107 (91.5)	96 (91.4)	0.995
Mechanical ventilation of ≥ 2 days after tracheal intubation	62 (19.7)	51 (25.4)	11 (9.6)	0.001	39 (17.6)	29 (24.8)	10 (9.5)	0.003
History of operation within 30 days	141 (44.8)	97 (48.3)	44 (38.6)	0.097	109 (49.1)	70 (59.8)	39 (37.1)	0.001
Past history of pneumonia	53 (16.8)	41 (20.4)	12 (10.5)	0.024	26 (11.7)	17 (14.5)	9 (8.6)	0.168
Alcoholism	13 (4.1)	8 (4.0)	5 (4.4)	0.538	12 (5.4)	7 (6.0)	5 (4.8)	0.688
Prior use of antibiotics within 90 days	242 (76.8)	168 (83.6)	74 (64.9)	< 0.001	157 (70.7)	91 (77.8)	66 (62.9)	0.015
History of prior DRP infection/colonization within a year	93 (29.5)	84 (41.8)	9 (7.9)	< 0.001				
Comorbidities								
Congestive heart failure	78 (24.8)	62 (30.8)	16 (14)	0.001	45 (20.3)	31 (26.5)	14 (13.3)	0.015
Chronic pulmonary diseases	68 (21.6)	45 (22.4)	23 (20.2)	0.646	46 (20.7)	26 (22.2)	20 (19.0)	0.560
Chronic kidney disease	57 (18.1)	50 (24.9)	7 (6.1)	< 0.001	39 (17.6)	32 (27.4)	7 (6.7)	< 0.001
Chronic liver diseases	23 (7.3)	13 (6.5)	10 (8.8)	0.450	16 (7.2)	7 (6.0)	9 (8.6)	0.457
Diabetes mellitus	70 (22.2)	44 (21.9)	26 (22.8)	0.851	47 (21.2)	23 (19.7)	24 (22.9)	0.560
Peripheral vascular disease	17 (5.4)	13 (6.5)	4 (3.5)	0.264	11 (5.0)	8 (6.8)	3 (2.9)	0.172
Immunosuppression [†]	59 (18.7)	31 (15.4)	28 (24.6)	0.046	46 (20.7)	20 (17.1)	26 (24.8)	0.159
Bedridden [‡]	119 (37.8)	99 (49.3)	20 (17.5)	< 0.001	65 (29.3)	48 (41.0)	17 (16.2)	< 0.001
Use of gastric acid suppressive agents [§]	200 (63.5)	125 (62.2)	75 (65.8)	0.524	138 (62.2)	70 (59.8)	68 (64.8)	0.449
Tube feeding	123 (39)	92 (45.8)	31 (27.2)	0.001	77 (34.7)	49 (41.9)	28 (26.7)	0.017
Manual ventilation within 7 days	34 (10.8)	21 (10.4)	13 (11.4)	0.793	28 (12.6)	15 (12.8)	13 (12.4)	0.922
Central intravenous catheter	117 (37.1)	87 (43.3)	30 (26.3)	0.003	78 (35.1)	50 (42.7)	28 (26.7)	0.012
Peripheral intravenous catheter	196 (62.2)	140 (69.7)	56 (49.1)	< 0.001	134 (60.4)	83 (70.9)	51 (48.6)	0.001
Physical findings								
Low blood pressure [¶]	157 (49.8)	106 (52.7)	51 (44.7)	0.172	105 (47.3)	60 (51.3)	45 (42.9)	0.209
Orientation disturbance (confusion) ^{††}	112 (35.7)	77 (38.3)	35 (31.0)	0.193	75 (33.9)	43 (36.8)	32 (30.8)	0.348
Laboratory findings								
Hematocrit $< 30\%$	131 (41.6)	97 (48.3)	34 (29.8)	0.001	85 (38.3)	53 (45.3)	32 (30.5)	0.023
Platelet $< 100,000/\text{mm}^3$	74 (23.5)	57 (28.4)	17 (14.9)	0.007	48 (21.6)	32 (27.4)	16 (15.2)	0.029
Na < 130 mEq/l	23 (7.3)	12 (6.0)	11 (9.6)	0.228	17 (7.7)	6 (5.1)	11 (10.5)	0.135
K < 3.5 or K ≥ 5.0 mEq/l	55 (17.5)	43 (21.4)	12 (10.5)	0.015	31 (14.0)	20 (17.1)	11 (10.5)	0.156
Albumin < 3.0 g/dl	205 (65.1)	135 (67.2)	70 (61.4)	0.303	144 (64.9)	80 (68.4)	64 (61.0)	0.247
BUN > 20 mg/dl	196 (62.2)	144 (71.6)	52 (45.6)	< 0.001	125 (56.3)	78 (66.7)	47 (44.8)	0.001
PaO ₂ /FIO ₂ ≤ 200	78 (24.8)	55 (27.4)	23 (20.2)	0.156	51 (23.0)	29 (24.8)	22 (21.0)	0.498
Radiographic findings								
Bilateral lung involvement	143 (45.4)	91 (45.3)	52 (45.6)	0.953	93 (41.9)	44 (37.6)	49 (46.7)	0.172
Pleural effusion	150 (47.6)	108 (53.7)	42 (36.8)	0.004	91 (41.0)	55 (47.0)	36 (34.3)	0.054
SOFA score, median (IQR)	4 (2-7)	4 (2-8)	3 (2-6)	< 0.001	3.5 (2-6.25)	4 (2-8)	3 (2-6)	0.011

Definition of abbreviations: BUN = blood urea nitrogen; ICU = intensive care unit; IQR = interquartile range; SOFA = sequential organ failure assessment.

[†]Data are presented as n (%) otherwise indicated.

^{††}Including any immunosuppressive diseases, such as congenital or acquired immunodeficiency, hematologic diseases, and neutropenia ($< 1,000/\text{mm}^3$), treatment with immunosuppressive drugs within the previous 30 days, or corticosteroids in daily dose of at least 10mg/day of a prednisone equivalent for more than 2 weeks.

[‡]Including patients who forced to be bedridden because of surgery.

[§]H₂-blockers or proton pump inhibitors.

[¶]Systolic blood pressure < 90 mmHg or diastolic blood pressure ≤ 60 mmHg or use of vasopressor.

^{†††}Glasgow coma scale ≤ 12 or use of sedative agents.

Table 3. Risk factors for DRPs in patients with HAP and VAP without prior DRP history

Variable	Resistant		Multivariate analysis	
	Yes	No	Adjusted OR (95% CI)	P value
Age ≥ 70 years old				
No (n = 99)	45	54	1 (ref)	
Yes (n = 123)	72	51	1.49 (0.78-2.84)	0.228
Male				
No (n = 34)	19	15	1 (ref)	
Yes (n = 188)	98	90	0.73 (0.31-1.69)	0.459
Prior use of antibiotics within 90 days				
No (n = 65)	26	39	1 (ref)	
Yes (n = 157)	91	66	2.02 (0.99-4.10)	0.051
≥ 5 days of hospitalization prior to the occurrence of HAP/VAP				
No (n = 19)	10	9	1 (ref)	
Yes (n = 203)	107	96	1.50 (0.44-5.15)	0.516
Immunosuppression [†]				
No (n = 176)	97	79	1 (ref)	
Yes (n = 46)	20	26	0.96 (0.43-2.16)	0.919
Mechanical ventilation of ≥ 2 days after tracheal intubation				
No (n = 183)	88	95	1 (ref)	
Yes (n = 39)	29	10	1.00 (0.28-3.56)	0.995
Chronic kidney disease [‡]				
No (n = 183)	85	98	1 (ref)	
Yes (n = 39)	32	7	11.52 (4.01-33.10)	< 0.001
Bedridden [‡]				
No (n = 157)	69	88	1 (ref)	
Yes (n = 65)	48	17	3.98 (1.48-10.69)	0.006
Peripheral intravenous catheter				
No (n = 88)	34	54	1 (ref)	
Yes (n = 134)	83	51	2.58 (1.31-5.08)	0.006
K < 3.5 mEq/l or K ≥ 5.0 mEq/l				
No (n = 191)	97	94	1 (ref)	
Yes (n = 31)	20	11	2.39 (0.95-5.97)	0.063

Definition of abbreviations: CI = confidence interval; OR = odds ratio.

[†]Including any immunosuppressive diseases, such as congenital or acquired immunodeficiency, hematologic diseases, and neutropenia ($< 1,000/\text{mm}^3$), treatment with immunosuppressive drugs within the previous 30 days, or corticosteroids in daily dose of at least 10mg/day of a prednisone equivalent for more than 2 weeks.

[‡]Including pre-existing renal disease with documented abnormal serum creatinine levels outside the pneumonia episode.

[‡]Including patients who forced to be bedridden because of surgery.