# [Original article]



# Drug resistance of *Pseudomonas aeruginosa* based on the isolation sites and types of gastrointestinal diseases: An observational study

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# Abstract

**Introduction :** We investigated the drug resistance status of *Pseudomonas aeruginosa (P. aerugino-sa)* focusing on its isolation sites and types of diseases.

**Materials and methods :** A microbiological laboratory database was searched to identify all clinical cultures positive for *P. aeruginosa*. Clinicopathologic features and susceptibility of *P. aeruginosa* to any antibiotics were evaluated in patients admitted to the division of upper (Upper-GI group) or lower gastrointestinal surgery (Lower-GI group). In addition, we investigated the susceptibility of *P. aeruginosa* to any antibiotics based on the isolation site.

**Results :** *P. aeruginosa* was frequently detected in the sputum and urine of the Upper-GI and Lower-GI groups, respectively. Among *P. aeruginosa* isolates from drain discharge, a significantly higher rate of resistance to imipenem, amikacin, and ciprofloxacin was observed ; among *P. aeruginosa* isolates from wounds, a substantially higher proportion had resistance to imipenem and cefozopran in the Upper-GI group. However, there was no difference between the two groups in the drug resistance of *P. aeruginosa* isolated from urine, sputum, blood, and ascites. *P. aeruginosa* isolated from sputum showed more resistance to imipenem and ciprofloxacin than those isolated from other sites. **Conclusion :** There were significant differences in the drug resistance of *P. aeruginosa* based on the isolation sites and types of diseases.

Key words : Pseudomonas aeruginosa, drug resistance, the isolation sites

# Introduction

*Pseudomonas aeruginosa (P. aeruginosa)* is one of the main microbes responsible for drug-resistant nosocomial infections<sup>1)</sup>. *P. aeruginosa* is naturally resistant to many antibiotics and has a remarkable capacity to acquire new resistance mechanisms, leading to increased therapeutic problems. Multidrug resistant-*P. aeruginosa* (MDRP) is a strain that has acquired resistance to three classes of antibacterial agents : fluoroquinolones, carbapenems, and aminoglycosides<sup>2)</sup>. Currently, the isolation rate of MDRP is reported to be 1-41%, and this varies greatly depending on the country and hospital environment<sup>3-6)</sup>. Because of the limited choice of antibiotics, MDRP is often difficult to treat and is associated with high morbidity and mortality rates<sup>7,8)</sup>.

The process of acquiring antibiotic resistance is

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©2024 The Fukushima Society of Medical Science. This article is licensed under a Creative Commons [Attribution-NonCommercial-ShareAlike 4.0 International] license. https://creativecommons.org/licenses/by-nc-sa/4.0/ influenced by various factors, including the immune status of the host, length of hospital stay, prolonged use of antibiotics, and environment. Moreover, there are potential differences in patient characteristics between upper- and lower- gastrointestinal surgery patients, such as esophageal cancer patients often suffering from postoperative pneumonia and rectal cancer patients suffering from urinary disturbance that require long-term placement of a urinary catheter, and these may lead to differences in the isolation of resistant bacteria. In this study, we investigated the drug resistance status of *P. aeruginosa*, focusing on the isolation sites and type of gastrointestinal disease.

# Materials and methods

### Study participants

The microbiology laboratory database of the National Defense Medical College Hospital in To-

korozawa, Japan, was searched to identify all clinical cultures positive for *P. aeruginosa* between 2015 and 2022. *P. aeruginosa* was isolated from 324 patients and 891 sites in the gastrointestinal surgical ward, where upper and lower gastrointestinal surgeries were primarily performed. Clinicopathologic features and susceptibility of *P. aeruginosa* to any antibiotics were evaluated in patients admitted to the division of upper gastrointestinal surgery (Upper-GI group, N = 97) and those admitted to the division of lower gastrointestinal surgery (Lower-GI group, N = 227). In addition, we investigated the susceptibility of *P. aeruginosa* to any antibiotics based on the isolation site.

All subjects provided written informed consent for the inclusion of their data. This study was conducted according to protocols approved by the National Defense Medical College Institutional Review Board (Permission number : 4147).

Imipenem (IPM), Meropener	m (MEPM), Dorip	enem (DRI	PM)		
MIC (µg/mL)	$\leq 1$	2	4	8	$16 \leq$
Breakpoint	S		Ι		R
Score	1	2	3	4	5
Amikacin (AMK)					
MIC (µg/mL)	$\leq 8$	16	32	64 ≤	
Breakpoint	S		Ι	R	
Score	1	2	3	4	
Ciprofloxacin (CPFX)					
MIC (µg/mL)	≤ 0.25	0.5	1	2	4≤
Breakpoint		S		Ι	R
Score	1	2	3	4	5
Piperacillin (PIPC), Tazobac	tam/piperacillin (	FAZ/PIPC)			
MIC (µg/mL)	$\leq 8$	16	32	64	128 ≤
Breakpoint	S			Ι	R
Score	1	2	3	4	5
Ceftazidime (CAZ), Cefozop	oran (CZOP)				
MIC (µg/mL)	≤ 4	8	16	32 ≤	
Breakpoint	S			Ι	
Score	1	2	3	4	
Levofloxacin (LVFX)					
MIC (µg/mL)	$\leq 0.5$	1	2	4	$8 \leq$
Breakpoint		S		Ι	R
Score	1	2	3	4	5

Table 1. Breakpoints and susceptibility scores for each antibiotic

MIC, minimal inhibitory concentration

		er GI =97)		er GI 227)	p-value
Age	73.1	± 8.9	68.6	0.03	
Male/ Female	78	8/19	140	6/81	< 0.01
Purpose of admission					
Surgery	67	69%	187	82%	
Intensive care	29	30%	38	17%	< 0.05
others	1	1%	2	1%	
Surgery					
Yes	67	69%	191	84%	0.01
No	30	31%	36	16%	< 0.01
Diagnosis on admission					
Esophageal cancer	52	54%	0	0%	
Gastric cancer	35	36%	0	0%	
Rectal cancer	0	0%	104	46%	
Colon cancer	0	0%	61	27%	
GI perforation	5	5%	15	7%	
Bowel obstruction	1	1%	11	5%	
Appendicitis	0	0%	6	3%	
IBD	0	0%	5	2%	
Others	4	4%	25	11%	
Antibiotic prophylaxis					
CEZ	61	97%	2	1%	
CMZ	2	3%	181	97%	< 0.01
Others	0	0%	4	2%	
Co-morbidity					
Diabetes mellitus					
Yes	17	18%	40	18%	
No	80	82%	187	82%	0.98
Hypertension					
Yes	43	44%	84	37%	
No	54	56%	143	63%	0.22
Steroid useage					
Yes	4	4%	12	5%	
No	93	96%	215	95%	0.65
Previous hospital stay					
Yes	67	69%	111	49%	
No	30	31%	116	51%	< 0.01
Hospital death	00	02/0	110	01/0	
Yes	15	15%	21	9%	
No	82	85%	206	91%	0.11
Hospital stay (days)		± 149.0		± 57.4	0.10
Endotracheal intubation	01.1 -		01.0		0.10
Yes	29	30%	25	11%	
No	20 68	70%	202	89%	< 0.01
Urinary catheterisation	50			0070	
Yes	66	68%	141	62%	
No	31	32%	86	38%	0.31
Central venous catheter	01	0270	00	0070	
Yes	60	62%	90	40%	
No	37	02 <i>%</i> 38%	90 137	40% 60%	< 0.01

 Table 2.
 Demographics and operative outcomes in the Upper-GI and Lower-GI groups

Blood purificatiuon therapy					
Yes	10	10%	10	4%	< 0.05
No	87	90%	217	96%	< 0.05
Isolation site					
Drain discharge	41	42%	96	42%	>0.99
Urine	13	13%	90	40%	< 0.01
Sputum	61	63%	36	16%	< 0.01
Wound	17	18%	43	19%	0.76
Blood	6	6%	12	5%	0.75
Ascites	5	5%	10	4%	0.77
Others	8	8%	5	2%	0.65

GI, gastrointestinal; IBD, inflammatory bowel disease; CEZ, cefazolin; CMZ, cefmetazole





### Scores of susceptibilities to antibiotics

Susceptibility to antibiotics was determined by measuring the minimal inhibitory concentrations (MIC) and was scored based on the MIC, as shown in Table 1. The MDRP score was defined as the sum of the imipenem (IPM), amikacin (AMK), and ciprofloxacin (CPFX) scores (minimum, 3 points; maximum,14 points). The breakpoints were classified as susceptible (S), intermediate (I), and resistant (R) according to the recommendations of the Clinical and Laboratory Standards Institute<sup>9</sup>. When *P. aeruginosa* was detected multiple times, the maximum score or breakpoint for each antibiotic was used.

### Statistical analysis

Continuous data were presented as mean  $\pm$  standard deviation (SD). Statistical analyses were performed using the Mann–Whitney *U* test, chi-square test, or Fisher's exact test, as appropriate. Statistical significance was set at p < 0.05. All analyses were performed using JMP Pro 15 software (SAS Institute, Cary, NC, USA).

# Results

Table 2 shows the demographic characteristics and operative outcomes of the Upper-GI and Lower-

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PIPC Break Point	S	Ι	R	p-value
Upper GI	71 (73.2%)	10 (10.3%)	16 (16.5%)	-0.05
Lower GI	183 (80.6%)	28 (12.3%)	16 (7.1%)	< 0.05
TAZ/PIPC Break Point	S	Ι	R	p-value
Upper GI	74 (76.3%)	9 (9.3%)	14 (14.4%)	-0.05
Lower GI	197 (86.8%)	16 (7.1%)	14 (6.2%)	< 0.05
MEPM Break Point	S	Ι	R	p-value
Upper GI	76 (78.4%)	6 (6.2%)	15 (15.5%)	< 0.05
Lower GI	206 (90.8%)	8 (3.5%)	13 (5.7%)	< 0.05
DRPM Break Point	S	Ι	R	p-value
Upper GI	82 (84.5%)	6 (6.2%)	9 (9.3%)	-0.01
Lower GI	217 (95.6%)	3 (1.3%)	7 (3.1%)	< 0.01
CAZ Break Point	S	Ι	R	p-value
Upper GI	79 (81.4%)	18 (18.6%)	NA	0.14
Lower GI	199 (87.7%)	28 (12.3%)	NA	0.14
CZOP Break Point	S	Ι	R	p-value
Upper GI	79 (81.4%)	18 (18.6%)	NA	-0.05
Lower GI	205 (90.3%)	22 (9.75%)	NA	< 0.05
LVFX Break Point	S	Ι	R	p-value
Upper GI	78 (80.4%)	5 (5.2%)	14 (14.4%)	0.19
Lower GI	199 (87.7%)	12 (5.3%)	16 (7.1%)	0.13

Table 3. Breakpoints for antibiotics in the Upper-GI and Lower-GI groups

GI, gastrointestinal; PIPC, piperacillin; TAZ/PIPC, tazobactam/piperacillin; MEPM, meropenem; DRPM, doripenem; CAZ, ceftazidime; CZOP, cefozopran; LVFX, levofloxacin; NA, not assigned

GI groups. The Upper-GI group had significantly older patients, predominantly male, and more patients admitted to intensive care than the Lower-GI group. Cefazolin was frequently used as a prophylactic antibiotic in the Upper-GI group, whereas cefmetazole was frequently used in the Lower-GI group. There were no significant differences in comorbidities, steroid use, length of hospital stay, or hospital death between the two groups; however, the number of patients with a previous hospitalization was significantly higher in the Upper-GI group than in the Lower-GI group. Furthermore, the Upper-GI group had a higher percentage of patients requiring endotracheal intubation, central venous catheterization, and blood purification therapy than the Lower-GI group. A higher percentage of P. aeruginosa was isolated from sputum in the Upper-GI group, whereas a higher percentage of *P. aeruginosa* was isolated from urine in the Lower-GI group.

The Upper–GI group had more cases with an IPM score of 4 or 5 (i.e. cases with a breakpoint of R as resistance to IPM) than the Lower–GI group, although there were no differences in either AMK or CPFX scores. The Upper-GI group had significantly higher MDRP scores than the Lower-GI group (Fig. 1). In addition, the Upper-GI group had higher meropenem (MEPM), doripenem (DRPM), and cefozopran (CZOP) scores than the Lower-GI group (Table 3).

Next, we investigated the antibiotic resistance according to the isolation sites in the two groups (Table 4). Among P. aeruginosa isolates from drain discharge, a significantly higher rate of resistance to IPM, AMK, CPFX, tazobactam/piperacillin (TAZ/ PIPC), MEPM, DRPM, CZOP, and levofloxacin was observed in the Upper-GI group. Similarly, among *P. aeruginosa* isolates from wounds, a significantly higher proportion was resistant to IPM, PIPC, TAZ/ PIPC, ceftazidime, and CZOP in the Upper-GI group. However, there was no difference between the two groups in the drug resistance of *P. aerugino*sa isolated from urine, sputum, blood, and ascites. *P. aeruginosa* isolated from sputum was more likely to show resistance to IPM (P=0.07) than that isolated from other sites (Fig. 2) and was more likely to have higher MDRP scores than that isolated from

			Drain c	Drain discharge			Urine	ne			Sputum	tum	
		S	I	R	p-value	S	I	R	<i>p</i> -value	S	Ι	R	p-value
IPM	Upper GI Lower GI	23 (56.1%) 80 (83.3%)	$\begin{array}{c} 3 \ (7.3\%) \\ 5 \ (5.2\%) \end{array}$	$\begin{array}{c} 15 \ (36.6\%) \\ 11 \ (11.5\%) \end{array}$	< 0.01	9 (69.2%) 76 (84.4%)	$\begin{array}{c} 0 \ (0\%) \\ 5 \ (5.6\%) \end{array}$	$\begin{array}{c} 4 \ (30.1\%) \\ 9 \ (10.0\%) \end{array}$	0.10	37 (60.7%) 26 (72.2%)	5 (8.2%) 4 (11.1%)	$19 (31.2\%) \\ 6 (16.7\%)$	0.27
AMK	Upper GI Lower GI	$\begin{array}{c} 39 \ (95.1\%) \\ 96 \ (100\%) \end{array}$	$\begin{array}{c} 2 \ (4.9\%) \\ 0 \ (0\%) \end{array}$	(960) 0 (0%)	< 0.05	13 $(100\%)$ 89 $(98.9\%)$	$\begin{array}{c} 0 (0\%) \\ 1 (1.1\%) \end{array}$	(%0) 0 (0%)	0.60	59 (96.7%) 36 (100%)	$\begin{array}{c} 1 \ (1.6\%) \\ 0 \ (0\%) \end{array}$	$\begin{array}{c} 1 \ (1.6\%) \\ 0 \ (0\%) \end{array}$	0.39
CPFX	Upper GI Lower GI	29 (70.7%) 86 (89.6%)	2 (4.9%) 2 (2.1%)	$\begin{array}{c} 10 \ (24.4\%) \\ 8 \ (8.3\%) \end{array}$	< 0.05	12 (92.3%) 83 (92.2%)	$\begin{array}{c} 0 \ (0\%) \\ 1 \ (1.1\%) \end{array}$	$\begin{array}{c} 1 \ (7.7\%) \\ 6 \ (6.7\%) \end{array}$	0.87	45 (73.8%) 29 (80.6%)	$\begin{array}{c} 2 & (3.3\%) \\ 2 & (5.6\%) \end{array}$	$\begin{array}{c} 14 \ (23.0\%) \\ 5 \ (13.9\%) \end{array}$	0.49
PIPC	Upper GI Lower GI	26 (63.4%) 73 (76.0%)	$\begin{array}{c} 5 \ (12.2\%) \\ 15 \ (15.6\%) \end{array}$	10 (24.4%) 8 (8.3%)	0.06	11 (84.6%) 76 (84.4%)	$\begin{array}{c} 2 \ (15.3\%) \\ 10 \ (11.1\%) \end{array}$	$\begin{array}{c} 0 \ (0\%) \\ 4 \ (4.4\%) \end{array}$	0.54	41 (67.2%) 23 (63.9%)	8 (13.1%) 7 (19.4%)	$\begin{array}{c} 12 \ (19.7\%) \\ 6 \ (16.7\%) \end{array}$	0.70
TAZ/PIPC	Upper GI Lower GI	27 (65.9%) 82 (85.4%)	3 (12.2%) 7 (7.3%)	9 (22.0%) 7 (7.3%)	< 0.05	12 (92.3%) 80 (88.9%)	$\frac{1}{6} (7.7\%) $	$\begin{array}{c} 0 \ (0\%) \\ 4 \ (4.4\%) \end{array}$	0.57	42 (72.4%) 26 (66.7%)	5 (8.6%) 7 (18.0%)	$\begin{array}{c} 11 \ (19.0\%) \\ 6 \ (15.4\%) \end{array}$	0.39
MEPM	Upper GI Lower GI	27 (65.9%) 87 (90.6%)	$\begin{array}{c} 4 \ (9.8\%) \\ 4 \ (4.2\%) \end{array}$	$\begin{array}{c} 10 \ (24.4\%) \\ 5 \ (5.2\%) \end{array}$	< 0.01	$10 (76.92\%) \\ 82 (91.1\%)$	$\frac{1}{2} (7.7\%)$	$\begin{array}{c} 2 \ (15.4\%) \\ 6 \ (6.7\%) \end{array}$	0.36	$\begin{array}{l} 43 \ (74.1\%) \\ 31 \ (79.5\%) \end{array}$	$5 (8.6\%) \\ 2 (5.1\%)$	$\begin{array}{c} 10 \ (17.2\%) \\ 6 \ (15.4\%) \end{array}$	0.76
DRPM	Upper GI Lower GI	30 (73.2%) 92 (95.8%)	$5 (12.2\%) \\ 3 (3.1\%)$	$\begin{array}{c} 6 (14.6\%) \\ 1 (1.0\%) \end{array}$	< 0.01	$11 (84.6\%) \\85 (94.4\%)$	$\frac{1}{1} (7.7\%) \\ 1 (1.1\%)$	$\frac{1}{4} (7.7\%)$	0.37	49 (84.5%) 33 (84.6%)	$\begin{array}{c} 3 \ (5.2\%) \\ 1 \ (2.6\%) \end{array}$	$\begin{array}{c} 6 \ (10.3\%) \\ 5 \ (12.8\%) \end{array}$	0.77
CAZ	Upper GI Lower GI	30 (73.2%) 83 (86.5%)	$\begin{array}{c} 11 \ (26.8\%) \\ 13 \ (13.5\%) \end{array}$	NA NA	0.07	12 (92.3%) 82 (91.1%)	$\frac{1}{8} (8.7\%)$	NA NA	0.88	45 (77.6%) 28 (71.8%)	13 (22.4%) 11 (28.2%)	NA NA	0.52
CZOP	Upper GI Lower GI	31 (75.6%) 86 (89.6%)	$\begin{array}{c} 10 \ (24.4\%) \\ 10 \ (10.4\%) \end{array}$	NA NA	< 0.05	12 (92.3%) 83 (92.2%)	$\frac{1}{7} (8.7\%)$	NA NA	0.99	44 (75.9%) 29 (74.4%)	$\begin{array}{c} 14 \ (24.1\%) \\ 10 \ (25.6\%) \end{array}$	NA NA	0.87
LVFX	Upper GI Lower GI	30 (73.2%) 84 (87.5%)	$\frac{1}{4} (2.4\%)$	$\begin{array}{c} 10 \ (24.4\%) \\ 8 \ (8.3\%) \end{array}$	< 0.05	12 (92.3%) 79 (87.8%)	$\begin{array}{c} 0 \ (0\%) \\ 6 \ (6.7\%) \end{array}$	$\frac{1}{5} (7.7\%)$	0.42	$\begin{array}{l} 43 \ (74.1\%) \\ 30 \ (76.9\%) \end{array}$	5 (8.6%) 3 (7.7%)	$\begin{array}{c} 10 \ (17.2\%) \\ 6 \ (15.4\%) \end{array}$	0.95

Table 4. Breakpoints for each antibiotic according to the isolation sites

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		<i>p</i> -value	0.13	0.36	>0.99	0.59	0.41	0.22	0.13	0.18	0.36	>0.99
	es	R	$\begin{array}{c} 1 \ (20.0\%) \\ 0 \ (0\%) \end{array}$	$\begin{array}{c} 0 (0\%) \\ 1 (10\%) \end{array}$	(%0) 0	$\begin{array}{c} 0 (0\%) \\ 1 (10.0\%) \end{array}$	$\begin{array}{c} 0 (0\%) \\ 1 (10.0\%) \end{array}$	$\begin{array}{c} 1 \ (20.0\%) \\ 0 \ (0\%) \end{array}$	$\begin{array}{c} 1 \ (20.0\%) \\ 0 \ (0\%) \end{array}$	NA NA	NA NA	(%0) 0 (%)
	Ascites	I	(%0) 0	(%0) 0 (%)	(%0) 0	$\frac{1}{1} (20.0\%)$ 1 (10.0%)	$\begin{array}{c} 0 (0\%) \\ 1 (10.0\%) \end{array}$	$\begin{array}{c} 0 \ (6.3\%) \\ 1 \ (10\%) \end{array}$	(%0) 0	$\begin{array}{c} 0 \ (0\%) \\ 2 \ (20\%) \end{array}$	$\begin{array}{c} 0 (0\%) \\ 1 (10\%) \end{array}$	(%0) 0 (\%) 0
		S	$\begin{array}{c} 4 \ (80.0\%) \\ 10 \ (100\%) \end{array}$	5 (100%) 9 (90%)	5(100%) 10(100%)	4 (80.0%) 8 (80.0%)	$5 (100\%) \\ 8 (80.0\%)$	4 (80.0%) 9 (90%)	$\begin{array}{c} 4 \ (80.0\%) \\ 10 \ (100\%) \end{array}$	$5 (100\%) \\ 8 (80.0\%)$	5 (100%) 9 (90%)	$\begin{array}{c} 5 \ (100\%) \\ 10 \ (100\%) \end{array}$
		<i>p</i> -value	0.59	>0.99	0.61	0.73	0.61	0.61	0.61	0.61	0.61	0.73
	po	R	$\frac{1}{1} (16.7\%)$ $\frac{1}{1} (8.3\%)$	(%0) 0	$\frac{1}{1} (16.7\%)$ $\frac{1}{1} (8.3\%)$	$\frac{1}{1} (16.7\%)$ $\frac{1}{1} (8.3\%)$	$\frac{1}{1} (16.7\%)$ $\frac{1}{1} (8.3\%)$	$\frac{1}{1} (16.7\%)$ $\frac{1}{1} (8.3\%)$	$\frac{1}{1} (16.7\%)$ $\frac{1}{1} (8.3\%)$	NA NA	NA NA	$\frac{1}{1} (17.2\%)$ $\frac{1}{1} (8.3\%)$
ontinued)	Blood	Ι	$\begin{array}{c} 0 (0\%) \\ 1 (8.3\%) \end{array}$	(%0) 0 (%)	(%0) 0 (%)	$\frac{1}{1} (16.7\%) \\ \frac{1}{1} (8.3\%)$	(%0) 0 (\%0) 0	(%0) 0 (\%0) 0	(%0) 0 (%)	$\frac{1}{1} (16.7\%) \\ \frac{1}{1} (8.3\%)$	$\frac{1}{1} (16.7\%) \\ \frac{1}{1} (8.3\%)$	$\frac{1}{1} \ (8.6\%)$ $\frac{1}{1} \ (8.3\%)$
Table 4. (Continued)		s	5 (83.3%) 10 (83.3%)	$\begin{array}{c} 6 & (96.6\%) \\ 12 & (100\%) \end{array}$	5 (83.3%) 11 (91.7%)	$\begin{array}{c} 4 \ (66.7\%) \\ 10 \ (83.3\%) \end{array}$	5 (83.3%) 11 (91.7%)	5 (83.3%) 11 (91.7%)	5 (83.3%) 11 (91.7%)	5 (83.3%) 11 (91.7%)	5 (83.3%) 11 (91.7%)	$\begin{array}{c} 4 \ (74.1\%) \\ 10 \ (83.3\%) \end{array}$
		<i>p</i> -value	< 0.05	0.10	0.17	< 0.05	< 0.05	0.06	0.08	< 0.05	< 0.05	0.08
	nd	R	5 (31.3%) 2 (4.6%)	$\begin{array}{c} 1 \ (6.3\%) \\ 0 \ (0\%) \end{array}$	$5 (31.3\%) \\5 (11.4\%)$	6 (37.5%) 3 (6.8%)	$5 (31.3\%) \\ 3 (6.8\%)$	$\begin{array}{c} 3 \ (18.8\%) \\ 2 \ (4.6\%) \end{array}$	$\begin{array}{c} 2 \ (12.5\%) \\ 1 \ (2.3\%) \end{array}$	NA NA	NA NA	$\begin{array}{c} 5 \ (31.3\%) \\ 4 \ (9.1\%) \end{array}$
	Wound	I	2 (12.5%) 3 (6.8%)	(%0) 0 (%)	$\begin{array}{c} 0 (0\%) \\ 1 (2.3\%) \end{array}$	$\begin{array}{c} 1 \ (6.3\%) \\ 4 \ (9.1\%) \end{array}$	$\begin{array}{c} 2 \ (12.5\%) \\ 1 \ (2.3\%) \end{array}$	$\begin{array}{c} 1 \ (6.3\%) \\ 0 \ (0\%) \end{array}$	$\frac{1}{0} (6.3\%) \\ 0 (0\%)$	6 (37.5%) 4 (9.1%)	6 (37.5%) 3 (6.8%)	$\begin{array}{c} 0 \ (0\%) \\ 2 \ (4.6\%) \end{array}$
		S	9 (56.3%) 39 (88.6%)	$15 (96.6\%) \\ 44 (100\%)$	11 (68.8%) 38 (86.4%)	9 $(56.3\%)$ 37 $(84.1\%)$	$\begin{array}{c} 9 & (56.3\%) \\ 40 & (90.9\%) \end{array}$	12 (75.0%) 42 (95.5%)	13 (81.3%) 43 (97.7%)	$\begin{array}{c} 10 \ (62.5\%) \\ 40 \ (90.9\%) \end{array}$	10 (62.5%) 41 (93.2%)	11 (68.8%) 38 (86.4%)
			Upper GI Lower GI	Upper GI Lower GI	Upper GI Lower GI	Upper GI Lower GI	Upper GI Lower GI	Upper GI Lower GI	Upper GI Lower GI	Upper GI Lower GI	Upper GI Lower GI	Upper GI Lower GI
			MdI	AMK	CPFX	PIPC	TAZ/PIPC	MEPM	DRPM	CAZ	CZOP	LVFX

# Drug-resistance of pseudomonas aeruginosa



Fig. 2. Breakpoints for IPM, AMK, and CPFX according to the isolation sites. *Pseudomonas aeruginosa* isolated from sputum was more likely to show drug resistance to IPM and CPFX than those isolated from other sites. IPM, imipenem; AMK, amikacin; CPFX, ciprofloxacin

other sites, specifically there were significant differences compared to that from wound and ascites (Fig. 3).

## Discussion

In this study, we demonstrated that there were significant differences in the drug resistance of *P. ae-ruginosa*, depending on the site of isolation and gastrointestinal disease type. In the Upper-GI group, resistance to PIPC, TAZ/PIPC, MEPM, DRPM, and CZOP as well as to the three classes of antibiotics used to define MDRP, was observed.

Endotracheal intubation, central venous catheter placement, and blood purification therapy were





performed more frequently in the Upper-GI group than in the Lower-GI group, suggesting that the Upper-GI group required intensive care and included more severely ill patients compared with the Lower-GI group. Resistance is more frequent in units for the management of patients with burns and cystic fibrosis and in intensive care units<sup>6,10,11)</sup>. In addition, Palacios-Baena *et al.* reported in a systematic review that the Acute Physiology and Chronic Health Evaluation II score is a risk factor for carbapenemresistant Gram-negative bacterial infections<sup>12)</sup>. Therefore, it has been suggested that patients with severe diseases are more likely to develop drug resistance to *P. aeruginosa*.

There were significant differences in the susceptibility of *P. aeruginosa* isolated from drains and wounds between the two groups ; however, no differences were observed in the susceptibility of P. aeruginosa isolated from urine, sputum, blood, or ascites. In this regard, the reason for the significantly higher IPM and MDRP scores in the Upper-GI group is considered to be that the frequency of isolation from sputum was higher in the Upper-GI group than in the Lower-GI group. More than half of the patients in the Upper-GI group were diagnosed with esophageal cancer. It is well-known that respiratory complications often occur after surgery for esophageal cancer, and the frequent isolation of *P. aeruginosa* from sputum is reasonable<sup>13</sup>. Livermore reported that P. aeruginosa isolated from the sputum of patients with cystic fibrosis showed higher resistance to anti-pseudomonal antibiotics

than that isolated from other sites in inpatients, intensive care unit patients, and outpatients in the United Kingdom<sup>14</sup>. Drug resistance is common among organisms isolated from the respiratory tract, particularly from patients in intensive care units and teaching hospitals<sup>8,15</sup>. These results suggested that *P. aeruginosa* isolates from sputum may have higher drug resistance than those isolated from other sites. *P. aeruginosa* was more frequently isolated in the urine in the Lower-GI group because rectal cancer patients often suffer from urinary disturbance and require long-term placement of a urinary catheter, although there was no difference in the rate of urinary catheter placement between the two groups.

This study had several limitations. First, this study was conducted in a retrospective nature and the data used in this study were obtained from the microbiology laboratory database, which includes both colonization and infection data. In addition, this study could not distinguish between community-acquired and hospital-acquired infections and the results should be interpreted with caution. Second, patients with postoperative infectious complications of gastrointestinal cancer and emergently hospitalized patients requiring intensive care were included in this study ; thus, the reasons for hospitalization were not uniform.

In conclusion, physicians should be aware, especially in the case of empirical treatment, that there were significant differences in the drug resistance of *P. aeruginosa* isolated from different sites and types of gastrointestinal tract diseases. Antimicrobial agents should be appropriately administered in the gastrointestinal ward under careful distinction between colonization and pathogen.

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## **Conflict of interest**

The authors have declared no conflicts of interest.

## **Ethical approval**

All subjects provided written informed consent for the inclusion of their data. This study was conducted according to protocols approved by the National Defense Medical College Institutional Review Board (Permission number: 4776).

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