



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

メタデータ	言語: English 出版者: The Fukushima Society of Medical Science 公開日: 2025-01-29 キーワード (Ja): キーワード (En): <i>Pseudomonas aeruginosa</i>, drug resistance, the isolation sites, Humans, <i>Pseudomonas aeruginosa</i>, Male, Female, Drug Resistance, Bacterial, Anti-Bacterial Agents, Aged, Gastrointestinal Diseases, <i>Pseudomonas</i> Infections, Middle Aged, Aged, 80 and over, Imipenem, Microbial Sensitivity Tests 作成者: Tsujimoto, Hironori, Fujikura, Yuji, Hamamoto, Taka-Aki, Horiguchi, Hiroyuki, Takahata, Risa, Ishibashi, Yusuke, Sugihara, Takao, Kouzu, Keita, Itazaki, Yujiro, Fujishima, Sei-Ichiro, Okamoto, Koichi, Kajiware, Yoshiki, Matsukuma, Susumu, Ueno, Hideki メールアドレス: 所属:
URL	https://fmu.repo.nii.ac.jp/records/2002349



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

Hironori Tsujimoto^{1,2)}, Yuji Fujikura²⁾, Taka-aki Hamamoto³⁾, Hiroyuki Horiguchi¹⁾, Risa Takahata²⁾, Yusuke Ishibashi¹⁾, Takao Sugihara¹⁾, Keita Kouzu¹⁾, Yujiro Itazaki¹⁾, Sei-ichiro Fujishima¹⁾, Koichi Okamoto¹⁾, Yoshiki Kajiwaru¹⁾, Susumu Matsukuma³⁾, Hideki Ueno¹⁾

¹⁾Department of Surgery, National Defense Medical College, Tokorozawa, Japan, ²⁾Department of Medical Risk Management and Infection Control, National Defense Medical College Hospital, National Defense Medical College, Tokorozawa, Japan, ³⁾Department of Laboratory Medicine, National Defense Medical College Hospital, Tokorozawa, Japan

(Received May 28, 2024, accepted July 25, 2024)

Abstract

Introduction : We investigated the drug resistance status of *Pseudomonas aeruginosa* (*P. aeruginosa*) 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 cefazopran 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 infections¹⁾. *P. aeruginosa* is naturally resistant to many antibiotics and has a remarkable capacity to acquire new resistance mechanisms, leading to increased therapeutic problems. Multi-drug resistant-*P. aeruginosa* (MDRP) is a strain that

has acquired resistance to three classes of antibacterial agents : fluoroquinolones, carbapenems, and aminoglycosides²⁾. Currently, the isolation rate of MDRP is reported to be 1–41%, and this varies greatly depending on the country and hospital environment^{3–6)}. Because of the limited choice of antibiotics, MDRP is often difficult to treat and is associated with high morbidity and mortality rates^{7,8)}.

The process of acquiring antibiotic resistance is

Corresponding author : Hironori Tsujimoto, MD E-mail : tsujihi@ndmc.ac.jp

©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).

Table 1. Breakpoints and susceptibility scores for each antibiotic

Imipenem (IPM), Meropenem (MEPM), Doripenem (DRPM)					
MIC (μg/mL)	≤ 1	2	4	8	16 ≤
Breakpoint	S		I		R
Score	1	2	3	4	5
Amikacin (AMK)					
MIC (μg/mL)	≤ 8	16	32	64 ≤	
Breakpoint	S		I	R	
Score	1	2	3	4	
Ciprofloxacin (CPFX)					
MIC (μg/mL)	≤ 0.25	0.5	1	2	4 ≤
Breakpoint		S		I	R
Score	1	2	3	4	5
Piperacillin (PIPC), Tazobactam/piperacillin (TAZ/PIPC)					
MIC (μg/mL)	≤ 8	16	32	64	128 ≤
Breakpoint	S			I	R
Score	1	2	3	4	5
Ceftazidime (CAZ), Cefozopran (CZOP)					
MIC (μg/mL)	≤ 4	8	16	32 ≤	
Breakpoint	S			I	
Score	1	2	3	4	
Levofloxacin (LVFX)					
MIC (μg/mL)	≤ 0.5	1	2	4	8 ≤
Breakpoint		S		I	R
Score	1	2	3	4	5

MIC, minimal inhibitory concentration

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

	Upper GI (n=97)		Lower GI (n=227)		p-value
Age	73.1 ± 8.9		68.6 ± 14.9		0.03
Male/ Female	78/19		146/81		<0.01
Purpose of admission					
Surgery	67	69%	187	82%	<0.05
Intensive care	29	30%	38	17%	
others	1	1%	2	1%	
Surgery					
Yes	67	69%	191	84%	<0.01
No	30	31%	36	16%	
Diagnosis on admission					
Esophageal cancer	52	54%	0	0%	<0.01
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%	<0.01
CMZ	2	3%	181	97%	
Others	0	0%	4	2%	
Co-morbidity					
Diabetes mellitus					
Yes	17	18%	40	18%	0.98
No	80	82%	187	82%	
Hypertension					
Yes	43	44%	84	37%	0.22
No	54	56%	143	63%	
Steroid useage					
Yes	4	4%	12	5%	0.65
No	93	96%	215	95%	
Previous hospital stay					
Yes	67	69%	111	49%	<0.01
No	30	31%	116	51%	
Hospital death					
Yes	15	15%	21	9%	0.11
No	82	85%	206	91%	
Hospital stay (days)	64.1 ± 149.0		37.9 ± 57.4		0.10
Endotracheal intubation					
Yes	29	30%	25	11%	<0.01
No	68	70%	202	89%	
Urinary catheterisation					
Yes	66	68%	141	62%	0.31
No	31	32%	86	38%	
Central venous catheter					
Yes	60	62%	90	40%	<0.01
No	37	38%	137	60%	

Blood purification therapy					
Yes	10	10%	10	4%	<0.05
No	87	90%	217	96%	
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

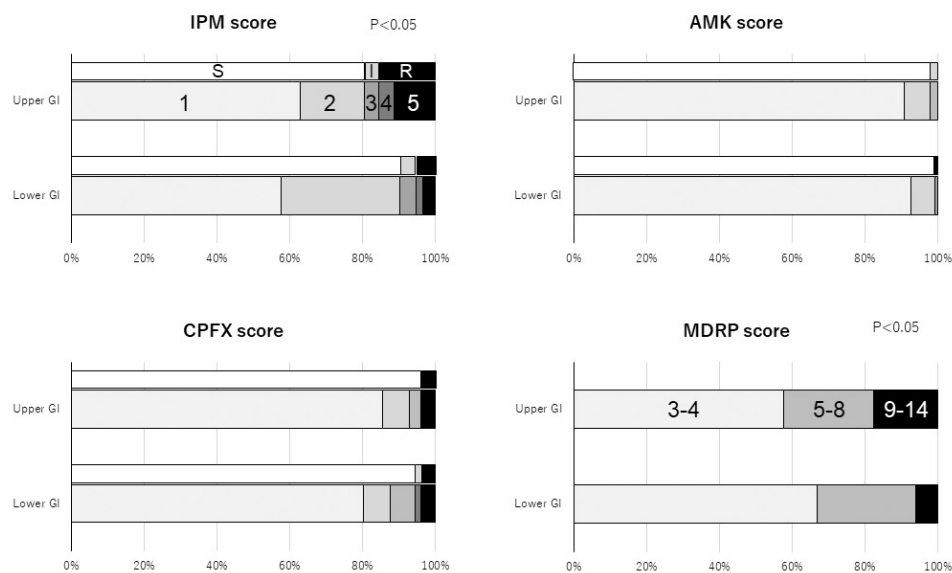


Fig. 1. Susceptibility to three classes of antibiotics and MDRP scores in the Upper-GI and Lower-GI groups
The Upper-GI group had more cases with an IPM score of 4 or 5 (i.e. cases with a breakpoint of R as resistance to IPM) than the Lower-GI group, although there were no differences in either AMK or CPFX scores. The Upper-GI group had significantly higher MDRP scores than the Lower-GI group.
GI, gastrointestinal ; IPM, imipenem ; AMK, amikacin ; CPFX, ciprofloxacin ; MDRP, multidrug resistant-*Pseudomonas aeruginosa*

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 (CPF) 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 Institute⁹⁾. 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-

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

PIPC Break Point	S	I	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%)	
TAZ/PIPC Break Point	S	I	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%)	
MEPM Break Point	S	I	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%)	
DRPM Break Point	S	I	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%)	
CAZ Break Point	S	I	R	p-value
Upper GI	79 (81.4%)	18 (18.6%)	NA	0.14
Lower GI	199 (87.7%)	28 (12.3%)	NA	
CZOP Break Point	S	I	R	p-value
Upper GI	79 (81.4%)	18 (18.6%)	NA	<0.05
Lower GI	205 (90.3%)	22 (9.75%)	NA	
LVFX Break Point	S	I	R	p-value
Upper GI	78 (80.4%)	5 (5.2%)	14 (14.4%)	0.13
Lower GI	199 (87.7%)	12 (5.3%)	16 (7.1%)	

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. aeruginosa* 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

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

	Drain discharge					Urine					Sputum				
	S	I	R	p-value	S	I	R	p-value	S	I	R	p-value	S	I	R
IPM	Upper GI	23 (56.1%)	3 (7.3%)	15 (36.6%)	<0.01	9 (69.2%)	0 (0%)	4 (30.1%)	0.10	37 (60.7%)	5 (8.2%)	19 (31.2%)	0.27	19 (31.2%)	6 (16.7%)
	Lower GI	80 (83.3%)	5 (5.2%)	11 (11.5%)		76 (84.4%)	5 (5.6%)	9 (10.0%)		26 (72.2%)	4 (11.1%)	6 (16.7%)		6 (16.7%)	
AMK	Upper GI	39 (95.1%)	2 (4.9%)	0 (0%)	<0.05	13 (100%)	0 (0%)	0 (0%)	0.60	59 (96.7%)	1 (1.6%)	1 (1.6%)	0.39	1 (1.6%)	
	Lower GI	96 (100%)	0 (0%)	0 (0%)		89 (98.9%)	1 (1.1%)	0 (0%)		36 (100%)	0 (0%)	0 (0%)		0 (0%)	
CPFX	Upper GI	29 (70.7%)	2 (4.9%)	10 (24.4%)	<0.05	12 (92.3%)	0 (0%)	1 (7.7%)	0.87	45 (73.8%)	2 (3.3%)	14 (23.0%)	0.49	14 (23.0%)	
	Lower GI	86 (89.6%)	2 (2.1%)	8 (8.3%)		83 (92.2%)	1 (1.1%)	6 (6.7%)		29 (80.6%)	2 (5.6%)	5 (13.9%)		5 (13.9%)	
PIPC	Upper GI	26 (63.4%)	5 (12.2%)	10 (24.4%)	0.06	11 (84.6%)	2 (15.3%)	0 (0%)	0.54	41 (67.2%)	8 (13.1%)	12 (19.7%)	0.70	12 (19.7%)	
	Lower GI	73 (76.0%)	15 (15.6%)	8 (8.3%)		76 (84.4%)	10 (11.1%)	4 (4.4%)		23 (63.9%)	7 (19.4%)	6 (16.7%)		6 (16.7%)	
TAZ/PIPC	Upper GI	27 (65.9%)	3 (12.2%)	9 (22.0%)	<0.05	12 (92.3%)	1 (7.7%)	0 (0%)	0.57	42 (72.4%)	5 (8.6%)	11 (19.0%)	0.39	11 (19.0%)	
	Lower GI	82 (85.4%)	7 (7.3%)	7 (7.3%)		80 (88.9%)	6 (6.7%)	4 (4.4%)		26 (66.7%)	7 (18.0%)	6 (15.4%)		6 (15.4%)	
MEPM	Upper GI	27 (65.9%)	4 (9.8%)	10 (24.4%)	<0.01	10 (76.92%)	1 (7.7%)	2 (15.4%)	0.36	43 (74.1%)	5 (8.6%)	10 (17.2%)	0.76	10 (17.2%)	
	Lower GI	87 (90.6%)	4 (4.2%)	5 (5.2%)		82 (91.1%)	2 (2.2%)	6 (6.7%)		31 (79.5%)	2 (5.1%)	6 (15.4%)		6 (15.4%)	
DRPM	Upper GI	30 (73.2%)	5 (12.2%)	6 (14.6%)	<0.01	11 (84.6%)	1 (7.7%)	1 (7.7%)	0.37	49 (84.5%)	3 (5.2%)	6 (10.3%)	0.77	6 (10.3%)	
	Lower GI	92 (95.8%)	3 (3.1%)	1 (1.0%)		85 (94.4%)	1 (1.1%)	4 (4.4%)		33 (84.6%)	1 (2.6%)	5 (12.8%)		5 (12.8%)	
CAZ	Upper GI	30 (73.2%)	11 (26.8%)	NA	0.07	12 (92.3%)	1 (8.7%)	NA	0.88	45 (77.6%)	13 (22.4%)	NA	0.52	NA	
	Lower GI	83 (86.5%)	13 (13.5%)	NA		82 (91.1%)	8 (8.9%)	NA		28 (71.8%)	11 (28.2%)	NA		NA	
CZOP	Upper GI	31 (75.6%)	10 (24.4%)	NA	<0.05	12 (92.3%)	1 (8.7%)	NA	0.99	44 (75.9%)	14 (24.1%)	NA	0.87	NA	
	Lower GI	86 (89.6%)	10 (10.4%)	NA		83 (92.2%)	7 (7.8%)	NA		29 (74.4%)	10 (25.6%)	NA		NA	
LVFX	Upper GI	30 (73.2%)	1 (2.4%)	10 (24.4%)	<0.05	12 (92.3%)	0 (0%)	1 (7.7%)	0.42	43 (74.1%)	5 (8.6%)	10 (17.2%)	0.95	10 (17.2%)	
	Lower GI	84 (87.5%)	4 (4.2%)	8 (8.3%)		79 (87.8%)	6 (6.7%)	5 (5.6%)		30 (76.9%)	3 (7.7%)	6 (15.4%)		6 (15.4%)	

GI, gastrointestinal ; IPM, imipenem ; AMK, amikacin ; CPFX, ciprofloxacin ; PIPC, piperacillin ; TAZ/PIPC, tazobactam/piperacillin ; MEPM, meropenem ; DRPM, doripenem ; CAZ, ceftazidime ; CZOP, ceftazopran ; LVFX, levofloxacin ; NA, not assigned ; S, susceptible ; I, intermediate ; R, resistant

Table 4. (Continued)

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

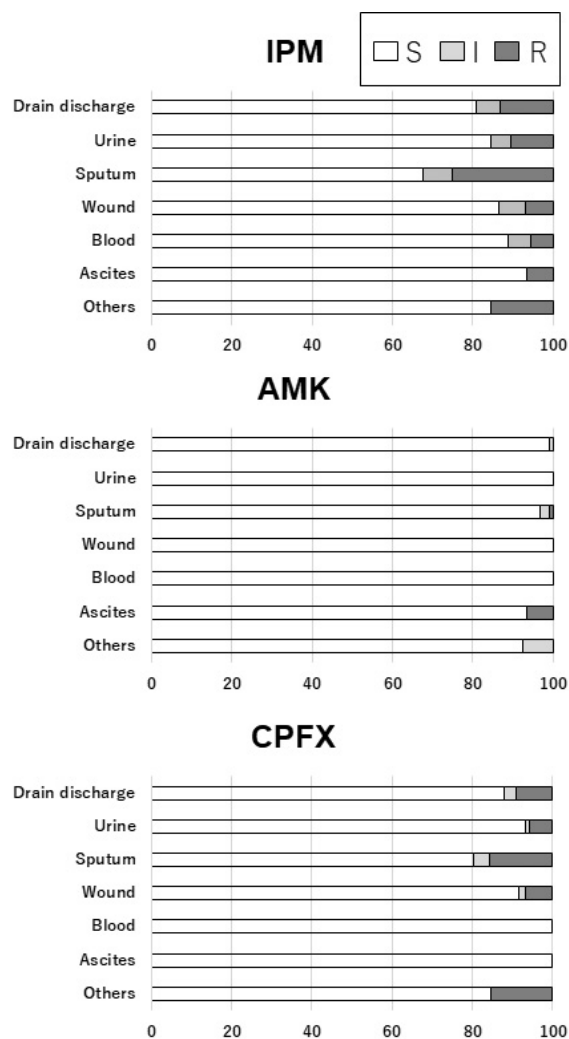


Fig. 2. Breakpoints for IPM, AMK, and CPFX according to the isolation sites.

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. aeruginosa*, 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

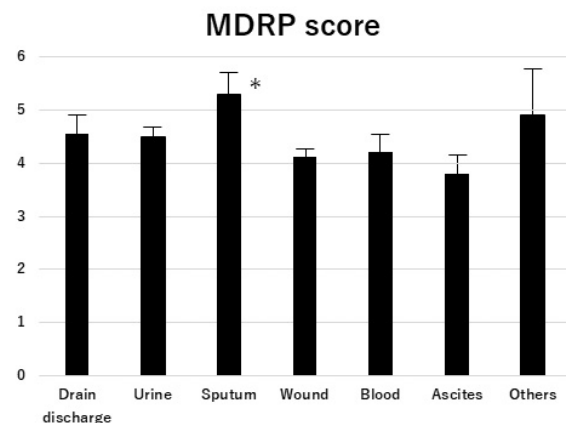


Fig. 3. MDRP score according to the isolation sites
Pseudomonas aeruginosa isolated from sputum more likely had higher MDRP scores than those isolated from other sites.

* $P < 0.05$ versus wound and ascites

MDRP, multidrug resistant-*Pseudomonas aeruginosa*

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^{6,10,11}. 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 carbapenem-resistant Gram-negative bacterial infections¹². 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 reasonable¹³. 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 Kingdom¹⁴). Drug resistance is common among organisms isolated from the respiratory tract, particularly from patients in intensive care units and teaching hospitals^{8,15}). 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.

Acknowledgments

We would like to thank Editage (www.editage.com) for English language editing.

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).

References

1. Kunz Coyne AJ, El Ghali A, Holger D, Rebold N, Rybak MJ. Therapeutic Strategies for Emerging Multidrug-Resistant *Pseudomonas aeruginosa*. *Infect Dis Ther*, **11** : 661-682, 2022.
2. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, *et al.* Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria : an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect*, **18** : 268-281, 2012.
3. Vaez H, Salehi-Abargouei A, Ghalehnoo ZR, Khadem F. Multidrug Resistant *Pseudomonas aeruginosa* in Iran : A Systematic Review and Metaanalysis. *J Glob Infect Dis*, **10** : 212-217, 2018.
4. Ichihara M, Ogino T, Fujii M, Haraguchi N, Takahashi H, Miyoshi N, *et al.* Usefulness of Bacterial Culture of Drainage Fluid for Predicting Surgical Site Infection After Crohn's Disease Surgery. *Ann Gastroenterol Surg*, **6** : 375-385, 2022.
5. Chang Y, Jeon K, Lee SM, Cho YJ, Kim YS, Chong YP, *et al.* The Distribution of Multidrug-resistant Microorganisms and Treatment Status of Hospital-acquired Pneumonia/Ventilator-associated Pneumonia in Adult Intensive Care Units : a Prospective Cohort Observational Study. *J Korean Med Sci*, **36** : e251, 2021.
6. Vincent JL, Sakr Y, Singer M, Martin-Loeches I, Machado FR, Marshall JC, *et al.* Prevalence and Outcomes of Infection Among Patients in Intensive Care Units in 2017. *JAMA*, **323** : 1478-1487, 2020.
7. Abubakar U, Al-Anazi M, Alanazi Z, Rodriguez-Bano J. Impact of COVID-19 pandemic on multidrug resistant gram positive and gram negative pathogens : A systematic review. *J Infect Public Health*, **16** : 320-331, 2022.
8. Oliveira ABS, Sacilotto GH, Neves MFB, Silva A, Moimaz TA, Gandolfi JV, *et al.* Prevalence, outcomes, and predictors of multidrug-resistant nosocomial lower respiratory tract infections among patients in an ICU. *J Bras Pneumol*, **49** : e20220235, 2023.
9. CLSI. Performance standards for antimicrobial susceptibility testing. In : CLSI supplement M100. 32nd ed. Clinical and Laboratory Standards Institute ; 2022.
10. Haghi F, Zeighami H, Monazami A, Toutouchi F, Nazarian S, Naderi G, *et al.* Diversity of virulence genes in multidrug resistant *Pseudomonas*

- aeruginosa isolated from burn wound infections. *Microb Pathog*, **115** : 251-256, 2018.
11. Blanchard AC, Rooney AM, Yau Y, Zhang Y, Stapleton PJ, Horton E, *et al.* Early detection using qPCR of *Pseudomonas aeruginosa* infection in children with cystic fibrosis undergoing eradication treatment. *J Cyst Fibros*, **17** : 723-728, 2018.
 12. Palacios-Baena ZR, Giannella M, Manissero D, Rodriguez-Bano J, Viale P, Lopes S, *et al.* Risk factors for carbapenem-resistant Gram-negative bacterial infections : a systematic review. *Clin Microbiol Infect*, **27** : 228-235, 2021.
 13. Tsujimoto H, Takahata R, Nomura S, Kumano I, Matsumoto Y, Yoshida K, *et al.* Predictive value of pleural and serum interleukin-6 levels for pneumonia and hypo-oxygenations after esophagectomy. *J Surg Res*, **182** : e61-67, 2013.
 14. Livermore DM. Multiple mechanisms of antimicrobial resistance in *Pseudomonas aeruginosa* : our worst nightmare? *Clin Infect Dis*, **34** : 634-640, 2002.
 15. Havens TN, Rosen DA, Rivera-Spoljaric K. Airway multidrug-resistant organisms in a population of tracheostomy and chronic ventilator-dependent children at a tertiary care pediatric hospital. *Pediatr Pulmonol*, **58** : 26-34, 2023.