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ORIGINAL ARTICLE

Risk factors for acquisition of multidrug-resistant bacteria in patients with anastomotic leakage after colorectal cancer surgery

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Abstract
Purpose The risk factors for acquiring an infection with multidrug-resistant (MDR) bacteria in patients with anastomotic leakage after colorectal cancer surgery are poorly understood. We evaluated the risk factors associated with the initial acquisition of MDR pathogens in patients with anastomotic leakage after colorectal cancer surgery.
Methods This study was a retrospective review of prospectively collected data at a university affiliated-tertiary referral hospital in South Korea. From January 2009 to April 2013, a total of 6767 consecutive patients with colorectal cancer who underwent surgery were registered. Of these patients, 190 (2.8 %) were diagnosed with anastomotic leakage. Finally, 143 (2.1 %) patients with culture test results were included in this study.
Results Of the 143 enrolled patients, 46 (32.2 %) were classified in the MDR group. The use of antibiotics for more than 5 days before diagnosis of anastomosis site leakage ($p=0.016$) and diabetes mellitus ($p=0.028$) was identified as independent risk factors for MDR acquisition by multivariate analysis. The rate of adequate initial empirical antibiotic therapy in the MDR group was lower than in the non-MDR group (35 vs. 75 %, $p<0.001$). Furthermore, the duration of antibiotic administration after the leak was longer in the MDR group ($p=0.013$). Patients in the MDR group also had a longer hospital stay ($p=0.012$).
Conclusions The length of antibiotic administration before the diagnosis of anastomotic leakage and diabetes mellitus were risk factors associated with the acquisition of MDR bacteria in patients with anastomotic leakage after colorectal cancer surgery.

Keywords Anastomotic leak · Colorectal neoplasms · Drug resistance · Multiple · Risk factors

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Introduction

Postoperative peritonitis, a serious complication following colorectal surgery, is associated with a high rate of septic shock (41 %) and mortality (19–40 %) [1, 2]. Furthermore, the treatment of postoperative peritonitis necessitates the use of significant hospital resources and is therefore costly [3]. In particular, anastomotic leakage accounts for 34 % of all cases of postoperative peritonitis [4], while the mortality rate associated with leakage after colorectal surgery is 8 % [5]. In spite of new operating techniques and materials, anastomotic leakage after colorectal surgery remains prevalent [6, 7]. Two treatment modalities exist for anastomotic leakage: operative or

nonoperative management. In both cases, the timely administration of suitable antibiotics is essential [8]. In recent years, the incidence of antimicrobial-resistant pathogens has increased rapidly, which has become a significant challenge for clinicians worldwide [9]. Inappropriate antimicrobial therapy for multidrug-resistant (MDR) infection is associated with significantly poorer outcomes [10–12]. The identification of the clinical characteristics that define patients at high risk for the acquisition of MDR bacteria could aid clinicians in their choice of antibiotics for patients with anastomotic leakage after colorectal cancer surgery. However, the risk factors, clinical features, and outcomes of patients who have MDR bacterial acquisition and anastomotic leakage after colorectal cancer surgery are not well understood.

In this study, we identified independent risk factors for the acquisition of MDR pathogens at the time of diagnosis of anastomotic leakage after colorectal cancer surgery. We also evaluated risk factors for MDR bacterial acquisition in the early phase of leakage to improve early antibiotic therapy after diagnosis of leakage. We compared the outcomes of patients with MDR pathogens to patients without MDR pathogens.

Materials and methods

Study design and study population

A retrospective cohort study was conducted. The local Institutional Review Board approved the study and waived the requirement for informed consent (IRB No. 2013-10-067-001).

From January 2009 to April 2013, a total of 6767 patients with colorectal cancer underwent surgery in the Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine. Of these patients, 2302 had low anterior resections. There were 1870 anterior resections, 1436 right colectomies, 283 left colectomies, 73 total colectomies, 42 intersphincteric resections, 38 transverse colectomies, and 723 nonanastomotic operations. Anastomotic leakage occurred in 190 patients (2.8 %): 138 (6.0 %) low anterior resection patients, 17 (0.9 %) anterior resection patients, 24 (1.7 %) right hemicolectomy patients, 6 (2.1 %) left hemicolectomy patients, 4 (5.5 %) total colectomy patients, and 1 (2.6 %) transverse colectomy patient. Of the 190 patients screened, 47 patients did not have blood or intra-abdominal fluid culture tests on the first day after diagnosis of anastomotic leakage and were thus excluded; therefore, a total of 143 patients were enrolled in this study.

The routine procedure for colorectal cancer surgery at our institution was as follows: Antibiotic prophylaxis using second-generation cephalosporin was administered, ideally within the hour prior to incision; the duration of antibiotic administration did not exceed 24 h. The bowel was prepared for surgery with an oral citric acid (19.5 g)/magnesium carbonate (10.75 g) solution and oral bisacodyl (10 mg) or 2000 ml of balanced lavage solution (containing 210 g of polyethylene glycol) in cases of low anterior resection without fecal diversion. Preoperative nonabsorbable oral antibiotics were not used for bowel preparation. From 2009 to 2011, feeding was delayed until the return of bowel function (defined as the presence of bowel sounds, passage of flatus, or stool). Starting in 2012, our institution has employed an early feeding strategy in which patients started a clear liquid diet on the first postoperative day and advanced to a regular diet after liquids were well tolerated.

Microbiological data

All culture tests were performed on the first day after diagnosis of anastomotic leakage; bacteriological profiles were based on these tests. Bacterial culture tests performed before anastomotic leakage or in the 2 days following anastomotic leakage were not included in this study. In cases of reoperation, abdominal fluid was taken for culture from the operative field, or in the immediate postoperative period, through closed suction drainage. If the patients had undergone percutaneous catheter drainage instead of reoperation, their drainage fluid was used. Blood and abdominal fluid cultures were not routinely ordered, and the need for these cultures was determined by the doctor on duty based on the condition of the patient in question.

Definitions

Patients with anastomotic leakage were defined as patients with confirmed anastomotic leakage at reoperation or patients for whom disruption of the anastomosis had been suspected and then confirmed by a colorectal surgeon based on imaging studies and clinical examination. Simple abscess or intra-abdominal fluid collection without any symptoms or signs of leakage was not considered to be anastomotic leakage.

The definition of MDR gram-positive and gram-negative organisms (i.e., methicillin-resistant *Staphylococcus aureus* [MRSA], extended-spectrum cephalosporin-resistant *Klebsiella pneumoniae*, *Escherichia coli*, and carbapenem-resistant *Pseudomonas aeruginosa*) was first described by Magiorakos et al. [13] and included resistance to one key antimicrobial agent. Briefly, it was defined as acquired nonsusceptibility to at least one agent in three or more antimicrobial categories.

Total antibiotic administration period before leakage was defined as the number of days that antibiotics were administered prior to diagnosis of leakage (including pre- and postoperative periods before diagnosis of leakage but during the same hospitalization).

Data collection and statistical analysis

All clinical data from patients with colorectal cancer who underwent colorectal cancer surgery were prospectively included in the colorectal cancer database of our hospital, and the medical records of all patients were retrospectively reviewed. Basic demographic parameters including age, sex, comorbidities, neo-adjuvant chemotherapy, operating report, microbial isolates and susceptibilities, mortality, peak temperature and systolic blood pressure on the day of diagnosis of anastomotic leakage, time from operation to leakage, duration of antibiotics administration, and duration of hospital stay were recorded. To assess potential relationships between patient outcomes and infections with MDR pathogens, the following parameters were included: vital signs 1 day before and 1 day after leakage, bacteriological profiles, treatment methods, length of hospital stay, antibiotics, and in-hospital mortality.

Continuous variables were compared using the Mann–Whitney *U* test and Student's *t* test. Qualitative variables were compared using the chi-square (χ^2) test. Backward stepwise logistic regression analysis was used to control for the effects of confounding variables while identifying independent risk factors for acquisition of MDR pathogens. All risk factors with an association of $p<0.2$ at the bivariate level were included in the multivariate logistic model to predict the acquisition of MDR pathogens. Continuous variables were recoded using receiver operating characteristic curves to define the appropriate cutoff points (represented by the values with the best sensitivity and specificity). The odds ratios (ORs) and their associated 95 % confidence intervals (CIs) were also calculated. For all analyses, a *p* value of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS software, version 20.0 (SPSS Inc., Chicago, IL).

Results

Study population

Of the 143 patients, more were males (81.8 %) than females (18.2 %). The mean patient age was 58.3±10.4 years. The median hospital stay was 24 days [interquartile range (IQR), 17–34 days]. The median duration of antibiotic administration after leakage was 11 days (IQR, 7–21 days), and adequate initial empirical antibiotic therapy was given to 89 patients (62.2 %). Anastomotic leakage was most common after rectal surgery ($n=121$, 84.6 %), followed by right colon surgery ($n=17$, 11.9 %) and left colon surgery ($n=5$, 3.5 %).

Clinical characteristics of the MDR and non-MDR groups

Of the 143 patients, 115 patients (80.4 %) were reported as having "growth," with the remaining 28 (19.6 %) having "no growth." A total of 232 microorganisms were cultured from either patient blood or abdominal fluid (Table 1) and 46 patients (32.2 %) were classified in the MDR group. The MDR bacteria isolated were the following: MDR *Enterococcus* spp. ($n=31$), MDR *Enterobacter* spp. ($n=9$), MDR *P. aeruginosa* ($n=4$), ESBL *E. coli* ($n=4$), *Acinetobacter* spp. ($n=3$), and MRSA ($n=1$). Patient baseline and demographic characteristics according to the group (MDR vs. non-MDR) are shown in Table 2. Univariate analysis revealed that a history of ICU admission after the first operation ($p=0.048$) and diabetes mellitus ($p=0.032$) were all factors associated with the acquisition of MDR pathogens in anastomotic leakage. However, age, sex, hospitalization within the 3-month period prior to admission, total length of antibiotic administration before diagnosis of anastomotic leakage, neo-adjuvant chemotherapy, protective ileostomy, bowel preparation status, and the presence of intestinal obstruction were not significant factors. In 134 patients (94 %), second-generation cephalosporin was administered as a preoperative antibiotic, but six patients (4 %) with suspicion of preoperative peritonitis were prescribed third-generation cephalosporin. Three patients with cephalosporin allergies (2 %) received quinolone without β-lactams. No relationship was observed between the preoperative antibiotics administered and the acquisition of MDR pathogens. In addition, the duration from initial admission to diagnosis of leakage, the duration from the first operation to leakage, and the site of anastomotic leakage were not associated with the acquisition of MDR pathogens. The total length

Table 1 Etiologic microorganisms isolated from blood or peritoneal fluid in the 143 patients with anastomotic leakage after colorectal cancer surgery

Microorganism	Number of isolates	MDR
Aerobes	189	52
Gram-positive	95	34
Enterococcus spp.	79	31
Streptococcus spp.	11	0
Staphylococcus spp.	5	3
Gram-negative	94	18
Enterobacter spp.	31	9
Pseudomonas aeruginosa	28	4
Escherichia coli	25	4
Klebsiella spp.	7	0
Acinetobacter spp.	3	1
Anaerobes	42	
Bacteroides fragilis	27	
Clostridium spp.	9	
Eggerthella lenta	5	
Fusobacterium varium	1	
Candida spp.	1	

Table 2 Clinical characteristics of the study population

	MDR (n=46)	Non-MDR (n=97)	p value
Age (years)	58.4±10.2	58.3±10.6	0.934
Sex (male)	39 (84.8 %)	78 (80.4 %)	0.527
Hospitalization within 3 months before admission	6 (13.0 %)	4 (4.1 %)	0.076[a]
History of ICU admission after first operation	13 (28.3 %)	14 (14.4 %)	0.048
Preoperative antibiotics			0.632
2nd generation cephalosporin	42 (91.3 %)	92 (94.8 %)	
3rd generation cephalosporin	3 (6.5 %)	3 (3.1 %)	
Quinolone	1 (2.2 %)	2 (2.1 %)	
Period of antibiotics administration from admission to end of prophylactic antibiotics administration	2 (2–2)	2 (2–2)	0.510[b]
Period of antibiotics administration from end of prophylactic antibiotics administration to diagnosis of leakage	3 (1–4)	2 (1–3)	0.123[b]
Total antibiotics administration period before diagnosis of anastomosis site leakage (day, median, IQR)	5 (3–6)	4 (3–5)	0.101[b]
Comorbidities			
Diabetes mellitus	11 (23.9 %)	10 (10.3 %)	0.032
Hypertension	19 (41.3 %)	32 (33.0 %)	0.332
Chronic obstructive pulmonary disease	2 (4.3 %)	1 (1.0 %)	0.242[a]
Atrial fibrillation	1 (2.2 %)	3 (3.1 %)	>0.999[a]
Chronic liver disease	3 (6.5 %)	7 (7.2 %)	>0.999[a]
Neo-adjuvant chemotherapy	5 (10.9 %)	15 (15.5 %)	0.459
Protective ileostomy in first operation	4 (8.7 %)	12 (12.4 %)	0.515
Minimal invasive surgery	20 (43.5 %)	59 (60.8 %)	0.051
Poor bowel preparation	2 (4.3 %)	8 (8.2 %)	0.501[a]
Intestinal obstruction	5 (10.9 %)	10 (10.3 %)	>0.999[a]
Site of leakage[c]			0.719[a]
Right side	4 (8.7 %)	13 (13.4 %)	
Left side	2 (4.3 %)	3 (3.1 %)	
Rectum	40 (87.0 %)	81 (83.5 %)	
Duration from admission to leakage (median (IQR))	7 (6–10)	7 (5–11)	0.760[b]
Duration from 1st operation to leakage (median (IQR))	5 (4–8)	5 (3–8)	0.520[b]

MDR multidrug-resistant bacteria; *Minimal invasive surgery* laparoscopic or robotic surgery

[a] Fisher's exact test

[b] Mann–Whitney test

[c] Right and left were divided by splenic flexure

of antibiotic administration before the diagnosis of anastomotic leakage was transformed into a binary variable using a cutoff point of 5 days, as determined by the receiver operating characteristic curve, to give the best sensitivity (50.0 %) and specificity (70.1 %). In a multiple logistic regression analysis, after adjusting for potential confounding factors, diabetes mellitus (adjusted OR, 2.96; 95 % CI, 1.13–7.81; p=0.028) and the total length of antibiotic administration for more than 5 days before diagnosis of anastomosis site leakage (adjusted OR, 2.48; 95 % CI, 1.18–5.20; p=0.016) significantly associated with MDR pathogen acquisition. The Hosmer-Lemeshow goodness-of-fit test showed good agreement between the observed and predicted values of the model (p=0.768).

In the subgroup analysis, 116 patients performed abdominal fluid culture irrespective of blood culture, history of ICU admission after the first operation (p=0.040), diabetes mellitus (p=0.029), and minimal invasive surgery (p=0.029), which were all factors associated with the acquisition of MDR pathogens in anastomotic leakage. In the multiple logistic backward regression analysis, diabetes mellitus (adjusted OR 3.18; 95 % CI, 1.01–9.98; p= 0.048), the total length of antibiotics administration per day (adjusted OR 1.20; 95 % CI, 1.02–1.41; p=0.032), and hospitalization within the 3-month period prior to admission (adjusted OR 6.44; 95 % 1.15–35.01; p=0.034) significantly associated with MDR pathogen acquisition (see details in the online supplement).

Clinical features, antibiotics, and outcomes

Patient clinical features and outcomes are presented in Table 3. Temperature, treatment method, and in-hospital mortality were similar between the two groups. Out of the 111 patients for whom blood cultures were available, bacteremia was more frequent in the patients with MDR pathogens compared with the patients with non-MDR pathogens; however, this trend was not statistically significant (22.2 % for MDR vs. 13.3 % for non-MDR; $p=0.234$). Hypotension (systolic blood pressure <90 mmHg) 1 day before and 1 day after leakage was more frequent in patients with MDR pathogens (37 vs. 13 %; $p=0.001$), and the length of hospital stay in the MDR group was longer than in the non-MDR group (30 vs. 24 days, $p=0.012$). In the MDR group, initial empirical antibiotics were adequate for 35 % (16/46) of all patients. On the other hand, in the non-MDR group, initial antibiotics were adequate for 76 % (73/97) of all patients. The average duration of antibiotic administration after leakage was also longer in the MDR group (14.5 vs. 10 days, $p=0.013$).

We analyzed the initial empirical antibiotics prescribed at the time of leakage. Piperacillin/tazobactam (pip/taz; $n=56$) and cephalosporin (second-generation cephalosporin=35, third-generation cephalosporin=24) were the main antimicrobial agents prescribed. In the MDR group, cephalosporin and pip/taz achieved poor adequacy rates, but in the non-MDR group, pip/taz achieved an initial empirical therapy adequacy rate above 90 %. Cephalosporin-based therapy yielded poor results, even in the non-MDR group.

Discussion

Previous studies examining postoperative peritonitis have tended to include a broad variety of pathological conditions, such as community or nosocomial settings, sites of primary surgical procedure, mechanisms of peritonitis, and underlying cancer [4, 14, 15]. However, to our knowledge, this is the first study to focus on patients with anastomotic leakage after colorectal cancer surgery.

In this study, *Enterococcus* spp. were the most dominant bacteria, followed by *Enterobacter*, *P. aeruginosa*, *Bacteroides fragilis*, *E. coli*, *K. pneumonia*, etc. (Table 1). The bacteriological profiles found in our study population were similar to those previously described in postoperative peritonitis [4, 15]. Our study revealed a 32.2 % incidence of MDR pathogens in patients with anastomotic leakage after colorectal cancer surgery. The bacteriological profiles were similar between the MDR and non-MDR groups (Table 1). The incidence of MDR pathogen acquisition was similar to figures reported in other postoperative peritonitis studies [10, 15].

Peritonitis is typically classified into three categories: community-acquired peritonitis, nosocomial postoperative peritonitis, and nosocomial nonpostoperative peritonitis (occurring without surgical intervention) [14]. Each category generally entails a different treatment strategy. In community-acquired peritonitis, antimicrobial selection focuses on *Enterobacteriaceae*, especially *E. coli* and anaerobes, while the most suitable course of therapy against *Enterococci* remains controversial [11, 16–18]. Routine coverage against *Enterococcus* is not necessary for patients with

Table 3 Clinical features, antibiotic treatment regimens, and outcomes of patients with MDR pathogens compared with the control group

	MDR ($n=46$)	Non-MDR ($n=97$)	p value
Temperature >38.0 °C	34 (73.9 %)	65 (67.0 %)	0.403
Hypotension (SBP <90 mmHg)	17 (37.0 %)	13 (13.4 %)	0.001
Bacteremia	($n=36$) 8 (22.2 %)	($n=75$) 10 (13.3 %)	0.234
Total length of hospital stay (days, median, IQR)	30 (18–52)	24 (17–32)	0.012[a]
Surgical repair of leakage	41 (89.1 %)	76 (78.4 %)	0.164
Treatment modality			0.357[b]
Reoperation	41 (89.1 %)	76 (78.4 %)	
Percutaneous catheter drainage	1 (2.2 %)	6 (6.2 %)	
Antibiotics only	4 (8.7 %)	15 (15.5 %)	
Adequate initial empirical antibiotics therapy	16 (34.8 %)	73 (75.3 %)	<0.001
Adequate empirical antibiotics within 3 days	21 (45.7 %)	79 (81.4 %)	<0.001
Duration of antibiotics administration after leakage [days, median (IQR)]	14.5 (7–34)	10 (7–18)	0.013[a]
In-hospital mortality	1 (2.2 %)	3 (3.1 %)	>0.999[b]

IQR, interquartile range

[a] Mann–Whitney test

[b] Fisher's exact test

community-acquired intra-abdominal infections [19–21]. However, antimicrobial therapy for *Enterococci* should be given when *Enterococci* are recovered from patients with nosocomial infections [11]. In the nosocomial setting, more resistant flora may be considered, including *Enterococcus*, *P. aeruginosa*, *Enterobacter* spp., MRSA, and *Candida* species. In this setting, it has also been shown that inadequate antimicrobial therapy prolongs hospitalization and is associated with poor outcomes [10–12, 22]. Thus, expanded spectrum multidrug regimens, which include either an aminoglycoside or a quinolone or a carbapenem and vancomycin, are recommended for these nosocomial infections [11].

The extent of leakage determined whether operative or nonoperative treatment would be used. Usually, patients with a simple abscess or intra-abdominal fluid collection without any symptoms or signs of leakage were treated in a nonoperative manner. To maximize the homogeneity of the study population, patients with a simple abscess or intra-abdominal fluid collection without any symptoms or signs of leakage were excluded. Our study focused on the acquisition of MDR bacteria at the time of diagnosis of leakage, irrespective of the extent of leakage or severity of peritonitis, and patients who underwent both operative and nonoperative interventions were analyzed to evaluate risk factors for acquisition of MDR pathogens.

Expanded spectrum multidrug regimens are important for patients with nosocomial postoperative peritonitis; however, it is perhaps more important to identify the relevant risk factors for acquiring an MDR pathogen among this group of patients. A prolonged preoperative length of stay and a prolonged (more than 2 days) period of preoperative antimicrobial therapy have both been shown to be related to resistance to empirical antimicrobial regimens; thus, such patients should be treated for nosocomial infection [11]. According to Seguin et al. [15], a prolonged preoperative hospital stay (>5 days) was associated with the acquisition of MDR pathogens. However, in the present study, the median duration from patient admission to leakage was not different between the MDR and non-MDR groups [median (IQR); 7 (6–10) for MDR group vs. 7 (5–11) for non-MDR group, $p=0.760$]. We also found that diabetes mellitus and the administration of antibiotics more than 5 days before the diagnosis of anastomotic site leakage were both strong independent risk factors for the acquisition of an MDR pathogen. Hospitalization within 3 months before admission also tended to be associated with the acquisition of an MDR pathogen. Thus, appropriate therapeutic approaches can be proposed based on the analysis of risk factors for the acquisition of MDR bacteria. For instance, complex multidrug regimens may be suitable empirical antimicrobial agents after leakage in patients with diabetes mellitus or in patients who underwent administration of antibiotics ≥5 days before the diagnosis of anastomotic site leakage. This proposal is suited for patients in a nosocomial setting, and the most suitable regimen may differ according to local epidemiology. Recent guidelines have emphasized the importance of early extended-spectrum empirical antibiotics, followed by rapid de-escalation after microbiologic identification of pathogens and susceptibility tests [8, 11, 23].

In this study, we observed that patients in the MDR group received inadequate empirical antimicrobial therapy more frequently than patients in the non-MDR group, and also that the average duration of antibiotic administration was longer in the MDR group. In addition, the median duration of patient hospitalization was longer in the MDR group. Hypotension was more likely to occur in patients who had recovered from infections with MDR pathogens. However, mortality rates were not significantly different between patients with and without MDR pathogens. Inadequate antibiotic selection has been shown in several studies to prolong hospital stay and has also been associated with a poor clinical outcome (prolonged hospital stay, treatment failure, and a higher mortality rate) [8, 22]. However, other studies of nosocomial peritoneal infections did not observe any relationships between inadequate antibiotic selection and poor clinical outcomes [4, 15, 24]. Although this perceived lack of effect on clinical outcomes may actually be due to a lack of power due to small sample sizes, the effect of inappropriate empirical antimicrobial selection on the outcomes of patients with postoperative peritonitis still remains controversial [1, 10]. In fact, a more critical aspect of managing postoperative peritonitis is surgical intervention, which can both control the source of infection and also decrease the bacterial load [4]. It is also well known that in cases of septic shock, each hour of delay in achieving administration of effective antibiotics is accompanied by a measurable increase in mortality [8]. Also, according to a surviving sepsis campaign, patients with severe sepsis or septic shock warrant broad-spectrum therapy until the causative organism and its antibiotic susceptibilities are defined [25]. For these reasons, and despite the uncertain link between outcome and inadequate empirical antibiotic selection, prompt initial antibiotic administration appears to be crucial for survival, at least for patients with severe sepsis or septic shock.

Our study does have several limitations. First, this study entailed a retrospective analysis of a prospectively collected database at a single center. Thus, hidden bias may have led to under- or overestimation of the true relationship between the risk factors and the acquisition of MDR pathogens. However, we attempted to address this limitation by performing multivariate logistic analyses to control for confounding factors. Second, blood or intra-abdominal culture tests were not conducted in 47 of the 190 patients with anastomotic leakage. Thus, the absence of culture tests for these 47 patients may have influenced the conclusions of this study. Third, detailed information for calculating severity scores was not available in our database. Therefore, the severity scores, which were not adjusted in our analysis, may have obscured the true result.

However, all patients in this study had colorectal cancer, and in all cases, surgery was elective. Finally, up to the present, there was no universal definition of anastomotic leakage. The definition of anastomotic leakage used in this study was not perfect; however, the definition was deemed the most simple and least prone to observer bias [7]. Nevertheless, it is important to note that the patient population was focused on anastomotic leakage after colorectal cancer surgery, and also that this study is the largest study published to date.

Anastomotic leakage is one of the most serious complications of colorectal surgery. Most previous reports have focused on leakage rates, risk factors for leakage, mortality, and oncological and bowel function outcomes. However, the epidemiology and clinical features of MDR bacteria in patients with anastomotic leakage after colorectal cancer surgery have not yet been identified. The identification of the clinical characteristics that define patients at high risk for the acquisition of MDR bacteria could aid clinicians in the appropriate management of these life-threatening conditions.

Conclusions

In patients with anastomotic leakage after colorectal cancer surgery, the incidence of MDR pathogen acquisition was 32.2 %. The acquisition of MDR pathogens was significantly associated with diabetes mellitus and the use of antibiotics for more than 5 days before the diagnosis of anastomotic leakage. In the context of these risk factors, complex multidrug regimens should be considered when selecting the appropriate empirical antibiotic therapy prior to a confirmed bacteriological profile in patients diagnosed with leakage after colorectal cancer surgery.

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