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Possible Risk Factors Related to Mortality in Intensive Care Patients after Gastroenterologic Surgery and Microorganisms Responsible for Infection

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Abstract: In this study, we aimed to investigate frequency of infections, infectious agents, treatment applied, and effects of these on mortality in patients who followed up in general surgery intensive care unit (ICU) after gastroenterologic surgery.Study data were obtained from a retrospective review of records of patients undergoing gastroenterologic surgery and followed up in general surgery ICU between January 2015 and December 2017. A total of 325 patients were included in the study, 54.2% male and 45.8% female. 36.6% of the patients were operated urgently, 63.4% were operated electively. Infection was developed in 31.3% of patients who were operated. Of the 103 patients who were infected, 88 abdominal infection, 4 genitourinary infection, 10 respiratory system infections were identified, whereas one patient's focus of infection could not be identified. The most frequently isolated gram (+) agent was Enterococcus species (64.7%), the most frequently isolated gram (-) agent was Escherichia coli (42.1%) and the most common fungal agent was Candida albicans. Twenty-four percent of infected patients were treated with monotherapy, while the rest received multiple antimicrobial agents. 4.6% (n=15) of the patients died in ICU and 1.5% (n=5) of them were infected. Age, urgent operation, operation due to colorectal or gastroduodenal and small bowel diseases, presence of comorbid diseases are effective parameters in the development of mortality in patients followed in ICU after gastroenterologic surgery. The most frequently detected agent in infectious disease is gram-negative bacteria. The results of this study support the fact that infections are not an independent risk factor in the development of mortality nowadays.
Keywords: Gastroenterologic surgery, mortality, infection, intensive care.

INTRODUCTION

Infection and high mortality rates in intensive care units, despite improvements in surgical technique and antimicrobial therapy, remain a serious problem. The focuses of infections seen in intensive care patients are often pulmonary, abdominal and blood circulatory system origin [1]. Infection rates in intensive care patients vary between 24.2 % and 60.1 %, depending on the type of ICU [2,3]. The mortality rates of intensive care units in the US ranges from 8% to 19% [4]. Mortality in intensive care patients may be based on preoperative, peroperative or postoperative reasons. Many studies have reported measures to reduce the incidence of intensive care infections. These are good handwashing, training, process control in invasive procedures, performance feedback, use of prophylactic antibiotics, aseptic techniques in catheterization, restriction in the use of urinary catheters, bloodbased infection control guidelines [5-10]. Base excess, high serum lactate and procalcitonin levels, advanced age, comorbid diseases, complex surgery, prolonged surgery, urgent surgery, surgeon's experience are only a part of the risk factors that have been shown to be effective on mortality [11-16]. While the American Society of Anesthesiologists' (ASA) physical status classification system, the Charlson Comorbidity Index, and the Revised Cardiac Risk Index (RCRI) are used to determine preoperative risk of patients, Acute Physiology and Chronic Health Evaluation (APACHE) score, the Simplified Acute Physiology Score (SAPS), the Mortality Probability Model (MPM), the Sequential Organ Failure Assessment (SOFA) and the Multiple Organ Dysfunction Score (MODS) are used to determine peroperative risk assessment [17]. Most of the patients undergoing gastroenterologic surgery have one or more serious underlying diseases. For this

reason, it is difficult to distinguish whether death is caused by primary disease or by developed abdominal infection in patients undergoing gastroenterologic surgery. Abdominal infections following gastroenterologic surgery are one of the most common causes of mortality in patients treated in intensive care unit [18]. However, there are reports that these infections do not effect mortality, but extend the length of stay in the hospital [20-22]. In this study, it was aimed to investigate the infections in patients followed up in ICU after major gastrointestinal system surgery and their relation with mortality.

MATERIALS AND METHODS

Study data were obtained from a retrospective review of records of patients undergoing gastrointestinal surgery and followed up in general surgery ICU in Kahramanmaraş Sütçü İmam University between January 2015 and December 2017. The local ethics committee approved the study (date 01.03.2018 number 02). Elective patients were operated within 48 hours and emergency patients were taken within 24 hours of application. In elective operations, the infection was detected before the operation and the patient was not operated. But the operation was taken after the infection was treated. Before the elective operation, hair in the incision region and surrounding area were cleaned with an electric shaver in the operating table. Depending on whether the patient is stable during an emergency operation, the hair in the operating area of the appropriate patient was cleaned with an electric shaver. All elective patients who were planned for intestinal resection and anastomosis were given bowel cleansing before the operation. A single dose of prophylactic antibiotics was administered 30-60 minutes before the operation of the elective patients with gastrointestinal system surgery. In emergency operations, it was applied just before the operation or during the operation. An additional dose of antibiotic was administered every four hours during long periods of operation. Malignant / benign distinction of pathologic indication of operation, first application form (urgent or elective), operation performed at the same or different sessions, distribution of operations according to systems (colorectal / pancreaticobiliary / gastroduodenal other bowel / related organs, esophagus-spleen and omentum operations), distribution of comorbid diseases (cerebral / respiratory / abdominal / cardiac / another) according to the systems that require chronic drug use in the patients or cause permanent organ dysfunction after the disease, length of stay in ICU, the type of infective agent that causes the infection, usage of antimicrobial therapy (single / multiple), and the survey status of the patients were examined data.

Statistical methods

SPSS 24.0 (IBM Corparation, Armonk, New York, United States) programs were used to analyze the variables. The normal distribution of data was evaluated by the Shapiro-Wilk test. The Mann-Whitney U test was used together with Monte Carlo results in comparing two independent groups according to quantitative results. Pearson Chi-Square, Fisher-Exact and Fisher-Freeman-Holton tests were tested with Monte Carlo Simulation technique to compare categorical variables and the column ratios were compared with each other and expressed according to Benjaminini-Hochberg corrected p-values. Odds ratios were used to show how many times those who have a risk factor are more than those who do not. Quantitative variables Mean ± Standard Deviation (std) and median range (minimum-maximum), and categorical variables as % (n) were shown. Variables were examined at 95% confidence level and $p< 0.05$.

RESULTS

A total of 325 patients, 54.2 % (n = 176) male and 45.8 % (n = 149) were included in the study. In 4.6% of patients (n = 15), intensive care unit deaths occurred. The mean age of the patients was 58 years, the mean age of the male patients was 55.9 ± 17.4 years and the mean age of the female patients was 58.7 ± 17.4 years. The median age of the survivors was 58 years (min-max: 18-59 years), and the median age of the deceased was 76 years (min-max: 45-91 years) (Graphic 1a). The difference between the ages of the survived and deceased was statistically significant ($p <0.001$). There was no statistically significant relationship between gender and mortality ($p> 0.05$). The initial reference center of the patients was our center in 88% (n = 286), while in 12% (n = 39) the patients were referred to our center. No significant difference was found between mortality and first reference center of the patients ($p> 0.05$). 34.8% of the patients (n = 113) underwent surgery for malignancy (Graph 1b). Of the 15 patients who deceased, 6.7 % (n = 1) were malignant and 36.1 % (n = 112) of 310 survived patients were malignant and this difference was statistically significant ($p<0,05$). The mortality rate in benign cases was 7.92-fold higher than the malignant rate, which was statistically significant (95% Confidence interval: 1.03-61.02). Of the patients, 36.6 % (n = 119) had an emergency operation and 63.4 % (n = 206) had elective operation (Graphic 1c). Surgery was performed in 80% (n = 12) of the 15 deceased under emergency conditions, while 34.5% (n = 107) of 310 survived patients underwent emergency surgery (Graphic 2c). The statistical difference between the development of mortality after emergency and elective operations was significant ($p<0.00.1$). The mortality rate in urgent operations was 7.59 times higher than elective operations in survived patients, which was statistically significant (95% confidence interval: 2.1-27.48). Single operation was performed in 84% of patients (n = 273) and two or more operations were performed in 16% (n = 52). It was determined that performing one or more of the operations was not a statistically significant risk factor on mortality development ($p> 0.05$). The mortality rate in patients

with colorectal disease, gastroduodenal or small bowel disease was statistically significantly higher than other groups (pancreaticobiliary diseases, other diseases) ($p < 0.05$). Cardiac comorbidity was found in 5, abdominal comorbidity in 4 and cerebral comorbidity in 2 patients who died in intensive care unit after gastroenterologic surgery (Table 1, Graphic 1d, Graphic2). The incidence of comorbidities in cases with mortality was statistically higher than survivors ($p<0.05$). The mortality rate in those with comorbidity was 5.5 times greater than survivors, and this difference was statistically significant (95% confidence interval: 1.72-17.87). Deaths developed in 2 of 11 patients with cerebral comorbidities, in 4 of 26 patients with abdominal comorbidities, and in 5 of 30 patients with cardiac comorbidities. The difference between surviving and dying patients groups was statistically significant ($p < 0.05$). However, there was no significant difference regarding respiratory comorbidities ($p > 0.05$). Median length of stay in intensive care unit was 3 days (1-68 days). There was no significant difference between the duration of intensive care unit stay and mortality ($p = 0.510$). The demographic distribution of the data of the patients included in the study is presented in Table 1. Mean time of hospitalization period after infection was 6.7±6.4 days for Gram-negative bacteria and 9.3±10.2 days for Gram-positive bacteria. There was no statistically significant difference between Gram-negative and Gram-positive bacteria ($p=0.155$). Infection developed in 31.7 % of patients (n = 103). Infection focus was detected as abdominal in 88, genitourinary in 4, respiratory system in 10 patients, but couldn't found in only one case. 23.3% (n = 24) of infected patients were treated with single antibiotic and the rest were treated with multiple antibiotics. In total, 55.7% (n = 93) of patients were treated with single antibiotic, and 44.3% (n = 74) of patients were treated with multiple antibiotics (Table 2). The types and distribution patterns of pathogens are presented in Table 3. In total, 167 patients received antimicrobial therapy, the frequency of usage of antibiotics in patients was shown in Table 4. Mean time of hospitalization period after infection was 4.7±5.4 days and 5.2±6.2 days for right preemptive therapy in single and multiple antibiotics used groups, respectively ($p>0.05$).

Table-1: Demographic distribution of patients data

		Alive	Died	Total	p
		% (n)	% (n)	% (n)	
Gender					
	Male	54.2(168)	53.3(8)	54.2(176)	1
	Female	45.8(142)	46.7(7)	45.8(149)	
Age median (min-max.) year		58 (18-89)	76(45-91)	58(18-91)	<0.001
Hospital	University Hospital	88.4(274)	80(12)	88(286)	0.404
	Another Hospital	11.6(36)	20(3)	12(39)	
Benign/malign					
	Benign	63.9(198)	93.3(14)	65.2 (212)	0.023
	Malign	36.1 (112)	6.7(1)	34.8(113)	7.92 (1.03-61.02)*
Surgery					
	Urgent	34.5(107)	80(12)	36.6(119)	<0.001
	Elective	65.5(203)	20(3)	63.4(206)	7.59 (2.1-27.48)*
Abdominal Surgery					
	First	83.5(259)	93.3(14)	84(273)	0.481
	Secondery-Multiple	16.5(51)	6.7(1)	16(52)	
Operation					
	Colorectal	33.2(103)	46.7(7)	33.8(110)	0.035
	Pancreaticobiliary	4.5(14)	0 (0)	4.3(14)	
	Gastroduodenal-small bowel	33.5(104)	53.3(8)	34.5(112)	
	Other	28.7(89)	0 (0)	27.4(89)	
Comorbidity					
	No	66.9(206)	26.7(4)	65(210)	5.5 (1.72-17.87)*
	Yes	33.1(102)	73.3(11)	35(113)	0.004
Comorbidity					
	Cerebral	8.8(9)	18.2(2)	9.7(11)	0.033
	Pulmonary	15.7(16)	0 (0,0)	14.2(16)	
	Abdominal	21.6(22)	36.4(4)	23(26)	
	Cardiac	24.5(25)	45.5(5)	26.5(30)	
	Other	29.4(30)	0 (0,0)	26.5(30)	
Hospitalization (day)					
	Median (min.-max)	3(1-68)	2(1-10)	3(1-68)	0.510

Table-2: Distribution of Infection data and antibiotic use

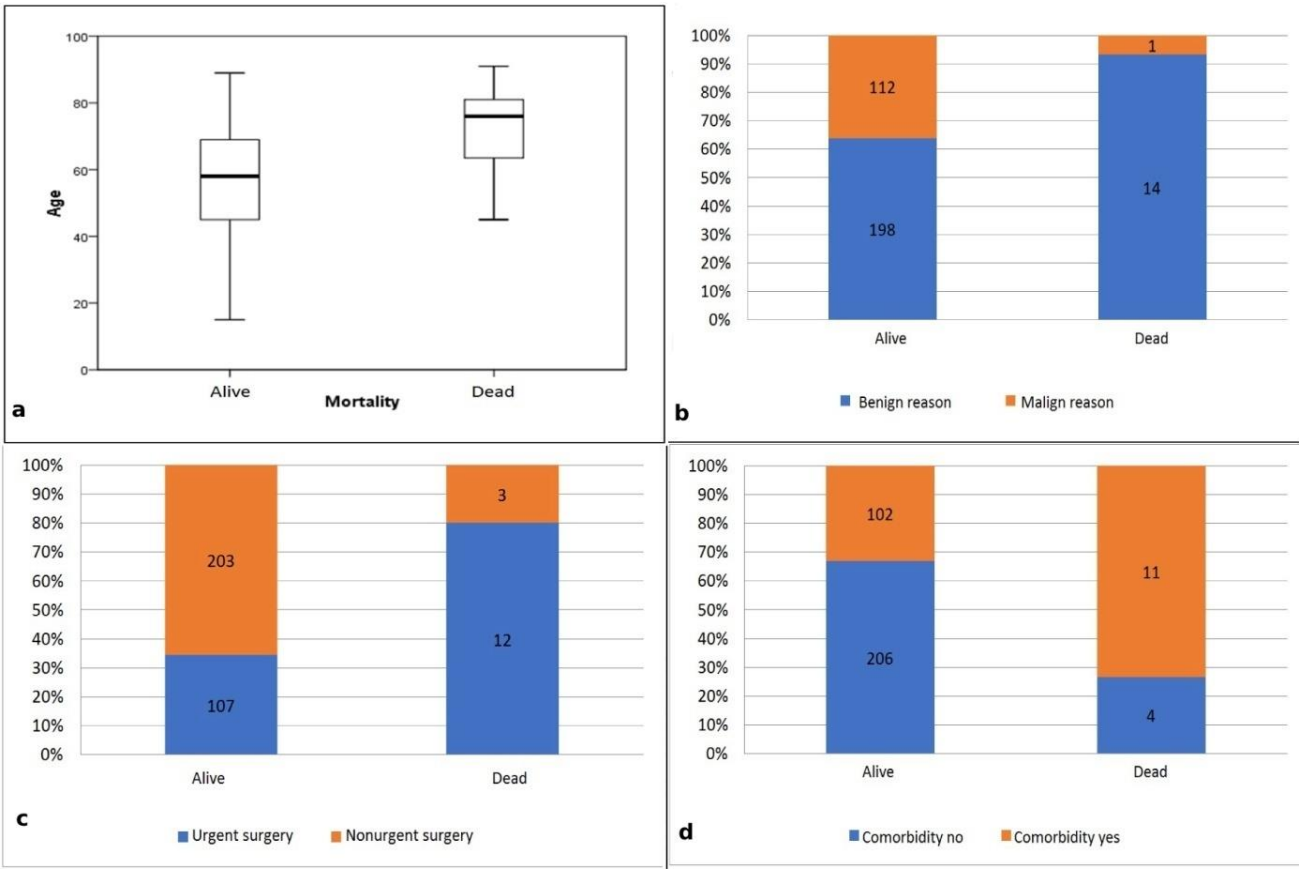
	Alive	Died	Total	p
	% (n)	% (n)	% (n)	
The focus of infection				
No	68.4(212)	66.7(10)	68.3(222)	1
Yes	31.6(98)	33.3(5)	31.7(103)	
Infection source				
Abdomen	84.7(83)	100(5)	85.4(88)	0.736
Respiratory	10.2(10)	0 (0)	9.7(10)	
Genitourinary	4.1 (4)	0 (0)	3.9(4)	
Nonavaliable	1 (1)	0 (0)	1 (1)	
Antibiotic Use				
Single	54.8(86)	70 (70)	55.7(93)	0.515
Multiple	45.2(71)	30 (3)	44.3(74)	
Fisher Freeman Halton (Monte Carlo) / Fisher Exact Test (Exact) - Pearson Chi Square Test(Monte Carlo/Exact) / *Odss Ratio (%95 Confidence Interval)				

Table-3: Gram (-) bacteria, gram (+) bacteria, and fungi

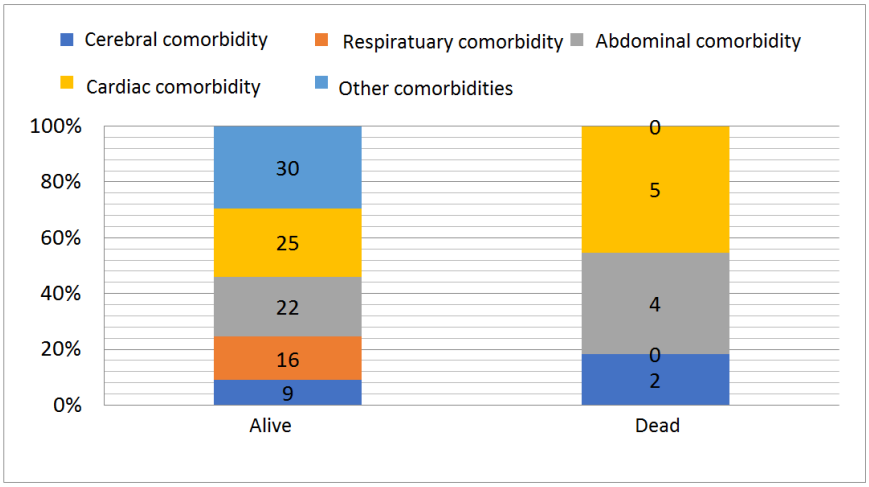
	n	**%**
Gram (-) bacteria		
Escherichia coli	16	42.1%
Escherichia coli, Candida albicans	1	2.6%
Acinetobacter baumannii	5	13.2%
Acinetobacter baumannii, Candida albicans	1	2.6%
Pseudomonas aeruginosa	3	7.9%
Escherichia coli, Enterococcus species	2	5.3%
Klebsiella pneumoniae	2	5.3%
Acinetobacter baumannii, Pseudomonas aeruginosa	1	2.6%
Escherichia coli, Proteus mirabilis	1	2.6%
Escherichia coli, Acinetobacter baumannii, Candida albicans	1	2.6%
Escherichia coli, Enterococcus hırae	1	2.6%
Enterobacter aerogenes	1	2.6%
Pseudomonas aeruginosa, Morganella morganni	1	2.6%
Pseudomonas aeruginosa, Escherichia coli	1	2.6%
Pseudomonas putida	1	2.6%
Gram (+) bacteria		
Enterococcus species	44	64.7%
Enterococcus species, Trichosporon asahii	1	1.5%
Methicillin resistant Staphylococcus epidermidis	5	7.4%
Methicillin resistant Staphylococcus epidermidis, Enterococcus faecalis	2	2.9%
Methicillin sensitive Staphylococcus epidermidis	2	2.9%
Methicillin resistant Staphylococcus capitis	2	2.9%
Methicillin resistant Staphylococcus aureus	2	2.9%
Enterococcus faecalis	1	1.5%
Methicillin sensitive Staphylococcus hominis, brevundimonas vesicularis	1	1.5%
Methicillin resistant Staphylococcus epidermidis, Staphylococcus xylosus	1	1.5%
Methicillin resistant Staphylococcus haemolyticus	2	3 %
Methicillin resistant Staphylococcus hominis	1	1.5%
Methicillin resistant Staphylococcus hominis, Candida albicans	1	1.5%
Methicillin resistant Staphylococcus capitis, Corynebacterium urealyticum	1	1.5%
Streptococcus agalactiae	1	1.5%
Isolated fungal agents		
Candida albicans	2	66.7%
Trichosporon asahii	1	33.3%

Table-4: The frequency of usage of antibiotics in patients

Antibiotic	Patients (n)	%
Ceftriaxone	48	28.7%
Cefazolin	27	16.2%
Ceftriaxone, Metronidazole	22	13.2%
Ceftriaxone, Rifamycin	8	4.8%
Cefazolin, Ceftriaxone	6	3.6%
Piperacillin Tazobactam	6	3.6%
Cefaperazon, Sulbactam	5	3.0%
İmipenem	5	3.0%
Cefazolin, Metronidazole	3	1.8%
Cefazolin, Rifamycin	3	1.8%
Ceftriaxone, İmipenem	3	1.8%
Ertapenem	3	1.8%
Rifamycin	3	1.8%
Amikacin,İmipenem	2	1.2%
Ampicillin Sulbactam	2	1.2%
Colistin,Meropenem	2	1.2%
Nystatin, Teikoplanin	1	0.6%
Amikacin, Ceftazidime	1	0.6%
Cefazolin, Ciprofloksasin	1	0.6%
Cefepim, Levofloksasin	1	0.6%
Ceftriaxone,Clarithromycin	1	0.6%
Daptomycin, Tigecycline	1	0.6%
Ertapenem, Metronidazole	1	0.6%
Gentamicin,Ceftriaxone	1	0.6%
İmipenem,Rifamycin	1	0.6%
Meropenem	1	0.6%
Meropenem, Fluconazole	1	0.6%
Meropenem, Gentamicin	1	0.6%
Meropenem, Levofloxacin	1	0.6%
Meropenem, Nystatin	1	0.6%
Meropenem, Sulbactam	1	0.6%
Metronidazole	1	0.6%
Ceftriaxone,Metronidazole	1	0.6%
Ceftriaxone, Rifamycin	1	0.6%
Tetracycline	1	0.6%



Graphic-1: a. Distribution of mean age in living and dying patients, b. Distribution of benign and malign diseases in living and dying patients. c. Distribution of emergency and elective surgery in living and dying patients d. Distribution of comorbidities in living and dying patients



Graphic-2: Distribution of comorbid diseases

DISCUSSION

In this study, advanced age was shown to be a very important risk factor in mortality development in patients (p<0,001). Similar results have been obtained in many studies in the literature, and advanced age has been shown to be an independent risk factor in the development of mortality [23-25]. In this study, urgent operations were shown to be a significant risk factor for mortality in patients as compared to elective operations (p<0,001). Studies in the literature have shown that urgent operations increase the risk of mortality similar to this study [23,24].In this study, cerebral, abdominal and cardiac comorbidities were found to be statistically significant risk factors in the development of mortality (p<0,05). Similar to the literature, it has been found that comorbidities in patients after gastrointestinal surgery are a risk factor in the development of mortality, except those with respiratory symptoms. In this study, the result was that respiratory comorbidity was not a significant risk factor for mortality development. This

situation contradicts many studies in the literature. In most of the previous studies, the mean mortality rate after gastrointestinal surgery was 15-20% [26,27]. The mortality rate after gastrointestinal surgery in this study was 4.6%, which is considerably lower than in previous studies. We think that this is related to the fact that our overall mortality ratio is low or that our successful approach to our patient group with respiratory comorbidities may have reduced mortality. Patients who were operated for colorectal or gastroduodenal and small bowel diseases were significantly higher in terms of mortality when compared to the other groups ($p< 0,035$, $p<0,031$, respectively). Both groups are risky groups in the development of mortality. In many studies in the literature, it is mentioned that the mortality rate of major abdominal surgical procedures increases [28,29]. The most frequently identified agents in intensive care infections following gastrointestinal surgeries are gram negative bacteria and the results of this study showed this. In this study, there was no statistically significant difference between the two groups in terms of mortality rates when the infected group and non-infected groups were compared. Although infections generally increase mortality rates in many other intensive care patients, mortality is seen as a rare result in the group of patients undergoing gastrointestinal surgery [12,13].There are many biomarkers and scoring systems used in predicting mortality in ICU patients. Biomarkers such as base excess, elevated levels of serum lactate and procalcitonin, and scoring systems such as APACHE, SAPS and MODS are the main ones [14-17]. Complex surgery, prolonged surgery, hypotension and tachycardia during surgery and the surgeon's experience are other risk factors that have been shown to be effective on mortality [12,30]. These mortality parameters could not be used because of the retrospective nature of the study and the lack of data in the records. There are publications in the literature reporting that infections after surgery are an effective risk factor for the high mortality rate in patients followed up in intensive care after gastrointestinal surgery, but infections only prolong patients' hospital stay but do not increase mortality rates [18-22]. The results of this study support that infections detected in patients undergoing gastrointestinal surgery are not an important but significant risk factor for the development of mortality nowadays. In this respect, this study contradicts the results of many studies in the literature. This contradiction can be explained as a natural consequence of the compliance of the intensive care unit with the general sterility and hygiene rules and the effective use of antibiotics.

CONCLUSION

Age, urgent operation, operations performed due to colorectal or gastroduodenal and small intestinal diseases, the presence of some comorbid diseases are effective on mortality in patients followed in intensive care after gastrointestinal surgery. The most frequently identified agents in intensive care infections are gram negative bacteria. The results of this study support that the identified infections are not an independent risk factor in the development of mortality nowadays, unlike what was known in the past.

Limitation

The retrospective nature of the study and the limited number of patients included in the study were considered limitations of the study.

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