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FULL PAPER

The assessment of predictor risk factors of anastomotic leakage after hemicolectomy with anastomotic: A prospective study

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Anastomotic leakage is one of the most concerning complications. The UK Surgical Infection Study Group in 1991 defined it as a discontinuity of the anastomotic, which connects between the intra-luminal and extra-luminal compartments. The aim of this study was to evaluate the risk factors of anastomotic leakage after hemicolectomy. This study design used a cohort prospective observational. Patients who underwent hemicolectomy and anastomotic for cancer pathology at Soetomo General Hospitals in Surabaya, Indonesia, between January 2018 and December 2022 were included. All patients who had colon anastomotic performed due to colon cancer met the inclusion criteria. Patients who were pregnant, under the age of 18, had incomplete or lost follow-up data, or both were eliminated. The total subjects in our study were 85 and anastomotic was found in 31 subjects. Anastomotic leakage was not found to be associated with any preoperative risk factors. The surgeon doing the procedure (p-value 0.02) and blood transfusion (p-value 0.007) are the intraoperative risk variables that significantly affect anastomotic leakage. In post-operative laboratory results, haemoglobin (p-value 0.007), PF Ratio (PO_2/FiO_2) (p-value 0.02), albumin (p-value 0.01), and CRP (p-value 0.01) are the variables that affect anastomotic leakage. Conversely, heart rate (p-value 0.01), body temperature (p-value 0.01), urine production (p-value 0.01), and retention (p-value 0.01) are clinical factors following surgery that affect anastomotic leakage.

KEYWORDS

Anastomotic leakage; risk factor; hemicolectomy.

Introduction

Anastomotic leakage (AL) is a highly concerning consequence [1]. In 1991, the UK Surgical Infection Study Group characterized it as a disruption of the anastomotic, which links the inner and outer compartments. These contents can be expelled by wounds or drains, or accumulate at the anastomotic site. Initial studies indicated that the interpretation of anastomotic breakdowns posed challenges. Leakage of anastomotic in patients with colon cancer following hemicolectomy and anastomotic is a complication that has a significant risk of death. Research data indicates that the occurrence of this problem

ranges from 6% to 22% of all cases [2]. Regarding oncology, individuals with colon cancer who encounter anastomotic leakage exhibit heightened rates of local recurrence and reduced disease-free survival. The Dutch Surgical Colorectal Audit published a study in 1992 that examined patients enrolled in the Netherlands in 2010. The study found that the occurrence of anastomotic leakage after colon cancer anastomotic resection surgery was 8.7%. To address the frequent occurrence of anastomotic leakage following colon cancer surgery, it is necessary to take further action to mitigate risk factors, promptly identify leakage, and implement preventive measures. These efforts are crucial in reducing the occurrence, complications, and death rates associated with anastomotic leakage in patients who have undergone tumor resection and anastomotic surgery for colon cancer [3]. Before clinical deterioration, patients with anastomotic leakage typically experience nonspecific signs and symptoms. Therefore, closely monitoring the initial clinical symptoms can help minimize the delay in diagnosing anastomotic leakage. Late diagnosis and treatment of this condition can lead to unfavorable outcomes, such as higher mortality rates. Thus, timely diagnosis is of utmost importance. In the research, delayed diagnosis of anastomotic leakage is associated with significant fatality rates. The occurrence of anastomotic leaks cannot be eliminated, so it is crucial to manage the symptoms associated with anastomotic leaks [4].

Anastomotic leakage is linked to numerous risk factors, which can be categorized into patient variables, preoperative factors, intraoperative factors, and postoperative factors [5]. Patient factors encompass age, gender, comorbidities, steroid use, and smoking. Preoperative factors include anemia, malnutrition, hypoalbuminemia, vitamin deficiency, previous irradiation, poor hydration status resulting from sepsis in the emergency setting, cancer location, and obstruction. Intraoperative factors encompass prolonged duration of surgery, heightened blood asas blood loss and transfusion, operator proficiency, anastomotic technique, bowel preparation, and surgical environment. Postoperative factors encompass postoperative infection, dietary regimen after surgery, wound dehiscence, and postoperative albumin levels. Comprehending the risk factors associated with anastomotic leakage is crucial, as it enables doctors to accurately evaluate these characteristics and identify patients who are at high risk. In turn, allows for the implementation of preventive measures against anastomotic leaking [6,7].

Materials and methods

The study was designed as a cohort prospective observational study. The study included patients who underwent hemicolectomy and anastomotic for cancer pathology at Soetomo General Hospitals in Surabaya, Indonesia, from January 2018 to December 2022. Among the 85 cases, a subset of patients experienced anastomotic leaking following the operation (referred to as the leaking group), whereas the remaining patients did not have any leakage (referred to as the no-leakage group). The inclusion criteria included all patients who received a colon anastomotic specifically for the treatment of colon cancer. Excluded from the study were patients who had lost follow-up or missing data, were pregnant, or were under the age of 18.

Preoperative evaluation in all cases, a comprehensive clinical examination and detailed history recording were performed. Thorough investigations were conducted for all cases. Laboratory test such as standard preoperative tests including C-reactive protein (CRP) and arterial blood gas (ABG) analysis. Radiological investigations for metastasis assessment in malignancy cases include plain chest X-ray, abdominal X-ray, abdominal ultrasound, and CT scan of the abdomen and

pelvic. Complete colonoscopy up to beyond the caecum was done in almost all elective patients.

Post-operative care: The majority of cases were transferred to the ward after surgery, except for those requiring intense monitoring in the ICU. A complete blood count (CBC) was requested daily for all patients during the first postoperative days (PODs), and C-reactive protein (CRP) was collected on the third postoperative day. The presence of aberrant findings in vital signs, clinical examination, and laboratory tests raised suspicion of AL. In cases where there was AL suspicion, specific radiologic tools were obtained for these patients.

The data analysis and interpretation were conducted using the SPSS v-26 software (IBM, Armonk, NY). The presentation of continuous data included the mean and standard deviation, or the median and range when suitable. Categorical data were given as numbers and percentages. The categorical variables were compared using Pearson's chi-square test and Fisher's exact test. The possible relative risks for postoperative factors and predictors of anastomotic leakage (AL) were evaluated by univariate analysis utilizing odds ratio (OR) with a 2-tailed 95% confidence interval (CI).

Results and discussion

This study obtained 85 research subjects who met the inclusion and exclusion criteria, from this number it was found that colon cancer patients who underwent hemicolectomy and anastomotic surgery, 54 patients without anastomotic leakage, only 31 patients (36.5%) experienced leakage after tumor resection and anastomotic surgery, as indicated in Table 1.

TABLE 1 Incidence of anastomotic leakage

	Frequency	Percentage (%)
Leakage Anastomotic (-)	54	63.5
Leakage Anastomotic (+)	31	36.5

Regarding gender, a study indicated that the occurrence of leakage anastomotic in colon cancer patients following resection surgery was higher in men (19 patients, 61.3%). However, no statistically significant was shown (p-value = 0.097) with an odds ratio of 0.469 and a 95% confidence interval of 0.19-1.15. A total of 47 patients diagnosed with colon cancer were found to be over the age of 50. Out of these patients, 16 (51.6%) experienced postoperative leaking anastomotic. However, no statistically significant link was observed between age and postoperative leakage anastomotic (p-value = 0.05). The study revealed a higher prevalence of colon cancer in the right colon, with a total of 44 patients. However, there was no significant difference in postoperative leakage between left and right colon cancer, with 15 patients (48.4%) experiencing this complication. The statistical analysis showed no significant relationship between the two variables, with a p-value of 0.63 and an odds ratio of 0.8 (95% confidence interval: 0.3-1.9). It is well-established in the field of surgery that patients who undergo emergency anastomotic resection surgery have a significantly higher risk of experiencing leakage rates compared to those who have elective surgery (17 patients, 45.9%). Nevertheless, the chi-square test findings did not indicate a statistically significant connection (p=0.11). The odds ratio (OR) is 0.48, with a 95% confidence interval (CI) ranging from 0.1 to 1.1. Patients who did not have bowel preparation had a greater likelihood of experiencing leakage after

undergoing anastomotic resection surgery compared to those who underwent stool preparation (17 patients, 45.9%). Nevertheless, the chi-square test findings indicated a lack of significant correlation (p=0.11) with an odds ratio (OR) of 0.48 and a 95% confidence interval (CI) ranging from 0.1 to 1.1 (Table 2).

TABLE 2 Preoperative factor of anastomotic leakage

Patient Variable		Leakage Anastomotic		Total	*P*-value	OR
		No	Yes			
Sex	Male	23 42.6%	19 61.3%	42 49.4%	0.097	0.4 (0.1-1.1)
	Female	31 57.4%	12 38.7%	43 50.6%		
Age (years)	< 35	4 7.4%	8 25.8%	12 14.1%	0.05	
	35 - 50	19 35.2%	7 22.6%	26 30.6%		
	> 50	31 57.4%	16 51.6%	47 55.3%		
Location	Right Colon	29 53.7%	15 48.4%	44 51.8%	0.63	0.8 (0.3-1.9)
	Left Colon	25 46.3%	15 48.4%	40 47.1%	0.85	1.08 (0.4-2.6)
Surgery Setting	Emergency	20 54.1%	17 45.9%	37 100.0%	0.11	0.48 (0.1-1.1)
	Elective	34 70.8%	14 29.2%	48 100.0%		
Bowel Preparation	Bowel Preparation (+)	34 70.8%	14 29.2%	48 100.0%	0.11	0.48 (0.1-1.1)
	Bowel Preparation (-)	20 54.1%	17 45.9%	37 100.0%		

TABLE 3 Intraoperative factor anastomotic leakage

Patient Variable		Leakage Anastomotic		Total	*P*-value	OR
		No	Yes			
Blood Transfusion	Transfusion (-)	37 68.5%	12 38.7%	49 57.6%	0.007	3.4 (1.3-8.6)
	Transfusion (+)	17 31.5%	19 61.3%	36 42.4%		
Operator	Resident	17 31.5%	21 67.7%	38 44.7%	0.02	
	Digestive surgery resident	23 42.6%	9 29.0%	32 37.6%		
	Digestive surgeon	14 25.9%	1 3.2%	15 17.6%		

TABLE 4 Postoperative laboratorium factor anastomotic leakage

Patient Variable		Leakage Anastomotic		Total	*P*-value	OR
		No	Yes			
HB	Normal	37 68.5%	12 38.7%	49 57.6%	0.007	3.4 (1.3-8.6)
	Anemia	17 31.5%	19 61.3%	36 42.4%		
PF Ratio	Normal	19 35.2%	5 16.1%	24 28.2%	0.02	
	Mild ARDS	20 37.0%	5 16.1%	25 29.4%		
	Severe ARDS	15 27.8%	21 67.7%	36 42.4%		
Albumin	Normal	11 20.4%	3 9.7%	14 16.5%	0.01	2.3 (0.6-93)
	Hypoalbuminemia	43 79.6%	28 90.3%	71 83.5%		
Creatinin	Normal	48 88.9%	25 80.6%	73 85.9%	0.29	1.9 (0.5-6)
	Increase of Creatinin Serum > 5%	6 11.1%	6 19.4%	12 14.1%		
Leukosit	Leukocytes < 10.000	20 37.0%	10 32.3%	30 35.3%	0.65	1.2 (0.4-3)
	Leukocytes > 10.000	34 63.0%	21 67.7%	55 64.7%		
CRP	CRP <2.5	35 64.8%	6 19.4%	41 48.2%	0.01	7.6 (2.6-21)
	CRP >2.5	19 35.2%	25 80.6%	44 51.8%		

TABLE 5 Postoperative clinical factor anastomotic leakage

Patient Variable		Leakage Anastomotic		Total	*P*-value	OR
		No	Yes			
Heart Rate	< 100 bpm	39 72.2%	11 35.5%	50 58.8%	0.01	4.7 (1.8-12)
	>100 bpm	15 27.8%	20 64.5%	35 41.2%		
Respiratory Rate	< 20 x/minute	46 85.2%	21 67.7%	67 78.8%	0.058	2.7 (0.9-7)
	>20 x/minute	8 14.8%	10 32.3%	18 21.2%		
Temperature	< 38 ºC	45 83.3%	15 48.4%	60 70.6%	0.01	5.3 (1.9-15)
	> 38 ºC	9 16.7%	16 51.6%	25 29.4%		
Urine Production	> 700 cc/ 24 hours	47 87.0%	13 41.9%	60 70.5%	0.02	4.8 (1.6-14)
	< 700 cc/ 24 hours	7 13.0%	18 58.1%	25 29.4%		
Sign of ileus	No	32 59.3%	20 64.5%	52 61.2%	0.63	0.8 (0.3-1.9)

Dehiscense of fascia	Yes	22 40.7%	11 35.5%	33 38.8%	0.01	7.1 (2.6-19)
	No	43 79.6%	11 35.5%	54 63.5%		
	Yes	11 20.4%	20 64.5%	31 36.5%		
Abdominal Pain	No	22 40.7%	4 12.9%	26 30.6%	0.07	4.6 (1.4-15)
	Yes	32 59.3%	27 87.1%	59 69.4%		
Retention	Retention < 200	38 70.4%	9 29.0%	47 55.3%	0.01	5.8 (2.1-15)
	Retention > 200	16 29.6%	22 71.0%	38 44.7%		
Post OP Nutrition	Normal	39 72.2%	17 54.8%	56 65.9%	0.10	2.1 (0.8-5)
	Tube	15 27.8%	14 45.2%	29 34.1%		

In patients with large amounts of blood loss that is enough to require transfusion, 19 patients (61.3%) experienced anastomotic leakage, and a statistically significant relationship was found with (p-value 0.007) OR 3.4 (1.3-8.6). In operators, it was found that the anastomotic leakage rate with resident operators was higher, namely 21 patients (67.7%) compared to senior or trainee operators, and a significant relationship was found between operators and the postoperative leakage rate of anastomotic resection (p-value 0.02) (Table 3).

In the postoperative laboratory items of patients suffering from colon cancer with anemia, 19 patients (61.3%) had leakage anastomotic, and a statistically significant relationship was found with (p-value 0.007) OR 3.4 (1.3 - 8.6). In patients who experienced severe ARDS, 21 patients (67.7%) had leakage anastomotic and a statistically significant relationship was found (p-value 0.02). Patients with hypoalbuminemia were found to have increased leakage anastomotic and a statistically significant relationship was found (p-value 0.007) OR 2.3 (0.6 - 93). Increased creatinine levels > 5% had a higher incidence of anastomotic leakage, namely 6 patients (19.4%) and there was no statistically significant relationship (p-value = 0.29) OR = 1.9; 95% CI (0.5-6). In the leukocyte item, patients with an increase in leukocytes > 10,000 had a higher incidence of anastomotic leakage, namely 21 patients (67.7%), but there was no statistically significant relationship (p-value =0.65) OR = 1.2; CI 95% (0.4-3). In the CRP item, patients with an increase in CRP > 2.5 had a higher incidence of anastomotic leakage, namely 25 patients (80.6%) and a statistically significant relationship (p-value = 0.02) OR = 7.6; CI 95% (2.6-21) (Table 4).

Addressing gender, a study indicated that the occurrence of leakage anastomotic in colon cancer patients following resection surgery was higher in men (19 patients, 61.3%). However, no statistically significant link was seen (p-value = 0.097) with an odds ratio of 0.469 and a 95% confidence interval of 0.19-1.15. A total of 47 patients diagnosed with colon cancer were seen to be over the age of 50. Among these patients, 16 individuals (51.6%) experienced postoperative leaking anastomotic. However, no statistically significant was identified between age and the occurrence of postoperative leakage anastomotic (p-value = 0.05). The study revealed that a higher proportion of patients with colon cancer had tumours located in the

right colon, specifically 44 patients. However, there was no significant difference in the occurrence of postoperative leakage after resection and anastomotic between left and right colon cancer. This was observed in 15 patients, accounting for 48.4% of the cases, and the statistical analysis showed no significant relationship (p-value = 0.63) with an odds ratio of 0.8 and a 95% confidence interval of 0.3-1.9. It is well-established in the field of surgical settings that patients undergoing emergency procedures have a greater likelihood of experiencing post-operative leakage rates following anastomotic resection surgery compared to those who undergo elective procedures (17 patients, 45.9%). Nevertheless, the chi-square test findings indicated a lack of significant correlation (p=0.11). The odds ratio (OR) is 0.48 with a 95% confidence interval (CI) ranging from 0.1 to 1.1. Patients who did not have bowel preparation had a greater likelihood of experiencing leakage after undergoing anastomotic resection surgery compared to those who underwent stool preparation (17 patients, 45.9%). Nevertheless, the chi-square test findings indicated a lack of significant correlation (p=0.11) with an odds ratio (OR) of 0.48 and a 95% confidence interval (CI) of 0.1-1.1 (Table 5).

Anastomotic leakage has been associated with numerous risk factors. Furthermore, certain research offered substantiation for the significance or insignificance of the majority of risk variables, contributing to the perplexity surrounding established risk factors. This study discovered that among colon cancer patients who had resection surgery and anastomotic, 31 out of 85 patients (36.5%) experienced leakage after the surgery. The incidence of anastomotic leakage in the Surabaya center was higher compared to a previous study conducted in Spain by Ortiz *et al.* (2016). In the Spanish study, out of 7231 surgical patients who underwent anastomotic, the rate of anastomotic leakage was 10.0%. According to a separate study conducted by Gray *et al.* (2021), the incidence of anastomotic leakage in patients having colonic anastomotic surgery might reach up to 24% [7,8].

Men have a higher likelihood of experiencing leakage compared to women. This study's findings align with the results of a previous study conducted by Ortiz *et al.* (2016) using multilevel regression analysis. The risk of anastomotic leakage is elevated in male patients, patients with tumors located less than 12 cm from the anus, and patients with advanced tumors [10] (Ortiz *et al.*, 2016). A review of 541 patients who underwent colonic and rectal anastomoses revealed that men had a leakage rate of 11%, whereas women had a leakage rate of just 3%. This difference can be attributed to the narrower male pelvis, which makes the dissection and anastomotic procedures more challenging during surgery. According to Gray *et al.* (2021), it has been established that individuals over the age of 50 are predominantly affected by leakage anastomotic in patients with colon cancer. The study also found that advancing age is associated with an increased risk of anastomotic leakage [7].

The study revealed a greater incidence of postoperative leakage of anastomotic resection in patients with left colon cancer, specifically affecting 15 individuals (37.5%) out of the entire left colon cancer patient population. The findings of this study align with the findings of a study conducted by Kryzauskas *et al.* (2020), which demonstrated that patients who received left hemicolectomy with high occlusion of the inferior mesenteric artery had a 2.35 times greater likelihood of experiencing anastomotic leakage (odds ratio: 0.939-5.856) [10]. Several investigations have indicated the distance from the anal verge as a significant risk factor that contributes to the occurrence of anastomotic leakage [5]. When it comes to surgical settings, it is well-established that patients undergoing emergency procedures face a greater risk of experiencing leakage rates after anastomotic resection surgery compared to those undergoing elective

procedures. Specifically, 17 patients (45.9%) were found to have higher rates of leakage in emergency settings. This is primarily due to the fact that emergency patients are not adequately prepared beforehand, such as through bowel preparation, unlike elective patients who undergo various preparations to improve their condition. Consequently, the higher incidence of anastomotic leakage in emergency settings can be attributed to these factors, as indicated by research conducted by Kryzauskas *et al.* (2020) [10].

Another study revealed that bowel preparation plays a crucial role in preventing anastomotic leakage due to the potential impact of fecal burdens on the integrity of the anastomotic. The objective of bowel preparation for elective surgery is to diminish the bacterial population in the colon. In one animal model, the presence of solid feces in the colon resulted in a higher rate of leakage in rats. However, in another study with dogs, where colonic anastomoses were examined similarly, there was no difference in the leakage rate between colons with or without bowel preparation. An analysis of 267 patients, chosen at random, revealed a 2% risk of leakage in patients who underwent bowel preparation, compared to a 4% rate in patients who did not undergo bowel preparation. However, this difference was not statistically significant (p=0.28). The literature has not provided a definitive solution to the question of whether the presence of solid stool with bacterial colonization contributes to anastomotic leaking. Despite the inconsistent findings in the literature regarding the efficacy of bowel preparation, it is nevertheless advised to undergo stool preparation to reduce contamination, as suggested by Kingham and Pachter (2009) [5].

The study revealed a significant correlation between blood transfusion and an increased likelihood of anastomotic leakage, which aligns with the findings of Bharathwaj and Arvind (2004). Intraoperative hemorrhage is a significant determinant in forecasting anastomotic leakage. Hemorrhage during surgery leads to tissue ischemia and imminent anastomotic recovery, hence elevating the likelihood of leaking. Leichtle *et al.* conducted a study that examined all cases of colectomy with primary anastomotic. The study found that intraoperative blood loss exceeding 100 mL (OR 1.62; 95% CI: 1.10 to 2.40; p = 0.02) and 300 mL (OR 2.22; 95% CI: 1.32 to 3.76; p = 0.003) were linked to an increased risk of developing anastomotic leak (AL). Another risk factor is bleeding, which may necessitate a blood transfusion. Blood transfusion can result in a decline in cell-mediated immune response, which heightens the vulnerability to infection in the vicinity of anastomoses and also hampers their healing process. Analysis of the resident operators' distribution revealed that 17 patients (45.9%) experienced a higher risk of anastomotic leakage compared to senior or trainee operators [11].

The investigation revealed a strong correlation between anastomotic leakage and elevated levels of hemoglobin, albumin, and PF Ratio> 300 (p-value <0.05). The findings of this study align with the research undertaken by Zarnescuand Costea (2021), which identified anemia as a risk factor for leakage. Hemoglobin plays a crucial role in the perfusion and oxygenation of the anastomotic. It is a significant determinant for the success of the anastomotic. Hemoglobin levels below 11 g/dL elevate the risk of leakage due to reduced ability to carry oxygen to tissues and the danger of ischemia. Anastomotic failure is significantly correlated with both intraoperative blood loss and blood transfusion. Hemorrhage can lead to ischemia at the site of surgical connection, resulting in compromised healing of the connection. Blood transfusion can lead to immunosuppression, which in turn raises the likelihood of infection complications at the anastomotic. The findings of this study align with the results of a study conducted by Zarnescu and Costea (2021),

which identified a preoperative albumin level below 3.5 g/dL as a significant factor for leakage. There was a notable disparity in preoperative serum albumin levels between the leakage group and the non-leakage group, and postoperative serum albumin levels were significantly lower in the leakage group [12].

Throughout the laboratory examination, it was seen that patients with colon cancer did not exhibit a statistically significant correlation between anastomotic leakage and a rise in creatinine levels exceeding 5%, or an increase in leukocytes over 10,000. This lack of correlation was determined based on a p-value more than 0.05. The study revealed that patients with a CRP level exceeding 2.5 had a significantly increased occurrence of anastomotic leakage following surgery for colon cancer excision (p-value < 0.05). The findings of this study represent the outcomes of extensive investigation. A significant association has been observed between acute phase liver protein (CRP) in the dulk and intraabdominal complications following surgery. The concentration of C-reactive protein (CRP) typically rises within 72 hours following surgery and subsequently decreases. CRP levels remain increased in patients experiencing surgical difficulties. Serum CRP is the most extensively researched biomarker for diagnosing colonic anastomotic leakage. Serum procalcitonin (PCT) and C-reactive protein (CRP) demonstrated a high degree of accuracy in predicting the absence of colonic anastomotic leakage. Within the heart rate category, it was observed that patients with a heart rate exceeding 100 had a greater incidence of postoperative leakage following colon cancer anastomotic resection. Within the context of body temperature, it was shown that individuals who experienced a rise in temperature above 38 °C had a greater incidence of postoperative leakage following colon cancer anastomotic resection. During the study on urine production, it was shown that individuals with urine production had a greater postoperative leakage rate following colon cancer anastomotic resection.

Concerning the breathing rate, it was observed that patients who had a breathing rate over 20 experienced a greater rate of postoperative leakage following colon cancer anastomotic resection. However, no significant correlation was identified between the rate of anastomotic leakage and the breathing rate (p-value>0.05). The findings of this study align with the research conducted by Rama *et al.* (2021) in a retrospective study involving 379 patients who underwent curative colorectal cancer resection. The study revealed that 22 out of these patients experienced anastomotic leakage, accounting for 6.0% of the total. Among these 22 patients, 68.0% exhibited symptoms of tachycardia and dyspnea [8]. Luo *et al.* conducted a retrospective study to assess the prognostic significance of anastomotic leakage based on various variables, with particular emphasis on pulse, respiration rate, and body temperature. It was discovered that individuals who had higher heart rate, respiration rate, and body temperature were more likely to suffer anastomotic leaks after surgery, compared to those who did not experience such leaks. Anastomotic leakage has been linked to elevated body temperature in previous studies [4, 13-15]. In the study conducted by Park *et al.* (2018), similar findings were observed. The earliest clinical symptoms for detecting anastomotic leakage exhibited distinct patterns in both the free leakage and anastomotic leakage groups (p<0.001) [16].

The presence of abdominal pain, along with a high fever and an increased number of white blood cells (leukocytosis), are the primary indicators used to identify anastomotic leaking. Nevertheless, significant clinical symptoms, such as low blood pressure and alterations in cognitive function, have a greater likelihood of identifying anastomotic leakage [16]. The findings of this study in the physical examination component indicate that there is no correlation between indicators of ileus and

abdominal pain and the extent of leakage following surgery for colon cancer anastomotic resection. This conclusion is supported by a p-value greater than 0.05. A significant correlation was observed between fascia dehiscence (+) and retention > 200, and the postoperative leak rate of colon cancer anastomotic resection (p-value < 0.05). The findings of this study contradict prior research that suggested postoperative ileus can sometimes be the first indication of symptoms related to anastomotic leaking [16]. Several studies have established a significant connection between ileus and anastomotic leakage. These studies have identified a group of inflammatory cytokines that play a role in the initial inflammatory response leading to ileus, while also hindering the healing process of anastomotic [17-20].

Abdominal pain might be a sign of a concerning complication following colorectal resection, such as iatrogenic damage or ischemia [21-23]. This may also suggest that the colorectal anastomotic is not healing properly, as a result of the pathophysiological mechanism of secondary peritonitis. Insufficient analgesics can cause abdominal pain [24-26]. Abdominal discomfort may also manifest as a symptom of other problems, including urinary tract infection, pneumonia, or acute urine retention. Pain can stimulate the sympathetic nervous system and trigger the release of stress-related hormones, which can interfere with the optimal conditions necessary for the healing of colorectal anastomotic [27,28]. Suton *et al.* conducted a retrospective analysis that involved 379 patients who underwent curative resection for colorectal cancer. The rate of anastomotic leakage was 6.0% (n=22), and 32% of patients had clear symptoms of peritonitis, including abdominal pain, fever, and increased white blood cell count [29]. Various scientists assessed the attributes of pain, particularly its severity, and established a correlation with clinical outcomes. In a recent study conducted by Regenbogen *et al.*, 7,221 patients from 52 hospitals in the Michigan Surgical Quality Collaborative were included. The study revealed that postoperative complications occurred in 20.3% of the patients compared to 26.4% in the control group ($p<0.001$). In addition, re-hospitalization rates were lower in the study group at 11.3% compared to 16.2% in the control group ($p=0.01$) [22].

Conclusion

The three risk factors for leakage anastomotic are divided into preoperative, intraoperative, and postoperative factors. In our study showed that no statistically significant relationship was observed between preoperative factors (gender, age, anastomotic location, surgery setting, and bowel preparation) and postoperative leakage anastomotic. The surgery operator and blood transfusion are intraoperative factors that impact leakage anastomotic. Laboratory results such as Hb, PF ratio, albumin, and CRP are post-operative factors that affect leakage anastomotic. In addition, leakage anastomotic is influenced by heart rate, body temperature, urine production, and retention, according to postoperative clinical examination.

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Authors' Contributions

The study's design and methodology were developed by Nazila Hana, who also carried out formal research and analysis and wrote the initial draught of the paper. Edwin Danardono

and Sahudi Salim read and edited the manuscript, curated the data, supplied resources, and oversaw project administration in addition to validating and supervising the study.

Conflict of Interest

The authors report no conflicts of interest in this work.

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