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A 48-Hour Regimen of Perioperative Antibiotic Prophylaxis in Laparoscopic-Assisted Radical Resection for Rectal Cancer: An Analysis of 124 Cases

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Abstract

Objective: It is widely accepted that antibiotic prophylaxis is useful for the prevention of surgical site infections, especially in colorectal surgery. But the standard protocol of perioperative antibiotic use in laparoscopic-assisted surgery for rectal cancer remains to be established. To evaluate the rate of perioperative infections following rectal cancer surgery and to determine the time of using prophylactic antibiotic, we retrospectively reviewed the clinical data of 124 patients receiving laparoscopic-assisted radical resection for rectal cancer to investigate the occurrence of perioperative infections following laparoscopic surgery.

Methods: This study included 124 cases receiving laparoscopic-assisted radical resection of rectal cancer from January 2014 to December 2014. A 48-hour treatment of intravenous antibiotic prophylaxis was used. The incidence of incisional surgical site infection (SSI), organ/space SSI, and remote infection was retrospectively investigated.

Results: The overall rate of SSIs following laparoscopic-assisted radical resection for rectal cancer was to be 13.71%. Incisional SSI occurred in 5 (4.03%) patients. Organ/space SSI occurred in 6 (4.84%) patients. Remote infection occurred in 6 (4.84%) patients.

Conclusion: The incidence of incisional SSI, organ/space SSI and remote infection was low using a 48-hour treatment of intravenous antibiotic prophylaxis after laparoscopic-assisted radical resection for rectal cancer. Thus, a 48-hour treatment of intravenous antibiotic prophylaxis should be enough to prevent the emergence of antibiotic-resistant bacterial infection in laparoscopic-assisted radical resection for rectal cancer.

Keywords: Intravenous antimicrobial prophylaxis; Laparoscopic-assisted surgery; Rectal cancer; Surgical site infection (SSI); Remote infection

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Introduction

Rectal cancer is one of the common digestive tract tumors, and the disease incidence rate rises by 2% per year continually in China. Surgical operation is the first-choice method to treat rectal cancer. In 1991, Jacobs introduced for the first time the laparoscopic technology in colorectal cancer surgical operation [1], which is considered a milestone-like progress in colorectal cancer treatment. Due to the development of minimally invasive techniques, the majority of colorectal procedures can be performed using a laparoscopic approach, and the indications for laparoscopic-assisted surgery have gradually expanded [2,3]. A number of available prospectively randomized trials and meta-analyses of laparoscopic-assisted surgery for colorectal cancer reported that laparoscopic-assisted colorectal surgery exhibited improved post-operative results, including less pain, a smaller incision, a faster recovery of gastrointestinal function, a shorter post-operative hospital stay and similar long-term survival, compared with those of open colorectal surgery [4-7]. Therefore, laparoscopic-assisted surgery has been widely accepted as an alternative to conventional open surgery for colorectal cancer.

Surgical site infections are simply defined as infections that occur after a surgical procedure at the

Table 1: Antibiotic prophylaxis for patients received laparoscopic-assisted radical resection for rectal cancer.

48-hour treatment protocol	48-hour treatment protocol if penicillin allergy	Additional antibiotics used when surgical site infection (SSI) or organ/space SSI was confirmed
(1) Cefuroxime sodium, 1.5 g, i.v. 30 min before surgery and continued twice daily up to 48-hour postoperatively.	(1) Clindamycin phosphate, 0.6 g, i.v. 30 min before surgery and continued twice daily up to 48-hour postoperatively.	Cefuroxime sodium, 1.5 g, i.v. twice daily up to 6-day postoperatively for the patient with incisional surgical site infection (SSI).
(2) Metronidazole, 1.0 g, i.v. twice daily up to 48-hour postoperatively.	(2) Metronidazole, 1.0 g, i.v. twice daily up to 48-hour postoperatively.	Piperacillin Sulbactam Sodium, 4.5 g, i.v. three times daily up to 5-day postoperatively for the patient with organ/space SSI.
		Meropenem for Injection, 1.5 g, i.v. three times daily up to 7-day postoperatively for the patient with remote infection.

site of the surgery. It is the most frequent nosocomial infection among surgical patients, accounting for 38% of all such infections [8,9]. It increases medical costs, prolongs hospital stay, and occasionally leads to mortality [10]. Antibiotic prophylaxis reduces the rate of SSI in gastrointestinal surgery, but a great deal of variation exists regarding the duration of antibiotic administration. In China, standardized national guidelines of antibiotic prophylaxis for colorectal surgery have not yet been established. Given the ever-increasing number of antibiotic options available, as well as the growing problem of antibiotic resistance, there is a need for research on this important topic.

In this study, we retrospectively reviewed the clinical data of 124 patients who received laparoscopic-assisted radical resection for rectal cancer. The occurrence of perioperative infections including incisional surgical site infection (SSI), organ/space SSI, and remote infection after a 48-hour treatment of antibiotic prophylaxis from January 2014 to December 2014 was evaluated.

Patients and Methods

The institutional ethical committee approved the current retrospective study (Number: 20140101). A written informed consent was obtained from all patients. We reviewed the electronic medical records of consecutive patients received Laparoscopic-assisted radical operation for rectal cancer. From January 2014 to December 2014, 124 patients were included in this study. The length of skin incision ranged between 3 and 15 cm at the discretion of the operator and was 5 cm in the majority of patients. A standard laparoscopic-assisted radical resection of rectal cancer was performed as previously described with slight modifications [11,12]. A closed suction drain was not routinely placed in the pelvic cavity. Pubic hair was removed using a surgical clipper after general endotracheal anesthesia was introduced. The first antibiotic was administered i.v. 30 min before the start of operation, while additional administration was given after the patient returned to the ward. Antibiotic prophylaxis for patients received Laparoscopic-assisted radical operation for rectal cancer was listed in (Table 1). Skin disinfection with povidone- iodine and dressing exchange was performed daily from postoperative day 2. Incisional SSI, organ/space SSI, and remote infection were observed up to the patient's departure and followed-up for 30 days accordingly [8]. Incisional SSI was defined as macroscopic abscess or purulent discharge observed on the operative wound. Organ/space SSI was defined as infection in the organ subjected to surgery. Culture tests were performed using abscess or purulent discharge. Abscess or purulent discharge was qualitatively cultured for aerobes and anaerobes using standard laboratory techniques. Remote infections including respiratory infection and urinary tract infection were evaluated by chest plain films, sputum, urine, blood, or catheter culture after surgery. Data were presented as means and standard deviations (SD) for continuous variables and as frequencies, ratios or rates for categorical variables.

Results

Of 124 patients in the study population, 17 (13.71%) developed a SSI. There were 59 women and 65 men with a median age of 63.02 (range from 27 to 89) years. During follow-up, 17 (13.71%) patients developed SSI. Incisional SSI occurred in 5 (4.03%) patient. Organ/space SSI occurred in 6 (4.84%) patients. Remote infection occurred in 6 (4.84%) patients. A 48-hour treatment of antibiotic prophylaxis was used (Table 1). The patients with SSI received additional antibiotics (Table 1). (Table 2) summarized the clinical characteristics and short-term surgical outcomes of patients in the study.

The causalmicro-organisms of incisional SSI, organ/space SSI and remote infection were isolated and identified in these patients. Microorganisms isolated in patient with incisional SSI were Staphylococcus epidermidis and *S* aureus as anaerobes, whereas those in patient with organ/space SSI were Enterococcus faecalis. And in patient with remote infection were both anaerobic and aerobic bacteria, such as Escherichia coli, Streptococcus, Staphylococcus aureus and so on.

The patient with incisional SSI did not develop fever, and were improved by removal of some sutures and abscess drainage and additional antibiotics. The patient with organ/space SSI developed fever and were treated with additional antibiotics as well as abscess drainage. The patient with remote infection developed fever and were treated with additional antibiotics.

Discussion

The overall rate of SSIs following laparoscopic-assisted radical resection of rectal cancer in the present study was 13.71%. This was similar to other large studies from developed countries, such as the United Kingdom (8-33%) [13,14], the United States of America (8-20%) [15,16], and Japan (4-30%) [17,18]. It was also low to the incidence rates reported from Canada (15-24%) [19] and countries in Southeast Asia such as Vietnam (14-20%) [20].

The differences in patient characteristics, surgical procedures, hospital settings, surveillance program, and criteria for diagnosis of incisional SSI could explain the various incidence of SSI among countries. As for patient resistance, intrinsic patient characteristics strictly correlating with an increased risk of SSI include advanced age, an American Society of Anesthesiologists (ASA) score of III, obesity, pre-existing illness, and host defense deficiency [21-24]. Moreover, risk factors for SSI related to the surgical procedure include quality of surgical care, diabetes mellitus, surgery type and duration, emergency procedure, blood transfusion, intraoperative hypothermia, and systemic hypoxemia [17–20].

Due to the high risk of bacterial contamination, colorectal surgery is associated with a particularly high risk of postoperative infection. SSI rates of up to 40% and of about 25% have been found in patients not receiving or receiving perioperative antibiotic prophylaxis,

Table 2: Clinical characteristics and short-term surgical outcomes of patients received laparoscopic-assisted radical resection for rectal cancer.

Characteristics	
Patients (n)	124
Age (years, mean ± SD)	63.02 ± 10.69
Gender (n, %)	
Male	65 (52.4)
Female	59 (47.6)
Diseases history (n, %)	
Diabetes	40 (32.3)
Hypertension	12 (9.7)
Cardiopathy	5 (4)
Surgical technique	Laparoscopic-assisted radical resection for rectal cancer
	Total mesorectal excision (TME)
Conversion to open surgery (n, %)	0
Tumor locations (n, %)	
Rectum	118 (95.2)
Colon sigmoideum	5 (4.0)
Descending colon	1 (0.8)
Operation time (minutes, mean ± SD)	137.83 ± 51.41
Estimated blood loss (mL, mean ± SD)	66.52 ± 68.16
Length of incision (cm, mean ± SD)	5.02 ± 1.27
Days to pull out gastrointestinal decompression tube(days, means ± SD)	1.11 ± 2.20
Days to liquid diet (days, mean ± SD)	7.19 ± 2.80
Days to first flatus (days, mean ± SD)	2.30 ± 1.21
Days to first defecation (days, mean ± SD)	4.52 ± 2.27
Days to pull out abdominal drainage tube(days, mean ± SD)	5.23 ± 2.92
Days to pull out catheter(days, means± SD)	3.98 ± 2.14
Days to independent ambulation(days, means ± SD)	6.57 ± 2.14
Intraoperative complications (n, %)	
Massive hemorrhage > 500 ml	0
Organ injury	0
Ileus	0
Post-operative complications (n, %)	
Intestinal adhesion	1 (0.8)
Ileus	1 (0.8)
Anastomotic stenosis	0
Anastomotic bleeding	2 (1.61)
Anastomotic leakage	1 (0.8)
Pulmonary infection	3 (2.4)
Urinary tract infection	0
Bacteremia	3 (2.4)
Incisional surgical site infection (SSI)	5 (4.03)
Organ/space SSI	6 (4.83)
Remote infection	6 (4.83)
Postoperative mortality (n, %)	0
Hospital stay (days, mean ± SD)	13.10 ± 5.74
Tumor size (diameter, cm, mean ± SD)	4.44 ± 1.45
Number of lymph node harvested (n, mean ± SD)	16.82 ± 10.28
Number of positive lymph node harvested (n, mean ± SD)	1.80 ± 2.81
R0 resection (0, %)	124 (100)
Proximal resection margin (cm, mean ± SD)	11.31± 3.54
Distal resection margin (cm, mean ± SD)	3.64 ± 2.28
Pathological types (n, %)	
Adenocarcinoma	118 (95.8)
Mucinous adenocarcinoma	6 (4.2)
Tumor differentiation (n, %)	
Poor	63 (50.8)
Moderate	59 (47.6)
Well	2 (1.6)
TNM stages (n, %)	
I	15 (12.1)
II	50 (40.32)
III	47(37.90)
IV	12 (9.68)
Cost for operation (RMB, mean ± SD)	20125.40 ± 5781.04
Total cost (RMB, mean ± SD)	42322.68 ± 10189.46

respectively [21,25]. Indeed, the efficacy of perioperative systemic antimicrobial agents is mainly related to suppression of bacterial growth in the tissues of the operative field once contamination occurs. Inappropriate timing of antimicrobial administration and inappropriate selection of the antimicrobial agent extend patient admission. It is universally accepted that antibiotic prophylaxis, perioperative administration of suitable antimicrobial agents, must be considered one of the most important measures for preventing SSI.

In digestive tract surgery, the benefits of prophylactic antibiotic administration for prevention of surgical site infection (SSI) have been established [25-27]. Based on the US guidelines, single-dose administration of an antibiotic within 1 hour before surgery and the duration of administration within 24 hours after the end of surgery had been recommended, even in clean-contaminated surgery [28,29]. The Japanese Association for Infectious Diseases and the Japanese Society of Chemotherapy published guidelines in 2005, in which the duration of prophylactic antibiotic administration should be 4 days or less in clean-contaminated surgery. Society of Infectious Diseases, Chinese Medical Association published guidelines in 2009, in which the duration of prophylactic antibiotic administration should be 48 hours or less in clean-contaminated surgery. However, the standard protocol of perioperative antibiotic use in laparoscopic resection for rectal cancer has not been established. In this study, we investigated the proper protocol of prophylactic antibiotic treatment for preventing perioperative infections in laparoscopic resection for rectal cancer.

The reported causal microorganisms are anaerobes and Escherichia coli in large-bowel surgery, which account for 56%and 46%, respectively, of such infections [30]. There are 10 [25-27] aerobes and 10 [31,32] anaerobes (mainly Bactericides) in 1g of feces. Therefore, the important factor in selecting a prophylactic antibiotic is antimicrobial activity against anaerobes [33]. The CDC guidelines

recommend use of antibiotics that are also effective against anaerobes, as a single agent or in combination to prevent postoperative infection in colorectal surgery [28]. In our clinical practice, a second-generation cephalosporin combined with metronidazole is mostly used (Table 1). Cefuroxime sodium, which shows bactericidal activity, is classified as a second-generation cephalosporin based on its antibacterial spectrum against Gram-positive and negative organisms. Cefuroxime sodium exhibits potent antimicrobial activity against anaerobes such as Bactericides fragilis [34]. Currently, Cefuroxime sodium is widely used to prevent postoperative infection after clean-contaminated surgery in China. Metronidazole is bactericidal against human pathogenic anaerobic bacteria, and administered in combination with Cefuroxime sodium, it has been shown to reduce the incidence of wound infections after colorectal surgery. Patients with early postoperative fever should be evaluated to identify the possible source of infection. However, there is evidence that most of these episodes are non-infectious in origin [35].

In our clinical study, the rate of SSIs was 13.71% using a 48-hour treatment of intravenous antimicrobial prophylaxis after Laparoscopic-assisted radical operation for rectal cancer. Incisional SSI was 4.03%, Organ/space SSI was 4.84%, and remote infection was 4.84%. The rate was similar to other studies from developed countries. Our results confirmed that the 48-hour protocol of prophylactic antibiotic treatment was adequate for preventing surgical site infection in laparoscopic-assisted radical resection for rectal cancer. It could both prevent the emergence of antibiotic-resistant bacterial infection and reduce hospital expenditure.

Conclusion

This present study found the overall rate of incisional SSI following laparoscopic-assisted radical resection for rectal cancer to be 13.71%, and antibiotic administration of longer than 48 hours postoperatively may not decrease the rate of this complication. Thus, we should be encouraged to using a shorter duration of antibiotics in order to prevent the emergence of antibiotic-resistant bacterial infection and reduce hospital expenditure. But whether a 24-hour protocol of prophylactic antibiotic treatment would be enough to prevent perioperative infections in laparoscopic-assisted radical resection for rectal cancer is not known and worth to be investigated further.

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