Perioperative Antibiotic Prophylaxis in Laparoscopic Right Hemicolectomy for Colon Cancer: A 48-Hour Regimen

Haibin Zhang¹, Xiongfei Yu¹, Ketao Jin², Lisong Teng¹

¹Department of Surgical Oncology, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310003, Zhejiang Province, P. R. China

²Department of Gastrointestinal Surgery, Shaoxing People's Hospital, Shaoxing Hospital of Zhejiang University, Shaoxing, 312000, Zhejiang Province, P. R. China

Corresponding author:

Ketao Jin, M.D.
Department of Gastrointestinal Surgery,
Shaoxing People's Hospital, Shaoxing
Hospital of Zhejiang University. No. 568
Zhongxing North Road, Shaoxing,
312000, Zhejiang Province, P.R. China
E-mail: jinketao2001@zju.edu.cn

ABSTRACT

Purpose: The standard protocol of perioperative antibiotic use in laparoscopic colectomy for colon cancer remains to be 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.

Methods: We retrospectively reviewed the clinical data of 45 patients receiving laparoscopic right hemicolectomy for colon cancer to investigate the occurrence of perioperative infections following laparoscopic surgery. This study included 45 cases receiving laparoscopic right hemicolectomy from January 2013 to December 2014. A 48-hour treatment of antibiotic prophylaxis was used.

Results: The incidence of incisional surgical site infection (SSI), organ/space SSI, and remote infection was retrospectively investigated. Incisional SSI occurred in 1 (2.3%) patient. Organ/space SSI occurred in 1 (2.3%) patient. No remote infection occurred.

Conclusions: The incidence of incisional SSI and organ/space SSI was low using a 48-hour treatment of antibiotic prophylaxis after laparoscopic right hemicolectomy for colon cancer. Therefore, the 48-hour protocol of prophylactic antibiotic treatment seems to be adequate for preventing perioperative infections in laparoscopic right hemicolectomy.

Key words: antibiotic prophylaxis, laparoscopic right hemicolectomy, colon cancer, surgical site infection (SSI), remote infection

INTRODUCTION

Colorectal cancer is one of the leading causes of mortality worldwide (1). Traditionally, cancers of the colon were removed through large abdominal incisions. Since the advent of laparoscopic surgery, it has become clear that patients benefit from a minimally invasive approach in a variety of ways (2). Therefore, laparoscopic-assisted surgery has been widely accepted as an alternative to conventional open surgery for colorectal cancer. Because of the

potential advantages, such as less invasiveness and postoperative pain, earlier recovery, better cosmetic results, milder morbidity, earlier time to walking, flatus, and oral intake, and quicker recovery with a shorter hospital stay, laparoscopic surgery for colorectal cancer was introduced into clinical practice in China in 2001 (3), was gradually implemented and is now commonplace in China. There has been booming interest in laparoscopic surgery for colorectal cancer since it was first described in 2001 (3). The last decade has witnessed national growth in the application of laparoscopic surgery for colorectal cancer yielding a significant amount of scientific data to support its clinical merits and advantages (4).

Surgical infections caused by the opening of contaminated cavities such as intestines, stomach or vagina have been feared by surgeons for many decades. It has been reported that wound infections occur in approximately 40% of patients undergoing colorectal surgery without antibiotic prophylaxis (5). Perioperative antibiotic use to prevent surgical site infection is a widely accepted procedure in general surgery, including laparoscopic surgery for colorectal cancer. Therefore different strategies have been developed to reduce the rate of complications associated to bacterial contamination. However, inappropriate antibiotic use increases environmental pressure favoring the emergence of antimicrobial-resistant bacteria that can cause surgical site infection, resulting in an increase in the cost of health care (6). A rational application of antibiotic agents is therefore essential and guidelines for appropriate use are currently under development. Results from the United States National Surgical Infection Prevention Project showed that among Medicare patients undergoing major surgery, antibiotic prophylaxis was begun within 1 hour before surgery in only 56% of patients and stopped within 24 hour of surgery in only 41%, as recommended (7).

Surgical wounds were classified as clean (class I), clean-contaminated (class II), contaminated (class III)

and dirty/infected (class IV) (8). According to this classification, laparoscopic right hemicolectomy is classified as clean-contaminated because the colon tract is opened. The optimal antibiotic prophylaxis for laparoscopic right hemicolectomy has not been investigated in China.

In this study, we retrospectively reviewed the clinical data of 45 patients receiving laparoscopic right hemicolectomy for colon cancer to investigate the occurrence of perioperative infections including incisional surgical site infection (SSI), organ/space SSI, and remote infection after a 48-hour antibiotic prophylaxis from January 2013 to December 2014.

PATIENTS AND METHODS

The institutional ethical committee approved the current retrospective study (Number: 20121220). A written informed consent was obtained from all patients. We reviewed the electronic medical records of consecutive patients receiving laparoscopic right hemicolectomy for colon cancer. From January 2013 to December 2014, 45 patients were included in this study. The length of skin incision ranged between 3 and 10 cm at the discretion of the operator and was 5 cm in the majority of patients. A standard laparoscopic right hemicolectomy was performed as previously described with slight modifications (9-11). 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 performed. 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 right hemicolectomy for colon 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

Table 1 - Antibiotic prophylaxis for patients received laparoscopic right hemicolectomy for colon 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.

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 numerical variables and as frequencies, ratios or rates for categorical variables.

RESULTS

The clinical characteristics and short-term surgical outcomes of patients were listed in *table 2*. This study included 45 cases receiving laparoscopic right hemicolectomy from January 2013 to December 2014. A 48-hour treatment of antibiotic prophylaxis was used (*table 1*). Incisional SSI occurred in 1 (2.3%) patient. Organ/space SSI, intra-abdominal abscess, occurred in 1 (2.3%) patient. No remote infection occurred. The patients with incisional SSI or organ/space SSI received additional antibiotics (*table 1*).

The causal microorganisms of incisional SSI and organ/space SSI were isolated and identified in these two patients. Microorganisms isolated in patient with incisional SSI were *Staphylococcus epidermidis* and *S aureus* as aerobes, whereas those in patient with organ/space SSI were *Enterococcus faecalis*.

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

DISCUSSION

Postoperative infection causes various problems, such as prolongation of hospital stay, increase in medical costs and decrease in patient satisfaction (12-14). Guidelines for the prevention of postoperative infection and proper antibiotic use have therefore been proposed by the Centers for Disease Control and Prevention (CDC) and other organizations (8,15). In digestive tract surgery, the benefits of prophylactic antibiotic administration for prevention of SSI have been established (16-18). Based on the US guidelines, single-dose administration of an antibiotic within 1

Table 2 - Clinical characteristics and short-term surgical outcomes of patients received laparoscopic right hemicolectomy for colon cancer

Characteristics	
Patients (n)	45
Age (years, mean $\pm$ SD)	61.08 $\pm$ 13.22
Gender (n, %)	
Male	17 (37.8)
Female	28 (62.2)
Surgical technique	Multiport laparoscopic right hemicolectomy total mesocolic excision (TME)
Conversion to open surgery (n, %)	0
Tumor locations (n, %)	
Cecum	3 (6.7)
Ascending colon	29 (64.4)
Hepatic flexure	8 (17.8)
Transverse colon	5 (11.1)
Operation time (minutes, mean $\pm$ SD)	142.56 $\pm$ 30.46
Estimated blood loss (mL, mean $\pm$ SD)	84.22 $\pm$ 72.15
Length of incision (cm, mean $\pm$ SD)	5.47 $\pm$ 1.24
Days to liquid diet (days, mean $\pm$ SD)	6.16 $\pm$ 2.15
Days to first flatus (days, mean $\pm$ SD)	3.33 $\pm$ 1.26
Days to first defecation (days, mean $\pm$ SD)	4.98 $\pm$ 1.96
Intraoperative complications (n, %)	
Massive hemorrhage > 500 ml	0
Organ injury	0
Ileus	0
Post-operative complications (n, %)	
Intestinal adhesion	0
Anastomotic stenosis	0
Anastomotic bleeding	0
Anastomotic leakage	0
Pulmonary infection	0
Urinary tract infection	0
Incisional surgical site infection (SSI)	1 (2.3)
Organ/space SSI	1 (2.3)
Postoperative mortality (n, %)	0
Hospital stay (days, mean $\pm$ SD)	13.78 $\pm$ 5.42
Tumor size (diameter, cm, mean $\pm$ SD)	5.68 $\pm$ 2.29
Number of lymph node harvested (n, mean $\pm$ SD)	26.00 $\pm$ 9.77
Number of positive lymph node harvested (n, mean $\pm$ SD)	1.78 $\pm$ 2.70
R0 resection (0, %)	43 (95.6)
Proximal resection margin (cm, mean $\pm$ SD)	10.33 $\pm$ 5.08
Distal resection margin (cm, mean $\pm$ SD)	9.76 $\pm$ 5.12
Pathological types (n, %)	
Adenocarcinoma	33 (73.3)
Mucinous adenocarcinoma	11 (24.4)
Signet-ring cell carcinoma	1 (2.2)
Tumor differentiation (n, %)	
Poor	16 (35.6)
Moderate	29 (64.4)
Well	0
TNM stages (n, %)	
I	3 (6.7)
II	19 (42.2)
III	22 (48.9)
IV	1 (2.2)

Neoadjuvant chemotherapy (n, %)	0
Adjuvant chemotherapy (n, %)	38 (84.4)
Cost for operation (RMB, mean $\pm$ SD)	7,528.65 $\pm$ 1441.78
Cost for drugs (RMB, mean $\pm$ SD)	20,287.11 $\pm$ 5311.30
Total cost (RMB, mean $\pm$ SD)	27,815.76 $\pm$ 5427.74

hour before surgery and the duration of administration within 24 hours after the end of surgery had been recommended, even in clean-contaminated surgery (8, 15). However, the Japanese Association for Infectious Diseases and the Japanese Society of Chemotherapy guidelines recommended the duration of prophylactic antibiotic administration should be 4 days or less in clean-contaminated surgery (19). 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 colectomy for colon cancer has not been established. This is the first study to investigate the proper protocol of prophylactic antibiotic treatment for preventing perioperative infections in laparoscopic colectomy for colon cancer.

According to the guidelines for the prevention of SSI published by the US Centers for Disease Control and Prevention (CDC) in 1999, various factors such as age, nutritional status, diabetes, smoking and obesity are thought to be related to the occurrence of SSI (20). Surgical stresses can weaken the immune systems of patients during the perioperative period, resulting in immuno-compromise and an increased susceptibility to pathogens. Under these circumstances, SSI is well known as a major complication of gastrointestinal surgery. Presence of SSI does not only make the patients lose their satisfaction with their treatment as a result of prolonged hospitalization, but also substantially increase morbidity, mortality, and the cost of care (21). Several surveillance reports regarding SSI have been carried out and have played important roles in SSI prevention (8,22,23). Patient factors (i.e., diabetes, smoking, obesity, steroid use, blood transfusion, etc.), environmental factors (i.e., ventilation in operating room, sterilization of surgical instruments, etc.), and bacterial factors are thought to be the main causes of SSI (24-30). Surgery of the colon is associated with a high incidence of SSI compared with surgery addressed to other parts of the digestive tract. Postoperative infection, including incisional SSI, organ/space SSI, or remote infection, occurs frequently after colorectal cancer surgery, causing not only a prolonged hospital stay and decrease in quality of life, but also a poorer

prognosis due to the delay in postoperative treatment. When considering which antimicrobial agent to use, a surgeon considers the risk of wound infection, cost, the risk of a drug side effects, and antibiotic resistance. The Society of Infectious Diseases, Chinese Medical Association guidelines recommends use of antibiotics that are also effective against aerobes, as a single agent or in combination to prevent postoperative infection in colorectal surgery. The large variety of continuously newly developed antibiotics makes an adequate therapy difficult for non-specialists. It has been shown that a single shot prophylaxis of a standard combination is sufficient to prevent postoperative infections. In our clinical practice, a second-generation cephalosporin combined with metronidazole is mostly used (*table 1*).

The present study showed that the overall rate of incisional SSI and organ/space SSI in patients received laparoscopic right hemicolectomy was 2.3% and 2.3%, respectively. No remote infection was found in these patients. Our results confirmed that the 48-hour protocol of prophylactic antibiotic treatment was adequate for preventing surgical site infection in laparoscopic right hemicolectomy. Our results suggest that a short perioperative course of antibiotics can adequately prevent remote infection. 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 of non-infectious origin (31).

CONCLUSION

Procedures for perioperative infection prophylaxis in laparoscopic colectomy for colon cancer consist of preoperative mechanical preparation, chemical preparation with oral antibiotic administration, and perioperative intravenous antibiotic administration. However, the optimal combination of these procedures and drugs and their durations of administration have not yet been established. Our results revealed that the incidence of incisional SSI and organ/space SSI was low using a 48-hour treatment of antibiotic prophylaxis after laparoscopic right hemicolectomy for colon cancer. Therefore, the 48-hour protocol of prophylactic antibiotic treatment seems to be adequate for preventing perioperative infections in laparoscopic right hemicolectomy. However, whether a 24-hour protocol of prophylactic antibiotic treatment would be enough to prevent perioperative infections in laparoscopic right hemicolectomy is not known and worth to be investigated in randomized control clinical trials further.

Authors' contributions

HBZ designed and carried out this study, analysed the data and wrote this manuscript. XFY was involved in designing this study and in drafting the manuscript. KTJ and LST involved in designing this study and in drafting the manuscript. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that they have no conflict of interest.

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