

# To Investigate the Impact of Laparoscopic Resection of Colorectal Carcinoma on the Peritoneal Metastases of Cancer

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## Abstract

**Objective:** To explore the effect of laparoscopy on cancer cells and the expressions of adhesion molecules (ICAM-1, CD44v6 & integrin  $\beta$ 1) in peritoneal tissue and abdominal rinse in patients with colorectal carcinoma (CC).

**Methods:** A total of 65 CC cases undergoing radical resection at our hospital were analyzed. They were divided into two groups of LAP (laparoscopy, n=35) and OP (open surgery, n=30). Peritoneal tissues were collected at incision and beyond. Also abdominal rinse was collected before tumor resection and abdomen closure. The expressions of adhesion molecules (ICAM-1, CD44v6 & integrin beta 1) in peritoneal and abdominal cavities of two groups were detected by immunohistochemistry and double-antibody sandwich ABC-ELISA. And cancer cells in abdominal rinse were detected by peritoneal lavage cytology (PLC) for comparing two surgical methods.

**Results:** In LAP group, PLC was positive in 3 cases (8.6%) before tumor resection and 8 cases (22.9%) before abdominal closure. In OP group, PLC was positive in 4 cases (13.3%) before tumor resection and 8 cases (26.7%) before abdominal closure. No inter-group difference existed in PLC ( $P>0.05$ ). The expressions of CD44v6, ICAM-1 and integrin beta 1 in abdominal cavity (before tumor resection & abdomen closure) were compared for LAP and OP groups. And there was no statistically significant difference ( $P>0.05$ ). The expressions of CD44v6, ICAM-1 and integrin beta 1 in peritoneal tissues (at incision and beyond) were compared between LAP and OP groups. And there was no statistically significant difference ( $P>0.05$ ).

**Conclusion:** Compared with CC patients undergoing traditional open surgery, the risk of exfoliated cancer cells in abdominal cavity shows no increase. And there is no impact upon the expressions of adhesion molecules.

**Keywords:** Laparoscopic surgery; Peritoneal metastases

## Introduction

In China, colorectal cancer is one type of gastrointestinal carcinoma with relatively high occurrence in the population. While surgical resection has been an effective way of getting rid of colorectal carcinoma, laparoscopic resection offers the benefits including shorter hospitalization, rapid recovery, and smaller incisions, and thus has been widely used in removing the colorectal carcinoma. For colorectal cancer, migration of tumor cells to distant organs leading to the metastases of cancer is the main cause of death in colorectal cancer patients [1,2]. Currently, there have been efforts in understanding whether the surgical resection and laparoscopic resection result in significant differences in the peritoneal metastases of cancer [3,4]. This paper reports a study assessing the impact of surgical resection and laparoscopic resection on the peritoneal metastases of cancer in colorectal cancer patients.

## Study Design and Methods

### A cohort study design

A total of 66 colorectal cancer patients treated between August 2013 and August 2015 were enlisted in a cohort study in which they were equally divided in random into two groups: a control group (33) and an observation group (33).

**Patient selection was based on the following criteria:** (1) The absence of distant metastasis based on preoperative images including CT, ultrasound, and X-ray; (2) No dysfunction of the liver, kidney, heart, and brain; (3) No history of operation for gastrointestinal carcinoma; (4) Patients' age between 40-65 years old.

**Patients were excluded in the study based on the following criteria:** (1) Abandoned operation due to tumor spreading to

peritoneal cavity and peritoneum; (2) palliative operation. The control group had 11 females and 22 males, with ages ranging from 40 to 64, and an average age of  $53.23 \pm 10.33$  years old. In this group the average tumor size was  $3.56 \pm 1.54$  cm. Based on the Dukes classification of tumors, there were 8 cases in Stage A, 15 cases in Stage B, and 10 cases in Stage C. The observation group had 10 females and 23 males, with ages ranging from 40 to 65, and an average age of  $53.09 \pm 10.13$  years old. In this group the average tumor size was  $4.10 \pm 1.65$  cm. Based on the Dukes classification, there were 9 cases in Stage A, 12 cases in Stage B, and 12 cases in Stage C. Comparison of the patients' sex, age and Dukes classification between these two groups demonstrated no statistical differences ( $P>0.05$ ).

## Treatment

Patients in the control group were subject to surgical resection. Please refer to the Surgical Procedures section for colorectal tumor separation, dissection, removal and digestive tract repair. Patients in the observation group were subject to laparoscopic resection, with the procedures detailed as below.

**Tumor site locationing:** Place the patient under a general anesthetic through endotracheal intubation and use carbon dioxide

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(CO<sub>2</sub>) gas to establish the pneumoperitoneum. Make a 10 mm Trocar incision around the navel to insert the laparoscope inside. Make a 10 mm and 5 mm Trocar incision at the lower left and right pneumoperitoneum respectively to insert the intestinal forceps. Pass the colonoscopy camera into the rectum and colon through the anus to locate the tumor site and determine the section to be surgically removed. Mark the tumor with a titanium forceps, and tie both ends of the colon approximately 10-15 cm from the tumor with cotton tapes. For rectal cancer, tie the proximal end first, followed by tying up the distal end during operation.

**Surgical procedures:** For transverse colon cancer, use Harmonic scalpel to cut and separate mesentery from the transverse colon. Based on the location of the tumor, clamp off the colic arteries, and make the hepatic flexure and the splenic flexure free. Remove the CO<sub>2</sub> pneumoperitoneum, and extend the middle-left Trocar incision up to 4-5 cm, take out the transverse colon, remove the tumor. Perform the colonic anastomosis, and put the colon back into the peritoneal cavity. Close off the incisions and reestablish CO<sub>2</sub> pneumoperitoneum to finish the operation. For ascending colon cancer, use Harmonic scalpel to cut and separate mesentery from the ascending colon. Make the hepatic flexure, ascending colon, and ilium free. Clamp off the right colic artery and right colic vein. Separate and cut the mesentery from the colon to the root of the right colonic artery. Remove the CO<sub>2</sub> pneumoperitoneum, and extend the middle-right Trocar incision up to 4-5 cm, take out the ascending colon, remove the tumor. Perform the ileum and transverse colon anastomosis, and put the colon back into the peritoneal cavity. Close off the incisions and reestablish CO<sub>2</sub> pneumoperitoneum to finish the operation. For sigmoid colon and rectum cancer, use Harmonic scalpel to cut and separate the mesentery from the sigmoid colon. Clamp off the artery roots of the mesentery. Make a ligation at the region 3-5 cm distal of the tumor using a cotton thread. Make a cut in the rectum. Extend the middle-left Trocar incision up to 4-5 cm, take out the colon, and remove the tumor. Suture the surgical ends together, and put the colon back into the peritoneal cavity. Close off the incisions and reestablish CO<sub>2</sub> pneumoperitoneum, insert the round stapler through the anus, and perform the rectal end anastomosis to complete the operation.

**Measurement:** Tumor cytology analysis: Collect the rinsing liquid of the peritoneal cavity and centrifuged for 10 minutes. Collect the precipitated cells, followed with H&E staining, fixing and conventional smearing under sterile conditions. Analyze the tumor cells under the light microscope. Tumor cytology analysis for the rinsing liquid of the surgical tools: At the end of the operation, rinse the surgical tools with SSPS (150 ml), collect and store the rinsing liquid under sterile conditions. Tumor cytology analysis of the CO<sub>2</sub> gas filtrate: When the CO<sub>2</sub> pneumoperitoneum was initially established draws the CO<sub>2</sub> through the Trocar, and pass it through the filter bottle with 150 ml SSPS until the end of the operation. Store the filter bottle under sterile conditions. Tumor cytology analysis for shedding tumor cells in the pneumoperitoneum rinsing liquid: Prior to the operation, rinsing the pneumoperitoneum cavity with tumor using 200 ml SSPS, and collect 100 ml rinsing liquid using a sterilized syringe. Post the operation, rinsing the pneumoperitoneum cavity with 500 ml SSPS, and collect 200 ml rinsing liquid using a sterilized syringe. Store the samples under sterile conditions.

### Statistical analysis

Data were analyzed using SPSS 15.0 Software. The counting data were analyzed by  $\chi^2$  test and expressed in percentages. The measurement data were analyzed by t test and expressed in  $\bar{x} \pm s$ . Data showed statistic difference whenever  $P < 0.05$ .

### Results

In this study, a comparison of the patients' sex, age and Dukes classification between the two groups (control group and observation group demonstrated no statistical differences ( $P > 0.05$ ).

#### A comparison of the tumor-positive percentages in the pneumoperitoneum rinsing liquid before and after the operation

No positive tumor cells were found in the CO<sub>2</sub> filtrate. In the observation group, the tumor-positive percentages in the pneumoperitoneum rinsing liquids before the operation and after the operation were 63.64% and 60.61%, respectively. Also in the observation group, the tumor-positive percentages in the pneumoperitoneum rinsing liquids where tumor was found to be negative prior to the operation but positive post the operation was 6.06%. In the control group, the tumor-positive percentages in the peritoneum rinsing liquids before the operation and after the operation were 69.70% and 45.45% respectively. Also in the control the tumor-positive percentages in the peritoneum rinsing liquids where tumor was found to be negative prior to the operation but positive post the operation was 9.09%. This two groups showed no statistical differences with  $P > 0.05$ . The results of the tumor-positive percentage in the pneumoperitoneum rinsing liquids before and after the operation were summarized in Table 1. In the observation group, the tumor-positive percentage in the device-rinsing liquid was 12.12%, in comparison to that of 9.09% in the control group. There is no statistical difference between these two groups ( $P > 0.05$ ). The results of the tumor-positive percentage in the device-rinsing liquids between the observation group and control group were summarized in Table 2.

### Discussion

It has been a clinical hot topic in understanding whether laparoscopic resection of colorectal cancer would result in the peritoneal metastases of cancer [5-7]. Related studies have found that during the laparoscopic surgery, the cancer cells might exist in vaporized form when the CO<sub>2</sub> pneumoperitoneum is established [8-10]. In our study, results showed the absence of positive tumor cells in the CO<sub>2</sub> filtrate, suggesting that the CO<sub>2</sub> pneumoperitoneum during the operation could not increase the rate of cancer metastases. Despite of the wide use of Harmonic scalpel in the laparoscopic surgery to remove cancerous tissues, whether the vaporization of the cancer tissue could increase the peritoneal metastases of the cancer remains to be controversial. When using Harmonic scalpel to remove gastric cancers, the resulting aerosol also contained some living cancer cells. The number of cancer cells is directly proportional to the cutting power and cutting time. Having a cutting time  $< 10s$  could prevent the peritoneal metastases of cancer cells [11]. Besides, the Harmonic scalpel may seal off the cutting end, causing the veins to be closed off. This would minimize the avenues of cancer cell metastases, preventing the peritoneal migration of cancer cells. This study also demonstrated that the tumor-positive percentage in the device-rinsing liquid from the observation group was 12.12%, in comparison to that of 9.09% in the control group. There was no statistical difference between these two groups. These results suggested that the devices contaminated with cancer cells might be one of the reasons for peritoneal metastases. However there was no significant difference in the metastatic rates between the surgical resection and laparoscopic resection.

Post the surgery, the shed cancer cells within the abdomen is one of the main reasons for peritoneal cancer metastases. This study compared the tumor shedding levels from the surgical resection and laparoscopic resection of colorectal cancer patients, and assessed their impact of these two surgical operations on the peritoneal cancer metastases. The study demonstrated no statistical differences in the peritoneal rinsing liquids between the control group and the observation group regarding

**Table I:** Tumor-positive percentages in the peritoneal rinsing liquid before and after the surgery

Groups	Patient Number	Preoperative tumor negative and post-operative tumor-positive rate	Tumor positive rates post-surgery	Tumor -positive rates prior to surgery
Observation Group	33	2 (6.06%)	17 (51.52%)	21 (63.64%)
Control Group	33	3 (9.09%)	15 (45.45%)	23 (69.70%)
$\chi^2$		0.216	0.243	0.273
P		>0.05	>0.05	>0.05

**Table II:** Tumor-positive rates in the device-rinsing liquid from the control group and observation group

Groups	Patient Number (N)	Tumor-positive Rate
Observation Group	33	4 (12.12%)
Control Group	33	3 (9.09%)
c2		0.16
P		>0.05

the preoperative tumor-positive rates, post-operative tumor-positive rates, and preoperative tumor-negative and postoperative tumor-positive rates. These results suggested that both surgical resection and laparoscopic resection could impact the peritoneal cancer metastases. The postoperative peritoneal rinsing liquids had a lower tumor-positive rate than the preoperative peritoneal rinsing liquids, suggesting that repeated peritoneal rinsing could decrease the tumor cell shedding and cancer metastases. Laparoscopic operation through changing the patient body position could decrease the pulling and dragging on the tumor and surrounding tissues, expand the operative view, lessen the injury to the peritoneal tissues, and avoid the stimulation of the lesions, thus lowering the cancer metastases. Overall, there is no significant difference in the peritoneal cancer metastases between the surgical resection and laparoscopic resection of the colorectal cancer. The application of CO<sub>2</sub> pneumoperitoneum does not increase the rate of peritoneal cancer metastases. Based on this study, we concluded that the laparoscopic resection of the colorectal cancer is safe, effective, and valuable for its clinical applications.

## Conclusion

The surgical resection and laparoscopic resection had no significant difference in their impact on the peritoneal cancer metastases.

## Conflict of Interest

Authors have no conflict of interest to disclose.

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