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Safety and efficacy evaluation of laparoscopy in colorectal cancer with liver metastasis

M.-F. YE, G.-G. XU, J.-F. GU, Q.-L. ZHOU, F.-Q. LIN, K.-L. TAO, F. TAO

Department of Gastrointestinal Surgery, Shaoxing People's Hospital, Shaoxing Hospital of Zhejiang University, Shaoxing, Zhejiang Province, China

Abstract. – OBJECTIVE: To study the safety and efficacy of simultaneous completion of colorectal cancer resection and liver metastasis resection by total laparoscopy.

PATIENTS AND METHODS: In the observation group, 40 patients with colorectal cancer combined with liver metastasis (CRCLM) were selected to receive total laparoscopic surgery. At the same time, 40 cases were selected for laparoscopic resection of colorectal cancer and hepatic resection as control group.

RESULTS: The outcomes of the two methods in the treatment of CRCLM were compared. The results showed that the difference in surgery time between the two groups was not statistically significant ($p>0.05$). The blood loss, drainage tube retention time and anal exhaust recovery time in the observation group were significantly less than those in control group ($p<0.05$). No significant difference in completion rate was found between the two groups ($p>0.05$); the prevalence rate of complications in the observation group was significantly lower than that in control group ($p<0.05$). No significant differences in the median survival period and the survival rate at 1 year, 2 years and 3 years after surgery were found between the two groups ($p>0.05$).

CONCLUSIONS: The outcomes of total laparoscopy in the treatment of CRCLM are not inferior to open surgery.

Key Words:
Total laparoscopic surgery, Colorectal cancer liver metastasis, Surgery completion rate, Complication, Median survival period.

Introduction

Liver metastasis is the most common metastasis type of colorectal cancer. Liver metastasis is observed in 25% of the patients with colorectal cancer when diagnosed, and up to 50% of the patients will have liver metastasis during the whole course of colorectal cancer[1]. The median survival time of the patients with colorectal cancer and liver metastasis (CRCLM) is only 6.9 months with surgical resection, and 5-year survival rate is 0. The median survival period of patients with surgical resection is up to 35 months, and 5-year survival rate is 35 to 58%[2]. At present, the surgical modes include staging operation, one stage operation, "Liver First Approach" and so on[3], in which the laparoscopic resection of colorectal cancer is relatively mature and widely applied[4]. However, the high risk of laparoscopic hepatectomy or liver lobectomy limits the application of total laparoscopic resection in the resection of lesions[5]. It has been demonstrated that the simultaneous surgery completion under the total laparoscopy has advantages over the staging and joint open surgery in reducing the perioperative complications and improving the survival prognosis[6]. In this study, we summarized our case load in total laparoscopic treatment.

Patients and Methods

Patients

CRCLM patients without contraindications were consecutively selected from January 2012 to January 2014 in our hospital. Inclusion criteria: (1) patients without obstruction, primary lesion and liver metastasis that affect RO resection; (2) patients with liver function: level A, residual liver volume: greater than 50%; (3) patients without lung, brain and bone metastasis. ASA rates were divided into Level 1 and 2. Patients without complete follow-up data or failed to finish follow-up visit were excluded. This study has been approved by the Ethics Committee of our hospital and all the patients signed informed consent. 40 patients received total laparoscopic

Corresponding Author: Kelong Tao, MD; e-mail: yemphon@aliyun.com
Feng Tao, MD; e-mail: tfzjsx@163.com

surgery as observation group. At the same time, 40 cases underwent laparoscopic resection of colorectal cancer and hepatic resection as control group. In observation group, there were 26 males and 14 females and the age ranged from 48 to 76 years with an average of 62.5±13.7 years. There were 22 cases with primary lesion located in the sigmoid colon, 13 cases in rectum, 4 cases in right semi-colon and 1 case in left semi-colon. There were 1 to 5 primary lesions observed in the patients, with the mean size of 2.2±1.3 cm. The maximum diameter of primary lesion was 1.5-5.6 cm with an average of 3.3±1.4 cm. There were 10 cases of left liver lobe metastasis and 30 cases of right liver lobe metastasis. There were 1 to 3 metastatic lesions with the mean value of 1.5±0.6 cm, the maximum diameter of metastatic lesion was 0.5-3.7 cm with an average of 2.0±0.6 cm. In the control group, there were 27 males and 13 females, and the age ranged from 46 to 77 years with an average of 62.3±12.5 years. There were 20 cases with the primary lesion located in the sigmoid colon, 14 cases in rectum, 3 cases in right semi-colon and 3 cases in left semi-colon; there were 1 to 4 primary semi-colons with the mean size of (2.0±1.6) cm. The maximum diameter of primary lesion was 1.0-5.5 cm with an average of 3.2±1.5 cm; there were 8 cases of left liver lobe metastasis, and 32 cases of right liver lobe metastasis. There were 1-4 metastatic lesions observed in the patients with the mean size of 1.8±0.7 cm, the maximum diameter of metastatic lesion was 1.0-3.5 cm with an average of 2.2±0.7 cm. No significant differences were found in baseline data between the two groups.

Surgical Methods

All patients in the two groups received the standard chemotherapy, biological and targeted treatment before and after surgery. For laparoscopic resection of colorectal cancer, the patients were allowed to lie down in horizontal position, and 15 mmHg of CO_2 pneumoperitoneum was maintained on the navel. Laparoscopic examination was performed to find the tumor location and to make sure that there were no distant metastasis sites. Puncture sites were selected according to the tumor sites. (1) The right semi-colon resection: the right arteries and veins of the colon, the ileocolic arteries and veins and the branches of the arteries and veins in the colon were separately isolated, a vascular clamp was used to clip the blood vessels and blood vessels were then cut. Colon mesentery was separated and placed about 5 cm under the lower edge of tumor from the mesocolon along the distal direction, one 6 cm-long incision was made in the abdominal wall and the liver metastasis specimen, which was loaded in the specimen bags, was firstly taken and then the intestinal canal dissociated well out of the incision, was pulled. The intestinal canal was cut respectively at 10 cm away from fat tumor proximal end and at 10 cm away from the distal end; then, end-to-end anastomosis was conducted. (2) Dixon surgery: rectum was horizontally cut at least 2 cm away from the edge of tumor and a 6 cm-long incision was made above the pubic symphysis. The liver metastasis cancer specimen was removed, the dissociated intestinal canal was dragged outside out of the incision site and the intestinal canal was cut. The sigmoid colon was cut 10 cm away from tumor. A circular stapler drill was inserted, and intestinal anastomosis through the anus was performed. (3) Miles surgery: the descending mesocolon was cut along the paracolic sulci. Colon was dislocated upward to the middle site of the descending colon middle section and then downward to the pelvic cavity rectum bladder excavation, arteries and veins were separated and cut under the mesenterium. Posterior wall of the rectum was bluntly dissected up to coccyx apex levator ani plane. The upper part of sigmoid colon was horizontally cut; inferior rectal artery was ligated, the link between the rectum and the basin tissue was cut off and the specimen was removed; perineal incision was sutured and closed. An orificium fistula was made at 1/3 of junction of the middle and inner parts of the left anterior superior spine and the umbilical connection line. The laparoscopic resection of liver metastatic lesion was performed by adding operation hole according to the surgery, which was generally established at right side of 2 cm under xiphoid process. (1) Left liver lateral lobe (liver section II and III) resection: the ultrasound knife was used to cut off the left liver coronary ligament and the deltoid ligament and separate them from the left lateral lobe; an ultrasonic knife was used to cut the liver capsule at 1 cm away from the falciform ligament, the liver parenchyma was separated from bottom to up and from deep to shadow. The “pedicles” in liver section II and III were separated from the place where the ligamentum teres hepatis was entered into the liver and blood vessels was clipped and cut. Subsequently, the liver parenchyma was cut and separated to the second porta hepatis direction, the

Figure 1. Schematic diagram for the resection via total laparoscopy (***A,*** the sigmoid colon tumor with a distance of 18 cm from the anus, with a 2 cm-long metastatic lesion on the left liver; ***B,*** a resected sigmoid colon cancer and separated blood vessel under the laparoscope; ***C,*** the left liver metastatic lesion cut under the laparoscope).

thinner canal was cut and closed with ultrasound knife and electrocoagulation, while the thicker ones were clipped with vascular clamp and cut. The left hepatic vein trunk was dissected out of the liver, and cut at the bottom. Finally, the left lateral lobe of liver was removed and the liver specimens were placed into the bag and temporarily placed on the left upper abdomen. (2) Right liver section V and VI (or signal section V or VI) resection: the gallbladder was cut first and the liver parenchyma was separated with ultrasound knife at the partial right side of the gallbladder fossa; the "pedicle" was dissected and separated in the liver section V for ligation and cutting. Then, the "pedicle" was dissected in the liver section VI for ligation and cutting if necessary. The liver parenchyma was separated according to the hepatic ischemia line showed on the liver surface, and section V and VI (or section V) was cut. (3) Non-anatomical liver resection: with the assistance of intra-operative orthophoria or intraoperative ultrasound assisted positioning, liver cutting line was made at 2 cm away from the tumor edge and liver metastatic lesion was separated and cut along the marking line.

Observation Indicators

The follow-up visit was carried out until January 2016 with the mean duration of 3 years. The differences in the operative time, blood loss, surgery completion rate, complication prevalence rate, drainage tube retention time, anal exhaust recovery time, median survival period and survival rate were compared between the two groups.

Statistical Analysis

SPSS20.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for data analysis. Measurement data were expressed as mean ± standard deviation and *t*-test was used for the comparisons between the two groups. The count data were expressed as cases or the percentage and the (corrected) X^2-test was used for comparison between the two groups. The survival analysis was carried out with Kaplan-Meier (KM) analysis and tested by Log Rank test. $p<0.05$ was considered to be statistically significant.

Results

Comparisons of the Operation Time, Blood Losses, Drainage Tube Retention Time and Anal Exhaust Recovery Time

No significant difference in operation time was found between the two groups ($p>0.05$). The blood loss, drainage tube retention time, and anal exhaust recovery time in observation group were significantly less than those in control group ($p<0.05$, Table I).

Comparisons of Surgery Completion Rate and Complication Prevalence Rate

In the control group, there was 1 case of severe bleeding due to liver metastasis rupture (more than 2000 ml) and 1 case of injury on the portal vein, and a total of 38 cases completed the surgery. In observation group, there were 2 cases of insufficiently exposed visual field, 2 cases of liver metastatic lesions that could not be cut completely and 1 case of severe bleeding due to damage to the portal vein, and a total of 35 cases completed the surgery. No significant difference in surgery completion rate was found between the two groups ($p>0.05$). The prevalence rate of complications in the observation group was significantly lower than that in control group ($p<0.05$, Table II).

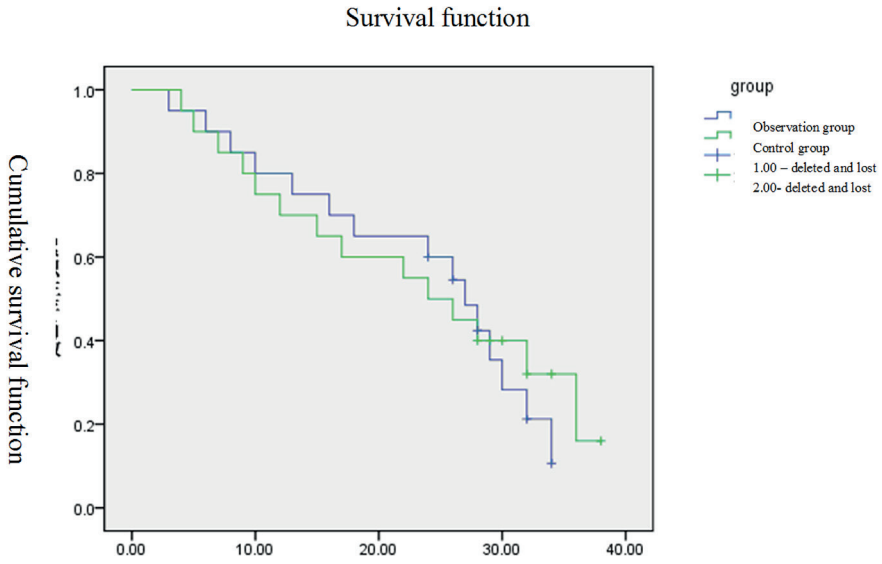

Figure 2. Analysis on median survival period via K-M method.

Table I. Comparison of operative times, blood losses, drainage tube indwelling times and anal exhaust recovery times.

Group category	Operative time (h)	Blood loss (ml)	Drainage tube indwelling time (d)	Anal exhaust recovery time (d)
Control group	2.5±0.6	562.4±52.9	20.6±3.7	3.7±0.5
Observation group	2.7±0.5	237.8±34.6	14.2±3.3	2.6±0.7
t	0.632	6.348	7.231	6.954
p	0.548	0.037	0.019	0.030

Compared to the data before treatment, $p<0.05$.

Comparison of Median Survival Period and Survival Rate

No significant differences in the median survival period and the survival rate at 1 year, 2 years and 3 years after surgery were found between the two groups ($p>0.05$, Table III and Figure 2).

Discussion

There are not many physicians with experience in both laparoscope and open half-liver resection, and multidisciplinary surgery has usually been applied; in other words, the joint surgery completed by more than one specialist physician also has higher requirements for the overall level of a hospital's general surgery[7]. With the application of new adjuvant treatment and biological treatment, the proportion of patients applicable for phase-I joint surgery has been gradually increased. Due to the definite safety of surgery, phase-I laparoscopic surgery will bring smaller trauma, fewer complications and better prognosis[8]. In a previous work, 11 CRCLM patients with phase-I colorectal cancer and liver metastasis received resection under total laparoscopy. In that study, there were many advantages, such as less pain, quicker recovery and shorter hospital stay, compared with the traditional laparotomy[9]. It has been showed that the risk of recurrence and distant metastasis would be increased with blood transfusion in colorectal cancer surgery. Laparoscope can reduce the probability of intraoperative blood infusion, thereby reducing the risk of recurrence and distant metastasis to some extent[10]. It has also confirmed that the total laparoscopy, which will not increase the prevalence rates of postoperative complications, is safe and feasible[11]. A controversial point for the

Table II. Comparison of the surgery completion rates and complication incidence rates [cases (%)].

Group category	Case number	Surgery completion RATE	Infection	Gas embolism	Intestinal fistula	Bile leakage	Others	Total incide rate
Control group	40	38 (95.0)	3	1	4	3	2	13 (32.5)
Observation group	40	35 (87.5)	1	1	2	1	0	5 (12.5)
χ^2		0.626						4.588
p		0.429						0.032

Table III. Comparison of median survival periods and survival rates.

Group category	Case number	Median survival period (month)	One year's survival rate [rate(%)]	Two years' survival rate [rate (%)]	Three years' survival rate [rate (%)]
Control group	40	27.0±2.6	32 (80.0)	27 (67.5)	20 (50.0)
Observation group	40	24.0±4.5	33 (82.5)	26 (65.0)	19 (47.5)
t (χ^2)		0.146	0.082	0.056	0.050
p		0.702	0.775	0.813	0.823

total laparoscopy in the treatment of patients with phase IV tumor is the tumor implantation rate of the incision[12]. In the study, a small incision was opened after the pneumoperitoneum was completely eliminated and the peritoneal layer was attached to the skin to protect the incision on the skin; then, the specimen bag was cut at the bottom and placed on the incision. Subsequently, a clinical specimen was withdrawn out of the incision through the specimen bag, and the digestive tract was reconstructed, followed by repeated washing with distilled water. A recent meta-analysis showed that there were no significant differences in survival rate and survival time within 1 year, 3 years and 5 years in total laparoscopy group. The possible explanations are the small sample size and the poor prognosis of patients with advanced colorectal cancer and liver metastases, which lead to a low survival rate[13]. Colorectal cancer at Duke IV phase is a contraindication of surgical surgery, but as long as the cardiopulmonary function of the patient is normal, the sufficient volume of liver residual primary lesion and metastases lesion can guarantee RO resection[14]. The preoperative multidisciplinary discussion and neoadjuvant treatment application make un-resectable parts of tumors resectable. There are mainly two liver resection orders and surgical modes. The first one is to dissociate the colorectal well without cutting it, remove the liver metastasis tumor and load it into the special bag, make a small incision in the lower abdomen, remove the specimen and make intestinal resection anastomosis. The other one is to firstly remove the liver metastasis cancer and re-resect colorectal cancer. Both orders were feasible, but the preferred one is the metastatic lesion preferential resection[15] due to the difficulties in the transfer of metastatic lesion resection, restriction of primary lesion resection, reduction of intestinal fistula, etc. The liver resection methods include anatomical and non-anatomical resection, and it is believed that the reason is related to the metastatic lesion site, diameter and size[16]. The determination of indications of liver laparoscopy should be based on the surgeon's liver resection technique, spleen tumor size, location, quantity and the possibility of RO resection. The intraoperative ultrasound can not only detect the size of the tumor, but also find new lesions[17,18]. It's believed that devices of laparoscopy may affect the surgeon's judgment on the tumor texture, especially when the metastatic lesion is in the deep liver, suggesting that RO resection should be performed during the surgery[19]. Based on the results of our work, the surgery time and surgical completion rates showed no significant differences between the two groups. In observation group, the blood loss, drainage tube retention time, anus exhaust recovery time and complication prevalence rate were significantly improved compared with those

in control group. The differences in survival rates in the median survival period and within 1 year, 2 years and 3 years between the two groups were not statistically significant.

Conclusions

The treatment effect of total laparoscopy on CRCLM is not inferior to open surgery.

Conflict of interest

The authors declare no conflicts of interest.

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