

Long-term outcome of laparoscopic-assisted right-hemicolectomy with D3 lymphadenectomy versus open surgery for colon carcinoma

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Abstract

Purpose To investigate the applicability, safety, short-term and long-term outcomes of laparoscopic surgery in the treatment of right-sided colon carcinomas with D3 lymphadenectomy.

Methods Between June 2003 and September 2010, 324 patients with right-sided colon carcinoma underwent surgical treatment in the same hospital, 177 cases were treated by laparoscopic surgery (LRH group) and 147 cases by open surgery (ORH group). We performed a retrospective analysis of the differences between the two groups in terms of the clinical data.

Results There were no significant differences between the two groups in the demographic data; however, the recovery time was significantly shorter in the LRH group, the number of overall lymph nodes harvested and principle lymph nodes harvested in the LRH group was significantly higher than in the ORH group, the incidence of

postoperative complications was 12.99 % in the LRH group and 22.45 % in the ORH group ($P < 0.05$), and the recurrence rate in the LRH group was lower than that in the ORH group, although the difference was not significant (15.25 vs 19.73 %). The cumulative overall survival for all stages at 1, 3 and 5 years in the LRH group (97.18, 83.73 and 70.37 %) were not significantly different compared to those in the ORH group (94.56, 77.84 and 66.97 %).

Conclusions Laparoscopic-assisted right hemicolectomy with D3 lymphadenectomy for colon carcinomas is safe and effective, while it is also superior to open surgery regarding the short-term outcomes, and the long-term outcomes are similar to those of open surgery.

Keywords Laparoscopic · Colon carcinoma · D3 lymphadenectomy

Introduction

Laparoscopic-assisted colectomy for colon cancer was first reported by Jacobs [1] in 1991, and it has become an increasingly popular surgical treatment for colorectal cancer in recent years. However, the development of laparoscopic-assisted radical right-hemicolectomy (LRH) is harder than laparoscopic-assisted surgery for cancers in the left hemicolon and rectum because of the complexity of the anatomy, wider range of surgical resection, and the special difficulty in achieving D3 lymphadenectomy. D3 lymphadenectomy has been proven to be a feasible and safe procedure for curable right-sided colon carcinomas [2]. However, few reports have examined the feasibility and safety of LRH with D3 lymphadenectomy. This study retrospectively analyzed the clinical data of 324 cases who underwent LRH with D3 lymphadenectomy or traditional

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open surgery, investigating the applicability, safety, short-term outcome and long-term outcome of laparoscopic surgery in the treatment of right-sided colon carcinomas with D3 lymphadenectomy.

Patients and methods

Patients

A total of 324 patients with colon carcinoma underwent LRH or open surgery at Shanghai Ruijin Hospital, China from June 2003 and September 2010. There were 177 patients who were included in the laparoscopic group (LRH group) and 147 cases in the open surgery group (ORH group). The surgical approach was selected by patients after being informed about the potential risks and benefits of both open surgery and laparoscopic surgery. All the patients underwent preoperative total colonoscopy, carcinoma biomarker testing, abdominal ultrasound and chest X-rays. The resected specimens were confirmed to be malignant by a preoperative biopsy or postoperative pathological diagnosis. We excluded the cases with the following criteria: patients with benign tumors, patients with TNM stage IV tumors, patients who underwent emergency surgery (due to obstruction or perforation), patients with serious organs dysfunction and pregnant patients. Patients with stage III or high-risk stage II tumors were advised to receive postoperative adjuvant chemotherapy.

Surgical techniques

Before surgery, all patients received bowel preparation (polyethylene glycol-electrolyte powder and oral gentamicin, combined with metronidazole). All the procedures strictly followed the radical principles of oncology, including en bloc resection, a no-touch technique, wound protection, adequate margins and complete lymphadenectomy. Extended D3 lymphadenectomy was performed using the medial to lateral (MtL) approach in LRH [2, 3]. The definition of lymph node mapping was grouped according to Japanese Society for Cancer of the Colon and Rectum [4]. The operations were performed by the same surgical team with extensive experience in laparoscopic-assisted gastrointestinal surgery. The surgeons performed several hundred laparoscopic surgeries per year.

The surgical procedure for D3 LRH was as follows: after placing the trocars, the viscera in the abdominal cavity were explored, and the tumor was located; a grasper was used gently, but with enough tension to pull the cecum (ileo-cecal junction) laterally in order to expose the ileocolic vessels' pedicle. Then, the mesentery

was opened at the projection of the ileocolic vessels, the vessel pedicle was isolated, and the lymph nodes extending to the left side of the superior mesenteric vein (SMV) and ileocolic artery and vein (ICA/ICV) were cut at their roots. Subsequently, dissections were made along the superior mesenteric vein to expose the gastrocolic trunk (the right colic vessels were often absent; if present, they were cut at their roots) and it was cut at its colic branch, retaining the gastric and pancreatic branches. The middle colic artery was then uncovered, and its right branch was cut. The middle colic vein was cut at its root to remove the lymph nodes around the vessels. Then, the lymph nodes along the superior mesenteric vessels were removed completely. A dissection was performed to separate the Toldt's fascia (posterior layer of mesocolon) from the Gerota fascia (prerenal fascia), exposing and protecting the descending part of the duodenum, the head of the pancreas, and the right gonadal vessels and ureter, followed by the dissections of the gastrocolic ligament, right side of the greater omentum and lateral peritoneum of the ascending colon. After detaching the hepatic flexure of the colon and ileocecum, the specimen was extracted from a small incision and a stapled side-to-side anastomosis was performed. A drainage tube was finally placed at the right paracolic sulcus.

Parameters

The demographic data (age, sex, TNM stage and pathological type), surgical outcome (length of operation, estimated blood loss and conversion rate in the LRH group), postoperative recovery outcome (time to first flatus, time to liquid diet, days of hospitalization and postoperative complication(s)), characterization of specimens (length, number of lymph nodes (including paracolic nodes, intermediate nodes and principle nodes)), and follow-up outcome (morbidity and mortality rates, local recurrence rate and metastasis rate and cumulative overall survival (OS)) were all examined. The pathological data are shown according to the AJCC colon and rectum cancer staging (7th edition).

Statistical analysis

The statistical analyses were performed using the SPSS software program (Statistical Package for Social Sciences, version 11.0). The measured data were presented as the mean \pm SD and analyzed by the Mann–Whitney *U* test. The numerical data were presented as ratios and were analyzed by the Chi-square test or Wilcoxon rank-sum test. The survival rate was estimated by the Kaplan–Meier method and the log-rank test. $P < 0.05$ was considered to be statistically significant.

Results

There were no significant differences between the two groups in the age (20–90 years in the ORH group, 43–84 in the LRH group), sex, TNM stage, pathological type, grade of differentiation or postoperative adjuvant chemotherapy. The demographic data are shown in Table 1. In the ORH group, the “others” column for the pathological type included two cases of carcinoid tumors.

The mean length of the operation in the LRH group (133 ± 36 min) was significantly longer than that of the ORH group (110 ± 41 min) ($P < 0.05$). The blood loss in the LRH group was significantly lower than that in the ORH group, with values of 94 ± 34 ml and 178 ± 79 ml, respectively, and the difference was significant ($P < 0.05$).

The outcomes with regard to the time to flatus, liquid diet, early ambulation and length of hospitalization (in days) in the ORH group were 3.6 ± 0.6, 5.7 ± 0.8, 6.0 ± 0.5 and 16.9 ± 4.3, respectively, while those in the LRH group were 2.1 ± 0.7, 3.2 ± 0.5, 3.6 ± 0.3 and 10.4 ± 2.7 respectively, and all were significantly different between the groups ($P < 0.01$, Table 2).

Table 1 Demographic data of the ORH and LRH groups, n (%)

	ORH, $n = 147$	LRH, $n = 177$	P value
Age (mean ± SD) ^a	65 ± 12	67 ± 12	0.135
Sex ^b			0.177
Male	80 (54.4)	83 (46.9)	
Female	67 (45.6)	94 (53.1)	
TNM stage ^c			0.305
I	20 (13.6)	23 (13.0)	
II	68 (46.3)	96 (54.2)	
III	59 (40.1)	58 (32.8)	
Pathological type ^b			0.053
Adenocarcinoma	129 (87.7)	169 (95.5)	
Mucinous adenocarcinoma	12 (8.2)	5 (2.8)	
Signet-ring cell carcinoma	4 (2.7)	3 (1.7)	
Others	2 (1.4)	0 (0)	
Differentiation of adenocarcinoma ^c			0.638
Poor	8 (6.2)	12 (7.1)	
Moderate	103 (79.8)	136 (80.5)	
Well	18 (14.0)	21 (12.4)	
Postoperative adjuvant chemotherapy ^b			0.427
Stage II	11 (16.2)	17 (17.7)	
Stage III	44 (74.6)	48 (82.8)	

^a U test

^b Chi-square test

^c Wilcoxon rank-sum test

Table 2 Comparison of the postoperative recovery and lymph node clearance (mean ± SD)

	ORH, $n = 147$	LRH, $n = 177$	P value
Time to flatus (days)	3.6 ± 0.6	2.1 ± 0.7	<0.01
Time to liquid diet (days)	5.7 ± 0.8	3.2 ± 0.5	<0.01
Early ambulation (days)	6.0 ± 0.5	3.6 ± 0.3	<0.01
Hospitalization (days)	16.9 ± 4.3	10.4 ± 2.7	<0.01
Overall LNs (n)	11.4 ± 4.1	15.2 ± 10.1	<0.01
Paracolic LNs (n)	7.7 ± 3.5	7.1 ± 4.0	0.150
Intermediate LNs (n)	3.1 ± 1.9	4.0 ± 6.3	0.071
Principle LNs (n)	0.6 ± 1.4	4.1 ± 5.1	<0.01

There was no significant difference between the ORH group (21.1 ± 6.9 cm) and the LRH group (19.88 ± 5.3 cm) in the lengths of specimens. The numbers of lymph nodes (LNs) (paracolic LNs, intermediate LNs and principle LNs) harvested in the LRH group were 15.2 ± 10.1, while that in the ORH group were 11.4 ± 4.1, with no significant differences being noted between the groups. However, more principle LNs were harvested in the LRH group than in the ORH group (4.1 ± 5.1 vs 0.6 ± 1.4, $P < 0.01$, Table 2).

None of the patients in this study died due to surgery. Five cases (2.82 %) in the LRH group were converted to open surgery, and three of these five cases required conversion because the tumor had invaded adjacent organs, one was required due to vessel injury and another required conversion for extensive abdominal cavity adhesions due to many previous abdominal surgeries. Four patients (2.36 %) in the LRH group were performed by hand-assisted laparoscopic surgery because of the large size of the tumor (one case) and the presence of abdominal wall adhesions (three cases). Twenty-three patients (12.99 %) developed postoperative complications in the LRH group, while 33 patients (22.45 %) in the ORH group developed complications ($P < 0.05$, Table 3). However, when the details of the complications were examined, only lung infections occurred significantly less often in the LRH group than in the ORH group (1.13 vs 7.48 %, $P < 0.01$, Table 3), while the incidence of other complications between the two groups did not show a significant difference.

The median follow-up time of the surviving patients was 54 (16–93) months for the ORH group and 54 months (15–104) for the LRH group, and the follow-up was ended in December 2011. Among all the patients, 17 cases (9.6 %) were lost in the LRH group, and 12 cases (8.2 %) were lost in the ORH group, with no significant difference between groups. At the end of the follow-up period, a total of 84 patients had died, and no significant difference was found between the two groups (Table 4). Metastasis

Table 3 Comparison of the postoperative complications, *n* (%)

	ORH, <i>n</i> = 147	LRH, <i>n</i> = 177	<i>P</i> value
Wound infection	7 (4.76)	3 (1.69)	0.205
Pulmonary infection	11 (7.48)	2 (1.13)	0.004
Urinary tract infection ^a	1 (0.68)	1 (0.56)	1.000
Urine retention	2 (1.36)	3 (1.69)	0.834
Ileus	5 (3.40)	3 (1.69)	0.531
Anastomotic leakage	6 (4.08)	7 (3.95)	0.954
Lymph leakage	0 (0)	4 (2.26)	0.184
Overall	33 (22.45)	23 (12.99)	0.025

^a Fisher's exact probability test

Table 4 Comparison of the follow-up outcomes, *n* (%)

	ORH, <i>n</i> = 147	LRH, <i>n</i> = 177	<i>P</i> value
Overall mortality	40 (27.21)	44 (24.86)	0.631
Local recurrence	3 (2.04)	5 (2.82)	0.926
Metastasis	25 (17.01)	21 (11.86)	0.187
Liver	10 (6.80)	9 (5.08)	0.512
Lung	6 (4.08)	5 (2.82)	0.754
Peritoneum	7 (4.76)	4 (2.26)	0.352
Other	2 (1.36)	3 (1.69)	0.834
Local recurrence + metastasis	3 (2.04)	2 (1.13)	0.834
Port-site/wound metastasis	1 (0.68)	1 (0.56)	1.000
Overall recurrence	29 (19.73)	27 (15.25)	0.289

occurred in 21 cases (11.86 %) in the LRH group, and in 25 cases (17.01 %) in the ORH group, again with no significant difference noted between the groups. In addition, one case in each group suffered port-site/wound metastasis. No difference was found between the two groups in terms of the local recurrence (five cases in the LRH group and three cases in the ORH group). The three patients with local recurrence in the ORH group have also developed metastasis, while two patients in the LRH group have suffered from both local recurrence and metastasis.

The cumulative overall survival probability for all stages at 12, 36, 60 and 75 months in the LRH group were 97.18, 83.73, 70.37 and 66.61 %, respectively, while the values in the ORH group were 94.56, 77.84, 66.97 and 62.10 %, respectively, with no significant differences being detectable between the groups ($P = 0.407$, Fig. 1a). In the cases with stage I and II tumors, the 5-year OS was 83.27 % in the ORH group and 75.09 % in the LRH group, which was not significantly different ($P = 0.477$, Fig. 1b). There was also no significant difference between the ORH group (44.81 %) and LRH group (60.94 %) in the 5-year OS of patients with stage III tumors ($P = 0.142$, Fig. 1c).

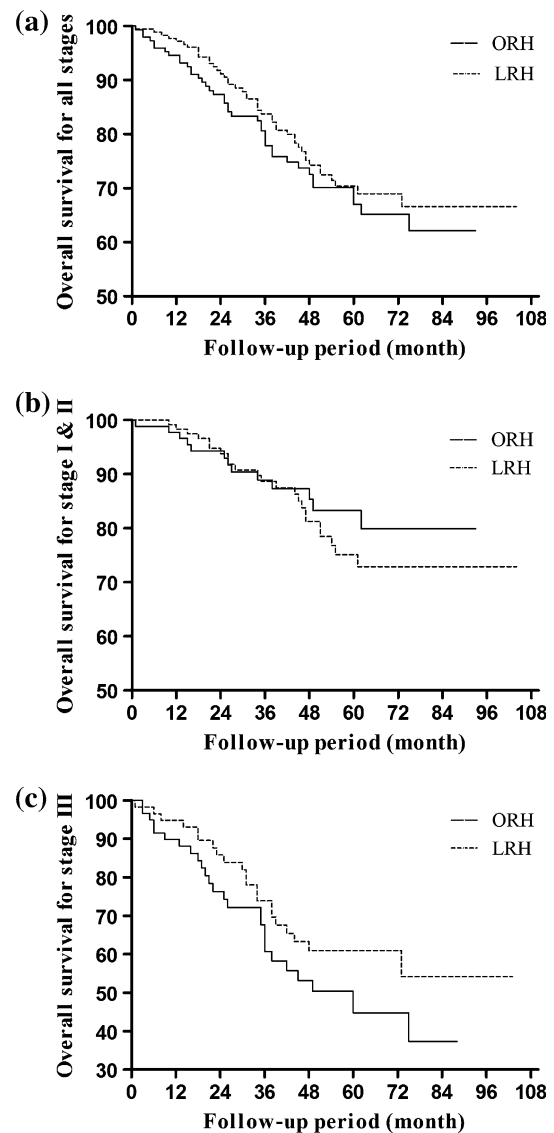


Fig. 1 The OS curves of the cases examined in this study. **a** The OS for all stages; **b** the OS for stage I and II patients; **c** the OS for stage III patients

Discussion

The safety and more rapid postoperative recovery associated with laparoscopic-assisted surgery for colorectal carcinoma have been widely confirmed [5–7]. However, there is still controversy about the long-term outcomes of laparoscopic-assisted colorectal surgery, especially about whether the laparoscopic-assisted surgery has an advantage over open surgery for the treatment of right-hemicolon carcinoma. Moreover, the role of extended lymph node dissection for colorectal carcinoma has been in dispute for years, with many Asian surgeons believing that extended lymphadenectomy may lead to a survival benefit, while Western surgeons think it may result in additional morbidity [8], and the related articles have been sporadic. In

recent years, the technical efficiency and feasibility of laparoscopic D3 lymphadenectomy by the MtL approach for right-hemicolon carcinoma have greatly progressed (with a steep learning curve) in our clinical center. We designed the present study to compare the safety, curative effect and oncological benefits of laparoscopic D3 lymphadenectomy for right-hemicolon carcinoma over the open procedure.

With the development of surgical instruments and techniques, a recent meta-analysis reported that the length of laparoscopic colorectal surgery was similar to that of open surgery [9]. However, as the present study showed, the length of a laparoscopic operation for right-sided colon carcinoma was much longer than that for open surgery [10, 11]; likely due to the complexity of the anatomy, wider range of surgical resection and D3 lymphadenectomy in the LRH group.

D3 lymphadenectomy requires the removal of mesenteric lymph nodes along the SMV/SMA [4]. Normally, the SMV is on the right side of the SMA, so D3 lymphadenectomy requires the division of the ICA and right colic artery (RCA) at the left side of the SMV [12]. However, the ICA and RCA have many patterns of crossing the SMV both anteriorly and posteriorly [13]. On average, 25 % of the length of the ICA and 50 % of the length of the RCA cross over the SMV. It is therefore sometimes difficult to completely expose the surgical trunk of the SMV, especially when the patient is obese. Therefore, if the ICA and RCA are cut at the right side of the SMV, 3.2–5.8 % of the positive lymph nodes along the SMV/SMA (principle nodes) are left behind [14]. The number of lymph nodes harvested is influenced by the extent of surgical resection and pathological techniques, and examining fewer than 12 lymph nodes could lead to downgrading. A few studies have reported that “fat-clearing” (pathological techniques) might increase the number of lymph nodes examined in specimens, so a greater extent of lymphadenectomy in surgical resection represents an alternative approach to increase the number of nodes harvested.

Although the optimum surgical procedure for colon carcinoma is still being debated, it has been reported that tumors resected with an intact mesocolon are associated with a better 5-year OS compared to patients with mesocolon defects [15]. Dr. Hohenberger [16] first proposed the concept of complete mesocolic excision (CME) in 2009, which was translated to colon carcinoma surgery according to the concept of TME for rectal carcinoma. CME with central vascular ligation (CVL) has been applied by many European centers for colon carcinoma. The surgical principles of D3 surgery are similar with CME with CVL, which emphasize maximizing the dissection of regional lymph nodes from the origin of supply vessels, the maintenance of embryonic anatomical surgical plains, and also keeping the intact resection of these planes. In the present

study, the D3 LRH also followed the principles of CME. Furthermore, the broader view in laparoscopic surgery was more conducive to a meticulous operation and keeping the intact planes. A previous study reported that no difference was found between D3 LRH and D3 open surgery in terms of the number of harvested LNs [17]. Based on our present results, the number of overall LNs and principle LNs harvested in the LRH group was higher than that in the ORH group. The wider range of surgical resection in D3 surgery might have contributed to this finding.

As many other papers have reported [5–7], this study also showed a more rapid postoperative recovery in the LRH group compared to the ORH group. This implied that LRH with anastomosis by a transverse incision could cause more postoperative pain and counteract the advantages over open surgery in terms of the recovery [18]. In this study, we applied a vertical incision to avoid cutting off the muscle of the abdominal wall, and finely adjusted the site of the incision according to the location of the tumor and/or the body type of the patients.

In the present study, five patients (2.82 %) in the LRH group were converted to open surgery, and this conversion rate was slightly lower than the reported 4.7–8.1 % [5, 19]. The reasons for conversion were most often that the tumor had invaded adjacent tissues, or that there were abdominal adhesions. It was demonstrated that conversion was associated with poor outcomes and increased complications, and the postoperative ileus rate in conversion cases was higher than that in open surgery cases [10]. Therefore, it is important to improve the safety of surgery by careful preoperative evaluation, by screening patients and by better mastering the occasion of conversion. There were no differences between the ORH and LRH groups in the overall postoperative complication rates in the present study and another study [20], suggesting that D3 laparoscopic procedures do not increase the morbidity. However, the lung infection rate in the LRH group was significantly lower than that in the ORH group, implying potential benefits for patients, especially for older patients, from laparoscopic surgery [21].

The recurrence rate is a crucial indication to evaluate the long-term outcomes of surgery. In the early period after the introduction of laparoscopic surgery for colorectal cancer, the oncological safety of laparoscopic surgery was doubted because of the development of port-site metastasis. Laparoscopic surgery for right-sided colon carcinoma strictly follows the oncological surgical principles. Furthermore, the laparoscopic MtL approach for D3 lymphadenectomy better complies with the “no touch” principle of oncology [2]. However, reports about the recurrence rate after D3 surgery are scarce. In this study, the recurrence rate in the LRH group was a little lower than that in the ORH group (15.25 vs 19.73 %), although the difference was not

significant. Based on the present results and those of three randomized clinical trials (RCTs), the COLOR [20], COST [22] and CLASSIC [23], we consider that laparoscopic D3 surgery for right-sided colon carcinomas is comparable to that of open surgery in terms of the oncological results.

With regard to survival, the impact of laparoscopic surgery has been controversial. In the present study, the 1-, 3- and 5-year OS of all cases were higher in the LRH group than in the ORH group, and metastasis also occurred in fewer patients in the LRH group than in the ORH group, although the differences were not significant. However, there have been few studies focusing on LRH. One retrospective study by Nakamura et al. [24] showed that no difference between laparoscopic and open surgery for right-sided colon carcinoma was observed in the OS (95.8 vs 95.0 % for stage I & II, 73.6 vs 64.1 % for stage III), and this finding was comparable with our results. Although Lacy et al. [25] and Kitano et al. [26] have reported the advantages in the 5-year OS for laparoscopic surgery over open surgery for the treatment of stages II and III colon carcinoma, respectively; there were some limitations to these studies, such as unequal administration of postoperative chemotherapy. Moreover, the present study was also an uncontrolled study, so the outcomes might have been influenced by a selection bias or differences in postoperative chemotherapy, cellular immunity and surgical stress. The results of the COLOR, COST and CLASSIC RCTs suggested that the disease-free survival (DFS) and OS were similar between laparoscopic surgery and open surgery. As no other long-term outcomes of laparoscopic D3 surgery for colon carcinoma have been reported, we think that further randomized controlled trials with more cases will be necessary to verify whether laparoscopic D3 surgery can provide additional benefits for patients with colon carcinoma.

The concept of CME was also related to the long-term results. The feasibility of CME in open surgery has been confirmed [16, 27], and the advantages of CME, as well as D3 surgery, for colon cancer over traditional open surgery in terms of the oncological outcomes have also been proved [28]. One study reported a 14.3 % rate of positive D3 LNs [8], and we consider that extended D3 lymphadenectomy may provide a better chance to achieve R0 resection for these colon cancers, especially for stage II/III tumors, which might partially explain the superiority of CME in the long-term outcomes. West et al. [29] reported a 5-year cancer-related survival of 89 % with CME. However, the papers about CME applied in laparoscopic surgery have been limited. A study from our surgical center made a preliminary exploration of the feasibility of CME by laparoscopy for right-sided colon carcinomas [30], while the present study focused on D3 lymphadenectomy has provided a potential basis for the safety of laparoscopic

CME procedures. However, whether CME or D3 should become the new standard for colon carcinoma surgery will require further research.

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Conflict of interest Drs. Ding-Pei Han, Ai-Guo Lu, Hao Feng, Pu-Xiong-Zhi Wang, Qi-Feng Cao, Ya-Ping Zong, Bo Feng, Min-Hua Zheng have no conflicts of interest.

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