# ORIGINAL ARTICLE

# The short- and long-term outcomes of laparoscopic versus open surgery for colorectal cancer: a meta-analysis

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#### Abstract

*Purpose* The aim of the study was to compare short- and long-term outcomes of laparoscopic surgery and conventional open surgery for colorectal cancer.

*Methods* Published randomized controlled trial (RCT) reports of laparoscopic surgery and open surgery for colorectal cancer were searched, and short- and long-term factors were extracted to perform meta-analysis.

Results A total of 15 RCT reports (6,557 colorectal cancer patients) were included in this study. Blood loss of laparoscopic surgery was less by 91.06 ml than open surgery (p=0.044). Operation time was longer by 49.34 min (p=0.000). The length of hospital stay was shorter by 2.64 days (p=0.003). Incisional length was shorter by 9.23 cm (p=0.000). Fluid intake was shorter by 0.70 day (p=0.001). Bowel movement was earlier by 0.95 day (p=0.000). Incidence of complications, blood transfusion, and 30 days death were significantly lower in laparoscopic surgery than in open surgery (p=0.011, 0.000, 0.01). But there was no significant difference in lymph nodes (p=0.535) and anastomotic leak (p=0.924). There was also no significant difference in 3 and 5 years overall survival (p=0.298, 0.966), diseasefree survival (p=0.487, 0.356), local recurrence (p=0.270, 0.649), and no difference in 5 years distant recurrence (p=0.838).

*Conclusions* Laparoscopic surgery is a mini-injured approach which can cure colorectal cancer safely and radically, and it is not different from conventional open surgery in long-term effectiveness, so laparoscopic surgery can be tried to widely use in colorectal cancer.

Chun-Li Wang and Gang Qu contributed equally to this work.

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C.-L. Wang e-mail: wangchunli808@126.com **Keywords** Colorectal cancer · Laparoscopy surgery · Open surgery · Meta-analysis

#### Introduction

Colorectal cancer is a common disease which is the fourth reason resulted to patients' death [1]. Since the first laparoscopic colorectal surgery was operated successfully in the year 1991 [2], laparoscopic surgery is widely performed in the colorectal cancer, and the skill is becoming more and more mature. Its' security, feasibility, and short-term curative effect have already been verified [3, 4]. Some randomized controlled trials (RCTs) have gotten the result that laparoscopic colorectal surgery (LCS) had the better short-term outcomes than open colorectal surgery (OCS), for example, less blood loss, better quality life, less pain, the shorter time of return to normal life and shorter length of hospital stay, and so on [5, 6]. But the post-operation recurrence is the most important problem which we should consider. And there are few reports about meta-analysis results of post-operation recurrence between laparoscopic and open surgery, while it is essential firstclass evidence of evidence-based medicine, so several RCTs comparing LCS and OCS's short- and long-term outcomes were selected to have been done meta-analysis. And the factors of 3 and 5 years following up period below were concluded to evaluate the long-term results of LCS.

#### Materials and methods

We looked up many materials about RCTs of colorectal cancer comparing LCS and OCS which were published from January 1991 to June 2013 and searched the major medical databases such as Pubmed, Embase, Ovid, ScienceDirect, Springer, Interscience, and so on. The search terms were used: "laparoscopy surgery," "colorectal cancer," "open surgery," "randomized controlled trial," and so on. Furthermore, we limited our search to those studies that involved a following up period of 3 or 5 years to evaluate the long-term outcomes of LCS. We conducted a meta-analysis for the short and long term. For the short-term analysis, we collected data of the operation time, blood loss, number of patients requiring blood transfusion, number of harvested lymph nodes, time of fluid intake, bowel movement, anastomotic leak, length of hospital stay, length of operation incision, complications, and 30 days death. For the long-term analysis, we used data of the rate of 3 years local recurrence, 3 years overall survival rate, 3 years disease-free survival rate, 5 years overall survival rate, 5 years disease-free survival rate, 5 years local recurrence rate, and 5 years distant recurrence.

#### Statistical analysis

Weighted mean difference (WMD) and odds ratio (OR) were used for the variables analysis of continuous and dichotomous, respectively.  $\chi^2$  test was used to evaluate heterogeneity among the studies, and  $\hat{I}^2$  was used to quantify the inconsistency (there were two models: fixed effect model and random effect model. The fixed effect model was used when the effects were deemed to be homogeneous (p>0.1,  $\hat{I}<50$  %); otherwise, the random effects model was used). And Z test was used to compare the overall difference. The confidence interval (CI) was established at 95 %, and p values of less than 0.05 were considered to indicate statistical significance. Begg's test and Egger's test were performed in order to evaluate the publication bias (in Begg's test p>0.05 and in

 Table 1
 Characteristics of the randomized control trials

Egger's test p>0.05 and 95 % CI includes 1; it is thought that there was no publication bias). Statistical analyses were performed using the stata12.0 (meta module) software.

# Results

At last 15 papers of RCTs that compared LCS and OCS for colorectal cancer [5–20] were selected. The characteristics of each RCT are presented in Table 1. This meta-analysis included 6,557 patients with colorectal cancer in all, of which 3,509 had performed LCS and 3,048 had OCS. The results of the short and long term are shown in Figs. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, and 18, respectively, and the data are presented in Tables 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

#### Short-term outcomes

The blood loss for LCS was significantly less than for OCS, by an average volume of 91.06 ml (WMD=-91.06; 95 % CI=-179.66 to -2.46; p=0.044); six of the 15 RCTs included data of blood loss. Operation time for LCS was significantly longer than for OCS, by 49.34 min (WMD=49.34; 95 % CI=29.57 to -69.12; p=0.000); five of the 15 RCTs included data of operation time. The length of hospital stay for LCS was significantly shorter than for OCS, by 2.64 days (WMD=-2.64; 95 % CI=-4.41 to -0.87; p=0.003); six of the 15 RCTs included data of the length of hospital stay. The incisional length for LCS was significantly shorter than for OCS, by an average of 9.23 cm (WMD=-9.23;

Studies	Year	Reference (n)	Study n	umber	Site	Follow-up (months)	Outcome
			LCS	OCS			
Milsom	1998	29	55	54	Colon and rectum	19 (mean)	Short and long term
Schwandner	1999	56	32	32	Colon and rectum	33 (mean)	Short and long term
Lacy	2002, 2008	30, 31	111	108	Colon	44 (mean)	Short and long term
Leung	2004	15	203	200	Rectosigmoid	40 (median)	Long term
Cost	2004		435	428	Colon	51 (max)	Long term
CLASICC	2005, 2007, 2010, 2012	32, 23, 29, 26	526	268	Colon and rectum	91.8 (mean)	Short and long term
Color	2005	30	627	621	Colon	36 (mean)	Short and long term
ColorII	2013	22	699	345	Rectum	1	Short term
Liang	2006	30	135	134	Left-sided colon	40 (max)	Long term
Park	2009	29	170	374	Rectum	36 (mean)	Short and long term
LAPKONII	2009	24	250	222	Colon		Short term
Braga	2010	21	134	134	Colon	73 (median)	Short and long term
Fujii	2010	36	35	27	Colon	62 (mean)	Short and long term
Jing Gong	2012	27	67	71	Rectum	21 (median)	Short term
Pappas-Gogos	2013	42	30	30	Colon and rectum		Short term

Fig. 1 Lymph node results of forest plot (fixed effect model)





Study			%
ID		WMD (95% CI)	Weight
	_		
Milsom		0.00 (-176.97, 176.97)	10.90
Lacy		-88.00 (-132.02, -43.98)	18.40
<b>↓</b> Liang		-186.00 (-192.10, -179.90	) 19.26
Braga		-81.00 (-130.98, -31.02)	18.16
Fujii	_	-129.00 (-251.85, -6.15)	14.06
Jing Gong	*	-32.20 (-43.99, -20.41)	19.21
<b>Overall</b> (I-squared = 99.1%, p = 0.000)		-91.06 (-179.66, -2.46)	100.00
NOTE: Weights are from random effects an	alysis		
-252	0	252	



Fig. 3 Operation time result of forest plot

Fig. 4 Length of hospital stay result of forest plot







Fig. 6 Bowel movement result of forest plot (fixed effect model)



**Fig. 7** Fluid intake result of forest plot





Fig. 8 Complication result of forest plot

Fig. 9 Blood transfusion result

of forest plot

95 % CI=-13.77 to -4.68; p=0.000); four of the 15 RCTs included data of incisional length. The bowel movement time for LCS was significantly shorter than for OCS, by an average of 0.95 day (WMD=-0.95; 95 % CI=-1.18 to -0.73; p=0.000); three of the 15 RCTs included data of bowel movement. The fluid intake for LCS was significantly

shorter than for OCS, by 0.70 day (WMD=-0.70; 95 % CI= -1.11 to -0.29; p=0.001); four of the 15 RCTs included data of the fluid intake. There were no significant differences in lymph nodes between the LCS group and the OCS group for treatment of the colorectal cancer. The rate of perioperative complications for patients in the LCS group was significantly lower than for those in the OCS group in this analysis of the pooled data for colorectal cancer treatment (OR=0.86; 95 % CI=0.77-0.97; p=0.011). Twelve of the 15 RCTs included data of perioperative complications. The number of blood transfusion in the LCS group was significantly lower than that in the OCS group in this analysis of the pooled data for colorectal cancer treatment (OR=0.46; 95 % CI=0.32-0.65; p=0.000). Three of the 15 RCTs included data of blood transfusion. There were no significant differences in anastomotic leak between the LCS group and the OCS group for the treatment of the colorectal cancer.

The rate of 30 days death in the LCS group was significantly lower than in the OCS group in this analysis of the pooled data for colorectal cancer treatment (OR=0.58; 95 % CI=0.38–0.88; p=0.01). Seven of the 15 RCTs included data of 30 days death.













**Fig. 12** Three-year overall survival result of forest plot

Fig. 13 Three-year disease-free survival result of forest plot











**Fig. 16** Five-year disease-free survival result of forest plot



# **Fig. 17** Five-year local recurrence result of forest plot

# Long-term outcomes

We found no significant differences in the rate of 3 years local recurrence between the surgery groups when we pooled data for the treatment of the colorectal cancer. Our analysis of the 5 years of local and distant recurrence between the LCS group and the OCS group for the treatment of the colorectal cancer indicated no significant difference. There were also no significant differences between the surgery groups for the overall survival in the 3 and 5 years. We also found no significant

differences in the 3- and 5-year disease-free survival rates between patients who underwent LCS and OCS.

### Heterogeneity

In the short-term period, significant heterogeneity was detected among studies with respect to the following six factors: blood loss, the length of hospital stay, operation time, time of fluid intake, the rate of perioperative complications, and the number of blood transfusion. In the long-term period,



Fig. 18 Five-year distant recurrence result of forest plot

**Table 2** Number of lymph nodes compared LCS and OCS (p=0.535) among four studies (n)

Study	LCS			OCS	OCS		
	N1	Mean1	SD1	N2	Mean2	SD2	
Schwandner	32	12.9	5.1	32	13	4.4	
Lacy	111	11.1	7.9	108	11.1	7.4	
Liang	135	15.6	3	134	16	6	
Fujii	35	24.1	13.4	27	25.2	15.3	

**Table 3** Blood loss compared LCS and OCS (p=0.044) among six studies (in milliliters)

Study	LCS			OCS	OCS		
	N1	Mean1	SD1	N2	Mean2	SD2	
Milsom	55	344	222	54	344	626	
Lacy	111	105	99	108	193	212	
Liang	135	54	12	134	240	34	
Braga	134	46	130	134	127	265	
Fujii	35	125	214	27	254	266	
Jing Gong	67	86.9	37.6	71	119.1	32.7	

 Table 4
 Operation time compared LCS and OCS (p=0.000) among five studies (in minutes)

Study	LCS			OCS	OCS		
	N1	Mean1	SD1	N2	Mean2	SD2	
Milsom	55	200	40	54	125	51	
Schwandner	32	281	80	32	209	66	
Lacy	111	142	52	108	118	45	
Liang	135	224.4	44.8	134	184	30.6	
Fujii	35	255	77	27	210	85	

**Table 5** Hospital length of stay compared LCS and OCS (p=0.003)among six studies (in days)

Study	LCS			OCS	OCS		
	Nl	Mean1	SD1	N2	Mean2	SD2	
Schwandner	32	15.3	6.1	32	21.9	18.9	
Lacy	111	5.2	2.1	108	7.9	9.3	
Liang	135	9.0	1.0	134	14.0	2.0	
Color	627	8.2	6.6	621	9.3	7.3	
ColorII	699	11.9	11.8	345	12.1	10.6	
Fujii	35	11.7	8.4	27	16.4	10.3	

**Table 6** Incisional length compared LCS and OCS (p=0.000) among four studies (in centimeters)

Study	LCS			OCS	OCS		
	Nl	Mean1	SD1	N2	Mean2	SD2	
Milsom	55	4.5	1.5	54	22	5	
Liang	135	10.6	1.6	134	18.0	3.1	
Braga	134	5.2	0.8	134	17.4	2.6	
LAPKONII	250	13.4	12	222	13	8.6	

**Table 7** Bowel movement compared LCS and OCS (p=0.000) among three studies (in days)

Study	LCS			OCS		
	Nl	Mean1	SD1	N2	Mean2	SD2
Schwandner	32	4.1	1.7	32	5.1	1.5
Color	627	3.6	1.7	621	4.6	3.0
ColorII	699	2.9	3.8	345	3.7	3.6

Table 8 Fluid intake compared LCS and OCS (p=0.001) during four studies (in days)

Study	LCS			OCS	OCS		
	Nl	Mean1	SD1	N2	Mean2	SD2	
Schwandner	32	3.1	1.2	32	3.6	1.4	
Lacy	111	2.3	1.8	108	3.5	2.8	
Color	627	2.9	1.9	621	3.8	3.4	
ColorII	699	2.6	4.3	345	2.8	3.6	

**Table 9** Number of complication compared LCS and OCS (p=0.011)among 12 studies (n)

Study LCS			OCS	
	NI	Morbidity1	N2	Morbidity2
Milsom	55	8	54	8
Schwandner	32	10	32	10
Lacy	111	14	108	37
Leung	203	40	200	45
Cost	435	92	428	85
CLASICC	526	54	268	27
Color	627	111	621	110
Liang	135	20	134	29
LAPKONII	250	63	222	53
Braga	134	20	134	33
Jing Gong	67	4	61	6
ColorII	694	81	344	49

**Table 10** Number of blood transfusion compared LCS and OCS (p=0.000) among three studies (n)

**Table 14** Three-year disease-free survival compared LCS and OCS (p=0.487) among five studies (n)

Study	LCS		OCS		
	NI	Morbidity1	N2	Morbidity2	
LAPKONII	250	29	222	39	
Braga	134	11	134	20	
Fujii	35	0	27	8	

Study	LCS		OCS	
	N1	Live1	N2	Live2
Cost	435	118	428	117
CLASICC	526	349	268	181
Park	170	132	374	309

**Table 11** Number of 30-day death compared LCS and OCS (p=0.011) among seven studies (n)

Study	LCS		OCS	
	NI	Death1	N2	Death2
Milsom	55	1	54	1
Schwandner	32	0	32	1
Lacy	111	1	108	3
Cost	435	2	428	4
Color	627	6	621	10
Braga	134	16	134	27
ColorII	694	8	344	6

**Table 15** Three-year local recurrence compared LCS and OCS (p=0.270) among five studies (n)

Study	LCS		OCS	
	Nl	Recurrence1	N2	Recurrence2
Schwandner	32	1	32	0
Park	170	6	374	5
CLASICC	526	41	268	19

**Table 12** Number of anastomotic leak compared LCS and OCS (p=0.924) among seven studies (n)

Study	LCS		OCS	
	N1	Morbidity1	N2	Morbidity2
Leung	203	1	200	4
Park	170	8	374	15
LAPKONII	250	8	222	5
Braga	134	4	134	5
Fujii	35	10	27	13
Jing Gong	67	1	71	1
ColorII	694	58	344	25

**Table 16** Five-year overall survival compared LCS and OCS (p=0.966) among five studies (n)

Study	LCS		OCS	
	N1	Survival1	N2	Survival2
Leung	203	154	200	146
cost	435	344	428	359
CLASICC	526	305	268	156
Braga	134	96	134	88
Fujii	35	33	27	25

**Table 13** Three-year overall survival compared LCS and OCS (p=0.298) among five studies (n)

Study	LCS		OCS	
	N1	Livel	N2	Live2
Schwandner	32	30	32	30
Leung	203	167	200	161
CLASICC	526	360	268	179
Braga	134	96	134	88

**Table 17** Five-year disease-free survival compared LCS and OCS (p=0.356) among five studies (n)

Study	LCS		OCS	
	N1	Survival1	N2	Survival2
Leung	203	153	200	157
CLASICC	526	291	268	157
Braga	134	84	134	84
Fujii	35	33	27	24

**Table 18** Five-year local recurrence compared LCS and OCS (p=0.649) among five studies (n)

Study	LCS	LCS		OCS	
	N1	Recurrencel1	N2	Recurrence2	
Lacy	111	7	108	14	
Leung	203	11	200	7	
CLASICC	526	57	268	23	

significant heterogeneity was detected among studies with respect to the following factors: 3 years disease-free survival, 3 years local recurrence, 5 years overall survival, 5 years disease-free survival, and 5 years distant recurrence. Random effect model was used in the above given factors. Fixed effect model was used in the rest factors. Begg's test and Egger's test were performed, respectively. And all factors below passed the tests (p>0.05 and 95 % CI includes 1).

#### Discussion

The biggest advantage of LCS than OCS lies to its minor injury. And many studies concluded that LCS had lower complications, less pain, shorter hospital stay, and less time to return to normal life than ORS in short-term period [9, 21, 22]. But the recurrence is the focus of debate laparoscopic approach and conventional open approach for the treatment of colorectal cancer. Therefore, we examined the results of LCS and compared to those of OCS in short- and long-term periods by a meta-analysis of 15 RCTs.

From the data meta-analysis, it is indicated that in shortterm period, LCS has less blood loss, lower length of hospital stay, lower incisional length, less time bowel movement, lower rate of perioperative complication, lower number of blood transfusion, and lower number of 30 days death than OCS. It fits to the LCS's consistent advantage. LCS is prior obviously to OCS in post-operation recovery. The length of hospital stay and time of bowel movement can be shown. But the operation time of LCS is longer than OCS because laparoscopic approach is more difficult than conventional open approach. And with surgeons' richer and richer experience, the operation time will decrease. LCS is similar to OCS with

Table 19Five-year distant recurrence compared LCS and OCS(p=0.838) among five studies (n)

Study	LCS	LCS		OCS	
	Nl	Recurrence1	N2	Recurrence2	
Lacy	111	7	108	9	
Leung	203	30	200	26	
CLASICC	526	110	268	55	

no significant differences in lymph nodes and anastomotic leak, while the number of lymph nodes is one of the most important factors of prognosis of colorectal cancer patients.

Long-term effectiveness is the basic criterion to evaluate the tumor radical operation. Long-term survival and recurrence are acknowledged standard criterion to detect if it is radical surgery-based disease free. There are no significant differences between LCS and OCS in 3 and 5 years overall survival and disease-free survival. There are also no significant differences in 3 and 5 years local and distant recurrence between two groups. So it can be concluded that there are similar long-term effectiveness between LCS and OCS.

It is considered that the hospital charges of LCS are higher than those of OCS [23, 24]. The use of disposable surgical instruments, the high cost of intraoperative anesthesia, and the higher technical operation requirements made the charges of LCS higher than those of OCS. But YS Choi et al. ever separated charge from cost. Cost encompassed anesthesia, laboratory, radiology, pharmacy, nursing, medical therapy, and consumables charges, so total hospital charges should be evaluated by cost-effectiveness analysis. JS Park et al. also provided that total hospital charges for laparoscopic surgery were higher than those of open surgery only during the early learning period and became similar during the experienced period. So it is hoped the emergence of reusable materials which can reduce the costs and the shortening of the learning period to achieve cost-effective. It is also expected to increase the intensity of insurance of consumables.

In conclusion, this meta-analysis shows that LCS has the advantage of less blood loss, lower length of hospital stay, earlier bowel movement, and lower rate of complications than OCS in the short-term period. And LCS is similar to OCS with no significant differences in the long-term results. LCS can safely cure colorectal cancer; anyway, this article also has shortcomings, due to the lack of relevant data reported on the application condition of LCS. We at least put forward a bold attempt; at the same time, it is also hoped that more scholars and researchers can come together to explore and apply laparoscopic surgery routinely to the treatment of colorectal cancer.

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