RESEARCH ARTICLE

Laparoscopic Versus Open Surgery for Rectal Cancer: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Background and Aim: Laparoscopic and open rectum surgery for rectal cancer remains controversial. This systematic review compared the short-term and long-term efficiency and complications associated with laparoscopic and open resection for rectal cancer. Materials and Methods: We searched PubMed, Embase, Cochrane Library, ISI Web of Knowledge and the China Biology Medicine Database to identify potential randomized controlled trials from their inception to March 31, 2014 without language restriction. Additional articles were identified from searching bibliographies of retrieved articles. Two reviewers independently assessed the full-text articles according to the pre-specified inclusion and exclusion criteria as well as the methodological quality of included trials. The meta-analysis was performed using RevMan 5.2. Results: A total of 16 randomized controlled trials involving 3,045 participants (laparoscopic group, 1,804 cases; open group, 1,241 cases) were reviewed. Laparoscopic surgery was associated with significantly lower intraoperative blood loss, earlier return of bowel movement and reduced length of hospital stay as compared to open surgery, although with increased operative time. It also showed an obvious advantage for minimizing late complications of adhesion-related bowel obstruction. Importantly, there were no significant differences in other postoperative complications, oncological clearance, 3-year and 5-year or 10 year recurrence and survival rates between two procedures. Conclusions: On the basis of this meta-analysis we conclude that laparoscopic surgery has advantages of earlier postoperative recovery, less blood loss and lower rates of adhesion-related bowel obstruction. In addition, oncological outcome is comparable after laparoscopic and open resection for rectal cancer.

Keywords: Laparoscopic surgery - rectum - cancer - systematic review - meta-analysis

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Introduction

Colorectal cancer including rectal cancer is the third and fifth most common cause of cancer deaths in the western world and in the Asian Pacific Rim region respectively (Yang et al., 2004). With an aging population over the next decade and changing lifestyle patterns, a higher colorectal cancer incidence will be translated into (Morrison et al., 2013; Tayyem et al., 2013). In recent years, accumulating evidence indicates that laparoscopic surgery for colon carcinoma is associated with earlier postoperative recovery, lower morbidity and with equivalent long-term outcomes (Bonjer et al., 2007; Kahnamoui et al., 2007; Di et al., 2013). However, these benefits of laparoscopic for rectum cancer were still controversy due to most studies were not randomized controlled trials (Strohlein et al., 2008; da Luz Moreira et al., 2011; Gezen et al., 2012), and few prospective randomized controlled trials (RCTs) or meta-analysis had only short-term (Huang et al., 2011; Xiong et al., 2012). Further more, so far there is no high quality evidence concerning 5-year recurrence and survival rate comparing laparoscopic rectum surgery and open rectum surgery. As a result, the latest NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines for Colon Cancer stated that laparoscopic colectomy has become an option in the surgical management of colon cancer (Benson et al., 2011), but for rectal cancer which said that laparoscopic surgery is preferred in the setting of a clinical trial (Benson et al., 2012). Based on these reasons, we intended to undertake this systematic review to comparing laparoscopic rectum surgery (LRS) and open rectum surgery (ORS) in patients with rectal cancer and to provide high level of evidence for clinical practice.

The aim of this systematic review was to compare the efficacy and safety of laparoscopic and open surgery for

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rectal Cancer, especially to find if the 5-year or 10-year oncological outcomes are comparable.

Materials and Methods

Search methods for identification of RCTs

To identify all relevant RCTs comparing laparoscopic surgery versus open surgery for rectal cancer, two reviewers (Zhang FW and Zhang JX) searched the following electronic databases independently: PubMed, Embase, the Cochrane Library, ISI Web of Knowledge, China Biology Medicine Database from their inception to March 31, 2014 without language restrictions. Additional articles were identified from searching bibliographies of retrieved articles. Two reviewers independently assessed the full-text articles according to the pre-specified inclusion and exclusion criteria as well as the methodological quality of included trials. Searches were carried out using the following medical subject headings (MeSH), free text words and their combinations: colorectal neoplasms, rectal neoplasm, rectum cancer, rectal tumor, rectal adenocarcinoma, laparoscopy, randomized controlled trials.

Inclusion criteria

The following criteria were used to select studies: (1) be an RCT comparing laparoscopic with open surgery in patients with rectal cancer; (2) studies that reported on at least one of the outcome measures mentioned below; (3) clearly documented rectal cancer surgery as either an "anterior resection" (AR) or "abdominoperineal resection" (APR) and described the technique as "laparoscopic" or "open". Studies including patients of any age and sex with rectal cancer were concerned with no limitation on language and publication status. Studies from the same multicentre trial whichever if it reported different outcomes were included, but total sample size was calculated only once.

Exclusion criteria

Studies were excluded if (1) the outcome of interest for the two techniques was not reported or it was impossible to determine it from the published results; (2) they reported either on rectal surgery for benign lesions and inflammatory bowel disease and did not include a distinct group of patients with rectal cancer; (3) included a patient group undergoing transanal endoscopic microsurgery, transanal excision or palliative treatment (not curative surgical intent).

Outcomes of interest

The primary end-points are long-term oncological outcomes including local and distant metastases (3-year and 5-year), port-site/incision recurrence, overall survival (OS) and disease-free survival (DFS).

The secondary end-points as follow: operative outcomes (operating time, estimated blood loss, bladder or urethral lesion), recovery outcomes (time to first bowel movement, time to feeding liquids, time to resume normal diet, time to walk independently, length of hospital stay), early postoperative outcomes [overall mortality, overall morbidity (number of patients who had any complication), hemorrhage, anastomotic leak, wound infection, postoperative bowel obstructions, pulmonary infection, urinary infection, urinary retention, deep vein thrombosis, abscess, sepsis, perianal wound complications (dehiscence or hernia only in the APR subgroup), perianal wound (infection or hematoma only in the APR subgroup], late postoperative outcomes (adhesion-related bowel obstruction, incisional hernia), histopathological oncological outcomes [mean number of lymph nodes harvested, positive circumferential margin (CRM)].

Data Extraction

Two investigators (Zhang FW and Zhang JX) independently reviewed the titles, abstracts, and full texts of retrieved articles to extract study data. Disagreements were resolved by a consensus and, if necessary, by involving an independent third person (Yang KH). The following information was extracted from each trial: (1) characteristics of trial participants; (2) inclusion and exclusion criteria of the trials; (3) type of intervention (AR or APR); (4) type of outcomes interested in; (5) the methodology characteristics of included study. Date of studies from the same multicentre trial and reporting different outcomes were extracted separately, for example, the three studies (Guillou et al., 2005; Jayne et al., 2007; Jayne et al., 2010) all came from the Medical Research Council CLASICC trial, which reported different outcomes of short-term endpoints, 3-year results and 5-year results of conventional versus laparoscopic assisted surgery in patients with colorectal cancer respectively, we extracted date of them respectively, but total sample size was calculated only once.

Assessment of methodological quality

The quality of the RCTs was assessed using the Cochrane Collaboration's tool for assessing risk of bias (Lundh et al., 2008) by two authors (Zhang FW and Zhang JX) independently. The criteria used for quality assessment were sequence generation of allocation, allocation concealment, blinding of outcome assessment, intent-to-treat analysis and patients lost to follow-up. The discrepancies were discussed until an agreement was reached. The quality of included trials was summarized in Table 1.

Statistical analysis

Statistical analysis for categorical variables was performed by using the odds ratio (OR) when the incidence of event is less than 20 percent to the Peto method in order to make the results of meta analysis the most effective and with minimum bias (Liu et al., 2011). In contrast, if the incidence of event is more than 20 percent, the relative risk (RR) and the Mantel-Haenszel method were used.

For continuous variables such as operating time, statistical analysis was performed by using the mean difference (MD) and inverse variance method. Data for continuous outcomes presented as means and range values, the standard deviations were calculated by using Hozo et al. (2005). Data for continuous outcomes expressed

as median and interquartile range, it was transformed in accordance with Liu M's method (Liu et al., 2011). Thus, all continuous data were standardized for analysis.

Subgroup analysis was also performed for the above-mentioned outcomes in patients undergoing anterior resection (AR), abdominoperineal excision (APR) and total mesorectal excision (TME) of the rectum cancers.

The heterogeneity for summary effects was assessed through χ^2 test (α=0.05) and I^2 statistics. A value for I^2 more than 50% was regarded as representing existing heterogeneity. The confidence interval was established at 95%, and p<0.05 was considered significant. When there was no statistics heterogeneity among studies (p>0.05, I^2<50%), we used fixed effect model; if there were (p<0.05, I^2>50%), we would try to find the cause. If there was no clinical/methodological heterogeneity among studies, we changed to random effect model. Statistical analysis was conducted by using Review Manager software version 5.2.

Results

Studies selected

We identified 20 potential RCTs comparing LRS with ORS for rectal cancer, of which, four studies were excluded for repeatedly published (Liang et al., 2010), outcomes of interest not studied(Buunen et al., 2009; Taylor et al., 2010) and data not available based on rectal cancer in trial of colorectal cancer (Kitano et al., 2005) (Figure 1). 16 RCTs (Araujo et al., 2003; Zhou et al., 2004; Guillou et al., 2005; Braga et al., 2007; Jayne et al., 2007; Pan et al., 2007; Pechlivanides et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Jayne et al., 2010; Kang et al., 2010; Liang et al., 2011; Zhang et al., 2012; Green et al., 2013; van der Pas et al., 2013) involving 3045 participants met the inclusion criteria were included in this meta-analysis, published year ranged from 2003 to 2013. All studies matching in age, sex and pathological stage, 1804 (59%) underwent laparoscopic surgery and 1241 (41%) underwent open rectal cancer surgery, four (Guillou et al., 2005; Jayne et al., 2007; Jayne et al., 2010; Green et al., 2013) of them reported different outcomes come from the same multicentre trial of the UK MRC CLASICC trial, therefore, the sample size is calculated only once. The rest multicentre studies are these trials (Pechlivanides et al., 2007; Kang et al., 2010; van der Pas et al., 2013). The mean follow-up ranged from 3 to112.5 months. AR was the only operation method for rectal cancer resection in two included trails (Zhou et al., 2004; Ng et al., 2009). In three studies (Araujo et al., 2003; Pan et al., 2007; Ng et al., 2008), APR was the only procedure. In the remaining trials both these procedures were performed. Eight RCTs (Araujo et al., 2003; Zhou et al., 2004; Pechlivanides et al., 2007; Ng et al., 2008; Lujan et al., 2009; Kang et al., 2010; Liang et al., 2011; Zhang et al., 2012) enrolled patients undergoing TME in both groups of laparoscopic and open. The characteristics of the included studies are listed in Table 2.

Quality of included RCTs

Of the 16 RCTs, 15 reported adequate randomized sequence generation (Zhou et al., 2004; Guillou et al., 2005; Braga et al., 2007; Jayne et al., 2007; Pan et al.,

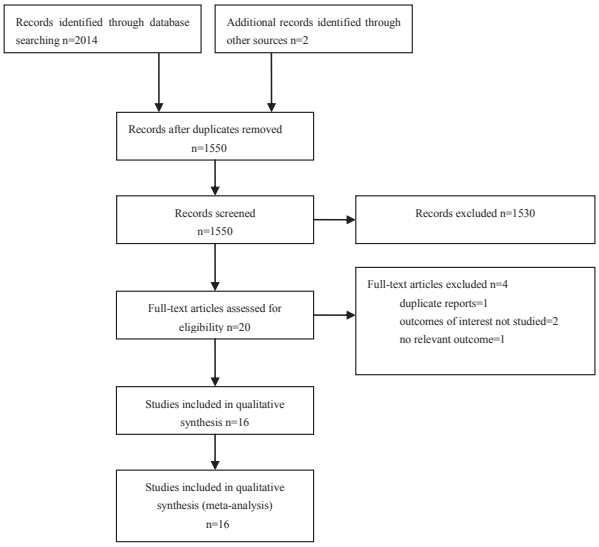

Figure 1. PRISMA Diagram of the Literature Search

Table 1. Quality of Included Trials

Study	adequate sequence generation	allocation concealment	blinding of outcome assement	intent-to-treat analysis	patients lost to follow-up
Araujo et al., 2003	Unclear	Unclear	Unclear	Unclear	Unclear
Zhou et al., 2004	Yes	Unclear	Unclear	Unclear	Unclear
Guillou et al., 2005	Yes	Yes	Unclear	Yes	Yes
Braga et al., 2007	Yes	Yes	Yes	Yes	Yes
Jayne et al., 2007	Yes	Yes	-	Yes	Yes
Pechlivanides et al., 2007	Yes	Unclear	Unclear	Unclear	Unclear
Pan et al., 2007	Yes	Unclear	Unclear	Unclear	Unclear
Ng et al., 2008	Yes	Yes	Unclear	Yes	Yes
Ng et al., 2009	Yes	Yes	Unclear	Yes	Yes
Lujan et al., 2009	Yes	Yes	Unclear	Yes	Unclear
Jayne et al., 2010	Yes	Yes	-	Yes	Yes
Kang et al., 2010	Yes	Yes	Unclear	Yes	Yes
Liang et al., 2011	Yes	Unclear	Yes	Yes	Yes
Zhang et al., 2012	Yes	Unclear	Unclear	Unclear	Yes
Green et al., 2013	Yes	Yes	-	Yes	Yes
van der Pas et al., 2013	Yes	Yes	No	Yes	Yes

*"-"means that outcomes are objective and not appropriate for evaluating this item

Table 2. Characteristics of Included Studies in Meta-analysis

CAuthor	Year	Tumor location	Resection Type	LRS/ORS	Conversion (%)	TME (%)	NE	Mean follow-up(mo) LRS/ORS
Araujo et al., 2003	2003	low	APR	13/15	0	100	Yes	47.2/47.2
Zhou et al., 2004	2004	low and ultralow	AR	82/89	NG	100	NG	1-16/1-16
Guillou et al., 2005	2005	colorectal	AR and APR	253/128	32	77 LRS 66 ORS	Yes	3/3
Braga et al., 2007	2007	rectal cancer	AR and APR	83/85	7.2	NG	Yes	53.6/53.6
Jayne et al., 2007	2007	colorectal	AR and APR	253/128	32	77 LRS 66 ORS	Yes	36.8/36.8
Pechlivanides et al., 2007	2007	middle and low	AR and APR	34/39	3	100	Yes	NG/NG
Pan et al., 2007	2007	low	APR	37/37	0	NG	NG	3-36/3-36
Ng et al., 2008	2008	low	APR	51/48	9.8	100	No	90.1/87.2
Ng et al., 2009	2009	upper	AR	76/77	30.3	0	Yes	71.1-168.3/ 69.8-168.7
Lujan et al., 2009	2009	low	AR and APR	101/103	7.9	100	Yes	32.8/34.1
Jayne et al., 2010	2010	colorectal	AR and APR	253/128	32	77 LRS 66 ORS	Yes	56.3/56.3
Kang et al., 2010	2010	mid and low	AR and APR	170/170	1.2	100	Yes	3/3
Liang et al., 2011	2011	rectal cancer	AR and APR	169/174	1	100	No	44/44
Zhang et al., 2012	2012	low	AR and APR	36/35	0	100	No	24-60/24-60
Green et al., 2013	2012	colorectal	AR and APR	253/128	32	77 LRS 66 ORS	Yes	62.9/62.9
van der Pas et al., 2013	2013	upper middle and lower	AR and APR	699/345	17	60 LRS 67 ORS	Yes	NG/NG

*LRS, laparoscopic rectal surgery; ORS, open rectal surgery; AR, anterior resection; APR, abdominoperineal excision; TME, total mesorectal excision; NE, neoadjuvant therapy; NG, not given

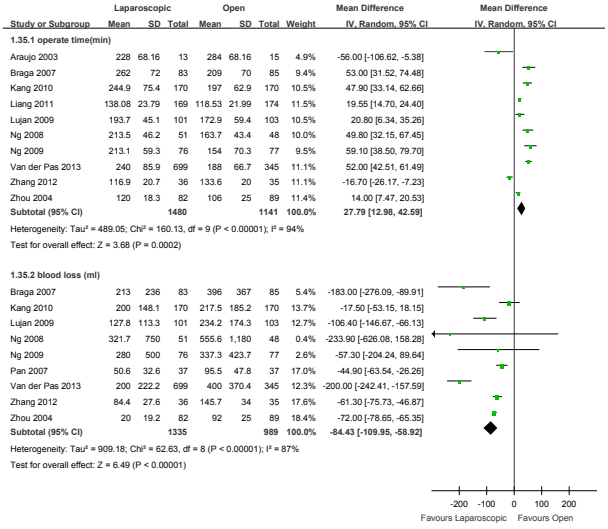

Figure 2. Laparoscopic (LRS) Compared with Open (ORS) Rectal Resection for Cancer: Operative Time (min), Blood Loss (ml)

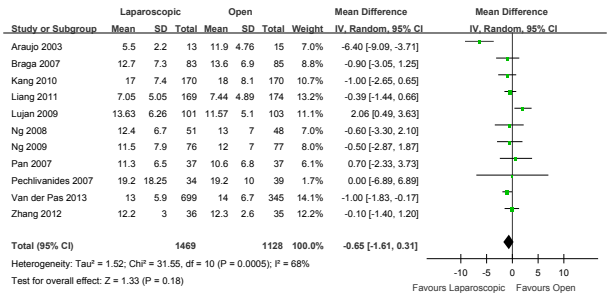

Figure 3. Laparoscopic (LRS) Compared with Open (ORS) Rectal Resection for Cancer: Number of Harvested Lymph Nodes

2007; Pechlivanides et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Jayne et al., 2010; Kang et al., 2010; Liang et al., 2011; Zhang et al., 2012; Green et al., 2013; van der Pas et al., 2013), 10 reported allocation concealment (Guillou et al., 2005; Braga et al., 2007; Jayne et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Jayne et al., 2010; Kang et al., 2010; Green et al., 2013; van der Pas et al., 2013). Only 2 reported blinding of outcome assessment (Braga et al., 2007; Liang et al., 2011) and 3 RCTs (Jayne et al., 2007; Jayne et al., 2010; Green et al., 2013) which's outcomes were objective such as overall survival, local recurrence were not appropriate for evaluating this item. Eleven did the intent-to-treat analysis (Guillou et al., 2005; Braga et al., 2007; Jayne et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Jayne et al., 2010; Kang et al., 2010; Liang et al., 2011; Green et al., 2013; van der Pas et al., 2013) and reported the patients lost to follow-up (Guillou et al., 2005; Braga et al., 2007; Jayne et al., 2007; Ng et al., 2008; Ng et al., 2009; Jayne et al., 2010; Kang et al., 2010; Liang et al., 2011; Zhang et al., 2012; Green et al., 2013; van der Pas et al., 2013) in detail.

Results of meta-analysis for LRS vs ORS considering all surgical procedures (AR and APR)

Results from outcome analysis including all selected studies independently from surgical procedure (AR and APR) are shown in Table 3.

Meta-analysis of operative outcomes

Ten studies focused on operative time (Araujo et al., 2003; Guillou et al., 2005; Braga et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Kang et al., 2010; Liang et al., 2011; Zhang et al., 2012; van der Pas

et al., 2013) , which was significantly increased in the laparoscopic compared with the open group (MD=27.79, 95%CI:12.98,42.59, p=0.0002). There is a fair amount of heterogeneity among the included studies (I^2=94%; p<0.00001) (Figure 2).

Nine papers measured intraoperative blood loss (Zhou et al., 2004; Braga et al., 2007; Pan et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Kang et al., 2010; Zhang et al., 2012; van der Pas et al., 2013). There was less blood loss in the laparoscopic compared with the open group (MD=-84.43, 95%CI:-109.95,-58.92, p<0.00001), with heterogeneity (I^2=87%; p<0.00001) (Figure 2). The intraoperative bladder or urethral lesion has no significant difference between the two groups (OR=1.14, 95%CI:0.52, 2.51, p=0.74).

Operative oncological outcomes

Eleven studies (Araujo et al., 2003; Braga et al., 2007; Pan et al., 2007; Pechlivanides et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Kang et al., 2010; Liang et al., 2011; Zhang et al., 2012; van der Pas et al., 2013) focused on the mean number of lymph nodes harvested during the surgical procedure, no significant difference was found (MD=-0.65, 95%CI:-1.61, 0.31, p=0.18), there was significant heterogeneity among the studies (I^2=68%; p<0.00005) (Figure 3). Sensitivity analysis showed that the heterogeneity of outcome among trials could be attributed mainly to the trial reported by Araujo et al. (2003).

Eight studies (Zhou et al., 2004; Guillou et al., 2005; Braga et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Kang et al., 2010; Zhang et al., 2012) of 2560 participants all matched for tumor stage reported data on CRM. Because there was no event for either the laparoscopic or open group in study of Zhou et al. (2004), therefore it was discarded from the meta-analysis.

Table 3. Results of a Meta-analysis Comparing Laparoscopic with Open Surgery for Rectal Cancer (All Procedures, AR and APR).

Outcome of Interest	No of Studies	Analysis Model	OR /MD (95%CI)	HG p-value/I^2 (%)	p-value
Operative outcomes					
Operative time	10	R	27.79 (12.98, 42.59)	<0.00001/94	0.0002
Blood loss	9	R	-84.43 (-109.95, -58.92)	<0.00001/87	<0.00001
Bladder or urethral lesion	8	F	1.14 (0.52, 2.51)	0.46/0	0.74
Operative oncological outcomes					
No of lymph nodes harvested	11	R	-0.65 (-1.61, 0.31)	0.00005/68	0.18
Positive circumferential margin	8	F	0.98 (0.70, 1.37)	0.96/0	0.89
Recovery outcomes					
Time to first bowel movement	9	R	-0.86 (-1.17, -0.55)	<0.00001/81	<0.00001
Time to feeding liquids	4	R	-0.48 (-0.82, -0.14)	0.002/80	0.006
Time to resume normal diet	6	R	-0.59 (-1.01, -0.17)	0.010/67	0.006
Time to walk independently	4	F	-0.69 (-0.87, -0.51)	0.27/23	<0.00001
Length of hospital stay	9	R	-2.06 (-3.43, -0.70)	<0.00001/86	0.003
Early postoperative outcomes					
Overall early postoperative mortality	9	F	0.70 (0.32, 1.50)	1.00/0	0.36
Overall early postoperative morbidity#	11	R	0.93 (0.79, 1.09)	0.02/54	0.38
Hemorrhage	7	F	0.77 (0.47, 1.27)	0.20/32	0.31
Anastomotic leak	8	F	1.00 (0.72, 1.38)	0.32/14	1
Wound infection	9	F	0.71 (0.51, 0.99)	0.13/36	0.05
Postoperative bowel obstructions	10	F	0.92 (0.64, 1.33)	0.59/0	0.66
Pulmonary infection	9	F	1.35 (0.86, 2.14)	0.65/0	0.19
Urinary infection	5	F	1.08 (0.60, 1.96)	0.41/0	0.79
Urinary retention	6	F	1.08 (0.62, 1.88)	0.91/0	0.77
Deep vein thrombosis	3	F	0.29 (0.06, 1.34)	0.42/0	0.11
Abscess	8	F	1.09 (0.70, 1.68)	0.90/0	0.71
Sepsis	3	F	1.68 (0.42, 6.78)	0.77/0	0.46
Perianal wound complications (dehiscence or hernia)**	2	R	0.75 (0.04, 14.38)	0.009/85	0.85
Perianal wound, infection or hematoma)	3	F	0.94 (0.51, 1.72)	0.38/0	0.83
Late complications					
Adhesion-related bowel obstruction	2	F	0.19 (0.07, 0.51)	0.87/0	0.001
Incisional hernia**	2	F	0.47 (0.15, 1.47)	0.21/36	0.19
3-year oncological outcomes					
Local recurrence	4	F	0.93 (0.51, 1.72)	0.99/0	0.83
Distance recurrence	4	F	1.06 (0.64, 1.76)	0.74/0	0.83
5-year or 10-year oncological outcomes					
Local recurrence	4	F	0.80 (0.37, 1.73)	0.49/0	0.57
Distance recurrence	2	F	0.60 (0.30, 1.19)	0.95/0	0.15
Incision/port site recurrence	3	F	0.13 (0.00, 6.42)	-	0.3
Overall survival#	4	F	1.06 (0.96, 1.18)	0.32/14	0.26
Disease free survival#	4	F	1.04 (0.95, 1.14)	0.98/0	0.38

*Mean difference, MD; OR, odds ratio; HG, heterogeneity; R, random; F, fix; **use Mantel-Haenszel and OR, #use Mantel-Haenszel and RR

Although the cumulative analysis of CRM was 6.7% in the LRS group and 5.6% in the ORS group, no significant difference was found (OR=0.98, 95%CI:0.70, 1.37, p=0.89), without heterogeneity (I^2=0%; p=0.96) between the two groups (Figure 4).

Meta-analysis of recovery outcomes

Nine papers (Zhou et al., 2004; Guillou et al., 2005; Braga et al., 2007; Pan et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Kang et al., 2010; van der Pas et al., 2013) addressed the time to first bowel movement which was significantly shorter in the LRS group compared with the ORS group (MD=-0.86, 95%CI:-1.17, -0.55, p<0.00001) (I^2=81%; p<0.00001) (Figure 5). The time to feeding liquids was earlier compared with the ORS group (MD=-0.48, 95%CI: -0.82, -0.14, p=0.006) (I^2=80%; p=0.002) , as well as the time to resume normal diet (MD=-0.59, 95%CI:-1.01, -0.17, p=0.006) (I^2=67%; p=0.01) and the time to walk independently (MD=-0.69, 95%CI:-0.87,-0.51, p<0.00001) (I^2=23%; p=0.23). Length of hospital stay reported in nine studies (Zhou et al., 2004; Guillou et al., 2005; Braga et al., 2007; Pan et al., 2007; Ng et al., 2008; Lujan et al., 2009; Ng et al., 2009; Kang et al., 2010; van der Pas et al., 2013) was significantly reduced in the LRS group compared with the ORS group (MD=-2.06, 95%CI:-3.43,-0.70, p=0.003). Heterogeneity of the studies on this parameter was significantly high (I^2=86%; p<0.00001) (Figure 5).

Meta-analysis of early postoperative complications

There was no significant difference between the laparoscopic and open groups not only in overall morbidity, but also in either of overall mortality, hemorrhage, anastomotic leak, wound infection, postoperative bowel obstructions, pulmonary infection, urinary infection, urinary retention, deep vein thrombosis, abscess, sepsis, perianal wound complications (dehiscence or hernia) and perianal wound (infection or hematoma).

Meta-analysis of late complications

Adhesion-related bowel obstruction described in only two RCTs (Braga et al., 2007; Ng et al., 2009) was significant less in the LRS group than ORS group (OR=0.19, 95%CI:0.07, 0.51; p=0.001) (I^2=0; p=0.87). There was no significant difference between LRS and ORS in incisional hernia (OR=0.47, 95%CI:0.15, 1.47; p=0.1).

Meta-analysis of long-term oncological outcomes

Four RCTs (Braga et al., 2007; Jayne et al., 2007; Pan et al., 2007; Zhang et al., 2012) focused on 3-year local recurrence and distance recurrence, meta-analysis of both outcomes didn't show any significant difference between the LRS and ORS groups (Table 3). Jayne et al. (2007) reported that there was no significant difference in 3-year of overall survival (OS) and disease-free survival (DFS) were seen between the groups for those undergoing AR or APR respectively, however, overall survival and disease-free survival for two groups undergoing AR and APR were not described. Liang et al. (2011) reported that there was no evidence to support a difference in 1-, 2-, and 3-year survival between LRS and ORS groups undergoing AR and APR, so that it was impossible to do quantitative synthesis based on 3-year of OS and DFS.

All of 5-year or longer time local recurrence (OR=0.80, 95%CI:0.37,1.73, p=0.57), distance recurrence (OR=0.60, 95%CI:0.30,1.19, p=0.15) and incision/port site recurrence (OR=0.13, 95%CI:0.00, 6.42, p=0.30) were not inferior in the LRS than in the ORS group. There was also no significant difference could be gotten

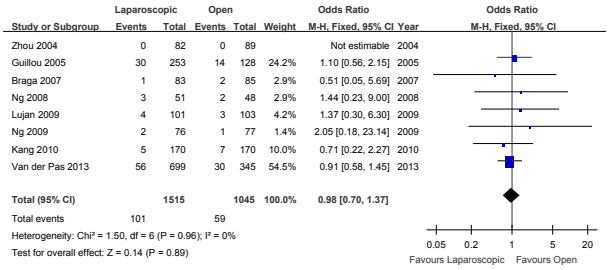

Figure 4. Laparoscopic (LRS) Compared with Open (ORS) Rectal Resection for Cancer: Positive Circumferential Margin

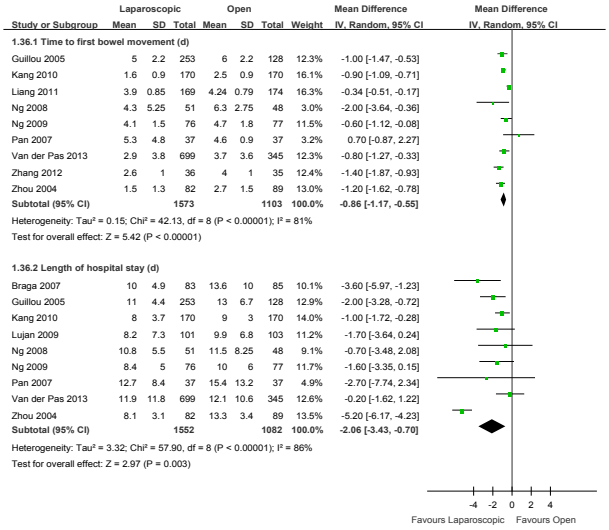

Figure 5. Laparoscopic (LRS) Compared with Open (ORS) Rectal Resection for Cancer: Time to First Bowel Movement (d), Length of Hospital Stay (d)

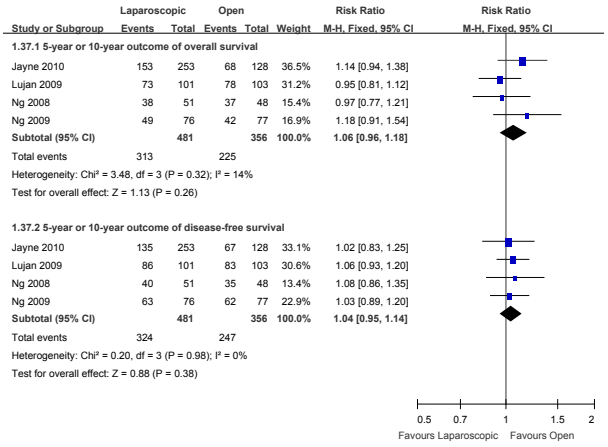

Figure 6. Laparoscopic (LRS) Compared with Open (ORS) Rectal Resection for Cancer: 5-year or 10-year Overall Survival (AR and APR), 5-year or 10-year Disease-free Survival (AR and APR)

Table 4. Results of A Meta-analysis Comparing Laparoscopic with Open Surgery for Rectal Cancer (AR)

Outcome of Interest	No of Studies	Analysis Model	OR/MD (95%CI)	HG *p*-value/I^2 (%)	*p*-value
Operative outcomes					
Operative time	3	R	32.06 (9.20, 54.91)	<0.0001/89	0.006
Blood loss	3	F	-72.52 (-79.06, -65.98)	0.64/0	<0.00001
Operative oncological outcomes					
No of lymph nodes harvested	1	F	-0.50 (-2.87, 1.87)	-	0.68
Positive circumferential margin	2	F	1.99 (0.20, 19.44)	-	0.55
Recovery outcomes					
Time to first bowel movement	3	R	-0.72 (-1.23, -0.21)	0.003/83	0.006
Time to feeding liquids	2	R	-0.50 (-1.12, -0.11)	0.003/88	0.11
Time to resume normal diet	1	F	-0.60 (-1.41, 0.21)	-	0.15
Time to walk independently	1	F	-0.70 (-1.37, -0.03)	-	0.04
Length of hospital stay	4	R	-2.23 (-4.98, 0.51)	<0.00001/97	0.11
Early postoperative outcomes					
Overall early postoperative mortality	2	F	0.67 (0.11, 3.97)	-	0.66
Overall early postoperative morbidity#	2	F	0.82 (0.54, 1.27)	0.23/31	0.38
Hemorrhage	2	F	0.37 (0.05, 2.65)	-	0.32
Anastomotic leak	2	F	0.34 (0.09, 1.26)	0.83/0	0.11
Wound infection	2	F	0.59 (0.23, 1.49)	0.79/0	0.26
Postoperative bowel obstructions	2	F	0.38 (0.05, 2.69)	0.59/0	0.33
Pulmonary infection	1	F	1.01 (0.14, 7.34)	-	0.99
Urinary infection	1	F	2.68 (0.79, 9.12)	-	0.11
Urinary retention	2	F	1.05 (0.36, 3.04)	0.30/7	0.94
Abscess	2	F	0.52 (0.05, 5.03)	-	0.57
Late complications					
Adhesion-related bowel obstruction	1	F	0.19 (0.07, 0.54)	-	0.002
Incisional hernia**	1	F	0.80 (0.21, 3.10)	-	0.75
5-year or 10-year oncological outcomes					
Local recurrence	1	F	1.28 (0.33, 4.91)	-	0.72
Distance recurrence	1	F	0.61 (0.25, 1.48)	-	0.27
Overall survival#	1	F	1.18 (0.91, 1.54)	-	0.21
Disease free survival#	1	F	1.03 (0.89, 1.20)	-	0.7

*Mean difference, MD; OR, odds ratio; HG, heterogeneity; R, random; F, fix; **use Mantel-Haenszel and OR, #use Mantel-Haenszel and RR

from the evidence in 5-year or longer time overall survival (313/481, 65.1% vs 225/356, 63.2%) (RR=1.06 95%CI:0.96, 1.18; p=0.26) (Figure 6) and disease-free survival (324/481, 67.3% vs 247/356, 69.4%) (RR=1.04, 95%CI:0.95, 1.14, p=0.38) (Figure 6).

Subgroup analysis of laparoscopic vs open AR for rectal cancer

Results from outcomes analysis including only the patients undergoing AR are shown in Table 4. Only two studies (Zhou et al., 2004; Ng et al., 2009) compared laparoscopic with open AR for rectal cancer while Lujan et al.'s RCT (Lujan et al., 2009) reported data on blood loss and operating time for this subgroup of patients and Liang et al.'s RCT (Liang et al., 2011) reported data on time to first bowel movement, time to feeding liquids and length of hospital stay for this subgroup of patients. The conclusion was the same as before that blood loss was less in the LRS group than in the ORS group (MD=-72.52, 95%CI:-79.06, -65.98, p<0.00001) (I^2=0; p=0.64). Operating time was longer in the LRS group than in the ORS.

Subgroup analysis of laparoscopic vs open APR for rectal cancer

Results from outcomes analysis including only the patients undergoing APR are shown in Table 5. Three RCTs (Araujo et al., 2003; Pan et al., 2007; Ng et al., 2008) compared laparoscopic with open APR for rectal cancer while Lujan et al. (2009) reported data on blood loss and operating time for this subgroup of patients and Liang et al. (2011) reported data on time to first bowel movement, time to feeding liquids and length of hospital stay for this subgroup of patients. Unlike AR, there was no significant difference comparing LRS group with OPS group in blood loss (MD=-109.3, 95%CI:-216.58,-2.01, p=0.05) (I^2=92%; p<0.00001) and operative time (MD=1.49, 95%CI:-109.3, 50.42, p=0.95) (I^2=93%; p<0.00001) for patients undergoing APR.

Outcomes of time to feeding liquids, time to walk independently, length of hospital stay and early postoperative wound infection have significant difference between the two groups characterized by p<0.05. No study reported data of late complications of this subgroup. There was no significant difference in remaining outcomes of operative, recovery, early postoperative, operative oncological outcomes and long term oncological outcomes.

Subgroup analysis of laparoscopic vs open TME

Eight RCTs (Araujo et al., 2003; Zhou et al., 2004; Pechlivanides et al., 2007; Ng et al., 2008; Lujan et al., 2009; Kang et al., 2010; Liang et al., 2011; Zhang et al., 2012) enrolled participants undergoing TME procedure in two groups (Table 6). Seven RCTs reported data on operative time, which was significantly increased in the LRS group (MD=16.91, 95%CI:1.71,32.11, p=0.03)

Table 5. Results of a Meta-analysis Comparing Laparoscopic with Open Surgery for Rectal Cancer (APR)

Outcome of interest	No of studies	Analysis model	OR /MD(95%CI)	HG P-value/I^2 (%)	P-value
Operative outcomes					
Operative time	3	R	1.49(-47.44,50.42)	<0.00001/93	0.95
Blood loss	3	R	-109.3(-216.58,-2.01)	<0.00001/92	0.05
Bladder or urethral lesion	3	F	0.81(0.17,3.87)	0.35/4	0.79
Operative oncological outcomes					
No of lymph nodes harvested	3	R	-2.13(-6.45,2.18)	0.00008/86	0.33
Positive circumferential margin	1	F	1.42(0.24,8.54)	-	0.7
Recovery outcomes					
Time to first bowel movement	3	R	-0.42(-1.55,-0.71)	0.05/66	0.47
Time to feeding liquids	1	F	-0.54(-0.89,-0.19)	-	0.003
Time to resume normal diet	1	F	-0.80(-2.63,1.03)	-	0.39
Time to walk independently	2	F	-1.25(-1.85,-0.65)	0.71/0	<0.0001
Length of hospital stay	3	F	-0.21(-0.38,-0.05)	0.59/0	0.01
Early postoperative outcomes					
Overall early postoperative mortality	2	F	0.94(0.06,15.27)	-	0.97
Overall early postoperative morbidity#	3	F	0.87(0.57,1.33)	0.04/69	0.51
Hemorrhage	1	F	0.12(0.01,2.02)	-	0.14
Wound infection	2	F	0.12(0.03,0.46)	0.99/0	0.002
Postoperative bowel obstructions	3	F	1.02(0.32,3.30)	0.12/52	0.97
Pulmonary infection	3	F	0.79(0.21,2.97)	0.35/4	0.72
Urinary infection	1	F	0.81(0.29,2.29)	-	0.69
Urinary retention	3	F	0.97(0.45,2.11)	0.94/0	0.94
Deep vein thrombosis	1	F	0.12(0.01,1.2)	-	0.07
Abscess	1	F	0.94(0.06,15.27)	-	0.97
Perianal wound complications (dehiscence or hernia)**	1	F	3.43(0.65,18.22)	-	0.15
Perianal wound (infection or hematoma)	2	F	0.97(0.47,2.00)	0.17/48	0.93
3-year oncological outcomes					
Local recurrence	1	F	1.00(0.06,16.30)	-	1
Distance recurrence	1	F	0.35(0.05,2.61)	-	0.31
5-year or 10-year oncological outcomes					
Local recurrence	2	F	0.35(0.08,1.43)	0.48/0	0.14
Distance recurrence	1	F	0.58(0.20,1.74)	-	0.34
Incision/port site recurrence	1	F	0.13(0.00,6.42)	-	0.3
Overall survival#	1	F	0.97(0.77,1.21)	-	0.76
Disease free survival#	1	F	1.08(0.86,1.35)	-	0.52

*Mean difference, MD; OR, odds ratio; HG, heterogeneity; R, random; F, fix; **use Mantel-Haenszel and OR, #use Mantel-Haenszel and RR

(I^2=93%; p<0.00001). Blood loss was described in five trials (Zhou et al., 2004; Ng et al., 2008; Lujan et al., 2009; Kang et al., 2010; Zhang et al., 2012), which was significant less in LRS group (MD=-64.87, 95%CI:-84.14,-45.59, p<0.00001) (I^2=71%; p=0.008).

Five RCTs (Zhou et al., 2004; Ng et al., 2008; Kang et al., 2010; Liang et al., 2011; Zhang et al., 2012) reported the time to first bowel movement after TME, which was significantly decreased in LRS (MD=-0.99, 95%CI:-1.44,-0.54, p<0.00001) (I^2=89%; p<0.00001). Three RCTs (Zhou et al., 2004; Kang et al., 2010; Liang et al., 2011) reported time to feeding liquids which was significantly lower in LRS (MD=-0.54, 95%CI:-0.94,-0.15, p=0.007) (I^2=85%; p=0.001).The time to resume normal diet given in three RCTs (Ng et al., 2008; Lujan et al., 2009; Kang et al., 2010) was significantly shorter in the LRS group (MD=-0.42, 95%CI:-0.63, -0.21, p<0.0001) (I^2=0; p=0.71). Two RCTs (Ng et al., 2008; Liang et al., 2011) reported the time to walk independently which was significantly decreased in LRS (MD=-0.65, 95%CI:-0.84,-0.46, p<0.00001) (I^2=30%; p=0.23). Deep vein thrombosis was reported in two RCTs (Ng et al., 2008; Liang et al., 2011), which was less in LRS (OR=0.13, 95%CI:0.02,0.91, p=0.04) (I^2=0; p=0.95). We were unable to find any studies that addressed late complications in this subgroup. There was no significant difference in other outcomes of operative, recovery, early postoperative, operative oncological outcomes and long term oncological outcomes.

Publication bias

A funnel plot of the studies used in the meta-analysis reporting on positive circumferential margin after laparoscopic rectal cancer surgery as compared with open rectal cancer surgery shows that none of the studies lay outside the limits of the 95% CI, and there was no evidence of publication bias among the studies (p=0.96).

Discussion

In 2005, the American Society of Colon and Rectal Surgeons (ASCRS) issued a statement regarding the role of laparoscopy in proctectomy for cancer: "The absence of five-year survival data makes it premature to endorse laparoscopic proctectomy for curable cancer" (Tjandra et al., 2005). Until 2012, the latest NCCN (National Comprehensive Cancer Network) Clinical Practice

Table 6. Results of a Meta-analysis Comparing Laparoscopic with Open Surgery for Rectal Cancer (TME)

Outcome of Interest	No of Studies	Analysis Model	OR/MD (95%CI)	HG P-value/I^2 (%)	*p*-value
Operative outcomes					
Operative time	7	R	16.91 (1.71, 32.11)	<0.00001/93	0.03
Blood loss	5	R	-64.87 (-84.14, -45.59)	0.008/71	<0.00001
Bladder or urethral lesion	5	F	0.81 (0.17, 3.88)	0.35/5	0.79
Operative oncological outcomes					
No of lymph nodes harvested	7	R	-0.80 (-2.36, 0.76)	0.0001/80	0.31
Positive circumferential margin	4	F	0.99 (0.44, 2.24)	0.72/0	0.99
Recovery outcomes					
Time to first bowel movement	5	R	-0.99 (-1.44, -0.54)	<0.00001/89	<0.00001
Time to feeding liquids	3	R	-0.54 (-0.94, -0.15)	0.001/85	0.007
Time to resume normal diet	3	F	-0.42 (-0.63, -0.21)	0.71/0	<0.0001
Time to walk independently	2	F	-0.65 (-0.84, -0.46)	0.23/30	<0.00001
Length of hospital stay	4	R	-2.24 (-4.81, -0.33)	<0.00001/94	0.09
Early postoperative outcomes					
Overall early postoperative mortality	6	F	0.75 (0.17, 3.32)	0.85/0	0.7
Overall early postoperative morbidity#	6	F	0.92 (0.75, 1.13)	0.57/0	0.45
Hemorrhage	3	F	0.25 (0.05, 1.27)	0.54/0	0.1
Anastomotic leak	4	F	0.64 (0.31, 1.32)	0.33/13	0.23
Wound infection	4	F	0.66 (0.31, 1.40)	0.14/44	0.28
Postoperative bowel obstructions	6	F	0.69 (0.42, 1.13)	0.95/0	0.15
Pulmonary infection	4	F	1.51 (0.43, 5.26)	0.62/0	0.52
Urinary infection	3	F	0.97 (0.45, 2.08)	0.87/0	0.94
Urinary retention	4	F	1.06 (0.54, 2.09)	0.82/0	0.86
Deepvein thrombosis	2	F	0.13 (0.02, 0.91)	0.95/0	0.04
Abscess	5	F	1.21 (0.37, 3.97)	0.68/0	0.75
Sepsis	2	F	1.99 (0.40, 9.94)	0.55/0	0.4
Perianal wound complications (dehiscence or hernia)**	2	R	0.75 (0.04, 14.38)	0.009/85	0.85
Perianal wound (infection or hematoma)	2	F	1.23 (0.57, 2.66)	0.40/0	0.6
3-year oncological outcomes					
Local recurrence	1	F	0.97 (0.06, 15.86)	-	0.98
Distance recurrence	1	F	0.97 (0.13, 7.20)	-	0.98
5-year or 10-year oncological outcomes					
Local recurrence	3	F	0.63 (0.25, 1.63)	0.42/0	0.34
Distance recurrence	1	F	0.58 (0.20, 1.74)	-	0.34
Incision/port site recurrence	2	F	0.13 (0.00, 6.42)	-	0.3
Overall survival#	2	F	0.96 (0.84, 1.09)	0.93/0	0.53
Disease free survival#	2	F	1.06 (0.95, 1.19)	0.89/0	0.28

*Mean difference, MD; OR, odds ratio; HG, heterogeneity; R, random; F, fix; **use Mantel-Haenszel and OR, #use Mantel-Haenszel and RR

Guidelines for rectal cancer showed that laparoscopic surgery was still preferred in the setting of a clinical trial owing to without long-term outcomes from laparoscopic surgery have been reported and current clinical trials are exploring open versus laparoscopic approach (Benson et al., 2012).

In recent years, there are some meta-analysises comparing LRS and ORS. A meta-analysis involving 2071 patients by Aziz et al. (2006) published in 2006. We must note that in spite of this meta-analysis includes 20 studies, of which only three are RCTs, therefore, which is at high risk of bias. A meta-anslysis by Trastulli et al. (2012) combined 3-year and 5-year oncological outcomes together showed no significant difference between the two groups in local, port-site and distant recurrence, which may cause confusion. There was still insufficient evidence to compare long-term oncologic outcomes between laparoscopic and open surgery for rectal cancer, so that, we decided to do this systematic review and meta-analysis.

Regarding to short-term outcomes, the present study drawn the conclusion that laparoscopic proctectomy for curable cancer is associated with a significantly less intraoperative blood loss compared with open radical surgery for patients with rectum cancer, however, the operative time was increased obviously. This findings are consistent with these studies previous (Breukink et al., 2006; Huang et al., 2011; Trastulli et al., 2012; Xiong et al., 2012). The pooled data of RCTs showed that there was no significant difference in bladder or urethral lesion between LRS and ORS, whether when it refer to all procedures of AR and APR or subgroup analysis of AR, APR, TME whichever.

The analysis of operative time and blood loss has high heterogeneity. One explanation for this finding is that the learning curve for laparoscopic proctectomy and different surgical procedure. Another possible explanation is that the different calculation methods in blood loss.

This meta-analysis suggests that evidence from RCTs published favoured LRS over ORS for treatment of rectal cancer with regard to recovery outcomes. All parameters of time to first bowel movement, time to feeding liquids, time to resume normal diet, time to walk independently

and length of hospital stay indicated statistical difference, which were similar to Trastulli's research (Trastulli et al., 2012). But among these parameters, only the length of hospital stay is relatively reliable. Although lack of uniformity of the criteria for patient discharge between the included RCTs such as these RCTs (Braga et al., 2007; Ng et al., 2008; Lujan et al., 2009). In contrast, the others are more subjective and can't accurate judgment.

The safety of LRS has been extensively reported in these systematic reviews (Breukink et al., 2006; Hotta and Yamaue, 2011; Trastulli et al., 2012; Xiong et al., 2012). No significant differences were found for overall mobidity, overall motality, anastomotic leak, postoperative bowel obstructions, pulmonary infection, urinary infection, urinary retention, deep vein thrombosis, abscess and sepsis between the two surgery groups, which were consistent with our review. Trastulli et al. (2012) research concluded that laparoscopic rectal surgery was associated with a significantly low rate of postoperative abdominal bleeding compared with the open approach. This was not in agreement with the present study, maybe our study included more RCTs and participants, as a result, the finding was more credible. A meta-analysis of RCTs comparing laparoscopic with open resection for colorectal cancer, identified that laparoscopic surgery has most obvious advantage in wound infection rates (Gao et al., 2006), this main benefits for laparoscopic surgery was further confirmed by our study, although wound infection rate was slightly lower in the laparoscopic rectum surgery groups (5.4% *vs* 7.0%, p=0.05). Additionally, the late complication of adhesive related obstruction decreased in laparoscopic group, the evidence was gained largely from the two studies (Braga et al., 2007; Ng et al., 2009), therefore, it should be interpreted with caution. It seemed that the safety and feasibility of LRS are similar to or better than those of conventional ORS.

In our meta-analysis, preoperative adjuvant therapy was carried out in eleven (Araujo et al., 2003; Guillou et al., 2005; Braga et al., 2007; Jayne et al., 2007; Pechlivanides et al., 2007; Lujan et al., 2009; Ng et al., 2009; Jayne et al., 2010; Kang et al., 2010; Green et al., 2013; van der Pas et al., 2013) of the sixteen RCTs, no adjuvant therapy (Ng et al., 2008; Liang et al., 2011; Zhang et al., 2012) or not record (Zhou et al., 2004; Pan et al., 2007) in five RCTs. Preoperative chemoradiotherapy not only may result in tumor downsizing and a decrease in tumor bulk and local recurrence, but also has the potential to increase rates of pathologic complete response and sphincter-saving procedures (Benson et al., 2012). In contrast to colon cancer, rectal cancer has the relatively high risk of locoregional recurrence and distant recurrence associated with its anatomical characters, although chemoradiotherapy was associated with increased toxicity, preoperative chemoradiotherapy for patients with stage II/III rectal cancer was recommended in NCCN guidelines for rectal cancer in 2012 (Benson et al., 2012).

The CRM has been shown to be a strong predic¬tor of both local recurrence and overall survival (Adam et al., 1994; Mawdsley et al., 2005; Glynne-Jones et al., 2006) including in patients undergoing neoadjuvant therapy (Nagtegaal and Quirke, 2008), and is an important consideration when post-operative treatment decisions are made. However, the number of lymph nodes harvested not only can vary with age of the patient, gender, tumor grade, and tumor site (Sarli et al., 2005), but also may be reduced after neoadjuvant, therefore, an intact CRM is considered a more accurate indicator of oncological adequacy than the number of lymph nodes retrieved (Nagtegaal et al., 2002).

In the CLASICC trial (Guillou et al., 2005), nearly half of the 794 patients were diagnosed with rectal cancer, no significant difference was found in CRM based on surgical approach (16% with LRS, 14% with ORS, p=0.8). In the COREAN trial (Kang et al., 2010) and the COLOR II trial (van der Pas et al., 2013), there were also no significant differences were found in terms of CRM and number of lymph nodes harvested as before. This present meta-analysis of RCTs confirmed the results of previous studies further.

The expected short-term benefits can only be of important when oncological results are at least equal. A recent meta-analysis comparing laparoscopic versus open surgery for colon cancer by Di et al. (2013) shown that lack of differences in total recurrence rate, 5-year tumor free survival rate and the overall 5-year survival, however, so far there is no high quality evidence concerning the oncological quality of resection comparing laparoscopic and open rectum surgery. In the CLASICC trial, no significant differences were found in local recur¬rence, OS and DFS in 3-year, 5-year and 10-year follow-up respectively. However, the CLASICC trial enrolled patients with colon and rectal cancer, which may confound conclusions for rectal cancer.

A meta-analysis by Huang et al. (2011) found no significant difference in 3-year OS, DFS, local and port site recurrence between laparoscopic and open surgery from six RCTs. Another recent meta-analysis by Trastulli et al. (2005) from nine RCTs found no significant difference between two surgical approaches in incision/port site recurrence, local and distance recurrence. Our analysis, of which the biggest sample size was 837 in these long-term outcomes, demonstrated that there was no statistically difference in 3-year local and distance recurrence, furthermore, no statistically difference was observed in these long term outcomes. However, Ng et al. (2008) calculated that nearly 4,000 patients needed to demonstrate that long-term survival was not different between LRS and ORS in a RCT. Although the present study is the first one concerning 5-year survival data and hardly encompassed all RCTs on this topic, the small sample size on these parameters limited the credibility of the conclusion. Additional clinical trials exploring open versus laparoscopic surgery for rectal cancer are ongoing (including ClinicalTrials.gov identifiers NCT00297791 [COLOR II], NCT00470951 [CTS-179], NCT00726622 [ACOSOG-Z6051], and NCT00147134 [JCOG0404]), the long term outcomes of these trials are to be expected.

Strengths and weaknesses

Although our study has multiple strengths, including its use of more RCTs than any other review published in the past and pooled date of 3-year and 5-year respectively to make the evidence more clearly, several limitations

should be noted. First, the small sample size limited power calculation for long-term survival outcomes and a rare event such as deep vein thrombosis. Furthermore, the inclusion of only published trials may have introduced publication bias. Third, the trials differed in tumor stage, the specific location of tumors and preoperative chemoradiotherapy, although all RCTs included matching in pathological stage of tumor, these factors may affect the surgery approach, so bring about clinical heterogeneity between trials. Finally, but not least, this study could not account for the learning curve associated with the technique and its effect on postoperative outcome, laparoscopic surgery for rectal cancer is otherwise a rather complicated surgery than other laparoscopic colectomy. Hence, the design and reporting of the future researches should have more details including preoperative adjuvant therapy, randomization, blinding outcome evaluation, doctor's experience in laparoscopic surgery. It is also important to have adequate following-up and pay more attention to long-term oncologic outcomes and quality of life of the patients.

In conclusion, through this study, we can clearly find that LRS has improved short-term outcomes in less blood loss, earlier return to bowel function, shorter hospital stay, while not incomparable in intraoperative complications and oncologic clearance adequacy. Furthermore, based on the 5-year and longer follow-up outcomes, we conclude that oncological outcome is comparable after laparoscopic and open resection for rectal cancer. In suitable patients, considering tumor stage, location, experience of the surgeon and the values of patients, laparoscopic approach could as one option.

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