Systematic Review and Meta-Analysis

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A meta-analysis of laparoscopic surgery versus conventional open surgery in the treatment of colorectal cancer

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Abstract

Background: This meta-analysis aimed to explore the overall effect and safety of anterior laparoscopic surgery versus conventional open surgery for patients with colorectal cancer based on eligible randomized controlled trials (RCTs), especially the difference in the postoperative incidence of deep venous thrombosis (DVT).

Methods: PubMed, Cochrane, and Embase were searched based on keywords to identify eligible studies before February 2018. Only RCTs were eligible. We analyzed the main outcomes using the relative risk (RR) or mean difference (MD) along with 95% confidence interval (95% CI).

Results: In this meta-analysis, we analyzed a total of 24 studies with 4592 patients in the laparoscopic surgery group and 3865 patients in the open surgery group. The results indicated that compared with the open surgery, laparoscopic surgery significantly decreased estimated blood loss (SMD: −1.14, 95%CI: −1.70 to −0.57), hospital stay (SMD: −1.12, 95%CI: −1.76 to −0.47), postoperative mortality (RR: 0.60, 95%CI: 0.41–0.86) and postoperative complication (RR: 0.83, 95%CI: 0.72–0.95). However, the operative time (WMD: 40.46, 95%CI: 35.94–44.9) was statistically higher in the laparoscopic surgery group than the open surgery group, and there was no significant difference in the incidence of DVT between the 2 groups (RR: 0.96, 95%CI: 0.46–2.02).

Conclusion: Laparoscopic surgery is superior to open surgery for patients with colorectal cancer. But the 2 surgeries showed no significant difference in the incidence of DVT.

Abbreviations: DVT = deep venous thrombosis, NCCN = National Comprehensive Cancer Network.

Keywords: colorectal cancer, laparoscopic surgery, meta-analysis, open surgery

1. Introduction

Colorectal cancer is among the top 3 common tumors worldwide,[1,2] and its morbidity has dramatically increased in Asians. Currently, surgery remain the best treatment for colorectal cancer, which includes conventional laparoscopic surgery, hand-assisted laparoscopic surgery, robotic surgery, single-pore laparoscopic surgery, and open surgery.[3,4]

Laparoscopic surgery combines features of the minimally invasive technique and open surgery. Compared with conventional open surgery, laparoscopic surgery has advantages such as smaller incision length, smaller blood loss, and less pain. However, previous studies demonstrated that laparoscopic surgery had some limitations like longer operative time and longer learning curve for surgeons.[6,7] For larger tumors, laparoscopic surgery is less effective due to the lack of tactile feedback and inadequate exposure.[7,8] Up to 2015, the National Comprehensive Cancer Network (NCCN) still did not recommend laparoscopic surgery for colorectal cancer.[9] Deep venous thrombosis (DVT) is one of the most common peripheral vascular diseases, and the post-thrombosis syndrome can influence the daily-life for a long time. Surgery can increase the incidence of DVT. In this study, we explored the influence of open surgery and laparoscopic surgery on the incidence of DVT.

In this meta-analysis, we explored the overall effect and safety of open surgery laparoscopic surgery for patients with colorectal cancer based on qualified RCTs.

2. Methods

2.1. Ethics statement

Ethics approval was waived because this study did not involve any human subjects or animals.

2.2. Literature search

Cochrane library, PubMed, and Embase database were identified for all the qualified studies up to February 2018 on open surgery versus laparoscopic surgery for patients with colorectal cancer. We also searched relevant publications as well as the reference

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materials. The literature search process was performed by 2 reviewers separately. Any arising disagreement was settled via the help of a third researcher.

2.3. Study selection

Studies should meet the following inclusion criteria: randomized controlled trials; the included patients were diagnosed with colorectal cancer; the test group were treated by laparoscopic surgery, and the control group were treated by open surgery; the outcomes included operative time, blood loss, hospital stay, wound infection, DVT, postoperative mortality, and postoperative complication.

Studies were excluded due to the following criteria: duplicate publications, or shared result; economic analysis, case report, expert comment, theoretical research, meta-analysis, systematic review and conference report; and irrelevant outcomes.

Two investigators identified all studies based on the predefined criteria independently. Any difference was settled by discussion via the aid of a third researcher.

2.4. Data collection and quality assessment

We extracted data from the included studies. The basic information was regarded as the first part: names of authors, publication year, the Jadad score, sample size, country, gender, and age. The second part was clinical outcomes: operative time, blood loss, hospital stay, wound infection, DVT, postoperative mortality, and postoperative complication. The Jadad score checklist was used to appraise the quality of the included studies. We evaluated all the RCTs from the 5 items: double blinding, detail of access and exit, randomized sequence, statement of randomization, and description of double blinding. Studies with a score <3 represented low-quality and high bias risks, studies with a score >3 indicated high-quality trial. The 2 investigators performed the mentioned process separately. A third investigator resolved differences by discussion.

2.5. Data synthesis and data analysis

We performed data synthesis as well as analysis using STATA 10.0 (Texas). Additionally, I^2 tests and Chi-squared test were utilized to determine the heterogeneity of clinical trial results to further decide the model for analyses (the random-effects model or the fixed-effects model). When the I^2 test value was >50% and Chi-squared test *P*-value was <.05, heterogeneity was defined to be high and the random-effects model was utilized. When the I^2 test value was less than 50% and Chi-squared test *P*-value was larger than .05, heterogeneity data were defined to be acceptable and the fixed-effects model was utilized. Mean ± standard deviation and mean difference (MD) were used to express and analyze continuous variables, respectively. Categorical data were presented as percentages and analyzed by relative risk (RR) or odds ratio (OR). DVT, postoperative mortality, and postoperative complication were analyzed by RR and 95%CI. Operative time, blood loss, and hospital stay were analyzed by MD and 95%CI. The primary endpoint of our research is postoperative mortality to evaluate the clinical efficacy of laparoscopic surgery and conventional open surgery. The indicators about operation contain operative time and hospital days. Indexes about adverse events include blood loss, DVT, and postoperative complication.

3. Results

3.1. Study characteristics

Totally, we identified 1347 publications based on index words. After screening abstracts or titles, we excluded 1269 publications, leaving 78 publications for further screening. During full-text screening, a total of 54 publications were excluded due to the following reasons: nonrandomized studies (22), no clinical outcomes (21), and theoretical research or review (11). Finally, in this meta-analysis, 24 studies[10–33] were included with 4592 patients in the laparoscopic surgery group and 3865 patients in the open surgery group. Figure 1 shows the selection process.

Table 1 summarizes the main characteristics of the included studies. The countries or districts of studies included United States, Japan, Germany, China, Hong Kong, Denmark, Singapore, Spain, Italy, Taiwan, Australia, Europe, the Netherlands, France, UK, and Greece. The main Jadad score was 4.54, indicating that the included studies were high quality. The mean age of all the included studies was more than 50 years old.

3.2. Operative time

Twenty-four studies with 4592 subjects in the laparoscopic surgery group and 3865 subjects in the open surgery group provided data on operative time. Based on the I^2 test (I^2 = 91.7%) and Chi-squared test (*P* = .000), we chose the random effects model to analyze operative time due to high variability. The pooled results showed that the laparoscopic surgery group dramatically increased operative time compared with the open surgery group (WMD: 40.46, 95%CI: 35.94–44.98, Fig. 2).

3.3. Blood loss

Seventeen studies with 2199 subjects in the open surgery group and 2568 subjects in the laparoscopic surgery group reported data on blood loss. Based on the I^2 test (I^2 = 98.6%) and Chi-squared test (*P* = .000), the random effects model was adopted to analyze blood loss. The pooled results showed that the laparoscopic surgery group dramatically decreased blood loss compared with the open surgery group (SMD: −1.14, 95%CI: −1.70 to −0.57, Fig. 3).

3.4. Hospital stay

Thirteen studies with 1567 subjects in the open surgery group and 1948 subjects in the laparoscopic surgery group provided data about on hospital stay. Based on the I^2 test (I^2 = 98.4%) and Chi-squared test

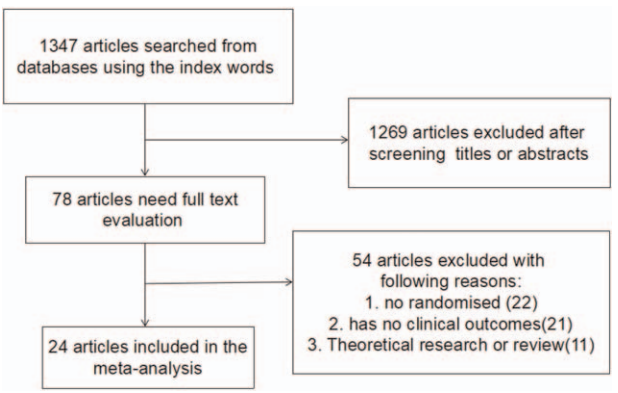

Figure 1. The flow diagram of the literature search and selection process.

Table 1

The basic characteristics description of included studies.

Study	Country	Jadad score	No. of patients		Gender		Age	
			L	O	L	O	L	O
FL Liu 2010	China	5	98	88	56M	50M	59.3	61.5
Chi Chiu Chung 2007	Hong Kong	5	41	40	25M	26M	71	72.5
Qin-Song Sheng 2012	China	5	59	57	32M	35M	62.4	64.6
J.G. Stage 1997	Denmark	4	15	14	8M	5M	72	73
W. Schwenk 1998	Germany	4	30	30	14M	16M	63.3	64.8
Jeffrey W Milsom 1998	Germany	4	55	54	26M	36M	69	69
C.L. Tang 2001	Singapore	5	118	118	61M	70M	64	62
Antonio M Lacy 2002	Spain	5	111	108	56M	50M	68	71
The Clinical Outcomes of Surgical Therapy Study Group 2004	America	5	435	428	223M	208M	70	69
Ka Lau Leung 2004	Hong Kong	5	203	200	104M	114M	67.1	66.5
Marco Braga 2005	Italy	5	258	259	137M	145M	63.7	65.1
Jin-Tung Liang 2006	Taiwan	5	135	134	76M	71M	64.4	64.2
Simon S.M.2008	Hong Kong	5	51	48	—	—	—	—
Peter J. Hewett 2008	Australia	5	294	298	139M	143M	71.1	69.4
The Colon Cancer Laparoscopic or Open Resection Study Group 2009	Europe	5	534	542	277M	289M	71	71
Martijn H G M van der Pas 2013	Netherlands	5	699	345	448M	211M	66.8	65.8
Emile Darai 2010	France	5	26	26	—	—	32	33.5
Pierre J Guillou 2005a	UK	5	526	268	230F	123F	69	69
Pierre J Guillou 2005b	UK	5	345	276	167F	121F	69	69
Shoichi Fujii 2014	Japan	5	100	100	50M	60M	79.8	80.1
Jing Gong 2012	China	3	67	71	38M	40M	58.4	59.6
Konstantinos E. Tsimogiannis 2012	Greece	3	20	20	8M	9M	67.77	70.17
J. Neudecker 2009	Germany	5	250	222	132M	116M	66.8	66.4
Wang Zhidu 2009	China	3	98	93	50M	51M	—	—
H. Hasegawa 2003	Japan	3	24	26	14M	18M	61	61

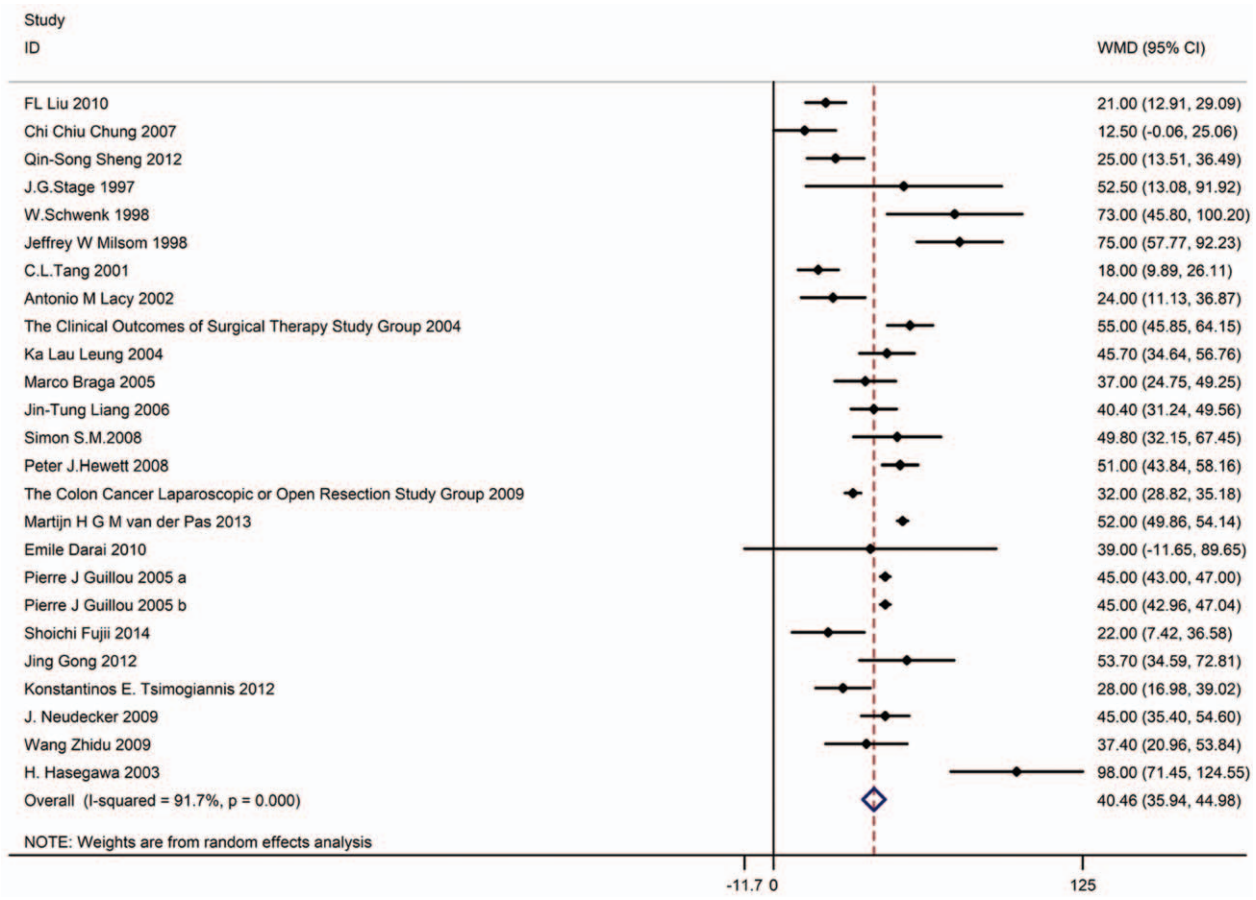

Figure 2. Forest plot showing operative time of laparoscopic surgery versus open surgery.

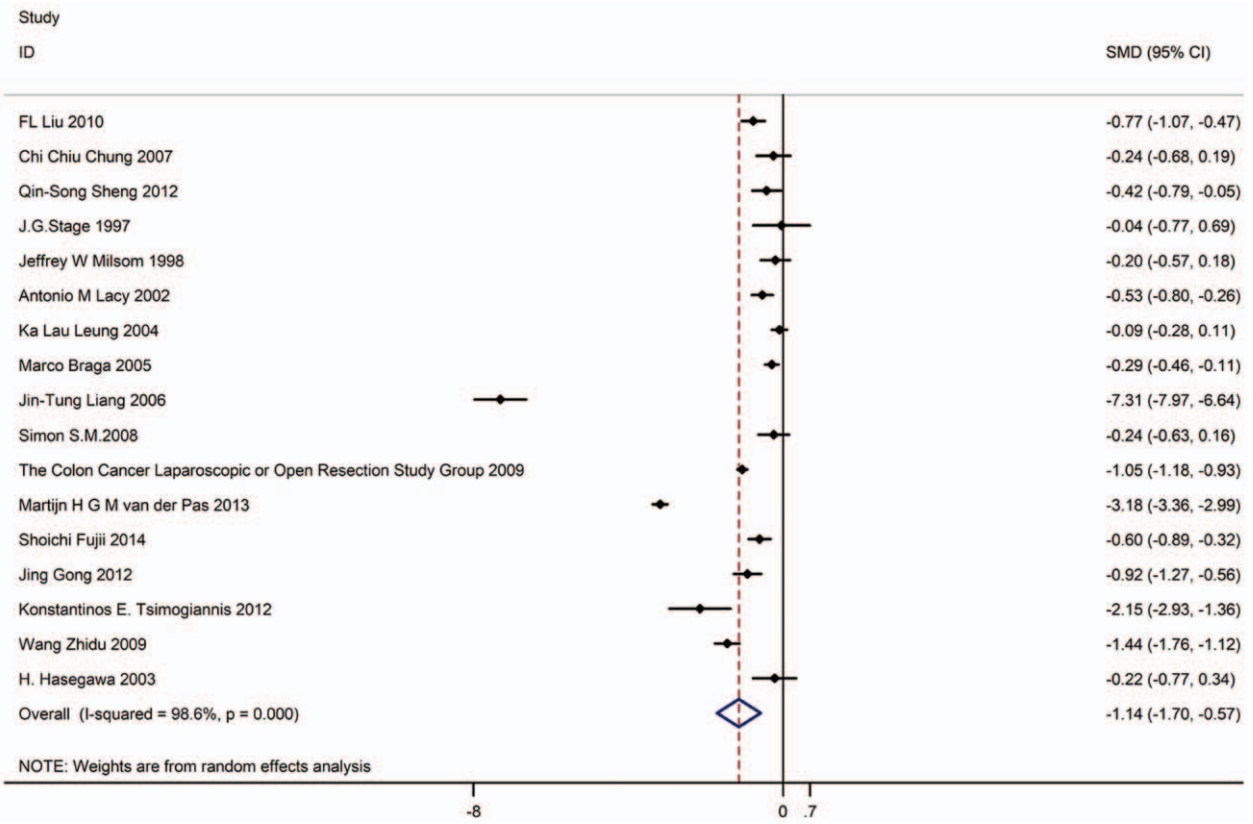

Figure 3. Forest plot showing blood loss that laparoscopic surgery versus open surgery.

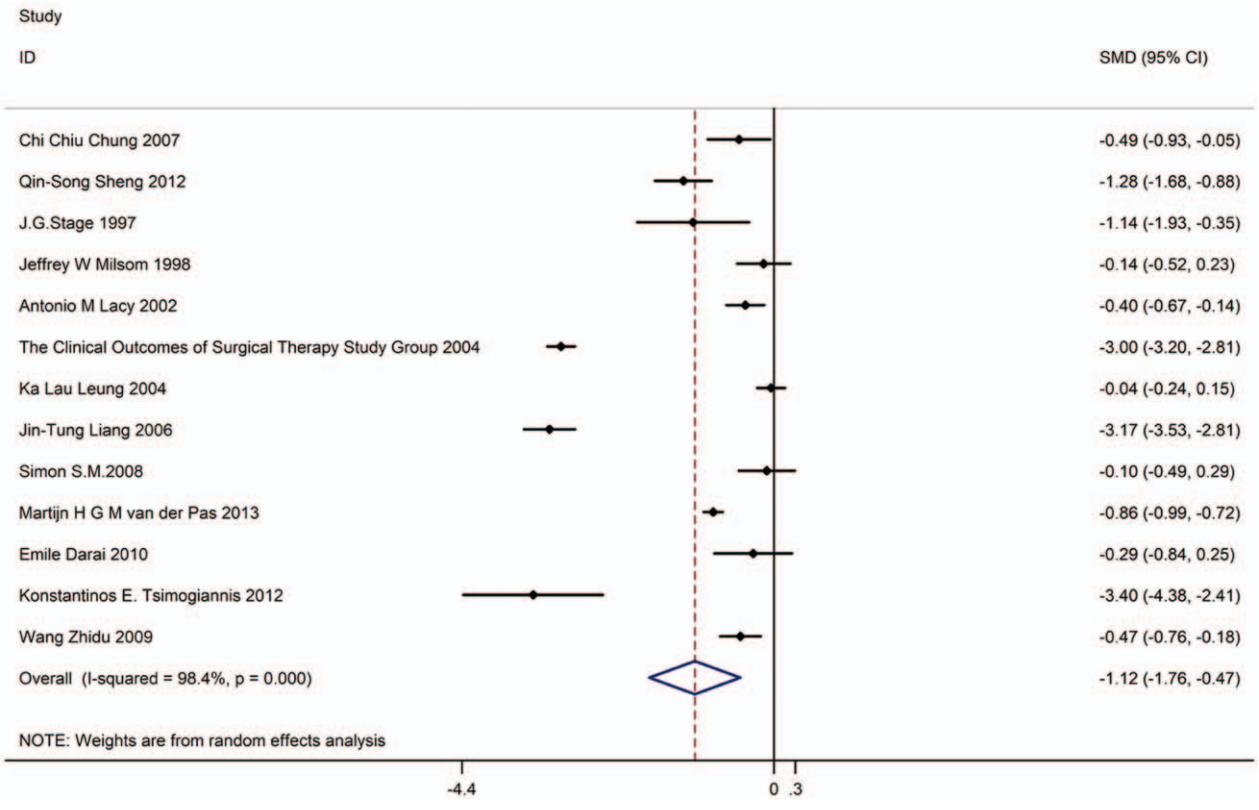

Figure 4. Forest plot showing hospital stay of laparoscopic surgery versus open surgery.

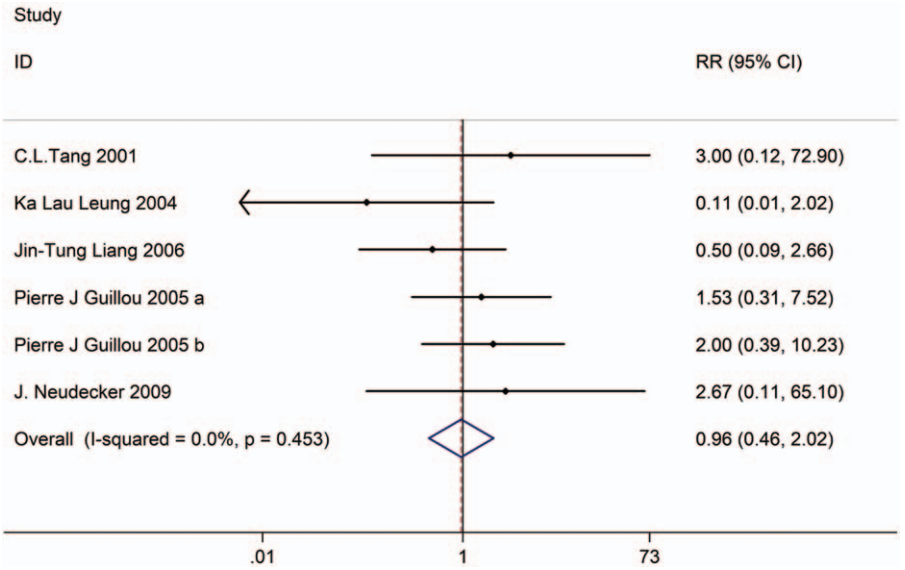

Figure 5. Forest plot showing DVT of laparoscopic surgery versus open surgery. DVT = deep venous thrombosis.

($P = .000$), we chose the random effects model to analyze hospital stay. The pooled results showed that the laparoscopic surgery group significantly decreased hospital stay compared with the open surgery group (SMD: −1.12, 95%CI: −1.76 to −0.47, Fig. 4).

3.5. DVT

Five studies with 1218 patients in the open surgery group and 1577 patients in the laparoscopic surgery group were included. Based on the I^2 test ($I^2 = 0.0\%$) and Chi-squared test ($P = .453$), the fixed effects model was used to analyze DVT. The pooled results showed no significant difference in the incidence of DVT between the 2 groups (RR: 0.96, 95%CI: 0.46–2.02, Fig. 5).

3.6. Postoperative mortality

Nine studies with 2108 patients in the open surgery group and 2470 patients in the laparoscopic surgery group provided data on postoperative mortality. Based on the I^2 test ($I^2 = 0.0\%$) and Chi-squared test ($P = .584$), we chose the fixed effects model to analyze postoperative mortality. The pooled results showed that the laparoscopic surgery group significantly decreased postoperative mortality compared with the open surgery group (RR: 0.60, 95%CI: 0.41–0.86, Fig. 6).

3.7. Postoperative complication

Nineteen studies with 3713 patients in the open surgery group and 4435 patients in the laparoscopic surgery group provided data on postoperative complications. Based on the I^2 test ($I^2 = 56.8\%$) and Chi-squared test ($P = .001$), we chose the random effects model to analyze postoperative complications. The pooled results showed that the laparoscopic surgery group significantly decreased the incidence of postoperative complication compared with the open surgery group (RR: 0.83, 95%CI: 0.72–0.95, Fig. 6).

3.8. Quality and bias assessment

According to the inclusion and exclusion criteria, 24 articles were included in this meta-analysis. Quality assessment and potential bias were accessed by funnel plot, Begg's and Mazumdar's rank test, and Egger's test. The funnel plot for log WMD in operative time of the included studies was notably symmetrical, suggesting that there was no significant publication bias (Fig. 7). Moreover, significant symmetry was determined using Begg's and Mazumdar's rank test ($Z = 0.72$, $P = .469$). However, Egger's test showed no significant publication bias ($P = .276$).

4. Discussion

Colorectal cancer (including colorectal cancer, rectal cancer, and anal cancer) is a common malignant tumor of the digestive tract. It is the third highest malignant tumor in men and the second highest malignant tumor in women worldwide. Colorectal cancer is the most common malignant tumor following lung cancer and breast cancer, which poses a serious threat to human health. In Western developed countries, the incidence of colorectal cancer tends to be stable or even declining with early intervention in the population. However, the incidence of colorectal cancer in the world is still increasing, especially in Japan, South Korea, China, and some Eastern Europe.

In our results, laparoscopic surgery group cost more operative time, less blood loss and less hospital stay than the open surgery group. The results also showed that the laparoscopic surgery group significantly decreased postoperative mortality compared with the open surgery group. At the same time, laparoscopic surgery group significantly decreased the incidence of postoperative complication compared with the open surgery group. Our study have the similar conclusion with other searches.[34,35] Besides, laparoscopic surgery group significantly decreased the incidence of postoperative complication compared with the open surgery group.

There were some similar meta-analyses of open surgery versus laparoscopic surgery for patients with colorectal cancer. Tong et al[34] summarized 9 clinical trials and supported that laparoscopic surgery appears to be a better alternative therapy for patients with colorectal cancer as compared to the open surgery. Zhang et al[35] summarized fifteen publications which

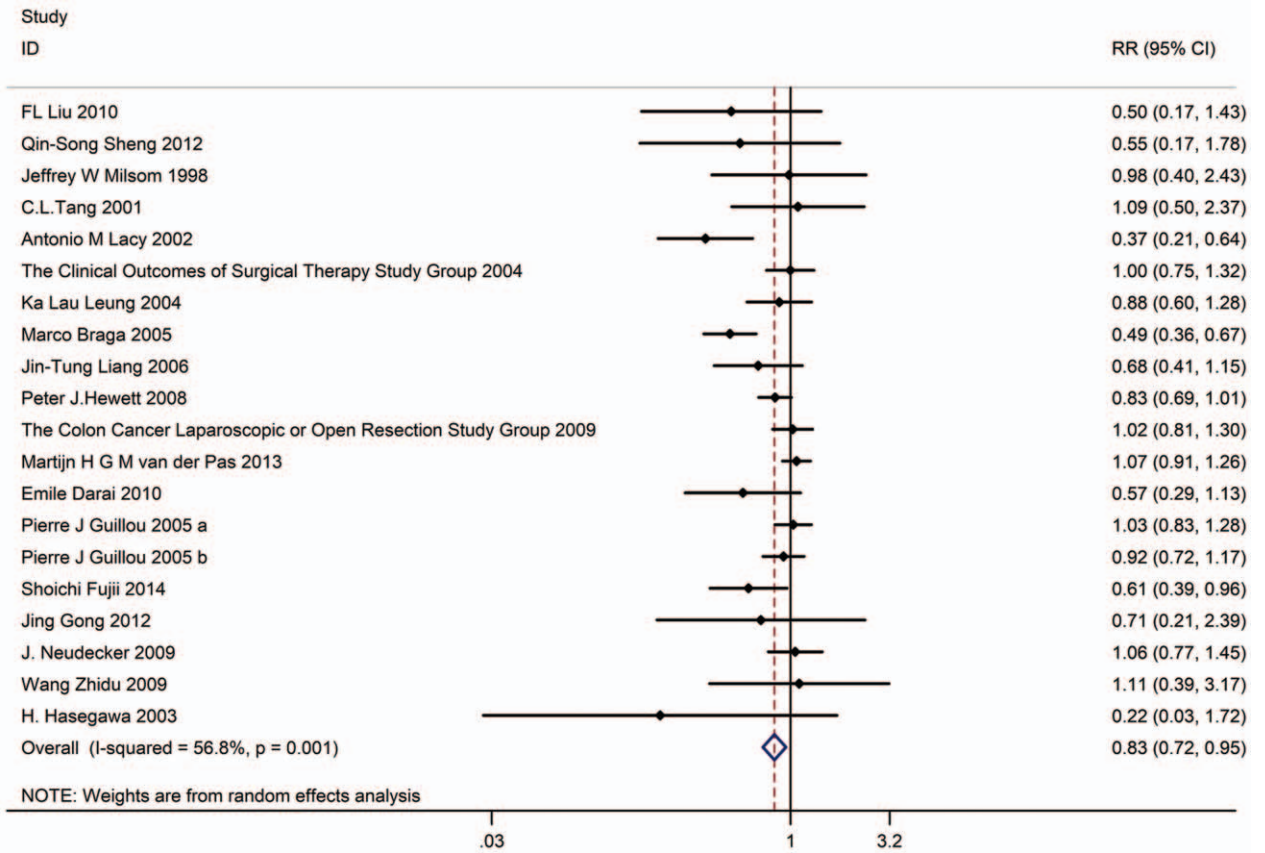

Figure 6. Forest plot showing postoperative complication of laparoscopic surgery versus open surgery.

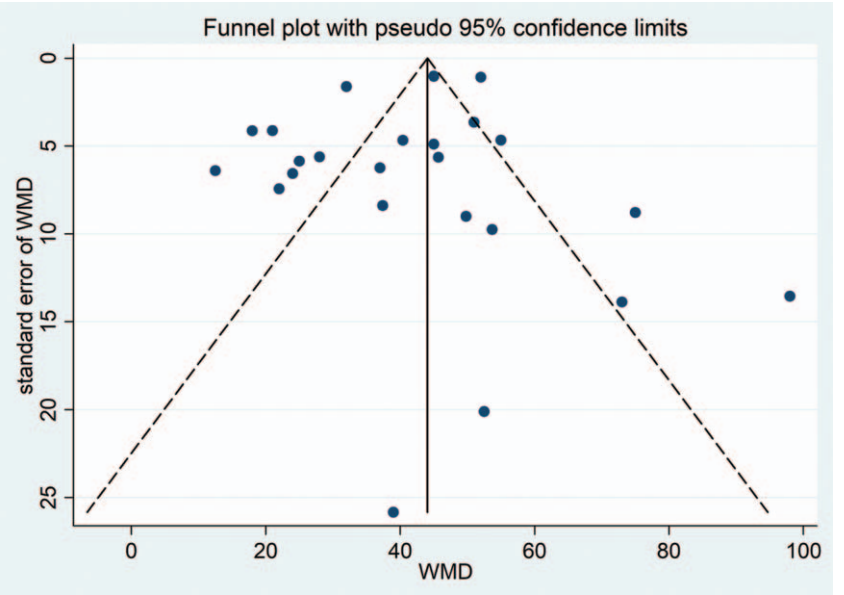

Figure 7. Funnel plot of studies in the meta-analysis.

were published between 2007 and 2017, and reported that hand-assisted laparoscopic surgery (HALS) was associated with shorter hospital days, postoperative hospital duration and so on. No difference was observed in the number of lymph nodes harvested, blood transfusion and so on.

However, in ASCOZOG6051 and ALACART studies,[36,37] they reported that laparoscopy in rectal cancer was not as safe as open surgery. This conclusion is different from our research, which is worth further study.

Admittedly, this meta-analysis had several limitations, such as: differences among patients in the mentioned predefined criteria. Patients' conditions were different in different studies; the surgical techniques in different studies are varied. We used pooled data for further analysis, and individual data were unavailable, which limited for a more comprehensive analysis. Postoperative DVT prophylaxis was not specifically evaluated. The differentiation in types of neoplasms could be analyzed in the future, since the related data was not enough in this article. Nonetheless, the main Jadad score of the included RCTs was more than 3, and no significant publication bias was found among the study, which confirmed our findings.

In conclusion, this systematic review and meta-analysis indeed revealed that laparoscopic surgery has several advantages in decreasing blood loss, hospital stay, postoperative mortality, as well as postoperative complication. Therefore, laparoscopic surgery could be a more effective therapy for patients with colorectal cancer.

Author contributions

Conceptualization: Wei Ye.
Data curation: Wei Ye.
Formal analysis: Zhi-Li Liu.
Methodology: Zhi-Li Liu.
Project administration: Rong Zeng.
Validation: Rong Zeng.
Writing – original draft: Xiao-Jun Song, Chang-Wei Liu.
Writing – review & editing: Xiao-Jun Song, Chang-Wei Liu.

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