Comparison of robot-assisted surgery, laparoscopic-assisted surgery, and open surgery for the treatment of colorectal cancer
A network meta-analysis

Shihou Sheng, PhD⁴, Tiancheng Zhao, PhD⁵, Xu Wang, PhD⁶,⁷

Abstract

Background: The aim of this study was to find the better treatment for colorectal cancer (CRC) by comparing robot-assisted colorectal surgery (RACS), laparoscopic-assisted colorectal surgery (LACS), and open surgery using network meta-analysis.

Methods: A literature search updated to August 15, 2017 was performed. All the included literatures were evaluated according to the quality evaluation criteria of bias risk recommended by the Cochrane Collaboration. All data were comprehensively analyzed by ADDIS. Odds ratio (OR), mean difference (MD), and 95% confidence interval (CI) were used to show the effect index of all data. The degree of convergence of the model was evaluated by the Brooks–Gelman–Rubin method with the potential scale reduction factor (PSRF) as the evaluation indicator.

Results: The PSRF values of operation time, estimated blood loss, length of hospital stay, complication, mortality, and anastomotic leakage ranged from 1.00 to 1.01, and those of wound infection, bleeding, and ileus ranged from 1.00 to 1.02. Open surgery had the shortest operation time compared with LACS and RACS. Furthermore, compared with LACS, the amount of blood loss, complication, mortality, bleeding rate, and ileus rate for RACS were the least, and the length of hospital stay for RACS was the shortest. The anastomotic leakage rate for LACS was the least, but there was no significant difference compared with those of RACS and open surgery. The wound infection rate for LACS was the least, but there was no significant difference compared with that of RACS.

Conclusion: RACS might be a better treatment for patients with CRC.

Abbreviations: CI = confidence interval, CRC = colorectal cancer, LACS = laparoscopic-assisted colorectal surgery, MD = mean difference, OR = odds ratio, PSRF = potential scale reduction factor, RACS = robot-assisted colorectal surgery.

Keywords: colorectal cancer, complication, estimated blood loss, length of hospital stay, network meta-analysis, operation time

Highlights

- Totally, 40 eligible papers published from 1998 to 2017 were included.
- The amount of bleeding and incidence rate of RACS was the least.
- The time of hospitalization of patients with RACS treatment was the shortest.
- RACS might be a better treatment for CRC patients.

1. Introduction

Colorectal cancer (CRC), one of the most common malignancies in the United States, seriously affects the health of people worldwide.

It is the 2nd most commonly diagnosed cancer in women and 3rd in men, with about 571,000 female and 663,000 male patients with CRC in 2012 worldwide.

The relative 5-year survival rate for patients with CRC is 65%, while the 10-year survival rate declines to 58%.

Risk factors for CRC include human papilloma virus infection, long-term constipation, inadequate physical activity, alcohol intake, smoking, and high protein and fat consumption.

Most of the patients with stage I and II CRC have to undergo colectomy, and the patients with stage III CRC receive chemotherapy to lower the risk of recurrence.

However, for CRC survivors, the risk of chronic diarrhea and cancer recurrence is increased. Thus, effective treatment for CRC is needed.

In the early 1990s, laparoscopic surgery was first proposed to be an alternative to open surgery for lesions of the rectum and colon.

Kitano indicated that compared with open surgery, laparoscopic surgery was a standard treatment for colon cancer with shorter hospital stay, faster recovery, improved incidence of wound infection, and decreased pain.

Furthermore, the long-term outcome with laparoscopic surgery has been identified by randomized controlled trials (RCTs). In addition, robotic systems especially Vinci 1 robot, CA, a robot for performing abdominal surgery, have been identified to be an alternative for standard laparoscopic surgery especially in complex pathology.

Robotic total mesorectal...
excision may have a better therapeutic effect than laparoscopic total mesorectal excision, especially in special cases, including low and middle rectal cancer.\cite{16} It is necessary to find optimal surgical methods for the treatment of CRC.

A network meta-analysis gains the certainty of all treatment comparisons by combination of direct and indirect evidence based on the randomized nature of the data.\cite{17} Recently, a network meta-analysis focused on the efficacy of laparoscopic and open surgery in CRC; however, the main outcomes were mortality and complications, and operation time, estimated blood loss, and length of hospital stay were not analyzed.\cite{18} Moreover, there was a rare study about the comparisons of laparoscopic-assisted colorectal surgery (LACS), robot-assisted colorectal surgery (RACS), and open surgery. Therefore, in the present study, we evaluated the curative effect of RACS, LACS, and open surgery on CRC using a network meta-analysis to find the best treatment for CRC. Our finding might provide a basis for the future clinical treatment.

2. Methods

This meta-analysis was performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.\cite{19}

2.1. Data sources

The related clinical researches were obtained from the electronic databases Pubmed (http://www.ncbi.nlm.nih.gov/pubmed/), Embase (http://www.embase.com), and the Cochrane Library (http://www.cochranelibrary.com) updated to August 15, 2017. The keywords were as follows: colorectal cancer (“colorectal cancer” OR “colorectal carcinoma” OR “rectal cancer” OR “rectal carcinoma” OR “colon cancer” OR “colorectal cancer” OR “colorectal carcinoma” OR “carcinoma of colon” OR “colorectal neoplasms”), robot support (“robot” OR “robotic” OR “da vinci” or davinci), laparoscopic support (“Laparoscopies” OR “laparoscopic” OR “laparoscopy”), open surgery (“open” OR “surgery”), and random-control study (Rando*).

2.2. Informed consent and ethical approval

This study was a meta-analysis of several eligible studies downloaded from the public database including PubMed, Embase, and Cochrane library, thus informed consent and ethical approval were not necessary.

2.3. Inclusion and exclusion criteria

Articles meeting the following criteria were selected (based on the PICOS principle): Published English literatures studied the efficacy of RACS, LACS, and open surgery in patients with CRC (P); participants in each group were patients with CRC treated with RACS, LACS, or open surgery (I, C); the outcomes of the study included operation time, estimated blood loss, and the occurrence of complication (O); and the type was a randomized controlled study (S). The following articles were removed: studies with incomplete data or cannot be used for statistical analysis; and literatures such as reviews, reports, comments, and letters. Besides, if multiple literatures were repeatedly published or from the same population data, only the latest research or the research with complete information was included.

![Figure 1. Literature search and study selection.](image-url)
| Study       | Year    | Country | Study year    | Stage | Group | N   | Age   | Gender (M/F) | BMI   |
|------------|---------|---------|---------------|-------|-------|-----|-------|--------------|-------|
| Jiménez Rodríguez | 2011    | Spain   | 2008.1–2009.1 | 0–IV | RACS | 28  | 68±9.1 | 12/16        | 28.5±2.5 |
| Park       | 2012    | Korea   | 2009.9–2011.7 | I–III| RACS | 35  | Mean 62.8 | 14/21        | Mean:24.4 |
| Kim        | 2017    | Korea   | 2012.2–2015.3 | I–II | RACS | 66  | 60.4±9.7 | 51/15        | 24.1±3.3  |
| Hewitt     | 1998    | Hong Kong | NA         | I–III| Open | 8   | 70 (38–77) | 3/5          | NA     |
| Millsom    | 1998    | Germany | 1993.10–1997.7 | I–II | Open | 54  | 69 (44–86) | 36/18        | NA     |
| Schwenk    | 1998    | Japan   | 1995.5–1996.11 | I–III| Open | 30  | 64.8±14.7 | 16/14        | NA     |
| Curet      | 2000    | USA     | 1993.1–1995.11 | NA   | Open | 18  | 69.2 (49–82) | 14/4       | NA     |
| Leung      | 2002    | Spain   | 1993.11–1998.7 | I–IV | Open | 108 | 71±11   | 50/58        | NA     |
| Araujo     | 2003    | Brazil  | 1997.9–2000.9 | I–IV | Open | 15  | 56.4 (24–78) | 10/5       | 25.6 (17.1–38.5) |
| Hasegawa   | 2003    | Japan   | 1998.6–2000.10 | II–III| Open | 26  | 61 (37–78) | 18/8        | NA     |
| Leung      | 2004    | Hong Kong | 1993.9–2002.10 | I–IV | Open | 180 | 66.5±12.3 | 114/86       | NA     |
| COST       | 2004    | USA     | 1994.8–2001.8 | 0–IV | Open | 428 | 69 (29–94) | 208/220     | NA     |
| Kaiser     | 2004    | Taiwan  | 1995.1–2001.2 | I–IV | Open | 20  | 60.5 (42–80) | 9/11       | NA     |
| Zhou       | 2004    | China   | 2001.6–2002.12 | NA   | Open | 89  | 45 (30–81) | 43/46       | NA     |
| Guillou    | 2005    | UK      | 1996.7–2002.7 | I–III| Open | 268 | 69±12    | 123/145     | 26±4    |
| Veldkamp   | 2005    | Canada  | 1997.3–2003.3 | I–IV | Open | 546 | 71 (31–95) | 336/210     | 24.9 (14.5–40.5) |
| Braga      | 2007    | Italy   | 1999.5–2000.5 | I–IV | Open | 85  | 65.3±10.3 | 64/21       | NA     |
| Liang      | 2006    | Taiwan  | 2000.1–2004.6 | I–II | Open | 134 | 64.2±12.0 | 71/83       | 25.6±4.0 |
| Ng         | 2008    | Hong Kong | 1994.9–2005.2 | I–IV | Open | 48  | 63.5±12.6 | 30/18       | NA     |
| Hewett     | 2008    | Australia | 1998.1–2005.4 | I–IV | Open | 298 | 69.4±11.4 | 143/155     | 26.0±4.3 |
| Lujan J    | 2009    | Spain   | 2002.1–2007.2 | I–IV | Open | 103 | 66.0±9.9  | 64/39       | NA     |
| Neudecker  | 2009    | Germany | 1998.9–2004.9 | I–III| Open | 222 | 66.4±11.1 | 116/106     | 25.8±3.2 |
| Kang       | 2010    | Korea   | 2006.4–2009.8 | I–III| Open | 170 | 59.1±9.9  | 110/60      | 24.1±3.2 |
| Liu        | 2010    | China   | 2005.2–2008.10 | NA   | Open | 88  | 61.5±8.9  | 50/38       | 26.1±1.7 |
| Liang      | 2011    | China   | 2004.5–2008.4 | NA   | Open | 174 | 57.3±13.0 | 92/82       | Mean:22.3 |
| Pascual    | 2010    | Spain   | 2004.7–2008.10 | I–IV | Open | 60  | 71.5±5.1  | 33/27       | NA     |
| Vilag      | 2011    | Netherlands | 2005.7–2009.8 | 0–IV | Open | 98  | 66±7.1   | 60/38       | 26.5±5.0 |
| Li         | 2011    | Hong Kong | 1996.7–2005.10 | I–IV | Open | 74  | 68±13.3  | 32/42       | NA     |
| van der Pas | 2013    | Eight countries | 2004.1–2010.5 | I–IV | Open | 345 | 65.8±10.9 | 211/134     | 26.5±4.7 |
| Fujii      | 2014    | Japan   | 2008.8–2012.8 | 0–IV | Open | 100 | 80.1±4.2 | 60/40       | 21.9±3.1 |
| Yamamoto   | 2014    | Japan   | 2004.10–2009.3 | II–IV| Open | 524 | 64 (33–75) | 309/215     | 22.7 (14.0–40.9) |
| Ng         | 2014    | Hong Kong | 2001.8–2007.8 | II–III| Open | 40  | 62.1±12.6 | 22/18       | 22.4±3.2 |
|           |         |         |               |       |      |     |        |              |        |
2.4. Data extraction and quality evaluation of literature

Data were independently extracted from the included literatures by 2 reviewers. For each study, the following data were collected: first author, published year, year of study, area of study, staging of CRC, and the total participants in each group, type of treatment, and general demographic data (e.g., sex, age, and body mass index) of participants in each group. The aggregate quality of the included studies was evaluated according to the quality evaluation criteria of risk bias, recommended by Cochrane Collaboration. Disagreement was resolved by discussions with a third reviewer.

2.5. Statistical analysis

All data were comprehensively analyzed by ADDIS (version 1.16.5, http://www.medfloss.org/node/812). ADDIS is a non-programming software used to assess and process data using Markov chain Monte Carlo theory based on the Bayesian framework. The network meta-analysis of operation time, estimated blood loss, length of hospital stay and complication, mortality, anastomotic leakage, wound infection, bleeding, and ileus was conducted based on the parameter set up in ADDIS software (number of chains, 4; tuning iterations, 20,000; simulation iterations, 50,000; thinning interval, 10; inference samples, 10,000; variance scaling factor, 2.5). Odds ratio (OR), mean difference (MD), and 95% confidence interval (CI) were used to show the effect index of all data. The test models used in this study were the random effects and consistency models. The degree of convergence of the model was evaluated by the Brooks–Gelman–Rubin method with the potential scale reduction factor (PSRF) as evaluation indicator. PSRF values close to 1 indicates better convergence effect of the model, and generally, PSRF values less than 1.2 are acceptable.

3. Results

3.1. Characteristics of the selected literature

A total of 5237 articles (1687 articles came from PubMed database, 2519 from Embase database, and 1031 from the Cochrane Library) were identified based on the literature search criteria. Among them, 1422 articles were repeated, and 3529 articles were irrelevant after reading the title and abstract. In addition, 246 articles (including 71 case series/reports, 102 literature reviews/meta-analyses, 11 reduplicative studies, 38 articles with irrelevant data) of the remaining 286 articles were removed by reviewing the full text. Finally, 40 eligible papers were included (Fig. 1).

In total, 12,825 patients with CRC who were mainly concentrated in the I–III periods in staging of CRC were included in the study, including 5947 patients in the open surgery group, 129 patients in the RACS group, and 6749 patients in the LACS group. Among them, there were more male than female patients (including 7249 male and 5576 female patients), but there was no difference for sex in each literature. The baseline characteristics in each group were comparable in terms of age and body mass index, with old age as the main characteristic. Besides, the areas of these studies were Germany, Japan, the United States, China, Spain, South Korea, and so on (Table 1). The result of RCT quality evaluation showed that the quality of the included literatures was not very good; especially, some of the literatures had no detailed description of the blinding of participants and personnel (performance bias) and blinding of outcome assessment (detection bias, Fig. 2A, B).

3.2. Network meta-analysis of operation time

The PSRF value of operation time ranged from 1.00 to 1.01, indicating complete convergence, good iterative effect, and stable results of the model. The results of the meta-analysis revealed that...
open surgery had the shortest operation time and statistically significant difference compared with LACS (MD = −43.40; 95% CI, −55.24 and −31.78) and RACS (MD = −109.19; 95% CI, −140.16 and −78.96; Table 2, Fig. 3A).

3.3. **Network meta-analysis of estimated blood loss**

The PSRF value of estimated blood loss ranged from 1.00 to 1.01, indicating complete convergence, good iterative effect, and stable results of the model. The results of the meta-analysis revealed that the amount of bleeding for RACS was the least, but there was no significant difference compared with that for open surgery (MD = −97.55; 95% CI, −260.39 and 68.03) and LACS (MD = −21.12; 95% CI, −175.07 and 133.17; Table 3, Fig. 3B).

3.4. **Network meta-analysis of length of hospital stay**

The model of length of hospital stay had complete convergence, good iterative effect, and stable results with the PSRF value = 1.00. The results of the meta-analysis revealed that patients who underwent RACS had the shortest length of hospital stay. It had a statistically significant difference compared with patients who underwent open surgery (MD = −2.90; 95% CI, −5.85 and −0.06), but had no significant difference compared with patients who underwent LACS (MD = −0.34; 95% CI, −2.93 and 2.21; Table 4, Fig. 3C).

3.5. **Network meta-analysis of complication**

The PSRF value of complication ranged from 1.00 to 1.01, indicating complete convergence, good iterative effect, and stable results of the model. The results of the meta-analysis revealed that the complication rate in patients who underwent RACS was the least, but there was no significant difference compared with those in patients who underwent open surgery (OR = 0.62; 95% CI, 0.21 and 1.68) and LACS (OR = 0.79; 95% CI, 0.28 and 2.13; Table 5, Fig. 3D).

3.6. **Network meta-analysis of mortality**

The PSRF value of mortality ranged from 1.00 to 1.01, indicating complete convergence, good iterative effect, and stable results of the model. The results showed that the mortality rate in patients who underwent RACS was the least, but there was no significant difference compared with those in patients who underwent LACS (OR = 0.84; 95% CI, 0.20 and 3.37) and open surgery (OR = 0.66; 95% CI, 0.15 and 2.70; Fig. 3E).

3.7. **Network meta-analysis of anastomotic leakage**

The PSRF value of anastomotic leakage ranged from 1.00 to 1.01, indicating complete convergence, good iterative effect, and stable result of the model. These results revealed that the rate of anastomotic leakage in patients who underwent LACS was the least, but there was no significant difference compared with those in patients who underwent RACS (OR = 0.46, 95% CI: 0.13, 1.58) and open surgery (OR = 0.92; 95% CI, 0.68 and 1.26; Fig. 3F).
3.8. Network meta-analysis of wound infection

The PSRF value of wound infection ranged from 1.00 to 1.02, indicating complete convergence, good iterative effect, and stable result of the model. The results revealed that the rate of wound infection in patients who underwent LACS was the least, and there was a statistically significant difference compared with that in patients who underwent open surgery (OR = 0.65; 95% CI, 0.49 and 0.82), but there was no significant difference compared with that in patients who underwent RACS (OR = 1.09; 95% CI, 0.11 and 8.45; Fig. 3G).

3.9. Network meta-analysis of bleeding

The PSRF value of bleeding ranged from 1.00 to 1.02, indicating complete convergence, good iterative effect, and stable result of the model. Figure 3H shows that the rate of bleeding in patients who underwent RACS was the least, but there was no significant difference compared with those in patients who underwent LACS (OR = 0.82; 95% CI, 0.05 and 20.06) and open surgery (OR = 0.44; 95% CI, 0.02 and 11.69).
3.10. **Network meta-analysis of ileus**

The PSRF value of ileus ranged from 1.00 to 1.02, indicating complete convergence, good iterative effect, and stable result of the model. Figure 3I shows that the rate of ileus in patients who underwent RACS was the least, but there was no significant difference compared with those in patients who underwent LACS (OR = 0.74; 95% CI, 0.20 and 2.05) and open surgery (OR = 0.42; 95% CI, 0.10 and 1.49).

Overall, the treatment effect of RACS was the best.

4. **Discussion**

A network meta-analysis evaluating the curative effect of RACS, LACS, and open surgery was conducted in this study. Our finding revealed that open surgery had the shortest operation time and statistically significant differences compared with LACS and RACS. Furthermore, compared with LACS and open surgery, the amount of bleeding and complication, mortality, bleeding, and ileus rates in RACS were the least, and the length of hospital stay in RACS was the shortest. However, in estimated blood loss and complication, there was no significant difference in RACS compared with open surgery and LACS, and in length of hospital stay, a statistically significant difference was found in RACS and open surgery but not in LACS.

The rate of anastomotic leakage in patients who underwent LACS was the least, but there was no significant difference compared with those in patients who underwent RACS and open surgery. The rate of wound infection in patients who underwent LACS was the least, but there was no significant difference compared with that in patients who underwent RACS.

The popularity of RACS, one of the latest developments in laparoscopic surgery, has been increasing since it was first performed in cholecystectomy in 2001. The surgical technique is improved by the properties of the robot system such as ambidextrous capability, 3-dimensional view, and tremor elimination. Similar to our study, previous studies reported that RACS had the longest operation time. However, it is worth noting that the operation time of RACS is minimal in more complex pelvic processes. Patients who underwent RACS and LACS have a similar quality of life, bowel function recovery, and postoperative morbidity. However, the autonomy of RACS is

| Table 3 | Results of meta-analysis in estimated blood loss. |
|---------|--------------------------------------------------|
| LACS    | 76.10 (19.99, 131.94)                             |
| −76.10 (−131.94, −19.99) | Open −97.55 (−260.39, 68.03) |
| 21.12 (133.17, 175.07)     | RACS 97.55 (68.03, 260.39) |

LACS = laparoscopic-assisted colorectal surgery, RACS = robot-assisted colorectal surgery.

| Table 4 | Results of meta-analysis in length of hospital stay. |
|---------|--------------------------------------------------|
| LACS    | 2.58 (1.32, 3.87)                                |
| −2.58 (−3.87, −1.32) | Open −2.90 (−5.85, −0.06) |
| 0.34 (−2.21, 2.93)     | RACS 2.90 (0.06, 5.85)  |

LACS = laparoscopic-assisted colorectal surgery, RACS = robot-assisted colorectal surgery.
better than that of LACS.[16] A previous study mentioned that the cost of RACS was much higher than that of LACS.[46] Park et al. suggested that the duration of surgery in the RACS group was longer than that in the LACS group, while the number of lymph nodes harvested, resection margin clearance, postoperative pain score, surgical complications, and hospital stay were similar.[143] The operation times were reported to be significantly longer in patients treated with robotic device than that treated with laparoscopy, whereas there were no differences between the 2 groups with regard to complications and hospital stay,[12] which was similar to our results. Two series comparing RACS and LACS in right colectomy have demonstrated that RACS has a longer case time and higher total hospital cost than LACS but similar estimated blood loss and length of hospital stay.[69] It is longer case time and higher total hospital cost than LACS but LACS in right colectomy have demonstrated that RACS has a similar estimated blood loss and length of hospital stay. Two series comparing RACS and LACS in right colectomy have demonstrated that RACS has a longer case time and higher total hospital cost than LACS but similar estimated blood loss and length of hospital stay.[69] It is longer case time and higher total hospital cost than LACS but LACS in right colectomy have demonstrated that RACS has a similar estimated blood loss and length of hospital stay.

### Table 5

|          | LACS | Open | RACS |
|----------|------|------|------|
| 0.78     | 0.67 | 0.88 | 0.62 |
| 1.26     | 0.47 | 3.54 | 1.62 |

LACS = laparoscopic-assisted colorectal surgery, RACS = robot-assisted colorectal surgery.

# Author contributions

**Conceptualization:** Shihou Sheng.

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**Formal analysis:** Xu Wang.

**Methodology:** Xu Wang.

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