Hand-assisted laparoscopic surgery versus conventional open surgery in intraoperative and postoperative outcomes for colorectal cancer
An updated systematic review and meta-analysis

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Abstract

\textbf{Aim:} This meta-analysis aims to compare hand-assisted laparoscopic surgery (HALS) and conventional open surgery (OS) for colorectal cancer (CRC) in terms of intraoperative and postoperative outcomes, and to explore the safety, feasibility of HALS for CRC surgery.

\textbf{Methods:} A systematic literature search with no limits was performed in PubMed, Embase, and Medline. The last search was performed on April 23, 2017. The outcomes of interests included intraoperative outcomes (operative time, blood loss, length of incision, transfusion, and lymph nodes harvested), postoperative outcomes (length of hospital stay, length of postoperative hospital stay, time to first flatus, time to first liquid diet, time to first soft diet, time to first bowel movement, postoperative complications, reoperation, ileus, anastomotic leakage, wound infection, urinary complication, pulmonary infection, and mortality).

\textbf{Results:} Fifteen articles published between 2007 and 2017 with a total of 1962 patients with CRC were included in our meta-analysis. HALS was associated with longer operative time, less blood loss, smaller length of incision, shorter hospital days and postoperative hospital days, less time to first flatus, less wound infection, and less postoperative complications. There was no difference in blood transfusion, lymph node harvested, time to first liquid or soft diet, time to first bowel movement, reoperation, ileus, anastomotic leakage, pulmonary infection, urinary complications, or mortality.

\textbf{Conclusions:} Our meta-analysis suggests that HALS in CRC surgery improves cosmesis and results in better postoperative recovery outcomes by reducing postoperative complications and hospital days. Furthermore, a large randomized control study is warranted to compare the short-term and long-term outcomes of those 2 techniques for CRC treatment.

\textbf{Abbreviations:} BMI = body mass index, CRC = colorectal cancer, HALS = hand-assisted laparoscopic surgery, LAS = laparoscopic surgery, OS = open surgery, PAS = previous abdominal surgery.

\textbf{Keywords:} colorectal cancer, conventional open surgery, hand-assisted laparoscopic surgery, outcomes

1. Introduction

Colorectal cancer (CRC) has become the third most common tumor in the world.\textsuperscript{[1–3]} Up to now, radical surgery is still the best choice for the treatment of CRC.\textsuperscript{[4]} In the past decades, several minimally invasive techniques have been increasingly used to colorectal surgery including conventional laparoscopic surgery (LAS), hand-assisted laparoscopic surgery (HALS), robotic surgery, and single-pore LAS.\textsuperscript{[5–10]}

Compared to conventional open surgery (OS), LAS has advantages in smaller incision length, less blood loss and pain, quicker recovery, and so on.\textsuperscript{[11,12]} However, LAS also has some limitations. Several previous studies demonstrated that LAS needed a significant longer operative time than OS in CRC. Besides, LAS is a complex procedure and will take a longer learning curve for clinicians. When it comes to large and heavy tumors, LAS becomes troublesome for dissection due to the lack of tactile feedback and adequate exposure.\textsuperscript{[11,13]} These conditions have stimulated the development of HALS.

HALS for CRC was firstly proposed in 1994.\textsuperscript{[14]} It is a minimally invasive technique which combines the features of LAS and OS. The most outstanding advantage of HALS is that surgeons can put a hand into the abdominal cavity through the hand-access device to help retraction and dissection. In addition, the specimen can be extracted from the incision which is created for the hand-access device.\textsuperscript{[11,12,13]} However, the safety and feasibility should be assessed before it can be widely accepted and used. Some studies have compared the outcomes of HALS and OS for CRC. However, the results may be different from each other.\textsuperscript{[11,16]} So we conduct this meta-analysis to compare the clinical outcomes between HALAS and OS for CRC.
We have also noticed some previous meta-analysis. However, one was LAS not HALS versus OS for rectal cancer\cite{17} and another was HALS versus OS for gastric cancer.\cite{18} Besides, we have included far more studies and patients than the previous similar meta-analysis.\cite{19} So we think our meta-analysis is different from previous studies.

2. Materials and methods

2.1. Study selection

We did a systematic literature searching in PubMed, Medline, and Embase for studies comparing HALS and OS in colorectal surgery. The search strategy included terms “hand-assisted laparoscopic surgery or hand-assisted laparoscopy” and “open or laparotomy” and “colorectal cancer or colorectal carcinoma or colon cancer or colon carcinoma or rectal cancer or rectal carcinoma.” The last research was performed on April 23, 2017. We also performed a manual search of references of articles and reviews for additional potentially eligible studies. The ethical approval was not necessary because this study was a meta-analysis.

2.2. Inclusion and exclusion criteria

The inclusion criteria for this meta-analysis were as follows: case-control study (HALS vs. OS); CRC; studies with total sample size more than 20; and intraoperative and/or postoperative outcomes were reported. The exclusion criteria studies were as follows: correspondences; review articles; studies including benign diseases; animal studies; single-arm studies; and studies not in English.

2.3. Data extraction

Two authors (XZ and QW) reviewed all the identified articles independently. They would solve the discrepancies by discussion first and a third reviewer (ZW) would be required if necessary. We extracted the following items from each study: first author’s name, year of publication, country, publication type, study type, bowel preparation, location of disease, number of total patients in each arm, numbers of male gender, age, body mass index (BMI), tumor stage, surgical procedure, previous abdominal surgery (PAS), and outcomes of interests.

2.4. Outcomes of interests

Intraoperative outcomes: operative time, blood loss, lymph node harvested, incision length, and blood transfusion.

Postoperative outcomes: hospital day, postoperative hospital day, time to first flatus, time to first liquid diet, time to first soft diet, time to first bowel movement, reoperation, ileus, anastomotic leakage, wound infection, pulmonary infection, urinary complication, postoperative complication, and mortality.

2.5. Quality assessment

The methodological quality of the enrolled retrospective studies was assessed using the revised and modified grading system of the Scottish Intercollegiate Guidelines Network.\cite{20} Articles achieving \(<8\) scores, \(8\) to \(14\) scores, and more than \(14\) scores (total score, \(20\)) were defined as poor quality, fair quality, and good quality, respectively. And the methodological quality of the randomized controlled trials was assessed by modified Jadad score system (total score, \(5\); 1 to \(2\), low quality; \(3\) to \(5\), high quality).\cite{21}

2.6. Statistical analysis

All data analyses were conducted using the Review Manager version 5.0 (The Cochrane Collaboration, Software Update, Oxford) and \(P<.05\) was considered statistically significant. Weighted mean difference (WMD) or standard mean difference (SMD) was calculated for the continuous outcomes, and pooled odds ratios (OR) or risk ratios (RR) were calculated for the dichotomous outcomes. For continuous outcomes, if the study only provided means and range values or median and range values, the means and standard deviations were calculated using methods described by Hozo et al.\cite{22} Chi-squared test and Higgins I-squared test were used for heterogeneity test. A value of \(P<.05\) and \(I^2>50\%\) was regarded as existing heterogeneity. If \(I^2>50\%\) and \(P<.05\), a random-effects model was applied. Correspondingly, if \(I^2<50\%\) and \(P>.05\), a fixed-effects model was applied. Begg funnel plot was used to evaluate publication bias.

3. Results

The procedure and result of literature search was shown in Fig. 1. A total of 249 studies were obtained from the original search algorithm. There remained 150 studies after removing duplications. After reviewing the titles and abstracts, only 31 relevant studies were further evaluated. There was no additional article identified from other sources. Among the 31 studies, 16 reports were excluded due to the following reasons: 6 studies included benign diseases; 5 studies were lack of independent data of HALS; 1 study had too small simple size; 1 study compared the outcome of LAS and OS; and 3 studies were review or correspondence. Thus, 15 articles\cite{21-37} published between 2007 and 2017 were included in our meta-analysis finally. Three\cite{30,35,36} of the 15 articles were randomized controlled trial. The characteristics of the included studies were summarized in Table 1. A total of 1962 patients (900 by HALS and 1062 by OS) were enrolled.

3.1. Patient demographics

There was no significant difference between the 2 groups in age (\(P=.13\), WMD = –1.12, confidence interval [CI –2.58, 0.33], \(I^2=55\%\)), male gender (\(P=.18\), OR = 1.15, CI [0.94, 1.90], \(I^2=0\%\)), or BMI (\(P=.65\), WMD = –0.12, CI [–0.66, 0.40], \(I^2=65\%\)). In addition, surgical procedures and tumor stage were similar in both groups.

3.2. Quality of included studies

The scores of methodological quality assessment of the enrolled retrospective studies were shown in Table 2 and the scores of randomized controlled trial were shown in Table 3. Of those 15 articles, 11 retrospective studies\cite{23-28,31-34,37} had fair quality (8–14 scores). Three randomized controlled trials\cite{30,35,36} had low quality (all were 2 scores). One other study\cite{29} was perspective but nonrandomized so we did not assess the quality.

3.3. Meta-analysis of intraoperative outcomes

There was no significant difference between HALS and OS in lymph node harvested (\(P=.25\), WMD = 0.76, 95\% CI [–0.53, 1.95].
Table 1

Characteristics of the included studies.

| Authors        | Year | Country | Publication type | Study type | Bowel preparation | Location | Disease | No. of patients | Gender (male) | Age | BMI |
|----------------|------|---------|------------------|------------|-------------------|----------|---------|----------------|---------------|-----|-----|
| Li              | 2015 | China   | Article          | RCCS       | Yes               | Right colon | Malignant | 10             | 6             | 14  | 64.5 ± 9.7 |
| Tajima          | 2014 | Japan   | Article          | RCCS       | NR                | Colon     | Malignant | 88             | 14            | 86  | 62.3 ± 10.2 |
| Sheng           | 2017 | China   | Article          | RCCS       | Yes               | Right colon | Malignant | 78             | 40            | 82  | 60.1 ± 10.8 |
| Li              | 2012 | China   | Article          | RCCS       | NR                | Colon     | Malignant | 42             | 23            | 25  | 62.0 ± 10.3 |
| Nam             | 2013 | Korea   | Article          | RCCS       | NR                | Sigmod colon | Malignant | 26             | 17            | 34  | 60.0 ± 12.6 |
| Osarogiagbo     | 2007 | USA     | Article          | RCCS       | NR                | Colon     | Malignant | 39             | 55            | —   | 71.0 ± 8.8  |
| Zhou            | 2015 | China   | Article          | PNCT       | Yes               | Rectum    | Malignant | 116            | 68            | 71  | 61.1 ± 11.2 |
| Liu             | 2012 | China   | Article          | RCCS       | NR                | Colon     | Malignant | 88             | 56            | 50  | 60.1 ± 10.4 |
| Nam             | 2013 | Korea   | Article          | RCCS       | NR                | Colon     | Malignant | 78             | 72            | 43  | 62.3 ± 10.2 |
| Liu             | 2010 | China   | Article          | RCCS       | NR                | Colon     | Malignant | 88             | 56            | 50  | 60.1 ± 10.8 |
| Gezen           | 2013 | USA     | Article          | RCCS       | NR                | Rectosigmod | Malignant | 25             | 11            | 18  | 67.2 ± 11.1 |
| Sm              | 2013 | Korea   | Article          | RCCS       | NR                | Right colon | Malignant | 16             | 9             | 18  | 61.0 ± 11.6 |
| Takakura        | 2009 | Japan   | Article          | RCCS       | NR                | Transverse colon | Malignant | 22             | 14            | 15  | 63.0 ± 14.5 |
| Zhu             | 2014 | China   | Article          | RCCS       | NR                | Rectosigmod | Malignant | 78             | 45            | 43  | 57.1 ± 11.6 |
| Chung           | 2007 | Hong Kong | Article       | PRCT       | Yes               | Rectum    | Malignant | 41             | 25            | 26  | 67.2 ± 12.3 |
| Sheng           | 2012 | China   | Article          | PRCT       | Yes               | Right colon | Malignant | 59             | 32            | 35  | 62.4 ± 12.8 |
| Jadlowiec       | 2014 | USA     | Article          | RCCS       | NR                | Colonrectum | Malignant | 152            | 77            | 78  | 64.7 ± 3.4  |

Stage

| Authors      | HALS | Open | No. of patients | Gender (male) | Age | BMI |
|--------------|------|------|-----------------|---------------|-----|-----|
| Li           | I 2, II 8, III 16 | — | 9, II 16 | — | 14 | 64.5 ± 9.7 |
| Tajima       | — | — | — | — | — | — |
| Sheng        | I 9, II 35, III 34 | I 11, II 30, III 31 | — | — | — | — |
| Li           | I 4, II 20, III 18 | I 13, II 22, III 20 | — | — | — | — |
| Nam          | 0.2, I 11, II 4, III 9 | 0.5, I 16, II 13, III 18 | — | — | — | — |
| Osarogiagbo  | 0.9, I 19, II 12, III 9 | 0.6, I 12, II 20, III 17 | — | — | — | — |
| Zhou         | I 30, II 45, III 41 | I 32, II 41, III 43 | — | — | — | — |
| Liu          | 0.1, II 7, III 6 | 0.1, II 12, III 12 | — | — | — | — |
| Gezen        | 0, I 19, II 3, III 4 | 0.2, I 18, II 14, III 9 | — | — | — | — |
| Sm           | I 12, II 4, III 5, IV 1 | I 13, II 8, III 12, IV 0 | — | — | — | — |
| Takakura     | — | — | — | — | — | — |
| Zhu          | — | — | — | — | — | — |
| Chung        | — | — | — | — | — | — |
| Sheng        | 1, II 25, III 27, IV 0 | I 11, II 24, III 22, IV 0 | — | — | — | — |
| Jadlowiec    | 0.29, I 37, II 29, III 47, IV 10 | 0.19, I 36, II 52, III 75, IV 22 | — | — | — | — |

Surgical procedures

| Authors | HALS | Open | No. of patients | Gender (male) | Age | BMI |
|---------|------|------|-----------------|---------------|-----|-----|
| —       | — | — | — | — | — | — |

PAS

| Authors | HALS | Open | No. of patients | Gender (male) | Age | BMI |
|---------|------|------|-----------------|---------------|-----|-----|
| —       | — | — | — | — | — | — |

APE = abdominopерineal excision, AR = anterior resection, BMI = body mass index, HALS = hand-assisted laparoscopic surgery, LAR = low anterior resection, LH = left hemicolectomy, NR = not report, PAS = previous abdominal surgery, PNCT = prospective nonrandomized controlled trials, PRCT = prospective randomized controlled trials, RCCS = retrospective case-control study, RH = right hemicolectomy, TC = transverse colectomy.
2.06] $I^2 = 77\%$) or blood transfusion ($P = .14, OR = 0.37, CI [0.10, 1.38], I^2 = 0\%$). However, although there existed heterogeneity, we observed a significant longer operative time ($P = .009, WMD = 14.97, CI [3.78, 26.15], I^2 = 92\%$), less blood loss ($P < .001, WMD = -0.68, CI [-1.08, -0.29], I^2 = 92\%$), and smaller incision length ($P < .001, WMD = -9.82, CI [-10.76, -8.89] I^2 = 95\%$) in HALS group (Fig. 2).

### 3.4. Meta-analysis of postoperative outcomes

The results demonstrated that HALS had shorter hospital day ($P < .001, WMD = -2.10, CI [-2.82, -1.37], I^2 = 83\%$), postoperative hospital day ($P < .001, WMD = -2.92, CI [-4.15, -1.83], I^2 = 77\%$), and time to first flatus ($P < .001, SMD = -1.81, CI [-2.76, -0.86], I^2 = 97\%$). Besides, there existed less wound infection ($P = .008, OR = 0.53, CI [0.33, 0.84], I^2 = 0\%$) and postoperative complications ($P = .007, OR = 0.61, CI [0.42, 0.87], I^2 = 0\%$) in HALS group. Nevertheless, we observed no significant difference in terms of time to first liquid diet ($P = .31, WMD = -0.31, CI [-0.92, 0.29], I^2 = 83\%$), time to first soft diet ($P = .15, WMD = 0.42, CI [-0.16, 1.00], I^2 = 0\%$), time to first bowel movement ($P = .25, WMD = -0.57, CI [-1.54, 0.40], I^2 = 77\%$), reoperation ($P = .75, OR = 1.20, CI [0.40, 3.64], I^2 = 0\%$), ileus ($P = .16, OR = 1.53, CI [0.84, 2.77], I^2 = 0\%$), anastomotic leakage ($P = .24, OR = 0.66, CI [0.33, 1.31], I^2 = 0\%$), pulmonary infection ($P = .05, OR = 0.40, CI [0.16, 0.99], I^2 = 0\%$), urinary complication ($P = .75, OR = 0.90, CI [0.48, 1.71], I^2 = 0\%$), or mortality ($P = .63, RR = 0.69, CI [0.16, 3.05], I^2 = 0\%$) between HALS and OS groups (Fig. 3).

### 3.5. Subgroup analysis of HALS versus OS for colon cancer

We did a subgroup analysis to compare the results of HALS and OS in patients with colon cancer. Nine studies were enrolled (333 by HALS and 412 by OS). We observed that HALS group had longer operative time ($P < .001, WMD = 18.53, CI [7.21, 29.84], I^2 = 84\%$), less blood loss ($P = .03, SMD = -0.51, CI [-0.96, -0.06], I^2 = 83\%$), smaller incision length ($P < .001, WMD = -10.39, CI [-12.35, -8.42], I^2 = 97\%$), shorter hospital day ($P < .001, WMD = -2.18, CI [-3.13, -1.23], I^2 = 61\%$), postoperative hospital day ($P < .001, WMD = -6.39, CI [-8.03,
-4.75, I² = 22%), and time to first flatus (P = .003, WMD = 2.15, CI [-3.56, -0.75], I² = 95%), less wound infection (P = .03, OR = 0.36, CI [0.14, 0.93], I² = 0%), and postoperative complication (P = .008, OR = 0.46, CI [0.26, 0.82], I² = 0%) (Table 4).

3.6. Publication bias

A funnel plot of the studies reporting on postoperative complications shows that there was no obvious publication bias among the studies (Fig. 4).

4. Discussion

Since the first report of HALS for CRC in 1994, it has been increasingly used in colorectal surgery. Although several studies have demonstrated the advantages of HALS, there still exists controversy about HALS. In our meta-analysis including 15 studies with 1962 patients, HALS group revealed a significantly less blood loss and smaller incision length, which are in line with the previous meta-analysis and reviews. This demonstrated that HALS can improve cosmesis for patients compared with OS.
Figure 3. Meta-analysis of postoperative outcomes. HALS = hand-assisted laparoscopic surgery.
Figure 3. (Continued.)
Interestingly, different from previous meta-analysis,[19] we observed significantly longer operative time in HALS group. This result is supported by some other reviews.[6,16] Ding et al thought that the operative time of HALS was related with technique skills and case accumulation.[19] However, we hold the opinion that HALS was belong to minimally invasive technique though it had part feature of OS. When performing HALS, surgeons can put one hand into abdominal cavity to assist dissection but both 2 hands to assist in OS. So HALS needs longer time than OS in CRC surgery.

Against previous meta-analysis,[19] there was no significant difference in ileus. The possible reason is that the occurrence of ileus is a complex procedure and many factors can contribute to it.[42] In colorectal surgery, both HALS and OS need a mobilization of the intestine which may be similar in the 2 groups. In addition, the similar results in time to first liquid diet, time to first soft diet, and time to first bowel movement of the 2 groups can also account for it. Although we observed significant less time to first flatus in HALS group, we thought that patients in HALS group had smaller incision length and less postoperative pain, so they could perform off-bed activities earlier which was beneficial to the recovery of intestinal function.

In line with previous review and meta-analysis,[6,19] there was no difference in lymph node harvested. We explained it that both HALS and OS need follow the principles of oncologic surgery. No significant difference was observed in blood transfusion, it might be because of the ability to rapidly control of unexpected bleeding by electrocaugulation equipment. In general, HALS has an incision of about 5 to 8 cm which is smaller in OS.[11,43] It will help to reduce the incidence of wound infection. So, we observed a significant less wound infection in HALS group. Besides, HALS group suggested significant shorter hospital days and postoperative hospital days, which are controversial in previous review.[39] The possible reason is that patients in HALS group had smaller incision length, faster recovery of gastrointestinal function, and lower incidence of wound infection or postoperative complications. Furthermore, no significant difference was observed in terms of reoperation, anastomotic leakage, pulmonary infection, urinary complication, or mortality. This might due to the advance of nursing level.

In the subgroup analysis of colon cancer, HALS can also improve cosmesis and result in better postoperative recovery outcomes. In addition, HALS can reduce the risk of postoperative complications. In regard to oncological outcomes, the result showed no significant difference in lymph node harvested of the 2 groups. The possible reason was that the 2 groups followed the similar dissection, mobilization, and vascular ligation which were based on the oncological principles.[44] We did not analyze the survival of cancer patients due to only 2 studies reporting the survival data and the survival outcomes could not be estimated for there was no death case in 1 article’s HALS group.

The strength of this meta-analysis: our meta-analysis included more articles and more patients than previous studies; we analyzed intraoperative and postoperative outcomes, and the pooled data showed that compared with OS, HALS could provide a smaller length of incision and faster postoperative recovery; our meta-analysis only included malignant diseases; and we also conducted subgroup analysis of HALS versus OS for colon cancer.

Some limitations of this study have to be highlighted. First, there existed high heterogeneity in some analyses. Though the sensitivity analysis was conducted by removing 1 study each time, the outcomes remained unchanged. We thought that it might be
influenced by many factors, such as the experience of surgeon, locations of diseases, bowel preparation, tumor stage and size, PAS, and so on. Second, most of the enrolled articles were retrospective studies. This might induce patient selection bias though there were 3 randomized controlled trials. And third, we did not compare survival outcomes for we could not get enough data from the included studies.

In conclusion, our meta-analysis suggests that the HALS in CRC surgery improves cosmosis and results in better postoperative recovery outcomes by reducing postoperative complications and hospital day. Furthermore, a large randomized control study is warranted to compare the short-term and long-term outcomes of those 2 techniques for CRC treatment.

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