Is the laparoscopic approach for rectal cancer superior to open surgery? A systematic review and meta-analysis on short-term surgical outcomes

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Abstract
Introduction: Over the past years the incidence of colorectal cancers has increased worldwide. Currently it is the most common gastrointestinal malignancy worldwide. The laparoscopic approach has become the gold standard for surgical treatment. However, a recently published meta-analysis showed no difference in short- and long-term oncological outcomes of laparoscopy for treating rectal cancer.

Aim: To assess current literature on short-term outcomes of rectal cancer treatment using laparoscopic surgery in comparison to the open approach.

Material and methods: We performed a systematic review and meta-analysis according to the PRISMA guidelines. The primary outcomes of interest were morbidity and short-term complications.

Results: We identified 4,328 potential references. In the end we included 13 randomized controlled trials (RCTs). We did not find any significant differences in terms of morbidity, haemorrhage, ureter injury, anastomotic leakage, mortality, intra-abdominal abscess or postoperative ileus. We found significant differences in the rate of surgical site infections, operative time, blood loss, length of hospital stay and time to first bowel movement.

Conclusions: This systematic review based on available RCTs confirms that laparoscopic rectal cancer surgery is associated with short-term outcomes comparable to the open approach. Moreover, in some aspects it provides better results (e.g. functional postoperative recovery, lower rate of surgical site infections (SSIs)). The quality of evidence is high; therefore in our opinion it is very unlikely that future trials will alter these results, and for this reason the laparoscopic approach can be considered the gold standard for the treatment of the majority of patients.

Key words: laparoscopy, rectal cancer, short-term outcomes.

Introduction
Over the past years the incidence of colorectal cancers has increased worldwide. Currently it is the most common gastrointestinal malignancy worldwide. Approximately one third of all large bowel cancers are located in the rectum [1]. So far, the primary treatment option for rectal adenocarcinoma remains surgery, supported by neoadjuvant and adjuvant therapy [2, 3].

Since the development of laparoscopic surgery, the minimally invasive approach for rectal opera-
tions has been rapidly replacing open procedures [4]. There have been many studies reporting better short-term outcomes after laparoscopic surgery such as lower morbidity, reduced blood loss, reduced pain and faster recovery [5]. Moreover, the operative technique is constantly modified in order to improve postoperative and oncological outcomes [6]. Although according to many surgeons, laparoscopy should be considered the gold standard for the treatment of rectal cancers, the results of recently published well-designed randomized controlled trials, such as COLOR II, ALACART, and ACOSOG Z6051, surprisingly showed no significant differences in terms of short-term morbidity between laparoscopy and open surgery, with very narrow 95% confidence intervals [7–9]. In addition, a recently published meta-analysis including randomized controlled trials showed no difference in short- and long-term oncological outcomes of laparoscopy for treating rectal cancer [10]. This raises the question whether in the era of modern perioperative care laparoscopy is still advantageous in terms of short-term outcomes.

Aim

Therefore, we aimed to answer whether laparoscopic surgery is clinically justified based on the highest quality studies.

Material and methods

Search strategy

A search was conducted by three researchers (MM, JW and GT) in November 2017 of Medline, Embase and the Cochrane library covering the period from January 1966 to November 2017. Aiming for the highest possible comprehensiveness of our review, our search had no language limitations. The full search strategy for the OVID platform is available in Figure 1. Reference lists of relevant publications were assessed for additional studies of interest. Furthermore, bibliographies from previous systematic reviews or meta-analyses on the subject were searched.

A paper was included when: the study concerned adult patients who underwent colorectal surgery for neoplasm and reported short-term morbidity. Included studies had to be randomized controlled trials (RCTs). All criteria mentioned above were required to enrol a study for further evaluation. Exclusion criteria were: the study was a review, guidelines, single group or non-randomized study.

Three researchers (MM, JW and GT) identified and selected citations from the search independently. In case of doubt about inclusion, a third reviewer was consulted (PM or MP) until a consensus was reached. Data from included studies were extracted independently by the three researchers. Study quality and risk of bias were assessed using The Cochrane Collaboration’s tool for assessing risk of bias.

Outcome measures

The primary outcome measures of this systematic review were overall short-term morbidity including intraoperative haemorrhage, ureter injury, anastomotic leakage, mortality, intra-abdominal abscesses, surgical site infections and postoperative ileus rate. Secondary outcomes were operative time, blood loss, length of hospital stay, and time to first flatus.

Statistical analysis

Analysis was performed using RevMan 5.3 (free-ware from The Cochrane Collaboration). Statistical
Table I. Baseline characteristics

| First author (trial name) | Year | Single or multicenter design (SC/MC) | Tumor stage exclusion criteria | Number of participants LAP/OPEN (n) | Mean age LAP/OPEN [years] | Mean distance of the tumor to anal verge LAP/OPEN [cm] | Types of surgery | Neoadjuvant treatment LAP/OPEN n (%) | Ileostomy LAP/OPEN n (%) | Conversion rate n (%) |
|---------------------------|------|--------------------------------------|--------------------------------|-----------------------------------|---------------------------|-----------------------------------------------------|-----------------|------------------------------------|------------------------|----------------------|
| Araujo 2003 SC Astler-Coller D | 2003 | SC | Astler-Coller D | 13/15 | 19/28 | 59.1/56.4 | ND | APR | 15/15 | ND | 0 |
| Zhou 2004 SC Dukes D | 2004 | SC | Dukes D | 82/89 | 82/89 | 44.0/45.0 | ND | TME | ND | ND | ND |
| Guillou (CLASICC) 2005 MC Acute intestinal obstruction | 2005 | MC | Acute intestinal obstruction | 253/128 | ND | ND | ND | TME, APR | ND | ND | 86 (34) |
| Braga 2006 SC T4 | 2006 | SC | T4 | 83/85 | 49/119 | 62.8/65.3 | 9.1/8.6 | TME, APR | 14 (16.9)/12 (14.1) | 22 (26.5)/21 (24.7) | 6 (7.2) |
| Pechlivanides 2007 SC T4 | 2007 | SC | T4 | 34/35 | 30/43 | 72.0/69.0 | 6/8 | TME, APR | 13 (38.2)/15 (43.6) | ND | 1 (3) |
| Ng 2008 SC T4, size > 6 cm | 2008 | SC | T4, size > 6 cm | 51/48 | 38/61 | 63.7/63.5 | ND | TME | 0/0 | ND | 5 (9.8) |
| Lujan 2009 SC T4 | 2009 | SC | T4 | 101/103 | 78/126 | 67.8/66.0 | 5.5/6.2 | TME, APR | 74 (73.0)/79 (77.0) | 48 (47.5)/48 (46.6) | 8 (7.9) |
| Kang (COREAN) 2010 MC T4, M1 | 2010 | MC | T4, M1 | 170/170 | 120/220 | 57.8/59.1 | 5.6/5.3 | TME, APR | 170 (100)/170 (100) | 138 (81.2)/129 (75.9) | 2 (1.2) |
| van der Pas (COLOR II) 2013 MC T4 | 2013 | MC | T4 | 699/345 | 385/669 | 66.8/65.8 | ND | PME, TME, APR | 63.6 (91.0)/317 (92.0) | 243 (34.8)/131 (38.0) | 119 (17) |
| Gong 2012 SC M1 | 2012 | SC | M1 | 67/71 | 60/78 | 58.4/59.6 | ND | TME, APR | ND | ND | 2 (3.0) |
| Kennedy (ENROL) 2014 MC Acute intestinal obstruction | 2014 | MC | Acute intestinal obstruction | 29/27 | ND | ND | ND | TME, APR | ND | 22 (75.9)/19 (70.4) | ND |
| Ng 2014 SC T4 | 2014 | SC | T4 | 40/40 | 34/46 | 60.2/62.1 | 6.9/7.1 | TME | ND | 20 (50.0)/26 (65.0) | 3 (7.5) |
| Fleshman (ACOSOG Z6051) 2015 MC T4, M1 | 2015 | MC | T4, M1 | 240/222 | 148/314 | 57.7/57.2 | 6.1/6.3 | TME, APR | 236 (98.3)/215 (96.7) | 171 (71.3)/165 (74.3) | 27 (11.3) |
| Stevenson (ALaCaRT) 2015 MC T4 | 2015 | MC | T4 | 238/237 | 162/311 | 65.0/65.0 | ND | TME, APR | 119 (50.0)/117 (49.4) | 68.1/59.5 | 21 (8.8) |

MC – multicenter, SC – single center, TME – total mesorectal excision (anterior resection), APR – abdominoperineal resection, PME – partial (upper) mesorectal excision, ND – no data, LAP – laparoscopic approach, OPEN – open approach.
heterogeneity and inconsistency were measured using Cochran’s Q tests and \( I^2 \), respectively. Qualitative outcomes from individual studies were analyzed to assess individual and pooled risk ratios (RR) with pertinent 95% confidence intervals (CI) favouring the mini-invasive approach over an open procedure and by means of the Mantel-Haenszel random-effects method. When study included medians and interquartile ranges, we calculated the mean ± SD using a method proposed by Hozo et al. [11]. Weighted mean differences (WMD) with 95% CI are presented for quantitative variables using the inverse variance fixed-effects or random-effects method. Statistical significance was observed with a two-tailed 0.05 level for a hypothesis and with 0.10 for heterogeneity testing, while unadjusted \( p \)-values were reported accordingly. This study was performed according to the Preferred Reporting Items for Systematic reviews (PRISMA) guidelines [12].

Results

Our strategy resulted in 4,328 references. After removing duplicates, and evaluating titles and abstracts, we chose 245 papers suitable for full-text review. In the end 16 studies were selected for extraction [7–9, 13–25]. There were 3 trials (COLOR II, CLASICC and COREAN) in which results were reported in more than one paper [8, 17, 18, 20, 21, 23, 26]. The relevant data were extracted only once from these studies. Two studies by Kennedy et al. (EnROL Trial) and Stevenson et al. (ALaCaRT Trial) reported complications, but they did not report overall complication rates. Due to lack of overall morbidity we decided to exclude these studies from the morbidity analysis to avoid potential bias of overestimation [9, 25]. However, we included them in secondary outcomes and specific complications. Our review covers 3,646 patients in total (2,066 patients in the laparoscopic group and 1,580 patients in the open group) (Table I). The PRISMA flowchart for the review is presented in Figure 2. Risk of bias in the studies is assessed in Figure 3. In general, the risk of bias in the presented studies is low. Due to the nature of the treatment (differences in operative technique), blinding of participants and personnel was impossible to perform. A factor which was mainly unclear was the outcome assessment, as most of the studies did not clearly define how and by whom they were performed.

Morbidity rate was reported in 11 studies. The total morbidity in the analysed material was 664/1797 (36.95%) in the laparoscopy group vs. 483/1316 (36.7%): \( p = 0.6, \) RR = 0.97; 95% CI: 0.87–1.08. Seven studies reported overall morbidity, whereas 4 other studies reported short-term morbidity only. Due to this fact we introduced subgroups to analyse potential differences. There were no significant variations within subgroups (\( p = 0.6 \) in overall group and \( p = 0.49 \) in short-term group) (Figure 4). Three of the included studies additionally provided information on intra-operative complications, but the analysis revealed similar results (RR = 1.01, 95% CI: 0.73–1.39). The heterogeneity of all mentioned outcomes was low.

Intra-operative haemorrhage was reported in 8 studies. There was no statistically significant difference between the groups, 61/1834 (3.33%) vs. 33/1342 (2.46%) (RR = 1.19, 95% CI: 0.78–1.81). There was no heterogeneity in the analysed material, \( I^2 = 0\% \) (Figure 5).

Ureter injuries were reported in 5 studies. There were 11/1341 (0.82%) cases in the laparoscopic group and 6/855 (0.7%) in the open group. Analysis revealed no significant difference: RR = 1.11, 95% CI: 0.78–1.81. There was no heterogeneity in the analysed material, \( I^2 = 0\% \) (Figure 6).

Anastomotic leakage was reported in 9 studies. There was no statistically significant difference between the groups, 107/1473 (7.26%) vs. 64/1126 (5.68%) (RR = 1.08, 95% CI: 0.79–1.47). There was
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no heterogeneity in the analysed material, $I^2 = 0\%$ (Figure 7).

Mortality was reported in 9 studies. There were 8 (0.5\%) cases of death in the laparoscopic group and 10 (0.8\%) cases in the open group (Figure 8). There was no significant difference between the groups (RR = 0.71, 95\% CI: 0.28–1.81).

Intra-abdominal abscess was reported in 8 studies. There was no statistically significant difference between the groups, 60/1466 (3.1\%) vs. 31/1102 (2.8\%) (RR = 1.11, 95\% CI: 0.73–1.70). There was no heterogeneity in the analysed material, $I^2 = 0\%$ (Figure 9).

Surgical site infection was reported in 10 studies. Analysis revealed a 33\% (89/1784 vs. 93/1316) low-

Figure 3. Risk of bias summary

Figure 4. Pooled estimates of morbidity comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.
er risk of developing surgical site infection in favour of laparoscopy (RR = 0.67, 95% CI: 0.46–0.96). The heterogeneity of the analysed outcome was at an acceptable level, $I^2 = 19\%$ (Figure 11).

Postoperative ileus was reported in 8 studies. There was no statistically significant difference between the groups, 74/1622 (4.56%) vs. 75/1250 (6%) (RR = 0.79, 95% CI: 0.57–1.1). There was no heterogeneity in the analysed material, $I^2 = 0\%$ (Figure 11).

Operative time was reported in 11 studies. Open procedures were significantly shorter in all studies (218 min in laparoscopy vs. 177 min in open) with a weighed mean difference of 40 min (MD = 40.01 min, 95% CI: 28.16–51.86). The heterogeneity of mentioned papers is high. We performed sensitivity analysis to study the influence of each study on the pooled estimate of operative time. The sensitivity analysis demonstrated that the results were not substantially affected by the exclusion of any single study. The pooled estimate of operative time in laparoscopy was 40 min shorter compared to open procedures with a SD of 12 min (MD = 40.01 min, 95% CI: 28.16–51.86, $I^2 = 0\%$).

### Table 1: Study or subgroup

| Study or subgroup | Laparoscopic | Open | Weight | Risk ratio | Year | Risk ratio |
|------------------|--------------|------|--------|------------|------|------------|
| Zhou             | 0            | 82   | 0      | Not estimable | 2004 |            |
| Guillou (CLASSIC) | 17           | 253  | 7      | 1.23 (0.52–2.89) | 2005 |            |
| Ng 2008          | 0            | 51   | 1      | 0.31 (0.00–7.53) | 2007 |            |
| Lujan            | 1            | 101  | 1      | 1.97 (0.06–16.08) | 2009 |            |
| Kang (COREAN)    | 0            | 170  | 1      | 3.00 (0.32–28.55) | 2010 |            |
| van der Pas (COLOR II) | 22          | 699  | 11     | 0.99 (0.48–2.01) | 2013 |            |
| Stevenson (ALaCaRT) | 10         | 238  | 4      | 2.49 (0.79–7.83) | 2015 |            |
| Total (95% CI)   | 1834         | 1342 | 100    | 1.19 (0.78–1.81) |      |            |

### Table 2: Study or subgroup

| Study or subgroup | Laparoscopic | Open | Weight | Risk ratio | Year | Risk ratio |
|------------------|--------------|------|--------|------------|------|------------|
| Zhou             | 0            | 82   | 0      | Not estimable | 2004 |            |
| Guillou (CLASSIC) | 0            | 253  | 4      | 0.06 (0.00–1.04) | 2005 |            |
| Gong             | 1            | 67   | 0      | 3.18 (0.13–76.64) | 2012 |            |
| van der Pas (COLOR II) | 9           | 699  | 2      | 2.22 (0.48–10.22) | 2013 |            |
| Fleshman (ACOSOG Z6051) | 1           | 240  | 0      | 2.78 (0.11–67.79) | 2015 |            |
| Total (95% CI)   | 1341         | 855  | 100.0  | 1.11 (0.18–6.67) |      |            |

### Table 3: Study or subgroup

| Study or subgroup | Laparoscopic | Open | Weight | Risk ratio | Year | Risk ratio |
|------------------|--------------|------|--------|------------|------|------------|
| Zhou             | 1            | 82   | 3      | 0.36 (0.04–3.41) | 2004 |            |
| Guillou (CLASSIC) | 26           | 253  | 9      | 1.46 (0.71–3.03) | 2005 |            |
| Braga            | 8            | 83   | 9      | 0.91 (0.37–2.25) | 2007 |            |
| Lujan            | 5            | 77   | 10     | 0.53 (0.19–1.47) | 2009 |            |
| Kang (COREAN)    | 2            | 170  | 0      | 5.00 (0.24–103.38) | 2010 |            |
| Gong             | 1            | 67   | 1      | 1.06 (0.07–16.60) | 2012 |            |
| van der Pas (COLOR II) | 58          | 461  | 25     | 1.21 (0.78–1.88) | 2013 |            |
| Ng 2014          | 1            | 40   | 2      | 0.50 (0.05–5.30) | 2014 |            |
| Fleshman (ACOSOG Z6051) | 5           | 240  | 5      | 0.93 (0.27–3.15) | 2015 |            |
| Total (95% CI)   | 1473         | 1126 | 100.0  | 1.08 (0.79–1.47) |      |            |

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**Figure 5.** Pooled estimates of intra-operative haemorrhage comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

**Figure 6.** Pooled estimates of ureter injury comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

**Figure 7.** Pooled estimates of anastomotic leakage comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.
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analysis which identified three papers that generated the whole heterogeneity: Zhou et al., Lujan et al. and Stevenson et al. Despite high heterogeneity generated by those papers, we decided to include the primary analysis (Figure 12) due to the fact that their exclusion did not alter the results (MD = 50.45 min, 95% CI: 44.71–56.18).

Blood loss was reported in 11 studies. Only three studies did not report smaller blood loss in laparoscopy [15, 17, 24]. There was a significant difference

| Study or subgroup | Laparoscopic | Open | Weight | Risk ratio  | Year | Risk ratio |
|-------------------|--------------|------|--------|-------------|------|------------|
| Zhou              | 0 82        | 89   | –      | Not estimable | 2004 |
| Braga             | 1 83        | 1 85 | 11.4   | 1.02 (0.07–16.10) | 2007 |
| Ng 2008           | 1 51        | 1 48 | 11.5   | 0.94 (0.06–14.63) | 2008 |
| Lujan             | 2 101       | 3 103 | 27.8   | 0.68 (0.12–3.98) | 2009 |
| Gong              | 0 67        | 0 71 | –      | Not estimable | 2012 |
| van der Pas (COLOR II) | 1 699 | 2 345 | 15.1   | 0.25 (0.02–2.71) | 2013 |
| Ng 2014           | 0 40        | 0 40 | –      | Not estimable | 2014 |
| Stevenson (ALaCaRT) | 1 238       | 1 237 | 11.3   | 1.00 (0.06–15.83) | 2015 |
| Fleshman (ACOSOG Z6051) | 2 240       | 2 222 | 22.8   | 0.93 (0.13–6.51) | 2015 |
| Total (95% CI)    | 1601        | 1240 | 100.0  | 0.71 (0.28–1.81) |         |

Heterogeneity: $t^2 = 0.00, \chi^2 = 0.99, df = 5 (p = 0.96), I^2 = 0%$

Test for overall effect: $Z = 0.72 (p = 0.47)$

**Figure 8.** Pooled estimates of mortality comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

| Study or subgroup | Laparoscopic | Open | Weight | Risk ratio  | Year | Risk ratio |
|-------------------|--------------|------|--------|-------------|------|------------|
| Zhou              | 0 82        | 89   | –      | Not estimable | 2004 |
| Braga             | 3 83        | 4 85 | 8.4    | 0.77 (0.18–3.33) | 2007 |
| Ng 2008           | 1 51        | 1 48 | 2.4    | 0.94 (0.06–14.63) | 2008 |
| Lujan             | 3 101       | 2 103 | 5.8    | 1.53 (0.26–8.96) | 2009 |
| Kang (COREAN)     | 0 170       | 1 170 | 1.8    | 0.33 (0.01–8.13) | 2010 |
| van der Pas (COLOR II) | 51 699     | 22 345 | 77.5   | 1.14 (0.71–1.85) | 2013 |
| Ng 2014           | 1 40        | 1 40 | 2.4    | 1.00 (0.06–15.44) | 2014 |
| Fleshman (ACOSOG Z6051) | 1 240 | 2 222 | 1.8    | 2.78 (0.11–67.79) | 2015 |
| Total (95% CI)    | 1466        | 1102 | 100.0  | 1.11 (0.73–1.70) |         |

Heterogeneity: $t^2 = 0.00, \chi^2 = 1.26, df = 6 (p = 0.97), I^2 = 0%$

Test for overall effect: $Z = 0.48 (p = 0.63)$

**Figure 9.** Pooled estimates of intra-abdominal abscess comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

| Study or subgroup | Laparoscopic | Open | Weight | Risk ratio  | Year | Risk ratio |
|-------------------|--------------|------|--------|-------------|------|------------|
| Zhou              | 2 82        | 3 89 | 3.9    | 0.72 (0.12–4.22) | 2004 |
| Guillou (CLASSIC) | 33 253      | 15 128 | 23.1  | 1.11 (0.63–1.97) | 2005 |
| Braga             | 6 83        | 13 85 | 12.1   | 0.47 (0.19–1.18) | 2007 |
| Ng 2008           | 10 51       | 10 48 | 15.3   | 0.94 (0.43–2.06) | 2008 |
| Lujan             | 0 101       | 2 103 | 1.4    | 0.20 (0.01–4.20) | 2009 |
| Kang (COREAN)     | 2 170       | 11 170 | 5.3    | 0.18 (0.04–0.81) | 2010 |
| Gong              | 1 67        | 2 71 | 2.2    | 0.53 (0.05–5.71) | 2012 |
| van der Pas (COLOR II) | 28 699    | 17 345 | 22.3  | 0.81 (0.45–1.46) | 2013 |
| Ng 2014           | 1 40        | 7 40 | 2.9    | 0.14 (0.02–1.11) | 2014 |
| Stevenson (ALaCaRT) | 6 238       | 13 237 | 11.4  | 0.46 (0.18–1.19) | 2015 |
| Total (95% CI)    | 1784        | 1316 | 100.0  | 0.67 (0.46–0.96) |         |

Heterogeneity: $t^2 = 0.06, \chi^2 = 11.15, df = 9 (p = 0.27), I^2 = 19%$

Test for overall effect: $Z = 2.21 (p = 0.03)$

**Figure 10.** Pooled estimates of surgical site infection comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.
among analysed groups (168 ml in laparoscopy vs. 303 ml in open group). Blood loss was on average 89 ml less (MD = –94.24, 95% CI: –123.12 – –65.36) (Figure 13). Due to high heterogeneity, \( I^2 = 90\% \), we performed a sensitivity test. Excluding studies by Kang et al., van der Pas et al. and Gong et al. reduced heterogeneity to \( I^2 = 60\% \), with no effect on the results (MD = –96.63, 95% CI: –122.68 – –69.97).

### Table 1

| Study or subgroup | Laparoscopic | Open | Weight | Risk ratio | Risk ratio |
|------------------|--------------|------|--------|------------|------------|
|                  | Events Total | Events Total | (%)  | M-H, random, 95% CI | M-H, random, 95% CI |
| Braga            | 2 83 2 85 2.9 | 1.02 (0.15–7.10) | |
| Fleshman (ACOSOG Z6051) | 1 240 0 222 1.0 | 2.78 (0.11–67.79) | |
| Kang (COREAN)    | 17 170 22 170 30.2 | 0.77 (0.43–1.40) | |
| Lujan            | 6 101 8 103 10.3 | 0.76 (0.28–2.13) | |
| Ng 2008          | 1 51 2 48 1.9 | 0.47 (0.04–5.02) | |
| Ng 2014          | 3 40 5 40 5.8 | 0.60 (0.15–2.34) | |
| Stevenson (ALaCaRT) | 11 238 24 237 22.5 | 0.46 (0.23–0.91) | |
| van der Pas (COLOR II) | 33 699 12 345 25.5 | 1.36 (0.71–2.59) | |
| **Total (95% CI)** | **1622 1250 100.0** | **0.79 (0.57–1.10)** | |

### Figure 11.
Pooled estimates of postoperative ileus comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

### Table 2

| Study or subgroup | Laparoscopic | Open | Weight | Mean difference | Year | Mean difference |
|------------------|--------------|------|--------|-----------------|------|----------------|
|                  | Mean SD Total | Mean SD Total | (%)  | IV, random, 95% CI | IV, random, 95% CI |
| Zhou             | 120 18.3 82 106 25 89 10.8 | 14.00 (7.47–20.53) | 2004 | |
| Braga            | 262 72 83 209 70 85 8.2 | 53.00 (31.52–74.48) | 2007 | |
| Ng 2008          | 213.5 46.2 51 163.7 43.4 | 49.80 (32.15–67.45) | 2008 | |
| Lujan            | 193.7 45.1 101 172.9 59.4 | 20.80 (6.34–35.26) | 2009 | |
| Kang (COREAN)    | 245 75 170 197 63 170 9.5 | 48.00 (33.28–62.72) | 2010 | |
| Gong             | 216 68 67 163 43 71 8.7 | 53.00 (33.89–72.11) | 2012 | |
| van der Pas (COLOR II) | 240 86 699 188 66.7 345 10.4 | 52.00 (42.50–61.50) | 2013 | |
| Kerley (EnROL)   | 220 67 29 186 48 27 8.4 | 34.00 (3.63–64.37) | 2014 | |
| Ng 2014          | 211.6 53 40 153 41.1 | 58.60 (37.82–79.38) | 2014 | |
| Stevenson (ALaCaRT) | 210 66.7 238 190 59.26 237 10.1 | 8.3 (8.65–31.35) | 2015 | |
| Fleshman (ACOSOG Z6051) | 266 102 240 221 92 222 8.9 | 45.00 (27.31–62.69) | 2015 | |
| **Total (95% CI)** | **1800 1437 100.0** | **40.01 (28.16–51.86)** | |

### Figure 12.
Pooled estimates of operative time comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

### Table 3

| Study or subgroup | Laparoscopic | Open | Weight | Mean difference | Year | Mean difference |
|------------------|--------------|------|--------|-----------------|------|----------------|
|                  | Mean SD Total | Mean SD Total | (%)  | IV, random, 95% CI | IV, random, 95% CI |
| Zhou             | 0 19.7 82 92 25 89 15.3 | –72.00 (–78.72, –65.28) | 2004 | |
| Braga            | 231.7 750 51 555.6 1180 48 6.5 | –233.90 (–626.08, 138.28) | 2007 | |
| Ng 2008          | 217.6 37.6 67 159.1 32.7 | –32.20 (–43.99, –20.41) | 2012 | |
| Lujan            | 127.8 113.3 101 234.2 174.3 | –106.40 (–146.67, –66.13) | 2009 | |
| Kang (COREAN)    | 200 148 170 217 185 170 12.5 | –17.00 (–52.61, 18.61) | 2010 | |
| Gong             | 86.9 37.6 67 159.1 32.7 | –32.20 (–43.99, –20.41) | 2012 | |
| van der Pas (COLOR II) | 200 222 699 400 370.35 89 51.6 | –200.0 (–242.41, –157.59) | 2013 | |
| Kennedy (EnROL)  | 181 146 29 450 397 27 7.7 | –269.00 (–427.90, –110.10) | 2014 | |
| Ng 2014          | 141.8 500 40 361.1 623.75 40 1.2 | –219.30 (–467.04, 28.44) | 2014 | |
| Stevenson (ALaCaRT) | 100 111 238 190 59.26 237 13.9 | –90.00 (–114.70, –65.30) | 2015 | |
| Fleshman (ACOSOG Z6051) | 256.1 305.8 240 318.4 331.7 222 9.5 | –62.30 (–126.62, –3.98) | 2015 | |
| **Total (95% CI)** | **1800 1437 100.0** | **–94.24 (–123.12, –65.36)** | |

### Figure 13.
Pooled estimates of blood loss comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.
Length of hospital stay (LOS) was reported in 12 studies. Five studies reported shorter LOS in favour of the laparoscopic approach, whereas the remainder did not reach a similar conclusion. In general LOS differed significantly between groups (9 days in the laparoscopic group vs. 11 days in the open open). Our analysis revealed that on average, the LOS is 1.6 days shorter in the case of laparoscopy (MD = −1.62, 95% CI: −2.37 − −0.86) (Figure 14). Due to high heterogeneity (I² = 92%) we performed sensitivity analysis and managed to reduce heterogeneity to 67% when studies by Zhou et al., Guillou et al. and Braga et al. were excluded (MD = −0.78, 95% CI: −1.44 − −0.12) [14, 20, 22].

Time to first flatus was reported in 5 studies, whereas time to first bowel movement was reported in 7 studies. Gong et al., Kang et al. and Stevenson et al. reported a shorter time to first flatus in favour of laparoscopy [9, 17, 19]. The mean time to first flatus was 1.93 days in the laparoscopic group, whereas in the open procedure it was 3 days. Due to high heterogeneity, we decided not to perform a meta-analysis of this outcome. In the case of time to first bowel movement only Stevenson et al. and Ng et al. did not report a shorter time for laparoscopy [9, 24]. The mean time to first bowel movement for laparoscopy was 2.97 days, while for the open group it was 3.82 days. Meta-analysis showed a 0.75 shorter time to first bowel movement in favour of laparoscopy (MD = −0.75, 95% CI: −1.29 − −0.22). The heterogeneity was high, I² = 92%; thus we performed a sensitivity test which revealed two studies generating all the heterogeneity. The result was not affected and still in favour of laparoscopy (MD = −1.03, 95% CI: −1.25 − −0.81) (Figure 15).

![Figure 14. Pooled estimates of length of hospital stay comparing laparoscopy and open surgery](image)

CI – confidence interval, df – degrees of freedom.

![Figure 15. Pooled estimates of time to first bowel movement comparing laparoscopy and open surgery](image)

CI – confidence interval, df – degrees of freedom.
Discussion

Our systematic review, based on 13 RCTs and 3,646 patients, revealed that although laparoscopy is associated with longer operative time it has significantly shorter LOS, lower blood loss and faster return of bowel function. In addition, there are no significant differences in intra-operative complications, postoperative overall morbidity and specific complications (postoperative ileus, anastomotic leakage and mortality). The quality of analysed studies was considered high. All of the studies lacked binding of the staff and patients, which in surgery is impossible to perform.

Since the first laparoscopic rectal resection over 25 years ago, the minimally invasive approach in rectal cancer treatment has established a well-based position in the medical world [27]. Currently nearly 45% (85% in some studies) of rectal resections in developed countries are performed laparoscopically [28]. Even though laparoscopic rectal resections are challenging and their learning curve is longer, most patients and surgeons consider the short-term benefits to be determining factors in the decision regarding choice of approach. Nowadays laparoscopy is the gold standard for the treatment of most benign conditions and has been shown to be safe and feasible or even beneficial in many oncologic indications. In terms of rectal cancer surgery, there are no differences in long-term outcomes between laparoscopic and open surgery when analysing all recently published randomized trials. This systematic review and meta-analyses aims to provide the best available evidence on short-term outcomes.

We identified 16 papers eligible for inclusion in the analysis, covering 3,618 patients (3 studies were based on the same database). Our primary outcome, morbidity rate, did not show any significant difference in all included studies, both in the early and in the latest publications. Studies by Kennedy et al. and Stevenson et al. were excluded from this analysis due to the impossibility of assessing the exact morbidity rate without overestimation. This, along with low heterogeneity within and among the groups, allows us to reach a strong conclusion that the laparoscopic approach is safe. Similar findings were presented by Zhang et al. [5] in their systematic review from 2014. Since that time the ACOSOG Z6051 and ALaCaRT trials and a study by Ng et al. have been published, and their results only strengthened Zhang’s conclusions in our updated review. This, however, stands in contrast to the results of a recent systematic review by Chen et al., which was based on studies published in the last 5 years, which shows lower morbidity in the laparoscopy group [29]. The reason for the discrepancies is that in their study they included high quality nonrandomized studies which alter the results, since subgroup analysis in fact revealed no differences in the RCT subgroup. Furthermore, the most recent studies by Stevenson et al. Fleshman et al. or Ng et al. were not included, probably leading to biased results. Apart from surgical site infection, there were no significant differences in terms of specific surgical complications or mortality. A lower rate of surgical site infection is typical for laparoscopic surgery and is mainly associated with smaller wounds.

All studies included in the analysis found operative time longer in the case of laparoscopic surgery. Our study shows on average a 40 min shorter time. We noted high heterogeneity among the studies in regard to this outcome. On one hand laparoscopy is for obvious reasons associated with a shorter time for wound closure, while on the other it is more technically demanding and the learning curve is longer. Most of the studies do not indicate whether surgeons are still on the learning curve or how far beyond it have they have come. In a study by Araujo et al. the operative time for laparoscopy was shorter, which is in contrast to all remaining RCTs [13]. However, this study was performed on a small group, which may underpower its results. It was not included in the meta-analysis due to lack of standard deviation in the results. Furthermore, some studies do not explicate how operative time is calculated – whether it is from the skin incision to closure or from entering to leaving the operating theatre. The differences between some studies are major. For example, the mean operative time for laparoscopy in the study by Zhou et al. is 120 min, whereas in the study by Fleshman et al. it is 266 min.

Time to first bowel movement was shorter for laparoscopy, which should result in faster recovery and thus shorter LOS. This is confirmed in our meta-analysis – LOS was 1.6 days shorter in the laparoscopic approach. Zhang et al., in their systematic review obtained similar results [5]. What is interesting is the fact that the most recent RCTs present data in which LOS does not differ [7, 9, 25]. There are several possible explanations for this observa-
Is the laparoscopic approach for rectal cancer superior to open surgery? A systematic review and meta-analysis on short-term surgical outcomes

Firstly, there is a change in the perioperative care and thanks to the introduction of multimodal clinical pathways to enhance patients’ recovery earlier recovery after open surgery has become feasible [30]. Enhanced recovery after surgery was first introduced by Kehlet several years ago. Currently this holistic approach to patient care has evolved and established a firm position in the surgical world. Many studies have shown that introduction of the ERAS protocol improved patients’ postoperative outcomes [31–33]. It has also been associated with reduced treatment costs, which is of great importance in the discussion on full acceptance and wider adoption of laparoscopic surgery, which is still very limited in some countries [34, 35]. Even though patients in the open arms had greater surgical trauma, there is a possibility that elements of modern perioperative care allowed for discharge at a comparable time to the laparoscopic group. Unfortunately, none of the analysed studies considered this aspect and the information regarding perioperative care was not included in the methodology. It is difficult to compare length of hospital stay between various countries and hospitals. In general the length of stay is usually too long and it is more associated with local customs rather than meeting objective discharge criteria.

Lower blood loss associated with laparoscopy is in line with what was presented by Zhang et al., as well as studies regarding laparoscopy in different surgical fields [36]. Low blood loss is enforced by laparoscopic technique since even a small amount of blood may obscure the view. Another advantage of lower blood loss is the fact greater blood loss and perioperative blood transfusions are associated with greater risk of postoperative adverse events and worse outcomes [37, 38]. Of course, there is always the chicken-or-egg causality dilemma as to what comes first: increased blood loss due to difficult operative conditions resulting in inferior quality of surgery or the real influence of blood loss. It seems that this question will long remain unanswered.

The quality of data in this review has several limitations. Surgeons’ experience and hospital volume in rectal surgery are beyond all doubt the most important factors influencing outcomes, and this aspect must be taken into consideration when analysing data of laparoscopic and open surgery. Most of the analysed studies where performed in high-volume centres. However, in this review surgeons’ experience was not analysed. In our study we focused only on surgical management of rectal cancer. The results may be biased by possible differences caused by neoadjuvant treatment which may alter post-operative complications occurrence, especially anastomotic leakage. Additionally, we did not analyse late complications such as hernias or adhesive bowel obstruction. We also did not consider postoperative functional disorders such as faecal incontinence or quality of life in general.

Conclusions

This systematic review based on available RCTs confirms that laparoscopic rectal cancer surgery is associated with short-term outcomes comparable to the open approach. Moreover, in some aspects it provides better results (e.g. functional postoperative recovery, lower rate of SSIs). The quality of evidence is high; therefore in our opinion it is very unlikely that future trials will alter these results, and for this reason the laparoscopic approach can be considered the gold standard for the treatment of majority of patients.

Conflict of interest

The authors declare no conflict of interest.

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