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-

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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 (freeware from The Cochrane Collaboration). Statistical

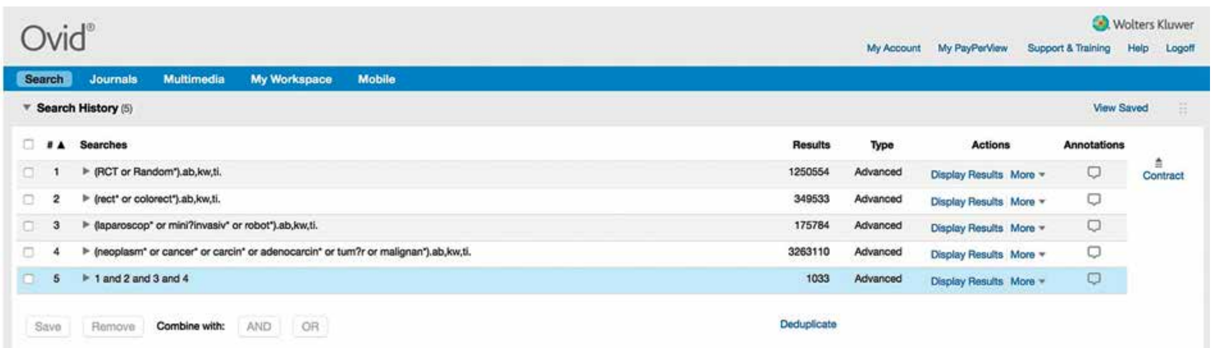

Figure 1. Search strategy for OVID

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*)	Female/ male (*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	13/15	19/28	59.1/56.4	ND	APR	15/15	ND	0
Zhou	2004	SC	Dukes D	82/89	82/89	44.0/45.0	ND	TME	ND	ND	ND
Guillou (CLASICC)	2005	MC	Acute intestinal obstruction	253/128	ND	ND	ND	TME, APR	ND	ND	86 (34)
Braga	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	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	51/48	38/61	63.7/63.5	ND	TME	0/0	ND	5 (9.8)
Lujan	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	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	699/345	385/669	66.8/65.8	ND	PME, TME, APR	636 (91.0)/ 317 (92.0)	243 (34.8)/ 131 (38.0)	119 (17)
Gong	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	29/27	ND	ND	ND	TME, APR	ND	22 (75.9)/ 19 (70.4)	ND
Ng	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	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	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.

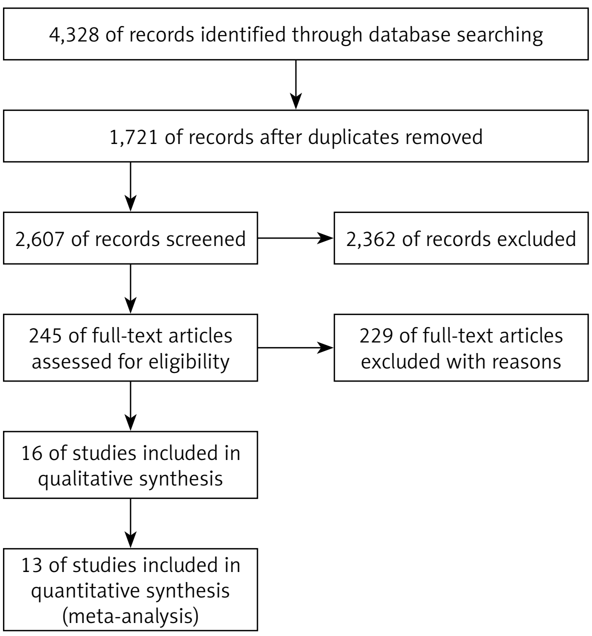

Figure 2. PRISMA flowchart

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: 0.18–6.67 (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

	Araujo	Braga	Fleshman (ACOSOG Z6051)	Gong	Guillou (CLASSIC)	Kang (COREAN)	Kennedy (EnROL)	Lujan	Ng 2008	Ng 2014	Pechlivanides	Stevenson (ALaCaRT)	van der Pas (COLOR II)	Zhou
Random sequence generation (selection bias)	+	+	+		+	+	+	+	+	+	+	+	+	
Allocation concealment (selection bias)	+				+		+	+	+	+		+	+	
Blinding of participants and personnel (performance bias)	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Blinding of outcome assessment (detection bias)						+					+	+	+	
Incomplete outcome data (attrition bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Selective reporting (reporting bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Other bias		+	+			+	+	–	+	+	+	+	+	+

Figure 3. Risk of bias summary

Study or subgroup	Laparoscopic Events	Laparoscopic Total	Open Events	Open Total	Weight (%)	Risk ratio M-H, random, 95% CI	Year
1.1.1. Overall							
Araujo	9	13	7	15	2.5	1.48 (0.77–2.85)	2003
Zhou	5	82	11	89	1.1	0.49 (0.18–1.36)	2004
Ng 2008	23	51	25	48	6.2	0.87 (0.58–1.30)	2008
Lujan	34	101	34	103	6.7	1.02 (0.69–1.50)	2009
Kang (COREAN)	36	170	40	170	6.5	0.90 (0.61–1.34)	2010
Gong	4	67	6	71	0.7	0.71 (0.21–2.39)	2012
Fleshman (ACOSOG Z6051)	137	240	129	222	28.1	0.98 (0.84–1.15)	2015
Subtotal (95% CI)		**724**		**718**	**51.8**	**0.97 (0.85–1.10)**	
Total events	248		252				
Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 4.22$, $df = 6$ ($p = 0.65$), $I^2 = 0\%$							
Test for overall effect: $Z = 0.52$ ($p = 0.60$)							
1.1.2. Short-term							
Guillou (CLASSIC)	101	253	47	128	12.4	1.09 (0.83–1.43)	2005
Braga	24	83	34	85	5.7	0.72 (0.47–1.11)	2007
van der Pas (COLOR II)	278	697	128	345	26.3	1.08 (0.91–1.27)	2013
Ng 2014	13	40	22	40	3.8	0.59 (0.35–1.00)	2014
Subtotal (95% CI)		**1073**		**598**	**48.2**	**0.92 (0.72–1.17)**	
Total events	416		231				
Heterogeneity: $\tau^2 = 0.03$, $\chi^2 = 7.15$, $df = 3$ ($p = 0.07$), $I^2 = 58\%$							
Test for overall effect: $Z = 0.69$ ($p = 0.49$)							
Total (95% CI)		**1797**		**1316**	**100.0**	**0.97 (0.87–1.08)**	
Total events	664		483				
Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 11.45$, $df = 10$ ($p = 0.32$), $I^2 = 13\%$							
Test for overall effect: $Z = 0.53$ ($p = 0.60$)							
Test for subgroup differences: $\chi^2 = 0.14$, $df = 1$ ($p = 0.71$), $I^2 = 0\%$							

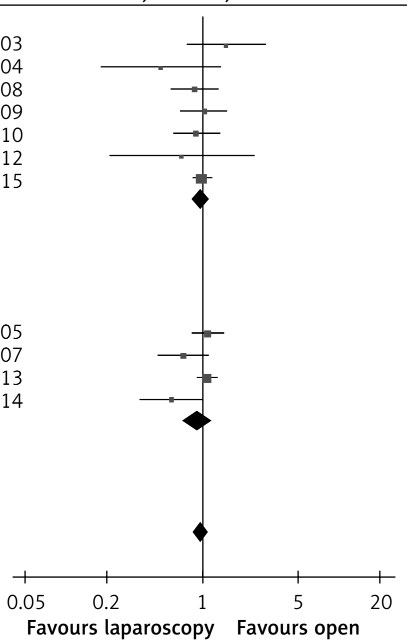

Figure 4. Pooled estimates of morbidity comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

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 (0.81%) 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 (3.14%) vs. 31/1102 (2.81%) (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) lower 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 10).

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

Study or subgroup	Laparoscopic		Open		Weight	Risk ratio	Year
	Events	Total	Events	Total	(%)	M-H, random, 95% CI	
Zhou	0	82	0	89	–	Not estimable	2004
Guillou (CLASSIC)	17	253	7	128	24.4	1.23 (0.52–2.89)	2005
Ng 2008	0	51	1	48	1.8	0.31 (0.01–7.53)	2008
Lujan	1	101	1	103	2.3	1.02 (0.06–16.08)	2009
Kang (COREAN)	3	170	1	170	3.5	3.00 (0.32–28.55)	2010
van der Pas (COLOR II)	22	699	11	345	35.1	0.99 (0.48–2.01)	2013
Fleshman (ACOSOG Z6051)	8	240	8	222	19.2	0.93 (0.35–2.42)	2015
Stevenson (ALaCaRT)	10	238	4	237	13.6	2.49 (0.79–7.83)	2015
Total (95% CI)		**1834**		**1342**	**100**	**1.19 (0.78–1.81)**	
Total events	61		33				

Heterogeneity: τ^2 = 0.00, χ^2 = 3.47, df = 6 (p = 0.75), I^2 = 0%
Test for overall effect: Z = 0.80 (p = 0.42)

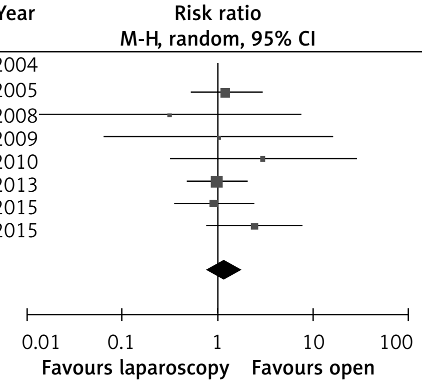

Figure 5. Pooled estimates of intra-operative haemorrhage comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

Study or subgroup	Laparoscopic		Open		Weight	Risk ratio	Year
	Events	Total	Events	Total	(%)	M-H, random, 95% CI	
Zhou	0	82	0	89	–	Not estimable	2004
Guillou (CLASSIC)	0	253	4	128	22.1	0.06 (0.00–1.04)	2005
Gong	1	67	0	71	19.9	3.18 (0.13–76.64)	2012
van der Pas (COLOR II)	9	699	2	345	38.2	2.22 (0.48–10.22)	2013
Fleshman (ACOSOG Z6051)	1	240	0	222	19.8	2.78 (0.11–67.79)	2015
Total (95% CI)		**1341**		**855**	**100.0**	**1.11 (0.18–6.67)**	
Total events	11		6				

Heterogeneity: τ^2 = 1.59, χ^2 = 5.76, df = 3 (p = 0.12), I^2 = 48%
Test for overall effect: Z = 0.11 (p = 0.91)

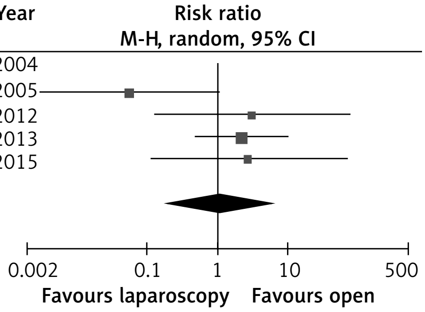

Figure 6. Pooled estimates of ureter injury comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

Study or subgroup	Laparoscopic		Open		Weight	Risk ratio	Year
	Events	Total	Events	Total	(%)	M-H, random, 95% CI	
Zhou	1	82	3	89	1.9	0.36 (0.04–3.41)	2004
Guillou (CLASSIC)	26	253	9	128	18.1	1.46 (0.71–3.03)	2005
Braga	8	83	9	85	11.7	0.91 (0.37–2.25)	2007
Lujan	5	77	10	81	9.1	0.53 (0.19–1.47)	2009
Kang (COREAN)	2	170	0	170	1.0	5.00 (0.24–103.38)	2010
Gong	1	67	1	71	1.3	1.06 (0.07–16.60)	2012
van der Pas (COLOR II)	58	461	25	240	48.9	1.21 (0.78–1.88)	2013
Ng 2014	1	40	2	40	1.7	0.50 (0.05–5.30)	2014
Fleshman (ACOSOG Z6051)	5	240	5	222	6.4	0.93 (0.27–3.15)	2015
Total (95% CI)		**1473**		**1126**	**100.0**	**1.08 (0.79–1.47)**	
Total events	107		64				

Heterogeneity: τ^2 = 0.00, χ^2 = 5.30, df = 8 (p = 0.73), I^2 = 0%
Test for overall effect: Z = 0.46 (p = 0.64)

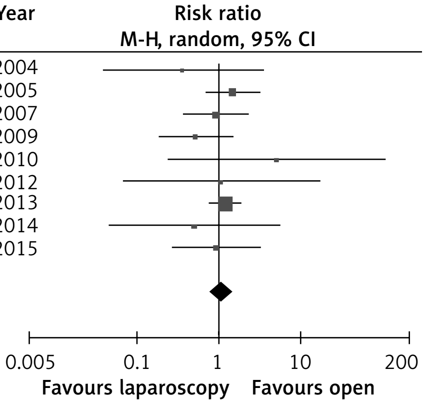

Figure 7. Pooled estimates of anastomotic leakage comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

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
	Events	Total	Events	Total	(%)	M-H, random, 95% CI	
Zhou	0	82	0	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)**	
Total events	8		10				

Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 0.99$, $df = 5$ ($p = 0.96$), $I^2 = 0\%$
Test for overall effect: $Z = 0.72$ ($p = 0.47$)

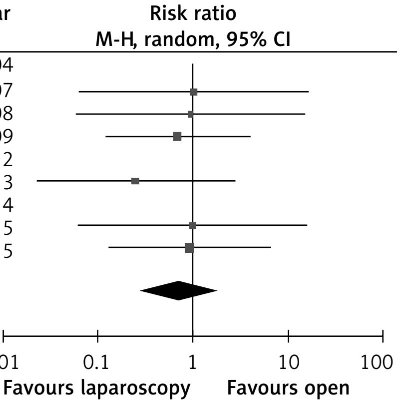

Figure 8. Pooled estimates of mortality comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

Study or subgroup	Laparoscopic		Open		Weight	Risk ratio	Year
	Events	Total	Events	Total	(%)	M-H, random, 95% CI	
Zhou	0	82	0	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	0	222	1.8	2.78 (0.11–67.79)	2015
Total (95% CI)		**1466**		**1102**	**100.0**	**1.11 (0.73–1.70)**	
Total events	60		31				

Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 1.26$, $df = 6$ ($p = 0.97$), $I^2 = 0\%$
Test for overall effect: $Z = 0.48$ ($p = 0.63$)

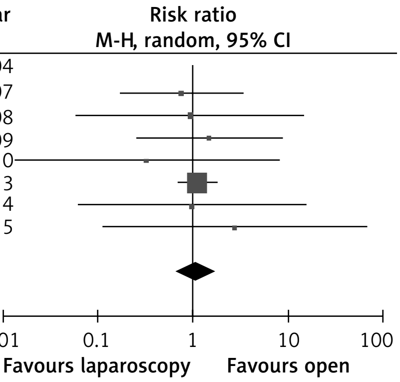

Figure 9. Pooled estimates of intra-abdominal abscess comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

Study or subgroup	Laparoscopic		Open		Weight	Risk ratio	Year
	Events	Total	Events	Total	(%)	M-H, random, 95% CI	
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)**	
Total events	89		93				

Heterogeneity: $\tau^2 = 0.06$, $\chi^2 = 11.15$, $df = 9$ ($p = 0.27$), $I^2 = 19\%$
Test for overall effect: $Z = 2.21$ ($p = 0.03$)

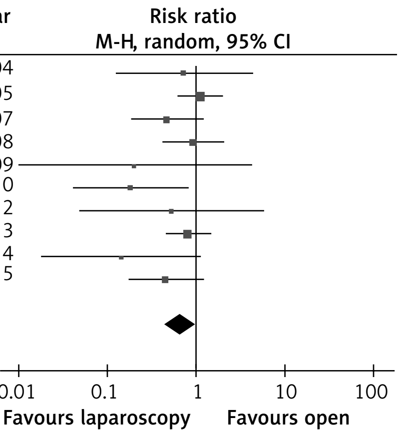

Figure 10. Pooled estimates of surgical site infection comparing laparoscopy and open surgery

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).

Study or subgroup	Laparoscopic		Open		Weight	Risk ratio
	Events	Total	Events	Total	(%)	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)**
Total events	74		75			

Heterogeneity: τ^2 = 0.00, χ^2 = 6.12, df = 7 (p = 0.53), I^2 = 0%
Test for overall effect: Z = 1.41 (p = 0.16)

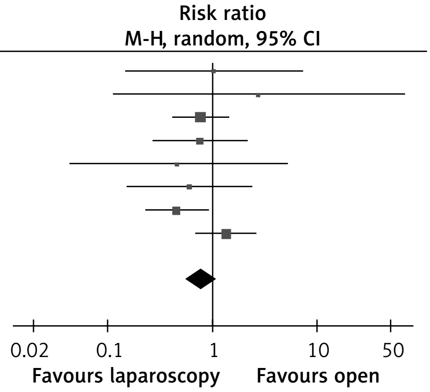

Figure 11. Pooled estimates of postoperative ileus comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

Study or subgroup	Laparoscopic			Open			Weight	Mean difference	Year
	Mean	SD	Total	Mean	SD	Total	(%)	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	48	9.0	49.80 (32.15–67.45)	2008
Lujan	193.7	45.1	101	172.9	59.4	103	9.6	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
Kennedy (EnROL)	220	67	29	186	48	27	6.4	34.00 (3.63–64.37)	2014
Ng 2014	211.6	53	40	153	41.1	40	8.3	58.60 (37.82–79.38)	2014
Stevenson (ALaCaRT)	210	66.7	238	190	59.26	237	10.1	20.00 (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)**	

Heterogeneity: τ^2 = 326.87, χ^2 = 77.95, df = 10 (p < 0.00001), I^2 = 87%
Test for overall effect: Z = 6.62 (p < 0.00001)

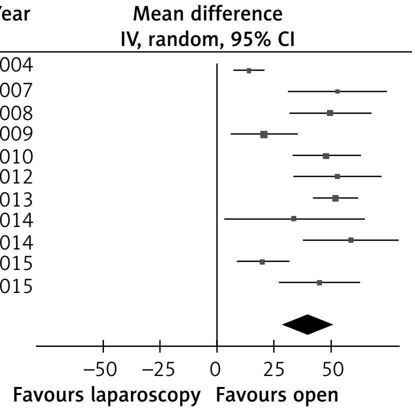

Figure 12. Pooled estimates of operative time comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

Study or subgroup	Laparoscopic			Open			Weight	Mean difference	Year
	Mean	SD	Total	Mean	SD	Total	(%)	IV, random, 95% CI	
Zhou	0	19.7	82	92	25	89	15.3	–72.00 (–78.72, –65.28)	2004
Braga	231	236	83	396	367	85	5.9	–183.00 (–276.09, –89.91)	2007
Ng 2008	321.7	750	51	555.6	1,180	48	0.5	–233.90 (–626.08, 158.28)	2008
Lujan	127.8	113.3	101	234.2	174.3	103	11.9	–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	119.1	32.7	71	15.0	–32.20 (–43.99, –20.41)	2012
van der Pas (COLOR II)	200	222	699	400	370.37	345	11.6	–200.00 (–242.41, –157.59)	2013
Kennedy (EnROL)	181	146	29	450	397	27	2.7	–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	159.26	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 (–120.62, –3.98)	2015
Total (95% CI)			**1800**			**1437**	**100.0**	**–94.24 (–123.12, –65.36)**	

Heterogeneity: τ^2 = 1407.61, χ^2 = 102.29, df = 10 (p < 0.00001), I^2 = 90%
Test for overall effect: Z = 6.40 (p < 0.00001)

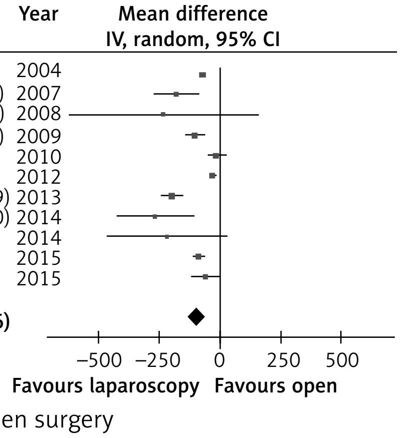

Figure 13. Pooled estimates of blood loss comparing laparoscopy and open surgery

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 (I^2 = 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, I^2 = 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).

Study or subgroup	Laparoscopic			Open			Weight	Mean difference	Year
	Mean	SD	Total	Mean	SD	Total	(%)	IV, random, 95% CI	
Zhou	8.1	3.1	82	13.3	3.4	89	10.5	–5.20 (–6.17, –4.23)	2004
Guillou (CLASSSIC)	11	1	253	13	1.5	128	12.5	–2.00 (–2.29, –1.71)	2005
Braga	10	4.9	83	13.6	10	85	5.6	–3.60 (–5.97, –1.23)	2007
Ng 2008	10.8	5.5	51	11.5	8.25	48	4.7	–0.70 (–3.48, 2.08)	2008
Lujan	8.2	7.3	101	9.9	6.8	103	6.9	–1.70 (–3.64, 0.24)	2009
Kang (COREAN)	8	0.83	170	9	0.67	170	12.6	–1.00 (–1.16, –0.84)	2010
Gong	10.4	4.3	67	13.8	5.9	71	7.7	–3.40 (–5.12, –1.68)	2012
van der Pas (COLOR II)	11.9	11.8	699	12.1	10.6	345	8.8	–0.20 (–1.62, 1.22)	2013
Ng 2014	10.5	7.5	40	15	40.25	40	0.3	–4.50 (–17.19, 8.19)	2014
Kennedy (EnROL)	5	1.85	29	6	3.7	27	8.3	–1.00 (–2.55, 0.55)	2014
Fleshman (ACOSOG Z6051)	7.3	5.4	240	7	3.4	222	11.1	0.30 (–0.52, 1.12)	2015
Stevenson (ALaCaRT)	8	4.44	238	8	4.44	237	11.1	0.00 (–0.80, 0.80)	2015
Total (95% CI)			**2053**			**1565**	**100.0**	**–1.62 (–2.37, –0.86)**	

Heterogeneity: τ^2 = 1.16, χ^2 = 134.47, d*f* = 11 ($p < 0.00001$), I^2 = 92%
Test for overall effect: Z = 4.21 ($p < 0.0001$)

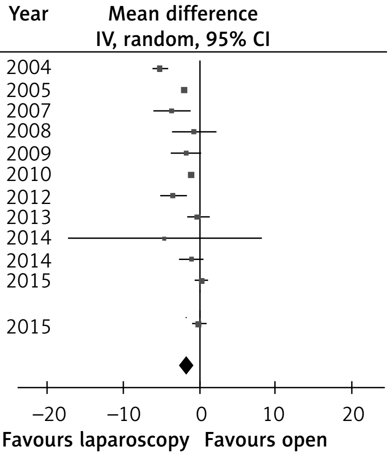

Figure 14. Pooled estimates of length of hospital stay comparing laparoscopy and open surgery

CI – confidence interval, df – degrees of freedom.

Study or subgroup	Laparoscopic			Open			Weight	Mean difference	Year
	Mean	SD	Total	Mean	SD	Total	(%)	IV, random, 95% CI	
Zhou	1.5	1.3	82	2.7	1.5	89	15.7	–1.20 (–1.62, –0.78)	2004
Guillou (CLASSSIC)	5	2.22	253	6	2.22	128	15.3	–1.00 (–1.47, –0.53)	2005
Ng 2008	4.3	5.25	51	6.3	2.75	48	6.7	–2.00 (–3.64, –0.36)	2008
van der Pas (COLOR II)	2.9	3.8	699	3.7	3.6	345	15.3	–0.80 (–1.27, –0.33)	2013
Ng 2014	3.1	1.3	40	3.1	1.5	40	14.1	0.00 (–0.62, 0.62)	2014
Fleshman (ACOSOG Z6051)	2	2.5	240	3	2	222	15.7	–1.00 (–1.41, –0.59)	2015
Stevenson (ALaCaRT)	2	0.3	234	2	0.5	233	17.3	0.00 (–0.07, 0.07)	2015
Total (95% CI)			**1599**			**1105**	**100.0**	**–0.75 (–1.29, –0.22)**	

Heterogeneity: τ^2 = 0.44, χ^2 = 79.24, d*f* = 6 ($p < 0.00001$), I^2 = 92%
Test for overall effect: Z = 2.74 (p = 0.006)

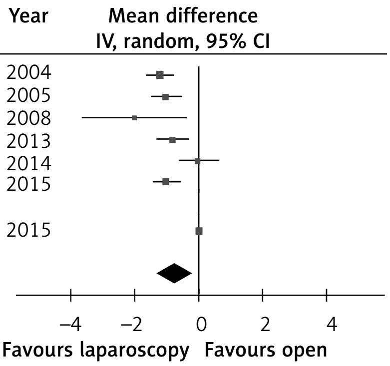

Figure 15. Pooled estimates of time to first bowel movement comparing laparoscopy and open surgery

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 blinding 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 observation. 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.

References

1. Brenner H, Bouvier AM, Foschi R, et al. Progress in colorectal cancer survival in Europe from the late 1980s to the early 21st century: the EUROCARE study. Int J Cancer 2012; 131: 1649-58.
2. van de Velde CJ, Boelens PG, Borras JM, et al. EURECCA colorectal: multidisciplinary management: European consensus conference colon & rectum. Eur J Cancer 2014; 50: 1.e1-34.
3. Monson JR, Weiser MR, Buie WD, et al. Practice parameters for the management of rectal cancer (revised). Dis Colon Rectum 2013; 56: 535-50.
4. Keller DS, Qiu J, Senagore AJ. Predicting opportunities to increase utilization of laparoscopy for rectal cancer. Surg Endosc 2018; 32: 1556-63.
5. Zhang FW, Zhou ZY, Wang HL, et al. Laparoscopic versus open surgery for rectal cancer: a systematic review and meta-analysis of randomized controlled trials. Asian Pac J Cancer Prev 2014; 15: 9985-96.
6. Piątkowski J, Jackowski M, Szeliga J, et al. Transanal total mesorectal excision (TATME) – preliminary findings. Videosurgery Miniinv 2015; 10: 495-8.
7. Fleshman J, Branda M, Sargent DJ, et al. Effect of laparoscopic-assisted resection vs. open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. JAMA 2015; 314: 1346-55.

8. van der Pas MH, Haglind E, Cuesta MA, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol 2013; 14: 210-8.
9. Stevenson AR, Solomon MJ, Lumley JW, et al. Effect of laparoscopic-assisted resection vs. open resection on pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. JAMA 2015; 314: 1356-63.
10. Pędziwiatr M, Małczak P, Mizera M, et al. There is no difference in outcome between laparoscopic and open surgery for rectal cancer: a systematic review and meta-analysis on short- and long-term oncologic outcomes. Tech Coloproctol 2017; 21: 595-604.
11. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 2005; 5: 13.
12. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg 2010; 8: 336-41.
13. Araujo SE, da Silva eSousa AH, de Campos FG, et al. Conventional approach x laparoscopic abdominoperineal resection for rectal cancer treatment after neoadjuvant chemoradiation: results of a prospective randomized trial. Rev Hosp Clin Fac Med Sao Paulo 2003; 58: 133-40.
14. Zhou ZG, Hu M, Li Y, et al. Laparoscopic versus open total mesorectal excision with anal sphincter preservation for low rectal cancer. Surg Endosc 2004; 18: 1211-5.
15. Ng SS, Leung KL, Lee JF, et al. Laparoscopic-assisted versus open abdominoperineal resection for low rectal cancer: a prospective randomized trial. Ann Surg Oncol 2008; 15: 2418-25.
16. Lujan J, Valero G, Hernandez Q, et al. Randomized clinical trial comparing laparoscopic and open surgery in patients with rectal cancer. Br J Surg 2009; 96: 982-9.
17. Kang SB, Park JW, Jeong SY, et al. Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. Lancet Oncol 2010; 11: 637-45.
18. Jeong SY, Park JW, Nam BH, et al. Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial. Lancet Oncol 2014; 15: 767-74.
19. Gong J, Shi DB, Li XX, et al. Short-term outcomes of laparoscopic total mesorectal excision compared to open surgery. World J Gastroenterol 2012; 18: 7308-13.
20. Guillou PJ, Quirke P, Thorpe H, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet 2005; 365: 1718-26.
21. Jayne DG, Thorpe HC, Copeland J, et al. Five-year follow-up of the Medical Research Council CLASICC trial of laparoscopically assisted versus open surgery for colorectal cancer. Br J Surg 2010; 97: 1638-45.
22. Braga M, Frasson M, Vignali A, et al. Laparoscopic resection in rectal cancer patients: outcome and cost-benefit analysis. Dis Colon Rectum 2007; 50: 464-71.
23. Bonjer HJ, Deijen CL, Haglind E, et al. A randomized trial of laparoscopic versus open surgery for rectal cancer. N Engl J Med 2015; 373: 194.
24. Ng SS, Lee JF, Yiu RY, et al. Laparoscopic-assisted versus open total mesorectal excision with anal sphincter preservation for mid and low rectal cancer: a prospective, randomized trial. Surg Endosc 2014; 28: 297-306.
25. Kennedy RH, Francis EA, Wharton R, et al. Multicenter randomized controlled trial of conventional versus laparoscopic surgery for colorectal cancer within an enhanced recovery programme: EnROL. J Clin Oncol 2014; 32: 1804-11.
26. Green BL, Marshall HC, Collinson F, et al. Long-term follow-up of the Medical Research Council CLASICC trial of conventional versus laparoscopically assisted resection in colorectal cancer. Br J Surg 2013; 100: 75-82.
27. Jacobs M, Verdeja JC, Goldstein HS. Minimally invasive colon resection (laparoscopic colectomy). Surg Laparosc Endosc 1991; 1: 144-50.
28. Askari A, Nachiappan S, Currie A, et al. Selection for laparoscopic resection confers a survival benefit in colorectal cancer surgery in England. Surg Endosc 2016; 30: 3839-47.
29. Chen K, Cao G, Chen B, et al. Laparoscopic versus open surgery for rectal cancer: a meta-analysis of classic randomized controlled trials and high-quality nonrandomized studies in the last 5 years. Int J Surg 2017; 39: 1-10.
30. Greco M, Capretti G, Beretta L, et al. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. World J Surg 2014; 38: 1531-41.
31. Pędziwiatr M, Pisarska M, Kisielewski M, et al. ERAS protocol in laparoscopic surgery for colonic versus rectal carcinoma: are there differences in short-term outcomes? Med Oncol 2016; 33: 56.
32. Pędziwiatr M, Pisarska M, Kisielewski M, et al. Is ERAS in laparoscopic surgery for colorectal cancer changing risk factors for delayed recovery? Med Oncol 2016; 33: 25.
33. Pędziwiatr M, Matłok M, Kisialeuski M, et al. Short hospital stays after laparoscopic gastric surgery under an enhanced recovery after surgery (ERAS) pathway: experience at a single center. Eur Surg 2014; 46: 128-32.
34. Pędziwiatr M, Wierdak M, Nowakowski M, et al. Cost minimization analysis of laparoscopic surgery for colorectal cancer within the enhanced recovery after surgery (ERAS) protocol: a single-centre, case-matched study. Videosurgery Miniinv 2016; 11: 14-21.
35. Kisielewski M, Rubinkiewicz M, Pędziwiatr M, et al. Are we ready for the ERAS protocol in colorectal surgery? Videosurgery Miniinv 2017; 12: 7-12.
36. Pędziwiatr M, Małczak P, Pisarska M, et al. Minimally invasive versus open pancreatoduodenectomy – systematic review and meta-analysis. Langenbecks Arch Surg 2017; 402: 841-51.
37. Okamura R, Hida K, Hasegawa S, et al. Impact of intraoperative blood loss on morbidity and survival after radical surgery for colorectal cancer patients aged 80 years or older. Int J Colorectal Dis 2016; 31: 327-34.
38. Musallam KM, Tamim HM, Richards T, et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. Lancet 2011; 378: 1396-407.

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