REVIEW



# Small bowel obstruction and incisional hernia after laparoscopic and open colorectal surgery: a meta-analysis of comparative trials

Nicolò Pecorelli<sup>1</sup> · Massimiliano Greco<sup>2</sup> · Salvatore Amodeo<sup>1</sup> · Marco Braga<sup>1</sup>

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#### Abstract

*Introduction* Recent studies show contrasting data on the impact of laparoscopy on long-term complications such as the occurrence of small bowel obstruction (SBO) and incisional hernia (IH). The objective of the study was to assess the impact of the laparoscopic approach on the occurrence of SBO and IH after colorectal resection.

*Methods* Two trained investigators independently searched MEDLINE, Embase, PubMed, and the Cochrane Central Register of clinical trials for studies comparing laparoscopy to open surgery for mid- to long-term outcomes after colorectal surgery. No language restriction was set. Sensitivity analyses for study design and quality, conversion rate, type of procedure (colon or rectal surgery), and length of follow-up were performed.

*Results* Eleven RCTs and 14 non-RCT comparative studies for a total of 6540 patients were included in the analysis. Laparoscopy was associated with a significant reduction in the occurrence of SBO (RR 0.57, [95 %CI 0.42–0.76], 16 trials) and IH (RR 0.60, [95 %CI 0.50–0.72], 19 trials). Sensitivity analysis including only RCTs confirmed the reduction in SBO (RR 0.58, [95 %CI 0.39–0.87], 8 trials), while the difference was close to significance for IH (RR 0.76, [95 %CI 0.56–1.03], 7 trials).

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Sensitivity analysis including only studies with conversion rate lower than 15 % showed a significant protective effect of laparoscopy for both SBO (RR 0.53, [95 %CI 0.37–0.77], 11 trials) and IH (RR 0.58, [95 %CI 0.47–0.72], 12 trials). No significant difference between laparoscopy and open surgery was found when the analysis was limited to studies with conversion rate >15 % (SBO: RR 0.60 [0.32–1.12], IH: RR 0.70 [0.46–1.06]). Length of follow-up did not substantially impact on results.

*Conclusion* Laparoscopic surgery is associated with a significant reduction in both SBO and IH compared to the open approach. A low conversion rate in the laparoscopic group plays a key role for reduction in both SBO and IH.

**Keywords** Ventral hernia · Intestinal obstruction · Colorectal surgery · Postoperative complications

It is well established that minimally invasive colorectal resection is associated with short-term benefits compared to traditional open surgery. Systematic reviews and metaanalyses have shown that laparoscopy (LPS) yields reduced postoperative analgesic requirements, lower morbidity, and faster recovery of gastrointestinal function resulting in reduced length of hospital stay [1]. In addition, oncologic non-inferiority of LPS has been reported in the setting of large multicenter trials for both colonic [2] and rectal cancers [3, 4].

The effect of LPS on long-term morbidity is still debated. Minimization of wound size and peritoneal trauma has the potential to protect from the occurrence of incisional hernia (IH) and small bowel obstruction (SBO), which are the most frequent late complications following colorectal resection. However, to our knowledge, no controlled trial has been specifically designed and powered to

Marco Braga braga.marco@hsr.it

<sup>&</sup>lt;sup>1</sup> Department of Surgery, San Raffaele Hospital, Vita-Salute San Raffaele University, Via Olgettina 60, 20132 Milan, Italy

<sup>&</sup>lt;sup>2</sup> Department of Anesthesiology, San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy

detect possible differences in long-term complications between minimally invasive and open surgery. Comparative studies including follow-ups of randomized controlled trials (RCTs) reported that LPS significantly reduced the incidence of IH and SBO [5], while other studies found no difference between surgical approaches [6, 7].

In the present meta-analysis, we aimed to summarize the available evidence and verify the effect of LPS on the occurrence of SBO and IH in patients undergoing elective colorectal resection.

## Methods

#### Search strategy and study selection

This systematic review and meta-analysis was conducted according to the Cochrane Collaboration and the Preferred Reporting Items for Systematic reviews (PRISMA) guidelines [8]. Our search strategy followed the principles of the PICO (patient, intervention, comparison, outcomes) framework [9]. The objective was to evaluate in patients undergoing colorectal surgery (P) the impact of laparoscopy (I) compared with open surgery (C) on long-term morbidity (O).

A systematic database search was performed using MEDLINE (via OvidSP), Embase (via OvidSP), the Cochrane Library, and PubMed for articles up to January 2015. The search strategy was developed according to Robinson et al. [10], using text words and relevant indexing to capture the concepts of laparoscopic colorectal procedures (e.g., laparoscopy, colon resection, rectal resection, sigmoidectomy) and postoperative complications (e.g., intestinal obstruction, incisional hernia). No language restrictions were considered. The search strategy used for the MEDLINE database is described in Supplemental digital content 1.

#### Inclusion and exclusion criteria

The following inclusion criteria were used for potentially relevant studies: (1) involves adult patients undergoing laparoscopic colorectal surgery, (2) a control group receiving open surgery, (3) random or non-random allocation to treatment, (4) reported at least one of the outcome measures of interest (see below) with no restriction on primary or secondary outcome. For the purpose of this review, we included both hand-assisted and conventional laparoscopic approaches. No language restrictions were set. Exclusion criteria were: (1) duplicate publications (in this case, only the article reporting the longest follow-up was abstracted), (2) non-human experimental studies, (3) more than 20 % of the cases were emergency surgeries, (4) patient follow-up was shorter than 12 months. The three investigators independently assessed compliance to selection criteria and selected studies for the final analysis with divergences finally being resolved by consensus.

#### **Outcome measures**

The primary outcome measures of interest were surgeryrelated SBO and IH occurring more than 30 days after surgery or after discharge from the primary admission. Secondary endpoints were reoperations due to surgery-related incisional hernia and small bowel obstruction occurring more than 30 days after surgery or after discharge from the primary admission.

# Study selection, data extraction, and quality assessment

Two expert investigators (NP, SA) independently screened the articles identified by the search. Clearly irrelevant articles were excluded after examination of titles and abstracts. Non-English-language articles were translated before further analysis. Full-text versions of all articles potentially suitable for inclusion were retrieved and evaluated against the selection criteria. Divergences regarding eligibility were resolved by consensus or by consulting the senior investigator (MB). Data were extracted independently by two investigators (NP, SA) and crosschecked. In addition to the outcome measures of interest, the following variables were obtained from the selected papers: patient demographics and body mass index (BMI), diagnosis, type of resection (e.g., colonic resection, rectal resection), conversion rate, duration and modality of follow-up, definition of relevant endpoints.

The internal validity and the quality of each trial were evaluated independently by two investigators (MG, SA) using the Cochrane Collaboration's tool [11] with divergences being resolved by consensus or by consulting a third investigator (MB). This tool appraises risk of bias across six domains: selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other risks of bias. Because of the impossibility to blind assessors to the intervention in assessing the occurrence of incisional hernia, for the domain "detection bias," we considered at low risk studies in which the clinical assessor was either independent (i.e., did not participate in the care of the patient) or was unaware of the type of surgery when reviewing questionnaire or radiological data. For the domain "other biases," we considered any potential source of bias not included in the previous domains (e.g.,

#### Fig. 1 PRISMA flow diagram



extreme imbalance in baseline characteristics, trial was stopped early). The Cochrane Collaboration's tool was originally designed to evaluate risk of bias in RCTs, but it has often been extended to non-randomized intervention studies [12]. Some domains of the tool are invariably negative in the absence of randomization (e.g., adequate sequence generation, allocation concealment). Studies with suboptimal scoring in up to three items were regarded at a moderate risk of bias, while studies with more than three suboptimal items and all non-randomized studies were qualified at high risk of bias.

#### Statistical analysis

Computations were performed with Stata 13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Statistical heterogeneity and inconsistency were measured using Cochran's Q tests and  $I^2$ , respectively. Binary outcomes from individual studies were analyzed to compute individual and pooled risk ratios (RR) with pertinent 95 % confidence intervals (CI, with

equivalence set at 1, RR < 1 favoring the first treatment, and RR > 1 favoring the second treatment), by means of a fixed effects method by inverse variance in the presence of low or moderate statistical inconsistency ( $I^2 \le 25$  %), and by means of a random effects method (which considers clinical and statistical variations) by DerSimonian and Laird in the presence of high statistical inconsistency ( $I^2 > 25$  %). Statistical significance was set at the twotailed 0.05 level for measure of effect testing and for heterogeneity testing.

A sensitivity analysis was performed by analyzing data from studies with low/intermediate risk of bias only. Subgroup analyses were planned a priori and performed, when possible, by clustering the studies according to whether they performed colon or rectal resection. Other subgroup analyses were also planned to verify the effect of conversion to open surgery and length of follow-up on the occurrence of SBO and IH. Studies reporting conversion to open surgery lower than 15 % were considered with low conversion rate, while trials with 15 % or higher conversion rate were considered with high conversion rate.

Table 1 Quality assessment of included studies

Study	Design	Quality asse	ssment accordir	t according to the Cochrane Collaboration's tool					
		Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall risk of bias
LAFA study [5]	Multicenter randomized controlled trial	(+)	(+)	(-)	(?)	(+)	(+)	(+)	Low
Ng et al. [15]	Randomized controlled trial	(+)	(-)	(-)	(?)	(+)	(+)	(+)	Moderate
COLOR study [6]	Multicenter randomized controlled trial	(+)	(+)	(-)	(?)	(-)	(+)	(+)	Moderate
Gervaz et al. [19]	Randomized controlled trial	(+)	(+)	(+)	(-)	(+)	(+)	(+)	Low
Braga et al. [17]	Randomized controlled trial	(+)	(+)	(-)	(+)	(+)	(+)	(+)	Low
Eshuis et al. [18]	Multicenter randomized controlled trial	(?)	(+)	(-)	(?)	(+)	(+)	(+)	Low
CLASICC study [7]	Multicenter randomized controlled trial	(?)	(+)	(-)	(?)	(—)	(+)	(+)	Moderate
Ng et al. [16]	Randomized controlled trial	(+)	(-)	(-)	(?)	(-)	(+)	(+)	Moderate
Stocchi et al. [21]	Randomized controlled trial	(-)	(-)	(-)	(?)	(+)	(+)	(-) <sup>a</sup>	High
Polle et al. [20]	Multicenter randomized controlled trial	(?)	(+)	(-)	(?)	(+)	(+)	(+)	Low
Winslow [22]	Multicenter randomized controlled trial	(?)	(+)	(-)	(-)	(—)	(+)	(+)	Moderate
Vignali et al. [36]	Retrospective matched cohort	(-)	(-)	(-)	(?)	(+)	(+)	(+)	High
Makni et al.	Retrospective cohort	(—)	(-)	(-)	(?)	(+)	(+)	(+)	High
Pereira et al. [34]	Retrospective cohort	(—)	(—)	(-)	(+)	(+)	(+)	(+)	High
Saklani et al. [35]	Retrospective cohort	(-)	(—)	(-)	(?)	(+)	(+)	(+)	High
Kellokumpu et al. [29]	Retrospective cohort	(-)	(—)	(-)	(?)	(+)	(+)	(+)	High
Llaguna et al. [31]	Retrospective cohort	(-)	(-)	(-)	(?)	(?)	(+)	(+)	High

Retrospective

Retrospective

matched cohort

Prospective

multicenter cohort

cohort Prospective

cohort

#### Table 1 continued

Study

Andersen

et al. [23]

Laurent et al.

Eshuis et al.

[30]

[26]

Ihedioha

[28]

Duepree

Patankar

et al. [25]

et al. [33]

Champault

Franklin

et al. [24]

et al. [27]

Design	Quality asse	ssment accordir	ng to the Cochrane	Collaboration'	s tool			
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall risk of bias
Retrospective matched cohort	(-)	(-)	(-)	(?)	(+)	(+)	(+)	High
Retrospective cohort	(-)	(-)	(-)	(-)	(?)	(+)	(+)	High
Retrospective multicenter cohort	(-)	(-)	(-)	(-)	(+)	(+)	(+)	High
Prospective cohort	(-)	(-)	(-)	(+)	(+)	(+)	(+)	High

(?)

(?)

(?)

(-)

(?)

(?)

(?)

(?)

(+)

(+)

(+)

(+)

(+)

(+)

(+)

(+)

High

High

High

High

(+) Low risk of bias; (-) high risk of bias; (?) unclear risk of bias

(-)

(-)

(-)

(-)

<sup>a</sup> Randomization to intervention only done after exploratory laparoscopy assessed feasibility

(-)

(-)

(-)

(-)

(-)

(-)

(-)

(-)

Previous publications showed that more than one-third of IH are diagnosed 5 years or longer after open surgery [13]. Thus, we performed subgroup analyses for studies with duration of follow-up lower than 5 years and studies with follow-up time of at least 5 years.

Publication bias was assessed by visually inspecting funnel plots, by sequential removal of individual studies, by analytical appraisal based on the Egger's regression test, and on the Peter test for publication bias [14]. According to the Egger or Peter methods for publication bias evaluation, a two-sided p value of 0.05 or less was regarded as significant.

#### Results

#### Literature search

Database searches and scanning of references of retrieved articles yielded a total of 12,437 articles. Excluding nonpertinent titles or abstracts, we retrieved 76 studies in complete form, which we assessed according to the selection criteria. A total of 51 studies were further excluded due to: no reporting of long-term complications (n = 38), duplicate publication (n = 3), study from a population-based registry (n = 3), high amount of missing data (n = 3), short follow-up (n = 2), only emergency surgery (n = 1), insufficient information on timing of complications (n = 1). The excluded articles and reasons for exclusion are listed in Supplemental digital content 2. Finally, twenty-five full-text articles fulfilled our selection criteria and were included in the review. The flowchart of articles selection is shown in Fig. 1.

#### Characteristics of the included studies

The 25 studies analyzed in this review included 11 RCTs [5-7, 15-22] and 14 non-randomized trials [23-36]. Of the latter, 11 were retrospective cohort studies including 3 matched studies, and 3 were prospective cohort trials. Table 1 summarizes the methodological quality of the 25 studies. Fifteen studies were considered at high risk of bias.

Study characteristics are summarized in Table 2. Eleven RCTs totaling 2831 patients (1485 LPS, 1346 open) and 14 non-randomized trials totaling 3709 patients (1524 LPS, 2185 open) were included in the analysis for an overall pool of 6540 patients (3009 LPS, 3531 open). Overall, 21 studies included patients undergoing colectomy, and 14 studies included rectal resection patients. Median conversion to open surgery rate was 11 % (interquartile range

Table 2 Characteristics of included studies

Study	Sam	ole size	Type of	Conversion	ITT	Length of follow-up	Follow-up modality
-	LPS	Open	resection	(%)	analysis	(months)	
LAFA study [5]	208	191	Colon	12	~	Median 40.8	Medical record review/Questionnaire interview
Ng et al. [15]	40	40	Rectum	8	~	Median 75.7 (LPS), 76.1 (open)	Office visits/Review of readmissions
COLOR study [6]	383	403	Colon	21	~	Median 60	Medical record review
Gervaz et al. [19]	54	51	Colon	9	~	Median 30 (LPS), 29 (open)	Office visits/Review of readmissions
Braga et al. [17]	330	332	Colon, rectum	5	~	Median 96	Office visits/Review of readmissions
Eshuis et al. [18]	29	26	Colon	10	~	Median 80.4	Office visits/Mailed questionnaire/ Telephone interview
CLASICC study [7]	280	131	Colon, rectum	24	~	Actual 36	Medical chart review
Ng et al. [16]	74	74	Rectum	30	~	Median 112.5 (LPS), 108.8 (open)	Office visits/Review of readmissions
Stocchi et al. [21]	27	29	Colon	6	~	Mean 126	Chart review/Mailed questionnaire/ Telephone interview
Polle et al. [20]	23	23	Colon, rectum	0	~	Median 32.4	Medical record review/Mailed questionnaire/Telephone interview
Winslow [22]	37	46	Colon	15		Mean 30.1	Office visits/Review of readmissions
Vignali et al. [36]	98	98	Colon	13	~	Median 62	Medical record review/Telephone interview
Makni et al. [32]	64	65	Colon	14	~	Mean 29.3	Medical record review
Pereira et al. [34]	89	249	Colon, rectum	10	~	Median 19.7	Medical record review
Saklani et al. [35]	144	187	Colon, rectum	13	~	Median 24.5 (LPS), 49 (open)	Medical record review
Kellokumpu et al. [29]	99	88	Rectum	22	~	Median 57.6	Medical record review
Llaguna et al. [31]	109	109	Colon, rectum	5		Mean 25.9	Medical record review
Andersen et al. [23]	58	143	Colon	8		Median 55.2 (LPS), 58.8 (open)	Telephone interview/Office visits
Laurent et al. [30]	155	165	Rectum	21	~	Median 51	Office visits
Eshuis et al. [26]	27	44	Colon	7	~	Median 103.2	Medical chart review/Office visits/Mailed questionnaire/Telephone interview
Ihedioha [28]	32	63	Colon, rectum	19	~	Median 22	Office visits
Duepree et al. [25]	211	505	Colon, small bowel	11		Median 32.5 (LPS), 29.0 (open)	Medical chart review/Mailed questionnaire/Telephone interview
Patankar et al. [33]	172	172	Colon, rectum	20	~	Mean 52 (LPS), 59 (open)	Office visits/Telephone interview/ Medical record review
Champault et al. [24]	74	83	Colon, rectum	8	~	Median 52.4 (LPS), 56.3 (open)	Office visits
Franklin et al. [27]	192	214	Colon, rectum	4	~	Median $> 30$ (LPS), $> 24$ (open)	Office visits

LPS laparoscopy, ITT intention to treat

### Table 3 Sample characteristics

Study	Age (years)		Male gend	ler	BMI (kg/m <sup>2</sup> )		Cancer	
	LPS	Open	LPS	Open	LPS	Open	LPS	Open
LAFA study [5]	Median 68 (60–74)	Median 67 (61–73)	121 (58)	113 (59)	Median 25.7 (23.4–27.7)	Median 26.1 (23.4–9.1)	177 (85)	160 (84)
Ng et al. [15]	Mean 60.2 (11.3)	Mean 62.1 (12.6)	24 (60)	22 (55)	Mean 23.1 (3.4)	Mean 22.4 (3.2)	40 (100)	40 (100)
COLOR study	≤70: 46 %	≤70: 46 %	197 (51)	212 (53)	≤25: 56 %	≤25: 50 %	379 (99)	398 (99)
Gervaz et al.	>70: 54 % Median 59	>70: 54 % Median 63	24 (44)	21 (41)	>25: 41 % 27 (19–35)	>25: 46 % 26 (20–37)	0	0
[19] Progo at al	(29–82) Maan 63 5	(38–84) Moon 65 6 (12 6)	182 (55)	186 (56)	ND	NID	258 (78)	268 (81)
[17]	(13.2)	Weall 05.0 (12.0)	182 (33)	180 (30)	INK	NK	238 (78)	208 (81)
Eshuis et al. [18]	Median 34.8 (29–41)	Median 38.9 (29.4–46.6)	12 (41)	9 (35)	Median 23.9 (22.8–26.6)	Median 24.3 (22.0–26.4)	0	0
CLASICC study [7]	Mean 68.9 (10.4)	Mean 69.9 (11.2)	162 (58)	73 (56)	Mean 25.5 (4.8)	Mean 26.1 (4.7)	280 (100)	131 (100)
Ng et al. [16]	Mean 66.5 (11.9)	Mean 65.7 (12.0)	37 (49)	48 (62)	NR	NR	74 (100)	74 (100)
Stocchi et al. [21]	Mean 36	Mean 35	24 (43)		NR	NR	0	0
Polle et al. [20]	Median 32.6 (19–59)	Median 37.5 (18–62)	6 (23)	13 (48)	Median 22.6 (18.1–34.7)	Median 23.3 (17.2–34.2)	0	0
Winslow [22]	Mean 69.4 (11.7)	Mean 65.7 (11.5)	NR	NR	NR	NR	37 (100)	46 (100)
Vignali et al. [36]	Mean 66.9 (12.2)	Mean 68.7 (15)	52 (53)	47 (48)	Mean 31.9 (2.1)	Mean 32.3 (2.5)	85 (87)	79 (81)
Makni et al. [32]	Mean 31 (9.9)	Mean 31 (11.8)	35 (55)	35 (54)	NR	NR	0	0
Pereira et al. [34]	Mean 68.9 (11.5)	Mean 68.7 (11.3)	43 (48)	149 (60)	Mean 27.6 (4.7)	Mean 27.8 (4.6)	89 (100)	249 (100)
Saklani et al. [35]	Median 73 (44–92)	Median 69.5 (42–92)	67 (47)	113 (60)	NR	NR	94 (65)	129 (69)
Kellokumpu et al. [29]	Mean 66.5 (11.8)	Mean 68.0 (10.2)	65 (65)	65 (71)	Mean 25.4 (3.1)	Mean 25.9 (4.6)	99 (100)	88 (100)
Llaguna et al. [31]	Mean 59.6 (14)	Mean 64.3 (13.5)	59 (54)	55 (51)	Mean 28.3 (5.4)	Mean 28.4 (4.6)	138 (63)	
Andersen et al. [23]	Median 78 (37–94)	Median 74 (41–95)	27 (47)	70 (49)	25.1	25.3	NR	NR
Laurent et al. [30]	Median 66 (25–84)	Median 64 (20–88)	91 (59)	104 (63)	Median 24.5 (16.2–33.2)	Median 25.0 (16.6–41.0)	155 (100)	165 (100)
Eshuis et al. [26]	Median 40 (26–66)	Median 44 (26–85)	7 (26)	10 (23)	Median 23.9 (19.1–34.5)	Median 23.1 (16.4–34.6)	0	0
Ihedioha [28]	Median 74	Median 74	17 (53)	30 (48)	NR	NR	30 (94)	47 (75)
Duepree et al. [25]	Mean 50.8 (10-85)	Mean 57.7 (11–92)	91 (43)	255 (51)	NR	NR	27 (13)	219 (43)
Patankar et al. [33]	Mean 67 (27–85)	Mean 69 (30–90)	73 (42)	77 (45)	NR	NR	172 (100)	172 (100)
Champault et al. [24]	Mean 66.8 (39–86)	Mean 61.3 (31–84)	38 (51)	45 (54)	NR	NR	74 (100)	83 (100)
Franklin et al. [27]	Mean 66.8	Mean 63.7	96 (50)	123 (58)	NR	NR	192 (100)	214 (100)

Values are mean (SD) or median (range), or number of patients (%), as specified

LPS laparoscopy, BMI body mass index, NR not reported

Study	Thirty-da	v reoperatio		Anastome	tic leak		Wound	infection		Ileus			Thirty-da	v readmissic	u
'n	SdT	Open	р	SdT	Open	d	SdT	Open	d	SdJ	Open	d	SdT	Open	d
LAFA study [5]	21 (10)	31 (16)	0.24	13 (6)	15 (8)	NR	14 (7)	26 (13.6 %)	NR	15 (7)	10 (5)	NR	13 (6)	14 (7)	0.97
Ng et al. [15]	1 (3)	0	NR	1 (3)	2 (5)	NR	1 (3)	7 (18)	NR	3 (8)	5 (13)	NR	NR	NR	I
COLOR study [6]	37 (7)	25 (5)	0.13	15 (3)	10 (2)	0.39	20 (4)	16 (3)	0.57	NR	NR	I	NR	NR	I
Gervaz et al. [19]	3 (5)	1 (2)	0.62	0	0	I	0	1 (2)	NR	0	1 (2)	NR	NR	NR	I
Braga et al. [17]	16 (5)	25 (8)	0.2	15 (5)	19 (6)	0.6	17 (5)	31 (9)	0.06	4 (1)	8 (2)	0.39	NR	NR	I
Eshuis et al. [18]	0	1 (3)	NR	0	0	I	0	6 (20)	NR	1 (3)	2 (7)	NR	0	4 (13)	NR
CLASICC study [7]	NR	NR	I	35 (7)	13 (5)	NR	47 (9)	22 (8)	NR	NR	NR	I	NR	NR	I
Ng et al. [16]	2 (3)	4 (5)	NR	1 (1)	4 (5)	NR	5 (7)	9 (12)	NR	1 (1)	2 (3)	NR	NR	NR	I
Stocchi et al. [21]	1 (3)	1 (3)	NR	1 (3)	0	NR	2 (7)	3 (10)	NR	2 (7)	3 (10)	NR	0	0	I
Polle et al. [20]	3 (10)	4 (13)	0.72	3 (10)	1 (3)	NR	1 (3)	1 (3)	NR	0	2 (7)	NR	NR	NR	I
Winslow [22]	NR	NR	I	NR	NR	I	5 (14)	5 (11)	> 0.05	2 (5.4)	14 (30)	0.0047	NR	NR	I
Vignali et al. [36]	8 (8)	6) 6)	0.8	(1) (2)	5 (5)	0.78	8 (8)	15 (15)	NR	3 (3)	3 (3)	NR	( <i>L</i> )	11 (11)	0.56
Makni et al. [32]	0	1 (2)	0.5	0	5 (8)	0.06	3 (5)	2 (3)	0.48	NR	NR	I	NR	NR	I
Pereira et al. [34]	5 (6)	19 (8)	0.52	2 (2)	8 (3)	0.21	8 (9)	39 (16)	0.04	NR	NR	I	NR	NR	I
Saklani et al. [35]	3 (2)	6 (3)	NR	1 (1)	5 (3)	NR	NR	NR	I	NR	NR	I	NR	NR	I
Kellokumpu et al. [29]	6 (6)	8 (9)	0.46	11 (11)	8 (9)	0.2	6 (6)	17 (19)	0.013	3 (3)	1 (1)	0.62	11 (11)	13 (15)	0.49
Llaguna et al. [31]	NR	NR	I	NR	NR	I	6 (6)	10 (9)	0.703	NR	NR	I	NR	NR	I
Andersen et al. [23]	NR	NR	I	NR	NR	I	NR	NR	I	NR	NR	I	NR	NR	I
Laurent et al. [30]	32 (21)	22 (13)	0.1	NR	NR	I	3 (2)	8 (5)	0.221	NR	NR	I	NR	NR	I
Eshuis et al. [26]	0	2 (4)	NR	0	1 (2)	NR	1 (3)	3 (6)	NR	NR	NR	I	NR	NR	I
Ihedioha [28]	NR	NR	I	NR	NR	Ι	3 (9)	6(10)	NR	NR	NR	Ι	NR	NR	I
Duepree et al. [25]	NR	NR	I	NR	NR	I	NR	NR	I	NR	NR	Ι	NR	NR	I
Patankar et al. [33]	NR	NR	I	0	2 (1)	NR	3 (2)	2 (1)	NR	5 (3)	0	NR	NR	NR	I
Champault et al. [24]	0	1 (1)	NR	0	2 (2)	NR	4 (5)	8 (10)	NR	1 (1)	9 (11)	0.01	NR	NR	I
Franklin et al. [27]	NR	NR	I	0	4 (2)	NR	1 (1)	14 (7)	NR	6 (3)	11 (5)	NR	10 (5)	19 (9)	NR
Values are number of pa	tients (%)														
LPS laparoscopy, IVA IIU	t reporteu														

8–19 %), including 5 studies with conversion exceeding 15 %. Mean or median length of patient follow-up was 5 years or longer in 8 studies. Follow-up modality was heterogeneous between studies, including office visits, medical record review, patient telephone interview, or mailed questionnaires.

Table 3 reports baseline characteristics of the patients included in the studies. Detailed short-term postoperative morbidity and hospital readmission are listed in Table 4. The amount of missing data for short-term outcomes is significant. Two non-randomized studies reported increased wound infection in the open group, while a single RCT and a non-randomized study showed reduced incidence of postoperative ileus in the LPS group.

#### Small bowel obstruction

Sixteen trials reported on the occurrence of SBO, 8 RCTs [5-7. 15-17. 19. 20] and 8 non-RCTs [24, 25, 27, 29, 32, 33, 35, 36]. When all trials have been pooled together, LPS significantly reduced SBO rate (2.78 %, 68/2446) compared to the open group (5.53 %, 147/2657) (RR 0.57, [0.42, 0.76] p for effect < 0.0001, p for heterogeneity = 0.7,  $I^2 = 0$  %) (Fig. 2). A significant difference in favor of LPS was found when the analysis was restricted to RCTs only (RR 0.58, [0.39, 0.87] p for effect < 0.008, p for heterogeneity = 0.3,  $I^2 = 4.2$  %), whereas the difference was barely significant when the analysis was limited to non-RCTs (RR 0.61, [0.36, 1.02] for effect = 0.057, *p* for heterogeneity = 0.86, р  $I^2 = 0$  %) (Fig. 3). SBO requiring surgery was comparable between patients undergoing LPS and open surgery (Supplemental digital content 3), also when RCTs and non-RCTs were considered separately (data not shown).

#### **Incisional hernia**

Nineteen studies reported on the incidence of incisional hernia, 7 RCTs [5, 7, 15–17, 20, 22] and 12 non-RCTs [23–25, 27–34, 36]. When all trials have been pooled together, LPS significantly reduced IH rate (7.08 %, 166/2345) compared to the open group (13.58 %, 379/2791) (RR 0.60, [0.50, 0.72] p for effect = 0.0001, p for heterogeneity = 0.19,  $I^2 = 21$  %) (Fig. 4). A significant difference in favor of LPS was found when the analysis was restricted to non-RCTs only (RR 0.57, [0.45, 0.72] p for effect = 0.0001, p for heterogeneity = 0.53,  $I^2 = 0$  %), whereas the difference was not significant when the analysis was limited to RCTs (RR 0.76, [0.56, 1.03] p for effect = 0.076, p for heterogeneity = 0.56,  $I^2 = 0$  %) (Fig. 5). The need for surgery due to IH was comparable between LPS and open

surgery (Supplemental digital content 4), also when RCTs and non-RCTs were considered separately (data not shown).

#### Sensitivity analyses and risk of bias

When the analysis was restricted to trials with low or intermediate risk of bias only, LPS significantly reduced SBO rate (RR 0.58, [0.39, 0.86] *p* for effect = 0.008, *p* for heterogeneity = 0.39,  $I^2 = 4$  %), whereas no significant difference for IH rate was found (RR 0.76, [0.56, 1.03] *p* for effect = 0.076) (Supplemental digital contents 5 and 6).

A sensitivity analysis was performed according to the conversion rate in the LPS group. Studies were split into high conversion rate (i.e., 15 % or higher) or low conversion rate (i.e., lower than 15 %). The occurrence of SBO remained significantly lower in the LPS group considering the 11 studies reporting low conversion rates only (RR 0.53, [0.37, 0.77] p for effect = 0.001, p for heterogeneity = 0.9,  $I^2 = 0$  %), whereas no difference was found between LPS and open surgery considering the 5 studies with high conversion rate only (RR 0.60, [0.32, 1.12] p for effect = 0.11, p for heterogeneity = 0.24,  $I^2 = 26 \%$ ) (Fig. 6). Similarly, the occurrence of IH remained significantly lower in the LPS group considering the 12 studies with low conversion rate only (RR 0.58, [0.47, 0.72] p for effect = 0.001, p for heterogeneity = 0.27,  $I^2 = 18 \%$ ), whereas a nonsignificant difference was found between LPS and open surgery considering the 7 studies where conversion rate exceed 15 % (RR 0.70, [0.46, 1.06] p for effect = 0.095, p for heterogeneity = 0.15,  $I^2 = 36 \%$ ) (Fig. 7).

LPS approach significantly reduced both SBO and IH considering studies with follow-up longer or shorter than 5 years (data not shown). Analyzing colonic and rectum resection separately, the occurrence of SBO was significantly lower in the LPS group considering 9 studies reporting data for colonic resection (RR 0.55, [0.38, 0.79] for effect = 0.001, p for heterogeneity = 0.91, р  $I^2 = 0$  %), whereas the difference was not significant considering 7 studies that included data for rectal resection (RR 0.59, [0.34, 1.02] p for effect = 0.058, p for heterogeneity = 0.32,  $I^2 = 14$  %) (Fig. 8). Conversely, the occurrence of IH was significantly different between LPS and open surgery for both colonic resection only (RR 0.54, [0.39, 0.76] p for effect < 0.001, p for heterogeneity = 0.15,  $I^2 = 34$  %) and rectum resection only (RR 0.54, [0.38, 0.77] p for effect = 0.001, p for heterogeneity = 0.27,  $I^2 = 21$  %) (Fig. 9). In studies reporting subgroup analysis for rectal resection [7, 17, 20, 29, 30, 35], median conversion rate was 16 % (interquartile range 8-22 %).

Fig. 2 Pooled estimates of small bowel obstruction comparing laparoscopic versus open surgery. All studies have been considered. *CI* confidence intervals, *df* degrees of freedom, *RR* risk ratio

		%
	RR (95% CI)	Weight
	0.75 (0.17, 3.35)	3.89
	0.16 (0.01, 3.05)	0.99
	0.82 (0.24, 2.75)	5.88
	0.74 (0.38, 1.44)	19.28
	0.43 (0.20, 0.94)	13.86
	0.37 (0.08, 1.82)	3.42
	0.32 (0.01, 7.56)	0.85
	0.53 (0.13, 2.17)	4.38
<b>•</b>	0.33 (0.12, 0.89)	8.58
	0.51 (0.13, 1.94)	4.78
•	0.14 (0.03, 0.61)	4.12
<b>_</b>	0.57 (0.18, 1.80)	6.54
	1.50 (0.25, 8.87)	2.73
	- 1.33 (0.34, 5.30)	4.52
	0.60 (0.23, 1.54)	9.70
	0.83 (0.26, 2.64)	6.48
0.0%, p = 0.793)	0.57 (0.42, 0.76)	100.00



Fig. 3 Pooled estimates of small bowel obstruction comparing laparoscopic versus open surgery. RCTs (*left plot*) and non-RCTs (*right plot*) have been considered separately. CI confidence intervals, RR risk ratio

Visual inspection of funnel plots did not identify a skewed or asymmetrical shape (Supplemental digital contents 7–8). Sequential removal of individual studies did not identify any study with excessive influence on results. Quantitative evaluation did not suggest the presence of publication bias, as measured by the Peter test (p = 0.74 for SBO analysis and p = 0.14 for IH analysis) and the Egger test (p = 0.60 for SBO analysis and p = 0.59 for IH analysis) on the overall complication rate.

# Discussion

The present meta-analysis found that laparoscopic colorectal surgery is associated with a significant reduction in SBO and IH compared to the open approach. Limiting the analysis to RCTs only, the incidence of SBO was significantly lower in patients treated with laparoscopy, while the reduction in IH only approached statistical significance. Sensitivity analyses showed that the laparoscopic approach **Fig. 4** Pooled estimates of incisional hernia comparing laparoscopic versus open surgery. All studies have been considered. *CI* confidence intervals, *RR* risk ratio





Fig. 5 Pooled estimates of incisional hernia comparing laparoscopic versus open surgery. RCTs (*left plot*) and non-RCTs (*right plot*) have been considered separately. CI confidence intervals, RR risk ratio

is associated with a significant reduction in both SBO and IH only in studies with low conversion rate.

The growing popularity of colorectal laparoscopic approach among surgeons and patients is due to its demonstrated advantages in the short term [1]. Moreover, RCTs confirmed that LPS did not adversely affect the chance of cure for colonic cancer [2]. Among the potential long-term advantages of LPS, a reduction in SBO and IH rates has been hypothesized in several comparative studies with contrasting results [5–7, 16]. The present meta-analysis explores this issue and represents a substantial update from a previous Cochrane review [37] in terms of number of studies and patients included. To clarify the effect of factors potentially influencing the occurrence of SBO and



**Fig. 6** Pooled estimates of small bowel obstruction comparing laparoscopic (LPS) versus open surgery. Studies have been split according to high ( $\geq$ 15 %, *right plot*) or low (<15 %, *left plot*) conversion rate in the LPS group. *CI* confidence intervals, *RR* risk ratio



Fig. 7 Pooled estimates of incisional hernia comparing laparoscopic (LPS) versus open surgery. Studies have been split according to high ( $\geq$ 15 %, *right plot*) or low (<15 %, *left plot*) conversion rate in the LPS group. *CI* confidence intervals, *RR* risk ratio



Fig. 8 Pooled estimates of small bowel occlusion comparing laparoscopic (LPS) versus open surgery. Studies have been split according to surgical site (colon surgery on *left plot*, rectum on *right plot*). *CI* confidence intervals, *RR* risk ratio

IH such as conversion to open surgery, length of follow-up, and type of procedure (colonic or rectal resection), specific sensitivity and subgroup analyses were performed. SBO is a frequent cause of hospital admission and eventually late reoperation after colorectal surgery [38, 39]. Postoperative adhesion formation takes place in response



Fig. 9 Pooled estimates of incisional hernia comparing laparoscopic (LPS) versus open surgery. Studies have been split according to surgical site (colon surgery on *left plot*, rectum on *right plot*). CI confidence intervals, df degrees of freedom, RR risk ratio

to injury of the peritoneal surfaces involving a complex interaction of many factors secreted by cells proximate to the traumatized areas [40]. The minimally invasive approach has the potential to reduce adhesion formation because of attenuated surgical trauma, less tissue handling, and smaller scars [41]. Our analysis found that LPS significantly reduced SBO by almost half when compared to open surgery. This was confirmed when limiting the analysis to RCTs and to trials at low risk of bias. Sensitivity analyses confirmed the reduction in SBO in LPS when considering subgroups with low conversion rate and colon resection, whereas no significant reduction was found including studies with high conversion rate and rectal resection.

Incisional hernia occurs in up to 30 % patients receiving a laparotomy and often enlarges over time leading to pain and potentially serious complication such as bowel obstruction, incarceration and strangulation [30, 31]. The possible reduction in IH in LPS surgery could derive from smaller incisions, better preservation of the abdominal wall, and lower wound infection rate compared to open approach. In the analysis we performed, LPS significantly reduced the risk of IH by 40 % when compared with open surgery. However, this effect was not confirmed when the analysis was limited to RCTs or when trials at high risk of bias were excluded. Sensitivity analyses confirmed the reduction in IH by LPS when considering studies with low conversion rate, whereas no difference was found including the studies with a high conversion rate only.

The impact of different factors on the occurrence of SBO and IH has been investigated by specifically focused sensitivity analyses. Conversion to open surgery was a key effect modifier when analyzing the impact of laparoscopy on both SBO and IH. When the analysis was limited to studies with conversion rate higher than 15 %, no advantage from the laparoscopic approach was found. In fact, as conversion rate increases, the number of patients initially

allocated to the LPS group who really benefit from the minimally invasive approach is reduced. Moreover, previous research has shown that patients converted from laparoscopic to open surgery experience more complications than those operated with a straightforward open approach [7]. A per-protocol analysis, which includes in the LPS arm only those patients who had a successful laparoscopic resection, would better ascertain the impact of the minimally invasive technique on long-term morbidity, but it would not reflect real-life clinical practice. Length of follow-up did not substantially impact on results, despite studies suggesting that long-term morbidity can occur several years after the primary surgery [13, 16].

No significant advantage from laparoscopic approach on SBO rates was found in patients who underwent rectal surgery. However, only few studies, most of which were non-randomized, reported subgroup data for rectal surgery. This limited the power of our analysis and increased the risk of bias. In addition, half of these trials [7, 29, 30] had conversion rates for rectal resection >20 %, which significantly reduces the protective effect of LPS. It should also be noted that rectal cancer patients are routinely undergoing neoadjuvant or adjuvant radiotherapy, which may have facilitated the occurrence of postoperative pelvic adhesions and SBO in both groups. Thus, to correctly identify the influence of the surgical approach on long-term complications following rectal resection, additional data from novel and specifically designed prospective studies accounting for confounding factors are required.

A limitation of our meta-analysis is that several included trials are of suboptimal quality especially non-randomized trials, carrying a high risk of bias. To avoid possible influences due to the poor quality of some studies, separate sensitivity analyses focused on RCTs and excluding trials at high risk of bias were performed. In addition, no risk of small studies bias or publication bias was detected, and no single study was identified as excessively influencing overall results. Another limitation concerning all studies included is that none of them was primarily designed and powered to detect possible differences in long-term complications between minimally invasive and open surgery, rather it represented a secondary analysis of studies powered on short-term results or cancer survival. Furthermore, subgroup analysis for colon and rectal resection were limited because of reduced sample size and a significant amount of missing data. Finally, it should also be noted that, although outcome measures and sensitivity analyses were planned ahead before pooling the data, the study protocol was not registered in a systematic review database (e.g., PROSPERO).

In conclusion, this meta-analysis found that laparoscopic colorectal surgery is associated with a significant reduction in SBO and IH compared to the open approach. When conversion rate is high, the protective role of laparoscopy for the occurrence of both SBO and IH disappears.

#### Compliance with ethical standards

Disclosures Drs. Nicolò Pecorelli, Massimiliano Greco, Salvatore Amodeo, and Marco Braga have no conflict of interest to disclose.

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