Laparoscopic right colectomy reduces short-term mortality and morbidity. Results of a systematic review and meta-analysis

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Laparoscopic right colectomy reduces short-term mortality and morbidity. Results of a systematic review and meta-analysis

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Abstract

Purpose

While definitive long-term results are not yet available, the global safety and oncologic adequacy of laparoscopic surgery for right colectomy remain controversial. The aim of the study was to evaluate differences in safety of laparoscopic right colectomy, compared with open surgery, with particular attention to cancer patients.

Methods

A systematic review from 1991 to 2014 was performed searching the MEDLINE and EMBASE databases (PROSPERO Registration number: CRD42014015256). We included randomised and controlled clinical studies comparing laparoscopic and open resection for rectal cancer. Primary endpoints were 30 days mortality and overall morbidity. Then, a meta-analysis was conducted by a fixed-effect model, performing a sensitivity analysis by a random-effect model. Relative risk (RR) was used as an indicator of treatment effect; a RR less than 1.0 was in favour of laparoscopy. Publication bias was assessed by funnel plot, heterogeneity by the I^2 test and subgroup analysis on oncologic patients.

Results

Twenty-seven studies, representing 3049 patients, met the inclusion criteria; only 2 were randomised for a total of 211 patients. Mortality was observed in 1.2 % of patients in the laparoscopic group and in 3.4 % of patients in the open group. The overall RR was 0.45

(95 % CI 0.21–0.93, $p = 0.031$). The raw incidence of overall complications was significantly lower in the laparoscopic group (16.8 %) compared to the open group (24.2 %). The overall RR was 0.81 (95 % CI 0.70–0.95, $p = 0.007$).

Conclusions

Based on the evidence of few randomised and mostly controlled series, mortality and morbidity were significantly lower after laparoscopy compared to open surgery.

Keywords

Colon cancer Colon neoplasms Right colectomy Laparoscopy Meta-analysis Systematic review

Introduction

Despite the evident advantages of laparoscopy in general when compared to open surgery, the uptake of laparoscopy in colorectal surgery was rather slow. It was not until 1991 that the first laparoscopic colectomy was reported [1] and the diffusion of the technique was much slower than expected. This was surely influenced by a reported risk of port site metastasis and concerns of oncological clearance [2, 3]. Trials and meta-analyses have shown that laparoscopic rectal resection and left colectomy as well as colorectal resections in general have better short-term outcomes compared with open surgery [4–9]. For some reasons, till now, few reports comparing laparoscopic to open right colonic resections have provided results on safety and efficacy. This was probably depending on the need of excellence of surgical technique, particularly relevant in the treatment of colorectal cancer, and possibly also because the attention was distracted by the discussion on the different techniques of laparoscopic right colectomy, in particular, regarding the opportunity of intracorporeal or extracorporeal anastomosis.

The aim of this study was to evaluate in a systematic review and meta-analysis whether there are clinically relevant short-term advantages of either laparoscopy or laparotomy for surgical treatment of benign and malignant right colon diseases requiring surgery in published literature. At the same time, we investigated the possible discrepancies in terms of oncologic outcomes between the two techniques in patients affected by cancer of the right colon.

Materials and methods

The methods for the analysis and generation of inclusion criteria were based on the recommendations of the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) Statement [10]. According to population, interventions, comparators, outcome measures and setting (PICOS) criteria, patients were included if affected with any benign or malignant diseases of the right colon requiring surgery, for which laparoscopic or laparotomic right colectomy was indicated. The study methods were documented in a protocol registered and accessible at http://www.crd.york.ac.uk/prospero/ (Registration number: CRD42014015256).

Types of studies

Only randomised controlled trials (RCTs) or controlled clinical trials (non-RCTs) were considered for this analysis, as suggested by the MOOSE group [11]. Studies were excluded if the study population included colorectal cancers in general, unless the data were presented separately, so to allow to distinguish data referred to right colectomies only. When multiple studies from the same institution were identified, the most recent or the most informative was selected. All and only full-text papers in English language were considered.

Types of participants

This meta-analysis compares laparoscopic and laparotomic right colectomies for both benign and malignant diseases, with regard to possible benefits of laparoscopy or laparotomy in the short-term post-operative period, defined as up to 30 days after surgery, as well as adherence to oncologic criteria and oncologic results at the latest follow-up available.

Types of intervention

All surgical procedures classified as right colectomy were considered, including both full laparoscopic and laparoscopic-assisted, as well as any kind of anastomosis, such as termino-lateral, termino-terminal and latero-terminal anastomoses. Type of interventions performed was noted in order to analyse separately different type of anastomosis when available. For the laparoscopic group, any right colon resection performed through a minimally invasive approach (i.e. in a space generated by an insufflated pneumoperitoneum with operative field visualisation obtained by a laparoscope and performed only through laparoscopic trocars) was included, while as open surgery, all procedures described as ‘open’ or ‘conventional’ and performed through an abdominal laparotomic incision were considered.

Types of outcome measures

Primary endpoints were overall mortality and morbidity at 30 days after surgery. Further parameters of potential interest taken into consideration were procedural time, parenteral use of narcotics, return to oral intake, day of first post-operative flatus, pulmonary infections, post-operative bleeding, blood loss, anastomotic leakage, wound infections, urinary complications and hospital stay. Finally, the following oncologic short-term and long-term outcomes were taken into considerations, such as number of lymph nodes harvested and recurrence rate at 5 years.

Search strategy and data collection

We searched MEDLINE and EMBASE databases from January 1991 to May 2014. The search strategy was performed using the following terms: ‘right’ and (‘hemicolectomy’/exp or ‘hemicolectomy’) and (‘laparoscopy’/exp or ‘laparoscopy’ or ‘laparoscopic’) and (‘laparotomy’/exp or ‘laparotomy’ or ‘laparotomic’ or ‘standard’/exp or ‘standard’ or ‘open’) and [1991–2014]/py.

The literature search was closed on 31 May 2014.

All abstracts retrieved from the electronic databases were screened independently by two authors (VF and FG). When an abstract was deemed relevant by at least one of them, the full text was retrieved. The reference lists of all relevant articles were manually searched for potentially relevant studies for inclusion.

Data extraction was carried out in duplicate independently by two authors (VF and FG). Disagreements were resolved by discussion with a third author (AA). The following data were collected when available: study features, patients’ characteristics (gender, age, BMI, ASA classification, cancer localization and stage, neoadjuvant therapy, type of procedures performed), data needed for study quality assessment and the outcomes measures.

Assessment of risk of bias

All studies meeting the selection criteria were assessed for methodological quality according to the Cochrane Collaboration guidelines [12] for RCTs and to the Newcastle-Ottawa Scale for non-RCTs [13]. This judgement was performed by three reviewers (AA, VF and FG); disagreements were resolved by discussion.

Statistical analysis

All analyses were performed according to original treatment allocation (intention-to-treat analysis). For binary outcome data, the relative risks (RR) and 95 % CIs were estimated using the Mantel-Haenszel method: RR <1 was in favour of laparoscopy. For continuous outcome data, the mean differences (MD) and 95 % CIs were estimated using the inverse variance weighting: MD negative value was in favour of laparoscopy. When means and/or SDs were not reported in the original paper, they were estimated from reported medians, ranges and sample size as described by Hozo [14].

A fixed-effects model was used in all meta-analyses, always redoing the same analyses by a random-effects model as described by DerSimonian and Laird [15]. Publication bias was assessed generating a funnel plot and performing the rank correlation test of funnel plot asymmetry. Heterogeneity was assessed by the I^2 measure of inconsistency, statistically significant if $I^2 > 50$ %; whenever I^2 was ≤ 50 %, the fixed-effects model was used; otherwise, the random-effects model was preferred.

Potential sources of heterogeneity were explored by different sensitivity analyses: comparing fixed- vs. random-effects models (thus incorporating heterogeneity by using the second method), performing sub-groups analyses (comparing single outcome studies [right colon cancer] vs. multiple ones), checking the results of cumulative (sequentially including studies by date of publication) and influence meta-analyses (calculating pooled estimates omitting one study at a time). Data were analysed as of December 2014 by R 3.1.2 package meta (R Foundation for Statistical Computing, Vienna-A, http://www.R-project.org) [16].

Results

Study selection

The search retrieved 371 studies. Figure 1 illustrates the PRISMA flowchart for study inclusion and exclusion criteria.

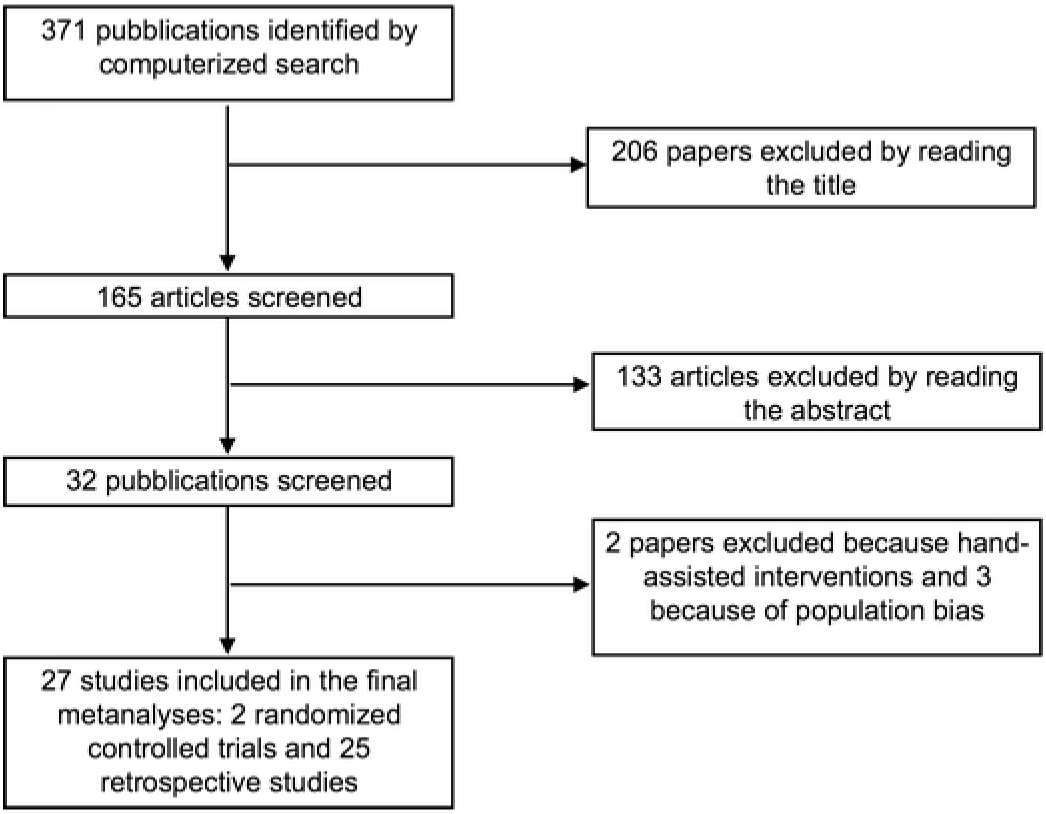


Fig. 1

Flowchart diagram detailing paper selection process

Characteristics of included studies

The characteristics of the 26 studies meeting the inclusion criteria are summarised in Table 1 [17–42]. Twenty studies were reported as full papers [17–36], while 6 were published as abstract only so far [37–42]. Altogether, they included a total of 3307 patients; 2 were RCTs for a total of 211 patients, and 24 were non-RCTs for a total of 3096 patients.

Table 1

Summary of the studies included in the systematic review and meta-analysis

Author and publication year	Country and study period	Type	Inclusion criteria	Exclusion criteria	Number	Lap surgery patients	Open surgery patients	Gender (M/F)		Age (mean ± SD or median and range)		BMI (mean ± SD or median and range)		Lap anastomosis	Conversion rate
								Lap	Open	Lap	Open	Lap	Open		
Ramacciato 2008	Italy January 2001 June 2005	Full paper	Right side colon cancer	1, 2, 3, 4, 11	66	33	33	N/A	N/A	66 (38–78)	72.5 (53–94)	24.4 (21–26)	24.1 (19–29)	EA	N/A
Li 2011	China July 1996	Full paper	Right side colon	1, 2, 5	145	71	74	33/38	32/42	68 ± 11.3	68 ± 13.3	N/A	N/A	EA	15.5 %

Author and publication year	Country and study period	Type	Inclusion criteria	Exclusion criteria	Number	Lap surgery patients	Open surgery patients	Gender (M/F)		Age (mean ± SD or median and range)		BMI (mean ± SD or median and range)		Lap anastomosis	Conversion rate
								Lap	Open	Lap	Open	Lap	Open		
	October 2005		cancer												
Bokey 1996	Australia January 1992 August 1994	Full paper	Right side colon cancer	N/A	67	34	33	N/A	17/16	73.9 ± 10.3	71.9 ± 10.2	N/A	N/A	EA	18 %
Leung 1999	Thailand January 1993 July 1997	Full paper	Right side colon cancer	1, 2, 5	84	28	56	15/13	30/26	69.6 ± 13.3	65.0 ± 13.4	N/A	N/A	EA	14 %
Lezoche 2003	Italy March 1992 February 2003	Full paper	Right side colon benign and malignant lesions	1, 3, 7, 8	166	108	58	58/50	31/27	66.9 (18–92)	67.2 (53–85)	N/A	N/A	EA	0 %
Baker 2004	UK 1993–2000	Full paper	Right side colon cancer	N/A	99	33	66	N/A	N/A	69.7	69.7	N/A	N/A	EA	18 %
Zheng 2005	China September 2000 February 2003	Full paper	Right side colon cancer	1, 3, 5, 6	64	30	34	16/14	20/14	60.2 ± 14.9	60 ± 12.7	N/A	N/A	EA	6 %
Del Rio 2006	Italy January 2001 December 2005	Full paper	Right side colon benign and malignant lesions	2, 3, 11	52	27	25	9/18	8/17	68.4 (32–79)	71.3 (43–87)	N/A	N/A	EA	7 %
Tong 2007	China June 2000 December 2004	Full paper	Right side colon cancer	1, 9	182	77	105	32/45	52/53	71.2 ± 11.9	71.6 ± 11.4	N/A	N/A	EA	9 %
Lohsiriwat 2007	Thailand March 2004 September 2006	Full paper	Right side colon cancer	1, 2, 4, 8, 10, 11, 12, 13, 14	36	13	20	6/7	7/13	56.9 ± 13.5	65.2 ± 16.0	20.8 ± 1.8	20.7 ± 4.2	EA	N/A
Nakamura 2009	Japan April 1990 December 2004	Full paper	Right side colon cancer	1, 14	333	100	100	65/35	65/35	64 (39–89)	65 (39–88)	22 (15–33)	22 (15–34)	EA	N/A
Tan 2009	Singapore May 2005 December 2007	Full paper	Right side colon benign and malignant lesions	15	77	37	40	19/18	22/18	68 (37–83)	67 (42–87)	23.5 (17.6–35.8)	22.9 (17.1–32.7)	EA	2.7 %

Author and publication year	Country and study period	Type	Inclusion criteria	Exclusion criteria	Number	Lap surgery patients	Open surgery patients	Gender (M/F)		Age (mean ± SD or median and range)		BMI (mean ± SD or median and range)		Lap anastomosis	Conversion rate
								Lap	Open	Lap	Open	Lap	Open		
Pommergaard 2009	Denmark N/A	Abstract	Right colon cancer	N/A	84	42	42	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Hemandas 2009	UK October 2006 February 2009	Abstract	Right colon cancer	N/A	164	89	75	N/A	N/A	N/A	N/A	N/A	N/A	N/A	4.5 %
Siani 2009	Italy January 2004 July 2009	Full paper	Right colon cancer	3, 4, 16	40	20	20	13/7	12/8	62 ± 13,5	63 ± 12.3	N/A	N/A	EA	N/A
Kahokehr 2010	New Zealand October 2005 August 2009	Full paper	Benign or malignant disease	11, 15, 21	113	39	74	19/20	24/50	73 (16–94)	72 (28–92)	26 ± 5.3	26.9 ± 4.5	EA	N/A
Abdel-Halim 2010	UK November 2003 March 2007	Full paper	Right colon cancer	1, 7, 22	56	22	34	5/17	22/12	77.5 (32–88)	76 (47–95)	26.9 (20–36)	26 (8–30)	EA	9 %
Leung 2010	UK January 2008 May 2009	Full paper	Right colon cancer	N/A	40	20	20	N/A	N/A	71 (47–89)	80 (42–88)	N/A	N/A	N/A	N/A
Khan 2011	UK October 2006 February 2009	Full paper	Right colon cancer	1	164	89	75	37/52	41/34	76 (53–92)	74 (46–89)	26 (17–47)	26 (18–35)	EA	4.5 %
Alkhamesi 2011	UK January 2005 April 2010	Full paper	Benign or malignant disease	1, 22	470	148	322	80/68	134/188	64, 97	67, 65	N/A	N/A	N/A	18.9 %
Beaumier 2011	Canada August 2003 December 2008	Abstract	Benign or malignant disease in >70 years old	7, 15	198	60	138	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Han 2013	China June 2003 September 2010	Full paper	Right colon cancer	1, 3, 9, 11, 17	324	177	147	83/94	80/67	67 ± 12	65 ± 12	N/A	N/A	EA	2.8 %
Kwon 2012	Korea 1999–2011	Full paper	Complicated right colonic diverticulitis	18	59	28	31	20/8	22/9	44 ± 13.2	44.7 ± 13.4	23.7 ± 3.5	23.8 ± 2.8	EA	0 %
Tanis 2012	Netherlands January 2006 April 2009	Full paper	Benign or malignant disease	1, 3, 7, 18, 20	75	30	45	12/18	19/26	75 (31–85)	73.5 (47–85)	25 (15–37)	24.5 (19–34)	EA	3 %

Author and publication year	Country and study period	Type	Inclusion criteria	Exclusion criteria	Number	Lap surgery patients	Open surgery patients	Gender (M/F)		Age (mean ± SD or median and range)		BMI (mean ± SD or median and range)		Lap anastomosis	Conversion rate
								Lap	Open	Lap	Open	Lap	Open		
Daniels 2013	UK January 2011 November 2011	Abstract	Right colon cancer	N/A	44	14	30	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Zhao 2013	China N/A	Abstract	Right colon cancer	N/A	105	48	57	N/A	N/A	N/A	N/A	N/A	N/A	N/A	10.4 %

LAP laparoscopic, *OPEN* laparotomic, *IA* intracorporeal anastomosis, *EA* extracorporeal anastomosis, *N/A* not available

1 emergency situations (e.g. acute obstruction, haemorrhage, perforation); *2* abdominal surgery; *3* T4; *4* presence of metastasis; *5* tumour >6 cm; *6* patients unwilling to take part in the study; *7* segmental resection, transverse colon resection, subtotal colectomy; *8* recurrent carcinoma; *9* benign disease; *10* peridural, perioperative analgesia; *11* ASA III–ASA IV, serious organ disfunction; *12* immune-compromised patients; *13* patients receiving antiplatelet and anticoagulant drugs; *14* conversion to open surgery; *15* laparoscopic exploration, colonic diversion without resection, stoma creation; *16* contraindication to pneumoperitoneum; *17* pregnant patients; *18* diverticulitis without complication, appendectomy, diverticulectomy; *19* age >80 years; *20* palliative resection; *21* mental illness; *22* associated procedure

Conversion rate to open procedures was as high as 18.9 % when tumour size and stage were not considered exclusion criteria [33] but still as high as 15.5 % when tumours >6 cm were excluded [18].

Table 2 shows baseline patients characteristics comparing open and laparoscopic procedures, substantially equivalent for gender distribution, mean age and mean BMI when available.

Table 2

Comparison of baseline patients' characteristics

	Number of patients		Gender (M/F)[a]		Mean age (years)		Mean BMI (Kg/m^2)	
	Lap	Open	Lap	Open	Lap	Open	Lap	Open
RCT	104	107	33/38	32/42	67.0	70.2	24.4	24.1
Non-RCT	1314	1735	502/487	604/603	68.2	68.5	23.8	23.6
Overall	1418	1842	535/525	636/645	67.6	69.4	24.1	23.8

[a]Data about the gender were not available in all studies

Table 3 shows distribution of patients according to tumour stage, with sufficient homogeneity.

Table 3

Comparison of cancer stage according to TNM classification

	Stage I (%)		Stage II (%)		Stage III (%)		Stage IV (%)	
	Lap	Open	Lap	Open	Lap	Open	Lap	Open
RCT	11.3	8.1	49.3	40.5	22.5	40.5	16.9	10.8
Non-RCT	15.6	14.5	43.3	45.9	34.5	33.7	6.6	5.9

Risk of bias of included studies

Assessment of quality according to the Cochrane Collaboration's tool for assessing risk of bias for RCTs and to the Newcastle-Ottawa Scale for non-RCTs is represented in Table 4 and Table 5, respectively. A subgroup analysis was conduced considering studies including only colon cancer patients.

Table 4

Quality assessment of the included randomised controlled studies based on the Cochrane Collaboration's tool for assessing risk of bias

Author and publication year	Random sequence generation	Allocation concealment	Blinding of participants, personnel and outcome	Incomplete outcome data	Selective outcome reporting	Other source of bias
Ramacciato 2008	Unclear	Unclear	No	Yes[a]	No	No
Li 2011	Yes	Yes	No	No	No	No

In all cases, *Yes* indicates a low risk of bias, *No* indicates high risk of bias and *Unclear* indicates unclear or unknown risk of bias

[a]Authors do not declare length of hospital stay in the two groups despite it was indicated in the "Materials and Methods" section

Table 5

Quality assessment of the included non-randomised controlled studies based on the Newcastle-Ottawa Scale

Author and publication year	Selections			Comparability		Outcome assessment		Score
	1	2	3	4	5	6	7	
Bokey 1996	*	*	*	**	*	*	*	8
Leung 1999	*	*	*	*	*	*	*	7
Lezoche 2003	*	*	*	**	–	*	*	7
Baker 2004	*	*	*	–	–	*	*	5
Zheng 2005	*	*	*	*	*	*	*	7
Del Rio 2006	*	*	*	*	–	*		5
Tong 2007	*	*	*	**	–	*	*	7
Lohsiriwat 2007	*	*	*	*	–	*	–	5
Nakamura 2009	*	*	*	**	*	*	*	8
Tan 2009	*	*	*	**	–	*	–	6
Pommergaard 2009	*	*	*	*	–	*	–	5
Hemandas 2009	*	*	*	**	–	*	–	6
Siani 2009	*	*	*	*	–	*	*	6
Kahokehr 2010	*	*	*	**	–	*	–	6
Abdel-Halim 2010	*	*	*	**	*	*	–	7
Leung 2010	*	*	*	*	–	*	–	5
Khan 2011	*	*	*	**	*	*	–	7

Selection

[1]Assignment for treatment (if yes, one point)

[2]How representative was the laparoscopic group in comparison to the general population undergoing rectal resections (if yes, one point; no points if the patients were selected or selection of group was not described)

[3]How representative was the open group in comparison to the general population undergoing rectal resections (if yes, one point; no points if the patients were selected or selection of group was not described)

Comparability

[4]Group comparable for 1–3 (if yes, two points; one point if one of these three characteristics was not reported even if there were no other differences between the two groups and other characteristics had been controlled for; no points were assigned if the two groups differed)

[5]Group comparable for 4–7 (if yes, two points; one point if one of these four characteristics was not reported even if there were no other differences between the two groups and other characteristics had been controlled for; no points were assigned if the two groups differed)

Outcome assessment

[6]Clearly defined outcome of interest (if yes, one point for information ascertained by medical records or interview; no points if this information was not reported)

[7]Follow-up equal between the two groups (if yes, one point; no points if follow-up not reported)

Comparability variables: 1 = age, 2 = gender, 3 = ASA, 4 = neoadjuvant/adjuvant therapy, 5 = tumour location, 6 = stage, 7 = procedure

Primary outcomes

The two primary outcomes investigated mortality and overall complications.

The raw incidence of mortality was significantly lower in the laparoscopic group (1.2 %) compared to the open one (3.4 %). The overall RR was 0.45 (95 % CI 0.21–0.93, $p = 0.031$) (Fig. 2). Neither heterogeneity ($I^2 = 0$ %) nor publication bias was detected ($p = 0.128$). Performing a cumulative meta-analysis with these 10 studies (2 RCTs and 8 non-RCTs), adding one study at a time by publication date, the RR progressively decreased over time from 3.53 to 0.44. Performing an influential meta-analysis, by omitting one study in turn, the RR was quite constant, ranging from 0.38 to 0.54 in the entire time frame.

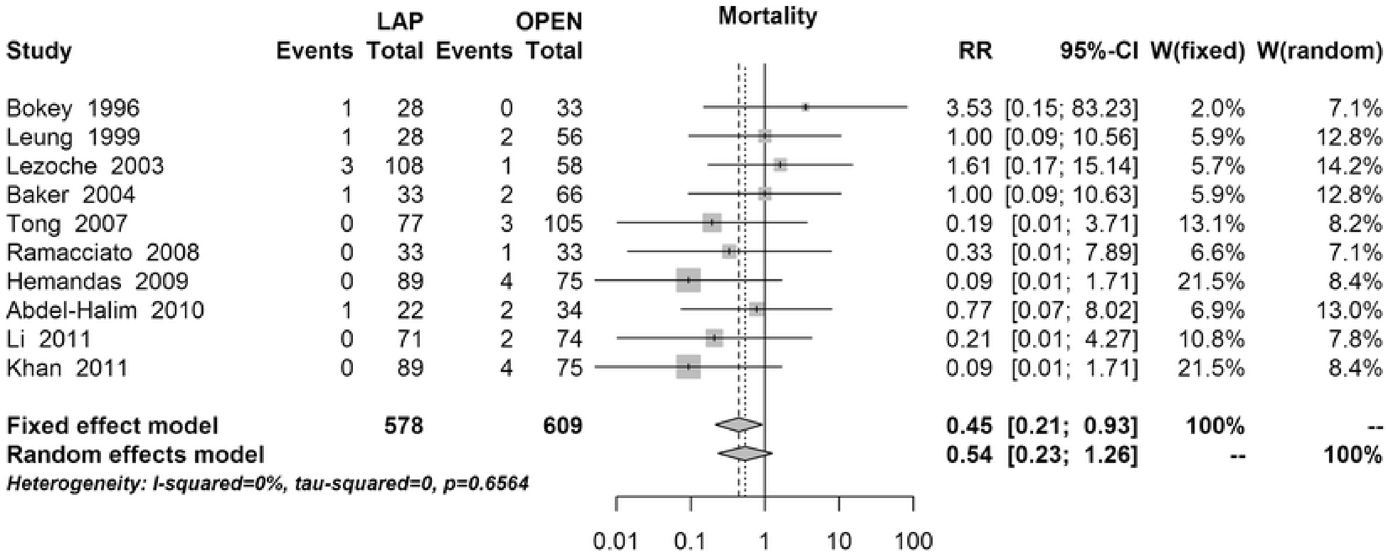


Fig. 2

Forest plot for 30 days mortality. *RR* relative risk, *95 % CI* confidence interval, *W* weight of the single study

The raw incidence of overall complications was significantly lower in the laparoscopic group (16.8 %) compared to the open group (24.2 %). The overall RR was 0.81 (95 % CI 0.70–0.95, $p = 0.007$) (Fig. 3), with a moderate heterogeneity ($I^2 = 50$ %). Once again, no publication bias was found ($p = 0.282$). Performing a cumulative meta-analysis with these 19 studies (2 RCTs and 17 non-RCTs), the RR decreased over time from 1.60 to 0.81, finally reaching a quite stable range (from 0.60 to 0.81) in the last 4 years (2011–2014). In the influential meta-analysis, the RR showed minor variations, ranging from 0.70 to 0.85 in the whole publication period.

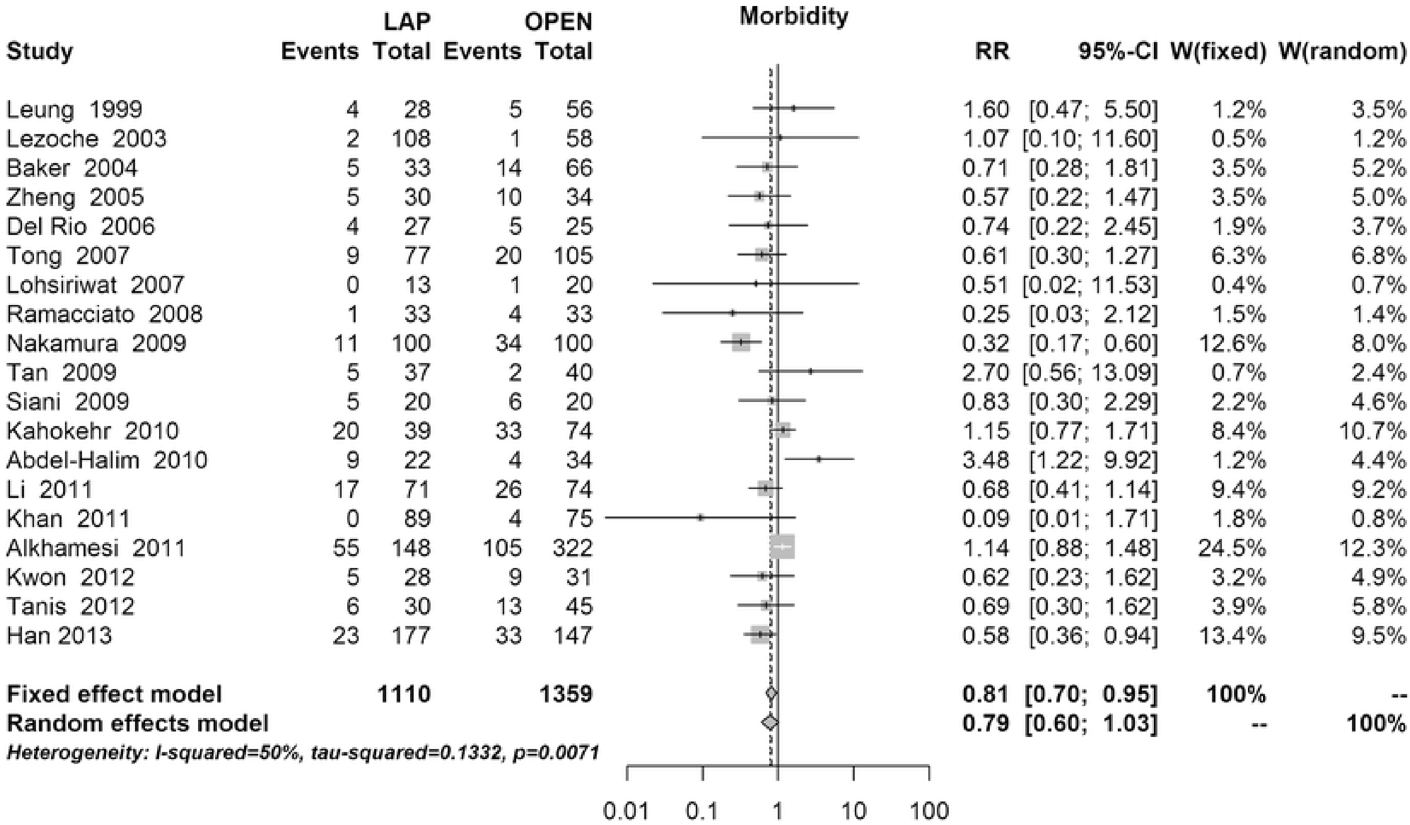


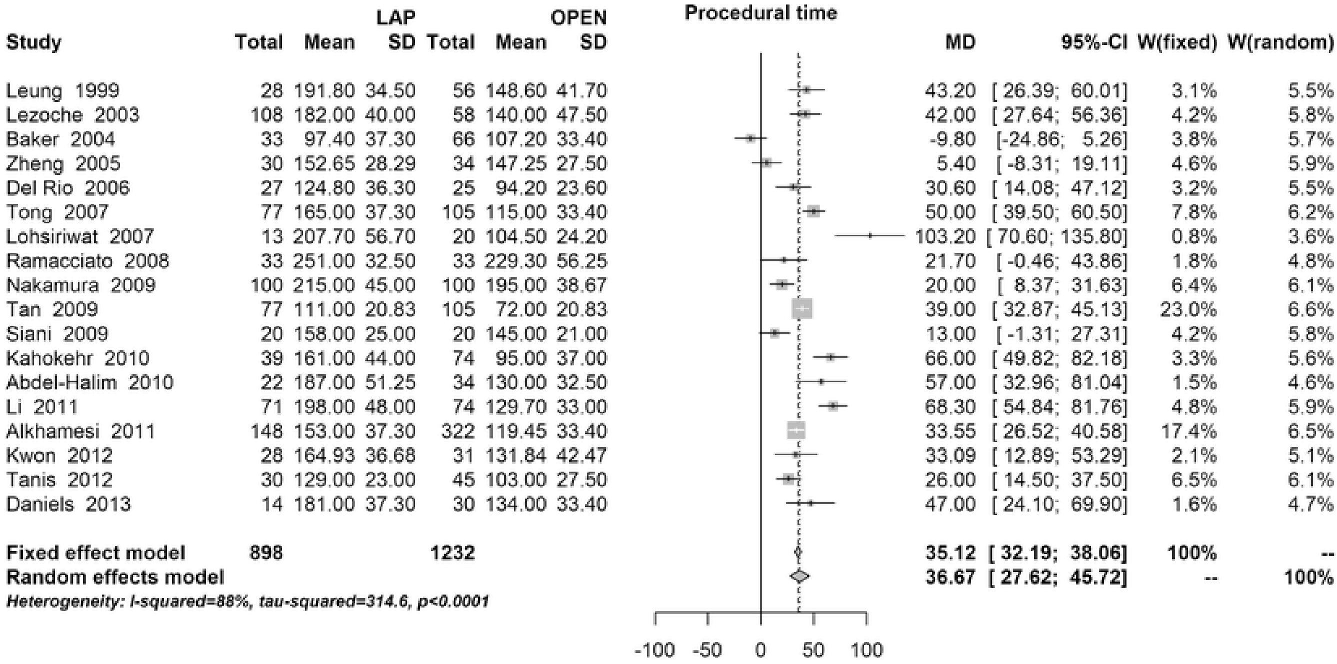
Fig. 3

Forest plot for 30 days morbidity. *RR* relative risk, *95 % CI* confidence interval, *W* weight of the single study

Secondary outcomes

As secondary outcomes, the meta-analysis investigated further parameters of potential interest such as procedural time, use of narcotics, oral intake, day of first flatus, pulmonary infections, post-operative bleeding, anastomotic leakage, wound infections, urinary complications, length of hospital stay lymph nodes harvested and recurrences at 5 years. The mean procedural time was available in 18 trials and was 168.7 min in the laparoscopic group and 125.7 min in the open surgery arm. The overall MD was 36.7 min (95 % CI

27.6–45.7, $p<0.001$) (Fig. 4), with an extreme heterogeneity ($I^2=88$ %). Thus, laparotomy resulted as a significantly faster surgical technique.



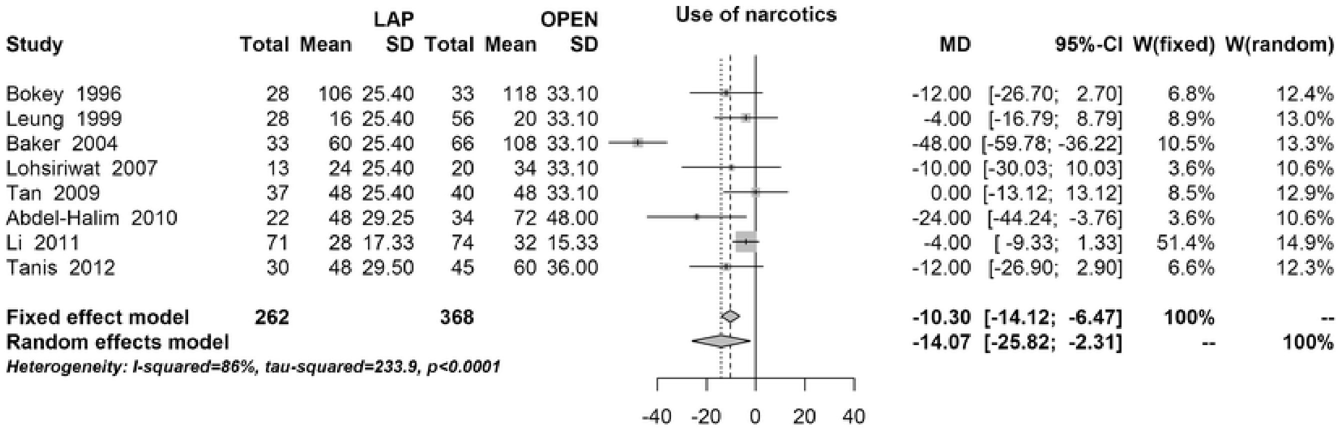
Study	LAP Total	LAP Mean	LAP SD	OPEN Total	OPEN Mean	OPEN SD	MD	95%-CI	W(fixed)	W(random)
Leung 1999	28	191.80	34.50	56	148.60	41.70	43.20	[26.39; 60.01]	3.1%	5.5%
Lezoche 2003	108	182.00	40.00	58	140.00	47.50	42.00	[27.64; 56.36]	4.2%	5.8%
Baker 2004	33	97.40	37.30	66	107.20	33.40	-9.80	[-24.86; 5.26]	3.8%	5.7%
Zheng 2005	30	152.65	28.29	34	147.25	27.50	5.40	[-8.31; 19.11]	4.6%	5.9%
Del Rio 2006	27	124.80	36.30	25	94.20	23.60	30.60	[14.08; 47.12]	3.2%	5.5%
Tong 2007	77	165.00	37.30	105	115.00	33.40	50.00	[39.50; 60.50]	7.8%	6.2%
Lohsiriwat 2007	13	207.70	56.70	20	104.50	24.20	103.20	[70.60; 135.80]	0.8%	3.6%
Ramacciato 2008	33	251.00	32.50	33	229.30	56.25	21.70	[-0.46; 43.86]	1.8%	4.8%
Nakamura 2009	100	215.00	45.00	100	195.00	38.67	20.00	[8.37; 31.63]	6.4%	6.1%
Tan 2009	77	111.00	20.83	105	72.00	20.83	39.00	[32.87; 45.13]	23.0%	6.6%
Siani 2009	20	158.00	25.00	20	145.00	21.00	13.00	[-1.31; 27.31]	4.2%	5.8%
Kahokehr 2010	39	161.00	44.00	74	95.00	37.00	66.00	[49.82; 82.18]	3.3%	5.6%
Abdel-Halim 2010	22	187.00	51.25	34	130.00	32.50	57.00	[32.96; 81.04]	1.5%	4.6%
Li 2011	71	198.00	48.00	74	129.70	33.00	68.30	[54.84; 81.76]	4.8%	5.9%
Alkhamesi 2011	148	153.00	37.30	322	119.45	33.40	33.55	[26.52; 40.58]	17.4%	6.5%
Kwon 2012	28	164.93	36.68	31	131.84	42.47	33.09	[12.89; 53.29]	2.1%	5.1%
Tanis 2012	30	129.00	23.00	45	103.00	27.50	26.00	[14.50; 37.50]	6.5%	6.1%
Daniels 2013	14	181.00	37.30	30	134.00	33.40	47.00	[24.10; 69.90]	1.6%	4.7%
Fixed effect model	**898**			**1232**			**35.12**	**[32.19; 38.06]**	**100%**	**--**
Random effects model							**36.67**	**[27.62; 45.72]**	**--**	**100%**

Heterogeneity: I-squared=88%, tau-squared=314.6, p<0.0001

Fig. 4

Forest plot for mean procedural time. *MD* mean difference, *95 % CI* confidence interval, *W* weight of the single study

The use of narcotics was reported in 8 trials. The median duration of their parenteral administration was 45.7 h in the laparoscopic group and 60.5 h in the open one. The overall MD was −14.1 h (95 % CI −25.8–−2.3, $p=0.019$) (Fig. 5), with an extreme heterogeneity ($I^2=86$ %). Thus, laparoscopy was associated with a less prolonged use of narcotics.



Study	LAP Total	LAP Mean	LAP SD	OPEN Total	OPEN Mean	OPEN SD	MD	95%-CI	W(fixed)	W(random)
Bokey 1996	28	106	25.40	33	118	33.10	-12.00	[-26.70; 2.70]	6.8%	12.4%
Leung 1999	28	16	25.40	56	20	33.10	-4.00	[-16.79; 8.79]	8.9%	13.0%
Baker 2004	33	60	25.40	66	108	33.10	-48.00	[-59.78; -36.22]	10.5%	13.3%
Lohsiriwat 2007	13	24	25.40	20	34	33.10	-10.00	[-30.03; 10.03]	3.6%	10.6%
Tan 2009	37	48	25.40	40	48	33.10	0.00	[-13.12; 13.12]	8.5%	12.9%
Abdel-Halim 2010	22	48	29.25	34	72	48.00	-24.00	[-44.24; -3.76]	3.6%	10.6%
Li 2011	71	28	17.33	74	32	15.33	-4.00	[-9.33; 1.33]	51.4%	14.9%
Tanis 2012	30	48	29.50	45	60	36.00	-12.00	[-26.90; 2.90]	6.6%	12.3%
Fixed effect model	**262**			**368**			**-10.30**	**[-14.12; -6.47]**	**100%**	**--**
Random effects model							**-14.07**	**[-25.82; -2.31]**	**--**	**100%**

Heterogeneity: I-squared=86%, tau-squared=233.9, p<0.0001

Fig. 5

Forest plot for perioperative use of narcotics. *MD* mean difference, *95 % CI* confidence interval, *W* weight of the single study

The oral intake recovery was reported in 13 trials. It meanly occurred after 3.87 days in the laparoscopic group and 4.97 days for the open surgery. The overall MD was −0.87 days (95 % CI −1.56–−0.18, $p=0.014$) (Fig. 6), with an extreme heterogeneity ($I^2=94$ %). Thus, laparoscopy was associated with a faster return to oral intake

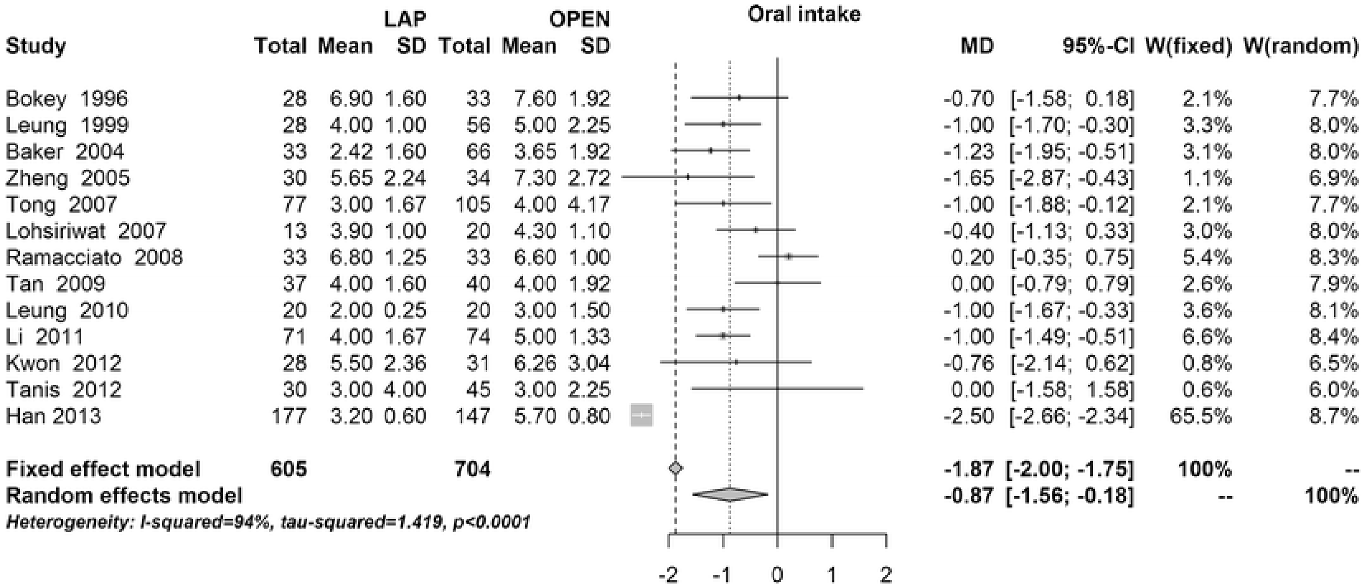


Fig. 6

Forest plot for oral food intake recovery. *MD* mean difference, *95 % CI* confidence interval, *W* weight of the single study

Thirteen trials reported the day of first flatus, which was meanly 2.68 days in the laparoscopic group and 3.71 days in the open surgery. The overall MD was −0.75 days (95 % CI −1.15–−0.35, $p<0.001$) (Fig. 7), with an extreme heterogeneity ($I^2=94$ %). Thus, laparoscopy was associated with a faster return to bowel function.

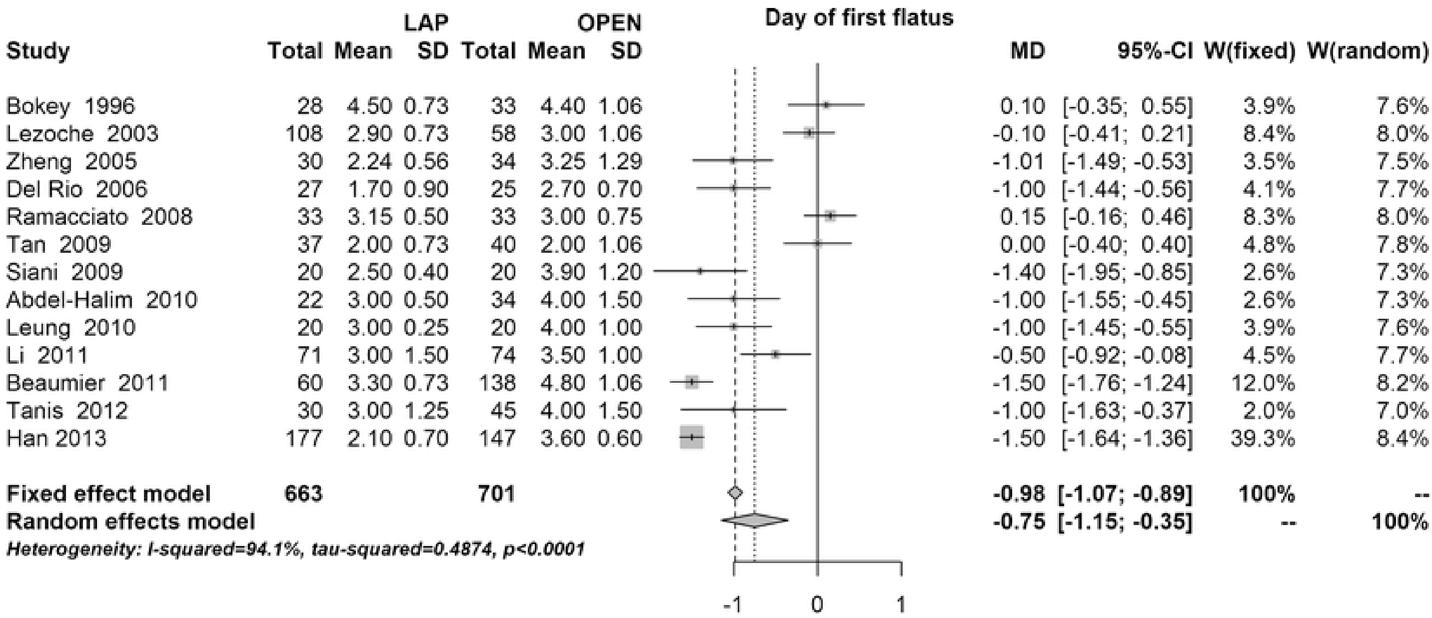


Fig. 7

Forest plot for bowel movement recovery. *MD* mean difference, *95 % CI* confidence interval, *W* weight of the single study

Pulmonary complications were reported in 13 trials, with a raw incidence of 2.4 % in the laparoscopic group and 3.7 % in the open group. The overall RR was 0.64 (95 % CI 0.38–1.07, $p = 0.086$) (Fig. 8), in the absence of any heterogeneity ($I^2 = 0$ %). Thus, despite pulmonary complications were fewer in the laparoscopic group, this difference did not reach statistical significance. Post-operative bleeding was reported in 6 trials, with a raw incidence of 0.9 % in the laparoscopic group and 1.9 % in the open group. The overall RR was 0.73 (95 % CI 0.25–2.16, $p = 0.572$) (Fig. 9), in the absence of any heterogeneity ($I^2 = 0$ %). Thus, laparoscopy and laparotomy showed an equivalent risk of post-operative bleeding.

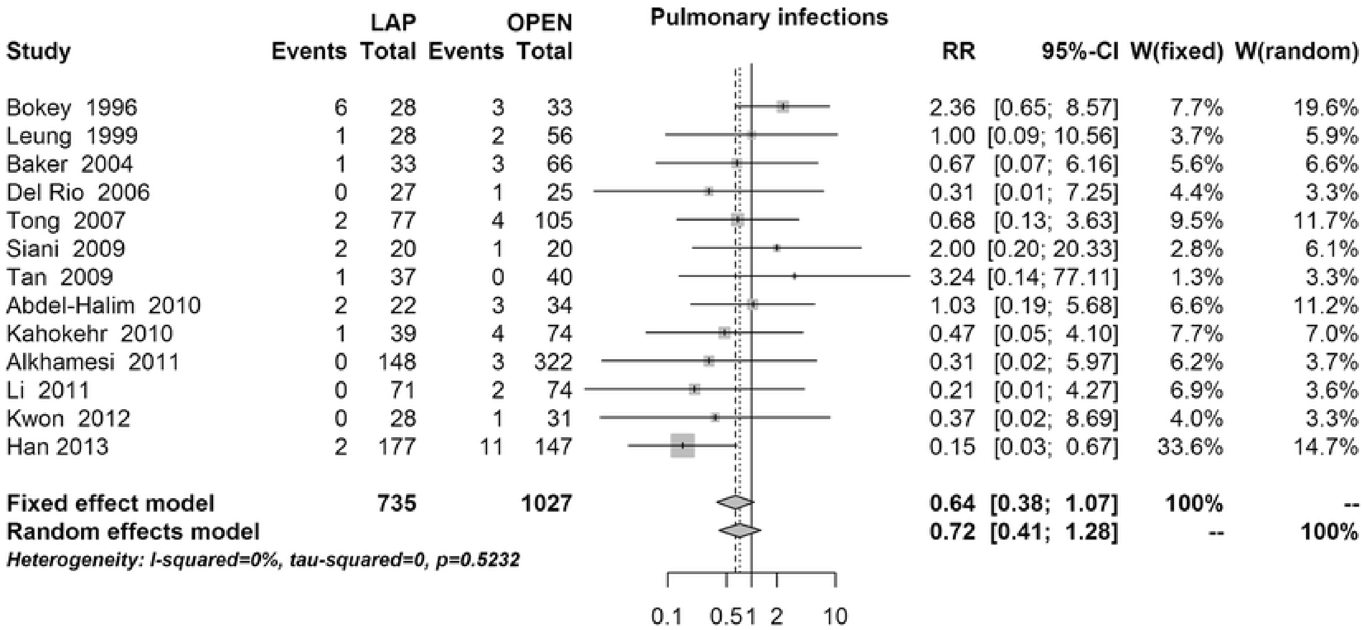


Fig. 8

Forest plot for incidence of pulmonary infections. *RR* relative risk, *95 % CI* confidence interval, *W* weight of the single study

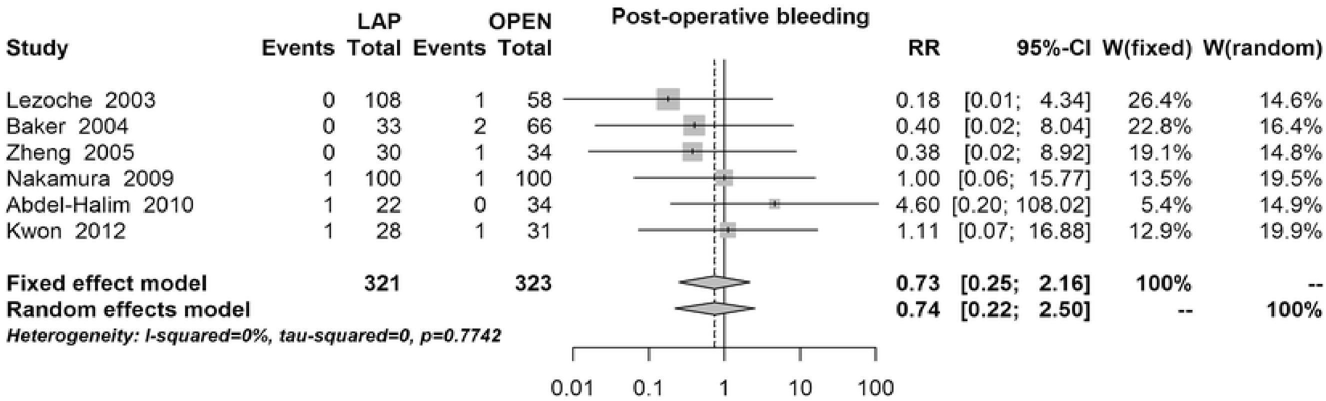


Fig. 9

Forest plot for incidence of post-operative bleeding. *RR* relative risk, *95 % CI* confidence interval, *W* weight of the single study

The mean blood loss, available in 9 researches, was 97.3 ml in the laparoscopic group and 182.5 ml in the open surgery; the overall MD was −89 ml (95 % CI −129–−48, $p<0.001$) (Fig. 10), with extreme heterogeneity ($I^2=91$ %). Thus, laparoscopy was associated with a reduced blood loss.

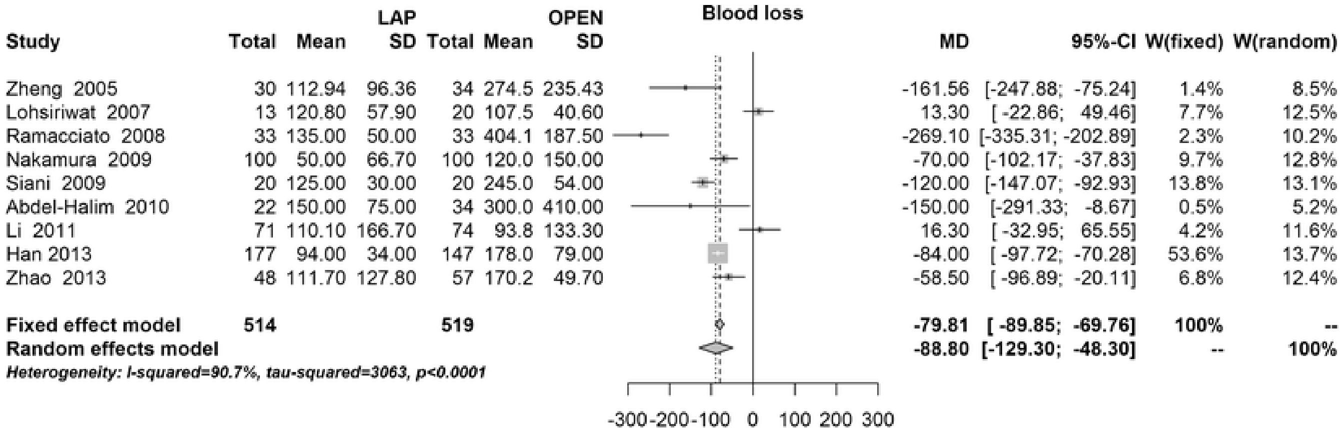


Fig. 10

Forest plot for incidence of blood loss. *MD* mean difference, *95 % CI* confidence interval, *W* weight of the single study

An anastomotic leakage occurred in 2.3 % of laparoscopic patients and 2.4 % of open surgery patients, as reported in 13 trials. The overall RR was 0.97 (95 % CI 0.57–1.65, $p=0.902$) (Fig. 11), with no heterogeneity ($I^2=0$ %). Thus, laparoscopy and laparotomy showed an equivalent risk of anastomotic leakage.

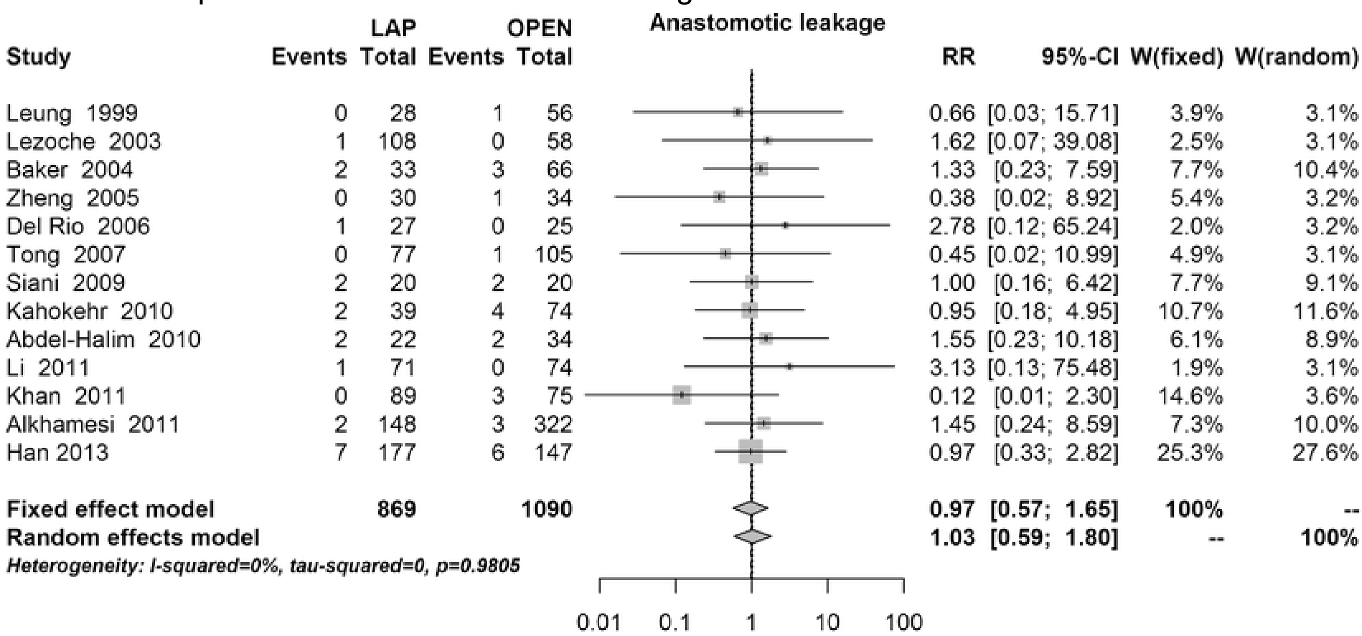


Fig. 11

Forest plot for incidence of anastomotic leakage. *RR* relative risk, *95 % CI* confidence interval, *W* weight of the single study

Wound complications were reported in 16 trials. They occurred in 4.8 % of laparoscopic patients and 9.0 % of open patients. The overall RR was 0.57 (95 % CI 0.41–0.80, $p = 0.011$) (Fig. 12), having a negligible heterogeneity ($I^2 = 7$ %). Thus, wound infections were almost halved in laparoscopic procedures.

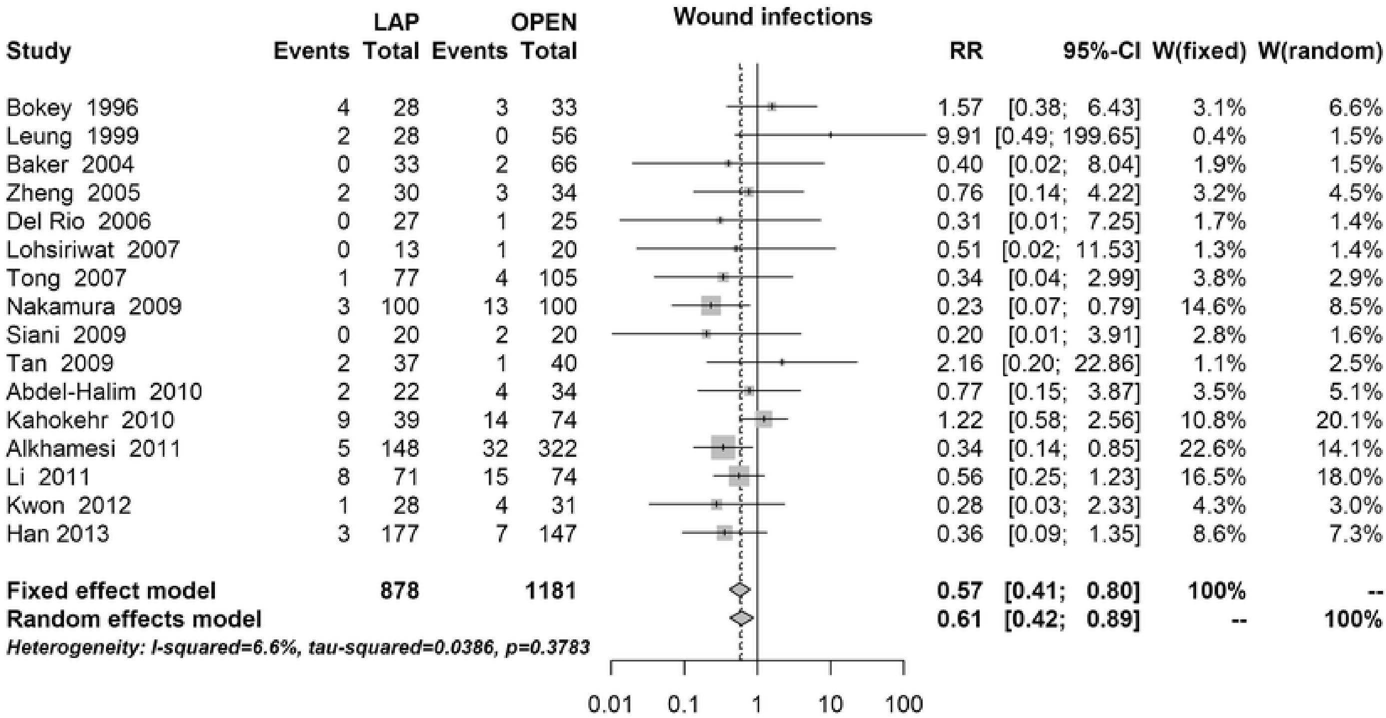


Fig. 12

Forest plot for incidence of wound infections. *RR* relative risk, *95 % CI* confidence interval, *W* weight of the single study

Urinary infections were reported in 10 papers. Their raw incidence was 3.6 % in the laparoscopic group and 4.3 % in the open group. The overall RR was 0.92 (95 % CI 0.54–1.57, $p = 0.771$) (Fig. 13), in the absence of any heterogeneity ($I^2 = 0$ %). Thus, laparoscopy and laparotomy showed an equivalent risk of urinary infections.

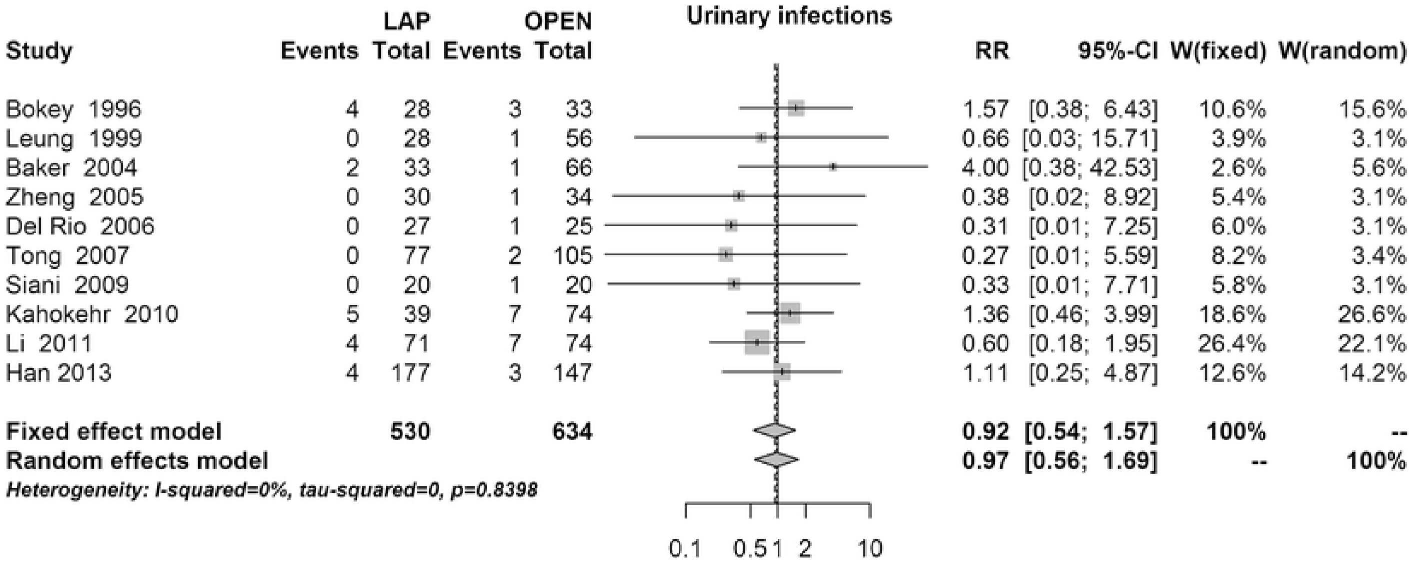


Fig. 13

Forest plot for incidence of urinary infections. *RR* relative risk, *95 % CI* confidence interval, *W* weight of the single study

The mean duration for hospital stay, as reported in 23 trials, was 7.4 days in the laparoscopic group and 10.2 days in the open group. The overall MD was −2.8 days (95 % CI −3.9–−1.7, $p<0.001$) (Fig. 14). Despite an extreme heterogeneity ($I^2=89$ %), laparoscopy reduced consistently the hospital stay.

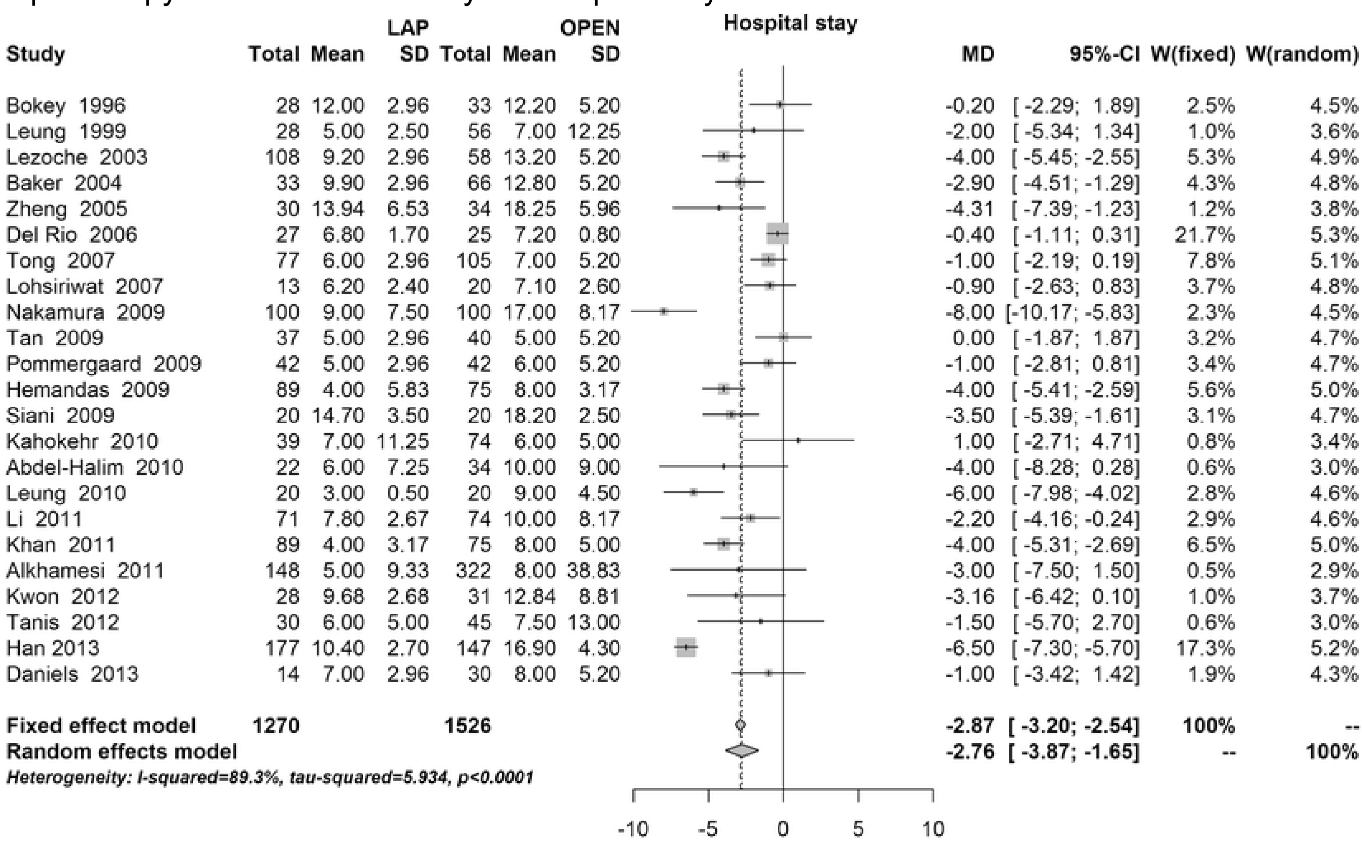


Fig. 14

Forest plot for length of hospital stay. *MD* mean difference, *95 % CI* confidence interval, *W* weight of the single study

Twenty authors reported the mean number of harvested lymph nodes, which was 16.5 lymph nodes after laparoscopic surgery and 15.8 after open surgery. The overall MD was 0.78 lymph nodes (95 % CI −0.41–1.97, $p=0.198$) (Fig. 15), with a very high heterogeneity ($I^2=82$ %). Thus, laparoscopy and laparotomy showed an equivalent number of harvested lymph nodes.

Study	LAP Total	LAP Mean	LAP SD	OPEN Total	OPEN Mean	OPEN SD	MD	95%-CI	W(fixed)	W(random)
Bokey 1996	28	17.00	8.95	33	16.00	4.97	1.00	[-2.72; 4.72]	0.9%	4.3%
Leung 1999	28	16.00	6.00	56	16.00	19.25	0.00	[-5.51; 5.51]	0.4%	2.9%
Lezoche 2003	108	14.90	8.95	58	13.80	4.97	1.10	[-1.02; 3.22]	2.7%	6.1%
Baker 2004	33	8.00	4.59	66	9.00	4.19	-1.00	[-2.86; 0.86]	3.5%	6.4%
Zheng 2005	30	11.24	8.02	34	9.75	6.04	1.49	[-2.03; 5.01]	1.0%	4.6%
Del Rio 2006	27	19.20	4.30	25	18.70	2.90	0.50	[-1.48; 2.48]	3.1%	6.3%
Tong 2007	77	15.80	1.40	105	16.70	1.58	-0.90	[-1.33; -0.47]	64.2%	7.5%
Lohsiriwat 2007	13	29.20	18.10	20	18.80	10.80	10.40	[-0.52; 21.32]	0.1%	1.0%
Ramacciato 2008	33	12.70	5.50	33	18.00	5.25	-5.30	[-7.89; -2.71]	1.8%	5.6%
Nakamura 2009	77	21.00	8.00	105	25.50	14.50	-4.50	[-7.80; -1.20]	1.1%	4.8%
Tan 2009	37	18.00	8.95	40	15.00	4.97	3.00	[-0.27; 6.27]	1.1%	4.8%
Pommergaard 2009	42	23.00	8.95	42	15.00	4.97	8.00	[4.90; 11.10]	1.3%	5.0%
Hemandas 2009	89	15.00	8.95	75	13.00	4.97	2.00	[-0.17; 4.17]	2.6%	6.0%
Siani 2009	20	23.00	3.00	20	24.00	2.00	-1.00	[-2.58; 0.58]	4.9%	6.7%
Abdel-Halim 2010	22	23.80	10.70	34	21.20	8.80	2.60	[-2.76; 7.96]	0.4%	3.0%
Li 2011	71	18.70	12.00	74	20.70	11.40	-2.00	[-5.81; 1.81]	0.8%	4.3%
Khan 2011	89	15.00	5.17	75	13.00	6.00	2.00	[0.27; 3.73]	4.1%	6.5%
Tanis 2012	30	15.00	6.75	45	13.50	9.00	1.50	[-2.07; 5.07]	1.0%	4.5%
Han 2013	177	15.20	10.10	147	11.40	4.10	3.80	[2.17; 5.43]	4.6%	6.6%
Daniels 2013	14	18.00	8.95	30	16.00	4.97	2.00	[-3.01; 7.01]	0.5%	3.2%
Fixed effect model	**1045**			**1117**			**-0.27**	**[-0.62; 0.08]**	**100%**	**--**
Random effects model							**0.78**	**[-0.41; 1.97]**	**--**	**100%**

Heterogeneity: I-squared=82.3%, tau-squared=4.837, p<0.0001

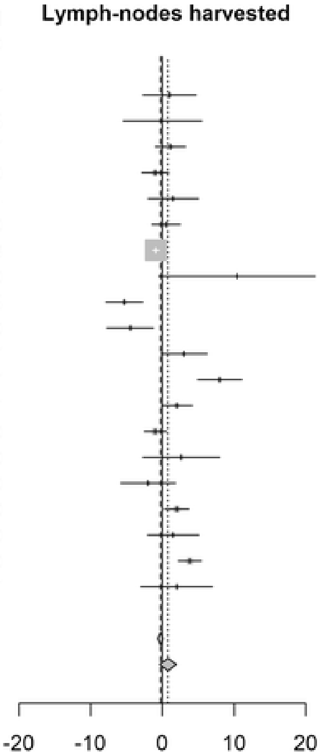


Fig. 15

Forest plot for number of lymph nodes harvested. *MD* mean difference, *95 % CI* confidence interval, *W* weight of the single study

The rate of recurrences at 5 years as reported in 6 trials, for a total of 1018 patients, was 14.3 % for laparoscopic patients and 15.6 % for open patients. The overall RR was 0.99 (95 % CI 0.55–1.76, $p=0.970$) (Fig. 16), with a high heterogeneity ($I^2=66$ %). Thus, laparoscopy and laparotomy showed an equivalent risk of recurrences at 5 years.

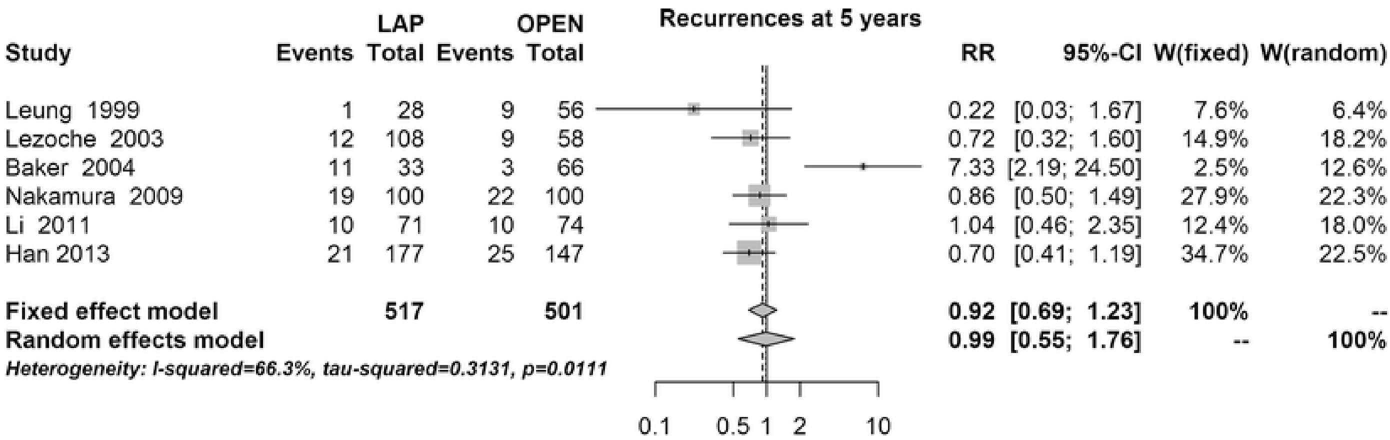


Fig. 16

Forest plot for recurrence rate at 5 years. *RR* relative risk, *95 % CI* confidence interval, *W* weight of the single study

Sensitivity analyses

The four most interesting outcomes were re-analysed, including in the meta-analyses only the trials in which right colectomy was indicated for primary malignant disease.

Overall complications, as reported in 12 trials, showed a RR of 0.62 (0.49–0.77, I^2=45 %) compared to 1.07 (0.87–1.31), as reported in the other studies (7 papers, I^2=0 %).

The RR for mortality were 0.37 (0.17–0.83) for only right colon cancer patients (9 papers, I^2=0 %) compared to 1.61 (0.17–15.14), as reported in the only excluded paper.

The MD for harvested lymph nodes was 0.62 (−0.81–2.05) for only right colon cancer studies (16 papers, I^2=85 %) compared to 1.19 (−0.05–2.43) for the other studies (4 papers, I^2=0 %).

The RR for recurrences at 5 years was 1.07 (0.53–2.18) for only right colon cancer studies (5 papers, I^2=72 %) vs. 0.72 (0.32–1.60), as reported in the only excluded paper.

Discussion

More than 2 years after the first report of a laparoscopic colorectal surgery procedure [1], laparoscopy has reached large diffusion in many fields, but its employment in the treatment of colorectal diseases is still debated. Interestingly, the attention till now has been mainly focused on the differences among the laparoscopic techniques proposed, which might be summarised as laparoscopically assisted right colectomy (with only the vascular ligation done intracorporeally), totally laparoscopic right colectomy (with both dissection and anastomosis done intracorporeally) and right colectomy with only the colonic dissection performed laparoscopically. But even here, hardly any conclusion could be achieved till now, despite a number of studies dedicated to this [43]. It is a fact that all the series included in this study who declared the technique of laparoscopic resection and anastomosis reported a laparoscopically assisted colectomy with extracorporeal anastomosis.

In truth, there is no evidence till now that laparoscopic right colectomy, whichever technique adopted, is superior to open surgery in terms of mortality, morbidity and oncologic appropriateness. Especially when treating cancer patients, where an R0 resection and systematic lymphadenectomy is considered the main step of curative therapy [44], available data did not allow till now to come to almost any reliable conclusion. While further long-term survival studies are awaited to focus on the oncologic adequacy of laparoscopic treatment of colon cancer, a short-term analysis of safety and oncologic adequacy can already be performed on existing data regarding right colectomy.

Since 1991, 26 studies [17–42] have been published comparing laparoscopic and open right colectomy in terms of safety and oncologic outcomes. Although a meta-analysis of only RCTs studies would be ideal, we decided to extend the inclusion criteria to non-randomised matched series, in order to increase the sample size, while maintaining an acceptable level of evidence, as confirmed by publication bias and heterogeneity tests. A subgroup analysis to verify the reliability of the results on cancer patients only was also performed. Due to these restrictions in papers selection, heterogeneity was kept into a reasonable frame, despite some of the included trials were relatively small; moreover, a formal sample size determination was not always performed, just to detect differences between laparoscopic and open surgery based on a well-defined primary outcome. The sensitivity analyses show that no study played an influential role on RR/MD in the whole time frame, and that heterogeneity was even reduced including only papers published in the last 4 years, as well as it was reduced in papers dealing with only cancer patients.

With these preliminary remarks, results obtained seem very interesting. The main finding of the present meta-analysis was that the incidence of mortality showed a significant reduction in the laparoscopic group compared to open surgery, and more precisely, this was more than halved in the laparoscopic group, or as low as 1.2 % compared to 3.4 %, with an RR of 0.45 and very low heterogeneity. Furthermore, the overall incidence of post-operative complications was also significantly lower in the laparoscopic group with a RR of

0.81, although a significant difference in specific complications such as urinary and pulmonary complications was not observed.
Another important finding of the present analysis was that no statistically significant difference in anastomotic leakage rate was observed. Despite the variety of possible anastomoses, including intracorporeal or extracorporeal techniques, the equivalence of leakages set at about 2 % of cases represents a remarkable result. Nor the post-operative risk of bleeding set between 1 and 2 % was different between the two groups, while the difference in estimated blood loss (97.3 vs. 182.5), although statistically significant, is biologically irrelevant. This is certainly influenced by the advent of new technologies, such as ultrasonic and radio frequency scalpels and multiple lines staplers, and the increasing surgical experience which resulted in a progressive optimization of the technique that most probably reflects in the equivalence of leakage rate and the lower incidence of surgical complications with the laparoscopic approach.
Laparoscopy also confirmed a clear advantage in terms of an earlier bowel activity restoration and time to oral intake, a reduced use of narcotics, wound infections and duration of post-operative hospital stay, whereas the only clear disadvantage was represented by the relatively longer operative time, meanly set at about 30 min.
The only two oncologic criteria which could be analysed were the number of lymph nodes harvested and the recurrence rate at 5 years: both showed a substantial equivalence between the two groups. Further analyses would have been of extreme interest, such as R0 achievement, but the lack of sufficient data on these topics forced us to stop. It was also not possible to analyse the overall survival and the disease-free survival at 5 years. In fact, as illustrated by Parmar [45], the correct way to do it would be to perform a survival meta-analysis, based on hazard ratios and standard errors deriving from Cox regression models. Unfortunately this data are not reported in the selected studies. Finally, no data was unfortunately available about post-operative quality of life.
Nevertheless, the outcomes analysed in this meta-analysis suggest that laparoscopy has different clinical advantages in the perioperative period when performing right colectomy, in line with the well-described results of laparoscopic left colectomy [2–4]. Nevertheless, these results should be interpreted cautiously as the present analysis is biased by some limitations. First, not only very few data are available of randomised trials but even most of the selected studies have a relatively low quality according to acknowledged scientific criteria such as the Cochrane Collaboration’s tool for Assessing Risk of Bias scale [12] and the Newcastle-Ottawa Scale [13]. Secondly, most of the studies did not have mortality and

short-term complications as primary outcome. Finally, scarce data regarding preoperative stage and patients' selection were reported in a consistent number of studies, so that it justifies in some cases a relevant heterogeneity among overall analysed patients.
Good quality randomised controlled trials comparing short-term and oncologic outcomes of laparoscopic right colectomy are strongly needed. While we have seen the results of the 5-year follow-up of the CLASICC trial [46] that confirms the oncological safety of laparoscopic surgery for colorectal cancer in general, as well as the long-term oncological outcome of the COLOR II-trial for rectal cancer [6], specific studies limited to right colectomy are still missing.
Notwithstanding the above-mentioned limitations, we can conclude that, based on the limited evidence of both randomised and case matched series, laparoscopic right colectomy appears to have clinically measurable short-term advantages in patients affected both by benign and malignant diseases of the right colon. Although technically demanding, laparoscopic right colectomy is safe; it guarantees a faster recovery and allows similar oncologic outcomes.

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