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REVIEW

Short-term outcomes of laparoscopic surgery for colorectal cancer in the elderly versus non-elderly: a systematic review and meta-analysis

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Abstract

Purpose Laparoscopic surgery for colorectal cancer has spread globally. The usefulness of laparoscopic surgery for elderly patients was initially indicated by comparison with open surgery. However, whether the procedure is safe for elderly as well as non-elderly patients with colorectal cancer remains unclear.

Methods In this review, patients aged ≥ 75 were defined as elderly. We conducted literature searches using PubMed, Scopus, and the Cochrane Central Register of Clinical Trials. Two authors independently reviewed resultant articles to identify relevant observational studies. Data synthesis was performed with a random-effects model. Heterogeneity was investigated by using forest plots and I^2 statistics. Risk of bias of included studies was assessed by the Risk of Bias Assessment Tool for Nonrandomized Studies. Publication bias was assessed by funnel plots.

Results Twenty-two studies were included. The incidence of overall complications was slightly higher in elderly patients than in non-elderly patients, with statistical significance (risk ratio (RR) 1.20, 95% confidence interval (CI) 1.08–1.34). There was no difference between them in the incidence of anastomotic leakage (RR 1.24, 95% CI 0.86–1.80) and mortality (risk difference 0.00, 95% CI − 0.01 to 0.01).

Conclusions Laparoscopic surgery for colorectal cancer is mostly safe for elderly patients as well as non-elderly patients. Preoperative comorbidities or poor physical capacity should be cared for in the elderly.

Keywords Colorectal neoplasms · Laparoscopy · Aged · Systematic review · Meta-analysis

Introduction

Laparoscopic surgery for colorectal cancer was introduced in 1991 and has spread widely because of its minimal invasiveness [1]. Many randomized controlled trials have been conducted to assess the usefulness of laparoscopic surgery, but most of the participants were non-elderly patients [2]. Recent systematic reviews reported that laparoscopic surgery, compared to open surgery, was effective for elderly patients with colorectal cancer [3–5]. Laparoscopic surgery may be useful for both elderly and non-elderly patients with colorectal cancer, but it is still unclear whether laparoscopic surgery is safe for elderly patients as well as non-elderly patients. Although many studies have tried to investigate the potential differences in the safety of laparoscopic colorectal surgery for elderly versus non-elderly patients, almost all such studies included small numbers of patients [6–27]. Thus, we performed a meta-analysis to compare the safety of laparoscopic surgery for elderly versus non-elderly patients with colorectal cancer.

Methods

Inclusion criteria

All observational studies were eligible for this review if the short-term outcomes of laparoscopic surgery for colorectal cancer were compared between elderly and non-elderly patients. Non-comparative studies such as case reports and case series were excluded because we considered that these studies had a higher risk of bias and could not be included in a meta-analysis. Patients aged ≥ 75 were defined as elderly in this review.

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Outcome measures

The primary outcomes were the incidence of overall complications, anastomotic leakage, and mortality. Secondary outcomes were the incidence of cardiac, pulmonary, urinary, and wound complications, postoperative ileus, and length of hospital stay.

Study search and selection

Literature searches were systematically conducted on October 14, 2017, using PubMed, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search terms used were "colorectal cancer," "elderly," "laparoscopy," "surgery," and related terms. Duplications were excluded by referring to study characteristics such as author names, study design, period, and setting. Titles and abstracts of the articles were independently screened by two authors (N.H. and Y.F.). After the screening, a full-text version of each article was assessed for final inclusion. After the study selection, reference lists of included studies were scanned to identify additional relevant studies.

Data extraction

Data were independently extracted and confirmed by the same review authors (N.H. and Y.F.). The extracted data included study design and period, setting, author names, characteristics of patients, and the primary and secondary outcomes of this meta-analysis. These data were entered into Review Manager 5.3 (Cochrane Collaboration software) and analyzed.

Assessment of risk of bias in included studies

Risk of bias of included studies was independently evaluated by the same review authors (N.H. and Y.F.) in each of the following domains: selection of participants, confounding variables, measurement of exposure, blinding of outcome assessments, incomplete outcome data, and selective outcome reporting. Risk of bias was classified as high, low, or unclear according to the Risk of Bias Assessment Tool for Nonrandomized Studies (RoBANS) [28]. Publication bias was assessed by funnel plots.

Statistical analysis

Data synthesis was conducted using Review Manager 5.3 (Cochrane Collaboration software). A random-effect model was used for all analyses, because studies were included from various countries with diverse cut-off values for the definition of elderly, leading to potential heterogeneity among study populations. The Mantel-Haenszel method was used for dichotomous variables, and the inverse-variance method was used for continuous variables. Risk ratio (RR) with 95% confidence interval (CI) was used for dichotomous variables in the meta-analysis. Risk difference (RD) with 95% CI was employed instead of RR when a rare outcome was investigated or when multiple studies in a meta-analysis included zero events in both elderly and non-elderly groups. For continuous variables, mean difference (MD) with 95% CI was used when a single outcome measure was used in a meta-analysis. All P values were two-sided, and P values less than 0.05 were considered statistically significant. Heterogeneity across included studies was assessed by visual inspection of a forest plot and then by the chi-square test. In the chi-square test, P values less than 0.10 were considered statistically significant, because this test has low power to detect heterogeneity when studies with a small number of participants are included in the analysis. Moreover, heterogeneity was quantified by I^2 statistics and interpreted as follows: 0–40%, low heterogeneity; 30–60%, moderate heterogeneity; 50–90%, substantial heterogeneity; and 75–100%, considerable heterogeneity [29].

Results

Characteristics of included studies

The comprehensive literature search using electronic databases identified 1799 articles. After duplications were removed, 1213 articles were screened by titles and abstracts to meet inclusion criteria. Full texts of 46 articles were examined for final inclusion. Twenty-two studies with 5466 patients were included (Fig. 1) [6–27]. These studies were reported from 7 countries. Of the 22 studies, 16 had a cohort design; 6 had a case-matched design; 19 were retrospective; and 3 were prospective (Table 1). The American Society of Anesthesiologists score was significantly higher in elderly patients than in non-elderly patients in most of the included studies. In contrast, there were no significant differences between them in tumor location and stage in most of the studies (Table 2).

Assessment of risk of bias in included studies

The risk of bias assessment is summarized in Table 3. Details of the assessment in each domain were as follows.

Selection of participants

All studies included in this analysis included all patients treated at their institutions and in a specific period. In addition, this meta-analysis investigated postoperative complications, so the complications were supposed not to exist preoperatively. Therefore, all included studies were judged to be at low risk of bias in this domain.

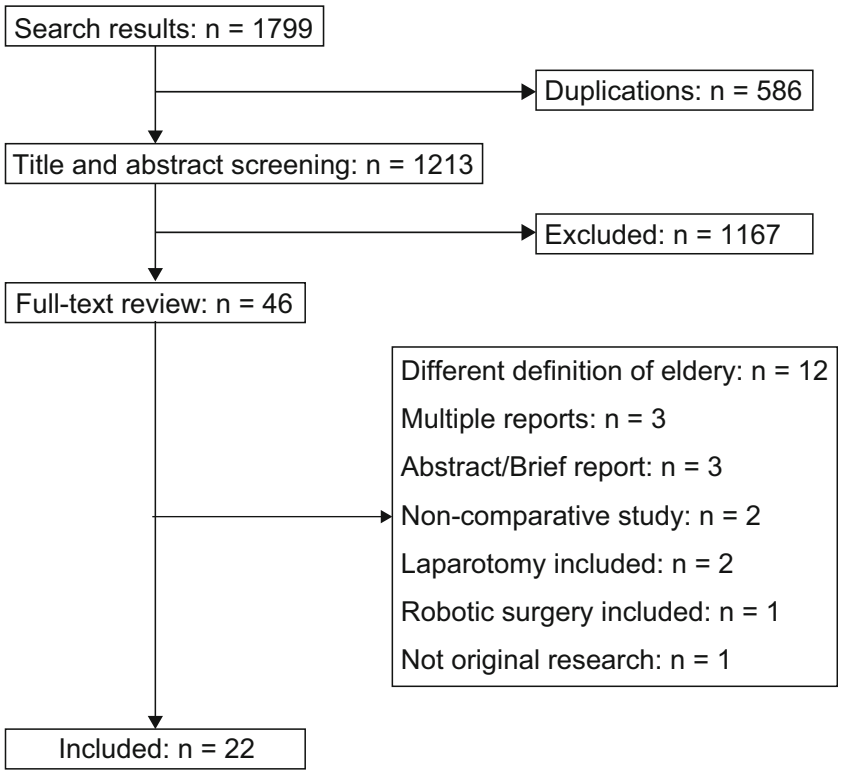

Fig. 1 Flow diagram of study selection

Table 1 Characteristics of included studies

Study	Year	Country	Design	Prospective/ retrospective
Akiyoshi [6]	2009	Japan	Cohort	Prospective
Arimoto [7]	2017	Japan	Case-matched	Retrospective
Bottino [8]	2012	Italy	Case-matched	Retrospective
Denet [9]	2017	France	Cohort	Retrospective
Fiscon [10]	2010	Italy	Case-matched	Prospective
Hirano [11]	2012	Japan	Cohort	Retrospective
Inoue [12]	2015	Japan	Cohort	Retrospective
Jeong [13]	2013	Korea	Cohort	Retrospective
Kang [14]	2015	Korea	Cohort	Retrospective
Kazama [15]	2017	Japan	Cohort	Retrospective
Kvasnovsky [16]	2015	UK	Cohort	Retrospective
Lim [17]	2017	Korea	Cohort	Retrospective
Matsuoka [18]	2004	Japan	Cohort	Retrospective
Nakamura [19]	2011	Japan	Case-matched	Retrospective
Otsuka [20]	2017	Japan	Case-matched	Retrospective
Pedziwiatr [21]	2015	Poland	Cohort	Prospective
Roscio [22]	2016	Italy	Cohort	Retrospective
Sklow [23]	2003	USA	Cohort	Retrospective
Tan [24]	2011	Japan	Cohort	Retrospective
Tokuhara [25]	2016	Japan	Cohort	Retrospective
Tomimaru [26]	2011	Japan	Cohort	Retrospective
Yamamoto [27]	2003	Japan	Case-matched	Retrospective

Table 2 Characteristics of participants

Study	Disease(s)	*n*		ASA score 1/2/3/4, *n*		Colon/Rectum, *n*		Stage 0-I/II/III/IV, *n*	
		Elderly	Non-elderly	Elderly	Non-elderly	Elderly	Non-elderly	Elderly	Non-elderly
Akiyoshi	Rectal cancer	44	228	2/36/6/0	120/105/3/0	0/44	0/228	19/6/18/1	117/44/57/10
Arimoto	Colorectal cancer	57	57	4/40/13/0	20/30/7/0	48/9	49/8	12/29/16/0	13/31/13/0
Bottino	Colorectal cancer	40	40	3.1 (a)	2.1	30/10	30/10	8/8/20/4	8/10/19/3
Denet	Colon cancer	168	339	78/90 (b)	280/59	168/0	339/0	29/84/39/16	113/85/91/21
Fiscon	Colorectal disease	50	50	1/28/19/2	1/28/19/2	35/15	35/15	36/26/36/2	40/30/22/8
Hirano	Colon cancer	9	10	NR	NR	9/0	10/0	NR	NR
Inoue	Colorectal cancer	48	100	13/17/18/0	51/28/21/0	39/9	82/18	6/14/13/15	8/33/34/25
Jeong	Colorectal cancer	92	824	18/67/7/0	444/364/16/0	35/57	268/556	21/36/34/1	271/262/269/22
Kang	Colorectal cancer	98	480	9/48/41/0	186/228/66/0	33/65	148/332	15/34/44/1	106/137/194/36
Kazama	Colorectal cancer	84	153	6/72/6/0	46/100/7/0	72/12	112/41	36/25/19/4	65/30/44/13
Kvasnovsky	Colorectal cancer	27	61	14/11 (b)	47/11	18/9	38/23	7/7/13/0	15/23/23/0
Lim	Colorectal cancer	115	404	3/89/23/0	244/158/2/0	67/48	190/214	18/55/31/11	120/128/129/27
Matsuoka	Colorectal neoplasm	14	60	13/1 (b)	51/9	12/2	51/9	12/0/0/0 (c)	45/3/3/0
Nakamura	Colon cancer	74	74	31/51/18/0	43/28/3/0	74/0	74/0	28/20/26/0	28/20/26/0
Otsuka	Colorectal cancer	93	133	40/47/6/0	81/50/2/0	65/28	90/43	30/32/21/10	51/36/33/13
Pedziwiatr	Colorectal cancer	34	43	0/5/25/4	3/38/2/0	26/6	23/20	13/12/4/5	18/9/11/5
Roscio	Colorectal cancer	129	302	0/43/79/7	53/185/64/0	96/33	220/82	116/13 (d)	279/23
Sklow	Colorectal cancer	39	38	1/18/18/2	3/25/9/1	34/5	31/7	9/15/8/7	18/7/6/7
Tan	Colorectal cancer	91	379	NR	NR	81/10	349/30	29/23/35/4	163/98/110/8
Tokuhara	Colorectal cancer	53	155	9/34/8/2	64/73/15/3	38/15	86/69	17/16/16/4	56/45/43/11
Tomimaru	Colon cancer	36	90	0/20/16/0	45/40/5/0	36/0	90/0	12/13/8/3 (c)	28/33/25/4
Yamamoto	Colon cancer	17	34	3/12/2/0	26/6/2/0	17/0	34/0	11/3/3/0	25/6/3/0

(a): mean, (b): score 1–2/3–4, (c): Dukes A/B/C/D, (d): stage 0–III/IV

ASA: American Society of Anesthesiologists, *NR*: not reported

Confounding variables

Sixteen studies had a cohort design, and confounding factors were not adjusted. These studies were judged to be at high risk of bias in this domain. Five studies had a case-matched design, and baseline characteristics between elderly and non-elderly patients were adjusted using a 1:1 or 1:2 matching method. Those studies were judged to be at low risk of bias in this domain. The remaining 1 study was case-matched design, but the matching method in each study was unclear, so it was judged to be at unclear risk of bias in this domain.

Measurement of exposure

Eighteen studies mentioned that the authors collected data prospectively or extracted data from their database and/or patients' charts. These studies were judged to be at low risk of bias in this domain. The remaining 4 studies did not mention their data sources, so they were judged to be at unclear risk of bias in this domain.

Blinding of outcome assessments

Included studies in this meta-analysis compared elderly and non-elderly patients who underwent laparoscopic colorectal surgery, so blinding of outcome assessments was impossible. Therefore, all included studies were judged to be at high risk of bias in this domain.

Incomplete outcome data

Two studies had a prospective design and reported short-term outcomes in all patients in each study, so they were judged to be at low risk of bias in this domain. Nineteen studies had a retrospective design or did not mention whether all patients in each study were assessed in the outcomes, so they were judged to be at unclear risk of bias in this domain. The remaining 1 study had missing patients, so it was judged to be at high risk of bias in this domain.

Table 3 Risk of bias assessment

Study	Selection of participants	Confounding variables	Measurement of exposure	Blinding of outcome assessments	Incomplete outcome data	Selective outcome reporting
Akiyoshi	Low	High	Low	High	Low	Unclear
Arimoto	Low	Low	Low	High	Unclear	Unclear
Bottino	Low	Low	Low	High	High	Unclear
Denet	Low	High	Low	High	Unclear	Unclear
Fiscon	Low	Low	Low	High	Low	Unclear
Hirano	Low	High	Unclear	High	Unclear	Unclear
Inoue	Low	High	Low	High	Unclear	Unclear
Jeong	Low	High	Low	High	Unclear	Unclear
Kang	Low	High	Low	High	Unclear	Unclear
Kazama	Low	High	Low	High	Unclear	Unclear
Kvasnovsky	Low	High	Low	High	Unclear	Unclear
Lim	Low	High	Unclear	High	Unclear	Unclear
Matsuoka	Low	High	Low	High	Unclear	Unclear
Nakamura	Low	Low	Unclear	High	Unclear	Unclear
Otsuka	Low	Unclear	Low	High	Unclear	Unclear
Pedziwiatr	Low	High	Low	High	Unclear	Unclear
Roscio	Low	High	Low	High	Unclear	Unclear
Sklow	Low	High	Low	High	Unclear	Unclear
Tan	Low	High	Low	High	Unclear	Unclear
Tokuhara	Low	High	Low	High	Unclear	Unclear
Tomimaru	Low	High	Low	High	Unclear	Unclear
Yamamoto	Low	Low	Unclear	High	Unclear	Unclear

Selective outcome reporting

Prospective registration was unclear in all included studies. Therefore, all studies were judged to be at unclear risk of bias in this domain.

Assessment of publication bias

Publication bias was assessed using funnel plots regarding primary outcomes. The shapes of the plots were all symmetrical, so no apparent publication bias was identified (Fig. 2).

Primary outcomes

Overall complications

All 22 studies with 5466 patients reported on the incidence of overall complications and were combined in a meta-analysis. The incidence was significantly higher in elderly patients than in non-elderly patients (RR 1.20, 95% CI 1.08–1.34, $P < 0.01$). Heterogeneity was low ($I^2 = 0\%$, $P = 0.71$; Fig. 3).

Anastomotic leakage

Sixteen studies with 4479 patients reported on the incidence of anastomotic leakage and were combined in a meta-analysis. There was no significant difference between elderly and non-elderly patients regarding the incidence of anastomotic leakage (RR 1.24, 95% CI 0.86–1.80, $P = 0.25$). Heterogeneity was low ($I^2 = 0\%$, $P = 0.72$; Fig. 4).

Mortality

Twenty studies with 5204 patients reported on the mortality and were combined in a meta-analysis. Mortality was low, and 12 studies reported 0% mortality. Therefore, mortality was assessed using RD. There was no significant difference between elderly and non-elderly patients regarding mortality (RD 0.00, 95% CI −0.01 to 0.01, $P = 0.89$). Heterogeneity was low ($I^2 = 0\%$, $P = 0.99$; Fig. 5).

Secondary outcomes

Cardiac complications

Nine studies with 1925 patients reported on the incidence of cardiac complications and were combined in a meta-analysis.

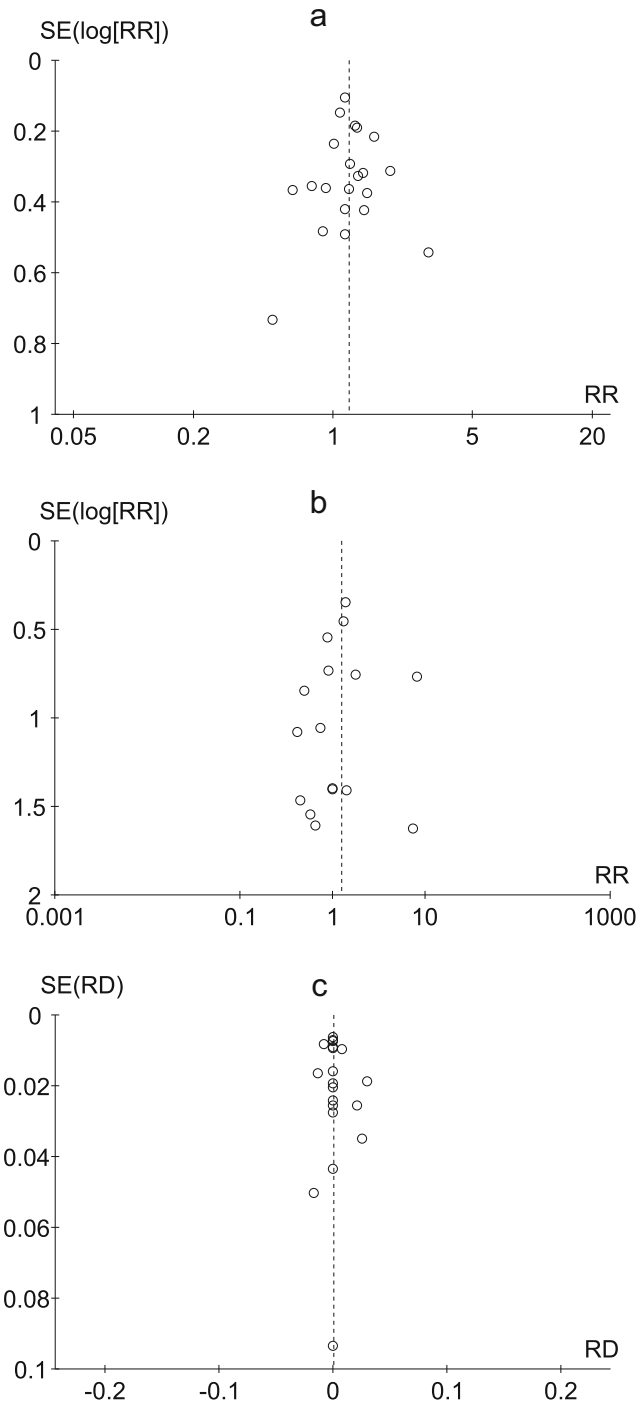

Fig. 2 Funnel plots. **a** The incidence of overall complications. **b** The incidence of anastomotic leakage. **c** Mortality. RD: risk difference, RR: risk ratio, SE: standard error

There was no significant difference between elderly and non-elderly patients regarding the incidence of cardiac complications (RR 1.68, 95% CI 0.79–3.54, $P = 0.18$). Heterogeneity was low ($I^2 = 0\%$, $P = 0.98$; Table 4).

Pulmonary complications

Thirteen studies with 3568 patients reported on the incidence of pulmonary complications and were combined in a meta-analysis. There was no significant difference between elderly and non-elderly patients regarding the incidence of pulmonary complications (RR 1.41, 95% CI 0.71–2.82, $P = 0.33$). Heterogeneity was low ($I^2 = 0\%$, $P = 0.53$; Table 4).

Wound complications

Eighteen studies with 4712 patients reported on the incidence of wound complications and were combined in a meta-analysis. There was no significant difference between elderly and non-elderly patients regarding the incidence of wound complications (RR 1.29, 95% CI 0.97–1.71, $P = 0.08$). Heterogeneity was low ($I^2 = 0\%$, $P = 0.92$; Table 4).

Postoperative ileus

Ten studies with 3310 patients reported on the incidence of postoperative ileus and were combined in a meta-analysis. There was no significant difference between elderly and non-elderly patients regarding the incidence of postoperative ileus (RR 1.47, 95% CI 0.83–2.62, $P = 0.19$). Heterogeneity was low ($I^2 = 0\%$, $P = 0.87$; Table 4).

Length of hospital stay

Nine studies with 1978 patients reported on the length of hospital stay as a mean with SD and were combined in a meta-analysis. There was no significant difference between elderly and non-elderly patients regarding the length of hospital stay (MD 0.50, 95% CI −0.28 to 1.29, $P = 0.21$). Heterogeneity was substantial ($I^2 = 73\%$, $P < 0.01$; Table 4).

Subgroup analyses

Primary outcomes were analyzed stratified by study design, specifically cohort study versus case-matched study. The incidences of overall complications and anastomotic leakage were slightly higher in cohort studies (RR 1.22, 95% CI 1.09–1.36 and RR 1.33, 95% CI 0.90–1.97, respectively) than in case-matched studies (RR 1.07, 95% CI 0.73–1.55 and RR 0.75, 95% CI 0.26–2.20, respectively). Mortalities in both cohort studies and case-matched studies (RD 0.00, 95% CI −0.01 to 0.01, RD 0.00, 95% CI −0.02 to 0.02, respectively) were not different (Table 5).

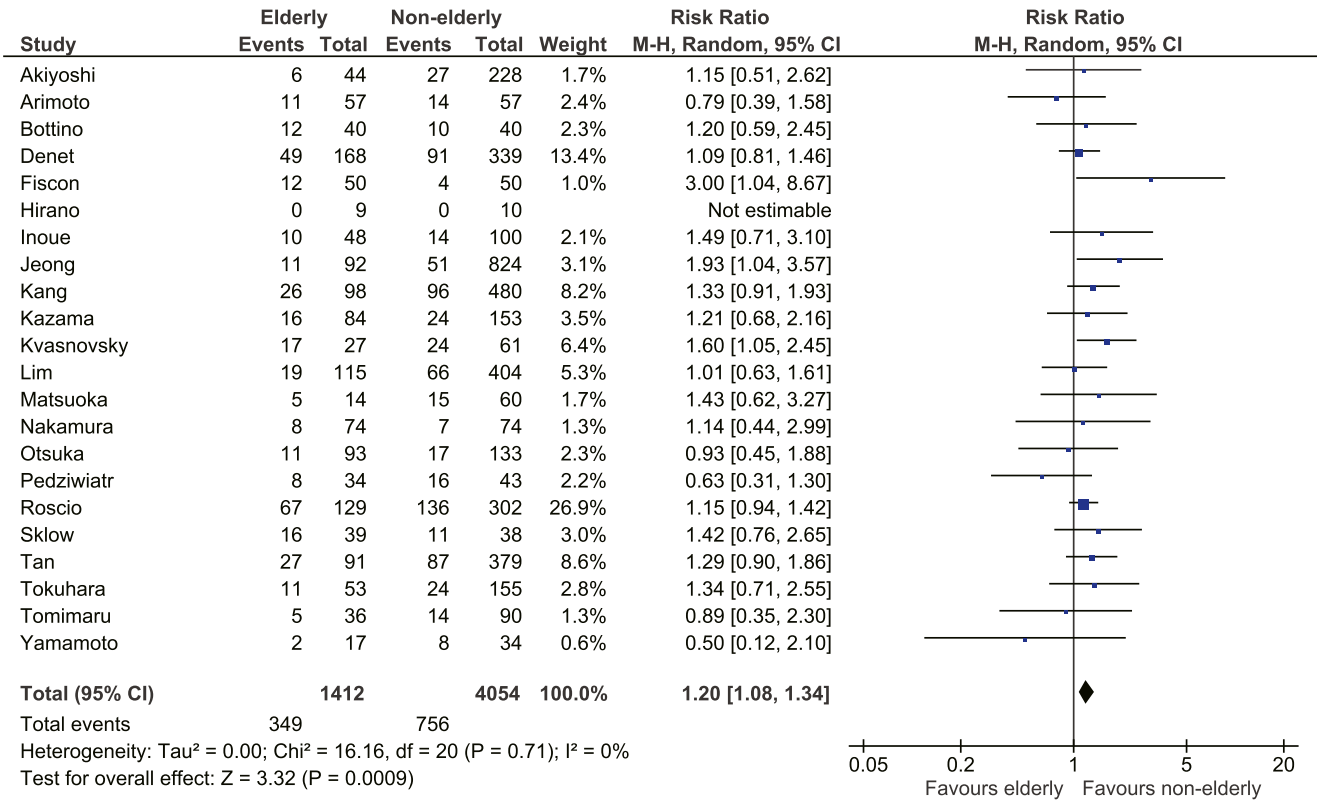

Fig. 3 Incidence of overall complications

Discussion

In this meta-analysis, we compared short-term outcomes of laparoscopic surgery between elderly and non-elderly patients with colorectal cancer. The incidence of overall complications was slightly higher in elderly patients than in non-elderly patients, but there was no significant difference between them in the incidence of anastomotic leakage and mortality.

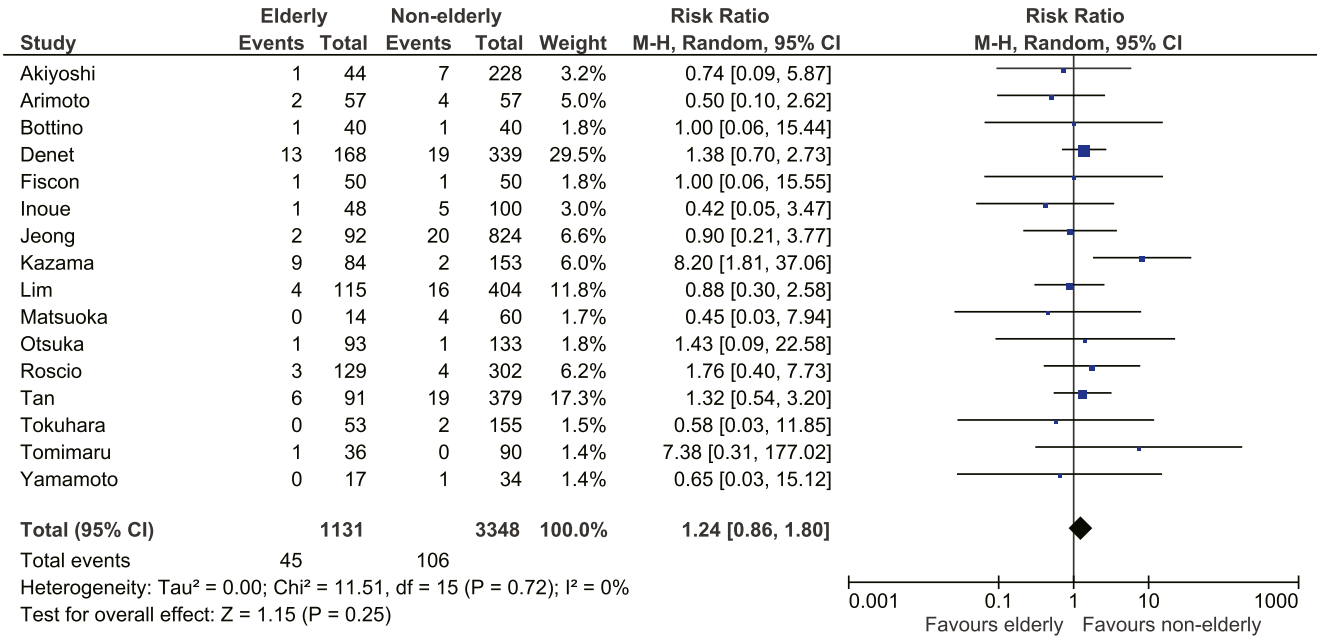

Fig. 4 Incidence of anastomotic leakage

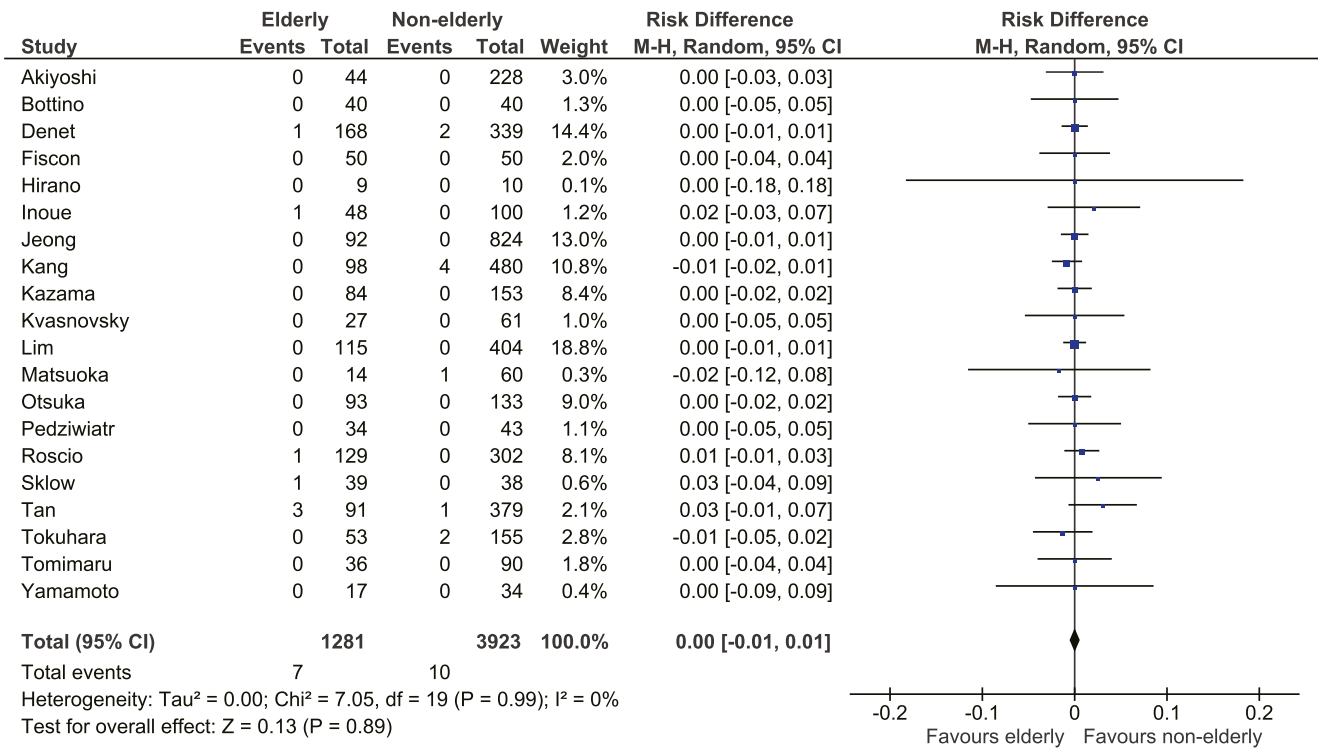

Fig. 5 Mortality

Table 4 Analysis of secondary outcomes

Outcome		Studies (*n*)	Elderly patients		Non-elderly patients		RR	95% CI	*P* value	Heterogeneity	
			Event (*n*)	Total (*n*)	Event (*n*)	Total (*n*)				I^2 (%)	*P* value
Incidence	Cardiac complications	9	11	595	14	1330	1.68	0.79–3.54	0.18	0	0.98
	Pulmonary complications	13	16	952	25	2611	1.41	0.71–2.82	0.33	0	0.53
	Wound complications	18	70	1231	141	3481	1.29	0.97–1.71	0.08	0	0.92
	Postoperative ileus	10	19	761	38	2549	1.47	0.83–2.62	0.19	0	0.87
Length of hospital stay (days)		9	–	525	–	1453	0.50 (a)	− 0.28 to 1.29	0.21	73	< 0.01

(a) Mean difference

CI: confidence interval, *RR*: risk ratio

Table 5 Subgroup analysis

Outcome		Cohort study			Case-matched study		
		RR	95% CI	*P* value	RR	95% CI	*P* value
Incidence	Overall complications	1.22	1.09–1.36	< 0.01	1.07	0.73–1.55	0.73
	Anastomotic leakage	1.33	0.90–1.97	0.16	0.75	0.26–2.20	0.60
	Mortality	0.00 (a)	-0.01 to 0.01	0.89	0.00 (a)	− 0.02 to 0.02	1.00

(a) Risk difference

CI: confidence interval, *RR*: risk ratio

Elderly patients have different characteristics from non-elderly patients including concomitant disease, poor performance status, and shorter life expectancy [30, 31]. Careful geriatric assessment is needed and individualized strategies are essential in treating elderly patients [30]. Although the survival benefit from surgery may be shorter in elderly patients than in non-elderly patients because of limited life expectancy, minimal invasiveness is no doubt favorable for all cancer patients. Several systematic reviews comparing laparoscopic and open surgeries for elderly colorectal cancer patients reported the advantage of laparoscopic surgery in short-term outcomes [3–5]. However, it remained unclear whether laparoscopic surgery is safe for elderly patients as well as non-elderly patients with colorectal cancer. Therefore, we compared the incidence of postoperative complications between elderly and non-elderly patients.

The results of meta-analyses indicated that the incidence of overall complications was significantly higher in the elderly patients. In addition, the incidence of anastomotic leakage, cardiac complications, pulmonary complications, wound complications, and postoperative ileus tended to be higher and length of hospital stay tended to be longer in elderly patients, without statistical significance. However, the degrees of difference were small, even for differences in outcomes that were statistically significant. We considered the small magnitude of differences to be influenced by the heterogeneity in baseline characteristics between elderly and non-elderly patients, as suggested by the results of the subgroup analysis. Most of the included studies had a retrospective cohort design, in which the characteristics of patients were not adjusted, and elderly patients naturally have more comorbidities and are more sensitive to surgical stress than non-elderly patients. By contrast, there were no differences between elderly and non-elderly patients in mortality and the incidence of anastomotic leakage in spite of the potential baseline heterogeneity of characteristics.

The strength of this meta-analysis was the inclusion of many studies from various countries, summing up large numbers of patients. The meta-analysis had enough power to detect even differences of small magnitude in short-term outcomes between elderly and non-elderly patients. Nonetheless, this analysis had several limitations. Included studies were mostly of a cohort design, in which the results were not adjusted for confounding factors. In addition, most of the included studies were retrospective, which have a potentially high risk of detection bias. Moreover, we could not obtain sufficient information about the definition of postoperative complications and the proportion of stoma creation in rectal cancer surgery. The definition of postoperative complications might not be unique across the included studies, and there might be an imbalance in stoma creation between elderly and non-elderly patients.

In conclusion, laparoscopic surgery for colorectal cancer was mostly safe for elderly patients as well as non-elderly patients; however, preoperative comorbidities or poor physical capacity in the elderly might lead to the increase of postoperative complications.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human rights For this type of study, formal consent is not required.

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