REVIEW ARTICLE

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Laparoscopic versus open surgery for elderly patients with colorectal cancer: a systematic review and meta-analysis of matched studies

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Key words
colorectal cancer, elderly, laparoscopic surgery, meta-analysis, open surgery.

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Abstract

Background: To compare clinical and survival outcomes between laparoscopic versus open surgery in elderly colorectal cancer patients.

Methods: PubMed, Embase and Scopus databases were systematically searched. The review included studies that were either randomized controlled trials (RCTs) or observational in design. STATA was used for statistical analysis.

Results: The meta-analysis was conducted with 24 studies. Compared with elderly subjects with open surgery, those undergoing laparoscopic surgery had a lower risk of mortality (within 3 months postoperatively) (RR 0.70, 95% CI: 0.53, 0.94). The long-term overall survival (HR 0.96, 95% CI: 0.89, 1.04), disease-free survival (HR 1.02, 95% CI: 0.93, 1.13), risk of recurrence (RR 1.44, 95% CI: 0.90, 2.30) and readmission (RR 1.11, 95% CI: 0.88, 1.40) rates were statistically similar in both the groups. The operative time (in minutes) was higher (WMD 30.37, 95% CI: 17.75, 43.0) and the blood loss (in ml) was lower (WMD −78.85, 95% CI: −101.96, −55.75) in those undergoing laparoscopic surgery. The length of hospital stay (in days) (WMD −2.53, 95% CI: −3.11, −1.95) and the time of return of bowel movements (in days) (WMD −1.06, 95% CI: −1.20, −0.93) was lower in those with laparoscopic surgery. The pooled risk of complications was lower in those with laparoscopic surgery (RR 0.66, 95% CI: 0.60, 0.74), compared with open surgery.

Conclusions: Findings suggest that in elderly subjects with colorectal cancer, laparoscopic surgery appears to be more beneficial than open surgery and should be prioritized, subject to the availability of required technical skills and facilities.

Introduction

Globally, colon and rectal cancer are among the top 10 cancer incidences, fourth and eighth in rankings respectively.[1] Combined, colorectal cancer constitutes around 10% of all cancer diagnoses and is among the third most diagnosed carcinoma.[2] Colorectal cancer exhibits a peak incidence in the seventh and eighth decade and ranks second in terms of the most common cause of cancer-related mortality in males and third in females.[2–4] Globally, advancements in medical care and increased access to health facilities have allowed the life expectancy to increase substantially.[5,6] With a greater elderly population there will be a global increase in elderly patient disease incidence, including colorectal cancer.

Currently, surgery is one of the promising management modality for colorectal cancer, specifically resection of the primary tumour with lymphadenectomy.[7] However, recent studies have shown that complete clinical response of rectal cancer can be achieved with neoadjuvant chemoradiotherapy and that a watch and wait approach is safe within similar survival outcomes in patients that achieve a complete pathological response.[8,9] Elderly subjects are usually frail and have reduced physiological reserve to undergo major surgery.[10] These patients often have associated metabolic, cardiac and respiratory comorbidities that increase the risk of peri and post-operative complications.[10,11] Studies specific to colorectal carcinoma have shown increasing age to be a significant factor associated with poor post-surgical outcomes and increased risk of morbidities.[12,13] Such studies have also indicated that elderly patients often have advanced disease progression and obstructive symptoms at the time of clinical presentation.[12,13] Like any other surgical intervention, colorectal surgery is often associated with an increased risk of morbidity and

mortality. Studies from the general population have demonstrated that in patients with colorectal cancer, laparoscopic surgery is more beneficial over open surgery with regards to better peri-operative outcomes.[14,15] However, evidence is inconclusive within the elderly population. Of potential concern, laparoscopic surgery in elderly patients may cause hemodynamic alterations resulting from increased intra-abdominal pressure due to pneumoperitoneum.[16] While open surgery is a major stress for the already weak and frail elderly subjects.

Recently, there have been several systematic reviews and meta-analyses which have compared the clinical and survival outcomes between laparoscopic and open surgery in elderly patients with colorectal cancer.[17–24] The included studies were primarily observational in design, which could prevent the adjustment for possible confounding variables. Additionally, there was often a lack of comparability of baseline characteristics among the groups which could affect the final reported effect sizes. One of the accepted methods to address this issue is the propensity score matching (PSM) statistical scoring technique.[25] PSM ensures that the subjects in the groups being compared are matched with each other based on a set of pre-defined characteristics. In this meta-analysis, we included studies that had conducted PSM and/or matched the subjects based on baseline clinical or socio-demographic characteristics. Through this meta-analytic effort, we intend to provide the most recent synthesized evidence through comparison of outcomes of laparoscopic versus open surgery in elderly colorectal cancer patients.

Materials and methods

This meta-analysis adhered to PRISMA guidelines.[26] The protocol was registered in the International Prospective Registry of Systematic Reviews (PROSPERO; registration number CRD42022299663). PubMed, Embase and Scopus databases were used to systematically search English language papers published until 15 December 2021. The search strategy incorporated the following: (elderly OR octogenarians OR nonagenarian OR geriatric) AND (Colorectal cancer OR gastrointestinal cancer OR colorectal) AND (open surgery OR laparoscopic surgery OR laparoscopy) AND (propensity matching OR matching OR propensity score match). The aim of the search was to select studies that compared the outcomes of interest among elderly subjects (aged ≥65 years) with colorectal cancer based on the type of surgical intervention, that is, laparoscopic or open surgery. The primary outcomes of interest were survival, that is, short-term and long-term, disease-free survival, risk of readmission and recurrence. The secondary outcomes were intra-operative parameters such as operation time and estimated blood loss, length of hospital stay, time to return of bowel movements and risk of postoperative complications.

The whole process of screening and selection of studies for inclusion in the meta-analysis was done by two study authors independently. As an initial step, the search strategy was run in the above-mentioned databases and after exclusion of duplicates, citations were thoroughly screened based on their title and abstract. As the next step, the full texts of the potentially relevant studies were retrieved and read. Through mutual discussions among the authors, disagreements regarding the inclusion of the studies were resolved. As a final step, the authors also reviewed the reference list of the included studies in an attempt to identify additional studies that they might have missed through the selection process they had followed.

We considered both randomized controlled trials (RCTs) and studies with an observational design for potential inclusion. Studies of interest were those that were done in elderly subjects with colorectal cancer and had compared relevant outcomes of interest based on the type of surgical management, that is, laparoscopy and open surgery. It is particularly important to note that for observational studies (i.e., retrospective, prospective or case–control), only those studies that had considered PSM were preferred for inclusion. This was done to reduce the selection bias arising out of differential characteristics among the subjects in the two groups. Studies conducted in younger population or those that did not provide comparative findings between laparoscopic and open surgery were excluded. Further, studies that did not involve PSM were also excluded.

Data from the eligible studies was extracted for analysis using a predefined sheet. This was done by two authors who were well versed with the meta-analytic process, study proposal and the subject under consideration. The quality assessment of the included studies was done using the Newcastle-Ottawa Quality Assessment Scale (NOS) for observational studies.[27] For RCTs, Cochrane risk of bias tool was used.[28]

Statistical analysis

We reported pooled effect sizes, along with 95% confidence intervals, either as relative risk (RR) or hazards ratio (HR) for categorical outcomes or weighted mean difference (WMD) for continuous outcomes. I^2 was used to denote heterogeneity and guided the selection of the analytic model, that is, random effects model if $I^2 \geq 40\%$ and fixed effects model if <40%.[29] We considered statistical significance to be present at a *P*-value of less than 0.05. Publication bias was assessed using Egger's test.[30]

Results

A total of 24 studies were considered for inclusion.[31–54] Table 1 presents the details of the studies included in the review. Figure 1 presents the process being followed for the final selection of studies. Most of the included studies ($n = 16$) were retrospective in design. There were six studies that were either RCTs or used primary data from an RCT. The remaining two studies were prospective in design. Seven studies were completed in Japan, eight studies in the USA and two studies each in Italy and Taiwan. One study each was done in China, South Korea, the UK and Israel. There were multicentre studies conducted in health facilities in New Zealand and Australia. The included studies were of modest to good quality (Tables S1, S2 and S3). For the observational studies, the NOS score ranged from six to nine, with nine being the maximum attainable score. The mean NOS score was 8.22. Among the 6 RCTs, all had adopted the process of random sequence generation and allocation concealment. Due to the trials being open label, owing to the nature of the interventions being tested, blinding was not possible.

Table 1 Characteristics of the studies included in the meta-analysis

Author (year of publication)	Study design	Country	Participant characteristics	Sample size	Key outcomes (laparoscopic vs. open)
Zhou *et al.* (2019)[31]	Retrospective	China	Elderly patients with colorectal cancer; mean age of 82 years; male (59%); mean BMI of 23.0 kg/m^2; ASA score I/II (54%); Tumour location (Rt. Colon- 33.8%; rectum- 38.7%); Poor tumour differentiation (25%); TNM II/III (88.7%)	Laparoscopic- 93; Open-93	*Mean follow up of 37.4 months* Operation time (min) (mean, *SD*): 161.2 (55.3); 149.1 (53.9) Blood loss (ml) (mean, *SD*): 50.9 (44.9); 108.1 (78.5) Length of hospital stay (days) (mean, *SD*): 9.6 (3.3); 12.2 (5.5) Return to normal bowel function (days) (mean, *SD*): 4.5 (1.6); 5.5 (2.1) Need for blood transfusion: RR 0.71 (95% CI: 0.39, 1.30) Overall post-operative complications: RR 0.40 (95% CI: 0.21, 0.79) Wound infection/sepsis: RR 0.20 (95% CI: 0.05, 0.89) Anastomosis leak: RR 0.50 (95% CI: 0.09, 2.66) Post-operative ileus: RR 0.40 (95% CI: 0.08, 2.01) Cardiac complication: RR 0.33 (95% CI: 0.04, 3.15) Pulmonary complication: RR 0.40 (95% CI: 0.08, 2.01) Overall survival (at latest follow up): HR 0.77 (95% CI: 0.47, 1.32) Disease free survival (at latest follow up): HR 0.71 (95% CI: 0.40, 1.25)
Moon *et al.* (2016)[32]	Retrospective	South Korea	Elderly patients with colorectal cancer; median age of 82 years; male (56%); median BMI of 22.0 kg/m^2; ASA score I/II (77.5%); Tumour location (Lt. Colon- 49.3%; rectum- 28%); TNM II/III (74%)	Laparoscopic- 71; Open-71	*Median follow up of 68.3 months* Operation time (min) (mean, *SD*): 182 (9.4); 130 (17.5) Blood loss (ml) (mean, *SD*): 100 (25); 100 (41.7) Length of hospital stay (days) (mean, *SD*): 9.0 (0.7); 10.0 (0.83) Return to normal bowel function (days) (mean, *SD*): 3 (0.3); 4 (0.3) Overall post-operative complications: RR 0.55 (95% CI: 0.33, 0.92) Wound infection/sepsis: RR 0.56 (95% CI: 0.20, 1.58) Post-operative ileus: RR 0.27 (95% CI: 0.08, 0.94) Urinary retention: RR 1.00 (95% CI: 0.42, 2.37) Pulmonary complication: RR 3.0 (95% CI: 0.12, 72.4) Intra-abdominal bleeding: RR 1.0 (95% CI: 0.06, 15.7) Overall survival (at latest follow up): HR 0.82 (95% CI: 0.48, 1.38) Disease free survival (at latest follow up): HR 0.67 (95% CI: 0.40, 1.12)
Frasson *et al.* (2008)[33]	Randomized controlled trial	Italy	Mean age of around 75 years; male (60%); mean ASA score of 2.2; Obesity (6.5%); diagnosis of cancer (85.5%)	Laparoscopic- 89; Open-112	*Follow up till 30 days post-operatively* Length of hospital stay (days) (mean, *SD*): 9.5 (3.8); 13 (9.4) Overall post-operative complications: RR 0.54 (95% CI: 0.33, 0.87) Wound infection/sepsis: RR 0.34 (95% CI: 0.15, 0.74) Post-operative ileus: RR 0.63 (95% CI: 0.16, 2.45) Urinary tract infection: RR 0.63 (95% CI: 0.06, 6.83) Pulmonary complication: RR 2.55 (95% CI: 0.24, 27.6) Intra-abdominal bleeding: RR 0.32 (95% CI: 0.04, 2.76) Anastomosis leak: RR 0.76 (95% CI: 0.19, 3.07) Cardiac complication: RR 0.72 (95% CI: 0.22, 2.38) Mortality (within 30-days): RR 2.51 (95% CI: 0.23, 27.3)

Table 1 Continued

Author (year of publication)	Study design	Country	Participant characteristics	Sample size	Key outcomes (laparoscopic vs. open)
Fujii *et al.* (2014)[34]	Randomized controlled trial	Japan	Elderly patients with colorectal cancer; age > 75 years; male (55%); mean BMI of 22.0 kg/m^2; ASA score II/III (93%); Tumour location (Lt. Colon- 43%; rectum- 29%); TNM II/III (67%)	Laparoscopic- 100; Open-100	*Short term follow up post-operatively (period of follow up not mentioned)* Operation time (min) (mean, *SD*): 172 (56); 150 (49) Blood loss (ml) (mean, *SD*): 63 (154); 157 (157) Length of hospital stay (days) (mean, *SD*): 11.7 (9.2); 14.4 (12.7) Overall post-operative complications: RR 0.64 (95% CI: 0.41, 0.99) Wound infection/sepsis: RR 0.42 (95% CI: 0.15, 1.14) Post-operative ileus: RR 0.33 (95% CI: 0.11, 0.99) Urinary tract infection: RR 1.00 (95% CI: 0.06, 15.7) Pulmonary complication: RR 0.20 (95% CI: 0.01, 4.11) Anastomosis leak: RR 0.63 (95% CI: 0.21, 1.85) Cardiac complication: RR 2.0 (95% CI: 0.18, 21.7) Renal complication: RR 0.33 (95% CI: 0.04, 3.15)
Fujii *et al.* (2021)[35]	Randomized controlled trial	Japan	Age > 75 years; male (54.7%); mean BMI of 22.0 kg/m^2; ASA score II/III (93%); Tumour location (Rt. Colon- 42.6%; rectum- 30%); TNM II/III (69%)	Laparoscopic- 98; Open-92	*Mean follow up of around 60 months* Overall survival (latest follow up; 5-year): HR 0.84 (95% CI: 0.47, 1.51) Disease free survival (latest follow up; 5-year): HR 0.80 (95% CI: 0.53, 1.20) Recurrence: RR 1.56 (95% CI: 0.81, 3.02)
Horsey *et al.* (2021)[36]	Retrospective	USA	Elderly patients with rectal cancer; age ≥ 65 years; male (>60%); White race (>85%); TNM II/III (68%)	Laparoscopic- 1891; Open-1891	Mortality (within 30-days): RR 0.62 (95% CI: 0.35, 1.09) Mortality (within 90-days): RR 0.66 (95% CI: 0.45, 0.97) Readmission: RR 1.12 (95% CI: 0.87, 1.44) Overall survival (latest follow up; 5-year): HR 0.87 (95% CI: 0.76, 1.01)
Ishibe *et al.* (2017)[37]	Randomized controlled trial	Japan	Elderly patients with colorectal cancer; male (55%); ASA score II/III (92.6%); Tumour location (Colon- 69.5%); No adjuvant chemotherapy (86.3%)	Laparoscopic- 98; Open-92	*Mean follow up of 43 months* Overall survival (latest follow up; 3-year): HR 0.83 (95% CI: 0.34, 2.07) Disease free survival (latest follow up;3-year): HR 1.28 (95% CI: 0.62, 2.64) Recurrence: RR 1.45 (95% CI: 0.72, 2.93)
Lin *et al.* (2010)[38]	Retrospective	Taiwan	Elderly patients with colorectal cancer; age ≥ 90 years; male (59%); Tumour stage II/III/IV (63.6%); associated diabetes (18%); associated hypertension (40%)	Laparoscopic- 11; Open-11	Length of hospital stay (days) (mean, *SD*): 16.9 (8.5); 23.9 (12.3) Overall post-operative complications: RR 0.80 (95% CI: 0.29, 2.21) Overall survival (latest follow up, 5 year): HR 0.71 (95% CI: 0.33, 1.57) Disease free survival (latest follow up, 5 year): HR 0.86 (95% CI: 0.43, 1.73) Recurrence: RR 0.50 (95% CI: 0.05, 4.75) Mortality (within 30-days): RR 3.0 (95% CI: 0.14, 66.5) Mortality (within 1 year): RR 0.67 (95% CI: 0.13, 3.24)
Miguchi *et al.* (2018)[39]	Retrospective	Japan	Elderly patients with colorectal cancer; median age of 85 years; female (61%); mean BMI of 21.0 kg/m^2; Tumour location (Rt. Colon- 64.4%; rectum- 14.4%); TNM II/III (84.6%)	Laparoscopic- 52; Open-52	Operation time (min) (mean, *SD*): 222 (59.8); 168 (81.5) Blood loss (ml) (mean, *SD*): 40 (180); 140 (403.3) Length of hospital stay (days) (mean, *SD*): 11 (4.8); 14 (9.3) Need for blood transfusion: RR 0.25 (95% CI: 0.08, 0.83) Overall post-operative complications: RR 0.52 (95% CI: 0.28, 0.97) Wound infection/sepsis: RR 0.50 (95% CI: 0.20, 1.23) Anastomosis leak: RR 5.0 (95% CI: 0.25, 101.6) Post-operative ileus: RR 0.67 (95% CI: 0.20, 2.23)

Table 1 Continued

Author (year of publication)	Study design	Country	Participant characteristics	Sample size	Key outcomes (laparoscopic vs. open)
					Cardiac complication: RR 0.33 (95% CI: 0.02, 7.9) Pulmonary complication: RR 1.00 (95% CI: 0.06, 15.6) Urinary tract infection: RR 3.0 (95% CI: 0.13, 71.9) Intra-abdominal bleeding: RR 0.33 (95% CI: 0.02, 7.9) Readmission: RR 2.0 (95% CI: 0.19, 21.4) Mortality (within 30-days): RR 0.33 (95% CI: 0.02, 7.9)
van Dalen *et al.* (2019)[40]	Retrospective	USA	Elderly patients with colorectal cancer; mean age of 68 years; white race (>70%); female (48%); mean BMI of 28.0 kg/m^2; ASA III/IV (62%)	Laparoscopic- 4020; Open-4014	Operation time (min) (mean, *SD*): 172 (87); 171.4 (101.8) Overall post-operative complications: RR 0.59 (95% CI: 0.56, 0.63) Wound infection/sepsis: RR 0.45 (95% CI: 0.37, 0.56) Cardiac complication: RR 0.70 (95% CI: 0.49, 1.00) Pulmonary complication: RR 0.50 (95% CI: 0.39, 0.65) Urinary tract infection: RR 0.50 (95% CI: 0.38, 0.64) Renal complication: RR 0.30 (95% CI: 0.15, 0.58)
Vignali *et al.* (2005)[41]	Retrospective	Italy	Elderly patients undergoing colectomy; mean age of around 83 years; female (52.5%); mean BMI of around 25.0 kg/m^2; TNM III/IV (52%)	Laparoscopic- 61; Open-61	*Mean follow up of 24.7 months* Operation time (min) (mean, *SD*): 220.3 (58.2); 171.2 (48.6) Blood loss (ml) (mean, *SD*): 135 (115); 270.4 (170) Return to normal bowel function (days) (mean, *SD*): 4.8 (2.1); 5.9 (2.0) Length of hospital stay (days) (mean, *SD*): 9.8 (5.3); 12.9 (10) Need for blood transfusion: RR 0.45 (95% CI: 0.22, 0.91) Overall post-operative complications: RR 0.68 (95% CI: 0.37, 1.26) Wound infection/sepsis: RR 0.45 (95% CI: 0.17, 1.23) Anastomosis leak: RR 1.33 (95% CI: 0.31, 5.71) Post-operative ileus: RR 0.50 (95% CI: 0.13, 1.91) Cardiac complication: RR 1.0 (95% CI: 0.26, 3.82) Pulmonary complication: RR 0.67 (95% CI: 0.12, 3.85) Urinary tract infection: RR 2.0 (95% CI: 0.19, 21.4) Mortality (within 30-days): RR 0.50 (95% CI: 0.05, 5.37) Readmission: RR 0.40 (95% CI: 0.08, 1.98) Overall survival (latest follow up, 2 year): HR 0.75 (95% CI: 0.28, 2.03)
Stocchi *et al.* (2000)[42]	Retrospective	USA	Mean age of around 81 years; female (50%); Right colectomy (82%); Indication being cancer (68%)	Laparoscopic- 42; Open-42	Operation time (min) (mean, *SD*): 190 (58.3); 142 (46.2) Return to normal bowel function (days) (mean, *SD*): 3.9 (1.7); 6.0 (2.2) Length of hospital stay (days) (mean, *SD*): 6.5 (4.0); 10.2 (4.4) Overall post-operative complications: RR 0.43 (95% CI: 0.18, 1.01) Post-operative ileus: RR 0.33 (95% CI: 0.02, 7.9) Cardiac complication: RR 0.25 (95% CI: 0.03, 2.14) Pulmonary complication: RR 0.80 (95% CI: 0.23, 2.77) Urinary tract infection: RR 0.33 (95% CI: 0.02, 7.9) Renal complication: RR 1.0 (95% CI: 0.06, 15.5)

Table 1 Continued

Author (year of publication)	Study design	Country	Participant characteristics	Sample size	Key outcomes (laparoscopic vs. open)
Sklow *et al.* (2003)[43]	Retrospective	USA	Mean age of around 82 years; male (55%); Right colectomy (69%); TNM 3/4 (38.5%)	Laparoscopic- 39; Open-39	Operation time (min) (mean, *SD*): 159.3 (6.9); 111.7 (6.7) Blood loss (ml) (mean, *SD*): 166.9 (17.7); 233.8 (35.5) Return to normal bowel function (days) (mean, *SD*): 3.9 (0.2); 4.9 (0.4) Length of hospital stay (days) (mean, *SD*): 6.1 (0.3); 7.8 (0.6) Overall post-operative complications: RR 1.0 (95% CI: 0.59, 1.70) Wound infection/sepsis: RR 1.03 (95% CI: 0.22, 4.77) Intra-abdominal bleeding: RR 3.0 (95% CI: 0.33, 27.6) Post-operative ileus: RR 0.75 (95% CI: 0.18, 3.13) Cardiac complication: RR 0.25 (95% CI: 0.03, 2.14) Pulmonary complication: RR 1.0 (95% CI: 0.15, 6.7) Urinary tract infection: RR 3.0 (95% CI: 0.13, 71.5) Renal complication: RR 0.50 (95% CI: 0.05, 5.3) Mortality (within 30-days): RR 3.0 (95% CI: 0.13, 71.5)
Senagore *et al.* (2003)[44]	Retrospective	USA	Mean age of around 78 years; male (55%); Right colectomy (65%); ASA score of 3/4 (85%)	Laparoscopic- 50; Open-123	Operation time (min) (mean, *SD*): 102 (41); 160.2 (53) Blood loss (ml) (mean, *SD*): 121 (100); 293 (311) Length of hospital stay (days) (mean, *SD*): 4.2 (3.0); 9.3 (7.6) Overall post-operative complications: RR 0.43 (95% CI: 0.22, 0.84) Wound infection/sepsis: RR 0.49 (95% CI: 0.06, 4.11) Post-operative ileus: RR 0.08 (95% CI: 0.01, 1.29) Cardiac complication: RR 0.98 (95% CI: 0.20, 4.91) Anastomosis leak: RR 0.27 (95% CI: 0.02, 4.93) Readmission: RR 0.92 (95% CI: 0.26, 3.34) Mortality (within 30-days): RR 0.49 (95% CI: 0.03, 9.95)
Hinoi *et al.* (2015)[45]	Retrospective	Japan	Median age of 83 years; males (47%); median BMI of 21.5 kg/m^2; Rt. Hemicolectomy in 43%; T3/4 (70%); N0 (69%)	Laparoscopic- 402; Open-402	*Median follow up of 39.5 months* Operation time (min) (mean, *SD*): 201 (14.2); 148 (12) Blood loss (ml) (mean, *SD*): 27 (10); 80 (28.3) Length of hospital stay (days) (mean, *SD*): 12 (1); 13 (1.5) Return to normal bowel function (days) (mean, *SD*): 2 (0.17); 3 (0.33) Overall post-operative complications: RR 0.69 (95% CI: 0.56, 0.85) Wound infection/sepsis: RR 0.72 (95% CI: 0.47, 1.10) Anastomosis leak: RR 2.00 (95% CI: 0.37, 10.8) Post-operative ileus: RR 0.75 (95% CI: 0.43, 1.30) Cardiac complication: RR 0.50 (95% CI: 0.05, 5.5) Pulmonary complication: RR 0.25 (95% CI: 0.07, 0.88) Intra-abdominal bleeding: RR 1.67 (95% CI: 0.40, 6.93) Overall survival (at latest follow up, 3 year): HR 1.02 (95% CI: 0.75, 1.38) Disease free survival (at latest follow up, 3 year): HR 1.01 (95% CI: 0.77, 1.32)

Table 1 Continued

Author (year of publication)	Study design	Country	Participant characteristics	Sample size	Key outcomes (laparoscopic vs. open)
Noblett *et al.* (2007)[46]	Prospective	United Kingdom	Mean age of around 65 years; males (57%); mean BMI of around 26 kg/m^2; mean ASA score of 2	Laparoscopic- 30; Open-30	Operation time (min) (mean, *SD*): 160 (43.3); 160 (26.7) Blood loss (ml) (mean, *SD*): 100 (90); 528 (389.2) Length of hospital stay (days) (mean, *SD*): 5 (7); 9 (2.5) Return to normal bowel function (days) (mean, *SD*): 3 (3.3); 4 (1.83) Overall post-operative complications: RR 0.29 (95% CI: 0.11, 0.77) Wound infection/sepsis: RR 1.00 (95% CI: 0.07, 15.3) Anastomosis leak: RR 3.00 (95% CI: 0.13, 70.8) Post-operative ileus: RR 0.50 (95% CI: 0.05, 5.22) Pulmonary complication: RR 0.14 (95% CI: 0.01, 2.65) Urinary tract infection: RR 0.14 (95% CI: 0.01, 2.65) Mortality (within 30 days): RR 3.0 (95% CI: 0.13, 70.8) Readmission: RR 0.33 (95% CI: 0.02, 7.87)
Issa *et al.* (2011)[47]	Retrospective	Israel	Elderly patients undergoing colonic resection; mean age of around 83 years; male (53%); mean BMI of around 25.0 kg/m^2; TNM III/IV (69%); Rt. Colectomy (51%); ASA II/IV (56%)	Laparoscopic- 47; Open-46	Operation time (min) (mean, *SD*): 157 (41); 121 (33) Length of hospital stay (days) (mean, *SD*): 7.6 (3.1); 8.8 (3.6) Return to normal bowel function (days) (mean, *SD*): 3.2 (1.4); 3.6 (1.5) Overall post-operative complications: RR 0.86 (95% CI: 0.47, 1.55) Wound infection/sepsis: RR 0.19 (95% CI: 0.01, 3.97) Anastomosis leak: RR 0.49 (95% CI: 0.05, 5.21) Post-operative ileus: RR 0.56 (95% CI: 0.18, 1.78) Pulmonary complication: RR 0.73 (95% CI: 0.17, 3.10) Urinary tract infection: RR 0.59 (95% CI: 0.15, 2.32) Mortality (within 30 days): RR 0.33 (95% CI: 0.04, 3.02) Readmission: RR 0.98 (95% CI: 0.14, 6.66)
Weeks *et al.* (2002)[48]	RCT	USA	Patients undergoing colectomy for colon cancer; mean age of around 68 years; male (50%); White race (86%); TNM III/IV (65%)	Laparoscopic- 228; Open-221	Length of hospital stay (days) (mean, *SD*): 5.6 (0.26); 6.4 (0.23) Mortality (within 60 days): RR 0.97 (95% CI: 0.14, 6.82) Readmission: RR 1.45 (95% CI: 0.25, 8.61)
Cummings *et al.* (2012)[49]	Retrospective	USA	Elderly patients (aged>65 years) undergoing colectomy for colon cancer; female (>50%); White race (>85%)	Laparoscopic- 424; Open-424	Length of hospital stay (days) (mean, *SD*): 8.3 (6.2); 10 (8.9) Mortality (within 30 days): RR 0.78 (95% CI: 0.39, 1.54) Overall post-operative complications: RR 0.81 (95% CI: 0.64, 1.04) Overall survival (at latest follow up, 5 year): HR 0.94 (95% CI: 0.76, 1.15)
Lian *et al.* (2010)[50]	Retrospective	USA	Elderly patients (Mean age of 82.8 years); female (53%); mean BMI of 26.1 kg/m^2; ASA score of 3 or 4 (83%)	Laparoscopic- 97; Open-97	Operation time (min) (mean, *SD*): 131 (41.3); 105.5 (46.7) Blood loss (ml) (mean, *SD*): 150 (165); 200 (408.3) Length of hospital stay (days) (mean, *SD*): 6 (11); 7 (8.5) Return to normal bowel function (days) (mean, *SD*): 4 (1.33); 5 (2) Need for blood transfusion: RR 0.33 (95% CI: 0.10, 1.19) Overall post-operative complications: RR 0.78 (95% CI: 0.56, 1.09) Wound infection/sepsis: RR 1.20 (95% CI: 0.38, 3.80)

Table 1 Continued

Author (year of publication)	Study design	Country	Participant characteristics	Sample size	Key outcomes (laparoscopic vs. open)
					Anastomosis leak: RR 1.33 (95% CI: 0.31, 5.80) Post-operative ileus: RR 0.95 (95% CI: 0.54, 1.66) Cardiac complication: RR 0.86 (95% CI: 0.30, 2.46) Pulmonary complication: RR 0.67 (95% CI: 0.25, 1.80) Urinary tract infection: RR 0.67 (95% CI: 0.11, 3.90) Renal complication: RR 0.67 (95% CI: 0.25, 1.80) Mortality (within 30 days): RR 1.0 (95% CI: 0.30, 3.34) Readmission: RR 1.5 (95% CI: 0.56, 4.05)
Allardyce *et al.* (2010)[51]	Analysis of RCT data	Muticentric (New Zealand and Australia)	Patients aged >70 years; males (48%); mean BMI of 26 kg/m^2; ASA score of 2 or 3 (83%)	Laparoscopic- 174; Open-152	Length of hospital stay (days) (mean, *SD*): 8 (8.83); 10 (9) Overall post-operative complications: RR 0.73 (95% CI: 0.56, 0.93)
Miyasaka *et al.* (2014)[52]	Retrospective	Japan	Patients aged >70 years; mean BMI of 22 kg/m^2, females (63%); ASA score of 2 or 3 (>85%)	Laparoscopic- 26; Open-26	Operation time (min) (mean, *SD*): 253 (58.3); 189 (63.3) Blood loss (ml) (mean, *SD*): 13 (33.8); 107 (443.3) Length of hospital stay (days) (mean, *SD*): 16 (7.2); 26 (14.3) Return to normal bowel function (days) (mean, *SD*): 4 (0.67); 6 (4.3) Overall post-operative complications: RR 0.33 (95% CI: 0.10, 1.09)
Takahashi *et al.* (2021)[53]	Prospective	Japan	Patients aged ≥80 years; mean age of 83 years; male (47.3%); mean BMI of 23 Kg/m^2; tumour stage III/IV (35%)	Laparoscopic- 76; Open-76	Operation time (min) (mean, *SD*): 248 (51.4); 186.5 (33.1) Blood loss (ml) (mean, *SD*): 20 (13.0); 87.5 (183) Return to normal bowel function (days) (mean, *SD*): 4 (0.83); 6.5 (2.9) Length of hospital stay (days) (mean, *SD*): 10.5 (1.4); 17 (3.9) Overall post-operative complications: RR 0.59 (95% CI: 0.40, 0.87) Wound infection/sepsis: RR 0.33 (95% CI: 0.04, 3.13) Anastomosis leak: RR 0.20 (95% CI: 0.01, 4.09) Post-operative ileus: RR 1.33 (95% CI: 0.31, 5.76) Renal complication: RR 5.0 (95% CI: 0.60, 41.8) Urinary tract infection: RR 1.0 (95% CI: 0.15, 6.92) Overall survival (latest follow up, 5 years): HR 0.97 (95% CI: 0.52, 1.79)
Chern *et al.* (2021)[54]	Retrospective	Taiwan	Elderly patients (aged ≥75 years); male (55%); BMI of ≥25.0 kg/m^2 (>30%); moderate tumour differentiation (80%); TNM II/III (>80%)	Laparoscopic- 504; Open-846	Length of hospital stay (days) (mean, *SD*): 8 (0.67); 10.5 (1) Overall post-operative complications: RR 0.87 (95% CI: 0.68, 1.10) Wound infection/sepsis: RR 0.57 (95% CI: 0.32, 1.04) Anastomosis leak: RR 3.35 (95% CI: 1.36, 8.26) Post-operative ileus: RR 0.84 (95% CI: 0.46, 1.54) Cardiac complication: RR 1.12 (95% CI: 0.19, 6.67) Pulmonary complication: RR 0.19 (95% CI: 0.03, 1.47) Renal complication: RR 0.73 (95% CI: 0.35, 1.52) Mortality (within 30 days): RR 0.42 (95% CI: 0.14, 1.25) Overall survival (latest follow up, 10 years): HR 1.07 (95% CI: 0.95, 1.21) Disease free survival (latest follow up, 10 years): HR 1.08 (95% CI: 0.96, 1.21)

Risk of mortality, recurrence and readmission

Compared to elderly patients who underwent open surgery, those undergoing laparoscopic surgery had a lower risk of mortality in the immediate post-operative period, that is, within 3 months (RR 0.70, 95% CI: 0.53, 0.94; $N = 13$; $I^2 = 0.0\%$; $n = 7476$) (Fig. 2). The long-term overall survival (HR 0.96, 95% CI: 0.89, 1.04; $N = 11$; $I^2 = 0.0\%$; $n = 7788$) and disease-free survival (HR 1.02, 95% CI: 0.93, 1.13; $N = 7$; $I^2 = 14.6\%$; n = 2884) was statistically similar in both the groups (Fig. 3). The risk of recurrence (RR 1.44, 95% CI: 0.90, 2.30; $N = 3$; $I^2 = 0.0\%$; $n = 402$) and readmission (RR 1.11, 95% CI: 0.88, 1.40; $N = 8$; $I^2 = 0.0\%$; $n = 4977$) was also similar in both the groups (Fig. 4). There was no evidence of publication bias for these outcomes (Egger's P-value >0.05).

Intra-operative and post-operative parameters

The operative time (in minutes) was higher (WMD 30.37, 95% CI: 17.75, 43.0; $N = 15$; $I^2 = 98.2\%$; $n = 10\,478$) and the blood loss (in ml) was lower (WMD −78.85, 95% CI: −101.96, −55.75; $N = 12$; $I^2 = 92.3\%$; $n = 2267$) in those undergoing laparoscopic surgery, compared with open surgery (Fig. 5). The length of hospital stay (in days) (WMD −2.53, 95% CI: −3.11, −1.95; $N = 20$; $I^2 = 98.6\%$; $n = 5640$) and the time of return of bowel movements (in days) (WMD −1.06, 95% CI: −1.20, −0.93; $N = 11$; $I^2 = 67.5\%$; $n = 1967$) was lower in those with laparoscopic, compared with open surgery (Fig. 6).

Complications

The pooled risk of overall complications was lower in those with laparoscopic surgery (RR 0.66, 95% CI: 0.60, 0.74; $N = 20$; $I^2 = 40.4\%$; $n = 13\,215$), compared with open surgery (Table 2). The risk of need for blood transfusion (RR 0.50, 95% CI: 0.33, 0.75; $N = 4$; $I^2 = 5.3\%$; $n = 606$), wound infection/sepsis (RR 0.49, 95% CI: 0.42, 0.58; $N = 15$; $I^2 = 0.0\%$; $n = 11\,883$), post-operative ileus (RR 0.68, 95% CI: 0.53, 0.88; $N = 15$; $I^2 = 0.0\%$; $n = 3933$), cardiac

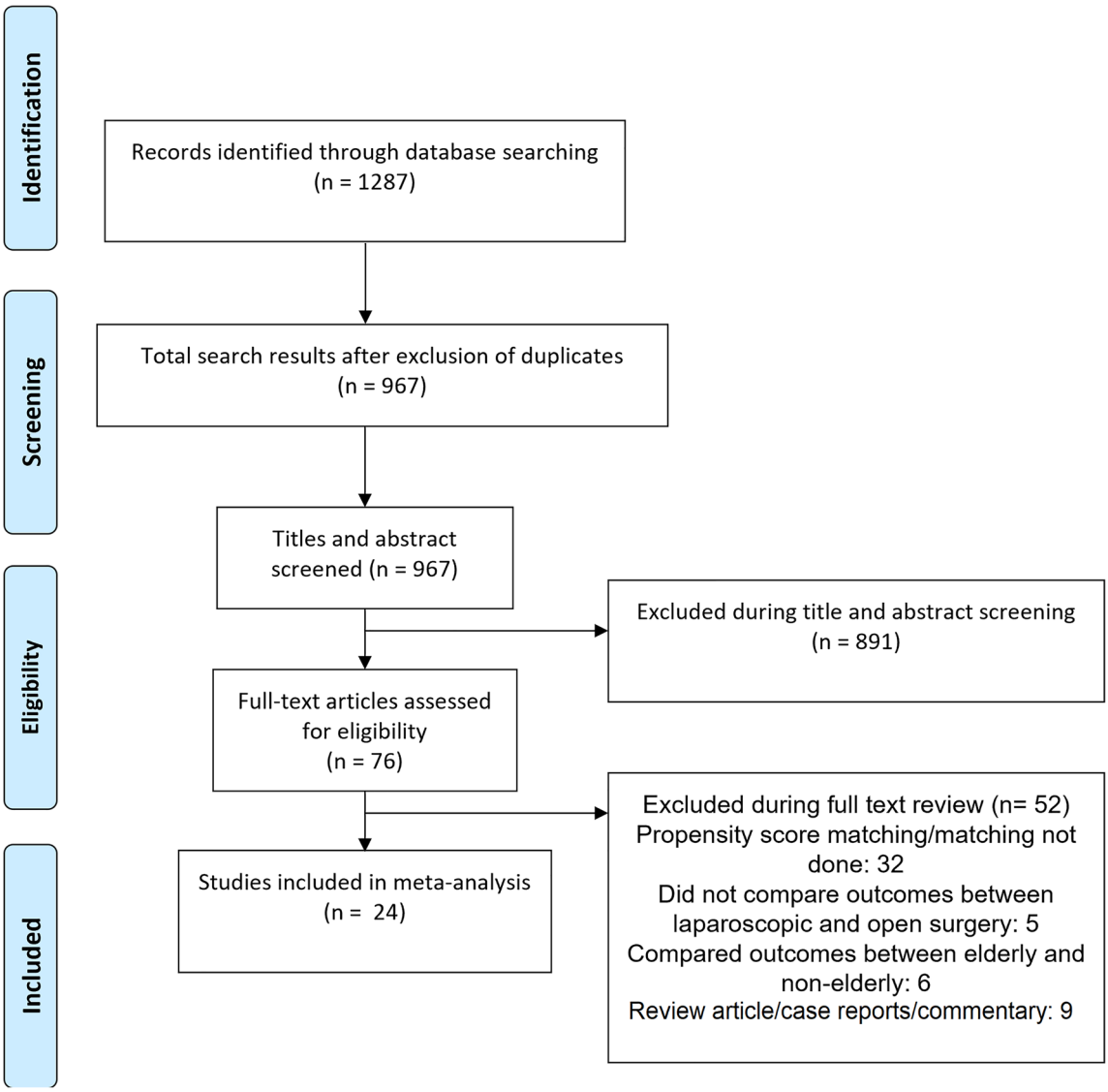

Fig. 1. Selection process of the studies included in the review.

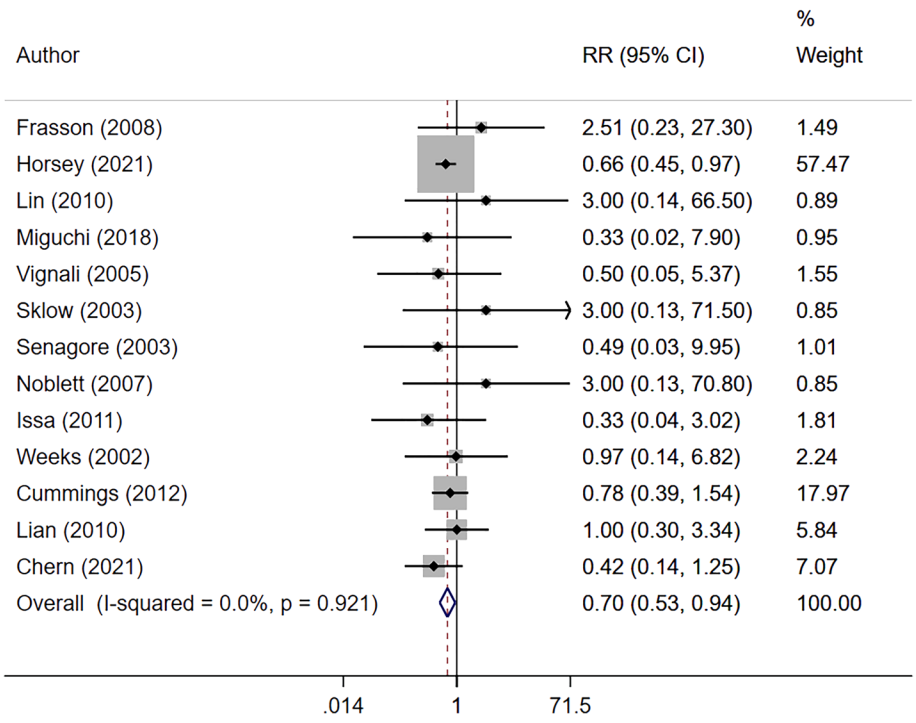

Fig. 2. Risk of short-term mortality among elderly patients with colorectal cancer undergoing laparoscopic surgery, compared with open surgery.

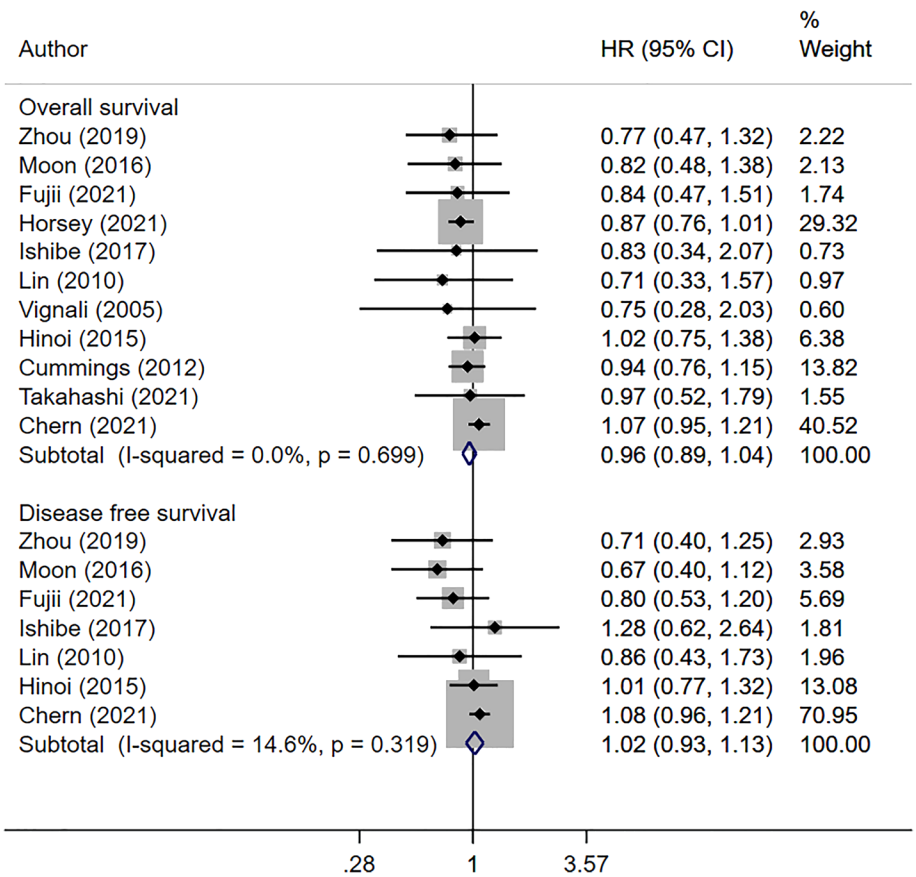

Fig. 3. Long-term survival and disease-free survival among elderly patients with colorectal cancer undergoing laparoscopic surgery, compared with open surgery.

complication (RR 0.71, 95% CI: 0.53, 0.94; $N = 12$; $I^2 = 0.0\%$; $n = 11\,430$), respiratory complication (RR 0.51, 95% CI: 0.41, 0.64; $N = 14$; $I^2 = 0.0\%$; $n = 11\,642$), renal complication (RR 0.60, 95% CI: 0.41, 0.87; $N = 8$; $I^2 = 29.8\%$; $n = 10\,224$) and urinary tract infection (RR 0.53, 95% CI: 0.41, 0.67; $N = 11$; $I^2 = 0.0\%$; $n = 9190$) was lower in those with laparoscopic surgery (Table 2).

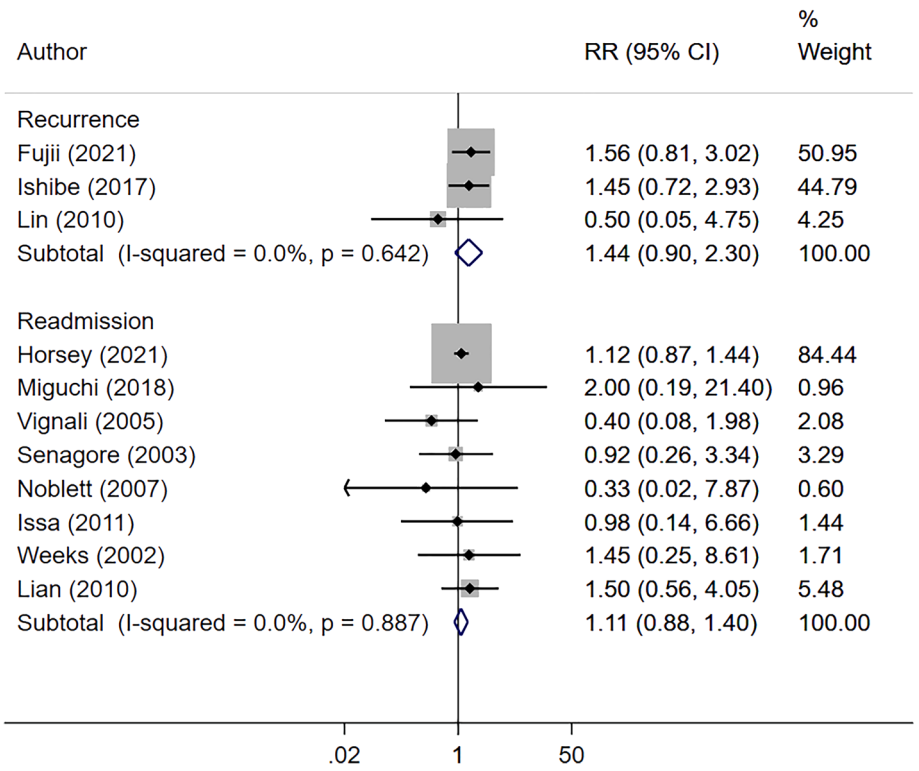

Fig. 4. Risk of readmission and recurrence among elderly patients with colorectal cancer undergoing laparoscopic surgery, compared with open surgery.

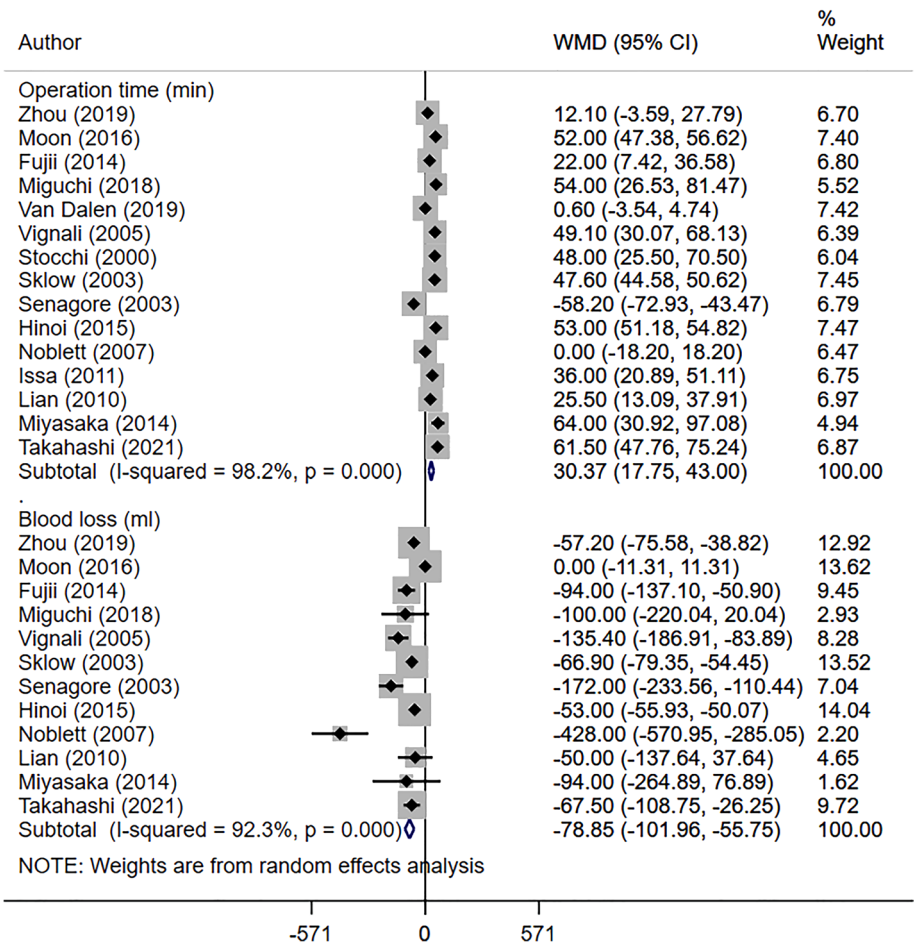

Fig. 5. Operative time and blood loss among elderly patients with colorectal cancer undergoing laparoscopic surgery, compared with open surgery.

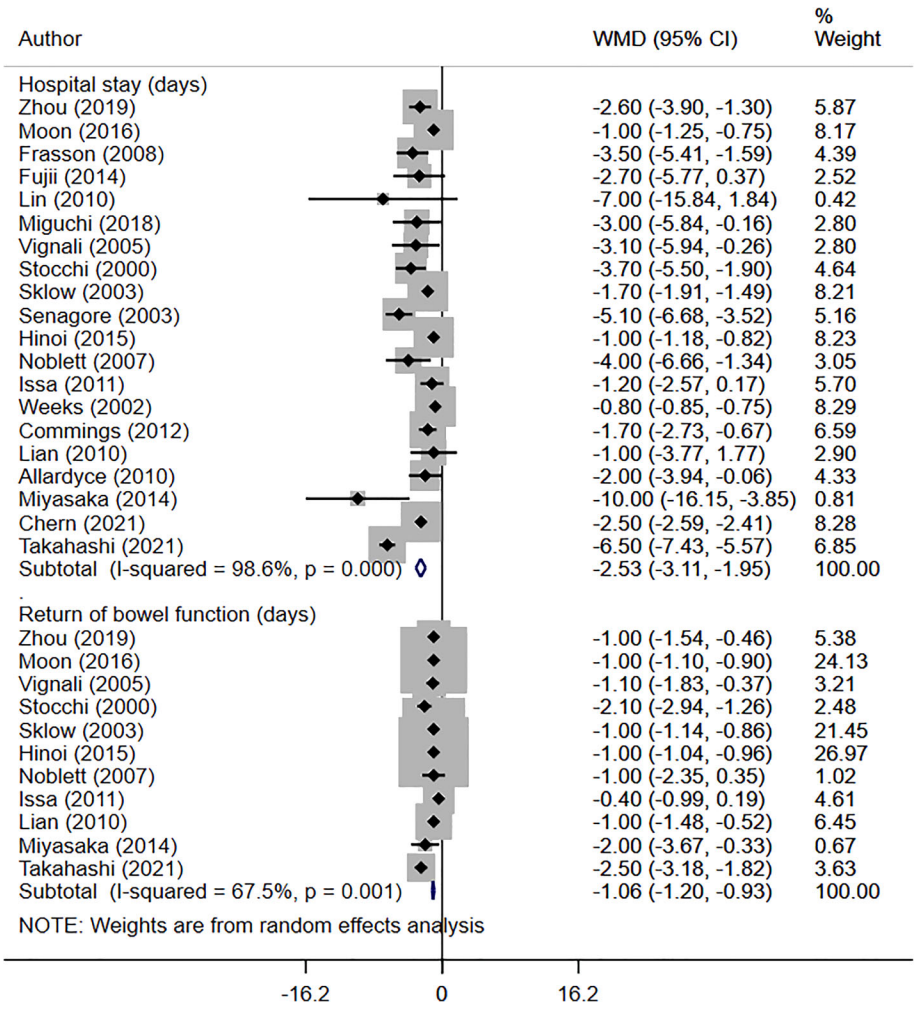

Fig. 6. Length of hospital stay and time to return of bowel movements among elderly patients with colorectal cancer undergoing laparoscopic surgery, compared with open surgery.

Table 2 Pooled effect size for the risk of complications

Outcomes	Pooled effect size (RR) with 95% Confidence interval	Number of studies (number of subjects)	I^2
Overall post-operative complication	0.66 (95% CI: 0.60, 0.74)*	20 ($n = 13\,215$)	40.4%
Need for blood transfusion	0.50 (95% CI: 0.33, 0.75)*	4 ($n = 606$)	5.3%
Risk of wound infection and/or sepsis	0.49 (95% CI: 0.42, 0.58)*	15 ($n = 11\,883$)	0.0%
Risk of anastomosis leak	1.24 (95% CI: 0.79, 1.94)	12 ($n = 3629$)	11.3%
Risk of post-operative ileus	0.68 (95% CI: 0.53, 0.88)*	15 ($n = 3933$)	0.0%
Risk of cardiac complication	0.71 (95% CI: 0.53, 0.94)*	12 ($n = 11\,430$)	0.0%
Risk of respiratory complication	0.51 (95% CI: 0.41, 0.64)*	14 ($n = 11\,642$)	0.0%
Risk of renal complication	0.60 (95% CI: 0.41, 0.87)*	8 ($n = 10\,224$)	29.8%
Risk of intra-abdominal bleeding	1.09 (95% CI: 0.43, 2.75)	5 ($n = 1329$)	0.0%
Risk of urinary tract infection	0.53 (95% CI: 0.41, 0.67)*	11 ($n = 9190$)	0.0%

*denotes statistical significance i.e., $P < 0.05$.

There were no differences in the risk of anastomotic leak and intra-abdominal bleeding among the two groups. There was no evidence of publication bias ($P > 0.05$).

Discussion

The review noted that laparoscopic surgery was associated with a lower risk of short-term mortality (within 3 months post-operatively) whereas the long-term overall survival, disease-free survival, risk of recurrence and readmission was statistically similar in both the groups. Laparoscopic surgery was also associated with lower blood loss, but the operative time was higher compared with open surgery. Benefits with respect to a shorter hospital stay, and an early return of bowel movements was noted in subjects undergoing laparoscopic surgery. Those patients who underwent laparoscopic surgery also had a considerably reduced risk of complications. The risk of a blood transfusion, wound infection/sepsis, post-operative ileus, cardiac complication, respiratory complication, renal complication and

urinary tract infection was lower in those patients who underwent laparoscopic surgery.

The findings are similar to those of the previous reviews on this subject.[17–24] A review by Antoniou *et al*. included 27 studies and reported that those with laparoscopic surgery had a decreased risk for mortality, overall morbidity as well as cardiac and respiratory complications.[19] Another review by Devoto *et al*. included six observational studies (retrospective in design) and found a reduced risk of morbidity in the laparoscopic group along with a shorter hospital stay and early return of bowel movements.[20] Based on these findings, the review concluded that laparoscopic surgery in elderly patients is safe and of similar clinical efficacy, compared with open surgery. Other reviews also noted that laparoscopic surgery in elderly patients with colorectal cancer led to a shorter hospital stay, reduced blood loss, reduced risk of post-operative complications and early return of normal bowel function.[21–23]

Elderly patients commonly have an increase in comorbidities, and the results presented here show a reduced risk of cardiac and respiratory complications following laparoscopic surgery. The reduction in the risk of cardiac complications could be due to the reduced blood loss and circulatory stress.[21] Reduced risk of respiratory complications, particularly pneumonia, may be due to reduced post-operative pain leading to lesser diaphragmatic splinting, that is, reduced inspiratory effort because of pain, thereby minimizing the risk of basal atelectasis and consequent pneumonia.[21] Though there could be many other major contributing factors, the observed benefits of reduced risk of respiratory complications might also be due to decreased blood loss, as indicated by the study by Fugita *et al*., wherein the authors found a correlation between intraoperative blood loss and development of postoperative pneumonia.[55] The current meta-analysis noted a shorter hospital stay in those undergoing laparoscopic surgery. This is an important finding as a prolonged hospital stay within elderly patients, could predispose them to an increased risk of hospital-acquired infections, leading to a substantial reduction in their functional capacity and increasing their out-of-pocket expenditure.[56,57] A decrease in functional status in these vulnerable patients could increase their risk of dependency and decrease their quality of life. The review also noted an increased operative time following laparoscopic surgery compared to open surgery. Increased operative time could mean greater physiological stress and an increased length of anaesthetic exposure. Hypotension is commonly observed with induction of anaesthesia and with the increase in operative time, the effect of hypotension on an elderly patient is concerning. Furthermore, previous research by Kojima *et al*., observed that elderly patients who did not have an independent functional status prior to surgery, had poor clinical outcomes following increased exposure to general anaesthesia.[58]

There are several strengths and limitations associated with this meta-analysis. One of the strengths is the comprehensive search of available studies and inclusion of only those observational studies that had utilized PSM. In this way, the selection bias and any bias arising from non-adjusted potential confounding variables was minimized to a certain extent. We also observed negligible heterogeneity for most of the outcomes considered. Limitations included a lack of subgroup analysis based on tumour characteristics. A subgroup analysis based on tumour size, location and stage would have been useful. However, the included studies did not provide sufficient relevant data to carry out this analysis. Another limitation was that the review focussed only on the clinical outcomes and not on the oncological outcomes of resection, for example, level of lymph node clearance or length of resected specimen. A potentially noteworthy limitation of this meta-analysis was to pool findings from studies that were different in design, that is, RCTs and observational. The adjustment of confounders in a well-conducted RCT is usually not required, whereas in observational studies, particularly those that use retrospective data, the adjustments in the analysis are prone to bias. However, as stated earlier, we attempted to reduce some of this bias by including only those observational studies that had used propensity score matching. Another limitation to note is that the type of colorectal resection was not differentiated in the analysis, and it could be possible that different resection types are pooled together or compared to each other, which would otherwise not make much clinical sense. For instance, it would not be meaningful to combine or compare outcomes associated with a laparoscopic right hemicolectomy with those of an open ultralow anterior resection for rectal cancer.

Conflict of interest

None declared.

Author contributions

Weimin Luo: Formal analysis; methodology; validation; visualization; writing – original draft; writing – review and editing. **Mengyuan Wu:** Data curation; formal analysis; methodology. **Yanling Chen:** Formal analysis; methodology; validation.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Author's judgements about study quality using the adapted Ottawa-Newcastle Risk of Bias Assessment tool (part 1)
Table S2. Author's judgements about study quality using the adapted Ottawa-Newcastle Risk of Bias Assessment tool (part 2)
Table S3. Author's judgements about risk of bias for each RCT included, based on Cochrane risk of bias assessment items