

Review

Adhesive small bowel obstruction after laparoscopic and open colorectal surgery: a systematic review and meta-analysis



Gi Won Ha, M.D., Min Ro Lee, M.D., Ph.D.*, Jong Hun Kim, M.D., Ph.D.

Research Institute of Clinical Medicine, Chonbuk National University Medical School, San 2-20
Geumam-dong, Deokjin-gu, Jeonju, Jeonbuk 561-180, South Korea

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Abstract

BACKGROUND: It is considered that laparoscopic surgery is associated with a much lower rate of postoperative formation of adhesions than open surgery. This meta-analysis assessed the incidence of adhesion-related readmissions and surgery for adhesive small bowel obstruction (SBO) in patients who underwent laparoscopic or open colorectal surgery.

METHODS: Multiple comprehensive databases were searched systematically to identify relevant studies and meta-analysis was done.

RESULTS: Meta-analysis showed that laparoscopic surgery was associated with a lower rate of adhesive SBO, both for randomized clinical trials (relative risk [RR] .26, 95% confidence interval [CI] .10 to .67, $I^2=41%$) and nonrandomized studies (RR .49, 95% CI .32 to .76, $I^2=91%$). Laparoscopic surgery was also associated with a lower rate of subsequent surgery for adhesive SBO, both for randomized clinical trials (RR .25, 95% CI .06 to .96, $I^2=0%$) and nonrandomized studies (RR .56, 95% CI .33 to .94, $I^2=77%$).

CONCLUSIONS: Laparoscopic colorectal surgery significantly reduced the rates of adhesive SBO and subsequent surgery for adhesive SBO, compared with open surgery.

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Small bowel obstruction (SBO) is defined as abdominal pain or distension, vomiting, and the appearance of a dilated small bowel loop on abdominal radiography or computed tomography. Postoperative adhesions, defined as abnormal fibrous bands between organs and/or tissues in

the abdominal cavity that are normally separated, are the most common complications of abdominal and pelvic surgery. About 65% to 75% of acute intestinal obstructions are caused by adhesions, predominantly involving the small bowel.¹

Of all types of abdominal surgery, open colorectal surgery was found to result in the highest rate of adhesion-related readmissions. Colorectal surgeries are associated with approximately 30% risk of adhesion-related complications over 4 years. Moreover, approximately 10% of the patients who undergo colorectal surgery are at risk for readmission directly related to adhesions.²⁻⁴ Theoretically, laparoscopic surgery is associated with a much lower rate of postoperative formation of adhesions than open surgery. Because adhesion

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* Corresponding author. Tel: +82-63-250-1570; fax: +82-63-271-6197.

E-mail address: gsmiro@jbnu.ac.kr

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formation represents a stepwise failure of peritoneal tissue repair mechanisms, clean dissection, and/or minimal blood loss and/or less-environmental exposure of the bowel during laparoscopic surgery may reduce the rate of adhesion formation.

However, it remains unclear whether laparoscopic colorectal resection reduces rates of adhesion formation and the incidence of adhesive SBO when compared with open colorectal surgery. Several recent studies have reported lower rates of adhesive SBO after laparoscopic than after open colorectal surgery,^{5–12} whereas other studies have reported comparable rates for the 2 approaches.^{13–16} These access-related complications have been associated with increased morbidity and mortality rates, as well as increased medical costs, because of rehospitalization and additional surgical procedures.^{17–20} The magnitude of health problems and costs related to adhesions indicate the need to develop methods that reduce the occurrence of postoperative adhesions.

This meta-analysis was designed to assess the incidence of adhesion-related readmissions and surgery for adhesive SBO in patients who underwent laparoscopic and open colorectal surgery.

Methods

This meta-analysis was performed in a manner consistent with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.²¹ Multiple comprehensive databases were searched for studies that compared rates of adhesive SBO in patients who underwent laparoscopic and open surgery for colorectal cancers. The study protocol was based on Cochrane review methods.²²

Data source and literature source

Multiple comprehensive databases, including PubMed (January 1, 1976 to June 24, 2015), EMBASE (January 1, 1985 to June 24, 2015), and the Cochrane Central Register of Controlled Trials (January 1, 1987 to June 24, 2015), were searched. There were no restrictions on the year of publication. Articles in all languages were sought, but only those published in English were included in this study. The search terms and combinations included: “colorectal surgery”, “colorectal cancer”, laparoscopy, adhesion, ileus, “small bowel obstruction”. After the initial electronic search, articles were manually searched to identify additional studies. Articles identified were assessed individually for inclusion.

Study selection

Article titles and abstracts were screened, and full texts were reviewed independently by 2 reviewers (Gi.W.H. and M.R.L.) based on the selection criteria. Discrepancies were

resolved by discussion between the reviewers. All studies investigating adhesive SBO in patients who underwent laparoscopic and open surgery for colorectal cancer were considered. Studies included in the meta-analysis were those in which most of the included patients had been diagnosed with malignant or benign tumors, and in which laparoscopic and open surgery were compared. Studies were excluded if they (1) mainly assessed patients with inflammatory bowel disease such as ulcerative colitis; (2) assessed only specific groups of patients, including elderly or obese patients; (3) assessed patients who developed adhesive SBO during the early postoperative period (<1 month follow-up); (4) had no extractable data and the authors could not be reached to provide additional information; (5) were case series with fewer than 10 patients; and (6) were not published in English.

Data extraction

All eligible studies were reviewed, and all relevant data were extracted independently by 2 reviewers using a predefined data extraction form. Variables recorded included: (1) study information, including last name of the first author, year of publication, country, and number of patients in each group; (2) demographic, clinical, and treatment characteristics of the patients; and (3) follow-up time and outcome measures. Any disagreements unresolved by discussion were reviewed by a 3rd reviewer. The primary outcome measure was incidence of adhesive SBO, and the secondary outcome measure was surgery for adhesive SBO.

Assessment of methodological quality

The methodological quality of randomized clinical trials (RCTs) was assessed using the Cochrane Collaboration risk of bias tool.²² The methodological quality of nonrandomized studies (NRSs) was assessed using the Newcastle-Ottawa Quality Scale, which allocates a maximum of 9 points to each study and in which a score of 6 or more indicated high quality.²³ Any unresolved disagreements between reviewers were resolved through consensus discussions or consultation with a 3rd reviewer.

Statistical analysis

The meta-analysis determined relative risk (RR) for dichotomous outcomes using the Mantel-Haenszel statistical method. Pooled estimates were presented with 95% confidence intervals (CIs). The presence and amount of heterogeneity were assessed with the Q test and I^2 index, respectively, with $P < .1$ considered statistically significant. I^2 indices of 25%, 50%, and 75% were considered indicative of low, moderate, and high heterogeneity, respectively. A random effects model was used for pooling when there was evidence of heterogeneity; otherwise a fixed effects

model was used. If sufficient data were available, planned subgroup analyses were performed to evaluate incidence of adhesive SBO. Sensitivity analyses were also performed for individual NRSs, and an alternative statistical effect model was used to reanalyze the data for the sensitivity analysis. Funnel plots were used to determine the presence of publication bias, with the asymmetry of funnel plots evaluated using the Egger-weighted linear regression test, with $P < .1$ considered statistically significant.²⁴

All data were analyzed using Review Manager software, version 5.3, from the Cochrane Collaboration and Comprehensive Meta-Analysis software (free trial version).

Results

Identification of studies

The initial search of databases identified 1,766 potentially relevant articles; of these, 1,743 were excluded because their titles and abstracts did not fulfill the selection criteria. Full-text review of the remaining 23 articles showed that 12 studies, comprised 2 RCTs^{10,11} and 10 NRSs,^{5-9,12-16} were suitable for inclusion (Fig. 1).

Study characteristics and patient populations

The 2 RCTs and 10 NRSs included a total of 198,228 patients. The 2 RCTs included 539 patients, 264 who underwent laparoscopic and 275 who underwent open surgery. The 10 NRSs included 197,689 patients, 16,563 who underwent laparoscopic and 181,126 who underwent

open surgery. Of the 10 NRSs, one study with large numbers of patients reported nation-wide intermediate-term admission rates for clinically apparent adhesions after laparoscopic and open colorectal surgery.⁸ The main characteristics of the 12 studies are summarized in Table 1. Two RCTs and 8 NRSs were full length articles, and the other 2 NRSs were abstracts; all 12 were published in English.

Quality of the included studies

Table 2 shows an evaluation of the risk of bias of the included RCTs. The 2 RCTs used adequate methods for generating allocation sequences and for concealment. None of the included trials included blinding of the surgeons, patients, and assessors because of the characteristics of surgery. Both included RCTs were at low risk of bias for incomplete outcome data and selective outcome reporting and were free of other bias. The quality of the 10 NRSs was determined by examining 3 factors: patient selection, comparability of the study groups, and assessment of outcomes. Studies were scored using an ordinal star scale, with higher scores (≥ 6) representing higher quality. The scores of the NRSs are also presented in Table 3.

Outcome measures

Outcomes in the 2 RCTs and 10 NRSs were assessed separately. Meta-analyses showed that laparoscopic surgery was associated with lower rates of adhesive SBO, both for

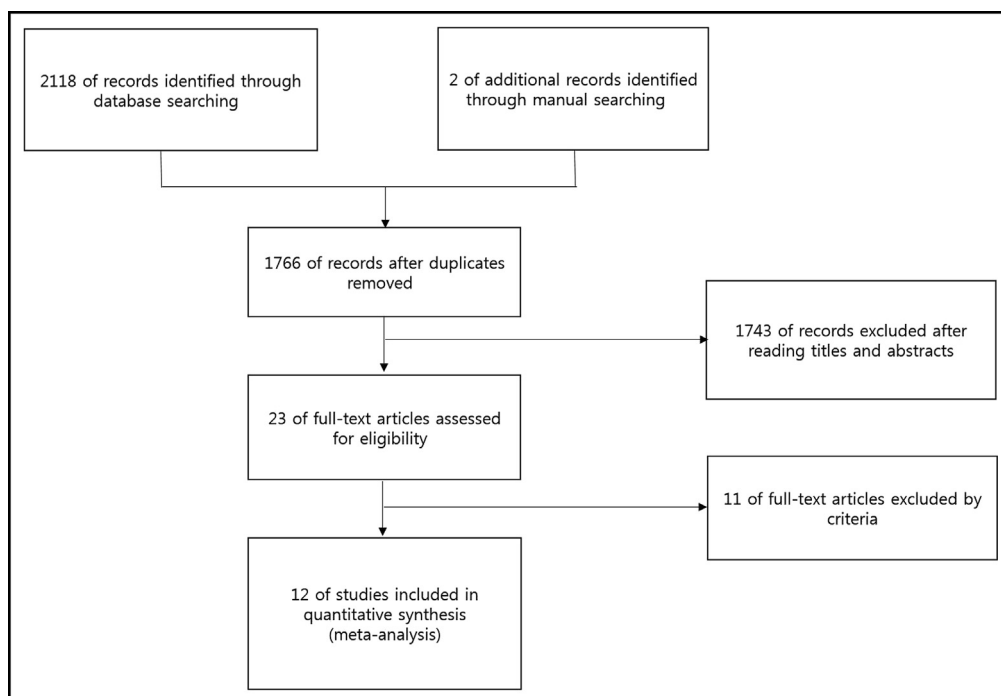


Figure 1 Flow chart of the literature search according to the PRISMA statement.

Table 1 Characteristics of the included studies

Authors	Year	Study design	No. of patients		Age (years)		Sex (M/F)		Median follow-up (years)	
			Lap	Open	Lap	Open	Lap	Open	Lap	Open
Klaristenfeld et al ⁵	2015	NRS, retrospective	2,790	1,823	63 (53-72)*	63 (54-72)*	1,390/1,400	942/881	2.4	
Chang et al ⁶	2015	NRS, retrospective	259	325	NA	NA	NA	NA	NA	NA
Bartels et al ⁷	2014	NRS, retrospective	208	191	68 (60-74)*	67 (61-73)*	121/87	113/78	3.4	
Burns et al ⁸	2013	NRS, retrospective	11,013	176,135	NA	NA	5,344/5,669	89,648/86,487	2.65	
Kim et al ⁹	2013	NRS, retrospective	827	1,087	NA	NA	NA	NA	NA	NA
Saklani et al ¹³	2012	NRS, retrospective	144	187	73 (44-92)*	69.5 (42-92)*	67/76	113/74	2.04	4.08
Scholin et al ¹⁴	2011	NRS, retrospective	383	403	NA	NA	197/186	212/191	5	5
Alvarez-Downing et al ¹⁵	2011	NRS, retrospective	448	339	64.8 ± 14.6	68.7 ± 14.8	231/217	150/189	1	1
Taylor et al ¹⁶	2010	NRS, retrospective	280	131	68.9 ± 10.4	69.9 ± 11.2	162/118	73/58	3	3
Ng et al ¹⁰	2009	RCT	74	74	66.5 ± 11.9	65.7 ± 12	37/39	48/29	9.38	9.07
Braga et al ¹¹	2005	RCT	190	201	65 ± 13	67 ± 11	115/75	121/80	3	
Duepree et al ¹²	2003	NRS, retrospective	211	505	50.8	57.7	91/120	255/250	2.71	2.42

Lap = laparoscopic colorectal surgery; NA = not available; NRS = nonrandomized study; Open = open colorectal surgery; RCT = randomized clinical trial.

*Median (range).

Table 2 The Cochrane Collaboration's tool for assessing risk of bias

Study	Sequence generation	Allocation concealment	Blinding of participants	Blinding of personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Braga, 2005	Low	Low	Unclear	Unclear	Unclear	Low	Low	Low
Ng, 2009	Low	Low	Unclear	Unclear	Unclear	Low	Low	Low

Table 3 Assessment of methodological quality of the cohort studies according to the Newcastle-Ottawa Scale

Cohort studies	Selection			Comparability		Outcome			Total score
	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Outcome of present at start of study	Control for important factor	Assessment of outcome	Follow-up long enough	Adequacy of follow-up	
Alvarez, 2011	★	★	★	—	—	★	—	★	5
Bartels, 2014	★	★	★	★	★	★	★	★	8
Burns, 2013	★	★	★	—	—	★	—	—	4
Chang, 2015	★	★	★	★	—	★	—	—	5
Duepre, 2003	★	★	★	—	—	★	—	—	4
Kim, 2013	★	★	★	★	—	★	—	★	6
Klaristenfeld, 2013	★	★	★	★	—	★	—	—	4
Saklani, 2012	★	★	★	★	—	★	★	—	6
Scholin, 2011	★	★	★	—	★	★	★	★	7
Taylor, 2010	★	★	★	—	★	★	★	★	7

Each star represents if individual criterion within the subsection was fulfilled.

the 2 RCTs involving 539 patients (RR .26, 95% CI .10 to .67, $I^2=41\%$) and the 10 NRSs involving 197,105 patients (RR .49, 95% CI .32 to .76, $I^2=91\%$; Fig. 2). In addition, laparoscopic surgery was associated with lower rates of subsequent surgery for adhesive SBO, both for the 2 RCTs (RR .25, 95% CI .06 to .96, $I^2=0\%$) and the 10 NRSs (RR .56, 95% CI .33 to .94, $I^2=77\%$; Fig. 3).

The incidence of adhesive SBO in the NRSs was determined in subgroups, including: (1) the intention-to-treat population, (2) the as-treated population, with patients converted from laparoscopic to open surgery excluded from the laparoscopic group (3) patients with tumor pathology including malignant or benign tumors, (4) patients who underwent colonic surgery, (5) patients who underwent rectal surgery, and (6) after excluding patients with a history of previous abdominal surgery or colorectal resection. All subgroup analyses found that the incidence of adhesive SBO was lower for laparoscopic than for open colorectal surgery, except for patients who underwent rectal surgery, in which no difference was observed (Fig. 4).

Sensitivity analysis was performed for NRSs by excluding studies with a high risk of bias, as determined using prespecified criteria. Overall estimates of effect for the incidence of adhesive SBO and the rate of surgery for adhesive SBO were robust in the face of this sensitivity analysis. In addition, reanalyzing the results using alternative (random or fixed effects) models found no significant difference in pooled effects between these 2 effects models.

Publication bias

Use of the Egger-weighted linear regression test to assess the asymmetry of funnel plots for all 10 NRSs showed that the funnel plots for both the incidence of adhesive SBO and the rate of subsequent surgery for SBO were symmetrical ($P = .12$ and $.18$, respectively), indicating no apparent publication bias (Fig. 5). Under the random effects model for the outcomes, using the Trim-and-Fill method, the results were not affected.

Comments

The present meta-analysis, based on 2 RCTs and 10 NRSs, found that laparoscopic colorectal surgery was associated with a lower incidence of adhesive SBO and a lower rate of surgery for adhesive SBO than open surgery. To our knowledge, this is the first systematic review and meta-analysis to evaluate the incidence of adhesive SBO in patients who underwent laparoscopic and open colorectal surgery. This meta-analysis had the advantage of including 2 large database studies, with larger numbers of patients than in each of the included studies.^{5,8} Although RCTs are a fundamental evaluation tool of medical research, resource and economic limitations often result in relatively low-patient numbers and a lack of long-term follow-up, leading

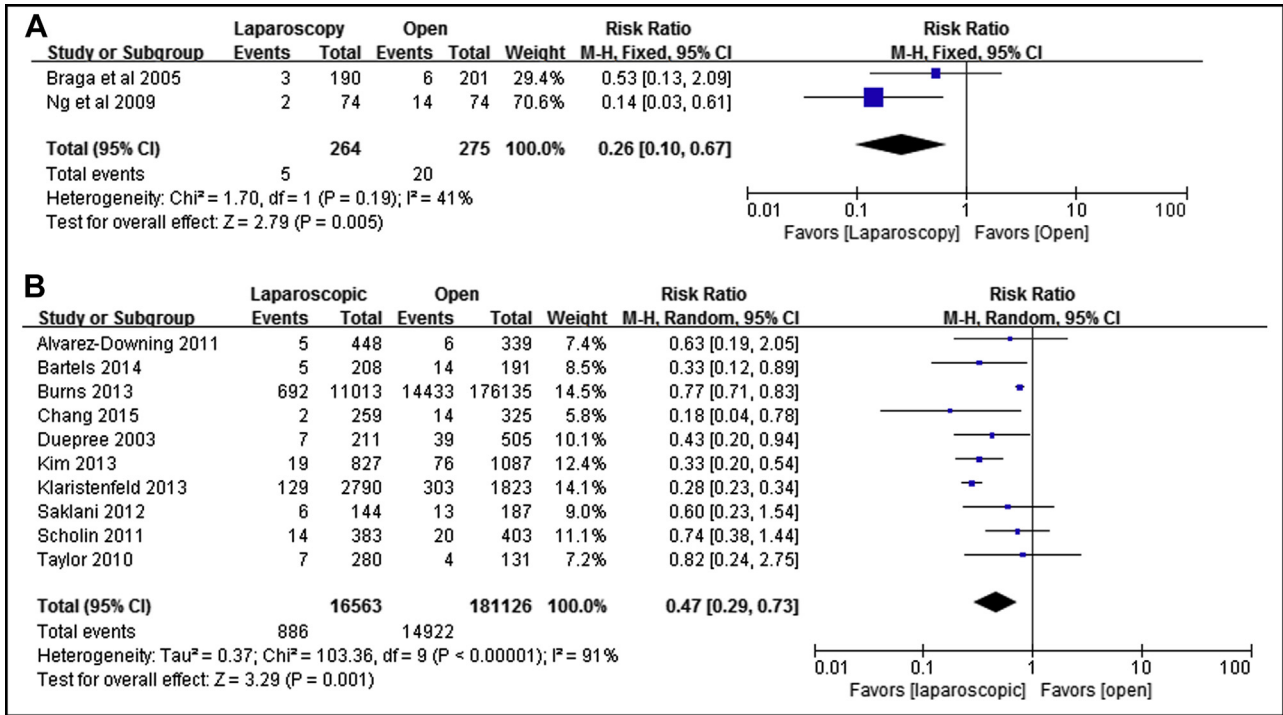


Figure 2 Forest plot and meta-analysis of the incidence of adhesive SBO in laparoscopic vs open colorectal surgery. (A) Analysis of RCTs. (B) Analysis of NRSs.

to an inability to detect differences between the groups. Therefore, if sufficient statistical power to detect associations requires long-term follow-up and large numbers of patients, analyses of large databases may be a viable alternative. Use of a large database has other advantages, in that

such studies may be able to evaluate the natural history of medical conditions and the outcomes of surgical interventions, because data collected to date in individual studies have been insufficient for assessing the long-term impact of laparoscopic surgery on the incidence of SBO.⁵

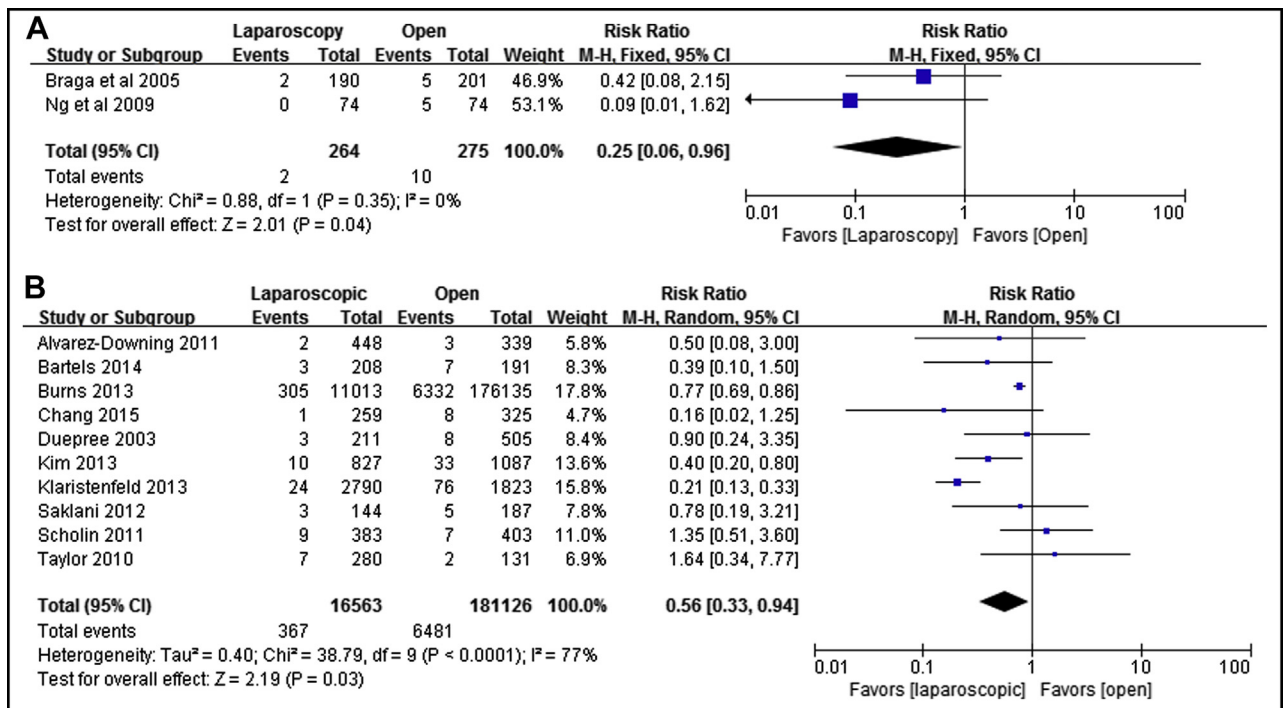


Figure 3 Forest plot and meta-analysis of the rate of subsequent surgery for adhesive SBO in laparoscopic versus open colorectal surgery. (A) Analysis of RCTs. (B) Analysis of NRSs.

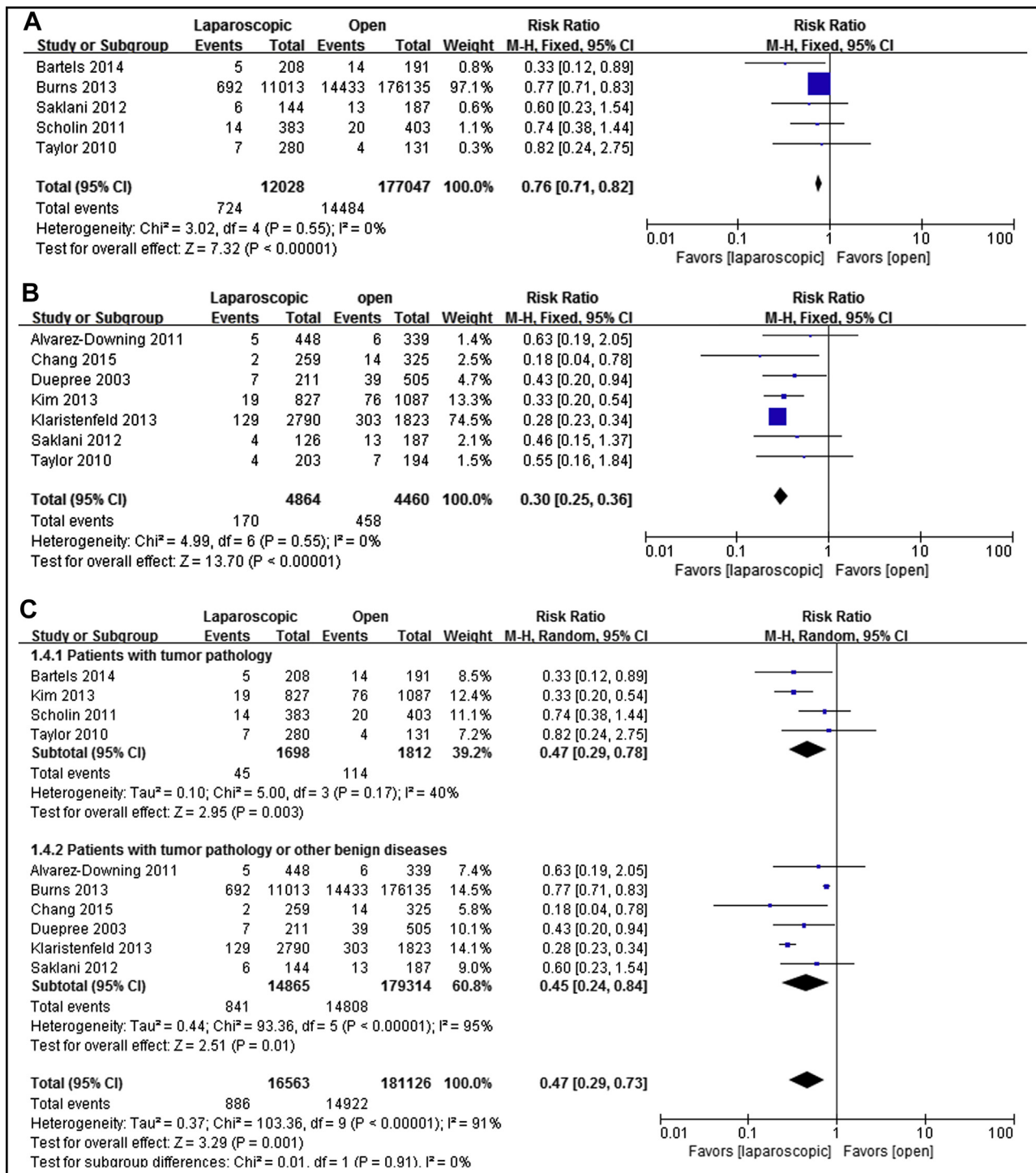


Figure 4 Subgroup analyses for NRSs, outcome: incidence of adhesive SBO in laparoscopic vs open colorectal surgery. (A) Including the ITT population. (B) Including the as-treated population. (C) Patients with tumor pathology including malignant or benign tumors. (D) Patients who underwent colonic surgery. (E) Patients who underwent rectal surgery. (F) After excluding patients with a history of previous abdominal surgery or colorectal resection.

Some of the studies included in this analysis found no significant differences in SBO rates between groups. These results may have been due to the small sample size of these studies and the likely low number of events. One large database study, however, reported a small but statistically significant difference in SBO rates, with a RR of .77 (95%

CI .71 to .83).⁸ This result was considered clinically relevant. With regard to this adverse event, although the effect size was small between groups, it would have clinical significance, leading to readmission and additional abdominal surgery with increased morbidity, mortality, and patient costs.

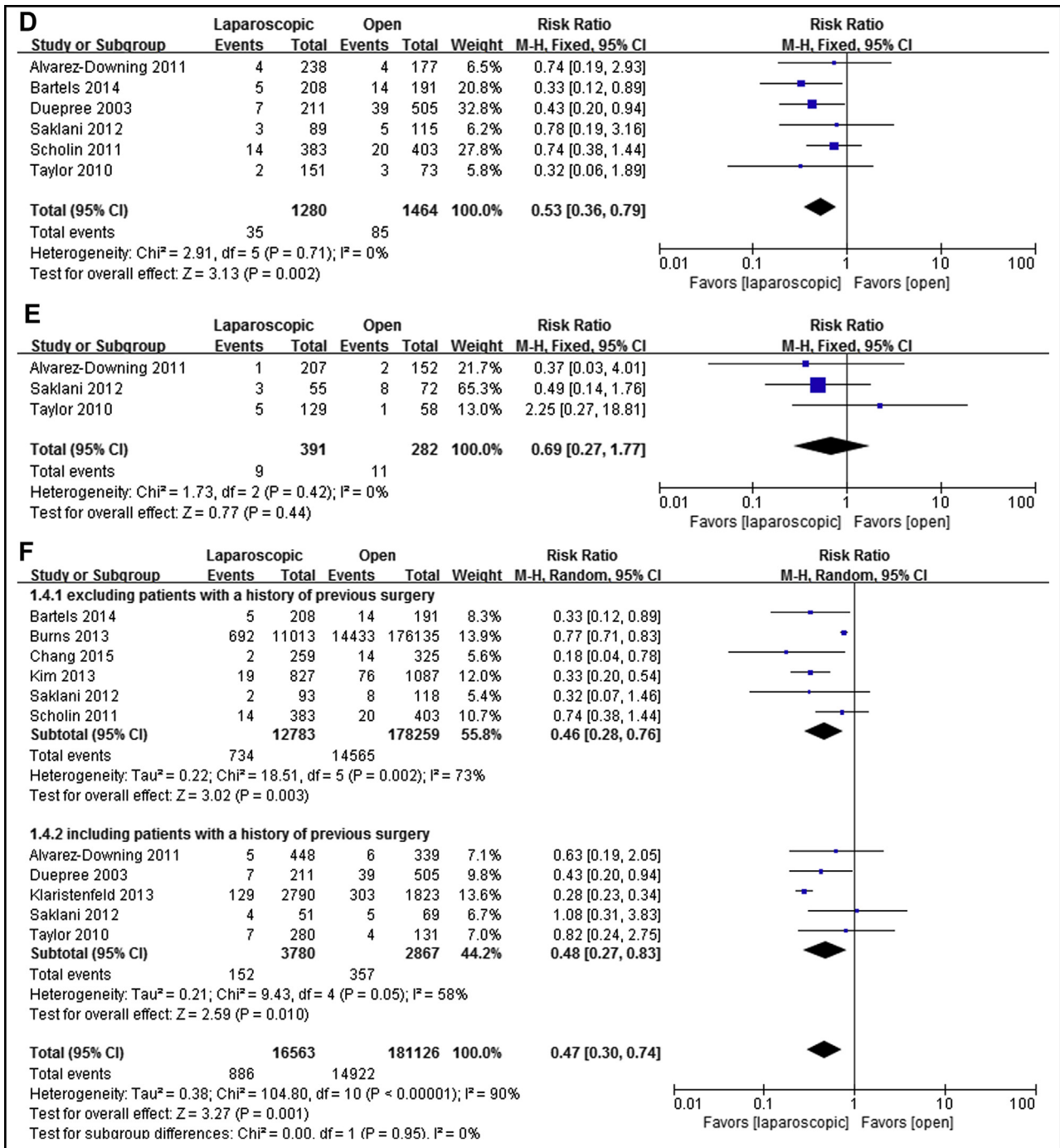


Figure 4 (Continued)

The incidence of adhesive SBO was also analyzed in subgroups of patients in the NRSs, all subgroup analyses except for one analysis showed that the incidence of adhesive SBO was lower with laparoscopic than open colorectal surgery. Analysis of the patients who underwent rectal surgery showed no significant difference in adhesive SBO rate between the laparoscopic and open groups, perhaps because of the relatively small sample size. As most NRSs did not distinguish between patients into underwent colonic and rectal surgery, the numbers of patients available for subgroup analysis were small and

unable to show statistical significance. Studies that evaluated patients undergoing laparoscopic rectal dissection showed that laparoscopic ileal pouch-anal anastomosis was associated with lower rates of adhesions, possibly because small bowel manipulation and incision length were reduced.^{25,26}

The time to onset of adhesive SBO varies greatly after index surgery. Studies have shown that the median time to adhesive SBO was 1.3 years, with up to 60% of all SBOs occurring during the first year after surgery for colorectal cancer.^{2,27} This SBO incidence was comparable to that of

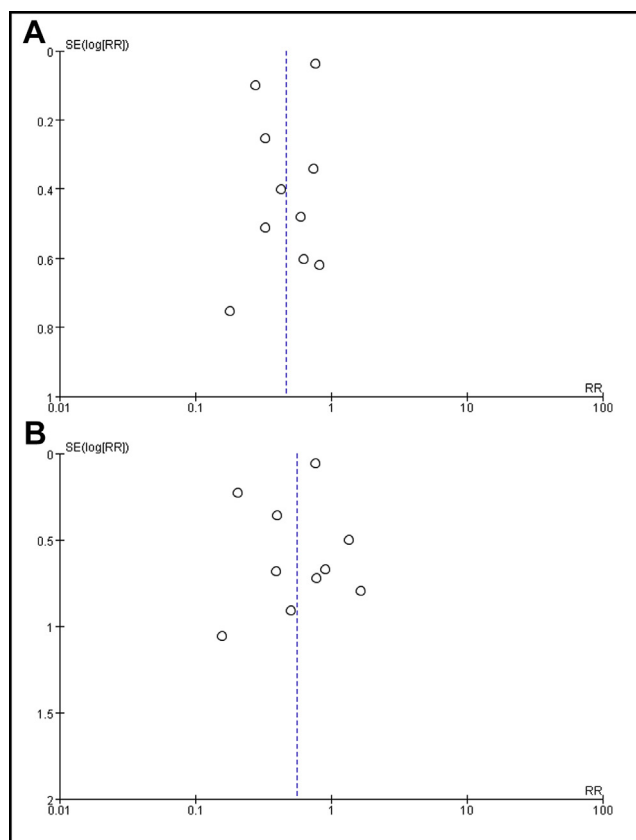


Figure 5 Outcome of publication bias. (A) Funnel plots of all studies included in the analysis for the incidence of adhesive SBO. (B) Funnel plots of all studies included in the analysis for the rate of subsequent surgery for adhesive SBO.

other studies with longer follow-up periods. Nevertheless, adequate median follow-up for outcomes was set at 3 years in our methodological quality assessment of NRSs. Event rates were calculated in a previous study to account for variations in time at risk and was found to be 3 years.¹⁶

There were several limitations in this analysis. First, it was based primarily on a review of NRSs. The retrospective nature of the NRSs made it difficult to exclude the possibility of selection bias resulting from baseline differences between the 2 groups. The open surgery group may have included a higher proportion of patients with a history of prior abdominopelvic surgery. Furthermore, included large database studies were limited by the reliability and specificity of data entered. Second, operations were performed by a large number of surgeons and techniques were not standardized, which may have affected the subsequent incidence of adhesive SBO. More laparoscopic procedures could be performed by experienced rather than inexperienced surgeons. In addition, most included studies did not define laparoscopic surgery or describe adjuncts to the surgical approach such as using adhesion barriers. Additional studies are needed that control for factors such as length of incision, extraction site, use of adhesion barriers, and laparoscopic techniques such as laparoscopically assisted or hand-assisted surgery. Third, only 4 of the 10 NRSs evaluated patients who underwent surgery for

colorectal cancer alone, with the remaining 7 NRSs including some patients with benign diseases. Finally, despite a median follow-up over 3 years, it was unclear whether the incidence of adhesive SBO would change after a much longer follow-up of at least 10 years.

Conclusions

This meta-analysis shows that laparoscopic colorectal surgery significantly reduced the incidence of adhesive SBO and the rate of subsequent surgery for adhesive SBO compared with open surgery. Despite these findings; however, well-designed, multicenter randomized trials are needed to confirm the benefit of laparoscopic colorectal surgery.

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