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SURGICAL ENDOSCOPY
and Other Interventional Techniques

Metaanalysis of trials comparing laparoscopic and open surgery for Crohn's disease

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Abstract
Background: Several studies in the literature have suggested that laparoscopic surgery for Crohn's disease is associated with faster postoperative recovery and a morbidity and recurrence rate similar to that for open surgery. Most of these studies have been limited by a small sample size and a short follow-up period.
Methods: To clarify whether open or laparoscopic resection results in a better outcome, a metaanalysis of studies was performed comparing the two procedures for Crohn's disease. Pooled effects were estimated using a random-effects model.
Results: Laparoscopic surgery required more operative time than open surgery (26.8 min; 95% confidence interval [CI], 6.4–47.2 min), but resulted in a shorter duration of ileus and a decreased hospital stay (−2.62 days; 95% CI, −3.62 to −1.62). Laparoscopic surgery also was associated with a decreased rate for postoperative bowel obstruction and surgical recurrences.
Conclusions: Laparoscopic surgery for Crohn's disease is feasible, safe, and associated with shorter duration of ileus and a shorter hospital stay.

Key words: Crohn's disease — Laparoscopic surgery — Metaanalysis

Despite improvements in medical therapy for Crohn's disease, 75% and 90% of patients still require surgery after 20 and 30 years of the disease, respectively [1–3]. Minimally invasive approaches developed for Crohn's disease over the past two decades have been shown to improve cosmetic results and potentially reduce postoperative ileus and hospital stay [4–10]. However, a laparoscopic approach to Crohn's disease is technically more demanding and requires additional training and operating time [5, 6]. Thus, the role of laparoscopy in the management of Crohn's disease still is evolving and debated.

Several studies have compared laparoscopic with open surgery for Crohn's disease [11–26]. Most of these studies recruited a relatively small number of subjects, resulting in limited power to evaluate significant outcome measures. Furthermore, some of these studies have reported conflicting results. To determine the potential benefit of laparoscopic surgery for Crohn's patients, we conducted a metaanalysis of the currently available published trials.

Materials and methods

Data identification

All relevant published studies were identified by computer-assisted search of the MEDLINE database from 1990 to 2004 using Silver Platter's MEDLINE (Ovid Technologies, New York NY). References were retrieved using key words that included "laparoscop*" and "Crohn*" or "granluomatous colitis" or "ileitis"or "inflammatory bowel" or regional enteritis". The cited references of each retrieved paper also were checked for relevance.

Studies were considered eligible for inclusion in the metaanalysis if they compared patients who had Crohn's disease and underwent laparoscopic surgery with a similar group of patients who underwent an open procedure. Two of the studies consisted of adolescent or pediatric cases [16, 25] and were included in the metaanalysis. One study [27] commented that the patients who underwent open procedures had more extensive disease than the laparoscopy group, and thus was excluded from the metaanalysis. In cases of multiple papers from the same institution with overlapping patients [12, 13, 28, 29], the most recent paper was included. Eligible reports were reviewed by two authors (A.S.R., A.F.) to determine final eligibility.

All the studies were abstracted for relevant study outcomes including operative time, hospital stay, time to first flatus, time to first bowel movement, time to solid intake, days requiring narcotics, rate of all postoperative complications, and rates of major complications (e.g., complications requiring reoperation, invasive procedures such as percutaneous drainage of abscesses). For the studies that included a reasonable long-term follow-up period, we also analyzed the rates for bowel obstruction, recurrent disease, and reoperation.

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Statistical methods

The rates of conversion from a laparoscopic to an open procedure were pooled using the inverse of the variance of the rates [30, 31]. The 95% confidence intervals for rates were calculated using standard statistical methods [32]. In dealing with rates equal to zero, an alternate method described by Hanley and Lippman-Hand [33] was used.

For data derived from contingency tables (e.g., complication rates for laparoscopic and open procedures), we computed the odds ratio and 95% confidence interval [34]. In cases of unstable estimators (which occur if the rate of an event is either 0 or 1), 0.5 was added to all the cells to estimate the odds ratio [32, 35]. An odds ratio significantly less than 1 favored laparoscopic surgery, whereas an odds ratio significantly greater than 1 favored the open procedure. For continuous variables (e.g., length of operation, days of hospital stay), we calculated the difference in mean values between the two procedures and its 95% confidence interval [34]. This method requires that the study report the standard errors of the mean, the standard deviations, or the confidence intervals. Thus, studies that did not report any of these parameters were not included in the statistical pooling of continuous variables.

The outcome variables (e.g., rates, odds ratios, and difference in mean values) were pooled using a random-effects model according to the method of DerSimonian and Laird [36], as further described by Fleiss [35]. We tested for homogeneity using the random-effects model to calculate the Q statistic and associated p value [34]. In two studies [16, 24], values were reported as bar graphs with error bars. Although the paper by Tabet et al. [24] did not specify whether the error bars represented standard deviation or standard error, we assumed that these values were standard deviations based on their corresponding p values.

We calculated the quantitative values after careful measurements of the distances on the bar graphs. In two studies [12, 20], the outcome variables for patients who underwent successful laparoscopy were reported separately from those who had an initial attempt at laparoscopy but then required conversion to an open procedure. To maximize the number of studies using an intent-to-treat analysis, the outcome values of both these groups were mathematically pooled to generate the laparoscopy group. For continuous variables, the pooled standard deviations were derived using standard statistical methods. The outcome values (either odds ratios or difference in means) and their 95% confidence intervals are reported. All p values less than 0.05 (two-tailed) were considered significant.

Results

Included studies

As shown in Table 1, 16 studies were included in the metaanalysis. One study was a randomized trial, whereas 15 were nonrandomized (13 were retrospective and 2 were prospective). Whereas 12 studies analyzed their results on an intent-to-treat basis [11, 13–18, 22–26], one study used a per protocol method [19], one study randomized patients after a diagnostic laparoscopy demonstrated feasibility [21], and two studies reported the results of the successful laparoscopy and converted laparoscopy groups separately [12, 20].

Two studies consisted primarily of pediatric and adolescent patients [16, 24]. All the selected studies included patients undergoing ileocolic resection as the most common laparoscopic procedure for Crohn's disease. Seven studies also reported that their patients underwent synchronous procedures such as a stricturoplasty [13, 17, 19], left or transverse colectomy [14, 18], small bowel resection [13–15, 17], drainage of intraabdominal abscess [13], and fistula closure [12, 14, 18]. Other studies also included patients undergoing laparoscopic procedures for their Crohn's disease other than an ileocolic resection such as small bowel resection [12, 17, 20, 22, 25], left or transverse colectomy [20, 24], segmental colectomy [20, 22], anastomotic site resection [20, 24], stricturoplasty [20], total colectomy or proctocolectomy [22], abdominoperineal resection [24], and Hartmann's procedure [24].

Surgical outcomes

The rates for conversion to an open procedure ranged from 0% to 29%. The pooled rate was 7% (95% confidence interval [CI], 4–10%; Table 1). Laparoscopic surgery required more operating time than the open procedures (26.8 min; 95% CI, 6.4–47.2 min; Fig. 1A). There was no significant difference in estimated blood loss between the two procedures (Fig. 1B).

Postoperative course

Laparoscopic surgery significantly reduced the duration of ileus, as measured by the time to first flatus (−0.82 days; 95% CI, −1.30 to −0.33 days; Fig. 2A), time to first bowel movement (−0.75 days; 95% CI, −1.32 to −0.17 days; Fig. 2B), time to oral intake (−1.52 days; 95% CI, −2.36 to −0.68 days; Fig. 2C), and time to solid intake (−1.54 days; 95% CI, −2.96 to −0.12 days; Fig. 2D). Laparoscopic surgery also was associated with fewer days of postoperative narcotic use (−2.3 days), although this pooled result did not reach statistical significance (95% CI, −4.81 to 0.18 days; Fig. 3A). Laparoscopic surgery resulted in a reduced hospital stay (−2.62 days; 95% CI, −3.62 to −1.62 days; Fig. 3B), which probably was secondary to shortened ileus and decreased narcotic use. Five studies reported that laparoscopic surgery had decreased hospital costs, as compared with the open procedure [11, 17, 22, 23, 26]. However, the lack of standardization prevented a formal pooling.

Postoperative complications

We looked at the rates for both reported total postoperative complications and major complications, defined as those requiring reoperation or an invasive procedure such as drainage of an abscess. Laparoscopic surgery resulted in reduced rates of total complications (odds ratio [OR], 0.62; 95% CI, 0.42–0.91; Fig. 4A) and major complications (OR, 0.50; 95% CI, 0.27–0.96; Fig. 4B). The tests for homogeneity of both total and major complication rates did not reach statistical significance (Q statistic 8.65 and 14.22, respectively; $p > 0.05$). There was no significant difference between the two procedures in terms of early reoperation for complications (OR, 0.81; 95% CI, 0.34–1.92).

Long-term follow-up assessment

Six studies also reported adequate postoperative follow-up assessment of their patients (Table 1) [11, 15, 21–24].

Table 1. Characteristics of studies included in the metaanalysis

Study	Study populations	Study design; analysis	No. of open procedure patients	No. of attempted laparoscopy patients	No. of laparoscopy patients with no conversion	Average postprocedure follow-up
Alabaz et al. [11]	Patients undergoing ileocolic resection	Retrospective; intent-to-treat	48	26	23	30 months
Bauer et al. [12]	Patients undergoing ileocolic resection or ileoileal anastomosis	Retrospective; pooled subgroups for intent-to-treat analysis	14	25	19	Not stated
Bemelman et al. [13]	Patients undergoing ileocolic resection	Retrospective; intent-to-treat	48	30	28	Not stated
Benoist et al. [14]	Patients undergoing ileocolic resection	Retrospective; intent-to-treat	32	24	20	Not stated
Bergamaschi et al. [15]	Patients undergoing ileocolic resection	Retrospective; intent-to-treat	53	39	39	60 months
Diamond and Langer 16]	Adolescents undergoing ileocolic resection	Retrospective; intent-to-treat	11	12	11	Not stated
Duepree et al. [17]	Adult patients undergoing ileocolic resection	Retrospective; intent-to-treat	24	21	20	Not stated
Huilgol et al. [18]	Patients undergoing ileocolic resection	Prospective; intent-to-treat	19	21	20	Not stated
Kishi et al. [19]	Patients undergoing ileocolic resection for stenosis	Retrospective; per protocol analysis after excluding patients	17	24	22 (4 patients were also excluded for technical reasons)	Not stated
Luan and Gross [20]	Patients undergoing intestinal surgery	Retrospective; pooled subgroups for intent-to-treat analysis	23	24	17	Not stated
Milsom et al. [21]	Patients undergoing ileocolic resection	Prospective; randomized after diagnostic laparoscopy excluded patients who were not candidates for laparoscopic resection	29	33	31	20.5 months
Msika et al. [22]	Patients undergoing intestinal surgery	Prospective, nonrandomized; intent-to-treat	26	20	20	30 months for open group, 10 months for laparoscopy group
Shore et al. [23]	Adult patients undergoing intestinal surgery	Retrospective; intent-to-treat	20	20	19	18.7 months for open group, 17.2 months for laparoscopy group
Tabet et al. [24]	Patients undergoing intestinal resection	Retrospective; intent-to-treat	29	32	28	40.2 months
von Allmen et al. [25]	Adolescents undergoing ileocolic resection	Retrospective; intent-to-treat	18	12	12	Not stated
Young-Fadok et al. [26]	Patients undergoing intestinal resection	Retrospective; intent-to-treat	33	33	31	Not stated

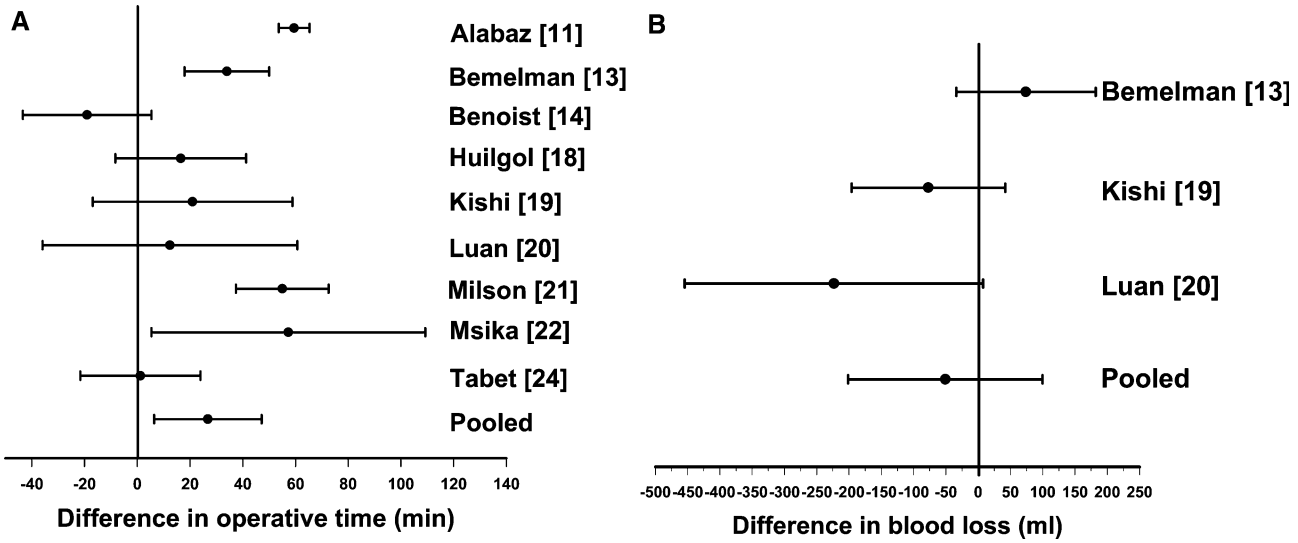

Fig. 1. **A** Metaanalysis of operative time. **B** Metaanalysis of intraoperative blood loss.

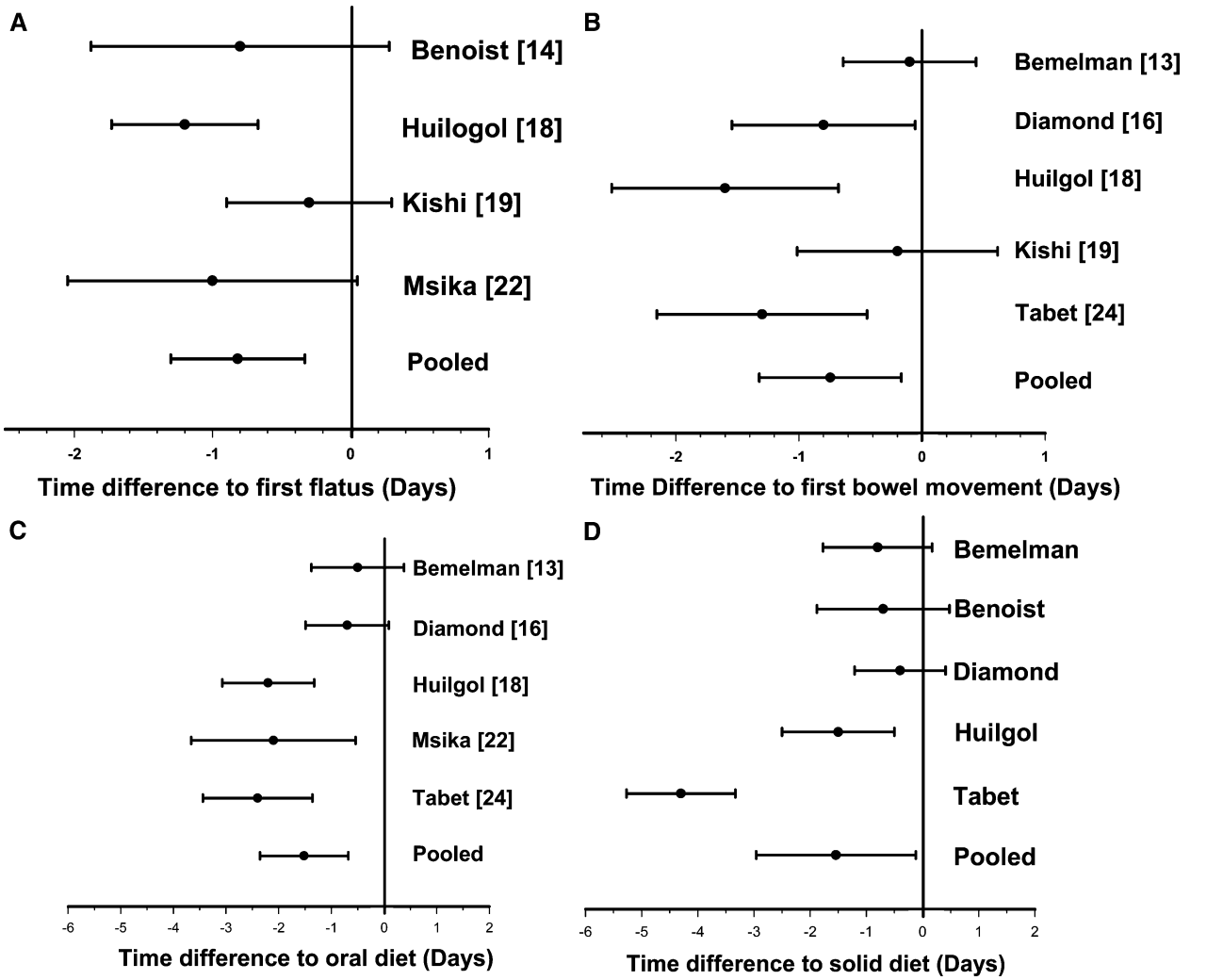

Fig. 2. **A** Metaanalysis of time to flatus. **B** Metaanalysis of time to bowel movement. **C** Metaanalysis of time to oral diet. **D** Metaanalysis of time to solid diet.

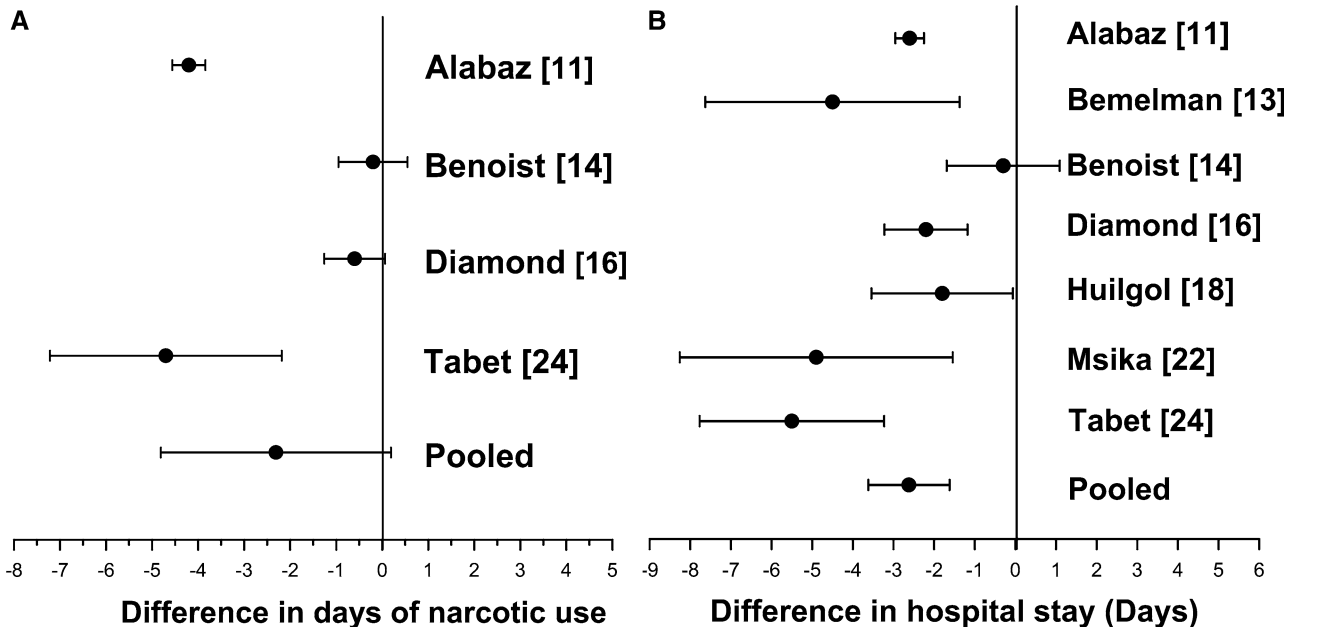

Fig. 3. **A** Metaanalysis of postoperative days of narcotic use. **B** Metaanalysis of hospital days.

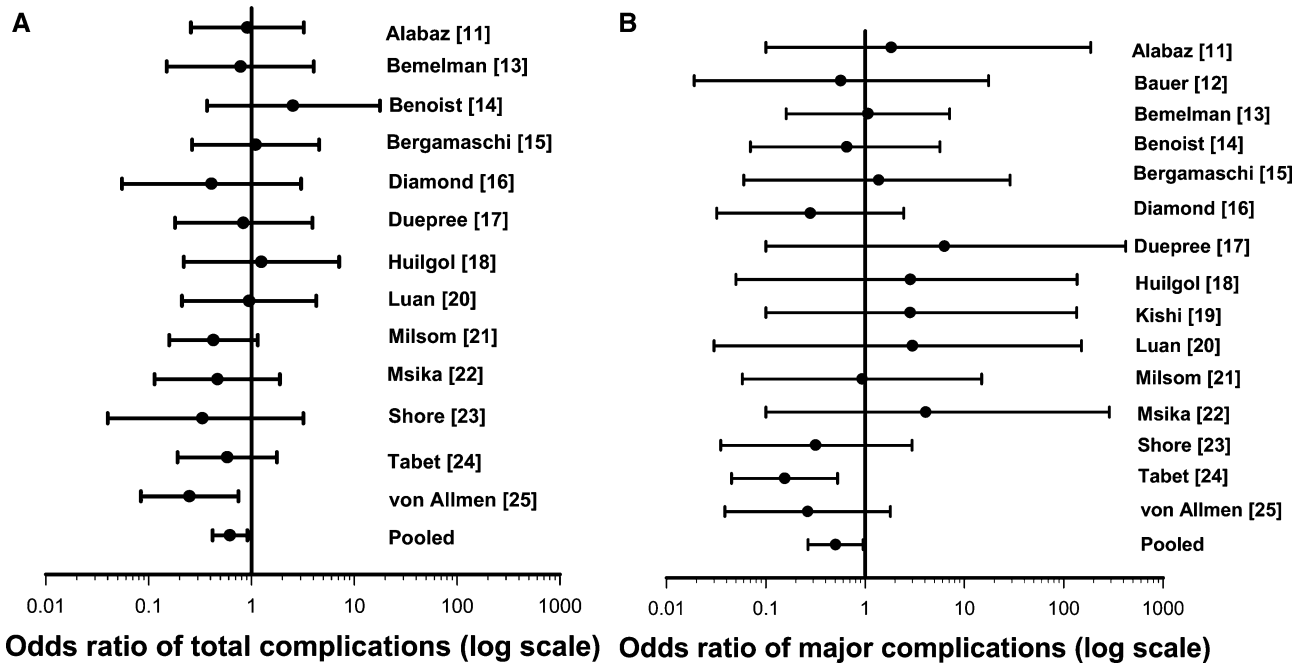

Fig. 4. **A** Metaanalysis of rates of total postoperative complications. **B** Metaanalysis of rates of major postoperative complications.

Laparoscopic surgery resulted in fewer small bowel obstructions than the open procedures (OR, 0.24; 95% CI, 0.14–0.41; Fig. 5A). Most of the reported small bowel obstruction cases were managed conservatively. Laparoscopic surgery also had a reduced rate of surgery for recurrences (OR, 0.51; 95% CI, 0.28–0.93; Fig. 5B). However, the statistical significance was driven by one study [24]. Finally, laparoscopic surgery also was associated with a lower rate of late reoperations for Crohn's recurrences (OR, 0.46, 95% CI, 0.27–0.80; Fig. 5C).

Discussion

According to our metaanalysis results, laparoscopic surgery for Crohn's disease is associated with prolonged operative time, shorter duration of postoperative ileus, shorter hospital stay, lower incidence of early postoperative complications, and postoperative small bowel obstruction. Furthermore, due to the significantly shorter length of hospital stay, a trend toward lower overall costs was noted with laparoscopic surgery. Most

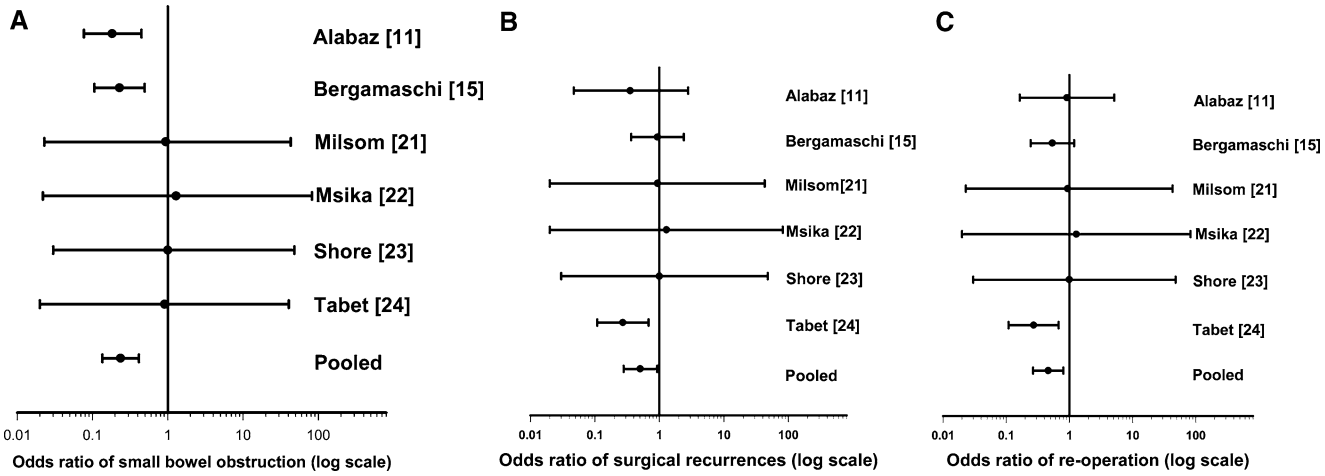

Fig. 5. **A** Metaanalysis of rates of total post small postoperative small bowel obstruction. **B** Meta-analysis of rates of postoperative recurrences requiring surgery. **C** Metaanalysis of reoperation rates.

of the studies permitted an intent-to-treat analysis that included patients who underwent conversion to an open procedure after an attempted laparoscopy in the "laparoscopic group." Even with this type of analysis, laparoscopic surgery appears to be a very valuable alternative to open surgery for Crohn's disease.

The relatively low pooled conversion rate of 7% suggests a selection bias for severity of disease and patient characteristics. Previous studies have identified factors associated with high conversion rates including internal fistula [37], smoking history [37], steroid administration [37], extracolonic disease [37], preoperative malnutrition [37], surgery for recurrent disease [37], and the presence of a palpable mass [28, 38]. However, none of the factors appears to be an absolute contraindication to laparoscopic surgery for appropriate patients [7, 9].

Patients undergoing laparoscopic surgery have a shorter duration of ileus, as reflected by the times to flatus and bowel movement and resumption of oral and solid diets. The reason for the decreased duration of ileus is clearly multifactorial. Extensive abdominal manipulation increases the production of inflammatory mediators and sympathetic stimulation, which inhibit intestinal motility [39]. Laparoscopy usually results in decreased intraoperative trauma, and thus decreased production of these mediators [40, 41] and less sympathetic stimulation [39]. Postoperative narcotic use also exacerbates ileus [42], and this is reduced by the laparoscopic approach, although not to a statistically significant extent in our analysis. This reduction in postoperative ileus translated to a decreased length of hospital stay.

On the other hand, laparoscopic surgery required additional operative time related to the increased technical demands for this procedure [5, 6]. Nevertheless, five studies reported decreased overall costs associated with laparoscopy [11, 17, 22, 23, 26]. Cost savings attributable to the shorter hospital stay outweighed the additional costs associated with increased operative time.

Laparoscopy was associated with reduced early postoperative complications. Because most of the studies were not randomized, it is difficult to discern whether these differences are attributable to the superiority of laparoscopy or rather to patient selection. Laparoscopy also was associated with decreased rates of postoperative small bowel obstruction. Experimental animal models and clinical studies have suggested that laparoscopic surgery results in fewer adhesions than open surgery [43]. Furthermore, laparoscopy also was associated with fewer surgical recurrences and a reduced need for reoperations. However, it is difficult to distinguish whether these differences are attributable to the superiority of laparoscopy or rather to confounding factors such as patient selection or the use of maintenance medical therapy, which may prevent postoperative recurrences. Thus, a large, randomized trial with long-term follow-up assessment probably will be needed for further evaluation of these issues.

In conclusion, laparoscopy for Crohn's disease appears to be feasible and safe. Our metaanalysis confirms that even in the challenging field of Crohn's disease inflammatory changes, laparoscopy offers a variety of significant clinical advantages. The length of the hospital stay is reduced with a trend toward reduction in overall costs. Postoperative bowel function recovers more readily, in part due to less use of narcotic pain medications and intraoperative manipulation. Laparoscopy also reduces postoperative complications such as small bowel obstruction, although these observations require further confirmation and longer follow-up evaluation.

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