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REVIEW

Intracorporeal versus extracorporeal anastomosis after laparoscopic right hemicolectomy for cancer: a systematic review and meta-analysis

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Abstract
Purpose The aim of this systematic review was to compare intracorporeal (IA) versus extracorporeal anastomosis (EA) after laparoscopic right hemicolectomy for cancer.
Methods The meta-analysis was conducted following all aspects of the Cochrane Handbook for systematic reviews and Preferred Reporting Items for Systematic Reviews and Meta-analysis statement. Studies published from 2009 to 2012 that compare IA and EA after laparoscopic right hemicolectomy were identified. The included non-randomized studies were assessed for their methodological quality using the revised and modified grading system of the Scottish Intercollegiate Guidelines Network. Intraoperative, early postoperative, and postoperative recovery outcomes were compared using weighted mean differences and odds ratios.
Results Five non-randomized controlled trials published between 2009 and 2011, comprising 425 patients, were included in this analysis. IA was associated with significant faster bowel movement, faster first flatus, shorter time to solid diet, decreased use of analgesics, and shorter duration of the hospital stay. No differences were observed for nasogastric tube reintroduction rate, operative time, incision length, number of nodes harvested, intraoperative complications, mortality, non-surgical site complications, surgical site complications (anastomotic leakage, anastomotic bleeding, wound infection, ileus), reintervention, and readmission rate.
Conclusions Even when the limitations are taken into account due to the observational nature of the included studies, the results suggest that the IA after laparoscopic right hemicolectomy for cancer results in better postoperative recovery outcomes, such as shorter hospital stay, faster bowel movement recovery, faster first flatus, faster time to solid diet, and lesser analgesic usage.

Keywords Laparoscopy · Intracorporeal anastomosis · Right hemicolectomy · Colon cancer

Background

The feasibility of laparoscopic colectomy procedures, in terms of both safety and oncological radicality, has been reported since 1991 [1], with data from several randomized trials [2–5]. These trials demonstrated that improvements in short-term postoperative results could be achieved without compromising long-term oncological results. The percentage of elective colectomies performed laparoscopically has increased over time; however, almost 90 % of the cases are still performed open, and utilization continues to be influenced by several factors [6]. A recent meta-analysis confirmed that laparoscopic right colectomy results in less blood loss, a shorter length of hospital stay, and lower postoperative short-term morbidity compared with open right colectomy, with equal oncological long-term results [7].

A survey by Jamail et al. [8] revealed that laparoscopic right colectomy with extracorporeal anastomosis is technically considered more difficult than laparoscopic sigmoidectomy and that the difficulty significantly increases when anastomosis is performed intracorporeally; this may explain why there are only a few publications [9–13] comparing these anastomotic techniques, and to date, no meta-analysis has been performed. For this reason, we conducted a

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systematic review and meta-analysis of all studies comparing intracorporeal (IA) versus extracorporeal anastomosis (EA) after laparoscopic right hemicolectomy for cancer.

Methods

Eligibility criteria

Types of studies

All published randomized and non-randomized comparative trials written in English, French, Spanish, German, and Italian comparing intracorporeal and extracorporeal anastomosis after laparoscopic right hemicolectomy for cancer were evaluated. Non-comparative studies, animal studies, and gray literature were excluded. Studies were excluded from the analysis when the outcome of interest for the two techniques was not reported. If two studies from the same institution were identified, the most recent or the most informative was selected, unless they were reports from different time periods or if the data from overlapping patients could be subtracted.

Types of interventions

Only laparoscopic right hemicolectomies were considered. After laparoscopy, the ileocolic vessels were identified and removed at their origin after applying hemostatic clips or mechanical staples. The colon was then mobilized. For IA patients, the division of the mesentery, colon, and ileum was carried out intracorporeally as the mechanical anastomosis. In patients who underwent an extracorporeal anastomosis, the colon and ileum were externalized and sectioned by widening the incision of one of the trocars or by performing a mini-laparotomy at another location (subcostal, suprapubic). Ileocolic anastomosis was subsequently performed manually or mechanically. Studies that included other types of resections or those that contained palliative resections were excluded unless the data were presented separately.

Types of outcome measures

The following end points were used to compare intracorporeal and extracorporeal patients:

Intraoperative: operative time, incision length (mm), number of nodes harvested, and intraoperative complications.

Early postoperative: mortality, non-surgical site complications, surgical site complications, anastomotic leakage, anastomotic bleeding, wound infection, ileus, and reintervention.

Postoperative recovery: bowel movement, first flatus, time to solid diet, nasogastric tube (NGT) reintroduction, day of analgesic usage, length of stay, and readmission.

Only morbidity in the first 30 days after surgery was considered. The postoperative complications were classified as non-surgical site (cardiovascular, respiratory, or metabolic events; non-surgical infections; deep venous thrombosis; and pulmonary embolism) or surgical site complications (anastomotic leakage, anastomotic bleeding, wound infection, ileus). Bowel movement, first flatus, time to solid diet, days of analgesic usage, and the length of stay were expressed as days from intervention.

Search

Two authors (AV and AG) independently carried out the electronic bibliographic research according to the validated methods of the PRISMA statement [14] using the following databases: Medline, Embase, Web of Science and The Cochrane Library. The database searches were performed using the following MeSH search terms: "colectomy," "right colectomy," "right colon cancer," "laparoscopic colectomy," "laparoscopic right colectomy," "laparoscopic-assisted right colectomy," and "comparative study." These terms, and their combination, were also used as key words. Special database functions, such as “related articles” and “explosion,” were used to maximize the search. To minimize retrieval bias, a manual search was performed using the Google Scholar database to manually search eight high-impact journals chosen on the basis of the frequency of articles found from 1991 to 2012 (Annals of Surgery, Surgical Endoscopy, Archives of Surgery, British Journal of Surgery, Diseases of the Colon & Rectum, Journal of American College of Surgeons, Colorectal Disease, and International Journal of Colorectal Disease) [15]. The searches were performed up to 5 August 2012. A manual bibliographic search was performed to individualize every bibliographic reference reported in the bibliography of the full-text articles examined. Because, to our knowledge, the first laparoscopic colectomy was reported in 1991 [1], the search was started in 1991.

Data collection process

One author (AV) extracted the data from the included study, and the second author (AG) checked the extracted data. Disagreements were resolved through discussion and, if necessary, by involving an independent third author (FF). The following information was extracted by one author (AG) for each included trial: number of participants, country, study design, inclusion and exclusion criteria, and the type of outcome.

Quality assessment

The included non-randomized studies were assessed for their methodological quality using the revised and modified grading system of the Scottish Intercollegiate Guidelines Network [16].

Statistical analysis

This study was performed in line with the recommendations of the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement [17]. The data analysis was performed using Revman 5.0 (Review Manager 5.0, Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008). Statistical analysis for dichotomous variables was performed using the odds ratio (OR) as the summary statistic (with a corresponding 95 % confidence interval—CI). The Mantel–Haenszel method was used to combine the OR for the outcomes of interest by using random-effect meta-analytical techniques [18]. Statistical analysis of the continuous variables was performed by calculating the weighted mean difference (WMD). Study heterogeneity was then assessed using the I^2 statistic, and the χ^2 test for heterogeneity was performed, with $P < 0.1$ considered to indicate statistically significant heterogeneity. I^2 values less than 25 % were defined as low heterogeneity; I^2 values between 25 and 50 % were considered to represent moderate heterogeneity; and values greater than 50 % were defined as representing high heterogeneity. Forest plots were constructed, with $P < 0.05$ considered to be statistically significant. A funnel plot was constructed to explore the possibility of publication bias.

Results

Evaluation of the 289 abstracts found through bibliographic research identified nine studies that could potentially be included in the meta-analysis. Following the full-text analysis, four of these studies were excluded [19–22] for being non-comparative. Five non-randomized controlled trials published between 2009 and 2011, comprising 425 patients, were included in this analysis [9–13]. Of these, 202 (47.5 %) had an IA, and 223 (52.5 %) had an EA. The characteristics of all five included studies are listed in Table 1. Three were case-controlled trials [10, 11, 13], and two were retrospective analyses [9, 12].

Quality assessment

An assessment of the non-randomized controlled trials is displayed in Table 2. Only the study from Scatizzi et al. [10] was of good quality (15 points on the modified grading

Table 1 Characteristics of the included studies

Authors	*N* of patients		Year	Country	Study design	Inclusion	Exclusion	Outcomes examined	Intracorporeal anastomosis	Extracorporeal anastomosis
	Intracorporeal	Extracorporeal								
Hellan et al.	23	57	2009	USA	RA	LRH for cancer	Open conversion	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 18, 19	LLS	LLS
Scatizzi et al.	40	40	2010	Italy	CCS	LRH for cancer	Advanced disease	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19	LLS	LLS
Grams et al.	54	51	2010	USA	RA	Laparoscopic hemicolectomy or colectomy for cancer	Intracorporeal anastomosis using a circular stapler	1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 18, 19	LLS	LLS
Fabozzi et al.	50	50	2010	Italy	CCS	LHR for non-metastatic cancer	Patients treated before 2001, ASA >2, previous abdominal surgery, previous neoplastic disease, immunodepression, acute complications of the tumor	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19	Not specified	Not specified
Chaves et al.	35	25	2011	Spain	CCS	LRH for cancer	None	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 15, 18, 19	LLS	LLS or LLM

CCS case–control study, *RA* retrospective analysis, *LRH* laparoscopic right hemicolectomy, *ASA* American Society of Anesthesiologists classification, *1* operative time, *2* incision length, *3* number of nodes harvested, *4* intraoperative complications, *5* mortality, *6* non-surgical site complications, *7* surgical site complications, *8* anastomotic leakage, *9* anastomotic bleeding, *10* wound infection, *11* ileus, *12* reintervention, *13* bowel movement, *14* first flatus, *15* time to solid diet, *16* NGT reintroduction, *17* day of analgesic usage, *18* length of stay, *19* readmissions, *LLS* laterolateral stapled ilecolonic anastomosis, *LLM* laterolateral manual ilecolonic anastomosis

Table 2 Evaluation of methodological qualities of included studies

Items/authors	Hellan	Scatizzi	Grams	Fabozzi	Chaves
Inclusion criteria	0	1	1	1	1
Exclusion criteria	0	1	1	1	1
Demographics comparable?	0	1	1	1	1
Can the number of participating centers be determined?	1	1	0	1	1
Can the number of surgeons who participated be determined?	1	1	0	0	1
Can the reader determine where the authors are on the learning curve for the reported procedure?	0	1	1	1	0
Are diagnostic criteria clearly stated for clinical outcomes if required?	1	1	1	1	1
Is the surgical technique adequately described?	1	1	1	0	1
Is there any way that they have tried to standardize the surgical technique?	0	1	1	0	1
Is there any way that they have tried to standardize perioperative care?	0	1	0	1	0
Is the age and range given for patients in the intracorporeal anastomosis group?	1	1	0	1	1
Do authors address whether there are any missing data?	0	0	0	0	0
Is the age and range given for patients in the extracorporeal anastomosis group?	1	1	0	1	1
Did all the patients asked to enter the study take part?	0	0	0	0	0
Drop-out rates stated?	0	0	0	0	0
Were patients in each group treated along similar timelines?	1	1	1	1	1
Outcomes clearly defined?	1	1	1	1	1
Blind assessors?	0	0	0	0	0
Standardized assessment tools?	1	1	1	1	1
Analysis by intention to treat?	0	0	0	0	0
Score	9	15	10	12	13

Total score, 21; <8, poor quality; 8–14, fair quality; ≥15, good quality

system of the Scottish Intercollegiate Guidelines Network). The remaining four studies were of fair quality (mean=11 points). None was of low quality (<8).

Intraoperative outcomes

There were no statistically significant differences between IA and EA concerning the operative time (P=0.25; WMD=9.66; 95 % CI, −6.68 to 25.99), incision length (P=0.30; WMD=−19.97; 95 % CI, −57.75 to 17.82), number of nodes harvested (P=0.47; WMD=1.33; 95 % CI, −2.26 to 4.93), or intraoperative complications (P=0.85; OR=0.84; 95 % CI, −0.14 to 5.20). However, except for intraoperative complications (Chi^2=2.08, P=0.35, I^2=4 %), the analyses were weakened by the elevated degree of heterogeneity for operative time (Chi^2=76.20, P<0.00001, I^2=95 %), incision length (Chi^2=76.20, P<0.00001, I^2=95 %), and number of nodes harvested (Chi^2=26.17, P<0.00001), I^2=89 %) (Fig. 1).

Early postoperative outcomes

No significant differences were observed from the analyses of mortality (P=0.79; OR=0.75; 95 % CI, 0.10 to 5.93), non-surgical site complications (P=0.74; OR=0.79; 95 % CI, 0.20 to 3.13), surgical site complications (P=0.16; OR=0.44; 95 % CI, 0.14 to 1.39), anastomotic leakage (P=0.92; OR=0.92; 95 % CI, 0.17 to 5.08), anastomotic bleeding (P=0.68; OR=0.60; 95 % CI, 0.05 to 6.96), wound infection (P=0.68; OR=0.74; 95 % CI, 0.18 to 3.09), ileus (P=0.45; OR=0.65; 95 % CI, 0.22 to 1.97), or reintervention (P=0.23; OR=0.43; 95 % CI, 0.11 to 1.70). High heterogeneity was observed for surgical site complications (Chi^2=8.61, P=0.07, I^2=54 %), while moderate heterogeneity was observed for non-surgical site complications (Chi^2=6.08, P=0.19, I^2=34 %), wound infection (Chi^2=7.78, P=0.10, I^2=49 %), and ileus (Chi^2=4.44, P=0.22, I^2=32 %) (Fig. 2a, b).

Postoperative recovery outcomes

In the IA group, we observed a significant faster bowel movement (P<0.00001; OR=−0.80; 95 % CI, −0.99 to −0.61), first flatus (P=0.002; OR=−0.48; 95 % CI, −0.78 to −0.18), and time to solid diet (P<0.00001; OR=−1.00; 95 % CI, −1.33 to −0.67). Furthermore, in the IA group, a decreased use of analgesic was noted (P<0.00001; OR=−1.00; 95 % CI, −1.34 to −0.66). A high level of heterogeneity was observed for bowel movement (Chi^2=34.06, P<0.00001, I^2=94 %), first flatus (Chi^2=13.08, P=0.001, I^2=85 %), and the use of analgesics (Chi^2=52.00, P<0.00001, I^2=98 %). The duration of the hospital stay was significantly shorter for the IA group

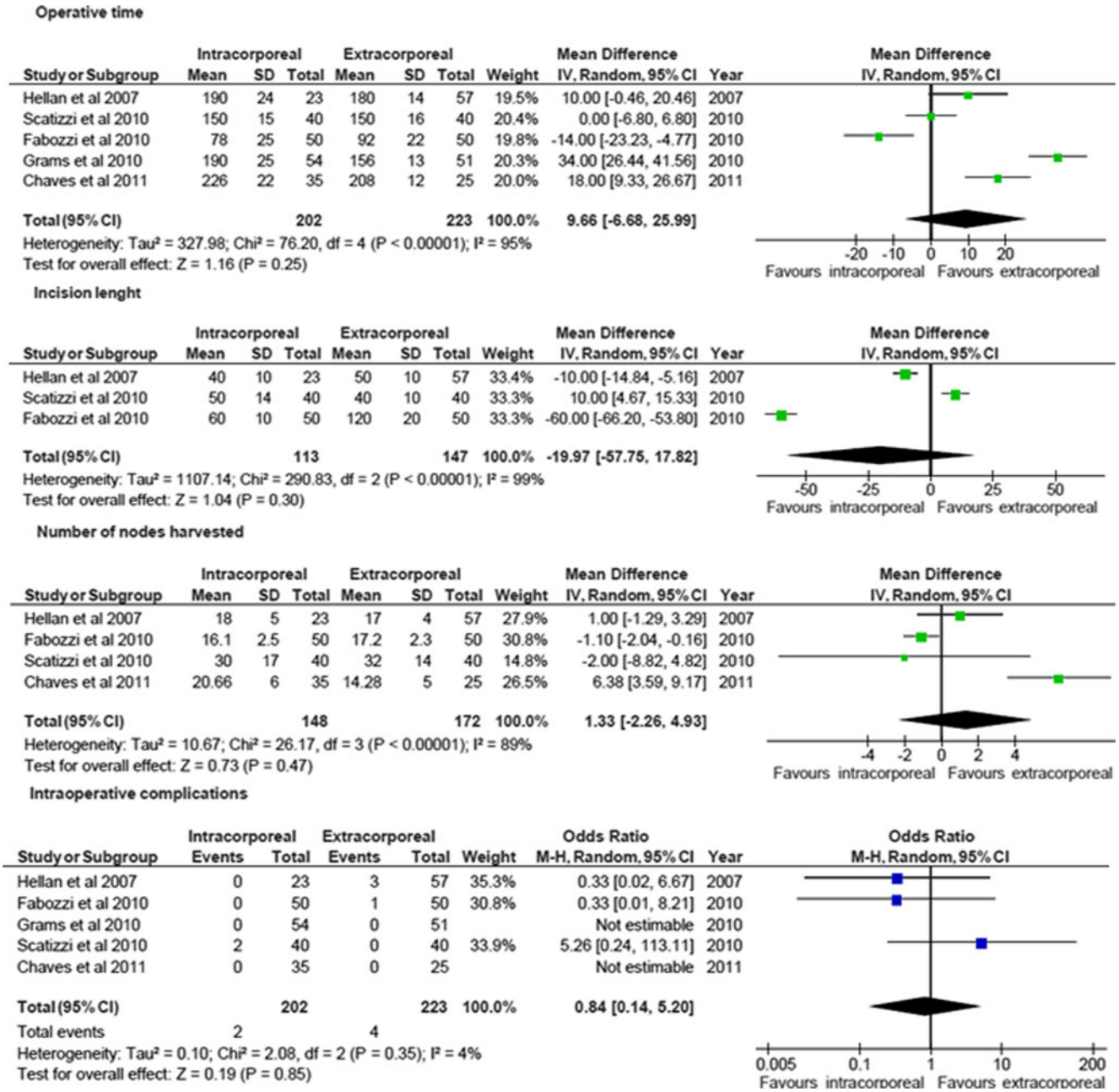

Fig. 1 Intraoperative outcomes

than for the EA group (P=0.003; OR=−0.93; 95 % CI, −1.79 to −0.07). This difference remained despite a degree of statistical heterogeneity and inconsistency (Chi^2=56.11, P< 0.00001, I^2=93 %). No differences were observed for NGT reintroduction and readmissions (P=0.55: OR=0.50; 95 % CI, 0.05 to 4.87) without heterogeneity (Fig. 3 and supplementary file 1).

Results of publication bias assessment

The funnel plots of the meta-analysis of all analyzed outcomes found that none exceeded the 95 % CI limit and that the studies were equally distributed on both sides of the vertical line. This result shows the absence of significant publication bias among the studies.

Discussion

Laparoscopic colonic resection is increasingly regarded as the gold standard for benign and malignant colonic lesions [23–28]. Short-term advantages include less postoperative analgesia, earlier resumption of ambulation, and a shorter hospital stay [25, 29]. The long-term oncological outcome is

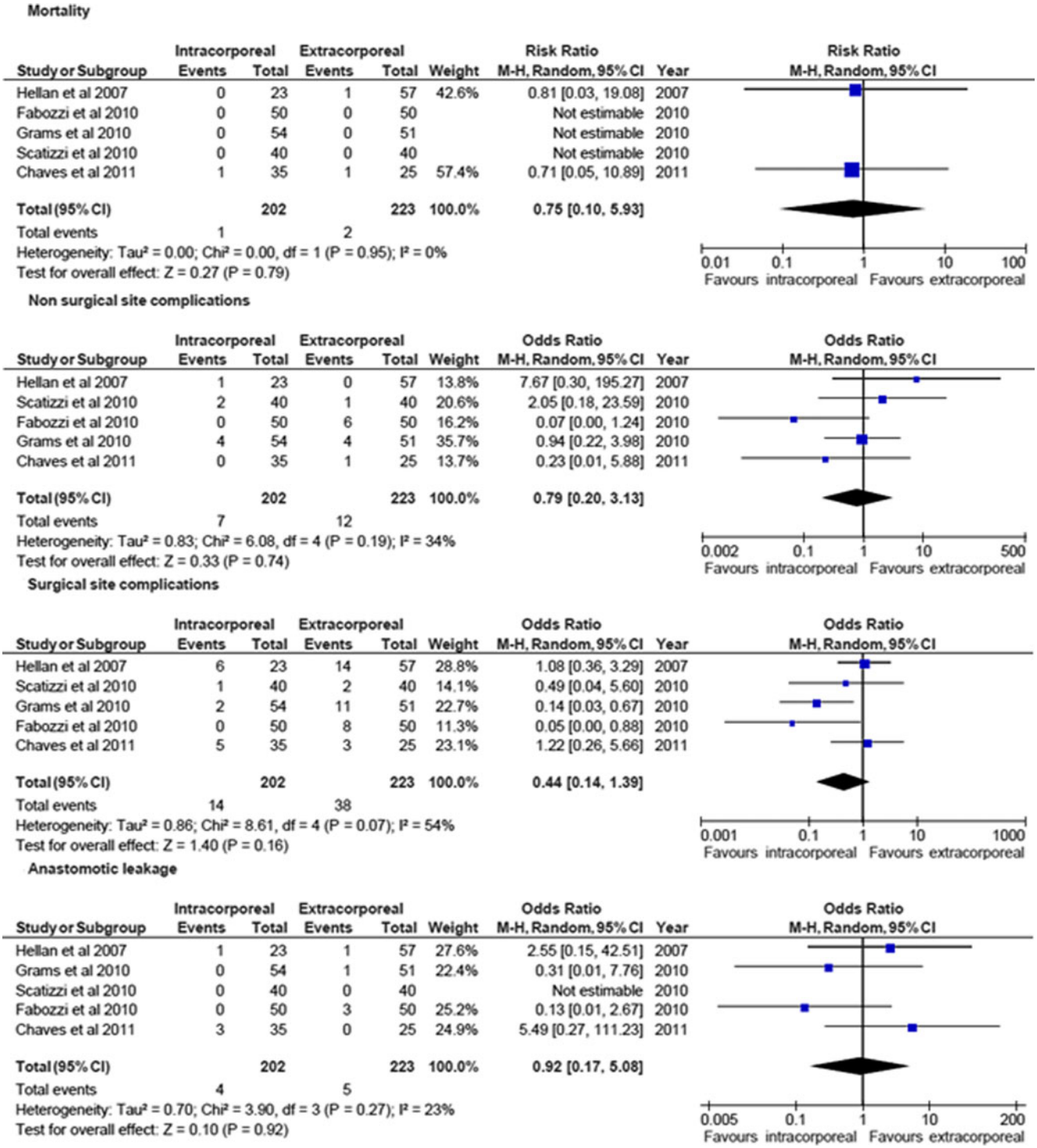

Fig. 2 Early postoperative outcomes

similar to that of open surgery [27, 30]. To date, no systematic review or meta-analysis exists that specifically compares intracorporeal versus extracorporeal anastomosis after laparoscopic right hemicolectomy for cancer.

A recent Cochrane systematic review [31] reported that stapled end-to-end ileocolic anastomosis was associated with a lower incidence of leakage compared with handsewn anastomosis. However, the marked heterogeneity between the studies leads to the present conclusion that there is no evidence for one procedure being better than the other. Nevertheless, due to the obvious technical complexity of manual anastomosis during laparoscopic surgery, the

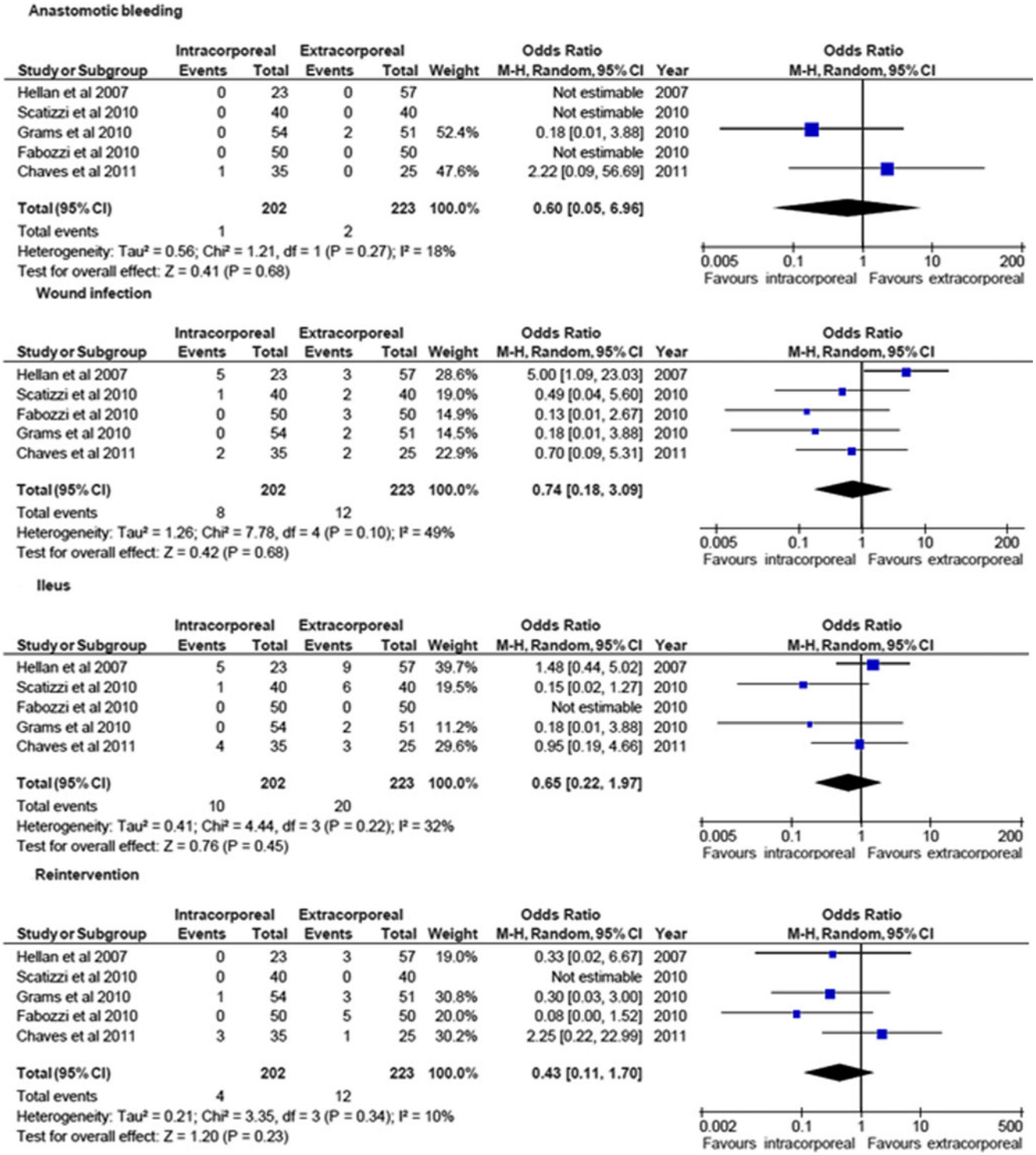

Fig. 2 (continued)

procedure of choice is the stapled method. Some authors have assessed and demonstrated the feasibility of this type of anastomosis, in terms of safety, recording an incidence of major surgical complications between 2 and 11 % [19, 20, 32]. All of the studies examined in this meta-analyses had both IA and EA performed with mechanical staplers, except the one from Fabozzi et al. [11] where the surgical technique was not specified and the one from Chaves et al. [13] in which both stapled and manual procedures were applied for EA. Confirming the safety of the stapled procedure, in this study, we observed no significant differences between the two groups concerning intraoperative complications and

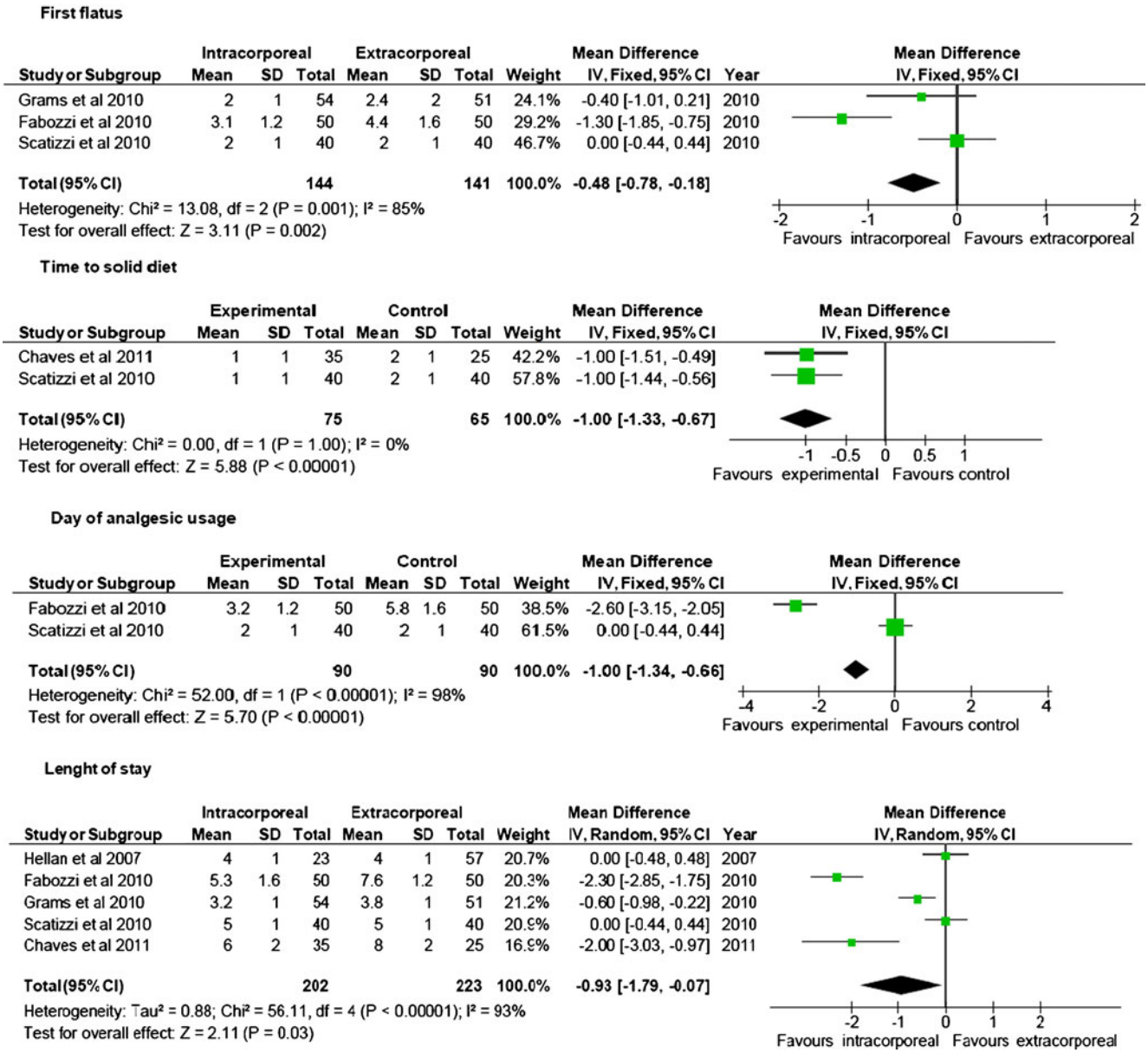

Fig. 3 Postoperative recovery outcomes

postoperative surgical site complications, such as anastomotic leakage, anastomotic bleeding, ileus, and wound infections. Notwithstanding the good results, we agree with other authors [8] regarding the technical difficulty of this procedure; therefore, to decrease the incidence of major complications, surgeons must be sufficiently trained to skillfully carry out laparoscopic sutures and be able to use linear mechanical staplers. This ability is necessary to keep the incidence of conversion to laparotomy as low as possible due to the high morbidity and cost for patients who undergo conversion [33].

It is also important to highlight the fact that laparoscopy results in a low incidence of postoperative non-surgical site complications, without differences between IA and EA. Some opponents of laparoscopic colectomy with IA argue that the operative time is longer, especially because the IA approach requires laparoscopic suturing skills, but our meta-analysis showed no differences, as well as regarding the length of the longer skin incision.

A completely intracorporeal technique implies a reduced manipulation of the abdominal organs [34] because the specimen is removed as the anastomosis is completed. The reduced manipulation of the bowel can explain the better recovery of the gastrointestinal tract (faster bowel movement, faster first flatus, and shorter time to a solid diet) in the IA group patients. This improves the patients' postoperative state/health and most likely explains the significant advantage in terms of the reduction of hospital stay for IA patients.

According to the latest TNM classification from the UICC, removal of at least 12 lymph nodes is fundamental to guarantee a sufficient oncological radicality [35]. To achieve this during laparoscopic right colectomy, the arterial branches must be ligated at the origin from the superior mesenteric artery. In laparoscopic-assisted techniques where vascular ligation is performed extra-corporeally through small incisions, it is difficult to obtain an adequate number of lymph nodes [36]. For this reason, for both techniques, vascular ligation and mesentery division were performed intracorporeally in all of the studies of this meta-analysis, and the number of excised lymph nodes in the two groups was similar.

This meta-analysis has certain limitations. First, the findings are all based on non-randomized studies, and this exposes the data to bias, even where other aspects of the methodology were satisfactory. The greatest risk, particularly when comparing two different surgical procedures with different levels of difficulty among non-randomized trials, is the introduction of selection bias in favor of the more technically demanding approach. This produces an overestimation of the treatment (IA) compared with the control (EA). This overestimation must be taken into consideration in the present study. Second, the selected studies are heterogeneous related to the applied anastomotic technique: one of the five selected studies does not refer to the type of anatomosis [11] and another study [13] applied both, stapled and manual procedures for extracorporeal anatomosis.

These findings, which are associated with the high degree of heterogeneity regarding some of the outcomes examined, could have resulted in bias. Nevertheless, the present manuscript reflects the current state of the literature on the subject, and therefore, more well-designed, multicenter, prospective randomized controlled trials are needed to allow for a more convincing evaluation. Despite these limitations, meta-analysis is a useful instrument for identifying variability and inconsistency in qualitative data derived from descriptive revisions [37].

Even when the limitations are taken into account due to the observational nature of the included studies, the results suggest that the intracorporeal anastomosis after laparoscopic right hemicolectomy for cancer results in better postoperative recovery outcomes, such as a shorter hospital stay, faster bowel movement recovery, faster first flatus, faster time to a solid diet, and lesser analgesic usage.

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