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Review

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## Open versus laparoscopic colectomy for colorectal cancer: A meta-analysis

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**Background:** Despite a decade experience of surgery by laparoscopy for colorectal cancer the safety and efficacy is still being debatable. We performed a meta-analysis of randomized controlled trials (RCTs), published between 1996 and July 2010 comparing laparoscopic vs open colonic resections for colorectal cancer.

**Methods:** A thorough search of the Medline, Embase and Cochrane library was made and identified RCTs were obtained and analyzed for short-term and long-term outcome variables. For continuous data mean difference and inverse variance were used for calculating the odds ratio (OR). Z test was used to calculate the overall effect and heterogeneity was tested by Chi-square and  $I^2$  values.

**Results:** A total of 43 studies were identified from 41 RCTs, not all variables were available in all studies, hence only those studies with particular variables were used for individual meta-analysis. A total of 35 studies evaluated 8940 participants with cumulative OR for operating time was 42 (95% CI 38.3 – 45.7); blood loss was evaluated in 19 studies with 5207 participants and an OR of 144.36 (95% CI 149.2-139.5) and 26 studies with 6460 participants reported on hospital stay with OR of 3.26 (95% CI 3.51 – 3.01) while lymph node yield was reported in 16 studies with 5515 participants and OR of 0.24 (0.82 – 0.34) respectively; all favoring laparoscopy. The meta analysis of present data suggest that laparoscopic resection of malignant esophageal or colonic carcinoma may be a better alternative as it has better short term outcome with no difference in survival at 5 years.

**Conclusion:** The results of present meta-analysis suggests that despite having a higher operating time, the blood loss and the hospital stay is significantly lower in laparoscopic group. The lymph node yield shows a trend favoring laparoscopy, however the effect is not significant. Laparoscopic colectomy appears to be a better method of surgery for colorectal cancer.

**Key words:** Colon cancer, Colorectal carcinoma, Laparoscopy.

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### Introduction

Laparoscopic surgery for colorectal cancer has been controversial from the beginning of its first introduction in late 1990s [1]. Since then several of the prospective randomized

controlled trials have demonstrated higher efficacy with regards to the short term outcomes like shorter hospital stay, reduced analgesic use, and earlier recovery to bowel movements [2-15]; however, the mean operating time and the average blood loss is higher while the number of lymph nodes retrieved has not been shown to differ significantly [3, 5, 6, 9, 11, 13, 16-43]. With regards to the long term survival data, again no difference in survival has been found with 3 years [16, 14, 22] and 5 years follow-up [3, 16-17, 22-24]. Thus, a meta-analysis appears to be the best way to recognize the congruity of these trials and studies.

## Material and Methods

### Search strategy

Randomized controlled trials (RCTs) of all the published data comparing laparoscopic and open surgery for colorectal cancer were searched in the electronic databases including Cochrane Library, MEDLINE, EMBASE, Pubmed and Google scholar for the years 1996–July 2010. Searches were carried out using medical subject headings (MeSH) and free text words in combination with the search strategy for randomized controlled trials described by Dickersin *et al.*, [26]. The following search was adapted for each database: laparoscopy [MeSH], surgery [MeSH], colon [MeSH], colectomy [MeSH], open [MeSH], colonic neoplasms [MeSH], colon cancer [MeSH], colorectal cancer [MeSH], and rectal neoplasms [MeSH].

All non-randomized studies and unpublished data were excluded. Trials reported in language other than in English were also excluded.

### Data extraction

The following data were collected in all randomized controlled trials: neoadjuvant therapy, tumor localization (Right/Transverse/Left colon, rectum), operating time, blood loss, hospital stay, time to pass flatus, time and duration of analgesic use, time to start oral feeds, type of resection

(right-sided, left-sided, rectal, abdominoperineal excision, extended colectomy, others), tumor stage (Dukes A,B,C and TNM I–IV), depth of invasion of bowel wall, grade of differentiation, number of lymph nodes harvested, pathological N stage, resection margins including distal and radial margins, complication rates, leakage rates, wound infection, morbidity and mortality rates, recurrence rates, mean follow-up, overall survival, disease free survival, adjuvant therapy.

### Assessment of methodological quality

- Review by MP, MS.
- Data analysis based on the ‘intention-to-treat’-principle.

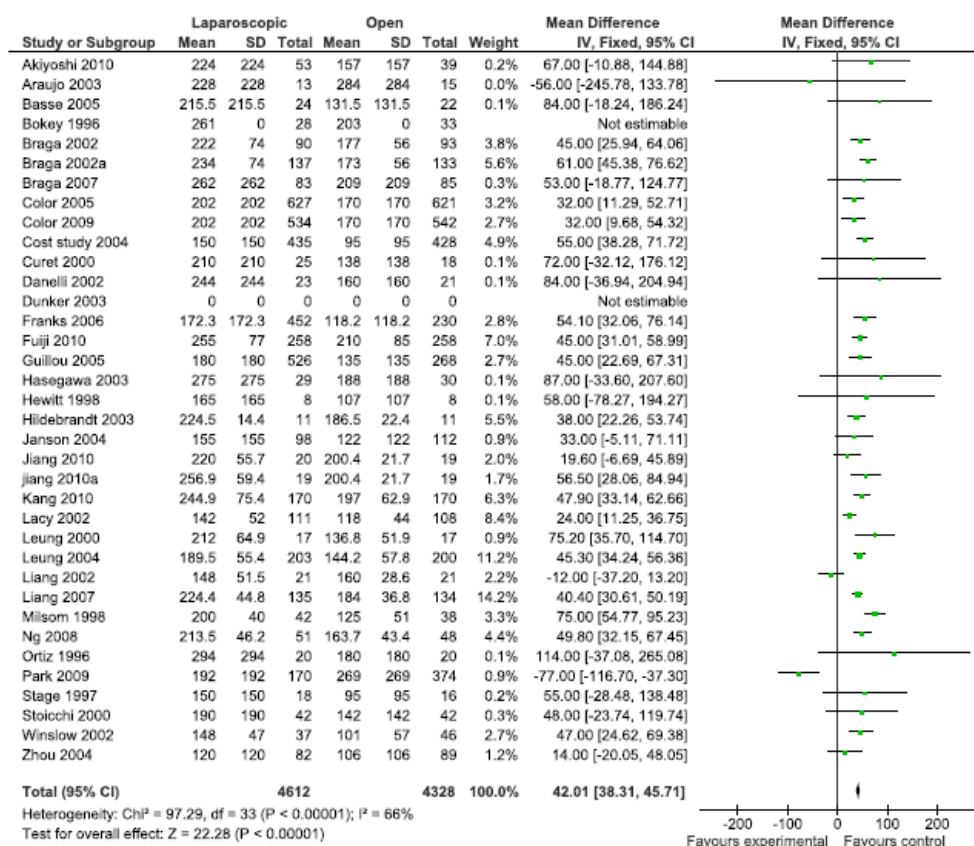
### Statistical analysis

The data regarding the short term and long term variables were extracted and entered in the Revman 5 software. For continuous data inverse variance method using mean difference was used to calculate the odds ratio and 95% CI using either random or fixed effect. For dichotomous variables odds ratios with their 95% confidence intervals were calculated. Analyses were performed using fixed effects models. Due to the large number of small studies that were included, these analyses were compared with analyses using random effects models. Heterogeneity was tested using Chi square and  $I^2$  test. Significance was tested with Z test.

## Result

A total of 61 published papers were identified. Of these 20 were excluded because 1 included benign diseases (Inflammatory bowel disease, polyps); one included advanced colorectal cancer; two were repetitions; and in 16 articles relevant data could not be extracted. Thus a total of 41 articles of RCTs were identified containing 43 studies. All of the included RCTs were published as full articles.

A total of 43 comparisons were identified from 41 RCTs, not all variables were available in all studies, and hence only those studies



**Figure 1: Operating time (36 studies, 8940 participants, favor open surgery).**

with particular variables were used for individual meta-analysis. Data on operating time was extracted from a total of 35 studies comprising 8940 participants. The mean/median operating time ranged from 120-256 minutes in; laparoscopy arm compared to 95-269 minutes in open surgery (Figure 1). The cumulative odds ratio was 42 with 95% CI of 38.3 – 45.7 favoring open surgery. Blood loss was evaluated in 19 studies with 5207 participants and cumulative OR of 144.36 favoring laparoscopy (95% CI 149.2-139.5). The average blood loss during Laparoscopic surgery was 20-320 ml versus 79-555 ml in open arm respectively (Figure 2). Hospital stay was studied in 26 studies with 6460 participants reported an OR of 3.26 (3.51 – 3.01) again favoring laparoscopy (Figure 3). Lymph node yield was reported in 16 studies with 5515 participants, an odds ratio -0.24 (0.82 – 0.34) was observed favoring laparoscopic procedures, although not clinically significant (Figure 4). Data from

three studies including 2733 participants revealed an odds ratio of 0.97(0.8-1.17) showing no significant difference in survival at three years of follow up (Figure 5). A total of 2966 participants from 5 studies showed an equivocal 5 years of survival between the two arms.(Odds ratio of 1.08 and 95% CI 0.9-1.28) (Figure 6).

**Discussion**

The introduction of Laparoscopic technique has been enthusiastically followed to the resection of colorectal cancer for more than 10 years. As of today, most of the colorectal surgeons routinely use the laparoscopic approach and attribute the advantages to the quicker functional recovery and comparable oncologic results. Till of date many trials have reported many benefits of the laparoscopic method, including the short term and the long term aspects. Short term benefits include reduction in surgical stress and

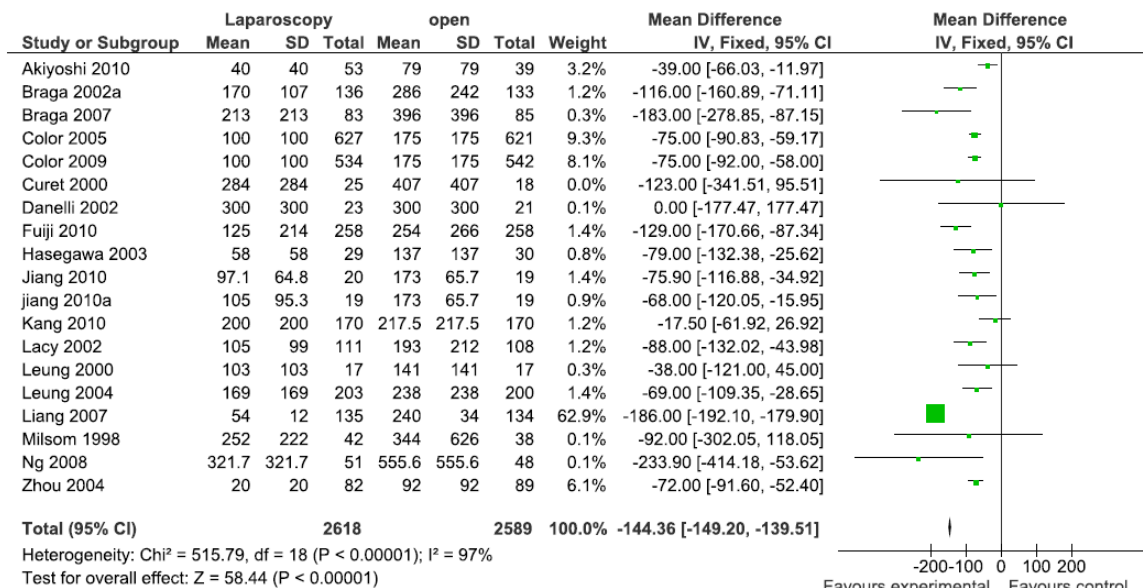


Figure 2: Blood loss (19 studies, 5207 participants; favors laparoscopy).

immunosuppression, less intraoperative blood loss, less postoperative pain and the requirement of analgesia, early recovery of bowel function in terms of flatus and feces, reduced hospital stay, and faster recovery to perform normal activities [15, 44-47]. This is also an important confirmatory finding that provides support for the laparoscopic

approach in terms of long-term survival by confirming from a surgical standpoint that the laparoscopic approach provides as good a resection as the open approach for treating CRC. But the feasibility of the technique will only be established if the long term outcomes are equally comparable and acceptable. Some of the studies have also concluded that

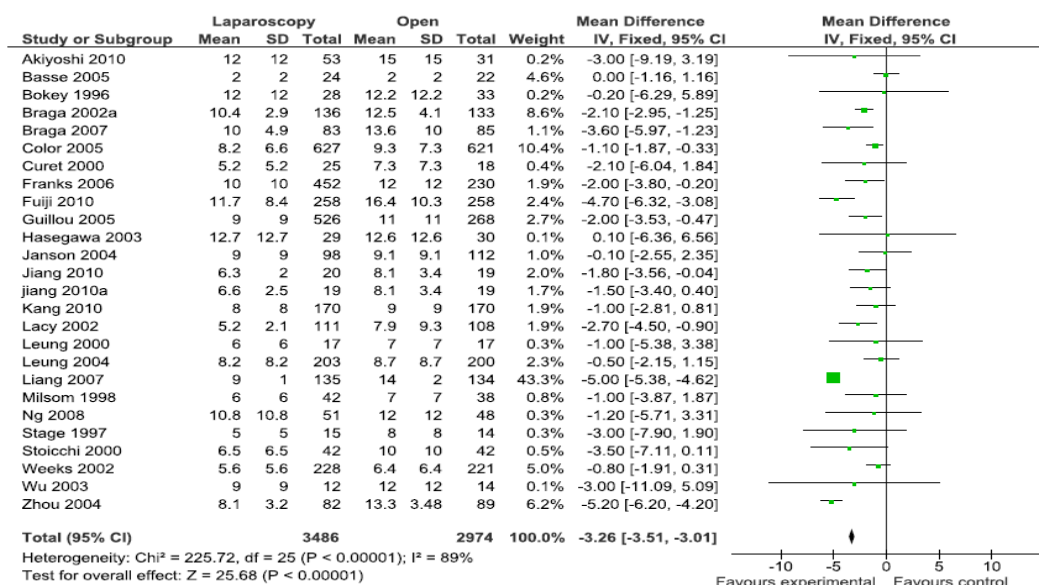


Figure 3: Hospital stay (26 studies, 6460 participants; favor laparoscopy).

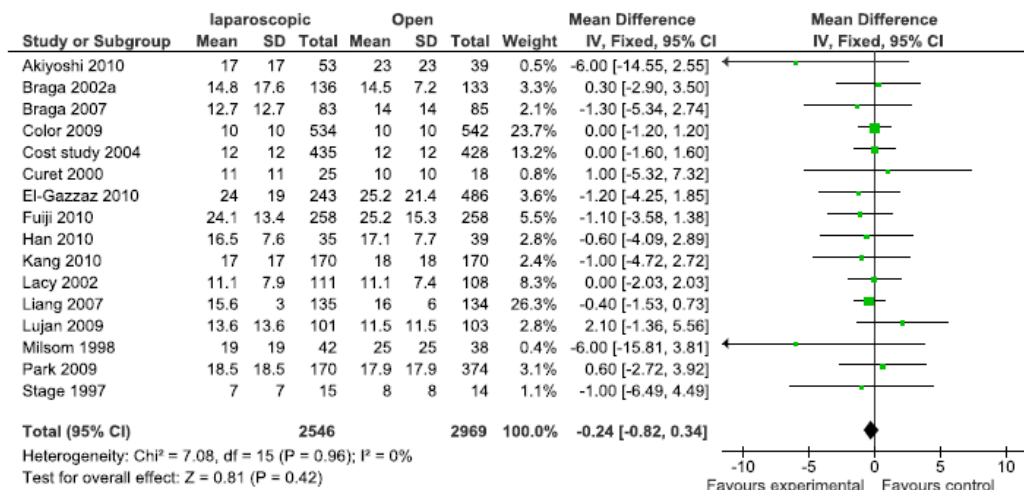


Figure 4: Lymph node yield (16 studies, 155 participants; No significant difference).

laparoscopy may even be detrimental to the patient with a higher recurrence and mortality rates [21, 48, 49]. The operative time was significantly longer with laparoscopic cancer surgery as compared with open surgery; a finding that has been consistent in laparoscopic colorectal surgery. Postoperative recovery was significantly better for patients who underwent laparoscopic resection in terms of bowel function and shortened hospital stay. This was also true for abdominoperineal resections, for which the requirement for parenteral analgesia was also significantly reduced in the laparoscopic group. It is important to note that time to feeding solids is a measure of recovery that is prone to bias, because surgeons with an interest in laparoscopic cancer surgery are likely to feed their patients earlier than for open rectal cancer surgery. Time to first bowel

movement is a better measure, but it may also be affected by the decision to commence oral intake. Improvement in the return of bowel function and reduced hospital stay has been shown by both the COST and Conventional versus Laparoscopic-Assisted Surgery in patients with Colorectal Cancer (CLASICC) trials for laparoscopic colorectal cancer surgery, although neither has demonstrated an improvement in quality of life. The results of this meta-analysis of patients have shown that there was no significant difference in the proportion of patients with the “number of lymph nodes harvested” when considering the laparoscopic groups. This finding suggests that specimens from laparoscopic and open surgery were comparable in terms of their adequacy of resection and oncological clearance. Because these operative factors strongly influence the likelihood of curative

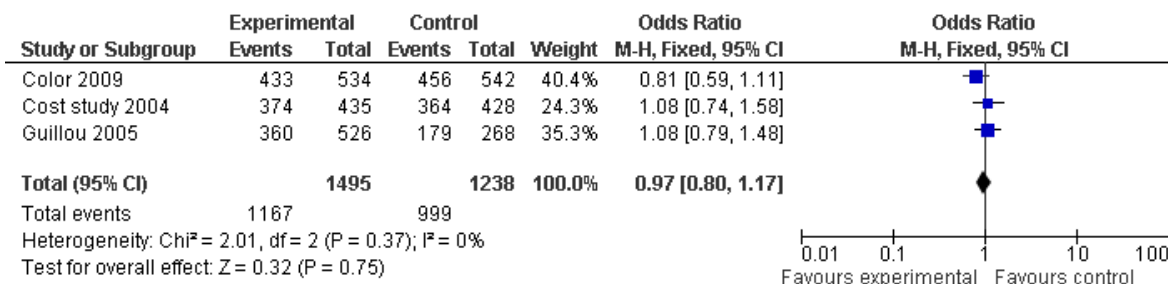
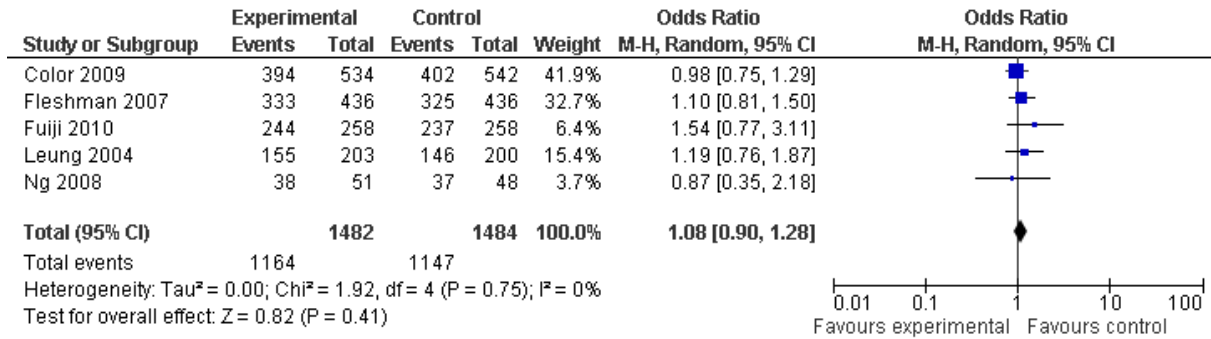


Figure 5: 3 year overall survival (3 studies; 2733 participants; no significant difference).



**Figure 6: 5 year overall survival (5 studies, 2966 participants; no statistically significant difference).**

resection and ultimately, survival after laparoscopic surgery for colorectal cancer, this is an important confirmatory finding. The presented meta-analysis shows that long term results in terms of 3 or 5 year survival are not different by two approaches. It should be noted that these studies has some limitations. Since patients who were lost to follow-up are excluded, thereby lowering both the power and the validity of the studies. This could cause a bias. Secondly, we did not perform a separate analysis comparing converted procedures, completed laparoscopic procedures, and open surgery procedures for CRC, since this analysis would be biased. Thirdly, it was not possible to match all patient groups for tumor grade, stage, and adjuvant treatment, all of which are factors known to affect outcome for patients with rectal cancer. This study could not account for the learning curve associated with the technique and its effect on postoperative outcome, and this is an important consideration because it has been suggested that laparoscopic resection of the rectum is more technically demanding and is associated with a longer learning curve than other laparoscopic colonic resections.

## Conclusion

The meta analysis of present data suggest that laparoscopic resection of malignant colonic carcinoma may be a better alternative as it has better short term outcome with no difference in survival at 5 years. Therefore,

successful laparoscopic colorectal resection for CRC is as effective as open surgery in terms of oncological outcomes, and these results support the continued use of laparoscopic surgery in patients with CRC.

## Authors' Contribution

**RKS:** Did the literature search and prepared the manuscript.

**MS:** Literature search, analysis and manuscript preparation.

**MP:** Concept, Design, Analysis and interpretation of data.

## Conflict of Interests

The authors declare that there are no conflicts of interests.

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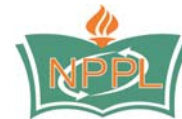
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