

Effect of cancer characteristics and oncological outcomes associated with laparoscopic colorectal resection converted to open surgery

A meta-analysis

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Abstract

Background: Although laparoscopic colorectal cancer resection is an oncologically safe procedure equivalent to open resection, the effects of conversion of a laparoscopic approach to an open approach remain unclear. This study evaluated the cancer characteristic and oncological outcomes associated with conversion of laparoscopic colorectal resection to open surgery.

Method: We conducted searches on PubMed, EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials. We included the literature published until 2018 that examined the impact of laparoscopic conversion to open colorectal resection. Only randomized control trials and prospective studies were included. Each study was reviewed and the data were extracted. Fixed-effects methods were used to combine data, and 95% confidence intervals (CIs) were used to evaluate the outcomes.

Results: Twelve studies with 5427 patients were included. Of these, 4672 patients underwent complete laparoscopic resection with no conversion (LAP group), whereas 755 underwent conversion to an open resection (CONV group). The meta-analysis showed significant differences between the LAP group and converted (CONV) group with respect to neoadjuvant therapy ($P = .002$), location of the rectal cancer ($P = .01$), and recurrence ($P = .01$). However, no difference in local recurrence ($P = .17$) was noted between both groups.

Conclusion: Conversion of laparoscopic to open colorectal cancer resection is influenced by tumor characteristics. Conversion of laparoscopic surgery for colorectal cancer is associated with a worse oncological outcome.

Abbreviations: CIs = confidence intervals, CONV = converted, CRC = Colorectal cancer, LAP = laparoscopic, LR = local recurrence, OS = overall survival, RR = risk ratio.

Keywords: cancer characteristic, colorectal cancer, conversion, laparoscopic, oncologic outcome

1. Introduction

Laparoscopic resection for colorectal cancer (CRC) was first reported by Jacobs and Verdeja in 1991,^[1] and it is considered a safe procedure. Considering that patients may require conversion has become important as conversion surgery can be associated with a worse postoperative course and may have a worse long-term oncological outcome.^[2–9] Conversion from a laparoscopic

resection to an open resection for CRC has been widely reported. In these studies, the conversion rates have been reported as approximately 13.9%.^[10–21] The effects of converting a laparoscopic (LAP) procedure to open surgery on postoperative outcomes have been disputed. To successfully complete the operation, the surgeon must possess advanced skills, including the ability to recognize the anatomy and perform the requisite surgical techniques. Most experts agree that LAP colorectal cancer resection has a learning curve.^[22] Despite the expertise of the surgeon, there remains a subset of patients who will never be suitable candidates for LAP surgery and in whom there can be little justification for attempting a LAP approach.

The benefits of LAP surgery has been greatly advantageous for the treatment of colorectal malignancy cancer. However, the application of minimally invasive techniques to treating CRC resulting in conversion to open colorectal cancer resection might be detrimental. Potential risks after curative resection of CRC involve cancer characteristics such as neoadjuvant therapy and location of tumor. Similarly, the oncologic outcomes after conversion of laparoscopic colorectal cancer resection remain unclear and are a concern when treating patients with CRC. Therefore, the aim of the meta-analysis was to analyze data to determine the cancer characteristics that were predictive of conversion from LAP resection to open resection in patients diagnosed with CRC and the long-term oncological outcomes of the conversion procedure.

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2. Materials and methods

2.1. Search strategy

The PubMed, EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials were searched to locate articles published until 2018, including articles referenced in the publications. The study was performed with approval from the institutional research ethics committee of Hongqi Affiliated Hospital to Mudanjiang Medical University. We also used the related articles function to broaden the search. Moreover, The following medical subject heading (MeSH) terms were searched using the Boolean terms (laparoscopic OR endoscopy) AND (cancer OR carcinoma OR adenocarcinoma OR tumor OR tumor) AND (colorectal OR rectal) AND (prognosis OR outcome) AND (conversion OR converted). (Table 1)

2.2. Inclusion and exclusion criteria

The inclusion criteria were as follows: studies that conversion from laparoscopic to open colorectal cancer resection clinical trials until 2018. The exclusion criteria were as follows:

studies of case reports, letters, or reviews without original data, non-English papers, articles that were not full-text and retrospective studies; non-colorectal cancer; benign disease and robotic-assisted surgery were excluded.

The endpoints of the study were to assess the laparoscopic to open colorectal cancer resection which is influenced by tumor characteristics and the impact of conversion on the long-term outcome of surgery for CRC.

2.3. Data extraction

Two review authors independently assessed the quality of the potentially eligible studies with disagreeing resolved by a third

reviewer. Data were extracted independently from each of the included studies such as, authors' names, year of publication, study type, tumor location, total number of patients included and number of patients who developed conversion from laparoscopic to open colorectal cancer resection.

2.4. Statistical analysis

Statistical analysis was performed by using the Review Manager (RevMan 5.0) software, version 5.0. A pooled risk ratio (RR) with 95% confidence intervals (CIs) was used to assess the outcomes of the studies. I^2 statistics were used to evaluate the between-study heterogeneity analysis in this meta-analysis. The heterogeneity among studies was tested by Q statistic and quantified by I^2 statistic. As a guide, I^2 values <50% indicated moderated and >50% indicated high heterogeneity. The quality assessment of included studies in this meta-analysis.

3. Result

3.1. Eligible studies

The initial search retrieved a total of 2533 references, and after screening the titles and abstracts of the identified articles, 2303 studies were excluded because they were not concerning converted patients. Among these studies, 230 studies were excluded after duplicate removed and we evaluated 18 potential candidate studies in the full text, 6 of which were retrospective studies. Finally, 12 studies were included in this meta-analysis, all of which were published until 2018. The definitions of conversion included a description of enlarging an incision or performing an unplanned laparotomy to achieve the remaining operative steps. The included study is presented in Table 2. There were prospective studies involving 5427 patients, of which 4672 had completed LAP surgery and 755 had undergone conversion

Table 1

Flow chart of the literature search and study selection process.

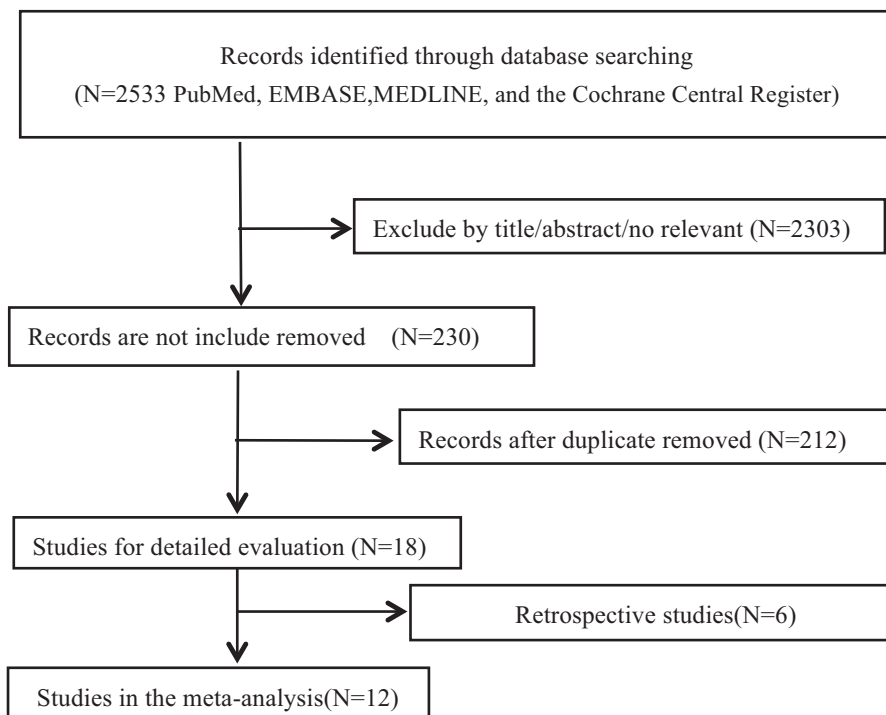


Table 2
Main characteristics of the 12 trial studies.

Ref.	Year	Study Type	Total of patients	Converted	Colon/rectal	Mortality 30-d		Recurrence	
						LAP	CONV	LAP	CONV
Chan A et al	2008	Prospective	470	41	Both	1	1	12	4
Franko et al	2008	Prospective	174	31	Both	1	2	N	N
Rottoli M et al	2009	Prospective	173	26	Rectal	0	0	17	7
Ptok H et al	2009	Prospective	346	56	Colon	1	1	N	N
White I et al	2011	Prospective	175	25	Both	0	1	N	N
Martinek L et al	2012	Prospective	243	17	Both	7	0	37	3
Rottoli M et al	2012	Prospective	93	31	Both	1	0	11	8
Rickert A et al	2013	Prospective	162	38	Rectal	0	1	15	5
Allaix M et al	2013	Prospective	1114	122	Both	3	0	N	N
Bondia et al	2014	Prospective	207	33	Both	N	N	N	N
Keller DS et al	2014	Prospective	141	25	Rectal	1	0	8	2
LI J et al	2015	Prospective	217	33	Colon	N	N	50	11

CONV=converted, LAP=laparoscopic.

surgery at an average rate of 13.9%. Besides, all studies reported the number of patients who developed completed LAP surgery and required a conversion after LAP.

3.2. Cancer characteristics and conversion

Conversion to open surgery resections have a risk of Neoadjuvant therapy, 6 studies including 1214 patients for analysis included data about Neoadjuvant therapy. (RR: 0.73,95% CI: 0.61-0.88, P=.0008)(Fig. 1); Conversion to open surgery resections have a risk of tumor location of rectal, 5 studies including 1188 patients for analysis included data about tumor location in the rectum (OR: 0.71,95% CI: 0.55-0.92, P=.01)(Fig. 2);

3.3. Follow-up outcome and conversion

Twelve studies including 5427 patients for analysis included data on conversion overall survival (OS). The range of OS follow up

was 36 to 60 months. Completed laparoscopic surgery was associated with a lower risk of over recurrence (RR: 0.67,95% CI: 0.49-0.92, P=.01) (Fig. 3), but not associated with a local recurrence (LR) (RR: 0.70,95% CI: 0.43-1.16, P=.17) (Fig. 4).

4. Discussion

The indications of “conversion” in laparoscopic colorectal surgery have not been defined. Cases of colorectal cancer for which a laparoscopic procedure is performed initially and is subsequently replaced by an open midline approach are defined as cases of conversion.^[16] However, conversion procedures have not been described in detail in the available literature. In some cases, a conversion is the necessary and responsible action to carry out. This study demonstrated that conversion to open operation in laparoscopic rectal resection is associated with greater mortality than only laparoscopic resection, and that certain cancer characteristics are predictive of conversion. The

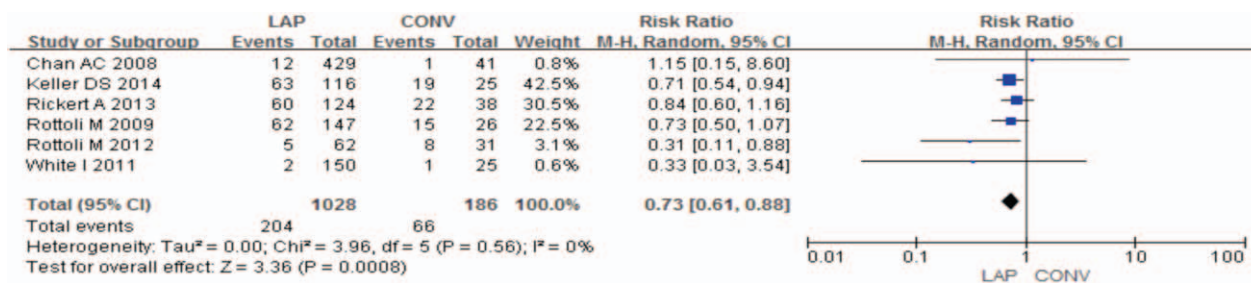


Figure 1. Conversion and Neoadjuvant therapy.

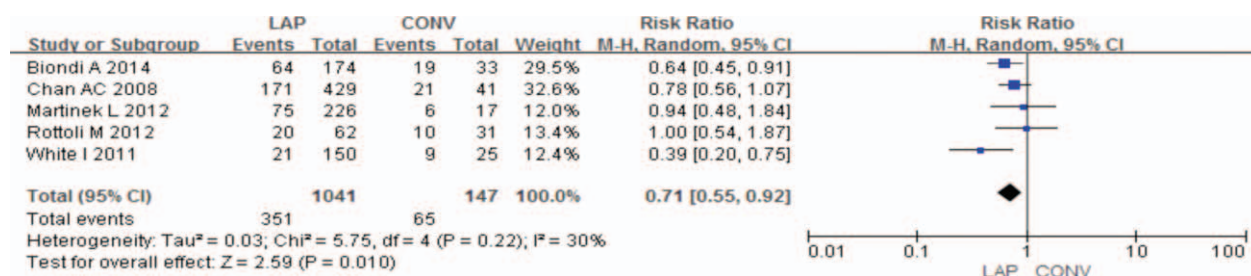


Figure 2. Conversion and Rectum location.

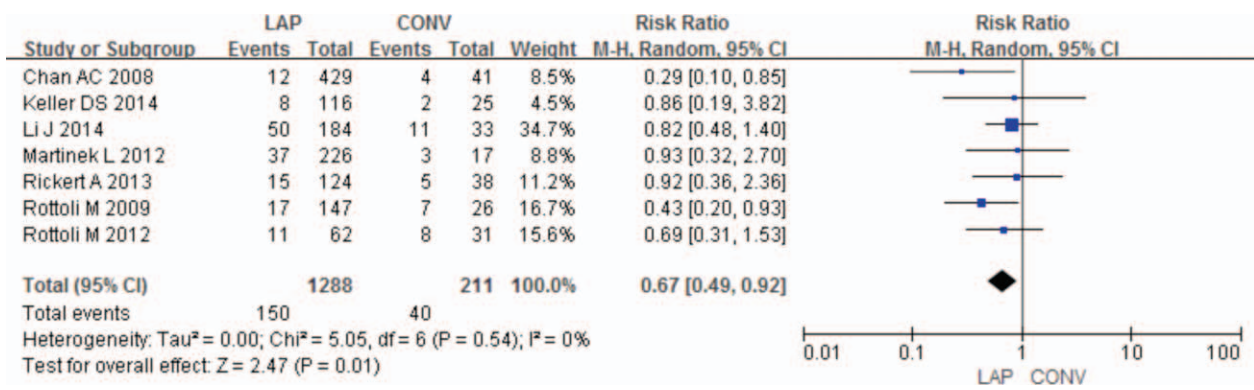


Figure 3. Conversion and Recurrence.

findings from the large number of patients included in the study suggest that conversion has negative effects on long-term outcomes in malignant colorectal tumors.^[18] Moreover, our findings show that the indications for laparoscopic procedure should be assessed carefully for malignant cancer characteristics in patients undergoing laparoscopic colorectal resection. Several factors influence the need to convert a laparoscopic to open colorectal operation. Generally, surgeon-related reasons for conversion can be controlled by adequate preparation and experience.^[12]

Our result indicated that the converted (CONV) group was characterized by an increased rate of complications, including neoadjuvant therapy, and tumor location, which lead to conversion. Therefore, patients who suffer from large and advanced tumors could present with difficulties during resection and these factors are associated with a high conversion rate and poor oncologic outcome.

Locally advanced cancers identified by an increased distance of tumor spread from the muscularis propria can possibly involve the adjacent viscera.^[23] It is recognized that laparoscopic surgery in patients with malignant cancer characteristics is technically challenging with a higher conversion rate. Although some researchers have demonstrated that obesity, male sex, BMI, adhesions, wound infections, anastomotic leakage, and large tumor size are risk factors for conversion, no studies have reported neoadjuvant preoperative therapy as a risk for conversion of laparoscopic colorectal resection.

Laparoscopic colorectal cancer resection is technically challenging; in this laparoscopic era, there has been little data in the literature on the conversion rates following neoadjuvant preoperative therapy. It remains unclear whether neoadjuvant preoperative therapy might result in an increased LAP group conversion rate and alter the postoperative morbidity in laparoscopic colorectal cancer resection. Neoadjuvant preoperative therapy is routinely administered to all patients with malignant cancer characteristics in China. However, neoadjuvant preoperative therapy is not routinely performed in Japan, owing to its adverse effects and recurrence rate.^[24] Neoadjuvant preoperative therapy is based on the clinical features at presentation such as histological features. However, there are no definitive findings indicating that neoadjuvant preoperative therapy introduces the conversion. We conducted this meta-analysis to evaluate the conversion rate of laparoscopic colorectal cancer surgery in patients who had received neoadjuvant preoperative therapy. The rate of conversion was influenced by neoadjuvant therapy in patients who underwent laparoscopic colorectal cancer resection, which may be because neoadjuvant therapy leads to severe fibrosis. Their study suggests that neoadjuvant therapy is the major cause of tissue degeneration around the tumor.^[25] The difference did not reach statistical significance, which might be attributable to the small sample size in the study.

We believe that the good results reported in CONV group of patients are associated with early conversion for locally advanced

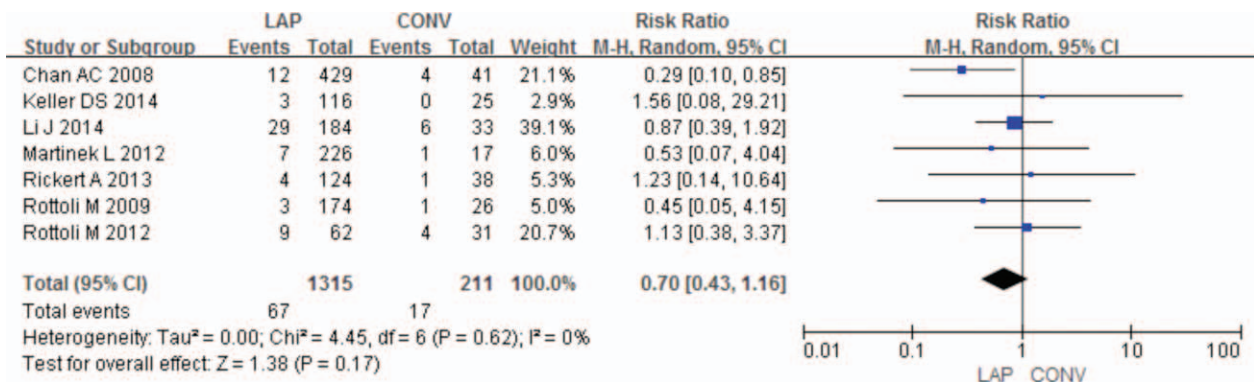


Figure 4. Conversion and Local Recurrence.

colorectal malignancies. This surgical aim avoids excessive tumor handling or incorrect oncologic dissection by the laparoscopic approach, reducing the risk of tumor cell spillage arising from local perforation. However, several studies have compared the short-term outcomes between the CONV group and LAP group. The evidence is controversial with some studies, showing a worse postoperative course in converted patients and others reporting no significant differences. In particular, among these studies that included only rectal cancer patients, one found better results in converted patients,^[26] whereas one found no differences.^[27] In addition, Green et al also found that converted colon cancer patients had significantly worse overall survival and disease-free survival, even after adjustment for stratification factors, age, sex, indicating that the disease itself adversely affects survival rather than the conversion procedure.^[28]

Recently, some retrospective studies have specifically investigated oncologic outcomes in T4 colorectal cancer patients after laparoscopic resection,^[29–31] concluding that a laparoscopic resection in T4 colorectal cancer is safe and does not affect oncologic outcomes in comparison with the open approach. However, future randomized control trials are needed to confirm these suggestions. Despite the limitations of a retrospective study, the results of these reports show that locally advanced cancer is the first reason for conversion to open surgery and that a T4 cancer is independently associated with poor survival. As there were no fixed criteria to determine the suitability for laparoscopic resection, the decision to perform either an open or a laparoscopic resection was left to the judgment of the consultant colorectal surgeon.

In this paper, the data collected on the long-term postoperative outcomes show a clear increase in mortality. The increase in the over survival and disease survival rates for converted patients completes this picture, showing that the postoperative long-term outcome for converted patients is markedly poorer. This clear evidence would appear to suggest that the long-term postoperative outcome is lower than that seen for open surgery, as already described in the direct comparison of LAP and CONV groups. In a comparison of the 2 groups, converted patients fared worse in terms of mortality of the LAP group. The evaluation of the long-term outcome in patients undergoing laparoscopic colorectal surgery plays a crucial role. Moloo et al^[32] reported their experience with 377 laparoscopic resections of colorectal carcinoma and found a lower survival rate in the converted group than in the completely laparoscopic group (75.7% vs. 87.2%). Our data show no relevant significant differences in the clinical outcomes regarding local recurrence and overall recurrence between patients in the CONV group and LAP group. A statistically significant difference in local recurrence was only found in one study. This large difference in the recurrence rate between the 2 groups can be explained by the difference in duration of follow-up time and tumor location.

Evidence regarding recurrence the following conversion to open surgery is controversial. Several series exist comparing recurrence rate between CONV and LAP groups. Ptok et al^[13] showed that oncological long-term results in the conversion group (35 patients) compared with the laparoscopic group (150 patients) and primarily open resection group (4611 patients) were lower with local recurrence rate and diminished average tumor-free survival ($P < .585$). There is no adequate evidence proving that the conversion of laparoscopic colorectal resection attempt does result in recurrence. However, the development of anastomotic leak has been associated with an increased risk of recurrence in patients undergoing resection for colorectal

cancer.^[33] Hence, careful selection of patients for laparoscopic colorectal resection is necessary.

We conclude from our findings that conversion of laparoscopic to open colorectal cancer resection is influenced by tumor characteristics and conversion of laparoscopic surgery to open surgery for colorectal cancer is associated with a worse oncological outcome.

Author contributions

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