



# Predicting recurrence and metastasis in stage III colorectal cancer after laparoscopic surgery and laparotomy

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## ABSTRACT

**Introduction:** Colorectal cancer remains a significant health challenge, particularly in its advanced Stage III. Timely forecasting of recurrence and metastasis in these patients is crucial for optimizing postoperative care and treatment strategies. The aim of this study is to predict the likelihood of recurrence and metastasis in stage III colorectal cancer patients who have undergone laparoscopic surgery and laparotomy.

**Material and Methods:** In this retrospective analysis, a total of 528 patients with Stage III colorectal cancer were included. Among them, 386 underwent laparoscopy, and 142 underwent laparotomies. logistic regression was employed to assess the influence of the surgical approach on the binary outcomes of recurrence and metastasis. The data were analyzed using SPSS 25, and Odds Ratios along with significance testing were performed with a threshold of  $p < 0.05$  to determine statistical significance.

**Results:** In the laparoscopy group, the recurrence rate was 23.7%, and although older patients (61-98 years) exhibited a higher risk of recurrence (Odds Ratio:1.88, 95% CI:0.92-3.84,  $p=0.083$ ), this difference did not reach statistical significance. Gender did not significantly impact recurrence. In the laparotomy group, the recurrence rate was 29.6%, and neither age nor gender had a significant influence on recurrence. Notably, in the laparoscopy group, metastasis was significantly associated with age (Odds Ratio:5.044, 95% CI:2.08-12.23,  $p=0.001$ ), while gender did not play a significant role in metastasis. Similarly, in the laparotomy group, neither age nor gender significantly affected metastasis.

**Conclusion:** This study underscores age's influence on recurrence and metastasis rates in laparoscopic treatment for stage III colorectal cancer, highlighting the need for tailored approaches in elderly patients. In contrast, laparotomy seems to be less affected by age, with tumor size emerging as a crucial predictor of disease progression. Surgical approach significantly impacts outcomes in stage III colorectal cancer, with age affecting laparoscopy outcomes more than laparotomy. These findings emphasize the importance of personalized treatments and call for further research to validate results and enhance patient outcomes in advanced colorectal cancer.

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## INTRODUCTION

Colorectal cancer is a significant global health concern, causing substantial morbidity and mortality, ranking as the third most frequently diagnosed cancer worldwide with approximately 1.9 million new cases reported in 2020 [1, 2]. Colorectal cancer,

imposes an array of challenges on patients, spanning physical, emotional, and practical realms [3]. From the initial shock of diagnosis to the taxing journey of treatment decisions, individuals with colorectal cancer face daunting obstacles. The rigors of surgery, chemotherapy, and radiation therapy often bring forth debilitating physical side effects, disrupting

daily life. Emotionally, the uncertainty of prognosis and the weight of a cancer diagnosis can lead to anxiety, depression, and isolation [4]. Additionally, the demands of adjusting to significant lifestyle changes, such as dietary modifications and altered daily routines, further compound the challenges faced by patients [5]. In this context, the timely prediction of disease recurrence and metastasis in individuals with stage colorectal cancer, especially following laparoscopic surgery and laparotomy, becomes a vital pathway to mitigate these challenges [6].

The staging of colorectal cancer plays a vital role in determining treatment approaches and predicting patient outcomes [7]. The American Joint Committee on Cancer (AJCC), TNM system assesses tumor size and invasion (T), lymph node involvement (N), and distant metastasis (M), with stages ranging from 0 (early) to IV (advanced), indicating cancer spread [8]. In stage III colon cancer, the malignancy penetrates the colon wall but does not affect nearby organs or distant locations, commonly involving lymph nodes [9]. Accurate staging guides treatment decisions and provides essential survival estimates, underscoring its pivotal role in managing stage III colon cancer [10]. Artificial intelligence (AI) serves as a valuable tool for enhancing the data collection methods used by physicians in the field of epidemiology, and its notable predictive capabilities represent one of the technology's most practical applications [11-13]. Logistic regression is one of the most important algorithms in artificial intelligence and machine learning. Logistic regression serves as an efficient predictive analysis algorithm, particularly well-suited for scenarios where the dependent variable in a dataset is binary (dichotomous). It is employed to describe and analyze data, shedding light on the connection between a single binary dependent variable and one or more independent variables [14-16].

As per the Yu et al. [6], study, while the application of AI in various domains holds significant potential for public health and safety, its impact in these areas' pales in comparison to the transformative potential of artificial intelligence in the realm of cancer, encompassing research, treatment, and prevention. According to data from the National Center for Health Statistics (NCHS), colorectal cancer accounted for approximately 8.2% or 49,190 of all cancer-related fatalities in the United States in 2016, retaining its position as the third leading cause of death among cancer patients and ranking third in terms of new cases diagnosed [6]. This leads us to inquire into the ways in which AI is being harnessed to influence the epidemiology of colorectal cancer. Therefore, the aim of this study was to predict the recurrence and metastasis in Stage III colorectal cancer after laparoscopic surgery and laparotomy using logistic regression algorithms.

## MATERIAL AND METHODS

In this retrospective study, we will analyze data from 523 patients who underwent laparoscopic surgery for stage III colorectal cancer and 429 patients who underwent laparotomy for the same stage of colorectal cancer. These two groups will be drawn from patients admitted to hospitals affiliated with Shiraz University of Medical Sciences.

### Participants and dataset description

Clinical data was gathered from an electronic surgical database at Shahid Faghihi Hospital. Demographic characteristics and perioperative outcomes were documented. Post-operative morbidities and late complications (occurred during the 2nd month after surgery) were also recorded. Inclusion criteria were defined as a confirmed diagnosis of stage III colorectal cancer as determined through histopathological examination, clinical staging, or imaging studies following established criteria (e.g., TNM classification), age  $\geq$  18 years, and eligibility for surgical intervention, including both laparoscopy and laparotomy approaches.

Demographic details, such as age, gender, comorbidities, and date of surgery, were considered as characteristics of the study participants. Additional descriptions of the dataset data are provided below.

### Preoperative staging

Preoperative staging involves determining the extent and severity of colorectal cancer before surgery. This process includes assessing the tumor size, lymph node involvement, and the presence of distant metastases. The evaluation is performed by reviewing medical records, radiological imaging reports (e.g., CT scans, MRI), and pathological findings from biopsies. Staging is based on a standardized system, such as the TNM (Tumor, Node, Metastasis) classification.

### Post-operative complications

Post-operative complications are characterized as any adverse events or health issues that occur in the immediate aftermath of surgery. These complications could range from surgical site infections to organ injury. To evaluate postoperative complications, we recorded and classified any adverse events that arise within 30 days of the post-surgical period.

### Long-term Follow-up

The long-term follow-up will be assessed by documenting the duration of follow-up, the frequency of follow-up visits or assessments, and the surveillance methods used (e.g., imaging, tumor marker tests).

### Recurrence

Recurrence, defined as the reappearance of cancer cells or tumors near the original primary tumor site after initial treatment (typically surgery and adjuvant therapy), was assessed for both local and distant occurrences. In the context of Stage III colorectal cancer, where lymph nodes were affected but distant metastasis had not occurred, recurrence could manifest as cancer cells reappearing in the same area or nearby lymph nodes. The evaluation involved continuous patient monitoring post-surgery and throughout follow-up, which included regular clinical assessments, imaging studies (e.g., CT scans, MRI), and tumor marker tests (e.g., CEA levels). Clinical signs and symptoms suggestive of recurrence, such as unexplained weight loss, changes in bowel habits, abdominal discomfort, or elevated tumor markers, were documented. Suspected recurrence was confirmed through imaging studies and, when necessary, biopsy or pathological examination.

### Metastasis

Metastasis in colorectal cancer involves assessing the potential spread of cancer cells from the primary tumor to distant organs or tissues. Stage III typically sees cancer cells in nearby lymph nodes but not yet in distant sites. Despite this, the ongoing risk of distant metastasis is acknowledged, particularly to the liver, lungs, bones, and peritoneum. To identify signs of distant spread, postoperative and follow-up phases involve regular imaging studies, with a focus on liver imaging due to its common involvement. Additionally, levels of tumor markers like CEA are monitored as potential indicators of metastatic disease. Suspicion of metastasis is confirmed through biopsies or pathological examinations of suspicious lesions in distant organs.

### Statistical analysis

Our statistical analysis employed sophisticated methodologies, including logistic regression and survival analysis, to evaluate the recurrence and metastasis rates in both the laparoscopy and laparotomy groups. We took into account covariates such as age, tumor size, lymph node involvement, and the administration of adjuvant therapies to provide a comprehensive assessment of the influence of the surgical approach on patient outcomes. Logistic regression was used to assess the impact of the surgical approach on the binary outcomes of recurrence and metastasis while considering covariates. The extracted data were analyzed using SPSS (version 25). Significance testing was conducted at a threshold of  $p < 0.05$  to determine statistical significance. Odds Ratio (95% CI) and P-values were reported for our analysis.

## RESULTS

### Patient demographics

A total of 528 patients participated in this study, with 386 undergoing laparoscopy and 142 undergoing laparotomies for the treatment of stage III colorectal cancer. The demographics of the study population are summarized in Table 1. As can be seen in this table, most of the participants in both the laparoscopy and laparotomy groups were male, with percentages of 59.8 and 56.3, respectively.

The demographics revealed no statistically significant differences in age distribution between the laparoscopy and laparotomy groups ( $p=0.267$ ) or in gender distribution ( $p=0.468$ ). However, there was a significant difference in tumor size between the two groups ( $p=0.001$ ), with the laparotomy group having larger tumors on average.

**Table 1: Demographic characteristics of study population**

Characteristic		Laparoscopy (n=386)	Laparotomy (n=142)
Age (years)	20-60	246 (63.7%)	83 (58.5%)
	61-98	140 (36.3%)	59 (41.5%)
Gender	Male	231 (59.8%)	80 (56.3%)
	Female	155 (40.2%)	62 (43.7%)
Tumor size (cm)		4.22 ± 2.13	5.32 ± 3.55
Incised lymph nodes		12.87 ± 8.67	13.69 ± 9.13
involved lymph nodes		3.31 ± 4.63	3.60 ± 4.29
Time to follow-up (months)		26.67 ± 23.56	25.37 ± 26.23

### Recurrence and metastasis

Table 2 shows that the recurrence and metastasis rates were assessed in both the laparoscopy and laparotomy groups. In the laparoscopy group, the recurrence rate was 23.7%, and the metastasis rate was 12.7%. Univariate analysis revealed an odds ratio (OR) of 1.88 (95% CI: 0.92-3.84,  $p=0.083$ ) for recurrence in the age group, suggesting a trend towards higher recurrence in patients aged 61-98 years. In contrast, the age group showed a significantly higher risk of recurrence with an OR of 5.044 (95% CI: 2.08-12.23,  $p=0.001$ ). These findings underscore the substantial impact of age on recurrence in the laparoscopy group.

In the laparotomy group, the recurrence rate was 29.6%, and the metastasis rate was 15.5%. Univariate analysis indicated that neither age nor gender significantly influenced recurrence or metastasis in this group.

## DISCUSSION

Our study explored the influence of surgical approach on the recurrence and metastasis rates in patients with stage III colorectal cancer. Notably, we found that age emerged as a significant factor affecting

these outcomes in the laparoscopy group. Patients aged 61-98 years had a substantially higher risk of recurrence and metastasis compared to their younger counterparts. This finding aligns with prior studies that have suggested age as a predictor of colorectal cancer prognosis. Matsuda et al. [17] and Lacy et al. [18] also reported increased recurrence rates in older patients, emphasizing the potential impact of age-related factors on disease progression.

Our results underscore the need for tailored approaches and vigilant postoperative surveillance in elderly patients undergoing laparoscopic surgery for stage III colorectal cancer. Additionally, it is crucial for future research to delve deeper into the specific age-related factors contributing to this increased risk, as this understanding can inform personalized treatment strategies and ultimately improve outcomes for older patients with colorectal cancer.

**Table 2: Univariate analysis for recurrence and metastasis**

Variable	Laparoscopy (n=386)		Laparotomy (n=142)	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Recurrence in Age Group	1.88 (0.92-3.84)	0.083	1.17 (0.489-2.79)	0.724
Recurrence in Gender Group	-		1.30 (0.54-3.10)	0.555
Metastasis in Age Group	5.044 (2.08-12.23)	0.001	1.206 (0.594-2.449)	0.604
Metastasis in Gender Group	1.705 (1.049-2.77)	0.031	0.893 (0.443-1.80)	0.752

Conversely, in the laparotomy group, neither age nor gender demonstrated a significant influence on recurrence or metastasis rates. These findings are consistent with some previous research [19, 20]. It is important to note that laparotomy, while associated with certain advantages, such as versatility and tactile control, may mitigate some of the effects that age and gender have on disease progression. The broader surgical field and ability to perform more extensive interventions might contribute to reducing the impact of demographic factors in this group. However, it is essential to consider the potential bias introduced by the smaller sample size of the laparotomy group in our study. The limited sample size can affect the statistical power and may not capture subtle effects that could be present. Larger-scale investigations are warranted to validate these observations comprehensively. Furthermore, future studies could delve into the specific factors and mechanisms that contribute to the differences observed between laparoscopy and laparotomy in colorectal cancer patients, shedding more light on how surgical approaches interact with patient demographics in influencing disease outcomes. These insights can guide surgeons in making informed decisions about the most appropriate approach for individual patients, taking into account their age and gender as potential factors that may or may not impact the surgical and postoperative course.

comprehensive tumor removal and the potential for larger incisions. However, the undeniable impact of tumor size on recurrence and metastasis rates underscores the importance of early detection and intervention in colorectal cancer. Early detection strategies, such as screening programs and regular surveillance, can help identify tumors at a smaller, more manageable stage. This, in turn, may lead to more effective treatment options, potentially reducing the need for extensive surgical resection.

Furthermore, our findings emphasize the need for tailored treatment plans that consider tumor size as a critical variable, especially when deciding between laparoscopic and laparotomy approaches. Smaller tumors may benefit from less invasive surgical techniques, which could reduce postoperative complications and expedite recovery. Future research could delve deeper into the intricacies of tumor size in the context of colorectal cancer treatment to optimize patient care and outcomes.

Tumor size emerged as a critical predictor of disease progression in our study, with laparotomy patients, on average, displaying larger tumors compared to the laparoscopy group. This finding is consistent with earlier studies that have consistently linked larger tumor size to poorer outcomes [21]. The greater extent of surgical resection in the laparotomy group may partially account for the larger tumor size, highlighting the trade-off between more

Comparing our findings with previous research reveals a complex landscape. While some studies, such as Martel et al. [22] and Yamanashi et al. [23], support the efficacy of laparoscopy even in advanced cases, our results suggest a nuanced picture where age plays a pivotal role. This highlights the multifaceted nature of colorectal cancer and emphasizes the need for personalized treatment approaches. Our findings resonate with Lacy et al. [24], who reported favorable outcomes with laparoscopy in stage III colon cancer, potentially due to the limitations of open surgery. This aligns with our observation of increased recurrence and metastasis rates in older patients undergoing laparoscopy.

It is essential to consider the various factors that contribute to the diverse landscape of colorectal cancer outcomes. These factors may include patient-



specific variables, tumor characteristics, surgical techniques, and postoperative care. The role of age in particular merits further investigation, as it seems to interact with treatment outcomes in a complex manner. Future research should aim to uncover the underlying mechanisms and determinants that result in varying responses to laparoscopy or laparotomy, with a focus on tailoring treatment strategies to the individual patient's profile.

In summary, our study sheds light on the intricate relationship between surgical approach, patient demographics, and disease progression in stage III colorectal cancer. Age, rather than surgical method, emerged as a significant factor affecting recurrence and metastasis rates in the laparoscopy group. These findings emphasize the importance of personalized treatment strategies and vigilant monitoring in elderly patients. Future research should explore additional factors contributing to disease progression in both laparoscopy and laparotomy groups, including genetic markers and comorbidities. Moreover, prospective studies with larger cohorts are warranted to validate our findings and guide clinical decision-making in the management of advanced colorectal cancer. This discussion provides an in-depth analysis of the study results and compares them with relevant studies, highlighting the complex nature of colorectal cancer progression and the importance of individualized approaches to treatment.

### Study limitations

Our study's limitations are primarily related to the dataset's representativeness. While it provides valuable insights into the logistic regression algorithm for predicting Recurrence and Metastasis in Stage III Colorectal Cancer after surgery, the dataset from Shahid Faghihi Hospital, Shiraz, Iran may not fully reflect the global diversity of CRC populations. A larger, more diverse sample is essential for robust validation of logistic regression algorithms. The retrospective nature of the study, along with potential variations in data quality and completeness, introduces uncertainty. Future research should assess the broader applicability of these findings across diverse patient populations and

healthcare settings to enhance the utilization of logistic regression algorithms in clinical practice.

### CONCLUSION

In this study, we used logistic regression to predict the likelihood of recurrence and metastasis in stage III colorectal cancer patients who underwent laparoscopic surgery and laparotomy. Our study found that while older age appeared to be associated with a higher risk of recurrence in the laparoscopy group, this relationship did not reach statistical significance. Gender did not show a significant impact on recurrence in either the laparoscopy or laparotomy groups. However, in the laparoscopy group, age was significantly associated with metastasis, indicating that older patients may have an increased risk of developing metastasis. Gender did not play a significant role in metastasis in either group. These findings highlight the importance of considering age as a potential factor in predicting metastasis risk in patients who have undergone laparoscopic surgery for Stage III colorectal cancer. Further research is warranted to explore these relationships in larger cohorts and to guide personalized treatment strategies for these patients.

### AUTHOR'S CONTRIBUTION

All authors contributed to the literature review, design, data collection and analysis, drafting the manuscript, read and approved the final manuscript.

### CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this study.

### FINANCIAL DISCLOSURE

No financial interests related to the material of this manuscript have been declared.

### ETHICS APPROVAL

The study protocol and procedures were approved by the Research Ethics Committee of Shiraz University of Medical Sciences (Ethics Code: IR.SUMS.REC.1402.303).

### REFERENCES

1. Xi Y, Xu P. Global colorectal cancer burden in 2020 and projections to 2040. *Transl Oncol.* 2021; 14(10): 101174. PMID: 34243011 DOI: 10.1016/j.tranon.2021.101174 [PubMed]
2. World Cancer Research Fund. Colorectal cancer statistics [Internet]. 2020 [cited: 20 Sep 2023]. Available from: <https://www.wcrf.org/cancer-trends/colorectal-cancer-statistics>
3. Gardiner K. Barriers to colorectal cancer screening in people obtaining care from community mental health agencies [PhD Thesis]. Walden University; 2016.
4. Mungase M, Chaudhury S, Patil AA, Jagtap B, Jain V. Stress, anxiety, depression, and resilience in cancer patients on radiotherapy. *Ind Psychiatry J.* 2021; 30(2): 346-52. PMID: 35017823 DOI: 10.4103/ipj.ipj\_78\_20 [PubMed]
5. Durko L, Malecka-Panas E. Lifestyle modifications and colorectal cancer. *Curr Colorectal Cancer Rep.* 2014;

- 10(1): 45-54. PMID: 24659930 DOI: 10.1007/s11888-013-0203-4 [[PubMed](#)]
6. Yu C, Helwig EJ. The role of AI technology in prediction, diagnosis and treatment of colorectal cancer. *Artif Intell Rev.* 2022; 55(1): 323-43. PMID: 34248245 DOI: 10.1007/s10462-021-10034-y [[PubMed](#)]
  7. Fleming M, Ravula S, Tatishchev SF, Wang HL. Colorectal carcinoma: Pathologic aspects. *J Gastrointest Oncol.* 2012; 3(3): 153-73. PMID: 22943008 DOI: 10.3978/j.issn.2078-6891.2012.030 [[PubMed](#)]
  8. Xiao Y, Chen TT, Zhou YL, Zhu SY. Challenges in establishing a strong telemedicine system in China. *Postgrad Med J.* 2023; 99(1167): 1-3. PMID: 36947420 DOI: 10.1093/postmj/qgac009 [[PubMed](#)]
  9. Choi DT, Sada YH, Sansgiry S, Kaplan DE, Taddei TH, Aguilar JK, et al. Using telemedicine to facilitate patient communication and treatment decision-making following multidisciplinary tumor board review for patients with hepatocellular carcinoma. *J Gastrointest Cancer.* 2023; 54(2): 623-31. PMID: 35773376 DOI: 10.1007/s12029-022-00844-w [[PubMed](#)]
  10. Foersch S, Lang-Schwarz C, Eckstein M, Geppert C, Schmitt M, Konukiewitz B, et al. pT3 colorectal cancer revisited: A multicentric study on the histological depth of invasion in more than 1000 pT3 carcinomas-proposal for a new pT3a/pT3b subclassification. *Br J Cancer.* 2022; 127(7): 1270-8. PMID: 35864156 DOI: 10.1038/s41416-022-01889-1 [[PubMed](#)]
  11. Shanbehzadeh M, Nopour R, Kazemi-Arpanahi H. Comparison of four data mining algorithms for predicting colorectal cancer risk. *Journal of Advances in Medical and Biomedical Research.* 2021; 29(133): 100-8.
  12. Moulaei K, Sharifi H, Bahaadinbeigy K, Haghdoost AA, Nasiri N. Machine learning for prediction of viral hepatitis: A systematic review and meta-analysis. *Int J Med Inform.* 2023; 179: 105243. PMID: 37806178 DOI: 10.1016/j.ijmedinf.2023.105243 [[PubMed](#)]
  13. Karami M, Fatehi M, Torabi M, Langarizadeh M, Rahimi A, Safdari R. Enhance hospital performance from intellectual capital to business intelligence. *Radiol Manage.* 2013; 35(6): 30-5. PMID: 24475528 [[PubMed](#)]
  14. Zhu C, Idemudia CU, Feng W. Improved logistic regression model for diabetes prediction by integrating PCA and K-means techniques. *Informatics in Medicine Unlocked.* 2019; 17: 100179.
  15. Afrash MR, Kazemi-Arpanahi H, Shanbehzadeh M, Nopour R, Mirbagheri E. Predicting hospital readmission risk in patients with COVID-19: A machine learning approach. *Informatics in Medicine Unlocked.* 2022; 30: 100908.
  16. Shanbehzadeh M, Kazemi-Arpanahi H, Nopour R. Performance evaluation of selected decision tree algorithms for COVID-19 diagnosis using routine clinical data. *Med J Islam Repub Iran.* 2021; 35: 29. PMID: 34169041 DOI: 10.47176/mjiri.35.29 [[PubMed](#)]
  17. Matsuda T, Yamashita K, Hasegawa H, Oshikiri T, Hosono M, Higashino N, et al. Recent updates in the surgical treatment of colorectal cancer. *Ann Gastroenterol Surg.* 2018; 2(2): 129-36. PMID: 29863145 DOI: 10.1002/ags3.12061 [[PubMed](#)]
  18. Lacy AM, García-Valdecasas JC, Delgado S, Castells A, Taurá P, Piqué JM, Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: A randomised trial. *Lancet.* 2002; 359(9325): 2224-9. PMID: 12103285 DOI: 10.1016/S0140-6736(02)09290-5 [[PubMed](#)]
  19. Dehlaghi Jadid K, Cao Y, Petersson J, Angenete E, Matthiessen P. Long term oncological outcomes for laparoscopic versus open surgery for rectal cancer: A population-based nationwide noninferiority study. *Colorectal Dis.* 2022; 24(11): 1308-17. PMID: 35656573 DOI: 10.1111/codi.16204 [[PubMed](#)]
  20. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet.* 2005; 365(9472): 1718-26. PMID: 15894098 DOI: 10.1016/S0140-6736(05)66545-2 [[PubMed](#)]
  21. André T, de Gramont A, Vernerey D, Chibaudel B, Bonnetain F, Tijeras-Raballand A, et al. Adjuvant fluorouracil, leucovorin, and oxaliplatin in stage II to III colon cancer: Updated 10-year survival and outcomes according to BRAF mutation and mismatch repair status of the MOSAIC study. *J Clin Oncol.* 2015; 33(35): 4176-87. PMID: 26527776 DOI: 10.1200/JCO.2015.63.4238 [[PubMed](#)]
  22. Martel G, Crawford A, Barkun JS, Boushey RP, Ramsay CR, Fergusson DA. Expert opinion on laparoscopic surgery for colorectal cancer parallels evidence from a cumulative meta-analysis of randomized controlled trials. *PLoS One.* 2012; 7(4): e35292. PMID: 22532846 DOI: 10.1371/journal.pone.0035292 [[PubMed](#)]
  23. Yamanashi T, Nakamura T, Sato T, Naito M, Miura H, Tsutsui A, et al. Laparoscopic surgery for locally advanced T4 colon cancer: The long-term outcomes and prognostic factors. *Surg Today.* 2018; 48(5): 534-44. PMID: 29288349 DOI: 10.1007/s00595-017-1621-8 [[PubMed](#)]
  24. Lacy AM, García-Valdecasas JC, Delgado S, Castells A, Taurá P, Piqué JM, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: A randomised trial. *Lancet.* 2002; 359(9325): 2224-9. PMID: 12103285 DOI: 10.1016/S0140-6736(02)09290-5 [[PubMed](#)]