# Evaluation of pathological outcomes and surgical radicality after laparoscopic resection of colon adenocarcinoma

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**Aim**
The aim of the present study was to assess the efficacy, pathological outcomes, and oncologic radicality after laparoscopic resection of colon adenocarcinoma.
**Patients and methods**
The study was conducted on 30 consecutive patients who had undergone laparoscopic resection of colon adenocarcinoma in the Surgical Oncology Unit, Department of Surgery, Faculty of Medicine, Alexandria University, Egypt (with exclusion criteria of patients with history of extensive abdominal surgery and obese patients with BMI>45 kg/m$^2$ and metastatic colorectal cancer).
**Results**
The mean age of the studied cases was 55.6 years, 53% of the studied cases had BMI more than 30 kg/m$^2$, 33% of the cases were sigmoid cancer, half of the cases (50%) were T2, and almost the other half were T3. The average procedure duration in the study was 190 min, 23% of the cases (seven cases) have been converted to open surgery, and the mean number of lymph nodes harvested was 13.5, with a range from 6 to 22. The analysis for the number of lymph nodes harvested by BMI showed that as the BMI increases, the likelihood for harvesting 12 lymph nodes or less increases as well. The Cramer's V test statistic (a measure of the degree of association between the two categorical variables 'lymph nodes harvested' and 'BMI') yielded a very strong correlation (value of '0.434').
**Conclusion**
Laparoscopy is a reliable method in colon cancer resection regarding surgical radicality, pathological outcomes, and efficacy.

**Keywords:**
BMI, colon cancer, laparoscopy, lymph nodes, surgical radicality

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## Introduction

According to the United States statistics, colon cancer is the third commonly diagnosed type of cancer among males and the second among females [1]. Laparoscopy has made a revolution in surgery since its introduction in 1980s, where the first laparoscopic appendectomy was done in 1983 [2] and the first laparoscopic cholecystectomy was done in 1987 [3]. The first laparoscopic resection for colon cancer was done in 1991 by Moises Jacobs in Miami, Florida, while performing a right hemicolectomy [4]. There are four main trials for laparoscopic resection of colon cancer. These are Clinical Outcomes of Surgical Therapy (COST) [5] trial, CLASSIC [6] trial, COLOR [7] trial, and Spanish trial [8].

The learning curve in laparoscopic colorectal surgery is technically demanding owing to the need to work in all quadrants on a mobile segment, need to expose and ligate substantial vascular structures, and the challenge of achieving an intracorporeal anastomosis [9]. At least 12 lymph nodes should be harvested in cancer colon surgery to attain adequate pathological reporting and staging [10]. Understaging by low number of harvested lymph nodes can affect the prognosis [11].

Regarding safety margins, 5-cm longitudinal resection margins (proximal and distal) are enough to decrease anastomotic site recurrence [12]. Circumferential resection margin is defined as the distance between the deepest point of the tumor (either direct tumor spread, neural or lymphovascular invasion, or nearest involved lymph node) and the resected mesenteric margin or the retroperitoneal fascia if found [13]. It should be noted here that the main objective of this study was to assess the efficacy, pathological outcomes, and oncologic radicality after laparoscopic resection of colon adenocarcinoma.

## Patients and methods

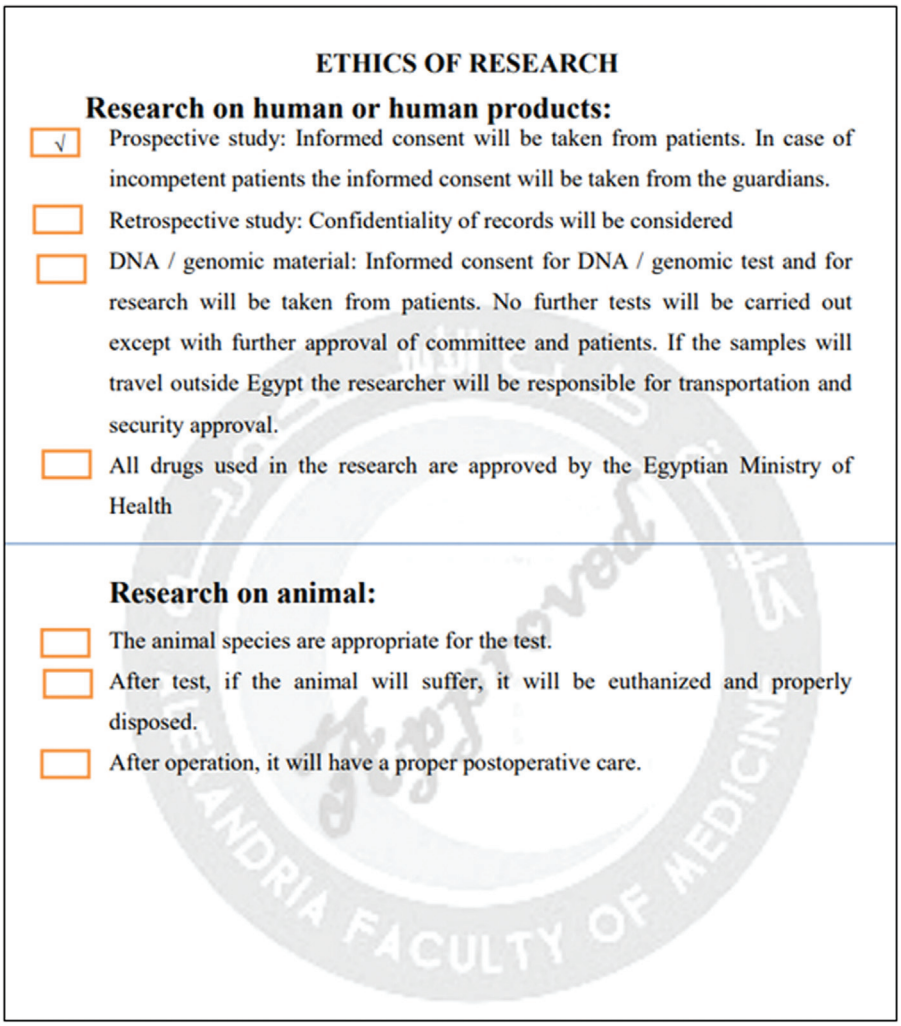
Before conducting the study, a formal approval from the 'Ethics of Research' Committee at Alexandria University was obtained (refer to Fig. 1). In addition, an informed written consent from each patient participating in the study was obtained. This study was then conducted on 30 patients who have done laparoscopic colectomy for colon adenocarcinoma, mainly in the Surgical Oncology Unit, Department of Surgery, Faculty of Medicine, Alexandria University, Egypt. It was very challenging to get more patients to participate in the study, mainly as the patients were found from only one unit (the Surgical Oncology Unit) at the Faculty of Medicine, Alexandria University in Egypt. Nevertheless, 30 samples are still significant enough to reach reliable conclusions. Specifically, in statistics, the typical minimum sample size is 30. For this, the research team made sure to have at least 30 patients to participate in this study. The exclusion criteria of patients were history of extensive abdominal surgery and obese patients with BMI greater than 45 $kg/m^2$ and metastatic colorectal cancer. Table 1 shows summary statistics of all explored variables in the study.

## Results

Regarding BMI variable, 53% of the studied cases had BMI more than 30, whereas 47% had BMI less than or equal to 30. A BMI value of 30 was used as the cutoff point to differentiate obese from nonobese patients.

Regarding the site of the tumor, all the sites of colon adenocarcinoma were included in this study, where their distribution was as follows: 33% of the cases were in the sigmoid, 27% in the recto-sigmoid region, 17% in the caecum or the ascending colon, 10% in the descending colon, 7% in the hepatic flexure, and 6% in the splenic flexure. The transverse colon tumors were not excluded, but there were no studied cases at that site.

**Figure 1**


ETHICS OF RESEARCH

Research on human or human products:

- [√] Prospective study: Informed consent will be taken from patients. In case of incompetent patients the informed consent will be taken from the guardians.
- [ ] Retrospective study: Confidentiality of records will be considered
- [ ] DNA / genomic material: Informed consent for DNA / genomic test and for research will be taken from patients. No further tests will be carried out except with further approval of committee and patients. If the samples will travel outside Egypt the researcher will be responsible for transportation and security approval.
- [ ] All drugs used in the research are approved by the Egyptian Ministry of Health

Research on animal:

- [ ] The animal species are appropriate for the test.
- [ ] After test, if the animal will suffer, it will be euthanized and properly disposed.
- [ ] After operation, it will have a proper postoperative care.

Formal approval from the 'Ethics of Research' Committee at Alexandria University for conducting the study.

**Table 1 Summary statistics of explored variables in the study**

| Continuous variables | | | |
|---|---|---|---|
| Variables of interest | Median | Mean | SD |
| Age (years) | 58 | 55.60 | 11.40 |
| Estimated blood level (ml) | 450 | 550 | 344.60 |
| Length of hospital stay (days) | 5 | 6.53 | 3.31 |
| Categorical (discrete) variables | | | |
| Variable of interest | Level | *n* (%) | |
| Sex | Male | 17 (56.67) | |
| | Female | 13 (43.33) | |
| BMI (kg/m$^2$) | ≤30 | 14 (46.67) | |
| | >30 | 16 (53.33) | |
| American Society of Anesthesiologists (ASA) level | I | 6 (20.00) | |
| | II | 14 (46.67) | |
| | III | 10 (33.33) | |
| Site | Caecum/ascending colon | 5 (16.67) | |
| | Splenic flexure | 2 (6.67) | |
| | Hepatic flexure | 2 (6.67) | |
| | Descending colon | 3 (10.00) | |
| | Sigmoid | 10 (33.33) | |
| | Recto sigmoid | 8 (26.67) | |
| (T) staging | 2 | 15 (50.00) | |
| | 3 and 4 | 15 (50.00) | |
| Obstruction | Nonpresent | 28 (93.33) | |
| | Present | 2 (6.67) | |
| Operation done | ELHC | 2 (6.67) | |
| | ERHC | 2 (6.67) | |
| | LHC | 3 (10.00) | |
| | RHC | 5 (16.67) | |
| | Sigmoidectomy | 10 (33.33) | |
| | Sigmoidectomy and anterior resection | 8 (26.67) | |
| Duration (min) | ≤180 | 17 (56.67) | |
| | >180 | 13 (43.33) | |
| Conversion to open? | None | 23 (76.67) | |
| | Applicable | 7 (23.33) | |
| Number of lymph nodes harvested | ≤12 | 11 (36.67) | |
| | >12 | 19 (63.33) | |
| Number of lymph nodes affected | ≤3 | 27 (90.00) | |
| | >3 | 3 (10.00) | |
| Lymphovascular and perineural invasion | Positive | 17 (56.67) | |
| | Negative | 13 (43.33) | |
| Deposits | Positive | 8 (26.67) | |
| | Negative | 22 (73.33) | |
| Morbidity | None | 24 (80.00) | |
| | Anastmotic leak, reoperation, and stoma | 1 (3.33) | |
| | Wound infection and burst | 2 (6.67) | |
| | Minor leakage, contained abscess, and pig tail | 1 (3.33) | |
| | Ureteric injury | 1 (3.33) | |
| | Wound infection | 1 (3.33) | |
| Days to return to diet | 3 days | 9 (30.00) | |
| | 4 days | 21 (70.00) | |

Regarding T staging of the tumor, half of the cases (50%) in this study were T2 and almost the other half was T3. No T1 tumors were among the studied cases, and there was only one case of T4 tumor that was invading the urinary bladder and the lateral abdominal wall. Two cases in the study presented with full blown picture of intestinal obstruction, whereas no cases in the study presented with signs of perforated viscus.

Regarding the type of the procedure done, the distribution of the laparoscopic procedures in this study was as follows: 33% of the cases had done sigmoidectomy, 27% had done sigmoidectomy with

anterior resection, 17% had done right hemicolectomy, 10% had done left hemicolectomy, 7% had done extended right hemicolectomy, and 6% had done extended left hemicolectomy.

Regarding the operative time, the mean duration of the procedure in this study was 190 min with a SD of 57.25 min. It should be mentioned that the duration of the procedure decreased with the progression in the learning curve. Regarding the estimated blood loss (EBL) variable, the mean EBL in this study was 550 ml, with a SD of 344.66 ml. This was measured by 'visual estimation method' done by the anesthesiologist.

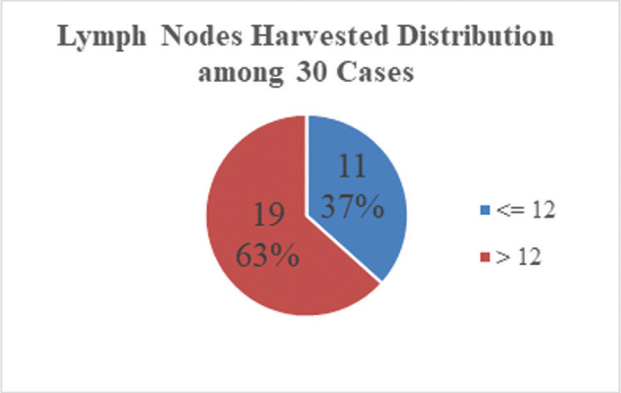
Regarding the rate of conversion to open, 23% of the cases (seven cases) in this study had been converted to open surgery. Two cases were the cases presented with intestinal obstruction, one case was T4 invading the urinary bladder and the lateral abdominal wall, one case was converted to repair ureteric injury by the urologist, and three cases were converted for making extracorporeal anastomosis owing to the unavailability of endo-GIA staplers or circular staplers.

Regarding the longitudinal (proximal and distal) and circumferential safety margins, all studied cases had negative margins except for one case which had positive circumferential margin. Regarding other pathological outcomes in the study, 90% of the studied cases had less than three lymph nodes affected, whereas 10% had more than three; 57% of the studied cases had positive lymphovascular and perneural invasion; 43% were negative for these invasions; and 27% had tumor deposits in their specimens, whereas 73% had no tumor deposits.

Regarding the number of lymph nodes harvested, the mean number of lymph nodes harvested was 13.5, with a range from 6 to 22. Furthermore, 63% of the studied cases had more than 12 lymph nodes harvested, whereas 37% had less than 12 lymph nodes. Figure 2 shows the distribution of lymph nodes harvested among the 30 cases, where the studied cases were divided in to those less than or equal to 12 lymph nodes harvested and those greater than 12.

The analysis for the number of lymph nodes harvested by BMI showed that as the BMI increases, the likelihood for harvesting 12 lymph nodes or less increases as well. More details are shown in the following points:

**Figure 2**



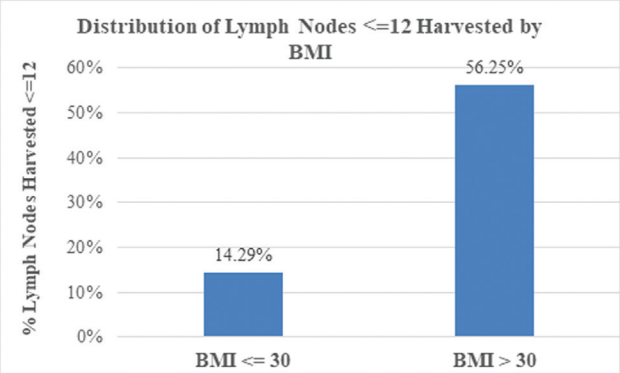

Lymph nodes harvested distribution among 30 cases.

**Table 2 Contingency table for 'lymph nodes harvested by BMI'**

| | BMI | | |
|---|---|---|---|
| | ≤30 | >30 | Total |
| Lymph nodes harvested | | | |
| ≤12 | 2 | 9 | 11 |
| >12 | 12 | 7 | 19 |
| Total | 14 | 16 | 30 |

(1) The contingency table for the distribution of 'lymph nodes harvested by BMI' is presented in Table 2.
(2) A $Z$ test of proportions was conducted to test whether a significant difference existed between the proportions of 'lymph nodes≤12' within 'BMI≤30' (14.29%) versus the proportion within 'BMI more than 30' (56.25%) per the data presented in Table 2. The test showed a significant difference at 5% significance level ($Z$ test statistic=−2.379 and $P$=0.017). For better visualization of this analysis, Fig. 3 is presented.
(3) A $\chi^2$ test of independence was also conducted to examine there existed a significant correlation (or association) between 'lymph nodes harvested' and 'BMI' per the data presented in Table 2. It was found that a significant correlation existed at 5% significance level ($\chi^2$ test statistic=5.662 and $P$=0.017).
(4) From the $\chi^2$ test, the Cramer's V test statistic (which is a measure of the degree of association between the two categorical variables 'lymph nodes harvested' and 'BMI') yielded a value of 0.434, which shows a very strong correlation. Typically, Cramer's V values range between 0 and 1. In general, the higher the value, the higher is the degree of correlation. The threshold values for Cramer's V test statistic values are shown in Fig. 4.

**Figure 3**




Distribution of lymph nodes harvested less than or equal to 12 by BMI.

**Figure 4**

| Phi and Cramer's V | Interpretation |
|---|---|
| > 0.25 | Very strong |
| > 0.15 | Strong |
| > 0.10 | Moderate |
| > 0.05 | Weak |
| > 0 | No or very weak |

Thresholds for degree of correlation based on Cramer's V values.

## Discussion

The review of literature has shown that very limited studies have investigated the correlation between the patient's BMI and the number of lymph nodes harvested during the laparoscopic resection of colon cancer. Thus, this correlation was investigated in this study, and this was one of the main contributions of this research.

Regarding the BMI, in their effort to determine the effect of visceral obesity and sarcoobesity on the outcomes of laparoscopic resection of colon cancer, Pedrazzani *et al.* [14] had about half of the patients studied in their research (50.6%) with BMI lower than 25 kg/m$^2$, 36.8% between 25 and 30 kg/m$^2$, and 12.6% higher than 30 kg/m$^2$. The authors found that increased visceral fat did not have a significant effect on the short-term outcomes after laparoscopic resection of cancer colon except for increased postoperative cardiac complications and increased incidence of prolonged postoperative ileus. In the Australian Laparoscopic Colon Cancer Study (ALCCaS) [15], 'BMI more than 35' was set as the exclusion criteria.

Regarding T staging of the tumor, in their effort to determine the outcomes of laparoscopic resection of colon cancer in Thailand as a new era, Tunruttanakul *et al.* [16] studied 58 cases in the laparoscopic arm; 24.1% of them were T1, 32.8% were T2, and 38% were T3. Leung *et al.* [17] published their results in 2004, and they excluded T4 tumors and those tumors presented with intestinal obstruction from their research. In the ALCCaS study [15], the CLASSIC study [18], the COST study [19], Braga *et al.* [20], Lacy *et al.* [21], and the COLOR trial [22], all of them excluded T4 tumors from their research.

Regarding the operative time, in the BARCELONA study [21], the mean operative time in the laparoscopic arm was 142 min. In the COST trial [19], the mean duration of the laparoscopic procedure was 150 min. In the CLASSIC trial [18], the mean duration for performing a laparoscopic colectomy was 180 min. In the COLOR trial [22], the mean operative time while performing the laparoscopic procedure was 145 min. Tunruttanakul *et al.* [16] found that the median operative time was 190 min, with a range of 90–420 min. In the meta-analysis of four RCTs (796 patients in the laparoscopic arm), Bonjer *et al.* [23] did not report the mean operative time.

Regarding the estimated blood loss variable, the median of EBL in the study by Tunruttanakul *et al.* [16] was 200 ml, with a range of 50–3000 ml. A Cochrane review of 25 RCTs assessing the short-term benefits of laparoscopic colorectal resection surgery has shown significantly reduced intraoperative blood loss compared with open surgery, with a weighted mean difference of 71.8 cm$^3$ (95% confidence interval of −113.0 to −30.8 cm$^3$; $P$=0.001) [24].

Regarding the rate of conversion to open, in the ALCCaS study [24], the number of participants was 592 and the rate of conversion to open surgery was 14.6%. In the CLASSIC study [18] in UK, there were 794 selected cases with a conversion to open rate of 29%. In the COLOR trial [22], 16% of the 1044 studied cases had been converted to open. In the COST study [19], there were 872 studied cases and the rate of conversion to open was 21%. In the BARCELONA study [21], there were 291 studied cases, and the published data in 2002 showed that the rate of conversion to open was 11%. In the study by Tunruttanakul *et al.* [16], the rate of conversion to open was 3.5% among the 58 studied cases in the laparoscopic arm. One case was due to a bulky descending colonic tumor invading the adjacent jejunum. The other conversion case was a sigmoid cancer in a portal hypertensive Child–Pugh B

cirrhosis patient, and the mesentery was markedly thickened and tended to bleed.

Regarding number of lymph nodes harvested, in the CLASSIC study [18], the mean number of lymph nodes harvested in the laparoscopic arm was 12. In the COLOR trial [22], the mean number of lymph nodes harvested in the laparoscopic arm was 10. In the COST study [19], the mean number of lymph nodes harvested in the laparoscopic arm was 12. In the BARCELONA study, Lacy *et al.* [21] found that the mean number of lymph nodes harvested in the laparoscopic arm was 11.1 with a SD of 7.9. In the meta-analysis of Bonjer *et al.* [23], the mean number of lymph nodes harvested in the laparoscopic arm was 11.8 with a SD of 7.4. Pedrazzani *et al* [14] found that the increased BMI is associated with increased visceral obesity, which led to decreased number of lymph nodes harvested. Choe *et al.* [25] found that the increased BMI is associated with deeper location of the lymph nodes in the mesocolic fat, which inversely affected the number of lymph nodes harvested. This was also confirmed by Yu *et al.* [26] and Watanabe *et al.* [27].

## Conclusions

Laparoscopy is a reliable method for resection of colon adenocarcinoma regarding the pathological outcomes and the surgical radicality. This study has shown that the number of the harvested lymph nodes and safety margins status are the most important indicators of the pathological and surgical radicality after laparoscopic resection of colon adenocarcinoma. To achieve this result, adequate learning curve is first needed. In addition, the patients' BMI greatly affects the number of the harvested lymph nodes, where the increase in the BMI decreases the number of the harvested lymph nodes.

It should be noted that the aforementioned conclusions are specifically applicable to those studied patient characteristics at Alexandria University in Egypt or those patients with very similar characteristics (i.e. BMI range, staging, and colon cancer site) as those used in this study. The study was also limited to only 30 patients due to the encountered difficulties of getting more cases at the Surgical Oncology Unit at Alexandria University in Egypt. For this, to produce a multicentric trial, future research could expand the current study by using more patient cases to validate the study findings. Another future research avenue is to assess the efficacy, pathological outcomes, and oncologic radicality after laparoscopic resection of colon adenocarcinoma in other countries with different patient characteristics. Afterward, a comparison could be made to evaluate how the results and conclusions gathered from this study would concur or differ with the other results.

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Nil.

**Conflicts of interest**

The authors declare no potential conflict of interest.

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