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Laparoscopic Versus Open Surgery for the Treatment of Colorectal Cancer: A Single Center Experience

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1. Abstract

Aim: The primary objective of this study was to comapare laparoscopic colorectal cancer surgery vs open colorectal surgery on postoperative morbidity and mortality.

Material and methods: In this study we enrolled 106 patients with colorectal cancer. We divided the patients in 2 two groups: open surgery group (n=59) and laparoscopic surgery group (n=47). The inclusion criteria were as follows: emergency surgery for rea-sons such as intestinal obstruction, bleeding or perforation; double primary cancers; treated by palliative surgery; treated by neoadju- vant therapy before surgery.

Results: The open group had significantly lower BMI (23.7 ± 2.3 kg/m2 vs. 25.7 ± 3.3 kg/m2, P = 0.009), preoperative HGB (12.3 ± 1.1 g/dL vs. 12.9 ± 2.7 g/dL, P = 0.045), and preoperative albumin (3.8 ± 1.3 g/dL vs. 4.2 ± 2.1 g/dL, P = 0.045), significantly higher preoperative ASA scores (ASA I-II 30.5% (18) vs 65.9% (31); ASA III-IV 69.5% (41) vs 34.1% (16), P < 0.001), and less comorbidities than the laparoscopic group (59.3% (35) vs 76.5% (36), P = 0.008.There were more patients with poor tumor differentiation in open group than the laparoscopic group (22.03% (13) vs 19.14% (9), P = 0.029. Besides, the 3-year OS rates in the open group were 67.6 % respectively in the laparoscopic group were 73.1%.

Conclusions: Laparoscopic surgery showed better resultsthan the open surgery in short-term outcomes. CEA level, III/IV stage, and perineural invasion were all reliable predictor of overall survival and disease-free survival for the treatment of laparoscopic surgery and open surgery for patients with colorectal cancer.

2. Introduction

Colorectal cancer is the third most common cancer in the world and one-third of this cancers are localized to the rectum. The Canadian Cancer Society estimated that approximately 23 800 new colorectal cases will be diagnosed in Canada per year and 78 000 in China. Surgery is the only curative treatment for colorectal can- cer. If we talk about curative options in treatment of colorectal cancer surgery is the only curative one. Curative surgery requires resection of the primary tumor with negative margins and com- plete oncologic lymphadenectomy. The resected segment depends on vascularization and lymphatic drainage at the tumor site and according to the American Joint Committee on Cancer, a mini- mum of 12 lymph nodes should be retrieved in surgical specimens. Otherwise tumor stage could be underestimated and suboptimal treatment could be offered. In most of the centers worldwide col- orectal cancer resection has been performed exclusively through open surgery. However following successful laparoscopic proce- dures, such as cholecystectomy, appendectomy and treatment of incisional hernias, this surgical approach has gradually been in- troduce first in the treatment of colorectal cancer. Jacobs in 1991 reported the first minimally invasive resection of a colon cancer. Since then, this treatment has been considered a landmark in the progress of surgical treatment. The controversial points include the intraoperative and postoperative complications, lymphadenec- tomy, long-term quality of life, and over-all and disease-free sur- vivals, postoperative outcomes.

There are numerous publications from the past 30 years that have evaluated and compared laparoscopic and open surgery for rectal cancer including the United Kingdom Medical Research Council

trial of Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASICC), the Comparison of Open versus laparoscopic surgery for mid- and low-Rectal.

Therefore, we designed a single-center and propensity score-matched analysis to investigate the short-term outcomes and survival rates of laparoscopic and open colorectal surgery, as well as the reliable predictors for OS and DFS in elderly patients with colorectal cancer.

3. Material and Methods

After approved by the ethics committee of Pius Brinzeu Clinical Hospital Timisoara all curatively operated colorectal cancer patients were collected between January 2016 and January 2017. The exclusion criteria were as follows: emergency surgery for reasons such as intestinal obstruction, bleeding or perforation; double primary cancers; treated by palliative surgery; treated by neoadjuvant therapy before surgery. Besides, written informed consent was obtained from each patient included in the study.

In this study, clinical data were collected based on electronic records and included age, gender, Body Mass Index (BMI), preoperative hemoglobin (HGB), preoperative albumin, American Society of Anesthesiologists (ASA) score, comorbidities, previous abdominal surgery, tumor location, tumor differentiation, and Tumor Nodes Metastasis (TNM) stage. Besides, the perioperative outcomes were also collected including the surgical outcomes, pathological outcomes, and the postoperative recovery. The surgical outcomes included the duration of operation, intraoperative blood loss, blood transfusion, intraoperative complication, postoperative complication, mortality, and Intensive Care Unit (ICU) stay. The pathological outcomes included the retrieved lymph node, tumor size, perineural invasion, vascular invasion, and positive Circumferential Resection Margin (CRM). Postoperative recovery included time to first flatus, time to oral feeding, and postoperative hospital days. The parameters of the postoperative recovery were all calculated based on the end of the operation. Postoperative complications were defined according to the Clavien-Dindo classification including wound infection, anastomosis leakage, ileus, urosepsis, pneumonia, pelvic abscess, arrhythmia, pleural effusion, delayed gastric emptying, and bacteremia [1-9].

After surgery all patients received a follow-up survey every 6 months in the first 2 years by outpatient visit. In these 2 years the patients were diagnosed by physical and laboratory examinations including biomarkers as CEA and CA 19-9 at each visit, CT scans of the chest, abdomen and pelvis at every 6 months.

SPSS version 22.0 was used for data analysis in the study. We decide to divide the patients according to the operations type in two groups: laparoscopic group of patients and open group. Quantitative data were analyzed by Mann-Whitney U test and presented as mean ± standard deviation. Categorical data were analyzed by the Chi-squared test and presented as frequency and percentage. The matching ratio was 1:1 and the covariates include age, gender, BMI, preoperative albumin level, preoperative HGB level, ASA score, comorbidity, previous abdominal surgery, tumor location, tumor differentiation, and TNM stage. The Kaplan-Meier method was performed to calculate the survivals of the patients treated with different operation types in the 2 groups, and the differences of the survival outcomes were compare by a log-rank test.

4. Results

In this study we enrolled 106 patients with colorectal cancer. We divided the patients in 2 two groups: open surgery group (n=59) and laparoscopic surgery group (n=47). The clinical and pathological characteristics before and post matching groups were shown in Table 1. Before matching there were significant differences in aspects of BMI, preoperative HGB, preoperative albumin, ASA, comorbidity, tumor location, differentiation ($P<0.05$) between the open group and laparoscopic group.

Before matching, the open group had significantly lower BMI (23.7 ± 2.3 kg/m2 vs. 25.7 ± 3.3 kg/m2, $P = 0.009$), preoperative HGB (12.3 ± 1.1 g/dL vs. 12.9 ± 2.7 g/dL, $P = 0.045$), and preoperative albumin (3.8 ± 1.3 g/dL vs. 4.2 ± 2.1 g/dL, $P = 0.045$), significantly higher preoperative ASA scores (ASA I-II 30.5% (18) vs 65.9% (31); ASA III-IV 69.5% (41)

vs 34.1% (16), $P < 0.001$), and less comorbidities than the laparoscopic group (59.3% (35)

vs 76.5% (36), $P = 0.008$). The primary tumor localization was more frequent in the right and left colon and less frequent in the sigmoid colon and rectum in the open group ($P = 0.007$). There were more patients with poor tumor differentiation in open group than the laparoscopic group (22.03% (13) vs 19.14% (9), $P = 0.029$). The laparoscopic group and open group were well balanced in aspects of age, gender, BMI, preoperative HGB, preoperative albumin, ASA score, comorbidity, previous abdominal surgery, tumor location, tumor differentiation, TNM stage, and preoperative CEA.

Table 1:

Variables	OPEN (n=59)	LAP (n-47)	*P*
Age	63±2.4	68±3.4	0.008
Gender			0.0432
M	64.4% (38)	57.4% (27)	
F	35.6% (21)	42.6% (20)	
BMI (kg/m2)	23.7±2.3	25.7±3.3	0.009
Preoperative HGB (g/dl)	12.3±1.1	12.9±2.7	0.045
Preoperative albumin (g/dl)	3.8±1.3	4.2±2.1	0.045
ASA score			0.001
I-II	30.5% (18)	65.9% (31)	
III-IV	69.5% (41)	34.1% (16)	
Comorbidity			0.008
Yes	59.3% (35)	76.5% (36)	
No	40.7% (24)	23.5% (11)	
Previous abdominal surgery			
Yes	25.4% (15)	19.4% (9)	0.456
No	74.6% (44)	80.6% (38)	
Tumor location			0.007
AC	32.2% (19)	23.4% (11)	
DC	11.86% (7)	12.76% (6)	
SC	16.9% (10)	19.14% (9)	
Rectum	38.98% (23)	44.68% (21)	
Tumor differentiation			0.029
Poor	22.03% (13)	19.14% (9)	
Median	66.10% (39)	70.21% (33)	
High	11.86% (7)	10.6% (5)	
TNM stage			0.213
I	6.7% (4)	17.02% (8)	
II	30.5% (18)	14.89% (7)	
III	49.15% (29)	61.7% (29)	
IV	13.55% (8)	6.98% (3)	
Preoperative CEA (ng/ml)			0.159
<5	67.7% (40)	78.7% (37)	
>5	32.3% (19)	21.27% (10)	

5. Short-Term Outcomes

The short-term outcomes, including the surgical outcomes, pathological outcomes, and postoperative recovery, in matched cohorts were as shown in Table 2. There was a significant difference in aspects of intraoperative blood loss and postoperative complication between the two groups. The laparoscopic group had significantly lower intraoperative blood loss (70 ± 49 mL vs. 118± 68 mL, P < 0.001) and lower occurrence of postoperative complication (12.7% (6) vs. 27.1% (16), P = 0.005). According to the Clavien Dindo classification, the incidence of grade I-II complications in open group was significantly higher (15.25% (9) vs 6.38% (3), P = 0.023). The most common morbidity in the open group was wound infection in 11.86% (7), followed by ileus in 8.47% (5), anastomosis leakage in 6.77% (4), and delayed gastric emptying in 3.38% (2). In the laparoscopic group, the most common morbidities were anastomosis leakage in 4.25% (2), ileus in 2.12% (1) and pneumonia in 2.12% (1). No patient died during the operation. For the pathological outcome, the retrieved lymph node was significantly higher in the laparoscopic group (31±13 (6-62) vs 23±11 (3-58), P=0.0213). Time to first flatus (1.9± 1.6 days vs. 2.5 ± 2.1 days, P = 0.001), time to oral feeding (2.8 ± 2.2 days vs. 3.9 ± 2.5 days, P = 0.003), and postoperative hospital stay (8.6 ± 3.3 days (LAP) vs. 12.2 ± 5.5 days (OP), P < 0.001) were all significantly lower in the laparoscopic group.

Table 2:

Variables	OPEN (n=59)	*LAP (n=47)*	*P*
Duration of operation (min, mean ± SD) (range)	179±35 (60-320)	189±21 (70-380)	0.065
Intraoperative blood loss (mL, mean ± SD) (range)	118±68 (50-500)	70±49 (30-200)	0.001
Blood transfusion	23.7% (14)	17.02% (8)	0.0265
Intraoperative complication	3.38% (2)	2.12% (1)	0.89
Postoperative complication	27.1% (16)	12.7% (6)	0.005
Wound infection	11.86% (7)	4.25% (2)	0.009
Anastomosis leakage	6.77% (4)	4.25% (2)	0.572
Ileus	8.47% (5)	2.12% (1)	0.456
Urosepsis	1.69 % (1)	0%	1
Pneumonia	3.38% (2)	2.12% (1)	0.987
Pelvic abscess	0%	2.12% (1)	1
Arrhythmia	3.38% (2)	2.12% (1)	0.923
Pleural effusion	1.69% (1)	0%	0.477

Delayed gastric emptying	3.38% (2)	4.25% (2)	0.362
Bacteremia	1.69% (1)	0%	1
Postoperative complication (ClavienDindo classification)			
I-II	15.25% (9)	6.38% (3)	0.023
III-IV	11.86% (7)	8.5% (4)	0.15
Mortality	0%	0%	-
Retrieved lymph node (mean ± SD) (range)	23±11 (3-58)	31±13 (6-62)	0.0213
Tumor size			0.038
< 5 cm	52.5% (31)	51.06% (24)	
≥ 5 cm	47.45% (28)	48.93% (23)	
Perineural invasion	28.81% (17)	17.02% (8)	0.475
Vascular invasion	32.2% (19)	25.53% (12)	0.513

6. Survival Analysis

The mean follow-up period in the matched cohort was 22.4 months (range, 5–42 mouths; open group: 15.4 months; laparoscopic group: 19.5 months). During the whole follow-up period, 28 of the 106 patients died (26.41%) and 19 of the 106 patients had local recurrence or distant metastasis (17.92%). If we talk about duration of the operation in Open vs Lap group (min, mean ± SD) (range) the average is 179±35 (60-320) vs 189±21 (70-380) and a P=0.064, which is not statistically significant. Intraoperative blood loss (mL, mean ± SD) (range) in the Open group was 118±68 (50-500) and in the Lap group 70±49 (30-200), and a P< 0.001. 23.7% (14) in the Open group vs 17.02% (8) in Lap group of patients have needed blood transfusion, with P=0.0265, that it is significantly statistic. **Intraoperative complication** in Open group were 3.38% (2) vs 2.12% (1), P=1.000.

We analyzed the postoperative complication and we found that 27.1% (16) of patients in Open group vs 12.7% (6) in Lap group, P=0.005. The most common complications in our study were (Open vs Lap): **Wound infection** 11.86% (7) vs 4.25% (2), P=0.009, **Anastomosis leakage** 6.77% (4) vs 4.25% (2), P=0.0572, **Ileus** 8.47% (5) vs 2.12% (1), P=0.456, Urosepsis 1.69 % (1) vs 0% (0), P= 1.000 Pneumonia 3.38% (2) vs 2.12% (1), P=0.987. Pelvic abscess 0% (0) vs 2.12% (1), P=1.000 Arrhythmia 3.38% (2) vs 2.12% (1), P=0.923. Pleural effusion 1.69% (1)vs 0% (0), P=0.477 **Delayed gastric emptying** 3.38% (2) vs 4.25% (2), P=0.362 Bacteremia 1.69% (1) vs 0% (0), P=1.000.

Postoperative complication (Clavien-Dindo classification) I-II 15.25% (9) vs 6.38% (3), P=0.023 and III-IV 11.86% (7) vs 8.5% (4). Mortality 0 (0%) vs 0 (0%) – ICU staying 13.9% vs 7.5 %, P=0.0156.

Pathological outcome: Retrieved lymph node (mean ± SD) (range) 23±11 (3-58) in open group vs 31±13 (6-62) in laparoscopic group. **Tumor size** < 5 cm 52.5% (31) in open group and 51.06% (24) in laparoscopic group, and > 5 cm in 47.45% (28) vs 48.93% (23), P=0.038. **Perineural invasion**, 28.81% (17) vs 17.02% (8), P=0.475. Vascular invasion, 32.2% (19) vs 25.53% (12), P=0.513.

7. Postoperative recovery

Kaplan curves showed no statistically significant difference in OS (P = 0.224) and DFS (P = 0.230) between the two groups. Besides, the 3-year OS rates in the open group were 67.6 % respectively in the laparoscopic group were 73.1%. At univariate analysis, CEA level, N stage, TNM stage, perineural invasion, and vascular invasion significantly affected both OS and DFS (P < 0.05). According to multivariate analysis, the OS was significantly affected by CEA (P = 0.032), TNM stage (P = 0.002) and perineural invasion (P = 0.041). Besides, DFS was significantly affected by the CEA level (P = 0.038), TNM stage (P = 0.012) and the perineural invasion (P = 0.020).

8. Discussion

According to this study, in patients with colorectal cancer, laparoscopic surgery has better short-term outcomes than the open surgery but there is no significant difference for the long-term survival outcomes.

CEA level, III/IV stage, and perineural invasion were all reliable predictor of overall survival and disease-free survival (DFS) for either laparoscopic or open surgery. Previous studies had already shown that colorectal cancer patients could also obtain better short-term outcomes through laparoscopic surgery [10, 14-19]. In the current study, it was found that the laparoscopic surgery could significantly reduce the intraoperative blood loss and postoperative complication. According to previous report, reduction of blood loss could reduce the stress reaction of surgery and further greatly reduce the incidence of postoperative complications, hence, the reduction of blood loss could effectively improve the postoperative recovery of patients [20]. Besides, among the postoperative complication, the laparoscopic surgery could significantly decrease the incidence of grade I-II complication (Table 2) such as wound infection compared to the open surgery. Moreover, laparoscopic surgery could significantly increase the number of the retrieved lymph node.

This was possibly attributed to clear and magnified visualization under laparoscopy, and was consistent with the report of Yang et al. which showed that the laparoscopic could significantly increase the number of retrieved lymph nodes for the early distal gastric cancer [12]. Previous studies had revealed the advantages of laparoscopic surgery about the faster recovery [21-24]. Vignali et al. had reported laparoscopic surgery could significantly decrease the time to first flatus, the time to liquid diet, and hospital stay [23]. Consistent with the above reports, the current study found that compared with the open group, the laparoscopic surgery could

significantly reduce the time to flatus, time to oral feeding, and postoperative hospital stay. Overall, the above findings reflected that the laparoscopic surgery had better short-term outcomes in the treatment in patients with colorectal cancer than the open surgery. Few studies reported data regarding long-term outcomes of laparoscopic surgery [25, 26]. In 2015, Hinoi et al. reported that there was no significant difference in patients with rectal or colon cancer in 3-year overall survival, disease-free survival, and cancer specific survival between laparoscopic and open groups [26]. Likewise, in 2016, Moon et al. reported that the laparoscopic surgery was without any significant difference for the 3- and 5-year overall survival, and 3-year and 5-year recurrence-free survival compared to the open surgery [25]. In this study, no difference in the 3- year OS rates (P = 0.224) and in 3- year DFS rates (P = 0.230) were observed between the open and laparoscopic surgery. Besides, it is noteworthy that the 3-year OS rates, and 3- DFS rates of patients in the laparoscopic group were generally higher than the open group. This difference might be due to the difference in the number of dissected lymph node between the open group and the laparoscopic group. Hence, although there was no significant difference in survival outcomes between the two surgical methods, the laparoscopic surgery in patients with colorectal cancer might achieve better survival outcomes than the open surgery. Prognostic factors affecting the survival of colorectal cancer patients have been previously reported [27–30]. Huh et al. had reported that both preoperative CEA level, TNM stage, and vascular or neural invasion were independent prognostic factors for the overall survival and disease-free survival in potentially curative colorectal cancer [30]. Besides, Tsai et al. reported the perineural invasion as a significant prognostic factor for postoperative relapse for stage II colorectal cancer undergoing radical resection [27]. Consistently with the previous studies, in this study, it was found that CEA level, III/IV stage, and perineural invasion were all independent predictors for the overall survival and the disease-free survival of elderly patients with colorectal cancer. This study has the limitations of any retrospective study. However, selection bias was reduced by propensity score matching through logistic regression. Multicenter large-scale prospective studies are needed to further confirm whether laparoscopic treatment is more suitable for patients with colorectal cancer in terms of short-term and survival outcomes. Cutoff values for CEA level, III/IV stage, and perineural invasion were not evaluated in this study, so large-scale studies are necessary to determine specific valid cutoff values for CEA level, III/IV stage, and perineural invasion.

9. Conclusions

Laparoscopic surgery showed better results than the open surgery in short-term outcomes. CEA level, III/IV stage, and perineural invasion were all reliable predictor of overall survival and disease-free survival for the treatment of laparoscopic surgery and open surgery for patients with colorectal cancer.

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