RESEARCH ARTICLE

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# Propensity Score-Matched Analysis of Laparoscopic versus Open Surgery for Non-Metastatic Rectal Cancer

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## Abstract

**Background:** Rectal cancer is a pervasive type of malignancy that accounts for one-third of colorectal cancers worldwide. Several studies have assessed the use of laparoscopic surgery as a treatment option. However, there is an ongoing debate regarding its oncological safety. **Methods:** This retrospective study included 270 patients with non-metastatic rectal cancer who underwent either laparoscopic resection (LR, n = 93) or open resection (OR, n = 177) in an academic medical center. The primary outcomes were overall survival (OS) and disease-free survival (DFS), whereas the secondary outcome was postoperative complications. We performed propensity score analyses and compared outcomes. Univariate survival analyses using Kaplan-Meier plots and Cox proportional hazard regression models were also conducted. **Results:** In the propensity score matching analyses, 93 LR- and 93 OR-matched patients were compared. The overall median follow-up time was 3.95 years (range, 1.98–5.55 years). The 3-year OS was similar between the groups (LR 79.1% vs OR 79.2%, p = 0.82). Meanwhile, the DFS rate was also comparable between the groups (LR 77.8% vs OR 73.2%, p = 0.53). No significant differences in operative blood loss or hospital stay between the groups were observed (150 vs 150 mL, p = 0.74; 9 vs 10 days, p = 0.077, respectively). Also, no difference was found in postoperative complications between the groups (p = 0.23). However, LR was associated with a longer operative time than OR (455 vs 356 min, p < 0.001) and the number of lymph nodes harvested in LR was slightly fewer than OR (10 vs 11, p = 0.045). **Conclusion:** LR of rectal cancer is safe, feasible, and comparable to standard OR in terms of the oncologic outcomes. However, LR required longer operative times. A well-designed prospective study with a large number of participants and long follow-up period is needed to show significant differences between the two groups.

**Keywords:** Propensity score-matched analysis- laparoscopic resection- open resection- non-metastatic rectal cancer

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## Introduction

Rectal cancer is a worldwide disease that constitutes one-third of colorectal cancers (Ferlay, Soerjomataram et al. 2015), and the incidence has increased significantly in the last few decades (Zhang et al., 2016) that has resulted in more than 80,000 fatalities per year. However. total mesorectal excision (TME) has significantly improved the outcome of surgery for this cancer during the last two decades. The TME procedure completely removes the adipose lymphatic tissue surrounding the rectum while preserving the pelvic autonomic nerves. Since radially disseminated cancer cells in the mesorectum are eradicated by total excision of this tissue, local recurrence rates of rectal cancer have dropped dramatically. In patients with advanced rectal cancer, radiotherapy and chemotherapy are crucial components of multimodal treatment.

In the early 1990s, TME was introduced during the same period that laparoscopic surgery was increasingly used in patients with colorectal illnesses. Laparoscopic colon cancer resection has been shown to be safe and results in reduced postoperative pain and faster recovery time. Furthermore, cancer survival rates are comparable to those obtained with traditional open colectomy. Although previous publications found that laparoscopic TME is safe, the number of trials with large patient populations has not been sufficient to allow clinical adoption of laparoscopic surgery in rectal cancer. Some studies have reported that laparoscopic TME is associated with higher rates of circumferential margin positivity and incomplete TME (Stevenson et al., 2015, Fleshman et al., 2019).

Due to its benefits in terms of recovery and complication rate, as well as its minimally invasive nature, laparoscopy has brought enormous changes to rectal cancer surgery since its introduction 22 years ago (Chen et al., 2017). Rectal cancer research has been considerable in recent years, due to advancements in equipment and techniques, and an increasing number of clinical doctors and patients

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have come to understand and accept laparoscopic rectal resection. The laparoscopic approach to rectal cancer differs from traditional open surgery, not just because of the rigorous requirements for laparoscopy, but also because of concerns regarding its safety and effectiveness.

Many scholars have attempted to answer the problem in recent years. Jiang performed a good meta-analysis of the short- and long-term outcomes of mid-low rectal cancer, which included 13 trials; however, only three papers were published in the previous three years. Furthermore, just a few of the meta-analyses included studies published after 2012, despite the fact that laparoscopic equipment and surgical procedures have evolved quickly in recent years.

For this rectal cancer study, we chose the most recent references over the last five years. The goal of this study was to compare oncologic results between laparoscopic and the conventional approach at Songklanagarind Hospital as the primary endpoint. We conducted an updated review of all high-quality published trials that compared laparoscopic surgery to traditional surgery. Materials and Methods

*Study population*

From January 2009 to December 2016, 270 consecutive non-metastatic rectal cancer patients underwent resection surgery at Songklanagarind Hospital, Prince of Songkhla University by either the laparoscopic resection (LR) (n = 93) or open resection (OR) (n = 177) approach. The data were collected retrospectively from the medical record system of the hospital. Figure 1 illustrates the selection process. The treatment protocol was based on the National Comprehensive Cancer Network (NCCN) guidelines. Patients with recurrent disease during the first postoperative year, emergency conditions such as intestinal obstruction or perforation, synchronous lesions, or a history of abdominal or pelvic surgery or radiation were excluded from the study. The patients were divided into several groups according to tumor location. The tumors were subdivided into three types according to the distance between the distal border and the anal verge (upper rectal cancer, 10–15 cm; middle rectal cancer, 5–10 cm; and lower rectal cancer, <5 cm). Neoadjuvant therapy and adjuvant therapy were given selectively following the standard protocol and in accordance with the patient's ability to tolerate the therapy.

The decision to proceed with laparoscopy or open surgery was made on an individual patient basis following multidisciplinary discussions and meetings. The patients chose the surgical approach of either LR or OR after receiving adequate information concerning the respective risks and benefits. Most of the surgeries were performed by two colorectal surgeons and one general surgeon, who were experts in these procedures.

*Preoperative staging work-up*

Before the operation, all patients underwent colonoscopy plus biopsy for a pathologic review of the adenocarcinoma as well as abdominal and chest computed tomography to work up the metastatic staging. Pelvic magnetic resonance imaging was used selectively to determine the preoperative clinical staging.

*Surgical technique*

During laparoscopic surgery for either abdominal perineal resection (APR) or low anterior resection (LAR), the patients were placed in the Trendelenburg lithotomy position (30°) with the left side tilted up. The surgeon stood on the patient's right side, and the first assistant stood on the patient's left side. Pneumoperitoneum was generated at a pressure of 12–15 mmHg. Six trocars were inserted: a 10-mm port at the supraumbilical region, a 12-mm port at the suprapubic area with an extension to extract the specimen (some surgeons used either an LLQ incision or the paraumbilical site for specimen extraction), a 12-mm port at the RLQ, and 5-mm ports at the LUQ, LLQ, and RUQ. The medial-to-lateral approach was used. The roots of the inferior mesenteric vascular pedicles were identified during lymphadenectomy and the autonomic nerves were preserved. A partial mesorectal excision was carried out for upper rectal cancers with a mesorectal margin of ≥5 cm distal to the cancer, and TME was performed for middle and lower rectal cancers. The port incision was extended 4–6 cm at the suprapubic area, LLQ, or the paraumbilical area for removal of specimens and intra-abdominal anastomosis. When indicated, the patients underwent a protective ileostomy. No extended abdominal incision was made when patients underwent APR. The decision for the one conversion case was made after inspection with laparoscopy. The data of this case were analyzed in the OR group.

In the OR group for either APR or LAR, a midline incision was created and the lateral-to-medial approach was followed. The other steps undertaken (i.e., divide the inferior mesenteric vascular pedicles, obtain the resection margin and achieve lymphadenectomy, and perform TME for the middle and lower rectal cancers as well as reach the decision to perform protective ileostomy) were the same methods followed during laparoscopic surgery, including the non-touch tumor technique.

*Postoperative management*

A liquid diet was started on postoperative days 2–3 after the nasogastric tube was removed and bowel function was achieved. The patients were encouraged to engage in early ambulation and do breathing exercises using an incentive spirometer on their own. The patients were discharged if they were intravenous analgesia-free, afebrile, and could tolerate food for 24 hours without major complications.

*Postoperative follow-up*

All patients were scheduled for follow-up following the NCCN guideline. Those with high-risk factors were recommended to undergo postoperative adjuvant chemotherapy with 5-fluorouracil-based regimens as per the routine protocol. Surveillance methods were applied to determine disease recurrence. The last follow-up was in December 2016. Patients lost to follow-up were contacted by telephone by the oncology center.

*Statistical analysis*

The statistical analyses were performed using the R software version 4.0.2 (R Core Team [2020]: R: A

language and environment for statistical computing. R Foundation for Statistical Computing). The Wilcoxon rank-sum test was used to assess differences in patient characteristics, whereas categorical data were compared using either Pearson's chi-square or Fisher's exact test. To balance the patient characteristics between the two groups and to diminish bias in the survival analyses, we also performed propensity score matching (i.e., 1:1 nearest neighbor matching, balancing for sex, age, body mass index, American Society of Anesthesiologists class, location of the tumor, stage of the disease, neoadjuvant treatment, and adjuvant treatment). Survival probability was estimated using the Kaplan-Meier method and compared using the Peto-Peto test. The independent prognostic effects of the surgical approaches on disease-free survival (DFS) and overall survival (OS) were estimated using Cox proportional hazard regression models. The results are reported as hazard ratio with a 95% confidence interval (CI). A p-value <0.05 was considered statistically significant.

*Compliance with ethical requirements*

The ethics committee of Prince of Songkla University approved this study. According to our institutional review board protocol for waiver of informed consent, the requirement for consent was waived because the participants had no more than minimal risk and the patients received standard treatment procedures. The ethical registration number was REC.62-432-10-3.

## Results

*Pre- and post-match baseline characteristics*

The use of laparoscopy increased steadily from 11% to 54% between 2009 and 2016. This was in stark contrast with the open surgery approach, which declined from 88% to 45% over the same period. The overall median follow-up in this study was 3.95 years (range, 1.98–5.55 years. After excluding the patients that did not match the selection criteria, 270 patients were eligible for the study analysis. A statistically meaningful difference was found in patients receiving neoadjuvant and adjuvant treatment in the LR group compared to the OR group (58.1% vs 42.9%, p = 0.025; 68.8% vs 78%, p = 0.019, respectively) (Table 1). After matching, the differences between the groups in terms of baseline demographics as well as neoadjuvant and adjuvant treatment were adjusted and balanced and the results are provided in Table 2.

*OS and DFS rates for the matched cohort*

The 3-year OS rate was 79.1% (95% CI 71.0–88.2) in the LR group and 79.2% (95% CI 71.1–88.3) in the OR group (p = 0.82) (Figure 2). Meanwhile, the DFS rate in the LR group was 77.8% (95% CI 69.3–87.5) and 73.2% (95%

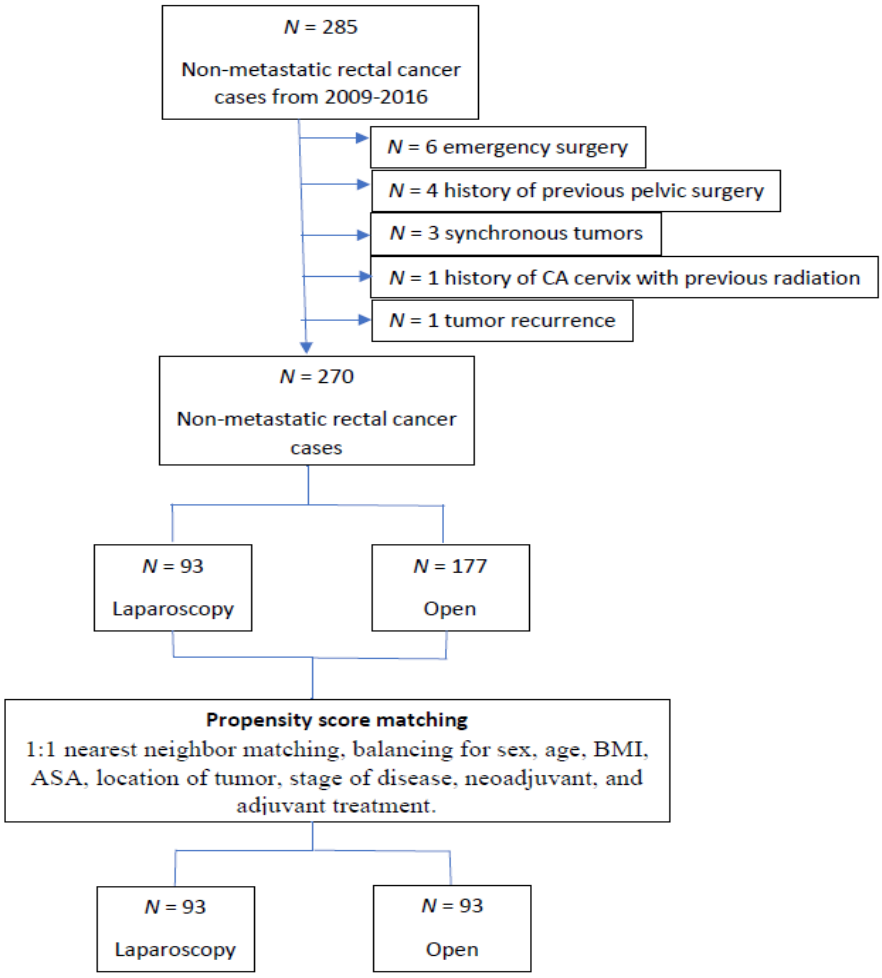


Figure 1. Study Flowchart Showing Patient Selection after Propensity Score-Matched Analysis

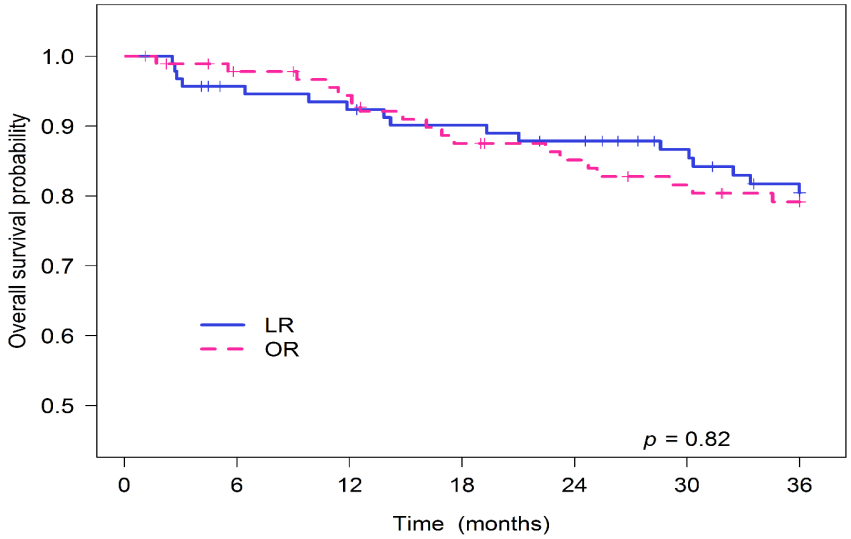


Figure 2. Overall Survival Rates between Laparoscopic Resection (LR, n = 93) and Open Resection (OR, n = 93) after Propensity Score-Matched Analysis

CI 64.2–83.5) in the OR group (p = 0.53) (Figure 3). The univariate analysis findings using the Cox proportional hazard regression model after propensity score matching are shown in Table 3.

## Discussion

In our study, the tumors were predominantly stage II and located in the lower rectum. More than half of patients in both groups received neoadjuvant chemoradiotherapy (LR 57% vs OR 55.9%, p = 1.000), which is in line with the findings of recent studies reporting higher neoadjuvant therapy rates (Arezzo et al., 2013; Boutros et al., 2013; Schnitzbauer et al., 2020). Meanwhile, some patients did not undergo neoadjuvant therapy either according to or in contradiction to the guidelines. This has been reported to be the case in other studies as well (Ströhlein et al., 2008, Zhou et al., 2015; Draeger et al., 2018; Schnitzbauer et al., 2020). The LR group had a shorter hospital stay (9 vs 10 days, p = 0.077). This finding was in agreement with several previous studies (Braga et al., 2011, Yamamoto et al, 2011, Kwon et al., 2012; Chen et al., 2014; Zhou et al., 2015). However, no statistically significant difference was detected. The duration of hospitalization in our study was longer than other studies because the length of stay in our cases included all hospitalization days beginning with admission, and the enhanced recovery after surgery protocol was not followed from the beginning of the study period. A disadvantage of the laparoscopic approach was that it required a significantly longer operative time compared to the open approach (455 vs 356 min, p < 0.001), which was a finding also reported by other studies (Yamamoto et al., 2011, van der Pas et al., 2013; Bedirli et al., 2014). Operative time also depends on the surgeon's level of expertise related to performing laparoscopic surgery for the treatment of rectal cancer. The LR group had statistically non-significant rates of complications (e.g., anastomotic leakage (3.2% vs 2.2%,

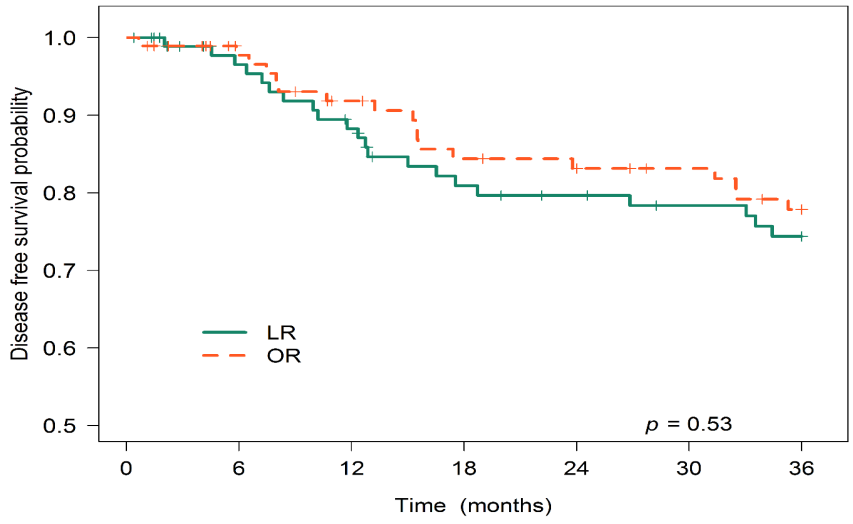


Figure 3. Disease-Free Survival Rates between Laparoscopic Resection (LR, n = 93) and open Resection (OR, n = 93) after Propensity Score-Matched Analysis.

Table 1. Comparison of Baseline Characteristics between Laparoscopic Resection (LR) and Open Resection (OR)

| | LR (n = 93) | OR (n = 177) | p-value |
|---|---|---|---|
| Demographic and clinical variables | | | |
| Sex (F/M), n | 41/52 | 84/93 | 0.689 |
| Age (year) | 62 (53–71) | 65 (56–73) | 0.298 |
| 15–50 | 18 (19.4) | 22 (12.4) | |
| 56–70 | 51 (54.8) | 102 (57.6) | |
| >70 | 24 (25.8) | 53 (29.9) | |
| BMI (kg/m$^2$) [median (range)] | 22.6 (20.2–25.3) | 22.1 (19.8–24.8) | 0.336 |
| ASA score I/II/III, n | 15/66/12 | 20/132/25 | 0.53 |
| Tumor location | | | 0.459 |
| Upper rectum | 22 (23.7) | 31 (17.5) | |
| Middle rectum | 29 (31.2) | 63 (35.6) | |
| Lower rectum | 42 (45.2) | 83 (46.9) | |
| Preoperative treatment | | | 0.033 |
| Neoadjuvant chemotherapy | 1 (1.1) | 1 (0.6) | |
| Neoadjuvant chemoradiotherapy | 53 (57) | 75 (42.4) | |
| Operation | | | 0.776 |
| APR | 24 (25.8) | 50 (28.2) | |
| LAR | 69 (74.2) | 127 (71.8) | |
| Histopathological variables | | | |
| pT stage | | | 0.402 |
| pT1 | 11 (11.8) | 11 (6.2) | |
| pT2 | 18 (19.4) | 31 (17.5) | |
| pT3 | 56 (60.2) | 118 (66.7) | |
| pT4 | 8 (8.6) | 17 (9.6) | |
| pN stage | | | 0.084 |
| N0 | 67 (72) | 104 (58.8) | |
| N1 | 17 (18.3) | 37 (20.9) | |
| N2a | 6 (6.5) | 18 (10.2) | |
| N2b | 3 (3.2) | 18 (10.2) | |
| Stage of disease AJCC | | | 0.053 |
| Stage I | 26 (28) | 32 (18.1) | |
| Stage II | 41 (44.1) | 72 (40.7) | |
| Stage III | 26 (28) | 73 (41.2) | |
| Positive resection margin | | | |
| Proximal | 0 (0) | 0 (0) | 1 |
| Distal | 0 (0) | 2 (1.1) | 0.547 |
| Circumferential | 5 (5.4) | 10 (5.6) | 1 |
| Harvest lymph node, median (range) | 10 (5–15) | 13 (7–24) | < 0.001 |
| Operative and postoperative outcome | | | |
| Operative time (min), median (range) | 455 (368–540) | 346 (267–440) | < 0.001 |
| Operative blood loss (mL), median (range) | 150 (50–400) | 175 (100–300) | 0.533 |
| Total hospital stay (day), median (range) | 9 (8–11) | 10 (9–13) | 0.004 |
| Postoperative morbidity | | | 0.128 |
| Leakage/collection | 3 (3.2) | 7 (4) | |
| Wound complication | 1 (1.1) | 3 (1.7) | |
| Anastomotic stenosis | 1 (1.1) | 3 (1.7) | |
| Hernia | 1 (1.1) | 3 (1.7) | |

Table 1. Continued

| | LR (n = 93) | OR (n = 177) | p-value |
|---|---|---|---|
| Postoperative morbidity | | | 0.128 |
| Ureter injury | 1 (1.1) | 2 (1.1) | |
| Small bowel obstruction | 0 (0) | 2 (1.1) | |
| RVF/perianal fistula | 3 (3.2) | 1 (0.6) | |
| Stroke | 0 (0) | 1 (0.6) | |
| Vaginal wall injury | 0 (0) | 1 (0.6) | |
| Acute urinary retention | 0 (0) | 1 (0.6) | |
| Prolapsed colostomy | 3 (3.2) | 0 (0) | |
| Erectile dysfunction | 2 (2.2) | 0 (0) | |
| Low anterior syndrome | 1 (1.1) | 0 (0) | |
| Postoperative treatment | | | 0.019 |
| Adjuvant chemotherapy | 49 (52.7) | 81 (45.8) | |
| Adjuvant chemoradiotherapy | 15 (16.1) | 56 (31.6) | |
| Adjuvant radiotherapy | 0 (0) | 1 (0.6) | |
| Oncologic outcome | | | |
| Local recurrence | 5 (5.4) | 13 (7.3) | 0.719 |
| Distant metastasis | 14 (15.1) | 38 (21.5) | 0.268 |
| Mortality | | | 0.296 |
| Disease-related | 18 (19.4) | 31 (17.5) | |
| Nondisease-related | 0 (0) | 5 (2.8) | |

Data are presented as n (%) unless otherwise indicated; BMI, body mass index; ASA, American Society of Anesthesiologists; APR, abdominal; perineal resection; LAR, low anterior resection; AJCC, The American Joint Committee on Cancer; RVF, rectovaginal fistula.

p = 0.230). This confirms the same trend reported by other studies where the major complication rates were similar between the LR and OR groups (5.4% vs 3.8%, p = 0.428) (Park et al., 2011). However, in contrast with the results from other studies (Braga et al., 2011, Yamamoto et al., 2011; Kwon et al., 2012; Chen et al., 2014; Zhao et al., 2015), which have suggested a significant superiority on the part of LR in ensuring less operative blood loss compared to OR, our study found similar blood loss volumes of the two surgical approaches (150 mL vs 150 mL, p = 0.740).

The median number of lymph nodes (LNs) harvested in our study was low in both groups compared to other studies and lower using the LR approach than the OR approach (10 vs 11, respectively, p = 0.045). This LN yield is likely attributable to the "learning curve" for both the surgeons and pathologists involved. Furthermore, more than half of our patients had chemoradiotherapy before surgery. Several studies have suggested that laparoscopic surgery could achieve the same effectiveness as open surgery concerning LN harvesting (Wu et al., 2012; Lujan et al., 2013; Zhou et al., 2015; Stracci et al., 2016; Balducci et al., 2017). Two studies reported greater LN harvesting using the LR approach compared to the OR approach (González et al., 2009; Boutros et al., 2013). In a retrospective comparative study involving

Table 2. Comparison of Baseline Characteristics between Laparoscopic Resection (LR) and Open Resection (OR) after Propensity Score-Matched Analysis

| | LR (n = 93) | OR (n = 93) | p-value |
|---|---|---|---|
| Demographic and clinical variables | | | |
| Sex (F/M), n | 41/52 | 43/50 | 0.883 |
| Age (year) | | | 0.279 |
| 15–50 | 18 (19.4) | 15 (16.1) | |
| 51–70 | 51 (54.8) | 49 (52.7) | |
| >70 | 24 (25.8) | 29 (31.2) | |
| BMI (kg/m$^2$), median (range) | 22.6 (20.2 - 25.3) | 22.7 (21 - 25.4) | 0.877 |
| ASA score I/II/III, n | 15/66/12 | 12/67/14 | 0.781 |
| Tumor location | | | 0.418 |
| Upper rectum | 22 (23.7) | 18 (19.4) | |
| Middle rectum | 29 (31.2) | 24 (25.8) | |
| Lower rectum | 42 (45.2) | 51 (54.8) | |
| Preoperative treatment | | | 1 |
| Neoadjuvant chemotherapy | 1 (1.1) | 1 (1.1) | |
| Neoadjuvant chemoradiotherapy | 53 (57) | 52 (55.9) | |
| Operation | | | 0.516 |
| LAR | 69 (74.2) | 64 (68.8) | |
| APR | 24 (25.8) | 29 (31.2) | |
| Histopathological variables | | | |
| pT stage | | | 0.983 |
| pT1 | 11 (11.8) | 10 (10.8) | |
| pT2 | 18 (19.4) | 20 (21.5) | |
| pT3 | 56 (60.2) | 55 (59.1) | |
| pT4 | 8 (8.6) | 8 (8.6) | |
| pN stage | | | 0.772 |
| N0 | 67 (72) | 67 (72) | |
| N1 | 17 (18.3) | 14 (15.1) | |
| N2a | 6 (6.5) | 6 (6.5) | |
| N2b | 3 (3.2) | 6 (6.5) | |
| Stage of disease AJCC | | | 0.985 |
| Stage I | 26 (28) | 27 (29) | |
| Stage II | 41 (44.1) | 40 (43) | |
| Stage III | 26 (28) | 26 (28) | |
| Positive resection margin | | | |
| Proximal | 0 (0) | 0 (0) | 1 |
| Distal | 0 (0) | 0 (0) | 1 |
| Circumferential | 5 (5.4) | 5 (5.4) | 1 |
| Harvest lymph node, median (range) | 10 (5–15) | 11 (7–20) | 0.045 |
| Operative and postoperative outcome | | | |
| Operative time (min), median (range) | 455 (368–540) | 356 (260–478) | < 0.001 |
| Operative blood loss (mL), median (range) | 150 (50–400) | 150 (100–300) | 0.74 |
| Total hospital stay (day), median (range) | 9 (8–11) | 10 (9–12) | 0.077 |
| Postoperative morbidity | | | 0.23 |
| Leakage/collection | 3 (3.2) | 2 (2.2) | |
| Wound complication | 1 (1.1) | 2 (2.2) | |
| RVF/perianal fistula | 3 (3.2) | 0 (0) | |
| Anastomotic stenosis | 1 (1.1) | 3 (3.2) | |
| Ureter injury | 1 (1.1) | 2 (2.2) | |
| Vaginal injury | 0 (0) | 1 (1.1) | |
| Acute urinary retention | 0 (0) | 1 (1.1) | |
| Low anterior syndrome | 1 (1.1) | 0 (0) | |
| Prolapsed colostomy | 3 (3.2) | 0 (0) | |
| Erectile dysfunction | 2 (2.2) | 0 (0) | |
| Hernia | 1 (1.1) | 1 (1.1) | |
| Postoperative treatment | | | 0.804 |
| Adjuvant chemotherapy | 49 (52.7) | 49 (52.7) | |
| Adjuvant chemoradiotherapy | 15 (16.1) | 18 (19.4) | |
| Oncologic outcome | | | |
| Local recurrence | 5 (5.4) | 6 (6.5) | 1 |
| Distant metastasis | 14 (15.1) | 18 (19.4) | 0.56 |
| Mortality | | | 1 |
| Disease-related | 18 (19.4) | 17 (18.3) | |
| Non disease-related | 0 (0) | 1 (1.1) | |

Data are presented as n (%) unless otherwise indicated; BMI, body mass index; ASA, American Society of Anesthesiologists; LAR, low anterior; resection; APR, anterior perineal resection; AJCC, The American Joint Committee on Cancer; RVF,rectovaginal fistula.

234 patients, Boutros et al et al., (2013) reported high or above-average LN harvests in both the open and laparoscopic groups (21 vs 27, respectively), which were significantly greater than the reported mean LN harvests (range, 8–18) following TME. This high LN yield can be attributed to the specialized techniques such as alcohol fixation to enhance LN visualization (Quirke et al. 1986). In a prospective comparative study including 56 patients, Gonzalez et al. (González et al., 2009) reported a mean of 12.1 versus 9.3 LNs harvested after laparoscopy and open TME, respectively. In contrast, Ströhlein et al., (2008) reported greater LN harvest yields using OR, and the results were 13.5 versus 16.9 LNs harvested in 89 laparoscopic and 275 open surgery cases. Interestingly, in their study, the LN harvest was higher in the open-access group, which might indicate a more extensive resection

Table 3. Univariate Cox Proportional Hazard Regression Model after Propensity Score Matching between Laparoscopic Resection (LR) and Open Resection (OR)

| | HR | 95.0% CI | p-value |
|---|---|---|---|
| Death | | | |
| Open | 1 | | |
| Laparoscopic | 1.02 | 0.53 - 1.96 | 0.951 |
| Local recurrence | | | |
| Open | 1 | | |
| Laparoscopic | 0.81 | 0.25 – 2.65 | 0.723 |
| Distant metastasis | | | |
| Open | 1 | | |
| Laparoscopic | 0.71 | 0.36 – 1.41 | 0.326 |

HR, hazard ratio; CI, confidence interval.

(Ströhlein et al., 2008). Besides, fewer LNs were reported to be associated with a short surgical specimen length and neoadjuvant treatment in rectal cancer patients (Stracci et al., 2016). Several studies indicated that LN status is the strongest predictor for cancer treatment because it is associated with higher survival rates. However, the increasing use of preoperative radiotherapy in patients with intermediate- and high-risk rectal cancers appears to have led to a decrease in the number of nodes examined (Baxter et al., 2005). The Chang study Chang et al., (2009), which aimed to investigate whether LN status after neoadjuvant radiotherapy for rectal cancer is a biologic predictor of outcome, reported that the median total number of LNs was lower preoperatively than postoperatively (6 vs 10, respectively). It was suggested that if one used a minimum of 12 nodes as the standard, only 20% of patients undergoing preoperative radiotherapy would have an adequate LN harvest (Baxteret et al., 2005). However, Orsenigo et al., (2019) found that rectal cancer patients with 12 or more lymph nodes removed did not have a statistically different survival compared to their counterparts. Multiple tumor- and patient-related factors are associated with LN yield, yet only the removal of at least 12 LNs can reliably determine LN status. Nevertheless, these considerations emphasize the need for further studies to assess these issues.

Negative proximal and distal margins were found in both groups. Furthermore, there was no significant difference regarding positive circumferential resection margin (CRM) (defined as CRM <1 mm) between the LR and OR groups in our study (5.4% vs 5.4%, p = 1.000). These findings were concordant with those of the ACOSOG Z6051 randomized clinical trial (Roxburgh and Guillem 2017), which reported negative CRM rates of 87.9% in the LR and 92.3% in the OR groups (p = 0.11). Meanwhile, three other trials, namely the COREAN, COLOR II, and ALaCaRT trials, (Jeong et al., 2014; Bonjer et al., 2015; Stevenson et al., 2015) reported high negative CRM rates of over 90% in every trial arm. The presence of involved CRMs in the COREAN trial had rates of 3% vs 4% for LR and OR, respectively (p = 0.77) (Jeong et al., 2014). In the COLOR II trial (Bonjer et al., 2015), the involved CRM rate was 10% for both arms. A positive finding was defined as the presence of tumor cells within 2 mm of the lateral surface of the mesorectum. In addition, the ALaCaRT randomized clinical trial reported that the CRM was clear among 222 patients (93%) in the laparoscopic surgery group and 228 patients (97%) in the open surgery group (risk difference = –3.7%, 95% CI –7.6%–0.1%, p = 0.06) (Stevenson, Solomon et al. 2015).

The OS rate in our study at postoperative 3 years was 79.1% (95% CI 71.0–88.2) after LR and 74.3% (95% CI 65.4–84.5) after OR (p = 0.514), whereas the DFS rate in the LR group was 77.8% (95% CI 69.3–87.5) and 63.3% (95% CI 53.1–75.5) in the OR group (p = 0.0378). In like fashion, the COREAN study (Jeong, Park et al. 2014) reported a 3-year OS rate of 91.7% (95% CI 86.3–95) in the LR group and 90.4% (95% CI 84.9–94.0) in the OR group, and DFS of 72.5% (95% CI 65.0–78.6) for the OR group and 79.2% (95% CI 72.3–84.6) for the LR group. Furthermore, similar findings were reported by Bonjer et al., (2015) in the COLOR II trial. The OS rates were 86.7% in the LR group and 83.6% in the OR group (difference = 3.1 percentage points, 95% CI –1.6–7.8), and the DFS rates were 74.8% in the LR group and 70.8% in the OR group (difference = 4.0 percentage points, 95% CI –1.9–9.9).

The univariate Cox proportional hazard ratios between the LR and OR groups in our study were not significantly different in terms of recurrence and survival rates, which were inconsistent with the findings of several earlier studies (Park et al., 2011; Lujan et al., 2013; Bonjer et al., 2015; Zhou et al., 2015; Chen et al., 2017; Yang et al., 2018). These results diverged from those of a study by Draeger et al., (2018), which concluded that laparoscopy was associated with superior local recurrence-free survival rates. Moreover, a study by Schnitzbauer et al., (2020) reported better 5-year recurrence-free survival and 5-year OS rates in favor of the laparoscopic group (p < 0.001). Veenhof et al., 2011) studied surgical stress response and immune competence following either open or laparoscopic TME surgery for rectal cancer. According to their findings, the postoperative immune and inflammatory functions tended to be better after laparoscopic rectal surgery compared with open rectal procedures. Furthermore, Makino et al., (2008) reported that the laparoscopic medial approach to carry out a resection without any tumor manipulation has a beneficial effect on cancer recurrence. This observation was not supported by the findings of this study.

A limitation of this study was due to the retrospective nature of the study. Some selection bias might have been present.

In conclusion, the LR approach in rectal cancer is safe, feasible, and comparable to the standard OR approach in terms of the oncologic outcomes at 3-year follow-up. However, LR required a longer operative time in this study. A prospective study with a larger number of patients and a longer follow-up period is needed to demonstrate significant differences between the LR and OR groups.

## Author Contribution Statement

Dr. Kanittha Sakolprakaikij and Praisuda Bualoy performed the literature research and study design. Dr. Kanittha Sakolprakaikij performed the data collection, data analysis, data interpretation, and writing the manuscript under the supervision and aid of Dr. Kamthorn Yolsuriyanwong and Dr. Piyanun Wangkulangkul who edited the tables and figures and constructed the manuscript. Miss Nannapat Pruphetkaew from the Epidemiology Unit, Faculty of Medicine did the statistical analysis. Dr. Kanittha Sakolprakaikij, Siripong Cheewatanakornkul revised the data and prepared the manuscript in its final form.

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*Conflict of interest statement*

The authors confirm that there are no conflicts of interest associated with this publication and there was no financial support for this work that could have influenced its outcome.

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