# Anastomotic leakage following laparoscopic resection of low and mid rectal cancer

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**Anastomotic leakage following laparoscopic resection of low and mid rectal cancer**

PURPOSE*: Anastomotic leakage is considered the commonest major complication after surgery for rectal cancer.*
MATERIALS AND METHODS: *Patients who underwent laparoscopic LAR or ULAR for rectal cancer were recruited. The primary outcome was the incidence of the AL during 30 days postoperative.*
RESULTS: *Fifty-nine consecutive patients were included in the study. Fifty-three patients underwent LAR with stapled colorectal anastomoses, while the remaining 6 patients underwent ULAR with hand-sewn coloanal anastomoses. The median duration of operation was 195 minutes (range; 120-315). The defunctioning ileostomy was created in 24 (7%) patients.*
*Overall, there was no recorded mortality. Only 10 (17%) patients developed complications. There were only 4 patients who developed AL. Three patients had a subclinical AL as they had defunctioning ileostomy at the time of the initial procedure, the diagnosis was made by CT with rectal contrast. They were treated conservatively with transanal anastomotic drainage under endoscopic guidance. One patient had a clinically significant AL, demonstrated as a peritonitis. This patient required reoperation during which pelvic abscess was drained, resection of the previous anastomosis, and hartmann's colostomy was performed.*
CONCLUSION: *Standardization of a definition, as well as, criteria for the diagnosis of AL, will help in comparison of the results and the surgical techniques in order to optimize the required care offered to rectal cancer patients. On expert hands, it is feasible to perform a laparoscopic sphincter-saving total mesorectal excision, additionally, it provides the advantages of a clear view of the deep pelvis and facilitates a precise sharp dissection.*

KEY WORDS: Anastomosis, Anastomotic Leakage, Rectal cancer, Total mesorectal excision

## Introduction

Anastomosis after radical cancer resection is considered one of the most daily practice in gastrointestinal (GI) surgery [1]. Turrentine et al. [2] conducted a retrospective analysis of the National Surgical Quality Improvement Program (NSQIP) database reported that rectal, esophageal, or pancreatic anastomoses were associated with the highest risk of leakage, this may be attributed to lacking serosa or furthermore, the under tension anastomoses in cases of esophagus and rectum. Also, technical difficulties in approaching these areas and their easily compromised blood supply may be considered main reasons for these higher incidences of anastomotic leakage (AL).
AL is considered the most feared and life-threatening complication after rectal cancer surgery, especially if not promptly diagnosed and correctly treated [3]. AL is asso-

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ciated with an increased morbidity, mortality, the length of hospital stay, the rate of re-intervention, and poor oncological outcomes [4,5]. Furthermore, the quality of life is usually affected with poor functional outcomes and a higher rate of a permeant stoma in 56% of patients [6,7]. The postoperative mortality following AL range between 6.0 to 39.3%. These variations may be attributed to the fact that little reports about the postoperative complications of colorectal cancer surgery were multicenter studies, most of the studies based on single-center experience, furthermore, distinguish rectal from colon cancer was addressed in few studies [8].

Despite the advance and extensive research, AL stands as a frequent postoperative complication. [1] The incidence of AL following rectal resection ranges between 1% and 30% [10]. In low anterior resection (LAR), the clinically significant leakage ranges between 3% and 21% with an average of 10% [11]. The subclinical type was reported to occur in up to 51% of patients [12]. An incidence of 11.6% of AL occurs in patients undergoing total mesorectal excision (TME) for rectal cancer [13].

Not surprisingly, the AL incidence following colorectal surgery varies according to the anatomic level of the anastomosis, for colorectal or coloanal AL 1% to 19% [14]; colocolic leakage 0% to 2% [15]; ileocolic leakage 0.02% to 4.0% [16]; and ileoileal leakage around 1% [17]. This great discrepancy in reported incidences of AL in rectal resection may be attributed to the lack of objective and easily applicable definition of AL [4].

One of the earlier definitions was proposed in 1991 by the Surgical Infection Study Group as the *"leak of luminal contents from a surgical join between two hollow viscera. The luminal contents may emerge either through the wound or at the drain site, or they may collect near the anastomosis, causing fever, abscess, septicemia, metabolic disturbance and/or multiple-organ failure"* [18].

Currently, the variable definitions of AL that have been applied in clinical studies on (AR) do not allow simple comparison of results between studies and therefore hinder clear conclusions of what type of operative and perioperative management should be preferred in daily practice. The term "anastomotic leakage" used most frequently to describe the failure of the integrity of the colorectal/coloanal anastomosis, while the terms like an anastomotic leak, insufficiency, failure, breakdown, defect, separation, and dehiscence were less frequently used [19].

In a review of the literature, Bruce et al. [20] found 56 different definitions from 97 studies with the lack of accepted universal definition for AL for whether upper or lower gastrointestinal, or hepato-pancreaticobiliary anastomoses. They suggested a grade of AL depending on the change in management plan varying from no change, prolonged hospital stay, and change with the need for re-intervention respectively for radiological, clinically minor, and clinically major [20].

International Study Group of Rectal Cancer (ISGRC) [19] in 2010 conducted a review of the literature, they recommended the use of term "anastomotic leakage" as a preferred term to describe this event and proposed their definition *"Defect of the intestinal wall integrity at the colorectal or coloanal anastomotic site (including suture and staple lines of neorectal reservoirs) leading to a communication between the intra- and extraluminal compartments. A pelvic abscess close to the anastomosis is also considered as anastomotic leakage"*. Moreover, they recommended a severity grading system depend on the required type of intervention. Grade A; need no active therapeutic intervention, Grade B; need active therapeutic intervention but not re-laparotomy, and Grade C; need re-laparotomy. This available grading distinguishes between an asymptomatic radiologic and a clinical leakage or between a minor and a major leakage.

Cong and his colleges [4] in 2013 conducted a systematic review on articles described AL they then pooled the data and determined the average rate of AL for each grade according to the grading system proposed by ISGRC. The pooled overall rate of AL was 8.58% for AR, 8.88% for LAR, and 7.44% for ULAR. The pooled rate of AL was significantly ($P < 0.001$) higher in European countries compared to Asian countries and USA.

AL may be categorized based on clinical presentation into subclinical and clinical leakage; subclinical in the case of absence of any abdominal signs and in this scenario the leakage diagnosed by routine radiological study, while for the clinical leakage there will the signs of generalized peritonitis or localized abscess [21].

## Materials and Methods

### Study Design

The patient's recruitment process was started from January 2015 until January 2017. The study was registered in ClinicalTrials.gov with the identifier of NCT02718729. The data had been collected and analyzed prospectively. A signed informed consent was obtained from every patient highlighting the possible future publication, after approval from the local ethical committee in both University of Mansoura and University of Rome Tor Vergata according to the Egyptian and the Italian bioethics laws in concordance with the Helsinki Declaration Principals.

### Inclusions and Exclusions

Patients underwent curative laparoscopic low anterior resection (LAR) or ultralow anterior resection (ULAR) with colorectal or coloanal anastomoses for biopsy proven primary rectal cancer were recruited for the study. We excluded patients who were pregnant, with recurrent disease, with tumor more than 12 cm from the anal verge undergoing abdominoperineal resection

(APR), colorectal or coloanal anastomoses after Hartmann's procedure, emergency surgery, or intraoperative evidence of leakage. The level of the tumor was defined by the aid of the flexible sigmoidoscopy from the tumor lower border to the anal verge considering it low, middle, upper rectal cancer for those laying less than 6 cm, between 6 to 12 cm, more than 12 cm, respectively.

### Preoperative Workup and Preparation

As a part of the preoperative workup, all cases were discussed on colorectal multidisciplinary meeting and underwent standard preoperative staging for rectal cancer including; colonoscopy with biopsy, CT chest, CT abdomen and pelvis, MRI pelvis, tumor markers (CEA, CA 19-9), and/or endorectal ultrasound (ERUS). All patients were also seen in pre-assessment clinic with careful evaluation by consultant anesthetists.

Neoadjuvant therapy was offered in form of long-course chemoradiotherapy to patients who had a nodal disease or locally advanced resectable rectal cancers with the surgery was scheduled 8 to 12 weeks after completion of therapy. Adjuvant chemotherapy was routinely recommended and radiotherapy was employed for close or positive resection margins.

The day before surgery all patient received mechanical bowel preparation (MBP) with PolyEthilene Glycol (PEG) and an additional liquid diet. An adequate thromboembolic prophylaxis with low molecular weight heparin (LMWH) was given the evening before the surgery. Antibiotic prophylaxis with 1 gm 2nd generation cephalosporin and 500 mg metronidazole were administered at the time of anesthesia induction.

### Surgical Technique

Using 4 trocars technique with 30° scope, medial to lateral dissection was started. The IMV vein was controlled at the level of the ligament of Treitz with the use of LigaSure™ vessel sealing device (Medtronic, Inc., Minneapolis, MN, USA). Then a high ligation of the IMA was performed, 1-1.5 cm distally to the origin by an Endo GIA™ 30 mm Articulating Vascular/Medium Reload with Tri-Staple ™ Technology (Medtronic, Inc., Minneapolis, MN, USA) loaded with white cartilage 45 mm. Full mobilization of the splenic flexure was routinely performed.

Total mesorectal excision (TME) was performed in the standardized way as described by Heald [22].

Transection of the rectum was done with an Endo GIA™ 30 mm Articulating Medium/Thick Reload with Tri-Staple ™ Technology loaded with violet cartilage 60 mm or Contour® Curved Cutter Stapler green (Ethicon, US, LLC., Cincinnati, OH, USA).

The specimen was extracted through a 4-5 cm Pfannenstiel incision. An end-to-end, side-to-end or side-to-side anastomosis was created extracorporeally, using a 29 or 33 mm circular stapler (Covidien "DST Series™ EEA™", Medtronic, Inc., Minneapolis, MN, USA). The integrity of anastomosis was tested by the competence doughnuts and by air leak test by immersion of pelvis with physiological saline with transanal air insufflation. Large Robinson or Blakes drain was placed in the presacral space. A defunctioning ileostomy was constructed if there was poor bowel preparation, technical difficulties in performing anastomosis, and for all anastomoses less than 6 cm from the anal verge.

### Postoperative Care

Patients were allowed clear fluid as soon as they tolerated it. The urinary catheter was removed on 1st day postoperative (POD) and from that day patients were encouraged for ambulation. Oral diet was resumed from the 2nd POD. A regimen of four weeks' prophylactic dose of LMWH was given to every patient. Antibiotic prophylaxis was continued for 24 hours after operation (3 more doses of IV 1 gm 2nd cephalosporin). The drain was removed after 48-72 hours depending on the volume of the discharge. Once the patients became fully ambulant combined with the absence of any major complications, they were discharged.

### Definition and Diagnosis of Anastomotic Leakage

Since there is no consensus in the literature about the definition of anastomotic leakage (AL) and there are multiple definitions used in different studies, for our study we adopted the definition published by Adams and Papagrigoriadis [23]. We defined AL when; there was a feculent material obtained from the drain or the wound, extravasation of dye on CT with rectal contrast, anastomotic defect directly visualized during colonoscopy, and finally the presence of peri-anastomotic air or fluid visualized on CT scan.

According to leakage patients were classified into no leakage group for patients without AL and leakage group for those with AL. Patients with AL were further subdivided into subclinical with no clinical symptoms and were diagnosed on routine CT with rectal contrast and clinical which was diagnosed with the presence of signs of localized abscesses or generalized peritonitis.

Furthermore, AL was graded according to the ISGRC [19] depending on the requirement of active therapeutic intervention into Grade A; requiring no active therapeutic intervention, Grade B; requiring active therapeutic intervention without re-laparotomy and Grade C; requiring re-laparotomy.

### Patient's Follow-Up, Outcomes, and Definitions

For the end-points of the study, patients were followed-up on the ward and then in the outpatients' department at two weeks and one month postoperative. When patients were suspected to have AL they underwent CT with rectal contrast to assess the integrity of the anastomosis. Six weeks after discharge all patients underwent follow-up flexible sigmoidoscopy at the outpatients' department.

The primary outcome was the incidence of the AL during 30 days postoperative. Secondary outcomes were the incidence of anastomotic stricture, conversion rate, operating time, the length of hospital stay, the clearness of safety margins, the role of diversion in decreasing the incidence of AL or urgent reoperation, overall 30 days' postoperative morbidities and mortality. Complications were classified according to the Clavien-Dindo [24] classification of surgical complications.

LAR was defined as complete mobilization of the extraperitoneal rectum and resection of more than the mid extraperitoneal rectum combined with TME with the anastomosis below the peritoneal reflection but beyond 2 cm of the dentate line, for ULAR the same previous definition was applied with the anastomosis within 2 cm of the dentate line (coloanal anastomosis).

Conversion to laparotomy was defined as any unplanned abdominal incision or an abdominal incision was made longer than or earlier than planned to complete any part of the surgery, a 5 cm incision for specimen extraction or extracorporeal anastomosis was not considered a conversion

A curative resection was defined as removal of all macroscopic primary and metastatic tumor if present at the time operation. The positive margin was defined as the presence of tumor within 1 mm from any resection margin; proximal, distal or circumferential.

### Variables Studied and Statistical Analysis

Basic patient's demographic data were recorded including age, sex, body mass index (BMI) status, American Society of Anesthesiology (ASA), tumor stage, the distance of the tumor from the anal verge, use of neoadjuvant chemoradiotherapy, duration of the operation, the length of hospital stay, time to resume feeding, postoperative morbidity, and mortality. Variables were categorized into patients, tumor, operation, and leakage-related variables. Data were collected in excel spreadsheet then analyzed using SPSS (Statistical Package for Social Science version 21 for Microsoft Windows). Continuous data were expressed as a mean ± (SD) or median (range) according to normality.

## Results

### Patients and Tumors Characteristics

Fifty-nine consecutive patients with primary rectal cancer were included in the study, of them, 27 were male and 32 females. The mean age was 63.49 ± 11.16 years and the mean BMI was 24.95 ± 3.56 kg/m$^2$. The median tumor distance from the anal verge was 7 cm (range; 4-12). Twenty-six (44%) patients were received neoadjuvant chemoradiotherapy for nodal disease and/or locally advanced rectal cancer (Table I). Fig. 1 displayed the recruitment process and the patients who were included, while Fig. 2 showed tumor size.

### Intra-Operative Details

All procedures were performed laparoscopic with only 5 (8%) patients needed conversion to open due to large size tumor (n=3) and failure to identify the ureter (n=2). Fifty-three patients underwent low anterior resection (LAR) with stapled colorectal anastomoses, while the remaining 6 patients underwent ultralow anterior resection (ULAR) with hand-sewn coloanal anastomoses. The

Table I - *Patients' and tumor's characteristics.*

| | **Patients N. (%)** |
|---|---|
| Total | 59 |
| Male | 27 (46%) |
| Female | 32 (54%) |
| Age (Mean ± SD) | 63.49 ± 11.16 years |
| BMI (Mean ± SD) | 24.95 ± 3.56 kg/m$^2$ |
| ASA | |
| I | 2 (3%) |
| II | 11 (19%) |
| III | 46 (78%) |
| Smoking | |
| Non-smoker | 47 (80%) |
| Ex-smoker | 5 (8%) |
| Smoker | 7 (12%) |
| Tumor location | |
| Low (0-6 cm) | 24 (41%) |
| Mid (7-12 cm) | 35 (59%) |
| Median distance from anal verge (range) | 7 cm (range; 4-12) |
| Patients received neoadjuvant CRT* | 26 (44%) |
| TNM stage | |
| I | 26 (44%) |
| IIA | 15 (25%) |
| IIIA | 1 (2%) |
| IIIB | 11 (19%) |
| IIIC | 5 (8%) |
| IVA** | 1 (2%) |

* CRT; chemoradiotherapy

** Liver metastasis

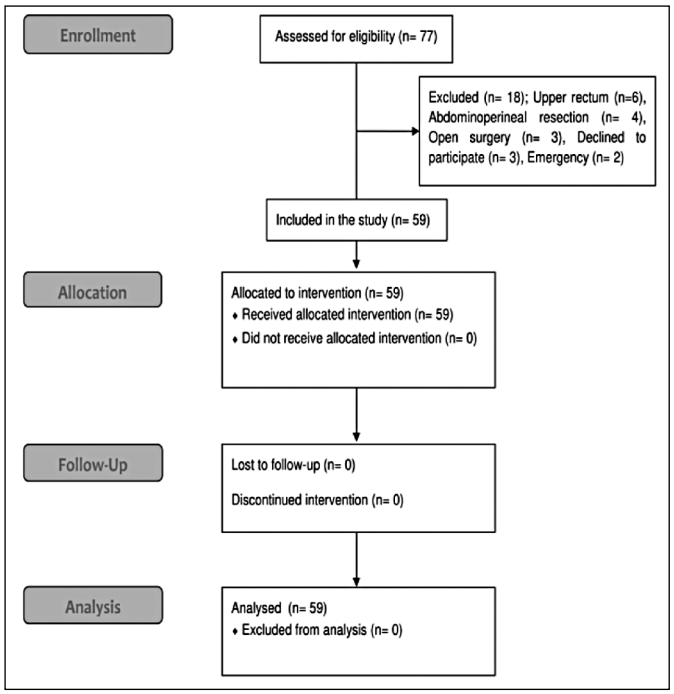


Fig. 1: A flow diagram illustrating the recruitment process.

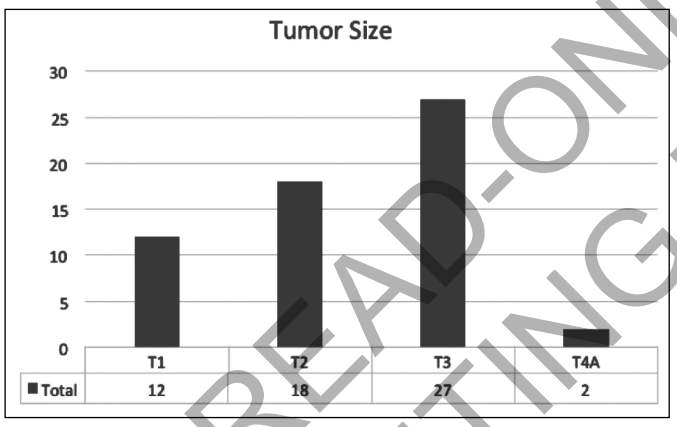


Fig. 2: Tumor characteristics; Tumor size.

median duration of operation was 195 minutes (range; 120- 315) (Table II).
Two fires were required in 48 patients to obtain a complete rectal division. Forty-two patients had end-to-end anastomoses created, whereas 16 patients had side-to-end anastomoses, and only one side-to-side anastomosis. The defunctioning ileostomy was created in 24 (41%) patients at the time of initial surgery (Table II).

## 30 Days' Postoperative Mortality and Morbidities

Overall, there was no recorded mortality during the study period. Only 10 (17%) patients developed complications;

Table II - *Operative details.*

| | **Patients N. (%)** |
|---|---|
| Rectal resection | |
| LAR* | 53 (90%) |
| ULAR** | 6 (10%) |
| Median duration of operation (range) | 195 min (range; 120-315 min) |
| Conversion | 5 (8%) |
| Two firing | 48 (81%) |
| Diversion | 24 (41%) |
| Anastomosis level | |
| Colorectal anastomosis | 53 (90%) |
| Coloanal anastomosis | 6 (10%) |
| Anastomosis configuration | |
| End-to-End | 42 (71%) |
| Side-to-End | 16 (27%) |
| Side-to-Side | 1 (2%) |
| Anastomosis | |
| Stapled | 53 (90%) |
| Hand-sewn | 6 (10%) |

* LAR; low anterior resection
** ULAR; ultralow anterior resection

Table III - *Post-operative course; time to resume eating and length of hospital stay.*

| | **Median in days (range)** |
|---|---|
| Length of hospital stay | 10 (6- 28) |
| Time to resume eating | 3 (2- 10) |

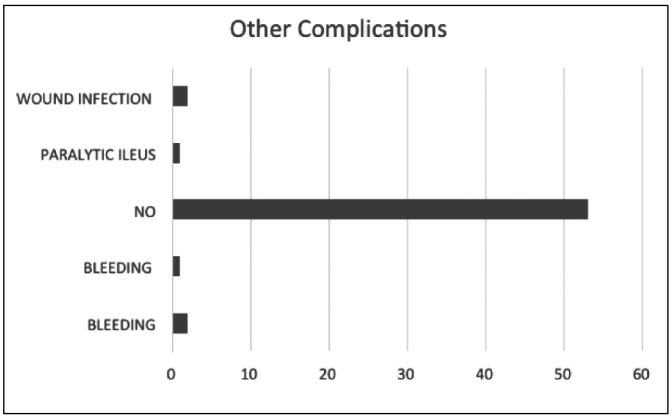


Fig. 3: Types of complications.

anastomotic leakage (AL) (n=4), postoperative bleeding (n=3), wound infection (n=2), and paralytic ileus (n=1). Postoperative complications were categorized based on the Clavien-Dindo classification of surgical complications (Table IV, V, Figs. 3, 4, 5).

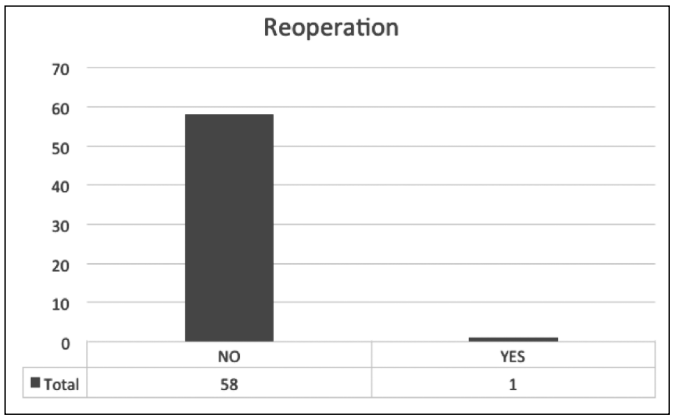


Fig. 4: Number of patients required reoperation.

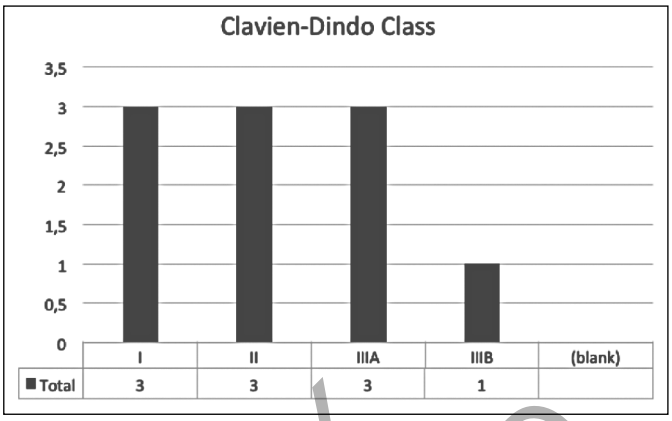


Fig. 5: Clavien-Dindo classifications of postoperative complications.

TABLE IV - *Post-operative complications, treatment, and Clavien-Dindo classification.*

| Complication | Patients N. (%) | Treatment | Clavien-Dindo classification |
|---|---|---|---|
| Total no | 10 | | |
| Anastomotic leakage | 4 | 3; Transanal anastomotic drainage/antibiotics | IIIA |
| | | 1; Hartmann's colostomy | IIIB |
| Postoperative bleeding | 3 | Blood transfusion (total transfusion 5 unit of blood) | II |
| Wound infection | 2 | Antibiotics treatment | II |
| Paralytic ileus | 1 | Conservative treatment | I |

TABLE V - *Patients with anastomotic leakage.*

| | Patient N. 23 | Patient N. 27 | Patient N. 42 | Patient N. 59 |
|---|---|---|---|---|
| Sex | F | F | M | M |
| Age | 66 years | 63 years | 66 years | 59 years |
| BMI | 24 kg/m2 | 26 kg/m2 | 28 kg/m2 | 25 kg/m2 |
| ASA | II | III | II | III |
| Smoking | No | No | No | Smoker |
| Distance | 9 cm | 5 cm | 5 cm | 4 cm |
| T | T3 | T2 | T3 | T3 |
| TNM Stage | IIIB | I | IIIC | IIIC |
| Neoadjuvant | Yes | No | Yes | Yes |
| Operation | LAR | LAR | LAR | ULAR |
| Duration | 205 min | 210 min | 200 min | 215 min |
| Conversion | No | No | No | Yes |
| Firing | 2 | 2 | 2 | 2 |
| Anastomotic level | Colorectal | Colorectal | Colorectal | Coloanal |
| Anastomotic configuration | End-To-End | End-To-End | Side-To-End | End-To-End |
| Anastomotic technique | Stapled | Stapled | Stapled | Hand-sewn |
| Ileostomy | Yes | Yes | No | Yes |
| Length of hospital stay | 15 days | 17 days | 28 days | 28 days |
| Resume eating | 2 days | 4 days | 10 days | 3 days |
| Other complications | No | No | No | No |
| Date of leakage diagnosis | 21st POD* | 8th POD | 3rd POD | 6th POD* |
| Leakage type | Sub-Clinical | Sub-Clinical | Clinical | Sub-Clinical |
| Leakage grade | B | B | C | B |
| Reoperation | No | No | Yes | No |
| Treatment | Transanal anastomotic drainage/antibiotics | Transanal anastomotic drainage/antibiotics | Hartman | Transanal anastomotic drainage/antibiotics |
| Clavien-Dindo Class | IIIA | IIIA | IIIB | IIIA |

*POD; postoperative day

### Anastomotic Leakage and Stricture Patients

There were only 4 patients who developed AL (7%) the characters of these patients were displayed in (Table V). Three patients had a subclinical AL as they had defunctioning ileostomy at the time of the initial procedure, the diagnosis was made by CT with rectal contrast at 6th, 8th and 21st postoperative day (POD). They were grade B according to the IGSRC [19] grading system and treated conservatively with transanal anastomotic drainage under endoscopic guidance and intravenous antibiotics. These 3 patients were discharged home on the 15th, 17th, 28th POD subsequently.

One patient had a clinically significant AL, demonstrated as a peritonitis at the 3rd POD. This patient was grade C according to the IGSRC [19] grading system and required reoperation during which pelvic abscess was drained, resection of the previous anastomosis and Hartmann's colostomy was performed.

Six weeks after discharge all the 59 patients underwent follow-up flexible sigmoidoscopy at the outpatients' department which showed completely healed anastomotic defect with no residual stenosis in those who developed AL. Only one patient developed anastomotic stricture which was treated with regular dilation in outpatients' department, this patient did not show any manifestations of AL.

### Postoperative Bleeding, Wound Infection, and Paralytic Ileus

None of these complications required any additional surgical intervention or ICU admission; postoperative bleeding required a blood transfusion, wound infection required antibiotics, and paralytic ileus required conservative management (Table IV).

### Postoperative Pathological Specimen

Pathological examination of the postoperative specimen showed tumor free proximal, distal and circumferential margins in all patients.

### Time to Resume Feeding and Length of Hospital Stay

The median length of hospital stay was 10 days (range 6-28). The median time to resume eating was 3 days (range 2-10) (Table III).

## Discussion

Through the study period starting from January 2015 till January 2017, we included 59 patients who underwent laparoscopic low anterior resection (LAR) and ultralow anterior resection (ULAR) for biopsy proven primary rectal cancers. All patients were consecutive patients, 80% of patients were ≥ ASA III, we did not exclude patients who needed conversion to open surgery, furthermore, our patients had a mean (±SD) age of 63.49 (± 11.16) years.

The first step was the identification of the inferior mesenteric artery (IMA), but the inferior mesenteric vein (IMV) was ligated first. It is important to identify the left ureter before ligation of the IMA, furthermore, we considered failure to identify the left ureter is an indication to convert to open surgery. We employed high ligation of the IMA 1 to 1.5 cm from its origin from the abdominal aorta. Tension-free anastomosis mandated full mobilization of the splenic flexure. All patients underwent total mesorectal excisions (TME) as prescribed by Heald [22] starting posteriorly, then laterally, and finally anteriorly. Rectal transection was done using Endo GIA ™ then an extracorporeal anastomosis was performed using a circular stapler. A leak test was performed in all patients by checking the competence of the doughnuts and air leak test (ALT). The decision of defunctioning stoma was individualized according to the anastomotic height and intraoperative difficulties.

According to Cheung et al. [25] in 2009 by a questionnaire among 368 surgeons worldwide, in whom 41.8%, 49.8%, and 8.4% perform 1-10, 10-40, and >40 laparoscopic TME resections per year respectively, our technique was comparable; 81.2% of European perform medial-to-lateral approach; 77.7% perform high ligation of IMA artery; 71.2% perform routine splenic flexure mobilization; 62.2% use blue cartridge in rectal transection; 91.5% of Americans and 61.2% of European create end-to-end anastomosis; 98.9% use circular stapler to create the anastomosis; 65.5% use anvil sizes of 28-29 mm; 67.7% perform ALT; 83.2% create a defunctioning stoma with 86% of these stomas were ileostomy; and 74.2% leave a drain.

Overall, we reported no mortality in this study which is comparable to the published results by Kang et al. [26], Barlehner et al. [27] and Miyajima et al. [28]. While the MRC CLASSIC [29] reported 4% mortality rate which is relatively higher than our results, this may be explained by the fact that this was the first trial to included laparoscopic rectal cancer resections.

Only 10 (17%) patients developed complications; anastomotic leakage (AL) in 4 patients, postoperative bleeding in 3 patients, wound infection in 2 patients, and paralytic ileus in 1 patient. This morbidity rate coincide with published results by Kim et al. [30], Pugliese et al. [31], and Ng et al. [32]. On the other hand, other authors as Staudacher et al. [33], Morino et al. [34], Dulucq et al. [35] published a higher incidence of morbidity ranging between 22-38% and in one study by Tsang et al. [36] reached 61%. This difference can be attributed to the fact that we did not include any emergency procedure [37] and

all of our patients were operated by the same team.

We used the Clavien-Dindo[24] classification of postoperative surgical complications as a precise method to report postoperative complications, as it was based on the therapeutic consequences which increase the objective information given and highlights further morbidity linked to the therapy-induced stress. The way in which complications were reported using terms such as early versus late complications or minor versus severe may hinder proper clarification of surgical outcomes. According to the Clavien-Dindo [24] classification of surgical complications we encountered; grade I in 1 patient, II in 5 patients, IIIA in 3 patients, and IIIB in 1 patient. Few series used this classification to report their complications. Laurent et al. [38] reported 44 patients were Grade III, 4 patients were Grade IV, and 2 patients were Grade V.

There were only 4 (7%) patients who developed AL in our study. These results coincide with published articles by the MRC CLASSIC [29], Park et al. [39], and Kim et al.[30], while other articles reported AL rate ranging between 0.4%-17% by Van der Pas et al. in the COLOR II trial [40], Staudacher et al. [33], Morino et al. [34], and Miyajima et al. [28]. These wide ranges of incidence may be attributed to lack of constant definition and criteria of diagnosis for AL.

Three of our patients who developed AL were treated conservatively with transanal anastomotic drainage and intravenous antibiotics. Six weeks after discharge those patients underwent follow-up flexible sigmoidoscopy which showed completely healed anastomotic defect with no residual stenosis. The remaining patient of those developed AL, required additional re-intervention to drain the pelvic abscess and resection of the anastomosis with the formation of Hartmann's colostomy.

The distance of the tumors from the anal verge was 4 cm in 1 patient, 5 cm in 2 patients and 9 cm in 1 patient of those developed AL. Anastomotic height is the most common factor associated with a significantly higher incidence of AL. [11] These results were confirmed by Cong et al. [41] Matthiessen et al. [42] , Wang and Gu [43], and Makela et al. [44]. While Park et al. [45] and Bertelsen et al. [46] did not find this significant association. This discrepancy may be attributed to the routine use of diversion in low-laying anastomoses which may lower the incidence of AL.

Three of our patients who developed AL were received neoadjuvant therapy. Twenty-six of our patients received neoadjuvant therapy, so a percentage of 12% of patient who received neoadjuvant therapy developed AL. Currently, the use of neoadjuvant therapy becomes crucial in rectal cancer treatment [47]. Kapiteijn et al. [48] found that the incidence of AL was similar in both groups of patients who were offered TME alone or with preoperative radiotherapy, same results reported by Sauer et al. [49] in the German trial. However, Cedermark et al. [50] in Stockholm trail I reported a higher AL in the neoadjuvant radiotherapy group but these numbers did not reach a significant level.

In our study, 48 patients from the whole 59 needed 2 fires for complete rectal transection, while the remaining 11 patients required only single fire. Rectal transection needed 2 fires in all AL patients, this gives a percentage of 8% of patients with 2 fires developed AL. Hotta and Yamaue [51] reported that rectal transection required multiple firings may cause AL. Also, Park et al. [45] reported a significant association between the number of fires needed for rectal transection and AL.

In patients who developed AL, anastomoses were coloanal hand-sewn in 1 patient and colorectal stapled in 3 patients, the configuration was end-to-end in 3 patients and side-to-end in 1 patient. In our study, anastomoses were end-to-end in 42 patients giving a 7% percentage of end-to-end anastomoses developed AL. Stapled colorectal anastomoses were 53 in the whole study giving a 6% percentage of stapled colorectal anastomoses developed AL. Slieker et al. [52] in a systematic review of the colorectal anastomoses technique testified a level 1A evidence of lack superiority of stapled versus hand-sewn anastomoses and a level 1B of a lower incidence of AL with side-to-end configuration, they also, found that studies on anastomotic configuration were often concentrating on pouch anastomosis for very low anastomoses with an end-point other than AL, so they gave this evidence from 2 experimental studies.

During the period of follow-up, only one patient developed anastomotic stricture which is considered a sequel for subtle AL, this stricture was treated by regular dilation in the outpatients' department [53]. Ng et al. [32] reported 117 complications in their study with 24 of these complications were an anastomotic stricture. Agha et al. [54] reported a 3.6% percentage of their patients developed anastomotic stricture. Barlehner et al. [27] reported an incidence of 2.1% for anastomotic stricture. The lower incidence we reported of anastomotic stricture could be explained by the fact that we employed full splenic flexure mobilization in all of our patients.

The defunctioning ileostomy was created in 3 patients of those developed AL at the time of initial operation, considering that 24 of our patients received defunctioning ileostomy at the time of initial procedures, so the percentage of patients with defunctioning ileostomy who developed AL was 13%. The decision for the construction of a defunctioning ileostomy was decided intraoperatively if there were any technical difficulties while performing the anastomosis. The role of diversion in the prevention of AL is still debatable, so patient selection should be justified [55,56]. Tan et al. [57] in a meta-analysis of 4 RCTs and 21 non-RCTs reported that the non-diverted anastomoses were associated with an increased incidence of AL combined with a higher rate of reoperation, but with no statistically significant difference in the mortality rate.

In our series, the median duration of operation was 195 minutes (range; 120-315), these results coincide with the results previously published in the MRC CLASSIC [29].

Park et al. [39], Delgado et al. [58], Kim et al. [30], and Agha et al. [54]. On the other hand, a shorter duration of 180 minutes (135-300) was reported by Tsang et al. [36], while Staudacher et al. [33] reported a mean operating time of 250 ± 116 minutes, which was not far from the published by Morino et al. [34] who reported 250 minutes (110-540). Longer duration of operation was reported by Laurent et al. [38] as they reported a median duration of 360 minutes (150-720). These variations of operating time may be explained by some of these studies included abdominoperineal resection (APR) and sphincter-saving procedures.

We testified a median time to resume eating of 3 days (range 2-10), which is comparable to published results by Kang et al. [26] , the COLOR II trial [40], and Delgado et al. [58]. Poon and Law [59] reported a range of 3-5 and 3-6 days postoperative to regain a bowel movement and tolerance to normal diet respectively.

We reported a median length of hospital stays of 10 days (range; 6-28), which is coincide with the published results by Staudacher et al. [33], Laurent et al. [60], and Leroy et al. [61]. Poon and Law [59] reported a mean length of hospital stay ranging between 8 to 11 days.

We defined conversion to laparotomy as any unplanned abdominal incision or an abdominal incision made longer or earlier than planned to complete any part of the surgery, a 5 cm incision for specimen extraction or extracorporeal anastomosis not considered a conversion. Braga et al. [62] defined conversion as an abdominal incision >7 cm, MRC CLASSIC trial group [29] defined it as an abdominal incision larger than required for retrieval of the specimen, Kim et al. [30] defined it as any unplanned incision in order to complete the procedure, Laurent et al. [60] defined it as a conventional midline laparotomy, Ng et al. [32] defined it as any part of the procedure with an open technique, and Staudacher et al. [63] defined it as laparoscopic procedure interruption.

In our study, all procedures were performed laparoscopic with only 5 (8%) cases needed conversion to open due to large size of the tumor in 3 patients and failure to identify the left ureter in 2 patients, this coincide with published results by Pugliese et al. [31], and lower than others as Morino et al. [34] and Dulucq et al. [35] this for articles on sphincter-saving resection only.

The conversion to open surgery was considered an indicator of inferior surgical outcomes in several reports [59]. However, in our study, only two patients who needed conversion to open surgery developed complications which were AL and wound infection and they were classified as Clvaian-Dindo class IIIA and I respectively.

Despite our efforts, this study still limited by certain factors. First, the fact that more patients should be recruited. Second, short duration of follow-up, which might be extended to include defunctioning ileostomy-related complications till the time of stoma reversal. Future multicenter international prospective study recruiting more patients is needed with a longer period of follow-up.

## Conclusion

Despite the recent advances in surgical techniques, anastomotic leakage (AL) remains a serious health problem which is associated with an increased mortality, morbidity, longer hospital stay, the rate of reoperation, with an additional cost. Many preventative measures are employed with no clear evidence of superiority over each other or even significant role in decreasing the incidence of AL. Justification and selection criteria should be identified for construction of defunctioning ileostomy. Standardization of a definition, as well as criteria for the diagnosis of AL, will help to compare the results and the surgical techniques in order to optimize the required care offered to rectal cancer patients.

On expert hands, it is feasible to perform a laparoscopic sphincter-saving total mesorectal excision (TME) for rectal cancer patients, additionally, it provides the advantages of a clear view of the deep pelvis and facilitates a precise sharp dissection. Despite the fact that laparoscopic TME has a relatively longer operative time compared to conventional open surgery, this can be compensated by the earlier return of bowel function shortening the hospital stay. The rates of morbidity, mortality, and AL show a non-significant difference between laparoscopic and conventional open surgery. However, these results came from case series, non-RCTs, with only a few RCTs, combined with the fact of absence of widely acceptable definition or criteria for the diagnosis of AL make these results confusing. Standardization of the technique of laparoscopic TME with a better reporting of the of operative details in concordance with short and long-term outcomes is required for better comparison of results. Subsequently, this will result in a predictable and reproducible operation.

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