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Transanal Inspection and Management of Low Colorectal Anastomosis Performed With a New Technique: the TICRANT Study

Francesco Crafa, MD[1], Sebastian Smolarek, MD[2], Giulia Missori, MD[2], Mostafa Shalaby, MD, MSc[2], Silvia Quareisma, MD[2], Adele Noviello, MD[1], Diletta Cassini, MD, PhD[3], Pasquale Ascenzi, MD[4], Luana Franceschilli, MD[2], Paolo Delrio, MD[5], Giannandrea Baldazzi, MD[3], Ucchino Giampiero, MD[4], Jacques Megevand, MD, PhD[6], Giovanni Maria Romano, MD, PhD[5], and Pierpaolo Sileri, MD, PhD[2]

Abstract

Background: Anastomotic leakage is one of the most serious complications after rectal cancer surgery. *Method:* A prospective multicenter interventional study to assess a newly described technique of creating the colorectal and coloanal anastomosis. The primary outcome was to access the safety and efficacy of this technique in the reduction of anastomotic leak. *Result:* Fifty-three patients with rectal cancer who underwent low or ultra-low anterior resection were included in the study. There were 35 males and 18 females, with a median age of 68 years (range = 49-89 years). The median tumor distance from the anal verge was 8 cm (range = 4-12 cm), and the median body mass index was 24 kg/m^2 (range = 20-35 kg/m^2). Thirty patients underwent open, 16 laparoscopic, and 7 robotic surgeries. Multiple firing (2-charges) was required in 30 patients to obtain a complete rectal division. Forty-five patients had colorectal anastomosis, and 8 patients had coloanal anastomosis. The protective ileostomy was created in 40 patients at the time of initial surgery. There was no mortality in the first 30 days postoperatively, and only 10 (19%) patients developed complications. There were 3 anastomotic leakages (6%); 2 of them were subclinical with ileostomy created at initial operation and both were treated conservatively with transanal drainage and intravenous antibiotics. One patient required reoperation and ileostomy. The median length of hospital stay was 10 days (range = 4-20 days). *Conclusion:* Our technique is a safe and efficient method of creation of colorectal anastomosis. It is also a universal method that can be used in open, laparoscopic, and robotic surgeries.

Keywords

rectal cancer, anterior resection, total mesorectal excision, double stapling technique, anastomosis, anastomotic leak

Introduction

Despite recent advances in colorectal surgery, anastomotic leakage remains one of the most feared complication after rectal cancer surgery.[1-3] Anastomotic leakage is more common after low anterior resection than any other type of gastrointestinal surgery. The lower the anastomosis, the higher is the risk of leakage.[4-7] The reported incidence of anastomotic leakage varies in literature, with an average of 10% (range = 3% to 21%).[1,8-11] There are some studies that reported a leakage rate as high as 36%[12,13] for clinically significant leak and 51%[1,14] for subclinical leakage.[12] The reported widespread incidence of leakage might be due to multiple definitions of anastomotic leakage existing in the literature.[8]

Anastomotic leakage is associated with the high mortality rate ranging from 6% to 39%. It also prolongs postoperative hospital stay, increasing the cost of treatment, as well as contributes to poor overall survival and high

[1]San Giuseppe Moscati Hospital, Avellino, Italy
[2]University of Rome Tor Vergata, Rome, Italy
[3]Policlinico di Abano Terme, Padova, Italy
[4]Chirurgia Generale, Ospedale Maggiore, Bologna Italy
[5]Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale," Naples, Italy
[6]Casa di Cura San Pio X, Milano, Italy

Corresponding Author:
Pierpaolo Sileri, University of Rome Tor Vergata, Policlinico Tor Vergata Hospital, Viale Oxford 81, 00133 Roma, Italy.
Email: piersileri@yahoo.com

local recurrence rate.[10] It also increases the incidence of emergency reoperation and a creation of stoma, which may become permanent in 25% of patients.[1,3,10-15]

Several risk factors for anastomotic leakage have been reported in the literature, with no clear consensus. The well-recognized risks factors for anastomotic leak are distance of the tumor from the anal verge (low rectal tumor), previous radiotherapy, emergency operation, male sex, advanced age, diabetes mellitus, vasculopathy, obesity, chronic obstructive pulmonary disease, malnutrition, chronic corticosteroid therapy, multiple numbers of stapler firings during rectal division, and finally low case volume for center (<20/year).[11,16-27]

Consequently, many protective measures were introduced to reduce the incidence of leakages such as intraoperative leakage testing, omentoplasty, a creation of diverting stoma, placement of a pelvic drain, and use of a biodegradable material. There is, however, no clear evidence supporting its effectiveness.[28-34]

Currently, the double stapling technique is the most widely performed procedure, which facilitates the creation of low colorectal anastomoses.[34] This technique is known to increase the incidence of anastomosis leak and strictures formation.[11] This is mainly caused by 2 factors: there are at least 2 staple lines crossing each other and use of 2 staplers creates stapled corners (the so-called "dog ears"), which can potentially lead to the creation of ischemic areas. Dog ear is also the "locus minoris resistantiae" point of the anastomosis, which can cause anastomotic leakage when intraluminal pressure increases.[35]

In the ideal situation, the 2 cross staple lines should be avoided and anastomosis should be inspected immediately after creation and reinforced it if necessary.

To overcome the weaknesses of the double stapling technique, we adopted a new technique to perform a colorectal and coloanal anastomosis.

The TICRANT study (Transanal Inspection and management of low ColoRectal Anastomosis performed with a New Technique) is a pilot study that describes a new surgical technique and evaluates its safety and efficacy. In this study, the primary outcome was to evaluate the incidence of anastomotic leak. Secondary outcomes were to evaluate the rate of postoperative mortality and morbidities and achievement of clear resection margins.

Materials and Methods

Study Design

Patients were prospectively enrolled into the study between January 2013 and January 2016 in the participating centers. The study was registered in ClinicalTrials.gov, with identifier NCT02879370. Six centers participated in the study where the principals' surgeons were a senior consultant of colorectal surgery or surgical oncology performing at least 20 rectal resections per year.

All patients signed written informed consent including the possibility of future publication according to the Italian bioethics laws. Institutional review board approval was obtained from the local ethical committee of each center in compliance with the principles of the Helsinki Declaration.

Inclusions and Exclusions

Patients undergoing curative low or ultra-low anterior resection for biopsy-proven primary rectal cancer were recruited for the study. Patients younger than 18 years of age, pregnant, with recurrent disease, with cancer less than 4 cm from the anal verge, undergoing abdominoperineal resection or emergency surgery were excluded from the study. A flow diagram illustrating the recruitment process is displayed in Figure 1.

Preoperative Assessment and Preparation

As a part of preoperative workup all cases were discussed on colorectal multidisciplinary meetings and underwent standard preoperative staging for rectal cancer, including colonoscopy with biopsy, computed tomography (CT) chest, CT abdomen and pelvis, magnetic resonance imaging pelvis, and/or endorectal ultrasound. All patients were also seen in preassessment clinics with careful evaluation by consultant anesthetists.

The day before surgery all patient received full mechanical bowel preparation with PEG (polyethylene glycol) with additional liquid diet. An adequate thromboembolic prophylaxis with low-molecular-weight heparin was given the evening before the surgery. Antibiotic prophylaxis with second-generation cephalosporin was administered at induction of anesthesia.

Surgical Technique

The low or ultra-low anterior resection with total mesorectal excision was performed in the standardized way as described by Heald.[36] Surgery was performed through open, laparoscopically, or robotic way. Just before rectal division, the circular anal dilator (CAD) device was inserted into the anal canal and fixed to the perianal skin by four 0-Silk sutures at the 4 cardinal's points. The rectal inspection was carried out by a purse suture anoscope to correctly identify the proximal and distal extension of the tumor. After that, the rectum was divided by linear or curved stapler under direct inspection through the CAD (Figure 2).

Four 2-0 Prolene sutures were placed: 2 of them at the extremities of the suture line (left and right), and then the

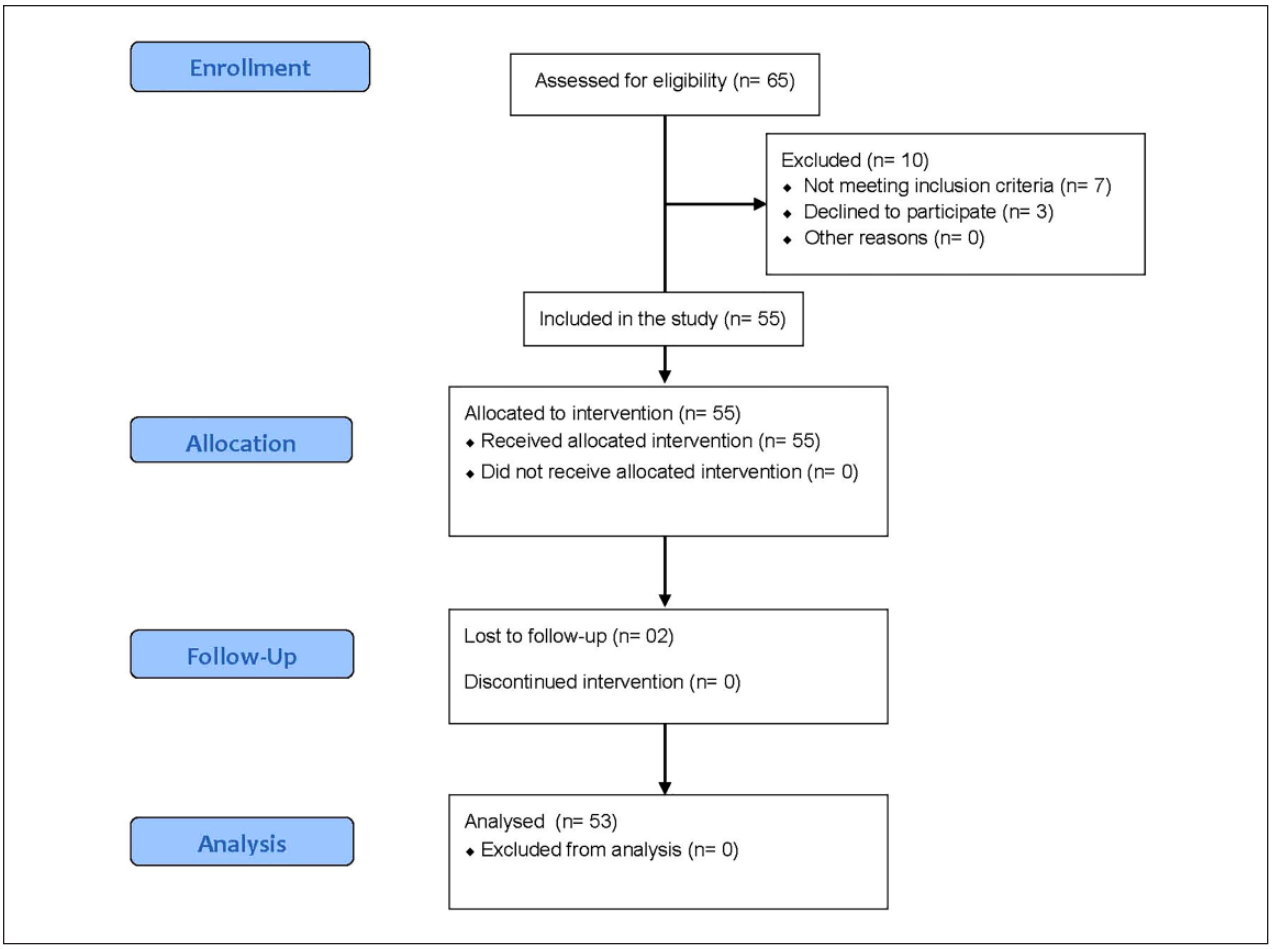

Figure 1. Flow diagram for patient recruitment process.

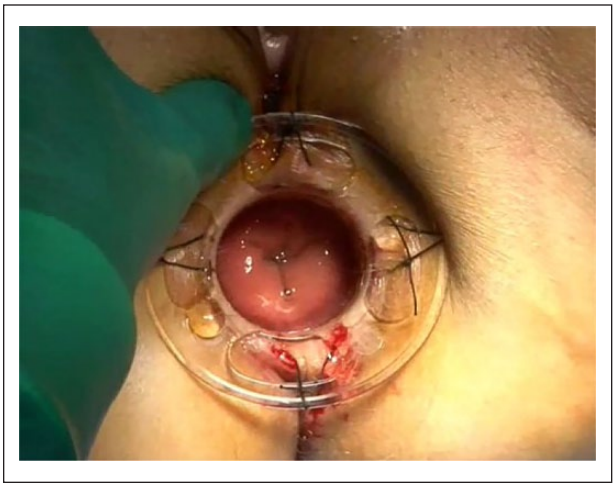

Figure 2. Circular anal dilator inserted and fixed to the perianal skin.

stump is pulled through the anus to allow the placement of the other 2 sutures transanally on the rectal stump 1 cm medially to the previous 2 sutures (Figure 3).

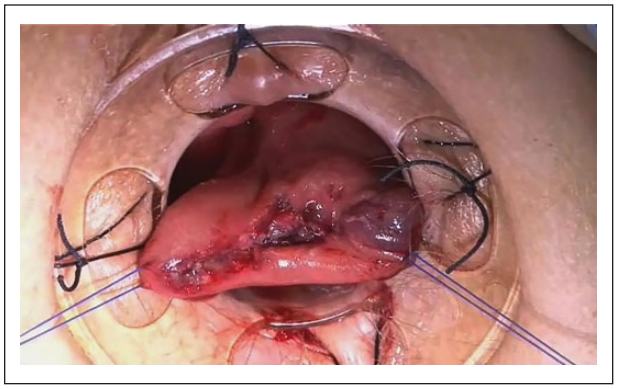

Figure 3. Two 2-0 Prolene sutures were placed transanally on the rectal stump at the extremities of the suture line (left and right).

The circular stapler was introduced through the CAD (29 or 33 mm KOL stapler, Touchstone International Medical Science Co, Ltd, Suzhou, China; Figure 4). The 4 tails of the Prolene stitches were introduced through the stapler channels (2 in the left and 2 in the right sides of the

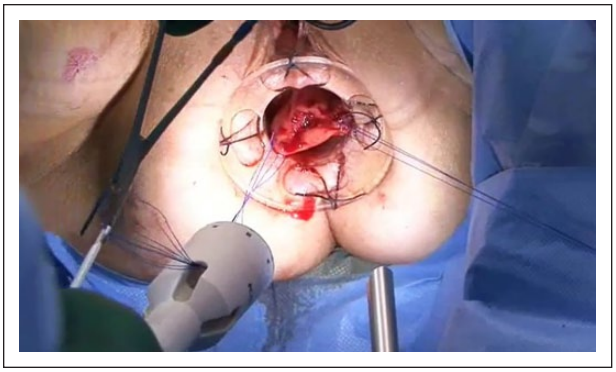

Figure 4. The 4 tails of the Prolene stitches were introduced through the stapler channels (2 in the left and 2 in the right sides of the instrument).

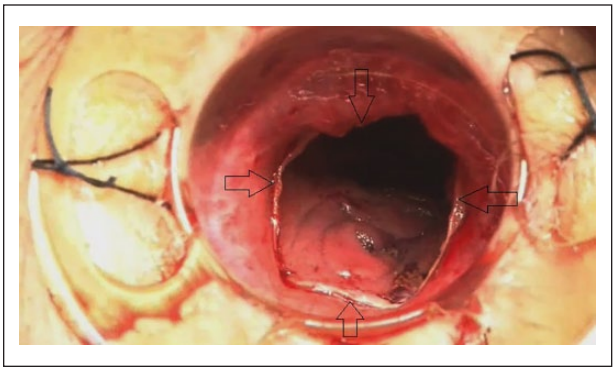

Figure 5. After anastomosis was created the presence of CAD allowed for careful transanal inspection of the anastomosis under direct vision.

instrument) and gentle traction was applied in order to obtain a gradual and homogeneous tension of the tissue. This maneuver allowed for the elimination of the previous staple line and dog ears. In the next step, the stapler anvil was introduced into the proximal colon and secured using purse string suture and one Prolene endo-loop. Subsequently, the circular stapler was opened, the spike was connected with the anvil, and the stapler was closed. After obtaining good healthy tissue plane the circular stapler was fired, and the competence of "donuts" was examined.

After anastomosis was created the presence of CAD allowed for careful transanal inspection of the anastomosis under direct vision (Figure 5). After satisfactory direct inspection, an air leak test was performed. The need for protective stoma was left to the discretion of operating surgeon. Large Robinson or Blakes drain was left in the pelvis at the end of the procedure.

Postoperative Care

The postoperative care was applied according to Enhanced Recovery After Surgery Protocol.[37] Patients were allowed clear fluid as soon as they tolerate it. Oral diet was introduced from the second postoperative day. All patients received 4 weeks' prophylactic dose of low-molecular-weight heparin. Antibiotic prophylaxis was continued for 24 hours after operation (3 more doses of IV 1 g cephalosporin). A urinary catheter was removed on the first postoperative day and from that day patients were encouraged for ambulation. The drain was removed after 48 to 72 hours depending on the volume of the discharge.

Definition of Anastomotic Leak

There is no consensus in the literature about the definition of anastomotic leak and there are multiple definitions used in different studies; for our study, we adapted the definition recently published by Adams and Papagrigoriadis.[8] We defined anastomotic leakage when there was a feculent material obtained from the drain or the wound, extravasation of dye on contrast Gastrografin enema or CT with rectal contrast, anastomotic defect directly visualized during colonoscopy, and finally the presence of perianastomotic air or fluid visualized on CT scan.

Patients' Follow-up and Outcomes

Patients were followed-up on the ward and then in the outpatient departments on the seventh day, 2 weeks, and 1 month postoperative. Follow-up was subsequently continued up to 12 months, and all patients underwent colonoscopy to assess the integrity of the anastomosis. All patients who received defunctioning ileostomy underwent Gastrografin enema or colonoscopy to assess the anastomosis prior to stoma reversal.

The primary outcome was the incidence of the anastomotic leak during 30 days postoperative, and to access the safety and efficacy of this newly prescribed technique in the reduction of anastomotic leak. Secondary outcomes were the clearness of safety margins and overall 30-day postoperative morbidities and mortality. Complications were classified according to the Clavien-Dindo classification of surgical complications.[38]

Variables Studied and Statistical Analysis

Basic patients' demographic data were recorded including age, sex, body mass index (BMI) status, American Society for Anesthesiologists (ASA) stage, tumor stage, the distance of the tumor from the anal verge, use of neo-adjuvant chemo-radiotherapy, type of surgical modality (open, laparoscopic, or robotic), duration of the operation, the length of hospital stay, and postoperative morbidity and mortality. Data were analyzed using Excel and SPSS (Statistical Package for Social Science version 21 for Microsoft Windows). Quantitative data were expressed as median and range.

Table 1. Patients and Tumor Characteristics.

	Patients, n (%)
Total	53
Male	35 (66%)
Female	18 (34%)
Age (median and range)	68 years (range = 49-89)
BMI (median and range)	24 kg/m^2 (range = 20-35)
ASA	
I	1 (2%)
II	18 (34%)
III	31 (58%)
IV	3 (6%)
V	
Mean tumor distance from anal verge (median and range)	8 cm (range = 4-12)
Patients underwent neo-adjuvant CRT	22 (42%)
Tumor stage	
0	
I	21 (40%)
IIA	4 (8%)
IIB	2 (4%)
IIC	
IIIA	5 (9%)
IIIB	15 (28%)
IIIC	1 (2%)
IVA[a]	5 (9%)
IVB	

Abbreviations: BMI, body mass index; ASA, American Society for Anesthesiologists; CRT, chemo-radiotherapy.
[a]Liver metastasis.

Table 2. Operative Details.

	Patients, n (%)
Approach	
Open	30 (57%)
Laparoscopic	16 (30%)
Robotic	7 (13%)
Rectal resection	
LAR	44 (83%)
Ultra LAR	9 (17%)
Rectal division	
Contour	20 (38%)
Endogia	28 (53%)
Linear	5 (9%)
Multiple firing (2-charges)	30 (57%)
Diversion	40 (75%)
Anastomosis level	
Colorectal anastomosis	45 (85%)
Coloanal anastomosis	8 (15%)
Anastomosis configuration	
End to end	48 (91%)
End to side	5 (9%)

Abbreviation: LAR, low anterior resection.

Results

Patients and Tumor Characteristics

Fifty-three patients with primary rectal cancer were enrolled to the study, 35 males and 18 females. The median age was 68 years (range = 49-89), and the median BMI was 24 kg/m^2 (range = 20-35; Table 1). The median tumor distance from the anal verge was 8 cm (range = 4-12). Twenty-two (42%) patients received neo-adjuvant chemo-radiotherapy for nodal disease and/or locally advanced rectal cancer (Table 1).

Intraoperative Details

Forty-four patients underwent low anterior resection, while the remaining 9 patients underwent ultra-low anterior resection. Thirty patients underwent open, 16 laparoscopic, and 7 robotic surgeries (Table 2).

Rectal division was performed by Contour Curved Cutter Stapler 64 mm (Ethicon Endosurgery, Somerville, NJ) device in 21 patients; Endo GIA 60 mm Reload with Tri-Staple Technology (Medtronic, Inc, Minneapolis, MN) in 28 patients; and GIA DST 60 mm Reload (Medtronic, Inc, Minneapolis, MN) or Proximate Linear Cutters 100 mm (Ethicon, US, LLC., Cincinnati, OH) in 4 patients. Multiple firing (2-charges) was required in 30 patients to obtain a complete rectal division. A single fire was applied in 23 patients, of which 18 had their rectum transected by a contour stapler, 4 by an Endo GIA, and 1 by a linear stapler. Of these 5 patients with a single fire with stapler other than contour 4 were female patients.

There were 45 colorectal anastomoses performed and 8 patients had coloanal anastomosis. Forty-eight patients had end-to-end anastomosis created whereas 5 patients had end-to-side anastomosis. The protective ileostomy was created in 40 patients at the time of initial surgery (Table 2).

Thirty-Day Postoperative Mortality and Morbidities

Overall, we did not record any mortality during the study period. Only 10 (19%) patients developed complications (Table 3). There were 3 patients who developed anastomotic leakage (6%); 2 of them were a subclinical leak in patients who had covering ileostomy at the time of the initial procedure, and the diagnosis was made during a routine colonoscopy. Both patients were treated conservatively with transanal drainage under endoscopic guidance and intravenous antibiotics. Both patients were discharged home on the 15th and 17th postoperative days subsequently. Six weeks after discharge both patients

Table 3. Postoperative Complications, Treatment, and Clavien-Dindo Classification.

Complication	Patients, n (%)	Treatment	Clavien-Dindo Class
Total number	10 (19%)		
Anastomotic leak	3 (6%)	2 patients; transanastomotic drainage and antibiotics	IIIA
		1 patient; reoperation	IIIB
Postoperative bleeding	3 (6%)	Blood transfusion	II
Pneumonia	2 (4%)	Antibiotics treatment	II
Wound infection	1 (2%)	Antibiotics treatment	II
Urinary tract infection	1 (2%)	Antibiotics treatment	II

underwent follow-up flexible sigmoidoscopy, which showed completely healed anastomotic defect with no residual stenosis.

One patient developed a clinically significant anastomotic leak, demonstrated as a peritonitis. This patient required reoperation during which pelvic abscess was drained, anastomotic defect repaired, and defunctioning ileostomy created.

The median length of hospital stay was 10 days (range = 4-20 days). Pathological examination of the postoperative specimen showed tumor-free distal, radial, and circumferential margins in all patients.

Discussion

The double stapling technique (DTS)[39] is currently the most widely performed procedure, which facilitates colorectal anastomoses at a lower level. Use of this technique has increased the number of sphincter-saving procedures in low rectal cancer, reducing the number of abdominoperineal resection and permanent colostomy. Despite improvement in technique, the leak rate in case of DST remains high.[4-7,9-11] Many risk factors of anastomotic leakage (AL) with DST are identified in the literature. Some of them are related strictly to the anastomosis-related technique such as the presence of so-called "locus minoris resistentiae" represented by the anastomotic "dog ear" and the crossing of the staple lines; it has been shown that in animal and phantom models they are the favorite sites for anastomotic disruption.[35,40] This is more frequent when the DST is performed by an end-to-end technique.[40] This is particularly important in ultra-low anterior resection where it is technically difficult to perform a side-to-end or side-to-side anastomosis.

In our series, the leak rate after the rectal resection is 6%, which is very low in comparison to that reported in the literature. When compared to the results documented in the literature, our results are in accordance with published articles,[41,42] while other articles reported AL rate ranging between 0.4% and 17%.[43-53] These wide ranges of incidence may be attributed to lack of constant definition of AL and criteria of diagnosis.[54]

In the authors' opinion, the AL rate reduction is due to the elimination of the double staple lines and so-called "dog ears" by using our new technique. The recently published articles reporting the results of transanal total mesorectal excision[55-59] confirmed a lower AL rate. This is most likely due to the technique used to perform the anastomosis that avoids a double staple suture lines, substituted by handmade purse strings suture. These data confirm the role of double staple suture lines as a risk factor for the AL pathogenesis.

Our technique provides a symmetric anastomosis and prevents the development of anastomotic weakness areas that can lead to leakage. Moreover, the anastomosis is performed under a direct vision, which allows easy performance of transanal air leak test and easy identification and repairs of any defect during the surgical procedure. Use of CAD facilitates a better transanal introduction of the circular stapler and gives the surgeon a better control of it. CAD also allows easy identification of the distal margin; this may be supported by the fact that all our patients underwent R0 resection with free distal margins.

Use of the direct vision to inspect the anastomosis can also reduce postoperative bleeding as reported by Shamiyeh et al.[60] The intraoperative anastomotic inspection could potentially also help the operating surgeon with the decision in relation to performing defunctioning ileostomy and reserve it only for high-risk and selected cases. This can significantly contribute to patients' postoperative quality of life as well as reduce the morbidity associated with ileostomy closure. In our series, protective stoma was created in 75% cases, which is still a high number taking into account only 6% anastomotic leak.

We believe that our described technique is simple to perform, reproducible, and safe in terms of complications, as reflected by our results. However, there are some challenges associated with this technique in relation to minimally invasive surgery. It requires higher laparoscopic suturing skills for the traction of lateral "dog ears" in the circular stapler, and this challenge does not pose particular difficulties in open surgery.

The main limitation of our study is the absence of a control group; however, this is the first description and assessment of this promising technique. We are planning for a randomized control trial for its better assessment.

Conclusion

Data obtained from the TICRANT study group suggest that the technique we propose to perform colorectal and coloanal anastomosis, for patients undergoing low and ultra-low anterior resection for rectal cancer, could potentially reduce the anastomotic leakage rate. This is mainly due to a better transanal introduction of the circular stapler, elimination of

the previous suture lines and dog ears, combined with a direct inspection of the anastomosis. This technique also allows easy performance of transanal air leak test and eventually direct repair of any small anastomotic defects. The use of CAD allows for better identification of the distal resection margin and can contribute to obtaining better oncological clearance. Finally, our technique is simple to perform, reproducible, and associated with low morbidity.

Author Contributions

Study concept and design: Francesco Crafa, Jacques Megevand, Giovanni Maria Romano, Pierpaolo Sileri
Acquisition of data: Paolo Delrio, Giannandrea Baldazzi, Ucchino Giampiero, Silvia Quareisma, Adele Noviello, Giulia Missori, Mostafa Shalaby, Diletta Cassini, Pasquale Ascenzi, Luana Franceschilli
Analysis and interpretation: Sebastian Smolarek, Mostafa Shalaby, Pierpaolo Sileri
Study supervision: Giulia Missori, Mostafa Shalaby, Pierpaolo Sileri

Declaration of Conflicting Interests

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