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Two-Stage Turnbull-Cutait Pull-Through Coloanal Anastomosis for Low Rectal Cancer
A Randomized Clinical Trial

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IMPORTANCE Two-stage Turnbull-Cutait pull-through hand-sewn coloanal anastomosis seems to provide benefits in terms of postoperative morbidity compared with standard hand-sewn coloanal anastomosis associated with diverting ileostomy and further ileostomy reversal in patients operated on for low rectal cancer.

OBJECTIVE To compare 30-day postoperative and 1-year follow-up results of Turnbull-Cutait pull-through hand-sewn coloanal anastomosis and standard hand-sewn coloanal anastomosis after ultralow rectal resection for rectal cancer.

DESIGN, SETTING, AND PARTICIPANTS Multicenter randomized clinical trial. Neither patients nor surgeons were blinded for technique. Patients were recruited in 3 centers, Bellvitge University Hospital and Valle d'Hebron University Hospital in Spain and Instituto Nazionale Tumori Fondazione G. Pascale–Istituto di Ricovero e Cura a Carattere Scientifico in Italy. Patients undergoing ultralow anterior rectal resection needing hand-sewn coloanal anastomosis were randomly assigned to 2-stage Turnbull-Cutait pull-through hand-sewn coloanal anastomosis or standard hand-sewn coloanal anastomosis associated with diverting ileostomy. Data were analyzed between June 2012 and October 2018.

INTERVENTIONS All patients underwent ultralow anterior resection. Patients assigned to the 2-stage Turnbull-Cutait pull-through group underwent exteriorization of a segment of left colon through the anal canal and, after 6 to 10 days, the exteriorized colon was resected and a delayed hand-sewn coloanal anastomosis was performed. For patients assigned to standard coloanal anastomosis, the hand-sewn coloanal anastomosis was performed with diverting ileostomy at first operation. Closure of the ileostomy was planned after 6 to 8 months.

MAIN OUTCOMES AND MEASURES Primary outcome was 30-day postoperative morbidity. For the standard hand-sewn coloanal anastomosis with diverting ileostomy group, overall postoperative morbidity includes 30-day postoperative complications of the ileostomy closure.

RESULTS Ninety-two white patients, 72 men and 20 women, with a median age of 62 years, were randomized and included in the analysis. Forty-six patients received standard hand-sewn coloanal anastomosis with diverting ileostomy and 46 received the 2-stage pull-through hand-sewn coloanal anastomosis. Seven patients (15.2%) in the standard hand-sewn coloanal anastomosis group did not undergo reversal ileostomy, and 1 patient (2.2%) in the 2-stage pull-through hand-sewn coloanal anastomosis group did not undergo delayed coloanal anastomosis. The 30-day overall composite postoperative complications rate was similar between the 2 groups (34.8% in 2-stage pull-through hand-sewn coloanal anastomosis group vs 45.7% in standard hand-sewn coloanal anastomosis group; $P = .40$), with a difference of −10.9 (95% CI, −29.5 to 8.9).

CONCLUSIONS AND RELEVANCE The 2-stage pull-through hand-sewn coloanal anastomosis after ultralow anterior resection for low rectal cancer is safe and does not increase the postoperative morbidity rate compared with standard coloanal anastomosis with covering ileostomy followed by ileostomy closure.

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Invited Commentary
Supplemental content

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Hand-sewn coloanal anastomosis after ultralow anterior rectal resection is considered the standard surgical technique for low rectal cancer, amenable to sphincter-saving procedure when stapled colorectal anastomosis cannot be performed for oncological or technical reasons.[1] Although universally accepted, hand-sewn coloanal anastomosis is associated with a high rate of anastomotic leakage and pelvic sepsis[2,3] leading to the indication of diverting ileostomy in these patients.[4-6] However, diverting stomas are not free of complications. Stoma-related morbidity is reported as high as 43% in patients bearing ileostomies (dehydration and acute or chronic renal failure and intestinal obstruction) and greater than 20% after stoma closure.[7-12] Moreover, having an ileostomy has been associated with a lower quality of life.[13,14]

In 1952 at the Cleveland Clinic, Ohio, R. B. Turnbull Jr, MD,[15] described a surgical technique of transanal colonic pull-through with 2-stage coloanal hand-sewn anastomosis for intestinal transit reconstruction in adults with rectal cancer and children with Hirschsprung disease to avoid a permanent colostomy. In the same period in Brazil, D. E. Cutait, MD,[16] described the same technique for adult patients with acquired megacolon secondary to Chagas disease. The pull-through procedure is performed in 2 stages, with resection of the affected colonic segment and exteriorization of the proximal colon through the anus during the first stage followed by delayed hand-sewn coloanal anastomosis some days later. Adherences and scarring between low pelvic walls and the colon formed during the interval are deemed to reduce the risk of coloanal anastomosis dehiscence permitting avoidance of a diverting stoma.

Over the years, the technique described by Turnbull and Cutait was gradually superseded in favor of stapled anastomosis[17] or standard hand-sewn coloanal anastomosis in association with diverting temporary stoma.[18] It remained indicated as salvage surgery for selected patients with colorectal anastomotic dehiscence, pelvic irradiation fistulae, chronic pelvic infection, and complex rectovaginal or rectourethral fistula to bring healthy tissue to the surgical site and to attempt avoidance of a permanent stoma.[19-23] In the last 2 decades, this technique has been reintroduced for the treatment of rectal cancer when trying to avoid diverting stoma and its related morbidity, with promising results.[20,24-26] Two systematic reviews[27,28] studying results of transanal colonic pull-through with 2-stage coloanal anastomosis for low rectal cancer showed a low rate of anastomotic leak, low pelvic morbidity, and low use of stoma, with reasonably good functional results. However, evidence of the advantages of the Turnbull-Cutait pull-through with 2-stage hand-sewn coloanal anastomosis (TCA) over standard hand-sewn coloanal anastomosis associated with diverting lateral ileostomy (CAA) in rectal cancer is scarce.

Based on the hypothesis that TCA provides significant benefits in terms of postoperative morbidity related to ileostomy when compared with CAA followed by ileostomy closure in patients operated on for low rectal cancer, a multicenter randomized clinical trial has been performed. Here, the 30-day postoperative and 1-year follow-up results are reported.

Key Points

Question Could 2-stage Turnbull-Cutait pull-through hand-sewn coloanal anastomosis be performed as an alternative to the standard coloanal anastomosis with diverting ileostomy after ultralow anterior resection for rectal cancer?

Findings In this multicenter randomized clincial trial comparing the 2 techniques, the 30-day postoperative morbidity was similar between groups.

Meaning Two-stage Turnbull-Cutait pull-through hand-sewn coloanal anastomosis may be considered after a sphincter-preserving ultralow anterior resection for low rectal cancer to avoid a temporary stoma.

Methods

Trial Design

This is a multicenter, 2-arm, parallel, 1-to-1, randomized clinical trial. Colorectal units of Bellvitge University Hospital and Valle d'Hebron University Hospital in Spain and Instituto Nazionale Tumori Fondazione G. Pascale–Istituto di Ricovero e Cura a Carattere Scientifico in Italy recruited patients between June 2012 and October 2018. The study followed the Declaration of Helsinki guidelines, was registered at http://www.clinicaltrials.gov (NCT01766661), and was approved by each local ethics committee. The study is closed for recruitment. The formal trial protocols can be found in Supplement 1.

Study Participants

According to the clinical study protocol,[29] all patients older than 17 years and younger than 75 years, diagnosed as having low rectal adenocarcinoma and potential candidates for radical ultralow anterior rectal resection with sphincter preservation and hand-sewn coloanal anastomosis during the study period, were evaluated for inclusion in the trial. Exclusion criteria were pregnancy and/or lactation, altered cognitive status preventing collaboration in the study or patients who could neither read nor write, history of fecal incontinence (baseline Wexner score equal to or greater than 6), previous coloproctological surgery or disease, synchronous colorectal tumor or any other active neoplasm, patients with desease classified as American Society of Anesthesiologists IV and V, patients on whom low colorectal stapler anastomosis could be performed, and refusal of the patient to sign the informed consent form.

Baseline evaluation included digital rectal examination, rigid rectoscopy, colonoscopy, endorectal ultrasonography, rectal magnetic resonance imaging, and chest and abdomen computed tomography scan. All cases were discussed by the colorectal cancer multidisciplinary team of each hospital. According to clinical treatment protocols for rectal cancer in the participating centers and following clinical practice guidelines for rectal cancer of the European Society for Medical Oncology,[30] patients with locally advanced rectal tumors underwent neoadjuvant treatment. Surgery was scheduled after 6 to 8 weeks from the end of neoadjuvant therapy. Baseline defecatory disfunctions were evaluated by the fecal

incontinence Wexner score,[31] the Low Anterior Resection Syndrome score,[32,33] and the Colorectal Functional Outcome questionnaire.[34]

Study Design

Patients who agreed to participate in the trial and who met the inclusion criteria were randomly allocated to CAA or to TCA after having signed informed consent (**Figure 1**). To avoid any unbalanced sample size between groups, randomization was carried out online by a computer-generated random code and stratified by center with blocks of 4 and 6 patients. Surgeons who recruited the patients and/or carried out surgery were responsible for randomization. Neither patients nor for surgeons were blind for allocation. A nurse or a surgical resident who was blind for the performed procedure was responsible for collecting functional follow-up data in each center. Data were collected by the investigators of each center and entered into an online database.

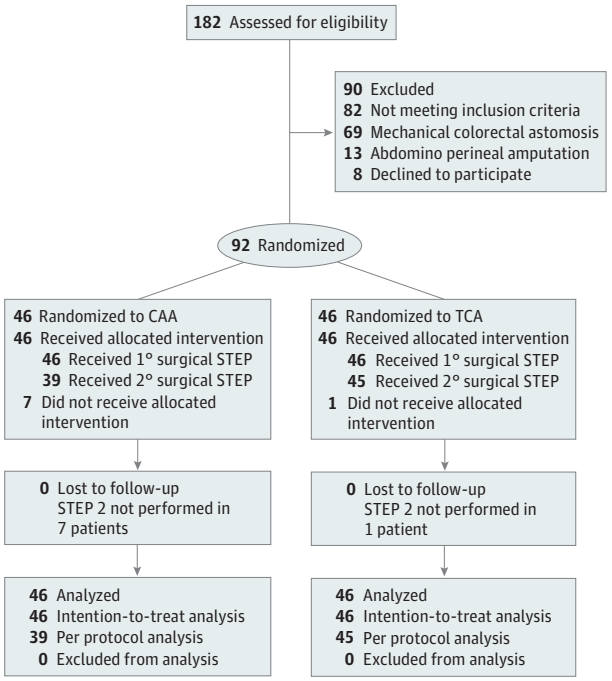
Procedures and Follow-up

All patients underwent mechanical bowel preparation and oral antibiotics. Both procedures were performed under general anesthesia in the lithotomy position, and parenteral antibiotic prophylaxis was prescribed following each center policy. All surgical procedures were performed by surgeons experienced in rectal cancer.

The operative management included 2 steps in both groups. First, all patients underwent ultralow anterior resection with total mesorectal excision.[35,36] Laparoscopy was the first-choice approach unless contraindication or technical intraoperative difficulties. The distal transection of the rectum was performed depending on the level of the tumor to achieve a free distal margin of at least 1 cm according the classification described by Rullier et al.[1] For supraanal tumors, the internal sphincter was preserved, and anal mucosectomy was performed above the dentate line. For juxtaanal and intraanal tumors, the internal sphincter was removed partially or totally, respectively, with the overlying anal mucosa. Patients assigned to the CAA group underwent hand-sewn coloanal anastomosis as described by Parks in 1972[18] with diverting loop ileostomy and patients randomized to TCA group underwent exteriorization of a short segment of left colon through the anal canal (pull-through) according to the technique described by Turnbull[15] and Cutait in 1961[16] (**Figure 2**A). The left colon was kept in place through the anal canal by tension-free mobilization and by the resting pressure of the anal canal. Additionally, 2 stitches fixed the colon to perianal skin.

The second step in the TCA group consisted of the resection of the exteriorized colon and construction of a delayed hand-sewn coloanal anastomosis with the same technique that for CAA group[37] (Figure 2B and C). The time between the first and second operation in the TCA group ranged between 6 and 10 days depending on the perfusion condition of the exteriorized colon that was checked daily for inspection at the anal margin level. In case of ischemia at its proximal end, the second step was performed earlier than planned. In the CAA group, the second step consisted of the closure of ileostomy. The time to closure of the stoma ranged between 6 and 8 months. All patients underwent clinical and/or radiological control of the coloanal anastomosis before closure of the diverting ileostomy.

Figure 1. Consolidated Standards of Reporting Trials 2010 Flow Diagram



CAA indicates hand-sewn coloanal anastomosis and diverting ileostomy; TCA, 2-stage Turnbull-Cutait pull-through anastomosis.

A visit at day 30 after discharge was scheduled for every patient independently of any other control deemed necessary for any individual patient, and periodical oncological follow-up was planned according to the protocol for rectal cancer of each participating center. Functional follow-up was performed as described in the previous published study protocol.[29]

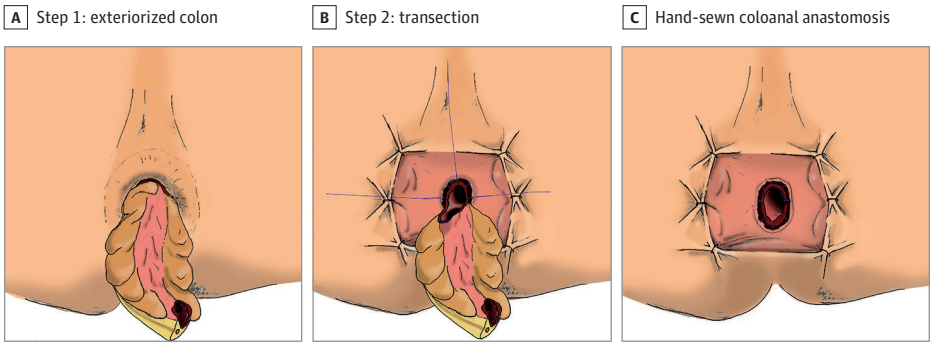
Outcomes

The primary outcome was comparison of composite 30-day overall postoperative morbidity between CAA and TCA. For the CAA group, composite morbidity included 30-day postoperative complications of the ileostomy closure. Postoperative complications have been classified using the Clavien-Dindo classification of surgical complications.[38]

Anastomotic leakage was defined as a communication between the intraluminal and extraluminal compartments owing to a defect of the integrity of the intestinal wall at the coloanal anastomosis. Any pelvic abscess has also been considered as anastomotic leakage.[39]

Secondary outcomes were surgical time, reoperations, length of hospital stay, and readmissions. Surgery-related morbidities have been assessed at 1 year after the first surgery. Functional outcomes assessed by the fecal incontinence Wexner score,[31] the Low Anterior Resection Syndrome score,[32] and the Colorectal Functional Outcome questionnaire[34] have been reported at 1 year after the first surgery.[29] Oncologic outcomes

Figure 2. Surgical Steps for 2-Stage Turnbull-Cutait Pull-Through Anastomosis



A, Step 1: the left colon is exteriorized through the anal canal and leaving 6 to 7 cm outside until step 2. B, Step 2: the exteriorized colon is transected at the level of the anal canal section. C, The hand-sewn coloanal anastomosis is performed with single stitch.

in term of local recurrence (LR), distant recurrence (DR), disease-free survival (DFS), and overall survival (OS) have been assessed at 1 year after surgery. Disease-free survival was defined as patients who were alive without signs of LR and/or DR, and OS was defined as patients alive independent of disease status. According to the published protocol,[29] functional and oncological outcomes at a minimum of 3-year follow-up will be reported in a future study.

Statistical Analysis

Sample size calculation was based on results of previously published studies and the authors' own data that show an estimated morbidity of 34% for the 2-stage Turnbull-Cutait pull-through coloanal anastomosis technique, 47% for standard hand-sewn coloanal anastomosis, and 27% for closure of the diverting ileostomy.[10,19,20,26,40,41] It was considered that, for patients assigned to the CAA group, the probability of complications in any of the 2 operations was 64.5%.

Assuming an α error of .05 and a β error of .20, a 2-tailed test determined a needed number of 46 patients randomized per arm (92 patients in total) to detect a difference between the 2 proportions (64.5% for the CAA group and 34% in the TCA group), with a loss to follow-up rate of 10%.

An interim analysis for the primary outcome has been performed, with 50% of patients recruited. The α error has been corrected with the Haybittle-Peto method. Assuming an overall α risk of .05, the corrected α levels for the interim and final analyses were .001 and .049, respectively. Because there was no statistically significant difference between the 2 groups in the primary end point, the trial continued.

The analysis of the primary outcome was performed using the χ^2 test and with confidence interval of the difference between the 2 proportions. For secondary outcomes, the confidence interval of 2 proportions or 2 means was calculated respectively for qualitative or quantitative variables. In the intention-to-treat (ITT) analysis, for patients who did not undergo a second step, a surgical time of 0 minutes, a hospital stay of 0 days, and no postoperative complications were assumed for step 2.

Quantitative data are presented as mean and standard deviation or median and percentile (25th-75th). Qualitative data are presented as absolute numbers and percentages. Differences between groups were evaluated using parametric or nonparametric test as appropriate. Qualitative variables were analyzed using the χ^2 test. Quantitative variables were analyzed using *t* or Mann-Whitney *U* test to compare 2 groups. Kaplan-Meier analysis was used to determine LR, DR, DFS, and OS at 1 year from the date of surgery. The statistical analysis was performed using software R, version 3.6 (R Foundation for Statistical Computing), and significance was set at a 2-sided *P* value less than .05.

Results

Patient Characteristics

During the study period, 182 patients were evaluated for inclusion. In following CONSORT guidelines,[42] the flow of participants from group assignment to final analysis is shown in Figure 1. Ninety-two patients met the inclusion criteria and were randomized. Thirty-nine patients (42.4%) were included in the Bellvitge University Hospital, 37 (40.2%) in the Valle d'Hebron Hospital, and 16 (17.4%) in the Istituto Nazionale Tumori Fondazione G. Pascale–Istituto di Ricovero e Cura a Carattere Scientifico. Forty-six patients received the CAA procedure, and 46 received the TCA procedure. Demographics, baseline characteristics, per and postoperative data are detailed **Table 1**.

During the first step, in the CAA group, 1 patient underwent 2 hepatic limited resections for synchronous metastasis and another patient underwent resection of a seminal vesicle en bloc with the tumor for local infiltration. In the TCA group, 8 patients needed additional surgical procedures in the first operation, including 1 concomitant single hepatic segmentectomy, 1 bisegmentectomy and cholecystectomy, 1 appendectomy, 1 cysto-prostatectomy on block with the rectum and Bricker reconstruction for tumor infiltration, and 4 pelvic lateral node dissections.

The reasons for conversion from laparoscopic to laparotomy in the 7 patients of the TCA group were technical difficulties owing to a narrow pelvis in 4 patients, intolerance of pneumoperitoneum and Trendelenburg position in 1 patient, difficult lateral pelvic node dissection in 1 patient, and the presence of a giant polycystic kidney in the last patient. In the CAA group, both conversions were owing to technical difficulties in narrow pelvis and/or obese patients.

Table 1. Characteristics of Patients, Perioperative Data, and Postoperative Data

Characteristic	No. (%)		
	All (N = 92)	CAA (n = 46)	TCA (n = 46)
Sex			
Women	20 (21.7)	9 (19.6)	11 (23.9)
Men	72 (78.3)	37 (80.4)	35 (76.1)
Age, median (IQR), y	62.3 (55.8-68.7)	63.8 (59.5-69.9)	58.9 (52.8-66.4)
ASA score			
II	73 (79.3)	34 (73.9)	39 (84.8)
III	19 (20.7)	12 (26.1)	7 (15.2)
BMI, median (IQR)	26.0 (24.8-28.4)	26.0 (25.4-29.1)	26.0 (24.7-26.9)
CEA, median (IQR), μg/L	2.8 (2.1-3.0)	3.0 (3.0-3.0)	2.1 (2.1-2.1)
Albumin, median (IQR), g/dL	4.3 (4.1-4.5)	4.2 (4.0-4.5)	4.4 (4.2-4.5)
Hemoglobin, median (IQR), g/dL	13.3 (12.2-14-6)	13.2 (12.2-14.6)	13.3 (12.3-14.6)
Clinical TNM			
T			
1	5 (5.4)	2 (4.4)	3 (6.5)
2	8 (8.7)	4 (8.70)	4 (8.7)
3	77 (83.7)	40 (87.0)	37 (80.4)
4	2 (2.2)	NA	2 (4.4)
N			
0	26 (28.3)	13 (28.3)	13 (28.3)
1	59 (64.1)	29 (63.0)	30 (65.2)
2	7 (7.6)	4 (8.7)	3 (6.5)
M			
0	78 (84.8)	38 (82.6)	40 (87.0)
1	14 (15.2)	8 (17.4)	6 (13.0)
Tumor height, median (IQR), cm	5.0 (4.0-6.0)	5.0 (4.0-6.0)	5.0 (4.0-6.0)
Neoadjuvant treatment			
No treatment	6 (6.5)	5 (10.9)	1 (2.2)
CRT	80 (87.0)	38 (82.6)	42 (91.3)
RT only	6 (6.5)	3 (6.5)	3 (6.5)
Wexner score, median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
LARS score, median (IQR)	2.0 (0.0-16.0)	2.5 (2.0-14.8)	0.0 (0.0-15.5)
CoREFO questionnaire, median (IQR)	7.3 (9.8)	7.4 (9.4)	7.3 (10.3)
Surgical technique			
Open	12 (13.0)	8 (17.4)	4 (8.7)
Laparoscopy	80 (87.0)	38 (82.6)	42 (91.3)
Conversion	9 (9.8)	2 (4.3)	7 (15.2)
Intersphincteric resection	22 (23.9)	12 (26.1)	10 (21.7)
Blood transfusion, patients			
Intraoperative	3 (3.3)	3 (6.5)	NA
Postoperative	9 (9.8)	6 (13)	3 (6.5)
Surgical pathology (TNM)			
T			
0	23 (25.0)	13 (28.3)	10 (21.7)
1	5 (5.5)	2 (4.4)	3 (6.5)
2	28 (30.4)	13 (28.3)	15 (32.6)
3	34 (37.0)	17 (37.0)	17 (37.0)
4	2 (2.2)	1 (2.2)	1 (2.2)

(continued)

Table 1. Characteristics of Patients, Perioperative Data, and Postoperative Data (continued)

Characteristic	No. (%)		
	All (N = 92)	CAA (n = 46)	TCA (n = 46)
N (N = 89)			
0	66 (71.7)	30 (65.2)	36 (78.3)
1	20 (21.7)	12 (26.1)	8 (17.4)
2	6 (6.6)	4 (8.7)	2 (4.3)
R			
0	86 (93.5)	41 (89.1)	45 (97.8)
1	6 (6.5)	5 (10.9)	1 (2.2)
Quality of mesorectum			
Complete	78 (84.8)	38 (82.6)	40 (87.0)
Partially complete	8 (8.7)	5 (10.9)	3 (6.5)
Incomplete	4 (4.4)	2 (4.4)	2 (4.4)
Not reported	2 (2.2)	1 (2.2)	1 (2.2)
Adjuvant treatment			
No treatment	32 (34.8)	13 (28.3)	19 (41.3)
CRT	7 (7.6)	5 (10.9)	2 (4.4)
CH only	52 (56.5)	27 (58.7)	25 (54.3)
RT only	1 (1.1)	1 (2.2)	NA

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CAA, hand-sewn coloanal anastomosis and diverting ileostomy; CEA, carcinoembryonic antigen; CH, chemotherapy; CoREFO, Colorectal Functional Outcome; CRT, chemoradiation therapy; IQR, interquartile range; LARS, Low Anterior Resection Syndrome score; NA, not applicable; RT, radiotherapy; TCA, 2-stage Turnbull-Cutait pull-through anastomosis.

SI conversion factors: To convert albumin to grams per liter, multiply by 10; hemoglobin to grams per liter, multiply by 10.

Seven patients (15.2%) in the CAA group did not undergo the second operation. Three of these patients were diagnosed as having distant nonresectable metastasis and were considered for palliative care, 2 patients refused further surgery, 1 died during follow-up for progression of the distant disease, and 1 patient needed a Hartmann procedure and simultaneous ileostomy reversal because of a left colonic ischemia. One patient (2.2%) in the TCA group did not complete surgical reconstructive management owing to pancolonic ischemia 2 days after the first operation and required a total colectomy with end ileostomy. Mean (SD) time between surgical steps was 9.8 (4.7) days and 320.0 (150.0) days for the TCA and CAA group, respectively.

Primary Outcomes

The 30-day overall composite postoperative complication rate was similar between the 2 groups in the ITT analysis. No differences were observed comparing the rate of greater than Clavien-Dindo 3b postoperative complications (**Table 2**). A detailed list of postoperative complications and treatments is shown in **Table 3**.

The overall rate of coloanal anastomotic leak was 18.5% (17 patients): 23.9% (11 patients) in the CAA group and 13.0% (6 patients) in the TCA group ($P = .28$). In the CAA group, 4 patients presented a posterior defect of the anastomosis, 1 presented an anterior defect, and 1 presented a lateral defect. Five patients had a pelvic abscess without a clear defect of the coloanal anastomosis. In the TCA group, 3 patients had a posterior defect, 1 had an anterior defect, and 2 patients presented a pelvic abscess without a clear defect of the anastomosis. Eleven patients (23.9%) developed postoperative paralytic ileus in the CAA group while no patients presented ileus in the TCA group ($P = .001$).

Secondary Outcomes

The median composite surgical time was lower in the TCA group compared with the CAA group, whereas hospital stay was similar comparing the single hospitalization of patients undergoing TCA with the composite time of the 2 admissions of patients undergoing CAA (Table 2).

During the first 30 postoperative days, the composite readmission rate was 4.4% (2 patients) in the TCA group and 8.7% (4 patients) in the CAA group ($P = .68$). Reason for readmission in the TCA group was pelvic abscess in both patients, whereas in the CAA group, 1 patient was readmitted for prostatitis, 2 for anastomotic leak with pelvic abscess, and 1 for a lower gastrointestinal bleeding after the ileostomy closure originating from the coloanal anastomosis. The rate of early definitive stoma as a result of postoperative complications was 2.2% (1 patient) in the CAA group and 4.3% (2 patients) in the TCA group ($P > .99$). No 30-day postoperative mortality was observed in the first step or second step in any of the 2 groups.

The 1-year morbidity rate, excluding 30-day postoperative complications, was similar between the 2 groups (Table 2). In the CAA group, 3 patients were readmitted for acute renal failure secondary to dehydration for high ileostomy output, 1 patient developed a stenosis of the coloanal anastomosis treated by dilatation undergoing anesthesia, 1 patient was readmitted for an adhesive small-bowel obstruction treated conservatively, and 1 patient was diagnosed as having an incisional hernia at the site of previous ileostomy. In the TCA group, 2 patients underwent dilation of anastomotic stricture, 1 patient was readmitted for adhesive small bowel obstruction successfully conservatively treated, and 1 patient underwent a Hartmann procedure owing to a chronic pelvic sepsis.

Local recurrence, DR, DFS, and OS at 1 year of follow-up were similar between the 2 groups (Table 2). Overall, 8 pa-

Table 2. Primary and Secondary Outcomes

Outcome	No. (%) All (N = 92)	CAA (n = 46)	TCA (n = 46)	*P* value	Difference (95% CI)
Overall 30-d postoperative morbidity					
1° Step	35 (38.0)	19 (41.3)	16 (34.8)	.67	−6.5 (−25.3 to 12.9)
2° Step	4 (4.4)	4 (8.7)	NA	NA	NA
Composite (ITT)	37 (40.2)	21 (45.7)	16 (34.8)	.40	−10.9 (−29.5 to 8.9)
1° Step (PP) (n = 84)	28 (33.3)	13 (33.3)	15 (33.3)	>.99	0.0 (−19.7 to 19.4)
Composite (PP) (n = 84)	30 (35.7)	15 (38.5)	15 (33.3)	.79	−5.1 (−24.8 to 14.8)
30-d Postoperative morbidity, ≥Dindo IIIb[38]					
Composite					
ITT	10 (10.9)	3 (6.5)	7 (15.2)	.32	8.7 (−4.7 to 22.4)
PP (n = 84)	8 (9.5)	2 (5.1)	6 (13.3)	.28	8.2 (−5.5 to 21.6)
Surgical time, median (IQR), min					
1° step	298 (248 to 336)	300 (270 to 350)	275 (249 to 320)	.09	−18.1 (−50.5 to 14.3)
2° step (n = 84)	60 (40.0 to 88.0)	88.0 (72.5 to 100)	40.0 (30.0 to 50.0)	<.001	−46.1 (−56.6 to −35.7)
Composite (ITT)	346 (300 to 416)	388 (324 to 437)	315 (275 to 360)	.003	−51.5 (−90.1 to −12.9)
Composite (PP) (n = 84)	359 (304 to 420)	400 (360 to 446)	315 (257 to 360)	<.001	−69.6 (−108.2 to −31.0)
Hospital stay, median (IQR), d					
1° Step	11.0 (7.0 to 15.2)	7.5 (6.0 to 12.0)	13.0 (10.2 to 17.8)	<.001	4.9 (0.7 to 9.2)
2° Step (n = 39)	5.0 (4.0 to 6.0)	5.0 (4.0 to 6.0)	NA	NA	
Composite (ITT)	13.5 (11.0 to 18.0)	13.5 (10.2 to 17.8)	13.5 (11.0 to 17.8)	.62	0.8 (−3.5 to 5.1)
Composite (PP) (n = 84)	13.5 (11.0 to 17.2)	14.0 (11.0 to 16.5)	13.0 (11.0 to 18.0)	.77	0.6 (−4.0 to 5.3)
1-y Postoperative morbidity[a]	10 (10.9)	5 (10.9)	5 (10.9)	>.99	0.0 (−13.6 to 13.6)
1-y Oncological outcomes, % (95% CI)[b]					
DFS	91.0 (85.3 to 97.2)	88.7 (79.9 to 98.5)	93.4 (86.4 to 100.0)	.47	NA
OS	97.8 (94.8 to 100.0)	97.8 (93.7 to 100.0)	97.7 (93.4 to 100.0)	.99	NA
LR	1.1 (0.0 to 3.3)	2.2 (0.0 to 6.4)	0.0 (0.0 to 0.0)	.32	NA
DR	9.0 (2.8 to 14.7)	11.3 (1.5 to 20.1)	6.6 (0.0 to 13.6)	.47	NA
1-y Functional outcomes					
Wexner score, median (IQR) (n = 65)	12.0 (7.0 to 16.0)	11.5 (8.0 to 15.2)	13.0 (7.0 to 16.0)	.70	0.21 (−2.4 to 2.8)
LARS score, median (IQR) (n = 65)	34.0 (26.0 to 39.0)	30.5 (25.2 to 38.2)	36.0 (27.0 to 39.0)	.45	1.2 (−3.9 to 6.3)
CoREFO questionnaire, median (IQR) (n = 65)	43.8 (26.7 to 55.0)	44.2 (26.9 to 55.3)	43.3 (25.0 to 54.8)	.68	−2.9 (−12.8 to 7.0)

Abbreviations: CAA, hand-sewn coloanal anastomosis and diverting ileostomy; CoREFO, Colorectal Functional Outcome; DFS, disease-free survival; DR, distance recurrence; IQR, interquartile range; ITT, intention-to-treat population; LARS, Low Anterior Resection Syndrome; LR, local recurrence; NA, not applicable; OS, overall survival; PP, per protocol population; TCA, 2-stage Turnbull-Cutait pull-through anastomosis.

[a] Calculated excluding 30-day postoperative composite complications.

[b] Calculated with Kaplan-Meier survival analysis.

tients (8.7%) presented distant recurrence, 5 patients (10.9%) were in the CAA group, and 3 patients (6.5%) in the TCA. In addition, 2 of 5 patients (4.3%) in the CAA group had LR. Two patients (2.2%), 1 in each group, died during the first year of follow-up of systemic disease progression.

Functional outcomes at 1-year of follow-up, censored for patients diagnosed as having LR and/or DR (4 patients), patients who died of systemic disease progression (2 patients), patients who had a stoma as a result of postoperative complication (4 patients) or because the patient was waiting ileostomy reversal surgery (9 patients), and patients who did not respond to the questionnaire (8 patients), were available for 65 patients (28 patients in the CCA group and 37 patients in the TCA group; *P* = .07). Results were comparable between the 2 groups (Table 2; eTable and eFigure in the Supplement). One patient in the CAA group was disconnected at 1 year owing to very poor quality of life.

Discussion

This study represents an attempt to investigate the safety of the TCA compared with CAA with diverting ileostomy in patients operated on for low rectal cancer. It shows similar rates

Table 3. Composite Postoperative Complications According to Clavien-Dindo Grading System[38]

	CAA (n = 46)		TCA (n = 46)	
Grade	Type (No.)	Treatment(s)	Type (No.)	Treatment(s)
I	Superficial wound infection (2)	Debridement	Superficial wound infection (1)	Debridement
	Anastomotic bleeding (1)	NA	NA	NA
	Hydrocele (1)	NA	NA	NA
	Diversion colitis after ileostomy reversal surgery (1)	Antibiotics	NA	NA
II	Anastomotic leak/pelvic abscess (2)	Antibiotics	NA	NA
	Infected pelvic hematoma (1)	Antibiotics	Infected pelvic hematoma (1)	Antibiotics
	Paralytic ileus (11)	NG tube and TPN	NA	NA
	Paralytic ileus after ileostomy reversal surgery (1)	NG tube and TPN	NA	NA
	Urinary tract infection and acute urinary retention (4)	Antibiotics and bladder catheterization	Urinary tract infection (2)	Antibiotics
	NA	NA	Acute urinary retention (3)	Bladder catheterization
	Postoperative pneumonia (1)	Antibiotics	Postoperative pneumonia (1)	Antibiotics
	Postoperative pancreatitis (1)	Medical support	NA	NA
III-a	Anastomotic leak/pelvic abscess (8)	Transanal drain and antibiotics	Anastomotic leak/pelvic abscess (1)	Transanal drain and antibiotics
	NA	NA	Anastomotic leak/pelvic abscess (1)	Percutaneous drain and antibiotics
	NA	NA	Prostatic abscess (1)	Perineal drain and antibiotics
	Superficial wound infection (1)	Debridement and NPWT	NA	NA
	Lower GI bleeding after ileostomy reversal surgery (1)	Colonoscopy	NA	NA
III-b	Anastomotic leak/pelvic abscess (1)	Surgical transanal drain	Anastomotic leak/pelvic abscess (4)	Surgical transanal drain
	NA	NA	Left colon ischemia (1)	End colostomy
	NA	NA	Hemoperitoneum (1)	Emergency laparotomy
	Mechanical intestinal obstruction after ileostomy reversal surgery (1)	Laparotomy and ileocecectomy	NA	NA
IV-b	Left colon ischemia with pelvic abscess and sepsis (1)	End colostomy and ileostomy closure, ICU	Pancolonic ischemia and sepsis (1)	Total colectomy with end ileostomy, ICU
	NA	NA	Exteriorized colon related sepsis (1)	Exploratory laparoscopy, delayed coloanal anastomosis, ICU

Abbreviations: CAA, hand-sewn coloanal anastomosis and diverting ileostomy; GI, gastrointestinal; ICU, intensive care unit; MOF, multiorgan failure; NG, nasogastric; NPWT, negative-pressure wound therapy; TCA, 2-stage Turnbull-Cutait pull-through anastomosis; TPN, total parenteral nutrition.

of short-term postoperative complications between the 2 groups. Moreover, 1-year oncological and functional outcomes were also comparable between the 2 groups.

To our knowledge, this is the first multicenter, randomized clinical trial comparing the 2 procedures. Although the study does not confirm the hypothesis that TCA provides significant benefits compared with CAA, the most important postoperative results are that the 2-staged anastomosis procedure is as safe as the conventional CAA, with the advantage of avoiding a diverting ileostomy and its potential associated complications.

Strengths and Limitations

The major strengths of this study are that it is multicentric (making results reproducible), it has been carried out only in centers with large experience in rectal cancer treatment and in TCA technique,[20,24,43-45] and that the same surgical techniques and perioperative and postoperative care were used in the involved centers. Furthermore, because we restricted inclusion only to patients who were candidates for hand-sewn coloanal anastomosis, the populations are homogenous.

The study has some limitations. First, the inclusion period is long. Time to complete recruitment can be explained by the very strict inclusion criteria. Only patients needing a hand-sewn coloanal anastomosis were randomized, thus excluding the so-called coloanal mechanical anastomosis. To compare strictly similar patients, it was assumed that whenever the anastomosis would be amenable to a mechanical double-stapled anastomosis, the patient would functionally benefit from the preservation of a slightly longer segment of mucosa in the upper anal canal. The other reason for the long recruitment was

related to the fact that only 3 centers were involved in the trial because not many surgeons were familiar with the TCA technique. Another limitation is that neither patients nor surgeons could be blinded. However, bias during functional follow-up was controlled by collecting functional tests and questionnaires by a dedicated nurse or surgical resident who had not been informed of the procedure performed.

In line with other studies,[46] we observed a high rate of coloanal anastomotic leak; around 24% in the CAA group and 13% in the TCA group. There is evidence that diverting stoma reduces the risk of anastomotic leak in patients with low colorectal or coloanal anastomosis.[4,6] It is interesting to observe that, in our study, the leak rate was not statistically different between groups. It seems that the adhesions between colonic serosa, pelvic tissues, and the anal canal wall that grow between the first and second surgical step contribute to reducing anastomotic leak as well as diverting ileostomy may do. Moreover, patients with anastomotic dehiscence presented only pelvic abscess and could be treated satisfactorily by transanal drainage without needing a laparotomy for peritonitis.

Several studies report that the most common cause of permanent stoma in patients operated on for rectal cancer is nonclosure of the diverting stoma owing to postoperative and adjuvant chemotherapy complications, progression of the disease, or because of the patient's refusal to undergo further operations.[7,47-49] In the Dutch total mesorectal excision trial,[50] 19% of patients did not have their stoma reversed during follow-up. In our study, 15% of the patients in the CAA group did not undergo temporary stoma closure, resulting in a permanent stoma. Because the TCA procedure avoids temporary stomas, it could potentially be helpful in reducing the rate of permanent stomas compared with standard CAA with diverting ileostomy.

Postoperative paralytic ileus in patients operated on for rectal cancer has been related in several studies to the presence of lateral ileostomy.[51] Similar results have been observed in this study, where 24% of the patients in the CAA group developed a paralytic ileus whereas no patients in the TCA group presented with this complication.

Unlike other studies[12] that report rates of complications related to the stoma between 21% and 70%, this study reports a lower rate. Only 3 patients were readmitted for acute renal failure while waiting for stoma closure. This could have been influenced by the fact that, in each center, all patients with a stoma are regularly closely followed up by a stoma nurse and a nutritional specialist team to reduce stoma complications. Additionally, it is possible that results could have been influenced by the fact the sphincter-saving surgery for low rectal cancer is generally offered to patients with a good family support network and/or who are able to take care of themselves. Furthermore, the trial could be underpowered to study stoma-related complications because only 46 patients received temporary stoma.

Although the study protocol plans to analyze oncological and functional results at 3 years, we considered it interesting to analyze and provide this information at the 1-year follow-up. No differences were observed in terms of oncological and functional results between the 2 procedures.

Conclusions

Hand-sewn staged coloanal anastomosis following TCA for low rectal cancer is safe and does not increase postoperative morbidity rates or need of permanent stomas in the short term compared with standard coloanal anastomosis with covering ileostomy followed by ileostomy closure. These results imply that 2-staged coloanal anastomosis can be considered a valid alternative strategy that avoids a temporary stoma after a sphincteric-preserving ultralow anterior resection for low rectal cancer. According to the protocol of this trial, long-term functional and oncological outcomes, late morbidity, and definitive stoma formation rates are awaited.

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