Trials

STUDY PROTOCOL

Open Access

Staged Turnbull-Cutait pull-through anastomosis comparing with direct anastomosis plus prophylactic ileostomy in the treatment of low rectal cancer after internal sphincter resection (STAR-TAR): study protocol for a randomized controlled trial

Wenhao Chen[1], Jianhua Ding[2], Jianbin Xiang[3], Yanlei Wang[4], Jiagang Han[5], Hui Ye[6], Donghua Wang[7], Binghu Lin[8], Junping Lei[8], Xiangbai Wu[9], Maojun Di[10], Yan Fu[10], Guiyi Yang[11], Chuanhui Qin[11], Aijun Chen[12], Jun Xu[12], Wenming Liu[13], Congqing Jiang[1*] and for the STAR-TAR study group

Abstract

Background Recent advancements in the understanding of lower rectum anatomy, rectal cancer biology, and surgical techniques have emphasized the importance of radical surgery for low rectal cancer that balances oncological safety and anal function preservation. After total mesorectal excision (TME) and coloanal anastomosis, participants face high risks of anastomotic leakage and infection, often requiring a protective ileostomy. However, ileostomies themselves lead to significant complications, such as dehydration and chronic renal failure, and many participants cannot have their stomas reversed as planned. The Turnbull-Cutait procedure, involving delayed transanal pull-through rectal resection, has emerged as a safer alternative, reducing leakage complications and avoiding the need for a protective stoma. Recent studies support its use in challenging rectal cases, showing comparable or better outcomes than standard techniques. Despite these promising results, limited data exists on its application to intersphincteric resection (ISR) or intersphincteric dissection (ISD), which itself has higher complication rates. Therefore, further research is needed to evaluate this Turnbull-Cutait anastomosis procedure (delayed transanal pull-through) in ISR, comparing its complications, oncological outcomes, and functional results to those of traditional methods (direct anastomosis).

This study is a prospective, multicenter, 1:1, non-inferiority, randomized controlled trial with 110 participants, divided into two groups: the staged Turnbull-Cutait pull-through anastomosis group ($n=55$) and the direct anastomosis group ($n=55$). The control group will undergo ISR with traditional anastomosis plus protective ileostomy, while the experimental group will receive the transanal pull-through and delayed anastomosis without ileostomy. The primary outcome is the 30-day overall postoperative complication rate, including anastomotic leakage, infection, and other complications. Secondary outcomes include long-term complications, total surgery time, anorectal

*Correspondence:
Congqing Jiang
wb002554@whu.edu.cn
Full list of author information is available at the end of the article

function (measured by LARS and Wexner scores), urinary and sexual function, quality of life (EORTC QLQ–CR29 and FIQL), and 3-year disease-free survival (DFS) and overall survival (OS).

Discussion Currently, there is a lack of systematic studies exploring the use of delayed pull-through anastomosis in intersphincteric resection (ISR) procedures. Existing research on this technique in low rectal cancer is limited to small, single-center, retrospective studies with low levels of evidence. Therefore, a multicenter, prospective, randomized controlled trial is needed to determine whether delayed pull-through anastomosis can serve as a viable alternative to ISR-coloanal anastomosis, offering comparable or lower rates of postoperative complications, as well as similar oncological outcomes and defecatory function. This study aims to provide higher-quality evidence through a larger, well-designed trial, which could significantly inform clinical practice in this under-explored area.

Trial registration ClinicalTrials.gov NCT06662643. Registered on October 29, 2024.

Keywords Low rectal cancer, Turnbull-Cutait, Pull-through, Internal sphincter resection, Delayed anastomosis, Protective stoma

Introduction

Background and rationale {6a}

In recent years, there has been increasing attention on radical surgical procedures for low rectal cancer that balance oncological safety with the preservation of anal function. In the early 1990 s, Schiessel introduced intersphincteric resection (ISR) for the treatment of low rectal cancer [1], marking a new era for extreme sphincter-preserving surgeries and offering an opportunity to preserve the anus in participants with ultra-low rectal cancer who would otherwise require abdominal-perineal resection. The use of laparoscopic and robotic techniques has further enhanced the minimally invasive effects of ISR. This extreme low rectal sphincter-preserving surgery enables some participants with low rectal cancer to avoid the debilitating loss of the anus while ensuring oncological efficacy, improving quality of life without compromising survival rates [2].

Based on the extent of sphincter resection, ISR is classified into partial ISR (PISR), subtotal ISR (subtotal-ISR), and total ISR (TISR). Correspondingly, the anastomosis site after coloanal anastomosis is located below the levator ani hiatus (PISR, near the dentate line; subtotal-ISR and TISR, below the dentate line). However, after low rectal total mesorectal excision (TME) and subsequent coloanal anastomosis, participants often face a high risk of anastomotic leakage and pelvic infections, which usually necessitates a protective ileostomy. The ileostomy helps divert fecal matter, providing a relatively low perfusion environment that promotes healing for ultra-low coloanal anastomoses. In case of an anastomotic leak, the protective stoma can mitigate infection and reduce the risk of secondary surgeries. However, complications from protective ileostomy, such as dehydration, chronic renal failure, and parastomal hernia, occur in up to 43% of cases [3]. Additionally, complications related to stoma reversal exceed 20% [4], significantly affecting participants' quality of life. Around one-fifth of participants with preventive stomas are unable to have them reversed and may require lifelong stoma formation [5].

In 1961, Turnbull and Cutait independently reported a surgical technique involving transanal pull-through rectal resection and delayed manual coloanal anastomosis [6, 7]. Surgical techniques based on this concept are now known as the Turnbull-Cutait (pull-through) procedure. The procedure generally involves pulling the proximal free colon (after resecting the affected rectum) through the anus by at least 2 cm, suturing the colonic muscular layer to the anal canal with several stitches, and performing delayed removal of the externalized bowel segment several weeks postoperatively, after sufficient adhesion and healing between the colon and surrounding pelvic wall tissues. From one perspective, this procedure is considered one of the safest reconstructive methods, effectively reducing anastomotic leakage-related complications and eliminating the need for a protective stoma. In recent years, its clinical application has gained attention for challenging cases such as radiation proctitis, complex rectovaginal/urethral fistulas, salvage surgeries for anastomotic leaks, and low-stage progressive rectal cancer [8–10].

In 2009, Remzi et al. conducted a retrospective analysis of 67 participants who underwent the Turnbull-Cutait procedure for various indications such as rectovaginal/urethral fistulas, anastomotic leaks, radiation proctitis, and rectal strictures. Compared to 88 participants undergoing standard coloanal anastomosis, the Turnbull-Cutait procedure (delayed anastomosis) significantly reduced the incidence of anastomotic leaks (3% vs. 7%) and pelvic abscesses (0% vs. 5%) without significant differences in defecation, urination, or sexual function [10]. The feasibility of Turnbull-Cutait anastomosis was recently validated in a multicenter RCT by Biondo et al. (JAMA Surg 2020), which demonstrated its short-term safety (leakage rate: 4.8% vs. 18.6% in direct anastomosis) for ultralow rectal resection. Their 2024 long-term

follow-up further confirmed comparable oncological outcomes (5-year local recurrence: 6.1% vs. 7.3%) and superior stoma-free survival (82% vs. 65%) [11, 12]. In a 2022 systematic review, the delayed anastomosis group showed comparable postoperative complication rates to the traditional surgery plus protective ileostomy group, with a significantly lower rate of pelvic infections (7% vs. 14%; $p = 0.02$) [13]. However, this technique may lead to complications such as colonic ischemia, necrosis, and anal stricture in participants with insufficient mobilization of the proximal colon, narrow anorectal rings, or short mesentery. Additionally, as the physiological function of the rectal-anal mucosal skin is abandoned, it may result in perianal eczema and impaired fecal control. Two systematic reviews, including over 1000 participants, demonstrated that delayed anastomosis techniques are not only associated with lower rates of anastomotic leaks, pelvic infections, and reduced stoma rates, but also maintaining satisfactory anal continence outcomes [14, 15].

Therefore, it is highly worthwhile to conduct a multicenter prospective randomized controlled study to determine whether this technique can serve as an effective alternative to ISR-coloanal anastomosis, achieving comparable or lower rates of postoperative complications, as well as equivalent oncological radicality and defecatory function. However, most research has focused on rectal cancers located higher in the rectum (requiring only TME) rather than specifically addressing ultra-low rectal cancers (which necessitate intersphincteric dissection, ISD) and there is limited data on its use in ISR—an extreme sphincter-preserving surgical procedure for low rectal lesions [15]. Unlike the aforementioned TURNBULL-BCN trial (NCT02394964) which focused on ultralow rectal cancer without ISR [11, 12], our protocol mandates histologically confirmed sphincter invasion requiring ISR. This research is urgently needed and could provide valuable guidance for clinical practice.

Objectives {7}

This study targets participants undergoing ultra-low rectal cancer surgery, which requires internal sphincter dissection for sphincter-saving procedures. The study compares the staged Turnbull-Cutait Pull-through anastomosis (a delayed transanal pull-through anastomosis without a protective stoma) as the experimental group with direct anastomosis (hand-sewn/stapled) plus protective ileostomy as the control group. The aim is to assess whether the Turnbull-Cutait Pull-through colon-anal anastomosis is non-inferior to direct anastomosis surgery in terms of complications (short-term such as anastomotic leakage/dehiscence, pelvic infection, anastomotic bleeding, ischemic bowel necrosis, bowel obstruction, and long-term complications such as anastomotic stricture, perianastomotic fistula, bowel obstruction, stoma-related complications, and others), postoperative anal function, quality of life, long-term oncological outcomes, hospital stay duration, and total hospitalization costs. Primary hypothesis: Turnbull-Cutait reduces 30-day major complications (Clavien-Dindo $\geq$IIIa) by $\geq$15% vs direct anastomosis. Secondary hypothesis: TC improves 1-year LARS scores ($\Delta \geq 5$ points) without compromising 3-year DFS.

Trial design {8}

This is a prospective, multicenter, non-inferiority, randomized controlled trial. The total planned enrollment is 110 participants, with the control and intervention groups being allocated in a 1:1 ratio. The Turnbull-Cutait Pull-through group will include 55 cases, while the direct anastomosis group will include 55 cases.

Methods: participants, interventions, and outcomes

Study setting {9}

This is a prospective, open-label, multicenter study that will be conducted in 13 centers in China, which included the following: Zhongnan Hospital, Wuhan University, Hubei, China; Rocket Force Special Medical Center of the People's Liberation Army, Beijing, China; Huashan Hospital, Fudan University, Shanghai, China; Qilu Hospital of Shandong University, Shandong, China; Beijing Chaoyang Hospital Affiliated to Capital Medical University, Beijing, China; Jingzhou Central Hospital, Hubei, China; Xiangyang Central Hospital, Hubei, China; Xiangyang First People's Hospital, Hubei, China; Yichang Second People's Hospital, Hubei, China; Taihe Hospital, Hubei, China; Suizhou Central Hospital, Hubei, China; Yichang Central People's Hospital, Hubei, China; Tianmen First People's Hospital, Hubei, China. These hospitals were selected based on their high annual caseloads of ISR procedures for low rectal cancer. All participating surgeons must (a) have performed $\geq$20 ISR procedures independently,

(b) demonstrated $\geq$10 Turnbull-Cutait cases (for the experimental arm), and (c) submitted unedited surgical videos for central review by the study's technical committee. Each center will obtain ethical approval from local ethics committee at each institution individually. The latest version of the protocol will be promptly distributed to all investigators.

Eligibility criteria {10}

Inclusion criteria

Participants must meet all of the following criteria to be eligible for inclusion in this study.

1) Histopathologically confirmed high- or moderate-grade adenocarcinoma or villous adenoma with malignancy on preoperative colonoscopy; tumor located ≤5 cm from the anal verge; primary tumor size <5 cm in diameter.
2) All enrolled participants require intersphincteric dissection. PISR surgery must be completed with hand-sewn (preferably) or stapled coloanal anastomosis. The anastomosis should be located near the dentate line (intraoperative photos or videos must be preserved).
3) Both male and female participants aged 18–75.
4) Non-recurrent rectal cancer.
5) No concurrent multiple primary colorectal cancers.
6) Initial staging or post-neoadjuvant therapy stage: T3 above the levator ani, T1–2 below.
7) Liver or lung oligometastases deemed resectable after evaluation by a Multi-Disciplinary treatment (MDT).
8) Participants may or may not have received neoadjuvant chemoradiotherapy.
9) Participants must understand and be willing to participate in this study, providing written informed consent.
10) Good anal function (Wexner Incontinence Score ≤5).

Exclusion criteria

Participants who meet any of the following criteria will be excluded from participation in this study.

1) History of malignant colorectal tumors.
2) Previous colorectal or anorectal surgeries or diseases.
3) Participants requiring emergency surgery due to intestinal obstruction, perforation, or bleeding.
4) Tumor invasion into the external sphincter, levator ani, or adjacent organs requiring combined organ resection.
5) Poor preoperative anal function or incontinence (Wexner Incontinence Score ≥6).
6) History of inflammatory bowel disease (IBD) or familial adenomatous polyposis (FAP).
7) Recent diagnosis of other malignancies.
8) Participation in other clinical trials within the 4 weeks prior to enrollment.
9) ASA classification ≥IV or ECOG performance status ≥2.
10) Severe hepatic, renal, cardiopulmonary, or coagulation dysfunction or serious underlying disease precluding surgery.
11) History of severe mental illness.
12) Pregnant or breastfeeding women.
13) Uncontrolled preoperative infection.
14) Other clinical or laboratory findings making the participant unsuitable for the study, as judged by the investigator.

Who will take informed consent? {26a}

Participants will be provided with detailed study information during recruitment to ensure informed consent, with written consent obtained from those who elect to participate.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

Not applicable.

Interventions

Explanation for the choice of comparators {6b}

The study compares the staged Turnbull-Cutait Pull-through anastomosis as the experimental group with direct anastomosis plus protective ileostomy as the control group. Both surgical procedures are well established and routinely performed in clinical practice, with proven safety and efficacy. During informed consent, participants will be clearly informed of the benefits, risks, and potential outcomes of each option, as well as the risks and benefits of the clinical trial, and written consent will be fully obtained.

Intervention description {11a}

Each surgical procedure can be divided into two stages.

1. For staged Turnbull-Cutait anastomosis, Stage 1: laparoscopic surgery is recommended. A standard 5-port method is used to create pneumoperitoneum after placing the trocar. The sigmoid colon and upper rectal mesentery are dissected along Toldt's fascia. Autonomic nerves should be preserved, and high ligation of the inferior mesenteric vessels with lymph node dissection is recommended. The surgeon can decide whether to preserve the left colic artery and whether to mobilize the splenic flexure based on intraoperative conditions. TME: using a posterior-to-anterior approach, the mesorectal plane is sharply dissected down to the pelvic floor. Intersphincteric space dissection (ISD): when TME dissection reaches the edge of the levator ani muscle hiatus, dissection starts either from the anterior or lateral rectal side, exposing and identifying the intersphincteric space. The intersphincteric space is then gradually exposed and dissected. Transecting the bowel: using a transanal approach, with the anal canal fully exposed—often assisted by a circular anal retractor—the bowel

is circumferentially transected at least 1 cm below the tumor(the internal sphincter was partially or totally resected). Dissection is then carried out in the intersphincteric space, where it meets the space previously dissected transabdominally. The rectum and proximal colon is exteriorized transanally, and the specimen is excised in accordance with the principles of oncologic resection, then at least 4 cm heathy proximal colon is leaving outside and sutured to the anal canal with 2 fixed stitches, without constructing a protective ileostomy. Stage 2: 2 to 4 weeks after the first surgery, after the colon has adhered well to the surrounding tissue, the exteriorized colon is trimmed and anal reconstruction performed.

2. For direct anastomosis plus protective ileostomy, Stage 1: the detailed techniques are the same as Stage 1 in staged Turnbull-Cutait anastomosis mentioned above (TME and intersphincteric space dissection), however, the subsequent step differ. A direct coloanal anastomosis will be performed using absorbable sutures under direct visualization and a protective ileostomy is created 25–30 cm from the ileocecal valve. Stage 2: 3 to 6 months after surgery (post-adjuvant chemoradiotherapy or chemotherapy), the ileostomy is closed. Prior to closure, digital rectal examination, defecography, MRI, colonoscopy, and other evaluations must confirm no recurrence, minimal anastomotic leakage, or rectovaginal fistula before ileostomy closure.

Criteria for discontinuing or modifying allocated interventions {11b}

Participants who, after enrollment, do not complete the two specified surgical procedures, such as converting to an APR (abdominoperineal resection) surgery, or participants in whom unexpected tumor involvement is discovered during surgery requiring combined pelvic organ resection, or those with peritoneal metastasis, need to be excluded from the trial. Modifications to the allocated interventions, such as preserving the left colic artery, mobilizing the splenic flexure, using ICG fluorescence laparoscopic guidance to assess bowel perfusion, and utilizing TaTME (transanal total mesorectal excision) technology to assist in retrograde transanal mobilization of the distal rectum are acceptable, as they do not fundamentally affect the basic process and outcome of the surgery. Other technical modifications, subject to approval by the steering committee, are also acceptable.

Strategies to improve adherence to interventions {11c}

To improve adherence to the intervention protocol, we will implement the following strategies: (1) preoperative education and training to ensure all trial staff are well-trained and fully informed about protocol requirements, (2) regular follow-up visits to monitor compliance and provide support, and (3) continuous monitoring with targeted interventions if non-compliance is detected.

Relevant concomitant care permitted or prohibited during the trial {11d}

Not applicable.

Provisions for post-trial care {30}

Post-trial care will be provided according to standard clinical practices for rectal cancer surgery. This includes the following: (1) Follow-up appointments: participants will be monitored regularly for signs of recurrence, complications, and quality of life assessments. The follow-up schedule will include clinical visits at 1, 3, 6, and 12 months post-surgery, then annually thereafter. (2) Oncological care: If indicated, participants will receive adjuvant chemotherapy or radiation therapy based on their cancer staging and the surgical outcomes. (3) Supportive care: Psychological and social support services will be available for participants facing challenges related to recovery and coping with the impact of cancer treatment.

Outcomes {12}

Primary endpoint

Primary outcome measure is 30-day overall composite postoperative complication rate, which includes anastomotic leakage/dehiscence, bleeding, ischemic bowel necrosis, pelvic infection (abscess), pelvic bleeding, bowel obstruction, stoma-related complications, and other complications occurring within 30 days. Anastomotic leakage is defined according to the criteria proposed by the International Study Group of Rectal Cancer (ISREC) in 2010, graded as A, B, or C, depending on severity and management.

Secondary endpoint(s)

- Long-term complications rate: include anastomotic stricture, anastomotic fistulas (e.g., rectovaginal or rectourethral fistula), bowel obstruction, stoma-related complications, inability to reverse stoma, chronic presacral sinus, and rectal prolapse (both mucosal and full-thickness).
- Total surgery time: defined as the combined time of the two stages (Stage 1 + Stage 2) of staged Turnbull-Cutait pull-through anastomosis with direct anastomosis or intersphincteric resection (ISR) plus stoma reversal time. This also includes total hospital stay (Stage 1 + Stage 2) and total hospitalization costs (Stage 1 + Stage 2).

- LARS Score Questionnaire: Low Anterior Resection Syndrome (LARS) Score is a tool used to assess bowel function after surgical treatment for rectal cancer, particularly following low anterior resection (LAR) procedures. The LARS score evaluates the presence and severity of bowel dysfunction, which can significantly impact the quality of life for participants. Interpretation: higher scores indicate worse bowel function and greater symptoms of LARS (minimum value: 0; maximum value: 42).
- Wexner Incontinence Score: The Wexner Incontinence Score is a validated tool used to assess the severity of fecal incontinence in participants. The Wexner score is calculated by summing the scores from each of the categories: 0: no incontinence; 1–5: mild incontinence; 6–10: moderate incontinence; 11–20: severe incontinence. Interpretation: higher scores indicate worse fecal incontinence and greater impact on quality of life (minimum value: 0; maximum value: 20).
- International Prostate Symptom Score (IPSS) Questionnaire: The International Prostate Symptom Score (IPSS) is a widely used tool for evaluating the severity of urinary symptoms in men and helps to assess the impact of these symptoms on participants' quality of life. Interpretation: higher scores indicate worse urinary symptoms and a greater impact on quality of life (minimum value: 0; maximum value: 35).
- International Index of Erectile Function (IIEF-5) Questionnaire: The International Index of Erectile Function (IIEF-5) is a widely used questionnaire designed to assess erectile function in men. IIEF-5 consists of five questions that evaluate different aspects of erectile function. Each question is scored on a scale from 0 to 5, with higher scores indicating better erectile function. Interpretation: higher scores indicate better erectile function and greater sexual satisfaction (minimum value: 0; maximum value: 25).
- Female Sexual Function Index (FSFI) Questionnaire: The Female Sexual Function Index (FSFI) is a widely used questionnaire designed to assess various dimensions of female sexual function. It is a reliable tool for identifying sexual dysfunction in women. Interpretation: higher scores indicate better sexual function. A total score below 26.55 suggests the presence of sexual dysfunction (minimum value: 2; maximum value: 36).
- EORTC QLQ-CR29 Questionnaire: The EORTC QLQ-CR29 is a specific quality of life questionnaire developed by the European Organisation for Research and Treatment of Cancer (EORTC) to assess the health-related quality of life in participants with colorectal cancer. This questionnaire is an extension of the EORTC Quality of Life Questionnaire (QLQ-C30) and is designed to evaluate the specific concerns and symptoms experienced by colorectal cancer participants. Interpretation: Higher scores indicate better functioning for functional scales and worse symptoms for symptom scales (number of items: 29 scoring range: 0 to 100).
- Three-year disease-free survival (3-year DFS): 3-year DFS refers to the duration during which participants remain free of disease following treatment (such as surgery, chemotherapy, or radiation) for a period of 3 years. Expressed as a percentage, with a higher percentage indicating that a greater proportion of participants remain disease-free at the 3-year mark, suggesting that the treatment may be effective in preventing recurrence or progression. Local recurrence is defined as evidence of recurrence within the pelvic area detected through digital rectal examination, colonoscopy, CT/MRI, PET-CT, or biopsy (when necessary) and confirmed to match the histopathology of the primary tumor. Distant metastasis is defined as evidence of metastasis found outside the pelvic area, including the liver, lungs, bones, or paraaortic lymph nodes.
- Three-year overall survival (3-year OS): Refers to the proportion of participants who remain alive 3 years after the beginning of the study period. Reported as a percentage, with a higher percentage indicating a greater proportion of participants alive at the 3-year mark, which may reflect improved survival due to the treatment.

Participant timeline {13}

The participant timeline is shown in Fig. 1.

Sample size {14}

The recruitment period for all subjects is estimated to be 2 years, with an average follow-up period of 3 years. Based on previously published studies and our own data, using the primary study endpoint—the anticipated 30-day overall composite postoperative complication rate—the expected 30-day overall composite postoperative complication rate is 34% for the staged Turnbull-Cutait anastomosis group and 62% for the direct anastomosis plus protective ileostomy group. With a 1:1 allocation ratio between the two groups, setting a two-sided $\alpha = 0.05$ and a power of $1\text{-}\beta = 80\%$ for a non-inferiority clinical study, using PASS 15.0 statistical software (USA)) and accounting for a 10% loss rate, the calculated sample size is 55 cases per group, totaling 110 cases. If necessary, the sample size may be increased after validation.

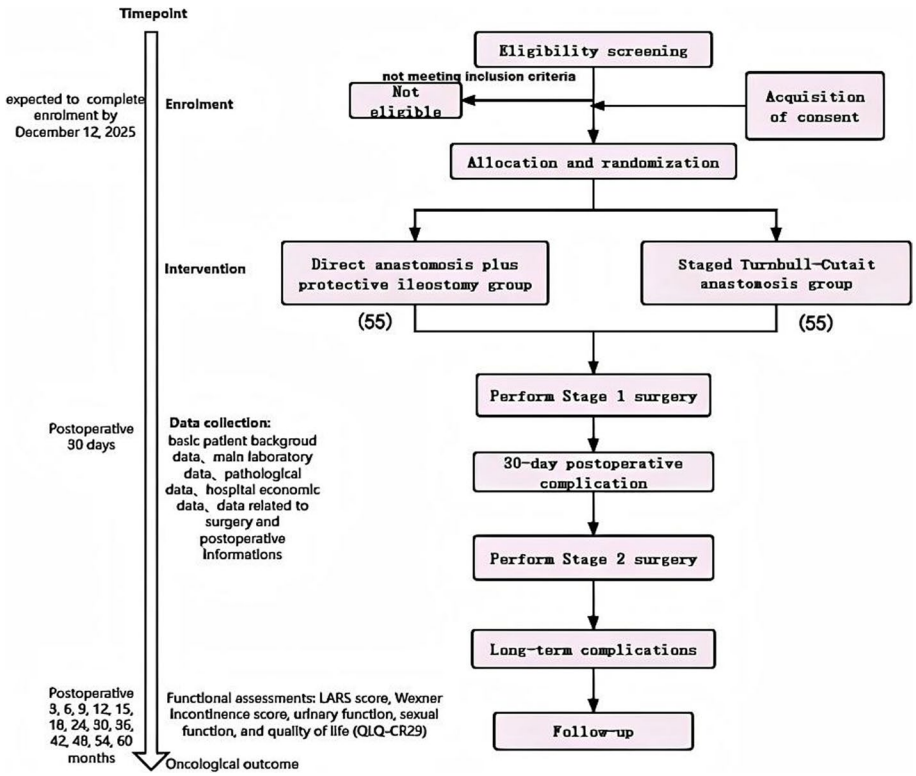

Fig. 1 Flow-chart of the study procedures

Recruitment {15}

Enrollment was commenced May 2024 and will continue until the required number of eligible participants is enrolled in the trial. Recruitment will take place at the aforementioned 14 institutions, where eligible participants will be identified and approached by trained research staff. Inclusion and exclusion criteria will be strictly followed. The recruitment period is expected to last 18 months, with the goal of enrolling 110 participants.

Assignment of interventions: allocation Sequence generation {16a}

The randomization process will use a computer-generated random number sequence to allocate participants to either the Turnbull-Cutait anastomosis group or direct anastomosis plus protective ileostomy group.

Concealment mechanism {16b}

The investigators will not be informed of the participants' enrollment status until after randomization and assignment to an intervention group.

Implementation {16c}

The allocation sequence will be generated by an independent statistician. Research assistants will enroll participants and assign interventions, while data analysis will be performed by a separate statistician not involved in the clinical data collection. Once eligible participants have been enrolled and informed consent is obtained, the randomization process will be carried out by the research team.

Assignment of interventions: blinding

Who will be blinded {17a}

Complete blinding is not feasible due to the nature of the interventions; however, the trial statistician and data analysts will be blinded to group allocation during the data analysis phase. Randomization will be disclosed to the investigators, participants, and clinical staff involved in treatment and follow-up.

Procedure for unblinding if needed {17b}

If unblinding is necessary (e.g., for safety reasons), the trial statistician will access the randomization data and reveal the intervention group. This will be done only after data analysis is completed or in the event of an adverse outcome requiring intervention.

Data collection and management

Plans for assessment and collection of outcomes {18a}

After treatment, participants will return for follow-up every 3 months for the first year. The follow-up assessments include digital rectal examination, routine blood tests, biochemical tests, tumor markers, pelvic MRI, chest and abdominal CT scans, and colonoscopy. Functional assessments, including anorectal manometry, LARS score, Wexner Incontinence Score, urinary function, sexual function, and quality of life (QLQ-CR29), will be dynamically evaluated at preoperative (1–3 days before surgery) and at postoperative time points: 1, 3, 6, 9, 12, 15, 18, 24, 30, 36, 42, 48, 54, and 60 months after the second stage of both two groups. A comprehensive database will be established, and a dedicated person will be responsible for filling, registering, and uploading follow-up data. Outside of scheduled follow-up visits, follow-up will be conducted via phone or WeChat (a popular Chinese social networking app).

Plans to promote participant retention and complete follow-up {18b}

To enhance retention, participants will be reminded of follow-up visits via phone calls or WeChat. The research team will maintain regular contact to address any concerns and encourage ongoing participation.

Data management {19}

The investigators will obtain informed consent from the participants at each institution. Data will be collected prospectively from all participants, and input into a customized electronic data capture system (EDC). All investigators should complete and submit the online version of the case report form promptly after each participant's visit.

Confidentiality {27}

Participant confidentiality will be strictly maintained, with only anonymized data used for research purposes.

Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Not applicable.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

All collected data will be analyzed by an independent statistician, who will remain blinded to the treatment group. Continuous variables will be expressed as mean ± standard deviation or median (interquartile range) and compared using the independent-samples *t*-test or Mann–Whitney *U* test. Categorical variables will be expressed as number (percentage) and compared using the chi-square test or Fisher's exact test. Long-term outcomes, including overall survival and disease-free survival, will be analyzed using the Kaplan–Meier method, with group differences assessed via the log-rank test. Multivariable Cox proportional hazards models will identify independent prognostic factors for both overall and disease-free survival. All statistical tests will be two-sided, and p-values less than 0.05 will be considered statistically significant.

Interim analyses {21b}

No interim analysis is scheduled for this study, and the study will not be terminated based on any interim results.

Methods for additional analyses (e.g., subgroup analyses) {20b}

Subgroup analyses will be conducted for exploratory purposes based on baseline characteristics, such as tumor staging and preoperative neoadjuvant chemoradiotherapy, to assess their impact on the primary endpoint. Additionally, according to the 2023 international ISOG-ISR expert consensus on standardizing and optimizing intersphincteric resection (ISR) [15], performing a coloanal anastomosis with a stapler during a fully transabdominal ISR (as defined in the "2023 Chinese Expert Consensus on Intersphincteric Resection for Low Rectal Cancer") should strictly be classified as ultra-low anterior resection (uLAR). Admittedly, this definition remains controversial, even among international expert groups, which reached consensus only after three rounds of voting. Therefore, in the statistical analysis of this clinical trial, in addition to the comparative analysis between the two main groups—direct anastomosis (manual/stapler) and delayed staged anastomosis—subgroup comparison should be conducted between participants in the stapled ISR group, manual ISR group (classic ISR group), and the delayed anastomosis group.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

An intention-to-treat analysis will be conducted, including all randomized participants based on their assigned group. Additionally, a per-protocol analysis will be performed as a sensitivity analysis. Missing data will be addressed in the publication, with multiple

imputation via predictive mean matching used to adjust for covariates.

Plans to give access to the full protocol, participant-level data, and statistical code {31c}

The protocol is available upon request, and the participant-level data can be accessed after publication upon reasonable request.

Oversight and monitoring

Composition of the coordinating center and trial steering committee {5 d}

The coordinating center, led by the Principal Investigator (PI) at Zhongnan Hospital, Wuhan University will manage the overall trial, including data collection, monitoring, and communication across sites. Quality Control Measures: Intraoperative photography of critical steps (e.g., completed pull-through) uploaded to the study database; Annual competency reassessment requiring submission of two recent case videos. Statistical Adjustment: We will record and adjust for: Individual surgeon volume (cases/year); Center experience (ISR caseload over past 5 years). The trial steering committee consists of Congqing Jiang, Wenhao Chen, Jianhua Ding, Jianbin Xiang, and Hui Ye, who will be responsible for scientific, ethical, and operational oversight.

Composition of the data monitoring committee, its role and reporting structure {21a}

The data monitoring committee, comprising two independent clinicians, researchers, and a statistician, will ensure participant safety and provide guidance to maintain the trial's integrity and validity.

Adverse event reporting and harms {22}

Adverse events (AE) related to this study are not anticipated as both two surgical techniques are well established and routinely performed in clinical practice. Postoperative complications should not be reported as adverse events.

Frequency and plans for auditing trial conduct {23}

Not applicable.

Plans for communicating important protocol amendments to relevant parties (e.g., trial participants, ethical committees) {25}

Any changes to the protocol will be reviewed and approved by the IRB before being implemented. These amendments will be promptly communicated to all relevant study personnel via email. Additionally, any applicable updates will be reflected on ClinicalTrials.gov.

Dissemination plans {31a}

The trial results will be shared through presentations at relevant meetings and submitted for publication in peer-reviewed journals. They will also be posted on ClinicalTrials.gov, with data made available per data-sharing requirements. All investigators will approve any publications before release.

Discussion

Advancements in technology have led to improved survival rates for rectal cancer participants, prompting a shift toward evaluating treatment outcomes based on postoperative morbidity, anorectal function, and quality of life. However, rectal cancer surgery still carries a high risk of complications, particularly anastomotic dehiscence and defecatory dysfunction. This study aims to show that the Turnbull-Cutait technique is at least as effective, if not more so, than the standard coloanal anastomosis with temporary ileostomy in reducing postoperative morbidity while maintaining comparable oncological and functional outcomes. We hypothesize that the Turnbull-Cutait pull-through procedure could be an optimal option for low rectal cancer participants, as it preserves normal intestinal continuity and avoids the need for a protective stoma. This could result in lower overall postoperative morbidity, reduced complications from stoma formation, and fewer hospital readmissions. Additionally, by eliminating the need for stoma closure, this technique could decrease healthcare costs. This randomized controlled trial will compare these two established surgical approaches and evaluate whether the two-stage Turnbull-Cutait pull-through procedure can offer superior results, reducing complications, improving participant outcomes, and enhancing both quality of life and cost-effectiveness in low rectal cancer treatment.

Trial status

Protocol Version 03 (29OCT2024).

The trial opened enrollment on May 05, 2024 and is expected to be completed by December 12, 2025.

Abbreviations

MDT	Multi-disciplinary treatment
EDC	Electronic data capture
TME	Total mesorectal excision
ISR	Intersphincteric resection
ISD	Intersphincteric dissection
LARS	Low anterior resection syndrome
IPSS	International Prostate Symptom Score
IIEF-5	International Index of Erectile Function
FSFI	Female Sexual Function Index
DFS	Disease-free survival
OS	Overall survival

Acknowledgements

None.

Authors' contributions {31b}
WHC, JHD, JBX, and CQJ conceived the trial. WHC, JHD, JBX, and CQJ designed the trial. YLW, JGH, HY, DHW, and BHL developed the statistical analysis plan. WHC drafted the manuscript. JHD, JBX, and CQJ revised the manuscript. All authors have given final approval for the version to be published.

Funding {4}
This work was supported by grants from the Project for the Development of Advantageous Disciplines of Zhongnan Hospital, Wuhan University (Grant No. XKJS202017).

Data availability {29}
The datasets generated during the study will be available after publication of the trials results upon written request made to the corresponding author.

Declarations

Ethics approval and consent to participate {24}
This prospective study was approved by the Zhongnan Hospital Institutional Review Board (Ethics number: 2024054). All methods were carried out in accordance with relevant guidelines and regulations. Research involving human participants, human material, or human data is conducted in accordance with the Declaration of Helsinki. The authors confirmed that informed consent was obtained from all subjects.

Consent for publication {32}
These are available from the corresponding author on request.

Competing interests {28}
The authors declare that they have no competing interests.

Author details
[1]Department of Colorectal and Anal Surgery, Zhongnan Hospital, Wuhan University, Hubei, China. [2]Department of Colorectal and Anal Surgery, Rocket Force Special Medical Center of the People's Liberation Army, Beijing, China. [3]Department of Colorectal and Anal Surgery, Huashan Hospital of Fudan University, Shanghai, China. [4]Department of Colorectal and Anal Surgery, Qilu Hospital of Shandong University, Shandong, China. [5]Department of Colorectal and Anal Surgery, Beijing Chaoyang Hospital Affiliated to Capital Medical University, Beijing, China. [6]Department of Colorectal and Anal Surgery, Jingzhou Central Hospital, Hubei, China. [7]Department of Colorectal and Anal Surgery, Xiangyang Central Hospital, Hubei, China. [8]Department of Colorectal and Anal Surgery, Xiangyang First People's Hospital, Hubei, China. [9]Department of Colorectal and Anal Surgery, Yichang Second People's Hospital, Hubei, China. [10]Department of Colorectal and Anal Surgery, Taihe Hospital, Hubei, China. [11]Department of Colorectal and Anal Surgery, Suizhou Central Hospital, Hubei, China. [12]Department of Colorectal and Anal Surgery, Yichang Central People's Hospital, Hubei, China. [13]Department of Colorectal and Anal Surgery, Tianmen First People's Hospital, Hubei, China.

Received: 7 February 2025 Accepted: 19 April 2025
Published online: 22 May 2025

References

1. Schiessel R, Karner-Hanusch J, Herbst F, et al. Intersphincteric resection for low rectal tumours. Br J Surg. 1994;81(9):1376–8. https://doi.org/10.1002/bjs.1800810944.
2. Martin ST, Heneghan HM, Winter DC. Systematic review of outcomes after intersphincteric resection for low rectal cancer. Br J Surg. 2012;99(5):603–12. https://doi.org/10.1002/bjs.8677.
3. Murken DR, Bleier JIS. Ostomy-related complications. Clin Colon Rectal Surg. 2019;32(3):176–82. https://doi.org/10.1055/s-0038-1676995.
4. Man VC, Choi HK, Law WL, et al. Morbidities after closure of ileostomy: Analysis of risk factors. Int J Colorectal Dis. 2016;31(1):51–7. https://doi.org/10.1007/s00384-015-2327-2.
5. Zhou X, Wang B, Li F, et al. Risk factors associated with nonclosure of defunctioning stomas after sphincter-preserving low anterior resection of rectal cancer: A meta-analysis. Dis Colon Rectum. 2017;60(5):544–54. https://doi.org/10.1097/DCR.0000000000000819.
6. Cutait DE, Figliolini FJ. A new method of colorectal anastomosis in abdominoperineal resection. Dis Colon Rectum. 1961;4:335–342.https://doi.org/10.1007/BF02627230.
7. Turnbull RB, Jr., Cuthbertson A. Abdominorectal pull-through resection for cancer and for hirschsprung's disease. Delayed posterior colorectal anastomosis. Cleve Clin Q. 1961;28:109–115. https://doi.org/10.3949/ccjm.28.2.109.
8. Corte H, Maggiori L, Treton X, et al. Rectovaginal fistula: What is the optimal strategy?: An analysis of 79 patients undergoing 286 procedures. Ann Surg. 2015:262(5):855–860. discussion 860–851.https://doi.org/10.1097/SLA.0000000000001461.
9. Patsouras D, Yassin NA, Phillips RK. Clinical outcomes of colo-anal pull-through procedure for complex rectal conditions. Colorectal Dis. 2014;16(4):253–8. https://doi.org/10.1111/codi.12532.
10. Remzi FH, El Gazzaz G, Kiran RP, et al. Outcomes following turnbull-cutait abdominoperineal pull-through compared with coloanal anastomosis. Br J Surg. 2009;96(4):424–9. https://doi.org/10.1002/bjs.6458.
11. Biondo S, Trenti L, Espin E, et al. Two-stage turnbull-cutait pull-through coloanal anastomosis for low rectal cancer: A randomized clinical trial. JAMA Surg. 2020;155(8): e201625. https://doi.org/10.1001/jamasurg.2020.1625.
12. Biondo S, Barrios O, Trenti L, Espin E, Bianco F, Falato A, De Franciscis S, Solis A, Kreisler E; TURNBULL-BCN Study Group. Long-Term Results of 2-Stage Turnbull-Cutait Pull-Through Coloanal Anastomosis for Low Rectal Cancer: A Randomized Clinical Trial. JAMA Surg. 2024;159(9):990–996. https://doi.org/10.1001/jamasurg.2024.2262.
13. La Raja C, Foppa C, Maroli A, et al. Surgical outcomes of turnbull-cutait delayed coloanal anastomosis with pull-through versus immediate coloanal anastomosis with diverting stoma after total mesorectal excision for low rectal cancer: A systematic review and meta-analysis. Tech Coloproctol. 2022;26(8):603–13. https://doi.org/10.1007/s10151-022-02601-4.
14. Hallet J, Milot H, Drolet S, et al. The clinical results of the turnbull-cutait delayed coloanal anastomosis: A systematic review. Tech Coloproctol. 2014;18(6):579–90. https://doi.org/10.1007/s10151-014-1132-1.
15. Portale G, Popesc GO, Parotto M, et al. Delayed colo-anal anastomosis for rectal cancer: Pelvic morbidity, functional results and oncological outcomes: A systematic review. World J Surg. 2019;43(5):1360–9. https://doi.org/10.1007/s00268-019-04918-y.

Publisher's Note