

Multicenter Controlled Study of Intracorporeal Mechanical Side-to-Side Isoperistaltic Anastomosis versus Extracorporeal Anastomosis in Laparoscopic Right Hemicolectomy: HEMI-D-TREND-Study

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Keywords

Right hemicolectomy · Anastomosis leak · Intracorporeal anastomosis · Extracorporeal anastomosis

Abstract

Colorectal cancer is the second most frequent cancer in the Western world. A third of colorectal tumors are located in the right colon, and right hemicolectomy is the treatment in nondisseminated right colon cancer. The most serious complication of this procedure is anastomotic leak, which occurs in 8.4% of cases. At present, there is no standardized technique for laparoscopic ileo-colic anastomosis. In previous observational studies, intracorporeal side-to-side ileo-colic

laparoscopic anastomosis has shown better results than extracorporeal anastomosis in terms of morbidity and mortality. It is known that randomized studies provide higher levels of evidence, but multicenter randomized controlled studies may imply a learning curve bias due to the differences in technical experience acquired at each hospital. As a result, we propose to carry out a prospective, controlled, nonrandomized TREND-study design (Transparent Reporting of Evaluations with Non-randomized Designs-TREND) in a large sample of 416 patients (208 per group) in order to assess the use of intracorporeal side-to-side ileo-colic laparoscopic anastomosis as the gold standard in right hemicolectomy.

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Introduction

Colorectal cancer is the second most frequent cancer in the Western world [1]. Roughly a third of colorectal tumors are located in the right colon [2], and right hemicolectomy surgery is the treatment of choice in nondisseminated right colon cancer and other benign pathologies [3]. Despite the introduction of laparoscopy and multimodal fast-track perioperative management programs in recent years, postoperative complication rates remain high [4, 5]. The most serious complication is anastomotic leak (AL), which is associated with increased mortality, longer hospital stay, and reduced quality of life due to the need for an ostomy [6]. For a long time, the importance of ileo-colic AL was underestimated. However, the ANACO study [2], conducted in 52 hospitals in our environment, reported a rate of AL of 8.4% (range 0–35%), the wide range being due to the differences in the surgical procedures and anastomoses used.

Currently, there is no standardized technique for ileo-colic anastomosis. The variability in the approaches used may increase the rate of anastomotic failure. Therefore, studies are now needed in order to homogenize the surgical technique and minimize the risks of surgery.

The results of intracorporeal laparoscopic anastomosis in the literature vary widely, although those reported so far estimate an AL rate below 2%. However, recent publications report low rates of morbidity and of surgical space infection [5, 7]. The main problem with this technique is that it requires a rather longer learning curve than others, and its results depend on the skill of the surgeon and his/her experience. As a result, comparative studies are needed to assess its use as gold standard.

Multicenter, randomized controlled studies have the disadvantage that randomization at centers with little experience in one or other of the techniques may imply a learning curve bias. Besides, if surgeons at a particular center believe that one of the techniques is superior to the other, randomization would be unethical. Because of this, we decided to perform a nonrandomized TREND-study design (Transparent Reporting of Evaluations with Non-randomized Designs-TREND).

In this multicenter TREND study, we aim to compare laparoscopic right hemicolectomy intracorporeal anastomosis with extracorporeal anastomosis. The study is currently underway. The first patient was included in April 2019, and patient recruitment is ongoing. The study is expected to finish in June 2021.

Methods/Design

Study Design

A multicenter prospective, nonrandomized, controlled study of intracorporeal mechanical side-to-side isoperistaltic anastomosis versus extracorporeal anastomosis in laparoscopic right hemicolectomy.

Hypothesis and Objectives

Hypothesis

Intracorporeal side-to-side ileo-lateral ileo-colic anastomosis in elective laparoscopic right hemicolectomy will achieve better results in terms of morbidity and mortality than the extracorporeal anastomoses.

Main Objective

To compare overall morbidity and mortality in laparoscopic right hemicolectomy with intracorporeal anastomosis and laparoscopic extracorporeal anastomosis and open surgery.

Secondary Objectives

To analyze the rate of AL and organ-cavitary infections; to compare the results with those published in the literature; to identify the risk factors associated with AL; to analyze the comorbidities associated with the type of incision made to extract the surgical specimen.

Study Setting and Participants

Population

Patients diagnosed with right colon adenocarcinoma after complete colonoscopy, biopsy, chest radiography, and thoracoabdominal and pelvic CT.

Inclusion Criteria

Patients over 18 years diagnosed with right colon neoplasia without metastasis. Indication of right hemicolectomy and ileo-colic anastomosis. Scheduled surgery performed by the Coloproctology Unit of each participating hospital. Compliance with the perioperative management program of each hospital.

Exclusion Criteria

Colon neoplasms at other locations. T4 tumor stage and stage IV of the TNM classification, American Society Anesthesiologists IV. Nonoptimal nutritional status (preoperative albumin ≤ 3.4 g/dL). Failure to sign informed consent, pregnancy, liver cirrhosis, dialysis treatment, and body mass index < 18 and > 35 Kg/m².

Withdrawal Criteria

Conversion to open surgery. Intracorporeal anastomosis technique other than the one described in the protocol.

Recruitment Plan

Intracorporeal group: Parc Taulí University Hospital, Hospital Universitari Joan XXIII de Tarragona, Hospital de Cancer de Barretos. Extracorporeal group: Consorci Hospitalari de Terrassa, Hospital de Universitari de Vic, Hospital Universitari Arnau de Vilanova de Lleida, Hospital Santa Tecla de Tarragona, Hospital Universitari Sant Joan de Reus.

Ethics, Informed Consent, and Legal Considerations

Patients who meet the inclusion criteria will sign the informed consent document. The processing of the data compiled by the main data managers during the trial will comply with the current legislation regarding data protection. The anonymity of the data is guaranteed. The study protocol, the information for patients, and the informed consent documents have been approved by the Clinical Research Ethics Committees of all the participating centers, in accordance with Royal Decree 1090/2015, of December 4. The Ethics Committee of the Parc Taulí University Hospital is the committee of reference (ID: 2018/658). The trial has been registered in the ClinicalTrials.gov database (ID: NCT03918369), and it is carried out in accordance with the seventh revision of the Declaration of Helsinki [8] and the 2013 SPIRIT Standard Protocol Articles for Clinical Trials [9].

Surgical Technique

The study comprises 2 groups: intracorporeal and extracorporeal anastomosis.

In the intracorporeal group, an intracorporeal mechanical side-to-side isoperistaltic anastomosis is made. In this procedure, intracorporeal division of the mesoileum and transverse colon is performed. The ileum and transverse colon are divided with the Endopath® Echelon Flex™ 60 stapler. The specimen is inserted into a plastic bag. Side-to-side isoperistaltic mechanical anastomosis is performed using the same endostapler. A running suture of the mechanical suture orifice is performed, with another reinforcing suture with Monocryl™ (poliglecaprone 25) or with STRATA-FIX™ Spiral Knotless barbed suture. The specimen is extracted through a Pfannenstiel laparotomy using a wound protector.

In the extracorporeal anastomosis, the anastomosis is performed applying the usual technique at each center.

Primary and Secondary Endpoints

Primary Endpoints

Overall morbidity, surgical space infection [10], AL [11], reinterventions, and hospital stay in the first 30 postoperative days.

Secondary Endpoints

Epidemiological variables: ID-patient, hospital, age, sex. Preoperative variables: American Society of Anesthesiologists, body mass index.

Surgical Variables

Type of hemicolectomy (extracorporeal anastomosis), surgical time, type of anastomosis, type of suture, type of anastomotic continuity, size and location of the laparotomy.

Postoperative Variables

Visual Analog Scale 1st and 2nd postoperative day, POSSUM [12], P-POSSUM [13], and CR-POSSUM [14] values, postoperative mortality, overall morbidity, Clavien-Dindo morbidity [15], relevant morbidity (Clavien-Dindo >II [15]), Comprehensive Complication Index [16], in the first 30 postoperative days.

Sample Size

The sample size has been calculated taking the AL as the main variable. ALs of 2% in the intracorporeal group and 8% in the extracorporeal group are estimated, with an α risk of 0.05 and $1-\beta$ of 0.9. The estimated number of cases to be included is 208 patients per group; with an estimated loss of 10%, the final number required is 416 patients.

Monitoring

Monitoring is centralized by the promoter center in a purpose-built online database.

Statistical Analysis

All patients will undergo intention-to-treat analysis. Per protocol analysis will also be carried out in both groups. Prospective data collection allows analysis without missing values.

The description of the variables and the statistical analysis will be carried out using the SPSS program version 23. The quantitative and categorical variables will be described in the standard way. Univariate analysis of the quantitative variables, with independent groups, will be performed by Student *t* test when their conditions of application are met; otherwise, the Mann-Whitney U will be used. For categorical variables, Pearson's chi-square or Fisher's exact statistic will be used, depending on the conditions. A *p* value <0.05 will be considered statistically significant, with a 95% CI.

Discussion

Extracorporeal anastomosis is the traditional technique for right hemicolectomy. The first description of intracorporeal mechanical ileo-colic anastomosis dates from the early 1990s [17]. It is noticeable that recent publications achieve better results with intracorporeal anastomosis, reporting percentages of AL below 3%. At present, however, there is no standardized anastomosis for right hemicolectomy, and intracorporeal and extracorporeal anastomosis are both used.

In the literature, observational studies show better results with intracorporeal anastomosis, despite its greater complexity and the effect of the learning curve. In our view, there are 3 factors that improve recovery and account for these good results: the absence of traction of the mesenteries because the specimen is not externalized, smaller suprapubic laparotomies, and the reinforcement of the anastomoses [18].

In conclusion, we believe that the positive results reported in the literature oblige us to determine whether intracorporeal mechanical side-to-side isoperistaltic anastomosis is the best option in right hemicolectomy. In this large multicenter, prospective, controlled study, we aim to strengthen the evidence to provide external validity for using intracorporeal anastomosis as a gold standard in right hemicolectomy.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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