Intracorporeal or Extracorporeal Ileocolic Anastomosis After Laparoscopic Right Colectomy

A Double-blinded Randomized Controlled Trial

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Objectives: The aim of the study was to determine whether there are clinically relevant differences in outcomes between laparoscopic right colectomy (LRC) with intracorporeal ileocolic anastomosis (IIA) and LRC with extracorporeal IA (EIA).

Background: IIA and EIA are 2 well-established techniques for restoration of bowel continuity after LRC. There are no high-quality studies demonstrating the superiority of one anastomotic technique over the other.

Methods: This is a double-blinded randomized controlled trial comparing the outcomes of LRC with IIA and LRC with EIA in patients with a benign or malignant right-sided colon neoplasm. Primary endpoint was length of hospital stay (LOS). This trial was registered with ClinicalTrials.gov, number NCT03045107.

Results: A total of 140 patients were randomized and analyzed. Median operative time was comparable in IIA versus EIA group {130 [interquartile range (IQR) 105–195] vs 130 (IQR 110–180) min; $P = 0.770$} and no intraoperative complications occurred. The quicker recovery of bowel function after IIA than EIA [gas: 2 (IQR 2–3) vs 3 (IQR 2–3) days, $P = 0.003$; stool: 4 (IQR 3–5) vs 4.5 (IQR 3–5) days, $P = 0.032$] was not reflected in any advantage in the primary endpoint: median LOS was similar in the 2 groups [6 (IQR 5–7) vs 6 (IQR 5–8) days; $P = 0.839$]. No significant differences were observed in the number of lymph nodes harvested, length of skin incision, 30-day morbidity (17.1% vs 15.7%, $P = 0.823$), reoperation rate, and readmission rate between the 2 groups.

Conclusions: LRC with IIA is associated with earlier recovery of postoperative bowel function than LRC with EIA; however, it does not reflect into a shorter LOS.

Keywords: anastomosis, extracorporeal, intracorporeal, laparoscopic right colectomy, randomized controlled trial

(*Ann Surg* 2019;270:762–767)

The first report on laparoscopic right colectomy (LRC) appeared in 1991.[1] Since then, several studies comparing laparoscopic and open RC (ORC) showed lower morbidity and mortality after LRC than ORC.[2]

Intracorporeal ileocolic anastomosis (IIA) and extracorporeal IA (EIA) are 2 well-established techniques for restoration of bowel continuity after LRC. Although there are no differences in oncologic principles (no touch technique, proximal vessel ligation, extent of lymphadenectomy), IIA has some potential advantages: reduced mesenteric traction, lower risk of ileum mesentery twisting while anastomosis construction, and shorter skin incision for the specimen extraction.[3]

Several retrospective studies have compared outcomes after LRC with IIA or EIA reporting controversial results: some showed earlier return of bowel function, lower morbidity, and shorter length of hospital stay (LOS) after IIA than EIA, whereas others did not find significant differences between the 2 techniques.[4–21] The rate of prolonged postoperative ileus does not seem to be affected by surgical technique.[21,22] The heterogeneity of the studies and the lack of randomization do not allow to clearly define possible clinical advantages of one technique over the other.[22–25]

The aim of this double-blinded randomized controlled trial (RCT) was to determine whether there are clinically relevant differences in outcomes between LRC with IIA and LRC with EIA.

METHODS

Patient Selection

This is a single-institution double-blind RCT comparing the outcomes in patients undergoing LRC with IIA or EIA between February 2017 and August 2018. All consecutive patients aged 18 years or older with a benign or malignant right-sided colon neoplasm were considered. Exclusion criteria were distant metastases, perioperative evidence of adjacent organs tumor invasion, emergent surgery, and scheduled synchronous intra-abdominal surgery. Patient characteristics, perioperative work-up, intraoperative results, and postoperative outcomes were recorded into a prospective database by an observer who was blinded to treatment. The protocol was approved by the ethical committee of our institution.

Randomization

All patients who provided written informed consent were randomly assigned in a 1:1 ratio to undergo either IIA or EIA according to a list of randomization numbers with treatment assignments used by an independent statistician. This list was computer generated and an Internet application allowed central randomization.

Blinding Process

Patients, care providers, staff collecting data, and those assessing the endpoints were all blinded to treatment allocation. Patients were blinded to the surgical procedure performed until the final assessment of the study endpoints. A big dressing covering all incisions was applied at the end of each surgical procedure. Patient's blinding was ensured by changing and keeping in place this dressing until discharge.

Because the blinding of the operating surgeons was not feasible, they were not involved in the data collection and outcome assessment. Physicians in charge of patients' management were not involved in the operating room and were blinded to the intervention.

The data were collected and analyzed by physicians who were not involved in the patient's management during the whole RCT.

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The authors report no conflicts of interest.
Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.annalsofsurgery.com).

ISSN: 0003-4932/19/27005-0762
DOI: 10.1097/SLA.0000000000003519

Surgical Technique

All surgical procedures were performed by 4 surgeons (M.Mo., M.D., A.A., M.Mi.) with extensive experience in laparoscopic and colorectal surgery: the overall case load of our unit was more than 2200 procedures and each surgeon had a personal experience of at least 50 LRCs with IIA before starting this RCT. Four trocars were used in all procedures: a 10-mm trocar (camera port) in left paraumbilical position, a 5- to 12-mm working trocar in the left upper quadrant, a 5-mm working trocar in suprapubic position, and a 5-mm working trocar in the right upper quadrant. A formal LRC was performed in all patients, regardless of the perioperative pathology of the colon neoplasm. The first steps (ileocolic vessels division, mesocolon dissection, and colon mobilization) of LRC with IIA or EIA were the same, following a medial to lateral approach: (1) ileocolic vessels identification and division after duodenum identification; (2) dissection starting at the origin of the ileocolic vessels, proceeding along the superior mesenteric vein in a cranial direction and ending at the origin of the Henle gastrocolic trunk from the superior mesenteric vein; division of the right colic vessels if present; (3) middle colic vessels identification by elevation of the transverse colon and division of the right branch of the middle colic vessels; (4) omentum division in a medial to lateral direction caudal to the right gastroepiploic vessels; (5) hepatic flexure mobilization and incision of lateral peritoneal attachments of the right colon to mobilize the colon medially.

- *LRC with EIA:* (1) exteriorization of terminal ileum, right colon, and proximal transverse colon for bowel division through a skin incision; (2) fashioning a handsewn or stapled IA, then the bowel is returned to the abdominal cavity; (3) after reinduction of pneumoperitoneum, the lack of EIA twists was checked and the mesenteric defect closed; (4) fascial defects and skin incisions closure. A big dressing covering all incisions was applied.
- *LRC with IIA*: (1) transection of terminal ileum and transverse colon with a laparoscopic stapler; (2) approximation of the antimesenteric side of colon and ileum stapled ends by an intracorporeal stay suture; (3) antimesenteric enterotomy and colotomy about 10 cm distal to the stapled ends of both colon and ileum; (4) fashioning a side-to-side anastomosis with a laparoscopic stapler; (5) enterotomy closure by a double-layer absorbable intracorporeal suture; (6) mesenteric defect closure; (7) specimen delivery through a skin incision; (8) fascial defects and skin incisions closure. A big dressing covering all incisions was applied, similar to that used for the EIA group.

Perioperative Management

Perioperative management was standardized for both groups. No perioperative mechanical bowel preparation was administered. Intraoperative anesthesia protocol included a targeted fluid therapy. The urinary catheter was removed on postoperative day (POD) 1. Pain management was based on tramadol in association with alizapride by continuous intravenous infusion through an elastomeric pump at a rate of 2 mL/h for 48 hours, and paracetamol 1000 mg iv up to 3 times per day during POD 1 and 2. Patients were mobilized on POD 1. Diet was resumed after the first flatus occurred. Patients were discharged after meeting the following criteria: absence of fever for more than 48 hours, satisfactory pain control with oral analgesics, adequate oral food intake, recovery of gastrointestinal functions, full mobilization, and acceptance of discharge by the patient in the absence of complications.

Study Outcomes

Primary endpoint was LOS, calculated as the number of days spent in the hospital between the end of the surgical procedure and discharge. Secondary outcomes included operative time, intraoperative complications, number of lymph nodes harvested, total length of skin incision, 30-day postoperative morbidity according to Clavien-Dindo classification,[26] return of bowel function, postoperative pain, reoperation rate, and hospital readmission.

Statistical Analyses

According to the existing literature[22] and our internal medical records, we considered a reduction of 1.5 days (with a standard deviation of 3 days) in the mean LOS clinically relevant. A sample size of 128 patients (64 per arm) was required to detect this difference, with alpha = 0.05 and power = 80%. Considering 10% of patients lost to follow-up, the total sample size was 140 patients. No interim analyses were planned. All analyses were performed on an intention-to-treat basis. Descriptive statistics for categorical variables were expressed as absolute/relative frequencies, whereas those for continuous covariates as median/IQR. Inferential statistics for associations has been performed by the Fisher exact test or Mann-Whitney one.

All *P* values were obtained by the 2-sided exact method, at the conventional 5% significance level. The statistical analyses were performed by using R 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria). This trial was registered with ClinicalTrials.gov, number NCT03045107.

RESULTS

A total of 145 patients were assessed for eligibility: 3 declined to participate and 2 did not meet inclusion criteria. A total of 140 patients were randomized: 70 in the IIA group and 70 in the EIA group (Fig. 1). Table 1 summarizes patient's characteristics.

Intraoperative Results

Median overall operative time and time to fashion the anastomosis were similar in IIA and EIA groups: 130 (IQR 105–195) versus 130 (IQR 110–180) minutes ($P = 0.770$), and 18 (15–25) versus 15 (15–20) minutes ($P = 0.335$). Median estimated blood loss was 50 (30–75) mL in the IIA group and 55 (35–100) mL in the EIA group ($P = 0.790$). No intraoperative complications occurred.

Conversion rate to open surgery was 0% in the IIA group and 8.6% in the EIA group ($P = 0.028$) (Table 2). The types of IA and the site of skin incision for the colon extraction are listed in Table 2. No significant differences were observed in the length of the skin incision used for the colon extraction.

Pathologic Results

Table 3 summarizes the pathologic findings.

Postoperative Results

A quicker recovery of bowel function was observed after IIA than EIA [gas: 2 (2–3) vs 3 (2–3) days, $P = 0.003$; stool: 4 (3–5) vs 4.5 (3–5) days, $P = 0.032$]. Resumption of solid diet occurred after 3 (3–5) days in the IIA group and 3.5 (3–5) days in the EIA group ($P = 0.294$). No significant differences were observed in the primary endpoint: 6 (5–7) days in the IIA group and 6 (5–8) days in the EIA group ($P = 0.839$). Pain assessment revealed a lower postoperative visual analogue scale (VAS) score in the IIA group, with a difference that was statistically significant on POD 3 ($P = 0.002$). Patients with a suprapubic Pfannenstiel incision reported a lower median VAS score on POD 3 than patients with a different incision (1 vs 2; $P = 0.008$).

Overall 30-day morbidity rates (17.1% vs 15.7%, $P = 0.823$) and the severity of complications were similar in the 2 groups (Table 4). Table 5, http://links.lww.com/SLA/B724 summarizes timing, type and outcomes of the treatment of the 8 patients who experienced a leak.

At 6-month clinical evaluation, an uncomplicated incisional hernia was detected in 1 (1.4%) IIA patient and 2 (2.9%) EIA

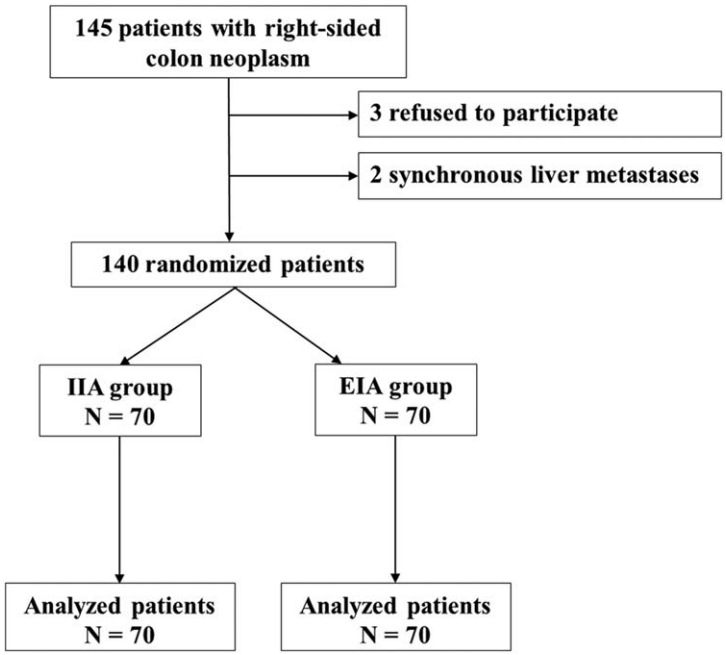

FIGURE 1. Flow chart of the study.

patients. No significant differences were observed in incisional hernia rates between patients with a suprapubic Pfannenstiel incision and patients with a different skin incision (0% vs 3%; $P = 0.645$).

DISCUSSION

Since the first report in 1991,[1] LRC has gained popularity for the surgical treatment of right-sided colon neoplasms, with better short-term results and similar oncologic outcomes when compared with ORC.[2] Several techniques for LRC have been described: (a) facilitated LRC[27]; (b) laparoscopic-assisted RC[28]; and (c) LRC with all steps performed laparoscopically.[29]

Even though LRC with IIA was first described in 1992, several factors, such as the need to perform hand-sewn sutures to close the enterotomies, prolonged operative time, and intraperitoneal spillage of bowel content, have limited its diffusion worldwide. A survey by Jamali et al[30] revealed that LRC with IIA is considered the most technically demanding laparoscopic colorectal procedure after Hartmann reversal and low anterior resection with total mesorectal excision.

TABLE 1. Preoperative Data

	IIA (N = 70)	EIA (N = 70)	*P*
Age, yr	70 (65–77)	72 (65–77)	0.498
Sex (male), N (%)	39 (55.7)	41 (58.6)	0.864
Body mass index, kg/m^2	24 (22.4–28.7)	25.2 (22.9–29.2)	0.282
ASA score, N (%)			0.425
1–2	37 (52.9)	30 (42.9)	
3–4	33 (47.1)	40 (57.1)	
Comorbidity, N (%)			
Cardiovascular	32 (45.7)	39 (55.7)	0.310
Pulmonary	7 (10)	9 (12.9)	0.790
Diabetes	13 (18.6)	10 (14.3)	0.648
Previous abdominal surgery, N (%)	29 (41.4)	34 (48.6)	0.497
Tumor site, N (%)			0.425
Cecum	39 (55.7)	41 (58.6)	
Ascending colon	18 (25.7)	12 (17.1)	
Hepatic flexure	13 (18.6)	17 (24.3)	

In the effort to identify potential advantages of IIA, several studies comparing perioperative outcomes after LRC with EIA or IIA have been published since 2009, reporting controversial results.[4–21] Some systematic reviews and meta-analyses showed that IIA might be associated with earlier bowel function recovery, lower morbidity rates, and shorter LOS.[22–25] The nonrandomized nature and the high heterogeneity of the studies, however, did not allow to draw any definitive conclusion, claiming for an RCT to better define the potential benefits of IIA.

Therefore, we designed an RCT to assess whether there are clinically relevant differences in outcomes between LRC with IIA and LRC with EIA. We observed a quicker recovery of bowel function after LCR with IIA. This finding might be related to several

TABLE 2. Intraoperative Results

	IIA (N = 70)	EIA (N = 70)	*P*
Operative time, min	130 (105–195)	130 (110–180)	0.770
Estimated blood loss, mL	50 (30–75)	55 (35–100)	0.790
Conversion to open surgery, N (%)		6 (8.6)	0.028
Locally advanced cancer	–	3	
Visceral obesity	–	2	
Adhesions	–	1	
Type of ileocolic anastomosis, N (%)			<0.001
Stapled	70 (100)	36 (51.4)	
Handsewn	0	34 (48.6)	<0.001
Side-to-side	70 (100)	47 (67.2)	
End-to-end	0	1 (1.4)	
End-to-side	0	22 (31.4)	
Site of skin incision, N (%)			
Transverse			
Right upper quadrant	17 (24.3)	29 (41.4)	0.048
Pfannenstiel incision	39 (55.7)	1 (1.4)	<0.001
Longitudinal			
Midline	11 (15.7)	20 (28.6)	0.103
Off-midline	3 (4.3)	20 (28.6)	<0.001
Length of skin incision, cm	7.5 (6–9)	8.0 (7–15)	0.291

TABLE 3. Pathology Results

	IIA (N = 70)	EIA (N = 70)	*P*
Histology, N (%)			0.185
Adenoma	16 (22.9)	9 (12.9)	
Cancer	54 (77.1)	61 (87.1)	
Length of specimen, cm	30 (25–35)	28.5 (25–35)	0.677
Tumor size, cm	4 (3–6.5)	4 (3.5–5.5)	0.862
Resection margins, cm			
Proximal	9 (6.5–11)	10 (6–18)	0.281
Distal	15 (10–20)	13 (8–16)	0.375
Number of lymph nodes harvested	17 (13–23)	16 (12–22)	0.539
Tumor staging, N (%)			0.380
1	5 (9.3)	7 (11.5)	
2	10 (18.5)	8 (13.1)	
3	39 (72.2)	46 (75.4)	

EIA, extracorporeal ileocolic anastomosis, IIA, intracorporeal ileocolic anastomosis.

factors, including reduced bowel manipulation and mesentery traction while performing the IIA, and lower postoperative pain with subsequent reduced use of pain medications.

LRC with IIA or EIA are both safe, with no significant differences in intraoperative blood loss, overall operative time, and anastomotic time. Postoperatively, there were no significant differences in overall morbidity rates (17.1% vs 15.7%): in particular, no intra-abdominal abscesses were detected suggesting that no significant intraperitoneal spillage occurred in the IIA group before the enterotomies were closed.

TABLE 4. Postoperative Results

	IIA (N = 70)	EIA (N = 70)	*P*
Postoperative complications, N (%)			0.823
Total	12 (17.1)	11 (15.7)	
Grade 1	1	2	
Grade 2	4	7	
Grade 3a			
Grade 3b	6	1	
Grade 4			
Grade 5	1*	1*	
Type of complications, N (%)			
Anastomotic leak	6 (8.6)	2 (2.9)	0.275
Bowel obstruction	–	2 (2.9)	
Prolonged postoperative ileus	1 (1.4)	1 (1.4)	1
Bleeding	1 (1.4)	1 (1.4)	
Pneumonia	2 (2.9)	3 (4.3)	1
Acute myocardial infarction	1 (1.4)	–	
Wound infection	1 (1.4)	2 (2.9)	1
VAS score			
POD 1	3 (2–5)	3 (2–5)	0.099
POD 2	2 (1–3)	2 (2–4)	0.180
POD 3	1 (0–2)	2 (2–3)	0.002
POD 4	0 (0–1)	1.5 (1–2)	0.084
POD 5	0 (0–1)	1 (0–1)	0.369
IV pain medication therapy duration, days	3 (2–5)	4 (3–6)	0.107
Bowel function, days			
Gas	2 (2.3)	3 (2–3)	0.003
Stool	4 (3–5)	4.5 (3–5)	0.032
Length of hospital stay, days	6 (5–7)	6 (5–8)	0.839
Readmission, N (%)	2 (2.9)	3 (4.3)	1
Acute intra-abdominal bleeding	–	–	
Anastomotic leak	1	–	
Bowel obstruction	1	2	
Pneumonia	–	1	

*1 Anastomotic leak.

Fashioning an IIA is one of the surgical steps that are rated highest in terms of difficulty, regardless of the surgeon's experience.[30] In the present study, to avoid the learning curve effect,[31] all LRCs were performed by 4 surgeons with extensive experience in laparoscopic and colorectal surgery. The anastomotic leak rate was, however, higher in the IIA group (8.6% vs 2.9%), even though this difference did not reach the statistical significance, confirming the technical challenge of IIA. Further large RCTs are warranted to define whether patients undergoing IIA are at higher risk of leak.

A further matter of debate is the way the IA is fashioned. While a Cochrane review[32] including studies published until 2010 reported significantly lower leak rates after stapled than hand-sewn anastomosis, recent studies seem to demonstrate that stapled anastomoses are associated with 2-fold increase in leak.[33,34] This evidence is, however, challenged by reporting bias regarding the type of stapler and the technique used, along with the surgeon's case volume.[35–37] In this RCT, all patients in the IIA group had a side-to-side isoperistaltic stapled IA, whereas a side-to-side isoperistaltic IA was constructed in 67% of patients in the EIA group (stapled in 51% of patients). A double-layer hand-sewn closure of the enterotomies was performed routinely in both groups.

No significant differences were detected in the primary endpoint: median LOS was 6 days in both groups. Median LOS observed in our RCT is 2 days longer than that reported in studies conducted in North America,[21] but consistent with those observed in Europe, reflecting substantial differences in health care systems.[10,15] It might be argued that our low adherence to the Enhanced Recovery After Surgery (ERAS) program[38] could have influenced the LOS in this RCT. Even though there is, however, evidence supporting ERAS, its implementation is still slow not only in Italy, but also in Europe[39,40] and North America.[41]

One potential advantage of IIA is the possibility to perform a shorter skin incision to extract the specimen in any quadrant of the abdomen that might be associated with lower postoperative morbidity and hernia rates than EIA. A recent systematic review and meta-analysis of the literature showed in patients undergoing laparoscopic colorectal resection that the risk of hernias is higher in case of midline than off-midline (transverse or suprapubic) incision.[42] This evidence is, however, limited by the poor quality of the studies. In this RCT, no significant differences were observed in pulmonary complications, superficial infections, and incisional hernias, even though a Pfannenstiel incision was more frequently used in the IIA group. We observed reduced postoperative pain in the IIA group in the first 3 PODs. This might reflect the fact that patients who had a suprapubic Pfannenstiel incision reported a significantly lower median VAS score than patients who had a longitudinal or a transverse incision in the right upper quadrant.

Both LRC with IIA and EIA are oncologically adequate. No differences in the number of lymph nodes harvested and in the distance of the tumor from the surgical margins were observed, reflecting the fact that the same oncologic principles are followed in both techniques, with proximal vessel ligation and lymphadenectomy, clear resection margins, ''no touch'' colon dissection and the use of a wound protector when the specimen is retrieved.

This study has some limitations. First, this is a single-institution RCT and, therefore, these results might not be generalized. Second, all LRCs were performed using a standard 2D imaging system. The last few years have witnessed continuous technological advances, including 3D[43] and near-infrared fluorescence angiography with indocyanine green (ICG)[44] as promising tools aiming at reducing the anastomotic leak rate in colorectal surgery. A challenging technique, as IIA, might particularly benefit from such technologies, thus reducing the leak rate.

CONCLUSIONS

IIA is associated with lower postoperative pain and earlier recovery of bowel function than EIA; however, it does not reflect into a shorter LOS. A word of caution concerning a possible higher risk of anastomotic leak after IIA is necessary.

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DISCUSSANTS

Fabrizio Michelassi (New York, NY):

Thank you for the privilege of commenting on this paper and for providing me with the manuscript well ahead of the meeting. The

authors, experts in the field, should be congratulated for executing a randomized controlled study so efficiently and enrolling 140 patients in 18 months. They randomized patients with intracorporeal versus extracorporeal anastomosis after a laparoscopic right hemicolectomy, and concluded that intracorporeal anastomosis is associated with lower postoperative pain and earlier recovery of postoperative bowel function than extracorporeal anastomosis. In their experience, it was, however, associated with a higher rate of anastomotic leakage.

I have a couple of questions:

First, there were 6 anastomotic dehiscences in the intracorporeal anastomotic group versus 2 in the extracorporeal anastomotic group. The difference is not statistically significant, but it may be clinically significant. A dehiscence rate of 8.6% seems high after a right hemicolectomy performed by very experienced surgeons. Following the end of your study, how have you modified your technique to address this concerning finding?

Second, the technique used by the authors calls for placing a 5- to 12-mm working trocar in the left upper quadrant. This lines up well with a side-to-side anastomosis between the transverse colon and the terminal ileum after a formal right hemicolectomy. Some of the lesions removed were benign and may have not needed a formal right hemicolectomy. How would you change the port placement to allow for a less radical right hemicolectomy, while still obtaining intestinal alignment for a subsequent side-to-side stapled anastomosis?

I would like to take this opportunity to thank the European Surgical Association for the privilege of the floor and honor of Honorary Membership.

Response From Marco E. Allaix (Torino, Italy):

Thank you for your questions. With regards to your first question, we could say that this difference was simply observed by chance, but we agree with you that it's a clinically relevant difference. A few years ago, a very nicely conducted survey showed that intracorporeal anastomosis and TME are the 2 most challenging colorectal procedures. During the last year, we have introduced the use of fluorescence with ICG to verify the bowel perfusion. We will see whether this will help in the near future because we currently lack well-designed studies, which clearly show that ICG per se reduces the risk of anastomotic leaks.

With regards to your second question, we used the same standardized technique for this study. We agree with you that benign lesions do not always need a formal right colectomy. On the contrary, we also know that there were very nice studies published a few years ago, which showed that 15% to 20% of adenomas actually harbor malignant cells, thus requiring a formal colectomy.

Yann Parc (Paris, France):

Thank you very much to the organizing committee for having given me the opportunity to review your manuscript. When you complete a randomized controlled study, your readers have great expectations. I was, however, very disappointed by your study. When you designed your study, you almost designed your unsuccessful results. You predicted a reduction of the length of stay at the hospital of 1.5 days. It's unrealistic, as hospitalization usually lasts 3, 5 or even 7 days. A simple change in surgical technique cannot have such an impact. Moreover, the size of the groups is too small to draw any relevant findings. You almost discovered a difference, in terms of anastomotic leakage. Your topic is how to perform the anastomosis. It was obvious, and it appears even more obvious with your results, that the anastomotic leak rate should be the primary end-point of such a study. Why haven't you taken the leak rate as the primary endpoint? It would have probably required much more patients, but it would have given a much stronger result.

Response From Marco E. Allaix (Torino, Italy):

Thank you very much. First of all, if you look at the literature, one of the theoretical benefits of intracorporeal anastomosis is the shorter hospital stay. The difference is, however, smaller than 1 day. So, we decided that having a 2-fold difference in the length of hospital stay, with respect to what has already been published in the literature, would have made the primary endpoint clinically relevant. Regarding the opportunity to choose the anastomotic leak rate as the primary endpoint of this trial, we acknowledge that the real leak rate of the intracorporeal anastomosis is actually unclear. As a consequence, and as stated in some recent meta-analyses, a sample size of an RCT cannot be calculated on the basis of the data currently available in the literature about the leak rate after intracorporeal anastomosis.

Eduardo M. Targarona (Barcelona, Spain):

Congratulations on a very nice trial. I believe that it's perfect because it's a double-blind trial. I have 3 questions. First, when did you randomize the patients? Was it before or at the beginning of the operation? Second, could the fact that you included intracorporeal mechanic anastomosis with extracorporeal manual anastomosis be considered as a bias? In fact, you should consider the same anastomotic method both inside and outside. Third, maintaining the double-blind protocol may be very difficult. Honestly, how many patients violated the blinding, or what was your experience with it?

Response From Marco E. Allaix (Torino, Italy):

Thank you very much for your questions. First, the randomization was done 1 day before the surgery, not during the operation. With regards to the type of anastomosis, of course, the intracorporeal anastomosis is a staple anastomosis. We believe it's something inherent to the technique, and therefore, we felt comfortable comparing these 2 different types of anastomoses.

With regards to the double blinding, it was challenging, but we did not encounter many difficulties. The operating surgeons were not involved in the data collection and outcome assessment; the physicians in charge of postoperative patient management were blinded to the intervention. Our patients knew that they would have received the standard operation according to the oncologic criteria, regardless of the type of anastomosis. Both patients and clinicians were unable to know the type of procedure performed, because the position of the trocars and the dressing used to cover the skin incisions were similar in both groups. No patient violated the blinding.

Peter Lodge (Leeds, United Kingdom):

I just have a brief question. I'm sorry if I missed it, but you were looking at a reduction in the length of stay using 2 surgical techniques. Did you standardize the anesthesia and analgesia for both groups, and did you use ERAS?

Response From Marco E. Allaix (Torino, Italy):

Thank you very much for your questions. All patients enrolled in the trial received exactly the same type of anesthesia intraoperatively and analgesia postoperatively. Regarding the ERAS, several published surveys from around the world show that adherence to ERAS is not as high as expected. We do follow some of the items, such as the intraoperative fluid restriction and early postoperative recovery. At the moment, we are, however, not following the perioperative ERAS items.