Rectal Cancer Surgery With or Without Bowel Preparation

The French Greccar III Multicenter Single-Blinded Randomized Trial

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Objective: To assess with a single-blinded, multicenter, randomized trial, the postoperative results in patients undergoing sphincter-saving rectal resection for cancer without preoperative mechanical bowel preparation (MBP).

Background: The collective evidence from literature strongly suggests that MBP, before elective colonic surgery, is of no benefit in terms of postoperative morbidity. Very few data and no randomized study are available for rectal surgery and preliminary results conclude toward the safety of rectal resection without MBP.

Methods: From October 2007 to January 2009, patients scheduled for elective rectal cancer sphincter-saving resection were randomized to receive preoperative MBP (ie, retrograde enema and oral laxatives) or not. Primary endpoint was the overall 30-day morbidity rate. Secondary endpoints included mortality rate, anastomotic leakage rate, major morbidity rate (Dindo III or more), degree of discomfort for the patient, and hospital stay.

Results: A total of 178 patients (103 men), including 89 in both groups (no-MBP and MBP groups), were included in the study. The overall and infectious morbidity rates were significantly higher in no-MBP versus MBP group, 44% versus 27%, $P = 0.018$, and 34% versus 16%, $P = 0.005$, respectively. Regarding both anastomotic leakage and major morbidity rates, there was no significant difference between no-MBP and MBP group: 19% versus 10% ($P = 0.09$) and 18% versus 11% ($P = 0.69$), respectively. Moderate or severe discomfort was reported by 40% of prepared patients. Mortality rate (1.1% vs 3.4%) and mean hospital stay (16 vs 14 days) did not differ significantly between both groups.

Conclusions: This first randomized trial demonstrated that rectal cancer surgery without MBP was associated with higher risk of overall and infectious morbidity rates without any significant increase of anastomotic leakage rate. Thus, it suggests continuing to perform MBP before elective rectal resection for cancer. This study is registered with ClinicalTrials.gov, number NCT00554892.

(*Ann Surg* 2010;252:863–868)

Although it is not yet a current clinical practice for colorectal surgeons, elective colonic resection without mechanical bowel preparation (MBP) (ie, including oral laxatives, retrograde enemas, and/or oral diet before surgery) is widely demonstrated in literature.[1–8] A recent updated meta-analysis of 14 randomized clinical trials concluded that any kind of MBP should be omitted before elective colonic surgery.[5] But, in contrast to previous studies,[6–8] the authors did not confirm the harmful effect of MBP in terms of septic complications, reporting similar anastomotic leakage rate between patients operated with and without MBP (4% vs 3.4%, $P = 0.46$). The only significant difference concerned was the rate of surgical site infections and favored the absence of MBP (15.7% after MBP vs 14.5%, $P = 0.02$).[5]

To date, these findings cannot be applied to rectal surgery because of insufficient published data. Indeed, rectal cancer location was considered as a noninclusion criterion in most of previous published trials. It is currently admitted that the risk of septic complications after rectal resection, as a result of the well-known risk factors, is higher than after colonic resection.[9,10] Thus, most of colorectal surgeons consider that no preparation regimen in rectal cancer surgery could represent an additive risk factor for postoperative morbidity.

However, because of these well-designed published data on colonic surgery without MBP, some colorectal surgeons begin to doubt this traditional dogma even in rectal surgery. Regarding rectal surgery without preoperative MBP, only 3 studies are available in the literature to date.[11–13] The Cochrane Group among 4700 patients included in all the 14 randomized studies on MBP and colorectal surgery, performed a subgroup analysis of patients with infraperitoneal colorectal anastomosis (119 patients with no MBP and 112 patients with MBP); it failed to show any benefit of MBP.[11] This subgroup analysis reported an anastomotic leakage rate of 6.6% in no-MBP patients versus 10% after MBP ($P = 0.21$). A second subgroup analysis performed among 449 patients undergoing low pelvic anastomosis, extracted from a randomized study including 1700 patients, was performed. In this subgroup analysis, in fact, only 48 patients presented a very low anastomosis with a temporary stoma, as it is the rule in rectal cancer surgery. In this analysis, the anastomotic leakage rate was similar between both no-MBP and MBP groups (6.6% vs 7.6%, $P = 0.71$).[12]

Only 1 study, conducted in our department, was specifically devoted to rectal surgery without MBP.[13] In this case-control study including 52 patients without MBP versus 60 with MBP, all undergoing sphincter-saving resection for rectal cancer, we observed that the anastomotic leakage rate was similar in both groups (15%) and that the overall morbidity rate was significantly lower in no-MBP versus MBP groups (31% vs 51%, $P = 0.036$).

Because, to date, a randomized study specifically devoted to the usefulness of MBP in rectal surgery is lacking, we performed a multicenter, single-blinded, randomized trial focusing on the postoperative results after sphincter-saving rectal resection for cancer.

PATIENTS AND METHODS

Patient Selection

Between October 2007 and January 2009, all patients with rectal cancer who presented to 8 participating national hospitals were screened for inclusion into the trial. The protocol was approved by

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ISSN: 0003-4932/10/25205-0863
DOI: 10.1097/SLA.0b013e3181fd8ea9

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the Comité de Protection des Personnes Ile-de France IV. Data management and statistical analyses were under the responsibility of the Unité de Recherche Clinique at Lariboisière Hospital. The trial was sponsored by the Direction de la Recherche Clinique at Assistance Publique-Hôpitaux de Paris (AP-HP) and mainly funded by a public grant from the Programme Hospitalier de Recherche Clinique. All patients provided written informed consent.

All the patients aged 18 years or older, with rectal cancer, (ie, within 15 cm from the anal verge) who underwent laparoscopic or open elective rectal resection with mesorectal excision and sphincter preservation, were eligible. Exclusion criteria were as follows: very low rectal tumors requiring abdominoperineal excision, metastases in the liver or lungs, T4 rectal cancer requiring extra-anatomical dissection, synchronous adenocarcinomas, and/or gastrointestinal disease (inflammatory bowel disease, familial polyposis) requiring extensive colonic surgery.

Patients were staged according to the TNM classification after endorectal ultrasound, abdominal-pelvic computed tomography scanning, and/or pelvic magnetic resonance imaging. Patients with advanced local disease (T3 and/or N1) received long-course preoperative radiotherapy or radiochemotherapy.

Randomization

Patients were randomly assigned to undergo rectal resection either with preoperative MBP or without MBP. All patients provided written informed consent. Randomization was performed centrally via an interactive voice randomization system. The treatment assignment was balanced with respect to 2 stratification variables: site of the primary tumor (upper part of the rectum vs mid and low parts) and type of surgical procedure (open vs laparoscopic surgery). The operating surgeon was blinded to the randomization process and the preparation status of all patients.

Bowel Preparation

All patients were admitted the day before surgery. Patients in the MBP group received bowel preparation including in combination oral laxatives and retrograde enemas. They were given senna solution (X-PREP sarget) (1 or 2 120-mg package of flavored powder diluted in a glass of water according to the cleanliness of the colon) 24 hours before the operation. For retrograde preparation, patients received 1 l of povidone-iodine enema on the evening before, and early in the morning, (at least 2 hours) before surgery.

After the preparation was taken (MBP patients), diet was confined to clear fluids all the day. Patients in the no-MBP group had no preoperative dietary restrictions up to midnight the day before operation. Fasting from midnight (ie, no clear fluids or carbohydrate) was used in all patients.

Perioperative prophylactic antibiotics with 500 mg of metronidazole and 1 g of ceftriaxone diluted in 125 mg of saline solution infused for 15 minutes were administered to all patients with and without MBP, intravenously at anesthetic induction and were continued every 2 hours during the surgical procedure.

Surgical Technique

In case of preoperative radiotherapy or radiochemotherapy, the operation was performed 6 to 8 weeks after the irradiation. The surgical procedure was performed through a midline laparotomy or with a total laparoscopic approach with only a 5-cm incision in the right iliac fossa for both specimen extraction and temporary ileostomy. Both techniques routinely involved high ligation of the inferior mesenteric vessels, complete mobilization of the splenic flexure, and partial or total mesorectal excision according to rectal cancer location. Rectal dissection was carried out 5 cm below the lower edge of the tumor in the upper third of the rectum and to the pelvic floor for mid and low rectal tumor with total mesorectal excision and nerve preservation. Reconstruction was either a conventional stapled colorectal anastomosis or a hand-sewn coloanal anastomosis. The doughnuts were always inspected for completeness. A temporary ileostomy was performed mainly for mid and low rectal tumors with low anastomosis. A colonic J pouch or a side-to-end anastomosis was performed, if possible, for very low anastomoses (ie, 5 cm or less from the anal verge). Anastomotic integrity was tested during operation by transanal instillation of fluid if surgeons had any intraoperative difficulty or subjective doubt after colorectal anastomosis. Aspirative pelvic drains were always used and placed behind the anastomosis. Ileostomy was closed 6 to 8 weeks after surgery if a water-soluble contrast enema control or CT scan did not show any anastomotic leakage.

Clinical Outcome

No patient was included in a fast-track surgery program. Both anesthesia procedures and postoperative care were conventional, and epidural anesthesia was not used. Postoperatively, concerning refeeding, patients were given liquids at day 1 and solid food from day 2. Concerning monitoring of intravenous perfusion during surgery, no standard protocol was used in this study. PCA must be suppressed. Opioids were given postoperatively for pain control.

The primary endpoint was the overall 30-day postoperative morbidity rate. Secondary endpoints included the postoperative mortality rate, the anastomotic leakage rate (asymptomatic or clinical), the infectious morbidity rate including abdominal (pelvic abscess, peritonitis, wound abscess, etc) and extra-abdominal (urinary tract infection, pneumopathy, etc) complications, the noninfectious complications rate, the major morbidity rate (ie, complications classified as Dindo III or more)[14] (Fig. 1), the hospital stay, the discomfort of the preparation for the patient, and the assessment of the colon cleansing by the operating surgeon.

Anastomotic leakage was defined as being asymptomatic if demonstrated by routine contrast enema before ileostomy closure and as clinical if symptoms related to leakage were noted (ie, gas, pus, or faecal discharge from the drain, peritonitis, discharge of pus per rectum). All clinical suspicion (ie, fever or abdominal pain) led to CT scan, which confirmed the diagnosis showing pelvic abcess or to a water-soluble contrast enema showing anastomotic dehiscence with leakage into the pelvic cavity. *Wound abscess* was defined as a wound requiring partial or complete opening for drainage of a purulent collection or erythema requiring initiation of antibiotic treatment.

Statistical Analysis

We calculated that a sample size of n = 90 in each group would ensure a power of at least 80% to detect a difference in the overall

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiologic interventions.
Grade II	Requiring pharmacological treatment – Blood transfusion.
Grade III	Requiring surgical, endoscopic or radiological intervention.
Grade IV	Life-threatening complication requiring intensive care unit management.
Grade V	Death of patient

FIGURE 1. Classification of surgical complications according to the Clavien-Dindo classification.

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morbidity rate corresponding to 50% in one group versus 30% in the second group using a 2-sided chi-square test with significance level fixed at 5%. Analysis was performed in all randomized patients (ie, intention to treat); in case of missing value of the morbidity, the status of the patient should be classified as presenting morbidity.

The primary endpoint and all secondary qualitative endpoints were tested by chi-square test. Durations of hospital stay were compared by log-rank test. A complementary analysis tested the possible heterogeneity of treatment effect size according to the tumor location (upper/mid-low part) and to the method (laparoscopy/laparotomy) using Cochran-Mantel-Haenszel test and Breslow-day test for homogeneity of the odds ratios. All tests were 2-sided with significance level fixed at 5%. We undertook all analyses with SAS software (version 9.2; from SAS Institute). This study is registered with ClinicalTrials.gov, number NCT00554892.

RESULTS

One hundred eighty-six patients were randomized. Seven patients were excluded for consent form missing (n = 5), refusal of surgical treatment (n = 1), and loss of follow-up (n = 1). One hundred seventy-eight patients were included and randomly assigned to the no-MBP group (n = 89) and the MBP group (n = 89). Demographic data of patients, tumor characteristics, and treatment are given in Table 1.

The overall 30-day mortality rate was similar between the 2 groups, 0% in the no-MBP group versus 1% (n = 1) in the MBP group.

The overall 30-day morbidity rate was significantly higher in patients without MBP compared with those with MBP, 44% (39/89) versus 27% (24/89), $P = 0.018$.

As shown in Table 2, infectious complications occurred significantly more frequently in the no-MBP group: 30 (34%) of 89 in the non-MBP group versus 14 (16%) of 89 in the MBP group ($P = 0.005$).

TABLE 1. Demographic and Clinical Characteristics of 178 Patients With or Without Mechanical Bowel Preparation Before Rectal Cancer Surgery

	MBP (n = 89)	no-MBP (n = 89)
Age (range), y	65 (57–73)	62 (54–71)
Sex (M/F) − ratio	56/33–1.7	46/43–1.0
BMI, kg/m^2	25.3 (23–27)	24.8 (22–27)
Tumor rectal location		
High	13	18
Mid/low	76 (85)	71 (80)
Preoperative radiotherapy	63 (71)	64 (72)
Laparoscopic rectal resection	73 (82)	74 (83)
Operative time*	260 (210–300)	268 (230–310)
Intraoperative complications	11 (12)	8 (9)
Blood transfusion	3 (3)	0
Type of anastomosis		
Stapled colorectal anastomosis	48 (54)	47 (53)
Hand-sewn coloanal anastomosis	41 (46)	42 (47)
Colonic pouch or side-to-end anastomosis	35 (39)	44 (49)
Temporary ileostomy	71 (80)	74 (83)
Pelvic drainage	85 (96)	88 (99)

Values are median unless indicated otherwise.
Values in parentheses are percentages unless indicated otherwise.
*Mean value.
BMI indicates body mass index; MBP, mechanical bowel preparation.

The noninfectious complications rate was similar between both groups: 16% in patients with no MBP versus 11% in MBP patients ($P = 0.42$). The major morbidity rate (ie, complications classified as Dindo III or more) was 18% in the no-MBP group versus 11% in the MBP group ($P = 0.69$). The rate of reoperation was not significantly different between patients without and with MBP: 12 (13%) 89 in the no-MBP versus 5 (6%) 89 in the MBP groups ($P = 0.63$). Main indications for reoperation in no-MBP versus MBP groups were clinical anastomotic leakage (3 vs 1), peritonitis (6 vs 2), pelvic abscess (2 vs 0), respectively. Other indications were wound dehiscence (n = 1), small bowel obstruction (n = 1), and acute leg ischemia (n = 1).

Regarding the infectious abdominal complications (Table 3), there was a trend toward more abdominal complications in no-MBP patients compared with those with MBP, 34 (38%) of 89 versus

TABLE 2. Postoperative Course After Rectal Cancer Surgery With and Without Preoperative Mechanical Bowel Preparation

	MBP (n = 89)	no-MBP (n = 89)	*P*
30-day overall morbidity	24 (27)	39 (44)	0.018
Mortality	1 (1)	0	
Infectious morbidity	14 (16)	30 (34)	0.005
Non infectious morbidity	11 (11)	14 (16)	0.42
Major morbidity (Dindo III or more)	10 (11)	16 (18)	0.69
Hospital stay (median range), d	11 (9–15)	12 (10–17)	0.15
6-month stoma closure, d	59 (97)	56 (92)	0.43

Values in parentheses are percentages unless indicated otherwise.
MBP indicates mechanical bowel preparation.

TABLE 3. Infectious and Noninfectious Complications After Rectal Cancer Surgery With and Without Preoperative Mechanical Bowel Preparation

	MBP (n = 89)	no-MBP (n = 89)
Infectious abdominal complications	15 (17)	34 (38)
Clinical anastomotic leakage	6 (7)	14 (16)
Isolated pelvic abscess	1 (1)	7 (8)
Wound abscess	3 (3)	1 (1)
Peristomial abscess	1 (1)	1 (1)
Urinary tract infection	4 (4)	11 (12)
Infectious extra abdominal complications	1 (1)	1 (1)
Pneumopathy	1 (1)	1 (1)
Non infectious abdominal complications	7 (8)	14 (16)
Small bowel obstruction	1 (1)	2 (2)
Urinary retention	3 (3)	10 (11)
Abdominal bleeding	0	1 (1)
Acute renal failure	3 (3)	1 (1)
Non infectious extra abdominal complications	5 (6)	1 (1)
Pulmonary embolism	1 (1)	0
Myocardial infarction	1 (1)	0
Phlebitis	2 (2)	0
Cardiac arrhythmia	1 (1)	1 (1)

Values in parentheses are percentages.
MBP indicates Mechanical bowel preparation.

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15 (17%) 89. The rate of wound abscess was not different between the 2 groups: 1% in the no-MBP group versus 3% in the MBP group. Although not significant, there was a 2-fold risk, in terms of noninfectious abdominal complications, for patients in the no-MBP group compared with the MBP group, 16% versus 8%, respectively.

The mean hospital stay was similar between the 2 groups: 16 ± 12 days in no-MBP patients versus 14 ± 9 days for patients with MBP, $P = 0.15$.

Table 4 details the 3-month anastomotic leakage rate. There was no significant difference in the overall anastomotic leakage rate (ie, including asymptomatic and clinical dehiscence) between the no-MBP and MBP groups, 19% (17 of 89) versus 10% (8 of 89), $P = 0.09$. Although not significant, clinical asymptomatic leakage was documented in 14 (16%) of 89 after no-MBP, which was higher than the incidence in the MBP group (7%), $P = 0.06$. Moreover, preparation seemed to influence the severity of pelvic sepsis because peritonitis, although not significant, was more frequent in no-MBP versus MBP patients [6 (7%) of 89 in the no-MBP group versus 2 (2%) 89 in the MBP group, $P = 0.15$, respectively].

Regarding the rate of 3-month stoma closure, there was no significant difference between the no-MBP and MBP groups, 92% versus 97%, $P = 0.43$, respectively (Table 2).

Regarding the preparation discomfort, 17% of patients complained about nausea or vomiting, 18% about abdominal pain, and 28% about abdominal bloating. These disorders let to stop preoperative MBP in 11% of cases. In practice, MBP was considered, by the patient, as excellent in 60% of cases, correct in 30% of cases, and poor in 10% of cases.

During the operation, surgeons were asked in a blinded fashion, to appreciate the cleansing of the colon. They rated the quality of the bowel preparation in the proximal colon and in the rectal stump as significantly worse in 11% of MBP patients compared with 31% with no-MBP ($P < 0.0001$) and in 5% of MBP patients compared with 22% in patients without MBP ($P < 0.0001$), respectively. Therefore, the necessity to perform intra operatively an additional rectal stump washout for bad preparation was not significantly different between no-MBP and MBP patients, 53% versus 48%, $P = 0.53$, respectively. Finally, there was no significant difference in terms of intraoperative faecal spillage, that is, 8% in no-MBP patients and 2% in MBP patients, $P = 0.16$.

We did not find any heterogeneity in the MBP group effect size between patients with tumor location in the upper or in the mid/low part of the rectum ($P = 0.91$) or between patients treated by laparoscopy or laparotomy ($P = 0.86$).

DISCUSSION

This study was designed to assess the value of preoperative MBP in patients undergoing sphincter-saving rectal resection for cancer. To our knowledge, this study is the first randomized trial focusing on MBP in patients undergoing rectal cancer surgery. We demonstrated that rectal resection without MBP was significantly associated with an increase of both the 30-day overall morbidity rate (44% vs 27%, $P = 0.01$) and the infectious complications rate (34% vs 16%, $P = 0.005$). Moreover, although not significant, there was, in no-MBP patients, a trend toward a 2-fold risk of anastomotic leakage (19% vs 10%) and peritonitis (7% vs 2%). This study suggests to continue to perform preoperative MBP before elective rectal resection for cancer.

Colorectal surgery without preoperative MBP (ie, no oral laxatives, retrograde enemas, or even oral diet) has been proposed in colorectal surgery (and in laparoscopy, minimal abdominal drainage, early diet, and ambulation) as a "more friendly approach" for the patient and in the aim to accelerate patient recovery.[15] No MBP is welcomed by both patients and nursing staff. Indeed, the preparation procedure is time-consuming and expensive, unpleasant to the patients, and sometimes dangerous, exposing the elderly population to the particular risk of fluid and electrolyte imbalance. Present data showed that, regarding the MBP discomfort, preparation was not so harmless and 20% of patients complained about nausea, abdominal pain, or abdominal bloating, leading to stop the preparation procedure in only 11% of cases.

Mechanical bowel preparation aims to provide a completely clean bowel to minimize the risk of intraoperative faecal spillage. This single-blinded randomized study (ie, the surgeon was blinded to the preparation status) confirmed that the cleansing of the colon was, according to the operating surgeon, defined as significantly worse in no-MBP patients. But, the necessity to use an additional rectal stump washout was not significantly different between no-MBP and MBP patients, 53% versus 48%, $P = 0.53$. Furthermore, in no MBP patients, the content of the bowel (bulky stools) can be manipulated into the bowel segment to be resected, enough to make the site of the anastomosis clear. Moreover, some studies showed that MBP, especially in case of "poor" preparation, caused a significant higher incidence of liquid bowel contents that led to peritoneal spillage and subsequent postoperative infectious complications.[16] A "poor prepared" colon is usually full of liquid feces that can be difficult to control, resulting in spillage into the abdominal cavity, which can cause significant contamination. Yu Yeh et al[17] demonstrated that one of the independent risk factors for anastomotic leakage was a poor colon preparation (OR, 2.58; 95% CI, 1.10-5.88). In our study, we did not show any difference in terms of intraoperative faecal spillage between the 2 groups, 8% in no-MBP versus 2% in MBP patients, $P = 0.16$.

Mechanical bowel preparation before colorectal surgery is a widely practiced treatment but many recent randomized studies and meta-analysis with high level of evidence clearly called into question this dogma underlining its detrimental effect by increasing the risk of postoperative infectious complications and/or anastomotic leakage rate.[1–8] A very recent updated meta-analysis, including 14 randomized trials with more than 4800 patients, confirmed the safety of elective colonic surgery without MBP but, in contrast with all previous published data, failed to demonstrate the negative effect of MBP in terms of anastomotic leakage, showing no statistical difference between the 2 groups, 3.4% after no-MBP versus 4% in MBP patients, $P = 0.46$.[5] In this latter meta-analysis, only the rate of surgical site infections was significantly lower in no-MBP versus MBP patients, 14.5% versus 15.7%, $P = 0.02$.

These findings, in colonic surgery, cannot be assessed for rectal surgery because of insufficient published data. Rectal tumor location was an exclusion criterion in most of published trials. Stratification, according to the level of anastomosis, was performed in few studies but the results were inconclusive, mainly because very few patients with infraperitoneal anastomosis were included in these studies.[2–4]

To date, most of the colorectal surgeons argue that the remaining feces in an unprepared colon could lead to a higher risk of

TABLE 4. Three-Month Anastomotic Leakage Rate in Patients Undergoing Rectal Cancer Surgery With or Without Preoperative Mechanical Bowel Preparation

	MBP (n = 89)	no-MBP (n = 89)	*P*
Overall anastomotic leakage	8 (11)	17 (19)	0.09
Asymptomatic leakage rate	2 (2)	3 (3)	–
Clinical anastomotic leakage rate	6 (7)	14 (16)	0.06
Peritonitis	2 (2)	6 (7)	0.15

Values in parentheses are percentages.
MBP indicates mechanical bowel preparation.

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postoperative septic complications, especially in case of infraperitoneal colorectal anastomosis and temporary stoma. Indeed, compared to colon surgery, anastomotic leakage remains the main complication after rectal resection with a widely reported incidence varying from 3% to 27% and significant clinical implications.[9,17,18] Such complication is well recognized as a cause of major morbidity with often long-term outcome and anorectal functional results affected but also as the major cause of postoperative death after rectal excision.[18,19] Moreover, it has been suggested that pelvic sepsis was associated with an increased risk of both local and distant recurrence and a decreased long-term survival.[20] For all these reasons, and mainly because of the use of a temporary stoma, the great majority of the surgeons continue to perform MBP before colorectal surgery.

Regarding rectal surgery without preoperative MBP, to date, 2 underpowered studies (ie, subgroup analysis)[11,12] are available and only 1 report was specifically devoted to rectal resection.[13] Both reviews[11,12] concluded that rectal resection with no-MBP could be performed safely without compromising the operative results. However, both subgroup analyses included a small number of patients in comparison with the number of patients undergoing colorectal surgery included in these randomized studies. The updated Cochrane systematic review compared a subgroup of 112 patients with MBP and 119 no-MBP patients and reported no significant difference after anterior resection in terms of anastomotic leakage (10% vs 6.6%, respectively).[11] Another subgroup analysis including 449 patients of a prior randomized multicenter trial, undergoing rectal surgery (anterior resection or Hartmann reversal), showed that MBP had no influence regarding the anastomotic leakage rate (6.6% without MBP versus 7.6% with MBP; $P = 0.71$).[12] Among them, only 48 patients underwent a diverting stoma for very low rectal tumors and there was no significant difference in terms of anastomotic leakage between no-MBP and MBP defunctioned patients (6.3 vs 7.2%, $P = 1.00$). In a control-case study reporting 52 patients with rectal resection for cancer with no-MBP, we demonstrated that although the incidence of anastomotic leakage was similar in the 2 groups (15%), the overall morbidity rate was significantly lower in no-MBP patients (31% vs 51% with MBP; $P = 0.036$).[13]

The present findings do not compare favorably with these previous published data and showed that no-MBP group was associated with increased overall and infectious morbidity. We do not have any specific reasons to explain this difference except that this randomized multicenter study provides stronger evidence than a case-control study and 2 subgroups analysis, to suggest not to extend the no-MBP regimen in rectal surgery. Moreover, in our previous study,[13] we noted that, although not significant, peritonitis seemed more frequent in no-MBP patients compared with MBP group (5.8% vs 1.6%; NS). In this study, we confirmed that although not significant, MBP seemed to influence the severity of pelvic sepsis. Indeed, despite defunctioning stoma, no-MBP patients had a 2-fold risk of major morbidity (complications defined as Dindo III or more) and peritonitis compared with MBP group, 18% versus 11% and 7% versus 2%, respectively.

CONCLUSION

This multicenter randomized study provides the first strong evidence data about rectal surgery for cancer without MBP. We showed that no-MBP patients presented significantly more overall postoperative complications (44% vs 27%) and more postoperative infectious complications (24% vs 16%). Moreover, although not significant, there was, in these latter patients, a trend toward a 2-fold risk of anastomotic leakage (19% vs 10%) and peritonitis (7% vs 2%).

Such data lead surgeons, in contrast to colonic surgery, to continue to perform preoperative MBP before elective rectal resection for cancer.

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DISCUSSION

ESA Paper 29: Rectal Cancer Surgery With or Without Bowel Preparation. The French Greccar III Multicenter Single-Blinded Randomized Trial

Y. Panis (Paris, France)

DISCUSSANTS

G. Carlson (Salford, UK)

This is a relatively small study compared with similar studies conducted in this setting and one important point to discuss is

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whether in fact there is still heterogeneity of the patient population. I think that most colorectal surgeons would conclude, in terms of rectal cancer surgery, that there are actually 2 populations of patients with rectal cancer. I would be particularly concerned about leaving patients with an unprepared bowel with an infraperitoneal anastomosis with a covering loop ileostomy as opposed to a patient with a high anterior resection who, in some ways, much more closely resembles the patients receiving colonic surgery. Do you think it is appropriate to use a protocol where almost 20% of your patients in each arm actually were high anterior resections rather than patients with infraperitoneal anastomoses and covering loop stomas, particularly given the fact that leak rates in your study are actually beginning to approach clinical significance. If you look at those patients who had infraperitoneal anastomoses, the difference may actually be clinically and statistically significant.

The second point I would ask you to comment on is the fact that you have not told as much about the perioperative care that these patients received. Because the mechanical bowel preparation group is more likely to be dehydrated, particularly if you did not provide preoperative fluid therapy, is it possible that your results may actually have been more significant than you have allowed for, given the fact that you may have seen some dehydration and hypovolemia in the mechanical bowel preparation group.

Third, you have not told us at all about the preoperative risk assessment for these 2 groups. In other words, how evenly matched were they for predicted postoperative complications? Can you assure us that your expected risks, for a septic complication for example, should have been similar when the 2 groups were compared?

In terms of your randomization technique, in your article, you mention interactive voice randomization. I do not know what that means. Do you mean you pick up a phone and say which group they will go into or is there something rather more subtle in terms of randomization? If there was a robust randomization process, how do you account for the fact that, there is a men-to-women ratio of 1.7:1 when the 2 groups were compared, suggesting that the sex ratio is not the same in the 2 groups, which is particularly important, given the fact that infective complications after colorectal surgery are well recognized to be more common in male patients.

Response From Y. Panis

Concerning the subgroup analysis between high and low rectal cancers, we made 2 subgroup analyses between open and laparoscopy and between high rectal cancer and low and mid rectal cancer. There are not a large number of patients with high rectal cancer but there is no heterogeneity and there is no difference. This is what my statistician tells me. It would be interesting to perform a new randomized study with a larger group of patients with stratification between high and low rectal cancers, but it is not easy to include patients with rectal cancer. We did this study, I think, in less than 18 months. It was very quick with almost 200 patients. It is not so easy to conduct larger studies. Perhaps that is the reason why the 14 randomized studies previously published did not include patients with rectal cancer. I think it is much easier with colonic surgery.

Concerning the randomization process, this was done by phone. The "Unité de Recherche Clinique" organized this study, and it provided the randomization process by phone. You say that there is a difference between males and females in the study between the 2 groups. I think the difference is not so large, but it was the randomization process that gave this result. As for your question regarding rehydration, we do not know. I have no answer to this question.

DISCUSSANTS

M. Braga (Milan, Italy)

There is no information in your article concerning perioperative care protocol. It is well known that intravenous administration load, postoperative analgesia technique, fasting period, and mobilization time after surgery are very important issues to prevent or reduce postoperative complications, especially infection. Did you standardize the perioperative protocol, and if yes, which perioperative protocol did you follow? My second question concerns your sample size calculation. I realize that your expected postoperative complication rate in the group receiving bowel preparation was 50%, according to your previous case-control study. In this trial, you found 27%. How do you explain this discrepancy? Do you think that it could bias the power calculation? Finally, concerning urinary complications, you found a 23% complication rate including both infection and retention in the no-bowel prep group versus 7% in the bowel prep group. How do you explain this difference?

Response From Y. Panis

For your first question, there is no fast track organization for all the patients. We had the same policy concerning the reduction of intravenous administration, for oral feeding at day 1 for all of the patients, but it was not a strict protocol. It is the same for preoperative immunonutrition. I think that we cannot give rules for 100% of the patients. Concerning the differences between our case-controlled study when we observed 30% and 50% and the randomized study when we observed 27% and 44%, the only answer I can give you is that it is a randomized study, and it is stronger than a case-controlled study. One cannot exclude the possibility in a case-controlled study that one might put easier patients in the good group and the more difficult patients in the bad group. It is the problem of the case-controlled study. I think that to avoid this bias, you must conduct a randomized study. Concerning urinary tract infection, it was 4% versus 12%, but there is no significant difference between the 2 groups.

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