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ORIGINAL ARTICLE

Safety, feasibility, and tolerance of early oral feeding after colorectal resection outside an enhanced recovery after surgery (ERAS) program

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Abstract
Introduction It is generally believed that resumption of feeding after colorectal resection is indicated only after recovery of bowel function. This study was designed to verify safety, feasibility, and tolerance of early oral postoperative feeding (EOF) outside an enhanced recovery after surgery (ERAS) program.
Materials and methods One hundred patient candidates to elective colorectal resection were prospectively enrolled in an EOF program. Feeding was started on postoperative day (POD) 1 with oral nutritional supplement (ONS). On POD 2, patients had normal food plus ONS to reach 1,000–1,200 kcal/day with progressive increase until 1,800–2,000 kcal/day. Results were compared with historical controls (n=100) in whom oral feeding was allowed only after full bowel function recovery. The ERAS program was not applied in both groups.
Results The EOF group had a better recovery of short half-life protein synthesis compared with the control group (P<0.001). Stool canalization occurred after a median of 3 days (range, 1–6 days) in the EOF group versus 5 days (range, 2–8 days) in the control group (P=0.001). The feeding protocol was completed in 89 patients within POD 5. Tolerance to resumption of feeding was similar in the two groups. The overall rate of postoperative complication was 22% in the EOF group vs. 27% in the control group (P=0.51). The median length of hospitalization was 9 days (range, 6–25 days) in the EOF group vs. 12 days (range, 6–31 days) in controls (P=0.01).
Conclusions EOF after colorectal operations is feasible and safe outside an ERAS program.

Keywords Colorectal surgery · Early feeding · Tolerance · Safety · Outcome · Fast track

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Introduction

Postoperative ileus after colorectal surgery remains a relevant clinical problem [1]. It was believed that maintaining gastric decompression could accelerate the recovery of bowel function [2]. Obviously, this delays the resumption of postoperative feeding. But, "nil by mouth" and prolonged fasting after major operations have been proven to be associated with longer convalescence and increased surgical morbidity [3, 4].

Recovery of bowel function after abdominal operations is controlled by several factors. Among the most important are the activity of the autonomic nervous system, the release of gastrointestinal hormones and inflammatory mediators and numerous tissue metabolic pathways. The type of anesthesia, drugs used for pain control, and severity of surgical trauma typically alters the action of one or more of these modifiers and therefore might have profound effects on intestinal motility [5, 6].

In the last years, a multimodal enhanced recovery program or "fast-track surgery" has been hypothesized as an efficacious way to preserve gut function [7, 8]. This program comprises several modalities and procedures [9] that also allow faster recovery of patients, improved outcome in terms of complications, and shorter length of hospital stay when compared with the traditional surgical treatment [10]. Nevertheless, this program is not yet largely applied even in countries that proposed it and is found difficult to implement worldwide [11–17]. Part of the reason may be due to the profound, radical, and numerous changes that surgeons and anesthetists should perform altogether to apply entirely the suggested program. This might contrast with the well-known establishment of surgical conservatism and the accepted wisdom of tradition. To overcome these limitations, a policy of one change at the time might convince the most hesitant physicians to change attitude and put into practice fast-track surgery even partially, which is indeed beneficial for the patients as previously demonstrated [15, 18–23].

The purpose of the study was to verify safety, feasibility, and tolerance of early oral feeding after major colorectal surgery in a surgical department where traditional perioperative patient care was routinely carried out.

Materials and methods

From January 2008 to December 2009, adult patients admitted at the Department of Surgery of the Milano-Bicocca University who required an elective colorectal resection were enrolled in a program of early postoperative oral feeding. Clinical data were recorded prospectively.

We excluded patients with the following conditions: undernutrition (weight loss >10% with respect to usual body weight), age >80 years, American Society of Anaesthetists (ASA) score >3, emergency operation, clinically relevant organ dysfunction as previously described [24], ongoing infections, immunosuppressive diseases, and refusal to sign a written informed consent.

The data obtained from studied patients were compared with historical controls that were selected to match age, gender, type of operation, and ASA score. These control patients were operated between 2005 and 2007.

The study was approved by the ethical committee of our hospital.

The program of early feeding after surgery is shown in details in Table 1. Briefly, feeding was started on POD 1 with oral nutritional supplement (700 kcal/day). On POD 2, patients could eat normal food plus oral nutritional supplement (ONS) to reach 1,000–1,200 kcal/day. From POD 3 until discharge, patients were allowed to eat solid food, and ONS were given only if subjects were unable to eat 1,800–2,000 kcal/day from normal food. As ONS, we used Ensure Plus, (Abbott SRL, Campoverde di Aprilia, Italy). The composition per 100 mL is: kcal, 150; carbohydrates, 20.2 g; proteins, 6.25 g; lipids, 4.92 g; and osmolarity, 563 mOsm/L.

A consultant dietician was available daily to support patient needs and calculate calorie intake. Patients were allowed to choose type of foodstuffs based on personal preference.

This protocol was discussed and approved by all senior staff surgeons and thus applied afterward without impediment. The policy was to convince the more reluctant ones to change only one behavior compared with traditional care. In particular, we asked to allow nasogastric tubes to be removed on POD 1 and to resume oral feeding at the same time. Moreover, we invited anesthetists to implement, as much as possible, the use of epidural analgesia.

Postoperative analgesia was obtained by epidural catheter (T9-T10) with continuous infusion of 0.2% ropivacaine plus sufentanil 0.75 μg/mL (4–6 mL/h). IV infusion of paracetamol (1 g) or ketoprofene (100 mg) was prescribed only in case of failure of pain control by epidural analgesia. The epidural catheter was removed on POD 3. In those patients without epidural catheter, we used patient-controlled analgesia (PCA) with morphine chloridrate for a maximum of 4 mg/h with a single bolus dose of 1 mg and free interval of 10 min. Additional

Table 1 Postoperative early oral feeding program

	POD 1 (700 kcal/day)	POD 2 (1,000–1,200 kcal/day)	From POD 3 until discharge (1,800–2,000 kcal/day)
Oral nutritional supplement	400 mL (600 kcal)	300 mL (450 kcal)	Given only if patients could not reached target calorie by foodstuff
Sugared clear fluids plus biscuits	100 kcal	100 kcal	300 kcal
Meat/fish	No	120 g	300 g
Pasta/rice	No	70 g	200 g
Vegetables/fruit	No	No	At patient's will

Total daily calories were reached with three to five meals

infusion of paracetamol (1 g) or ketoprofene (100 mg) was given in case of failure of pain control by PCA.

Side effects of early postoperative feeding were defined as previously described [25]. Persistent ileus was defined as absence of peristaltic bowel sounds after 72 h after surgery, and/or gastric residual of >200 mL/24 h.

Blood samples were collected at admission (baseline), at POD 3, and POD 6 for routine biochemical parameters and to evaluate protein metabolism by short-life proteins such as prealbumin and retinol-binding protein (RBP).

At the beginning of surgery, the anesthesiologist placed a nasogastric tube that was removed the morning (8 AM) after operation, unless the gastric residual was >300 mL.

Statistics

Simple descriptive statistics were calculated to describe the distribution of categorical or continuous variables. Two-sided *P* values were obtained from the Pearson Chi-square test for categorical variables and the Wilcoxon rank-sum test or Kruskal–Wallis test when appropriate for continuous variables and were considered significant if lower than the conventional 5% threshold.

Data are shown as mean±standard deviation, median (range), or number of cases (%).

Results

One hundred and seventy-seven patients with colorectal disease were admitted during the study period, but, due to exclusion criteria, 100 patients were enrolled.

By comparing the two study periods, the only variables that changed in the clinical management of the patients was the early removal of the nasogastric tube, the rate of epidural analgesia, and the timing of resumption of oral feeding (Table 2). From the items considered, it is quite clear that the enhanced recovery program was basically not applied during the two studied periods except for early removal of the nasogastric tube (NGT) and resumption of oral feeding and the greater use (58%) of epidural analgesia in the 2008–2009 period vs. the 2005–2007 period (31%; $P=0.001$). Based on this consideration, we could evaluate if early oral feeding was feasible, safe, and tolerated outside a fast-track program.

The two groups of patients were well matched for baseline and surgical characteristics (Table 3) and also for routine laboratory parameters (Table 4). In the EOF group, we observed a better recovery of short half-life protein synthesis as shown by the plasma levels of prealbumin and RBP on POD 6 when compared with the control group ($P<0.001$; Table 4).

Patient mobilization was obtained after a median of 2 days (range, 1–5 days) in the EOF group and after 3 days (range, 2–6 days) in controls ($P=0.02$).

Defecation occurred after a median of 3 days (range, 1–6 days) in the EOF group versus 5 days (range, 2–8 days) in the control group ($P=0.001$).

In the control group, NGT tube was removed after a median of 4 days (range, 3–8 days) after operation, and oral feeding was allowed after a median of 6 (range, 5–11) days.

Early oral feeding was well tolerated in 67/100 patients with no side effects. Thirty-three patients had some complication related to early feeding, but this was, in most of the cases, transient, and the feeding protocol was completed in 89/100 of the patients within the fifth postoperative day (Table 5). Eleven patients did not complete the EOF protocol for persistent vomiting ($n=5$), anastomotic dehiscence ($n=3$), persistent nausea ($n=2$), and intestinal obstruction ($n=1$). In those patients, oral feeding program was interrupted definitively. The overall rate of EOF tolerance was 95% (55/58) in patients with epidural analgesia and 81% (34/42) in patients with PCA ($P=0.005$).

The rate and type of side effects were similar in the two groups with the exception of vomiting (8% in the EOF group vs. 4% in controls) and the need of NGT re-insertion (4% in the EOF group vs. 1% in the control group). None of these events reached statistical significance.

The overall rate of postoperative complication was 22% (22/100) in the EOF group vs. 27% (27/100) in the control group ($P=0.51$). In the EOF group, four patients had more than one complication versus six patients in the control group. Complications in detail are described in Table 6. There was one death in each group.

The median length of hospitalization was 9 days (range, 6–25 days) in the EOF group vs. 12 days (range, 6–31 days) in controls ($P=0.01$).

Discussion

Despite the limitation of a non-randomized trial and a retrospective control group, the present results suggest that EOF is feasible, safe, and well tolerated in the vast majority of patients undergoing colorectal resection even not applying an ERAS program. This observation may stimulate also the most doubtful and traditional surgeons to allow immediate resumption of oral food intake without radical transformation of their established practice. Faster recovery of oral feeding seems associated with an earlier recovery of bowel function, and both of them appear correlated with the surgeon's confidence to discharge patients more rapidly.

The fast-track program has been described as a set of numerous procedures, originally promulgated as a bundle to be applied altogether to be effective [26, 27]. The numerous

Table 2 Fast-track items undertaken in the two studied periods as compared with recommendations

Procedure	Fast-track as described by others [9, 10, 15]	Period, 2005–2007	Period, 2008–2009
Pre-operative counseling	Recommended	Not applied	Same
Pre-medication	Not recommended	Diazepam 0.2 mg/kg	Same
Pre-operative fasting	Not recommended	From midnight	Same
Pre-operative carbohydrate loading	Recommended	None applied	Same
Bowel preparation	Not recommended	Applied in 87/100	Applied in 82/100
Active prevention of intra-operative hypothermia	Recommended	Warming blanket (75/100)	(72/100)
		Hot infusion line (21/100)	(19/100)
		None (4/100)	(9/100)
Analgesia	Mainly by epidural catheter and oral nonsteroidal anti-inflammatory drugs	Epidural (31/100)	(58/100)
		PCA (69/100)	(42/100)
Laparoscopic resection	Not routinely	Performed in 23/100	Performed in 27/100
Transverse incision	Recommended	All midline	Same
Surgical team	Trained	Not trained, four seniors and five residents	Not trained, five seniors and six residents
Surgical drainage	Not recommended	Placed in 83/100 patients and removed after canalization to stools	Same (78/100)
Mobilization	Forced and early	According to patient motivation	Same
Nasogastric tube	Not recommended	Removed when gastric outlet was <50 mL	Removed on POD 1 (8 AM) unless gastric outlet was >300 mL
Postoperative oral feeding	Early	After NGT removal and stool canalization	On POD1 (according to program in Table 1)
Postoperative IV infusion (saline or electrolyte solution)	Restricted	According to fluid and electrolyte balance to even in and out	Same
Postoperative laxative	Recommended	Not applied	Same
Removal of bladder catheter	Early	After patient full mobilization	Same
Discharge criteria	Adequate oral intake, gastrointestinal functions restored, pain controlled by oral analgesics and no signs of complications	Not fixed; according to reference surgeon	Same

and radical changes proposed to modify the traditional surgical care may be the reason for its difficult application and limited use in several countries and surgical departments [10–17]. More recently, it has been reported that similar beneficial results on surgical outcome can be also obtained, if only a part of this program is carried out [9, 15]. Therefore, it is not completely understood which component of this program is really essential for the proven quicker patient recovery and the reduced postoperative morbidity as consistently reported by several authors [18–23]. From a recent multivariate analysis, early oral feeding and intravenous fluid interruption after operation and specific trainee of the surgical staff seem the most important elements for success [14]. In our team, only one of the senior surgeons had a specific experience in the field of enteral feeding. Moreover, it was believed that early oral feeding to be safe and tolerated, postoperative ileus need to be fully recovered. Our data challenge this concept. In fact, from our results, it seems the opposite is true. Recovery of bowel function was faster in the group receiving EOF than in controls in whom nasogastric tubes were left in place until bowel canalization and gastric outlet was <50 mL. Furthermore, the rate and type of gastrointestinal side effects did not differ between groups with the exception of vomiting and need of gastric tube re-insertion in favor of the conventional care. Taking into consideration the drawback of a retrospective control group, our results are somehow consistent with a recent RCT by Han-Geurts and colleagues [28]. They reported that patients randomized to postoperative free diet resumption had a slightly higher rate of nasogastric tube re-insertion and vomiting when compared with subjects receiving a conventional care. In contrast to our data, they showed that tolerance rate to a solid diet was higher and faster in the experimental group,

Table 3 Baseline and surgical characteristics

	EOF (n=100)	Controls (n=100)	P value
Age, years	61.2±8.1	59.8±10.6	0.295
Sex (male, %)	57	61	0.670
Body mass index	25.3±4.7	26.0±5.2	0.319
ASA score			0.432
I	17	21	
II	53	55	
III	30	24	
Co-morbidities	37	34	0.772
Primary disease			0.472
Malignant/benign	84/16	79/21	
Type of surgery			0.755
Left colectomy	51	47	
Rectal resection	15	18	
Sigmoid resection	8	6	
Right colectomy	21	24	
Transverse resection	4	3	
Subtotal colectomy	1	2	
Protecting stoma	15	17	0.855
Operative blood loss, mL	210 (50–1,200)	260 (50–1,550)	0.164
Duration of operation, min	190 (120–310)	180 (110–290)	0.226

Data are shown as mean±standard deviation, median (range), or number of patients

but this event was independent from the resolution of postoperative ileus.

Several things may be done to accelerate the recovery of peristalsis such as reduce the use of opioids, minimize tissue trauma, implement minimally invasive surgical techniques, optimize fluid and electrolyte infusion and acid–base balance, maintain normothermia, stimulate mobilization, and reduce the use of nasogastric decompression [5, 6]. Epidural analgesia has been shown by some authors [29] as the most effective approach to accelerate recovery, even though results are conflicting [30–32]. In particular, Zutshi et al. [30] reported that epidural analgesia had no advantages over PCA

Table 4 Peri-operative biochemical parameters

Parameter	Baseline		POD 3		POD 6	
	EOF	Control	EOF	Control	EOF	Control
Hematocrit (%)	36.3±5.7	37.1±6.0	31.8±5.2	32.0±5.8	33.8±13.7	34.2±12.9
Glucose (mg/dL)	90.2±18.1	92.1±16.8	99.5±19.8	102.1±33.3	90.9±14.5	99.1±20.2
Creatinine (mg/dL)	1.0±0.1	1.1±0.2	0.9±0.2	1.0±0.2	0.9±0.2	0.9±0.3
Total bilirubin (mg/dL)	0.5±0.2	0.5±0.3	0.6±0.4	0.7±0.3	0.6±0.2	0.7±0.3
ALT (UI/L)	17.0±6.6	20.1±7.4	21.8±12.2	23.7±19.9	24.9±15.8	22.9±14.5
AST (UI/L)	16.9±9.5	18.5±8.5	25.7±22.8	22.2±13.4	36.7±36.1	31.7±26.1
γ-GT (UI/L)	24.8±34.1	22.9±26.0	34.7±41.1	32.5±30.7	42.4±31.2	35.9±28.2
Iron (μg/dL)	52.9±30.8	49.8±36.5	37.4±17.6	36.6±20.8	28.8±10.9	31.7±13.3
Cholesterol (mg/dL)	174.4±44.3	183.3±51.7	120.5±29.2	126.3±31.2	142.7±21.2	131.0±30.8
Triglycerides (mg/dL)	82.8±26.1	87.4±21.8	96.2±17.30	90.1±22.3	104.5±21.1	97.4±28.9
Lymphocytes (cells/mm^3)	1,616±585	1,670±632	1,595±945	1,485±712	1,505±771	1,437±672
RBP (mg/dL)	3.1±1.4	3.2±1.3	1.8±0.4	1.9±0.8	2.6±0.7*	2.0±0.5
Prealbumin (mg/dL)	17.8±7.5	18.2±6.6	10.1±2.7	10.3±3.4	14.5±3.1*	11.9±2.5
Albumin (g/dL)	3.9±0.5	4.0±0.8	3.1±0.4	3.2±0.5	3.5±1.1	3.3±0.9

Data are shown as mean±standard deviation

*P<0.001 vs. controls

Table 5 Side effects of the two type of postoperative feeding schemes

Protocol complication	EOF (n=100)	Controls (n=100)	P value
Nausea	11	10	0.998
Vomiting	8	4	0.375
Diarrhea	6	5	0.998
Abdominal distension	4	5	0.998
NGT re-insertion	4	1	0.369
EOF program completed (number of patients)	89/100	NA	

Data as shown as number of events or number of patients

NGT nasogastric tube, *NA* not applicable

if patients were on a fast-track care, and Marret et al. [31], in their meta-analysis, concluded that epidural anesthesia allowed a faster recovery of ileus but did not affect the postoperative incidence of nausea and vomiting, resumption of oral feeding, and length of hospitalization. This review also suggested that, rather than the analgesic technique, it was an ERAS program that improved postoperative recovery. Our data suggest that, outside an ERAS program, the rate of EOF tolerance was significantly higher in the patients treated with epidural analgesia compared with PCA. This observation partially confirms that this type of analgesia may be a key factor but probably not the only one to accelerate patient recovery of bowel function, mobility, and early oral feeding when fast-track care is not applied. Indeed, the rate of tolerance of oral feeding was acceptable (81%) even in those patients receiving PCA. This rate is comparable with other experiences in the pre-ERAS period [33, 34] and implies that epidural analgesia may not be the only measure that facilitates tolerance to oral feeding after colorectal operations.

The present data show a trend toward an improved surgical morbidity in the group treated with EOF when compared with conventional care but without reaching significance. Notably, the rate of anastomotic leak was similar suggesting that EOF and a faster passage of stool do not jeopardize the healing of intestinal sutures as shown by others [28]. Furthermore, we observed a 50% reduction in the pneumonia rate in subjects receiving EOF. This may be attributed to the early removal of the nasogastric tube [35].

The lack of statistical significance may be due to the limitation of the comparison of this treatment with historical controls or more probably to the fact that we did not apply the vast majority of the actions suggested by the ERAS program. Hence, we consider the present experience as the beginning to develop a more efficient surgical care with the progressive application of the ERAS program. We chose the prudent policy of one step at the time instead of the proposing the whole ERAS program at once. This strategy might be more appropriate to convince the more skeptical to modify attitudes. Once this change has been proven feasible and safe, with reliable data, other modalities may be introduced easily until reaching the entire bundle. In fact, numerous randomized trials and meta-analysis [9, 10, 16–23] clearly showed that the methodical implementation of fast-track surgery is a key intervention to significantly reduce postoperative complication rate and length of hospitalization.

We observed that patients receiving EOF had a more efficient protein synthesis as shown by the higher, short half-life protein plasma levels on postoperative day 6. An improved protein synthesis is essential for most metabolic pathways, wound healing, and immune response. The near-normalization of prealbumin and RBP levels after 6 days from surgery may be attributed to the type of oral nutrition. In fact, we chose to give ONS in the first days because these may have a more favorable ratio between volume taken and calorie/protein intake when compared with foodstuff.

It is difficult to speculate on the causes related to a shorter hospitalization in the EOF group. But, since the our surgical team was the same over the two study periods, the discharge criteria not fixed, and the overall rate of postoperative complications similar, the most probable reason for shorter hospital stay observed in the treated group may be attributed to the attitude and confidence of surgeons to discharge patients earlier because of faster mobilization, recovery of bowel function, and oral feeding tolerance.

Conclusions

The present data suggest that early feeding after surgery is safe and feasible also outside an ERAS program. This might convince surgeons devoted to a more traditional and

Table 6 Details of postoperative morbidity

Type of complications	EOF (n=100)	Controls (n=100)
Wound infection	10	12
Pneumonia	4	8
Wound dehiscence	2	3
Anastomotic leak	4	5
Deep organ space collection	2	3
Persistent ileus	2	4
Intestinal obstruction	1	1
Bleeding	3	2
Sepsis	1	1
Total	29*	37

Data shown as number of events

*P=0.294 vs. controls

conservative surgical care that limited changes in daily practice are possible without jeopardizing patient outcome. This policy of one step at the time may, in the future, lead to a wider application and acceptance of a fast-track program in colorectal surgery.

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