

# Effect of early oral feeding on gastrointestinal motility in patients undergoing colorectal resection: a meta-analysis of randomized clinical trials

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**Background:** The use of early oral feeding (EOF) to enhance the recovery of gastrointestinal (GI) motility after elective colorectal cancer surgery remains controversial. There was no updated meta-analysis to determine the efficacy and safety of this invention.

**Methods:** Randomized controlled trials (RCTs) were identified from PubMed, Embase, and the Cochrance Central Register of Controlled Trials (CENTRAL). Eleven RCTs (1,216 participants) were included in our meta-analysis.

**Results:** The EOF was associated with a shorter time of first flatus (MD =-0.58, 95% CI: -0.70 to -0.47, P<0.00001,  $I^2 = 19\%$ ), shorter first defecation (MD =-0.79, 95% CI: -1.00 to -0.59, P<0.00001,  $I^2 = 0\%$ ), and reduced length of hospital stay (MD =-1.48, 95% CI: -2.11 to -0.85,  $I^2 = 78\%$ ) compared to conventional oral feeding (COF). There was no significant difference between the EOF and COF group in the incidence of nausea, vomiting, nasogastric tube (NGT) reinsertion, the risk of wound infection, and the occurrence of pneumonia and anastomotic dehiscence. The risk of total postoperative complications was much lower in the EOF group than the COF group [relative risk (RR) 0.59, 95% CI: 0.48 to 0.73,  $I^2 = 46\%$ , P<0.00001].

**Conclusions:** Our findings suggest that EOF is appropriate for patients after elective colorectal cancer surgery and it is good for the recovery of GI motility.

Keywords: Early oral feeding (EOF); conventional oral feeding (COF); gastrointestinal motility

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Introduction

Colorectal cancer (CRC) has been a serious threat to human health and high mortality rate in the world (1). Surgery is currently the first-line treatment, however CRC surgery is a relatively big trauma to patients. There are still two major issues for postoperative treatment: how to improve the gastrointestinal (GI) function while improving the wound healing, and how to offer enough and efficient nutrition to patients to improve recovery from surgery. The commonly supportive treatment is nutrition feeding after the resumption of bowel sounds and first flatus or defecation. However, the time of feeding and the feeding path remains controversial. The conventional oral feeding (COF) is gradually introduced following the first bowel sounds and flatus or defecation. This strategy is mainly based on the concern that early oral feeding (EOF) may increase anastomotic leakage and prolonged postoperative ileus (2,3). However, this practice has been challenged

by findings from several GI physiologic studies stating that the optimal nutritional status and maintenance of GI function significantly contribute to wound healing (4,5). These findings show that EOF will lead to postoperative ileus as a paralysis of the entire bowel with the complete absence of any functional contractile activity is misleading. Postoperative ileus is usually transient and clinically not obvious. In actuality, oral feeding within 24 hours after colorectal surgery is tolerated, and the feed is absorbed (6-9). Although EOF might be a promising one, whether early or later oral feeding benefit patients still remains unsure. Enteral nutrition includes oral and enteral tubes. Feeding through enteral tubes could lead to various complications, including aspiration pneumonia, discomfort, tube occlusion, tube malposition, and epistaxis, which may affect the recovery of postoperative GI function. Although it is a general opinion that oral feeding is superior to feeding via other paths, the benefits and adverse effects of oral feeding has not been fully evaluated. There are increasingly more reports of randomized controlled trials (RCTs) on nutritional support after CRC surgery. There are previous meta-analyses combined studies of oral feeding and transcatheter feeding or upper GI track operation. The current meta-analysis focuses on the benefits and adverse effects of EOF and COF on the recovery of GI function.

#### Methods

The present meta-analysis was carried out using a protocol designed according to the Cochrane Handbook recommendations; it was performed in consistency with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (10).

### Data sources and search strategy

We searched PubMed, the Cochrane Database of Systematic Reviews (Cochrane Reviews), and EMBASE for appropriate RCTs published between January 1966 and October 2017. The full PubMed search strategy is presented as follows: ((early OR immediate) AND (oral OR enteral) AND (feed OR nutrition OR diet)) AND ((Colorect, rect, sigmoid, bowel, intestine, Colorectal Neoplasms, Neoplasms, Colorectal, or Neoplasm, Colorectal or Cancers, Colorectal)) AND ((Resection OR surgery OR operation OR Laparotomy OR laparoscopy or laparoscope)) AND ((Colonic Diseases OR surgery)) AND ((Gastrointestinal Motilities or Motilities, Gastrointestinal or Motility, Gastrointestinal or Intestinal Motility or Intestinal Motilities or Motilities, Intestinal or Motility, Intestinal)) AND ((randomized controlled trial or random or human)). The search strategy was designed to identify RCTs of EOF therapy compared to the COF in patients that underwent colorectal surgery. There were no language restrictions. References of retrieved studies and identified reviews were manually searched.

#### Study selection

Titles and abstracts of records obtained from searches were first independently examined by two well trained researchers (Z Jiang and QC Chen). Following the initial abstract assessment, the full-text of all identified studies was acquired. Eligible studies were RCTs that met the following criteria: (I) population: patients underwent elective CRC surgery; (II) experimental intervention: administration of EOF program, without tube feeding; (III) comparison intervention: conventional (traditional) oral feeding; and (IV) outcomes: primary outcomes include time to first bowel sounds, first flatus, defecation, and length of hospital stay. Secondary outcomes include nausea and vomiting and nasogastric tube reinsertion and complications (wound infection, pneumonia, anastomotic dehiscence and postoperative total complications). We defined EOF as any oral caloric intake commencing within 24 h postoperatively. COF was defined as withholding oral intake until passage of flatus or bowel movement or longer than 24 h postoperatively. To be included, a study should have reported at least one of the relevant outcome measures listed above. Studies were excluded according to the following exclusion criteria: tube feeding, emergency surgery, parenteral nutrition, use of immune-enhancing feeding products fast-track programs, including other interventions that might influence postoperative GI motility except EOF, inability to identify whether feeding was given within 24 h, or no data available for meta-analysis. Two investigators (Z Jiang and QC Chen) independently assessed studies for inclusion, and any disagreements between the two reviewers were resolved by consensus or the involvement of another author (LX Cao).

#### Data extraction and study characteristics

Two authors (Z Jiang and QC Chen) independently extracted data from studies and entered them into a predefined database. Any discrepancies were identified and resolved through discussion with a third author (LX Cao)

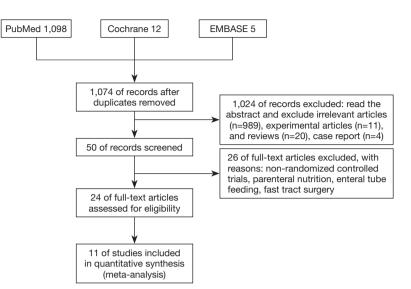


Figure 1 A flow-chart of study selection.

if necessary. Extracted information from each eligible study included: (I) study bibliographic information including the name of the first author, year of publication, and number of patients in each group; (II) patient information including age, gender; (III) EOF detailed protocol and control interventions; and (IV) outcome measurements. The outcomes were time to first bowel sounds, flatus, defecation, length of hospital stays and all complications. If data on the postoperative outcomes were absent or incomplete, the corresponding author of the study was contacted to request for the missing data. The data extraction followed the intention-to-treat basis whenever possible.

#### Assessment of quality of the included studies

Two authors (Z Jiang and QC Chen) independently assessed the methodological quality of the included studies by using the Cochrane approach (11,12). Each trial was judged for low, unclear, or high risk of bias. The quality of the evidence for each outcome was evaluated with the grading of recommendations assessment, development, and evaluation (GRADE) (11-13). Disagreement was resolved through consensus and deep discussion.

#### Data synthesis and analysis

Treatment effects for dichotomous outcomes were measured with relative risk (RR), and for continuous outcome measures were measured with weighted mean difference (WMD). Pooled estimates were presented with 95% CI. Heterogeneity was explored by the Cochran Q statistic and characterized with  $I^2$ . A fixed-effect model was used for meta-analysis in the absence of significant heterogeneity, defined as a P value >0.10 and  $I^2$  <50%. In case of significant heterogeneity, we employed the random-effects model; the exception was if few trials dominated the available evidence or if small-trial bias was statistically significant (14,15). For all other comparisons, a P value <0.05 was considered statistically significant, and all tests were two-sided. Data analysis was performed with Review Manager (RevMan, Version 5.3. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014).

#### **Results**

#### Study characteristics

The initial search of electronic databases identified 1,074 published studies (*Figure 1*). After applying the study exclusion criteria, 11 RCTs (1,216 patients) (16-26) were included in the analysis; there was a total of 611 patients in the EOF group and 605 in the COF group. The main characteristics of the 11 trials are shown in *Tables 1,2*. The results of risk of bias are shown in *Figure 2*. Eight of the 11 included studies detailed the methods of randomization used (17-22,25,26), and two provided inadequate information on randomization methods (23,24). Six studies described the blinding methods used: blinding numbers and blinding of the study assessors (17,18,20,21,25,26). We categorized

Table 1 Chamastanistics of non-domin	ad alinical suisle of ansau	al narterision aftern acloneetal	surgery included in the meta-analysis
Table I Characteristics of randomiz	ed chilical trials of enters	al nutrition after colorectal	surgery included in the meta-analysis

Author			nple size Age			Randomization	Main outcomes	Type of
Author	Dala	EOF	COF	EOF	COF	Randomization	Main outcomes	surgery
Vang D (16)	2014	43	45	60.4±6.5	60.3±4.9	Random number table	Duration of postoperative fever; interval to flatus; hospital stay; medical cost; complication morbidity	LS
Zhou T (17)	2006	161	155	55.3±16.7	57.1±19.8	Random number table	Time to first flatus; defecation; hospital stay; complication	OS
da Fonseca LM (18)	2011	24	26	57.4±16.3	51.7±13.3	Patients were randomly assigned to groups by a computer program	Time to first flatus; defecation; hospital stay; tolerance of solid diet; complication	LS
Vang ZH (19)	2013	24	24	56.3±11.5	54.7±12.5	Random number table	Time to first flatus; hospital stay; complication; hospital cost; complication	LS
Dag A (20)	2011	99	100	62±12.33	8 61±15.82	A computer-generated list immediately after surgery by an independent computer consultant	Time to first flatus; hospital stay; complication; intestinal movements; time to defecation	LS
El Nakeeb A (21)	2009	60	60	52.3±12.5	56.3±11.6	Randomization was achieved using sealed envelopes	Hospital stay; complications; times to first passage of flatus; time to first stool; vomiting	OS
Feo CV (22)	2004	50	50	67.6±10.2	67.6±10.4	Patients were assigned by means of a computerized randomization list	Bowel movement; hospital stay; nausea and vomiting; complications	OS
Hartsell PA (23)	1997	29	29	N/A	N/A	Patients were prospectively randomized	Hospital stay; complications; nausea and vomiting	OS
Lobato Dias Consoil M (24)	2010	14	15	47.4±16.7	54.5±10.1	Patients were randomized to either traditional care or the early fed group	hospital stay; complications; first flatus	LS & OS
Stewart BT (25)	1998	40	40	N/A	N/A	Pre-operatively the patients were randomly assigned according to a computer number generator to one of two groups	Passed flatus; bowel sounds; hospital stay; complications; rate of vomiting	OS
Han-Geurts IJ (26)	2007	67	61	N/A	N/A	Randomization was according to a computer- generated list with blocked sequences, and was carried out by telephone call in the operating theatre before surgery	hospital stay; complications;	OS

N/A, not available; LS, laparoscopy; OS, open surgery.

two studies as of unclear risk bias based on the assessment of reporting bias (19,25). All of the included studies had a high risk of performance bias because the experimental and control interventions could not be blindly implemented.

#### Primary outcomes

Time to first flatus was reported in six studies incorporated after screening. Three of the 11 studies did not report the

Trial	Protocol	Duration of observation
Wang D (16)	Water POD 1, gradually increase fluid diet to semiliquid diet; POD 2 in take TPF-FOS	POD 1 to POD 7
Zhou T (17)	Water immediately, gradually to a liquid fiberless diet POD 1, and a semi-liquid fiber diet POD 3	Hospital discharge
da Fonseca LM (18)	Liquid diet (approximately 500 cm <sup>3</sup> ) on POD 1, and regular diet within the next 24 h, as tolerated and at their discretion	Hospital discharge (POD 7)
Wang ZH (19)	Water POD 1, gradually increase fluid diet to semiliquid diet; POD 2 in take TPF-FOS	Until discharge (tolerated solid diet and normal defecation)
Dag A (20)	Fluid diet approximately 12 h after the operation, gradually increased to a solid diet as tolerated	During hospital stay
El Nakeeb A (21)	Began fluids on POD 1 and advanced to a regular diet within the next 24–48 h when tolerated	During hospital stay
Feo CV (22)	Drink the day after the operation, eat a soft diet the following day regardless of the passage of flatus, and then advanced to solid food as tolerated	Until on the day of discharge
Hartsell PA (23)	Began a full liquid diet on POD 1	During hospital stay
Lobato Dias Consoi M (24)	I 500 mL of restricted fluid were received on POD 1, and a free diet was received immediately if no nausea or vomiting was observed	Until hospital discharge
Stewart BT (25)	Free fluids from 4 h after the surgery and progressed to a solid diet from POD 1 at their own discretion	Until hospital discharge
Han-Geurts IJ (26)	Resumed an oral diet on any day after surgery	Until hospital discharge
POD postoporativo	day: TPE-EOS, enteral nutritional suspension	

Table 2 Early feeding protocol and risk of bias of the included studies

POD, postoperative day; TPF-FOS, enteral nutritional suspension.

mean or SD for this outcome; authors were contacted for additional information but with none responding. Based on the reported data, time to first flatus was significantly shorter in the EOF group (WMD –0.58 days; 95% CI: –0.70 to –0.47 days; P<0.00001, from a fixed effects model), with significant heterogeneity across trials ( $\chi^2$  =4.97, P=0.29, I<sup>2</sup> =19%) compared to the COF group (*Figure 3A*).

According to data from four trials, time to first defecation was reduced in the EOF group (WMD –0.79 days; 95% CI: –1.00 to –0.59 days; P<0.00001, from a fixed effects model) with heterogeneity across trials ( $\chi^2$  =1.28, P=0.53, I<sup>2</sup> =0%) compared to the COF group (*Figure 3B*).

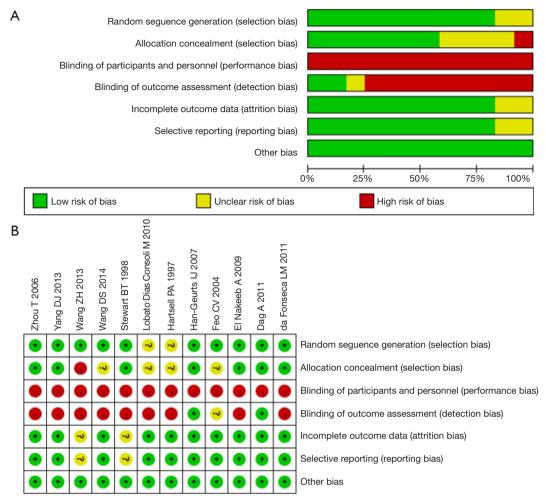
Length of hospital stay was also assessed in all of the included studies. Three of the trials did not report the mean or SD for length of hospital stay; authors were contacted for additional information but did not respond. Thus, the analysis for length of hospital stay was based on eight trials. Compared with the COF group, hospital stay was significantly reduced in the EOF group (WMD –1.48 days; 95% CI: –2.11 to –0.85 days; P<0.00001, from a random effects model), with some evidence of heterogeneity

between trials ( $\chi^2$  =31.22, P<0.0001, I<sup>2</sup> =78%) (*Figure 3C*).

#### Secondary outcomes

Nausea and vomiting were reported in six studies. EOF tended to be associated with a higher risk of nausea and vomiting compared to COF, although the difference was statistically non-significant (RR 1.28; 95% CI: 0.94 to 1.73; P=0.12). According to data from five studies, the difference in NGT reinsertion was not statistically significant between the EOF and COF groups (RR 1.31; 95% CI: 0.75 to 2.31; P=0.35) with no heterogeneity ( $\chi^2$  =0.81, P=0.85, I<sup>2</sup> =0%) (*Figure 4*).

Postoperative complications were analyzed in the included studies. Wound infection was reported in 7 studies, pneumonia in 7 studies, and anastomotic dehiscence in 8 studies. There were 10 total studies reported with postoperative complications. There were no statistically significant differences between the EOF and the COF groups in the risk of wound infection, pneumonia, and anastomotic dehiscence (respectively RR 0.74; 95%



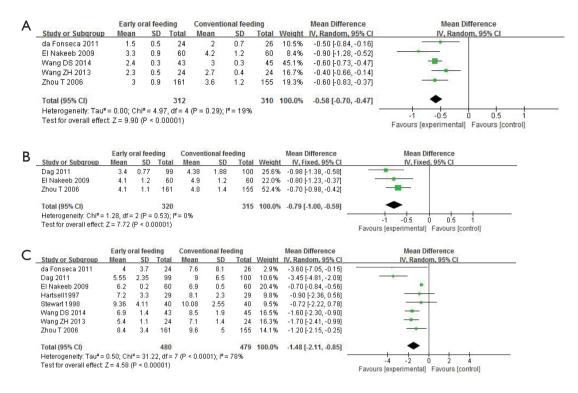
**Figure 2** Risk of bias analysis. (A) Risk of bias graph: review authors' judgments about each risk of bias item presented as percentage across all included studies. Green circles indicate low risk of bias, yellow circles indicate unclear risk of bias, and red circles indicate high risk of bias. (B) Risk of bias summary: review authors' judgments about each risk of bias item for each included study. Green circles indicate low risk of bias, and red circles indicate low risk of bias, yellow circles indicate high risk of bias.

CI: 0.42 to 1.29; P=0.29; RR 0.55; 95% CI: 0.29 to 1.02; P=0.06; RR 0.53; 95% CI: 0.26 to 1.07; P=0.08), with little heterogeneity between trials (respectively  $\chi^2$  =2.69, P=0.85, I<sup>2</sup> =0%;  $\chi^2$  =4.89, P=0.56, I<sup>2</sup> =0%;  $\chi^2$  =4.06, P=0.77, I<sup>2</sup> =0%). The results showed that EOF reduced the risk of total complications compared to COF (RR 0.59; 95% CI: 0.48 to 0.73; P<0.00001), with little heterogeneity between trials ( $\chi^2$ =16.63, P=0.05, I<sup>2</sup> =46%) (*Figure 5*).

#### Discussion

This meta-analysis determined the effect of EOF on several postoperative GI motility outcomes in patients undergoing

elective colorectal surgery. Our primary analysis included trials with low risk of bias and that showed EOF being associated with a significant reduction in time to first flatus, defecation, length of hospital stay, and actually decreasing total postoperative complications compared with COF. There were no statistical differences in the risk of wound infection, pneumonia, anastomotic dehiscence, rate of NGT reinsertion, nausea, and vomiting. EOF is one of some important elements in fast-track surgery which can enhance recovery after colorectal surgery (27,28), and the evidence is mainly based on two meta-analyses (7,29,30). However, there is inadequate evidence. Firstly, both metaanalyses included many studies in which all or some patients



**Figure 3** EOF versus COF for time to first flatus, first defecation, and length of hospital stay. (A) EOF versus COF for time to first flatus (a fixed effects model). (B) EOF versus COF for time to first defecation (a fixed effects model). (C) EOF versus COF for length of hospital stay (a random effects model). EOF, early oral feeding; COF, conventional oral feeding.

	Early oral fe	eeding	<b>Conventional</b>	feeding		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
5.2.1 nausea and vor	miting						
da Fonseca 2011	4	24	10	26	13.5%	0.43 [0.16, 1.20]	
El Nakeeb 2009	15	60	10	60	14.0%	1.50 [0.73, 3.07]	
Feo 2004	16	50	7	50	9.8%	2.29 [1.03, 5.07]	
Hartsell1997	14	29	10	29	14.0%	1.40 [0.75, 2.62]	
Stewart 1998	16	40	15	40	21.1%	1.07 [0.61, 1.85]	
Wang ZH 2013	2	24	1	24	1.4%	2.00 [0.19, 20.61]	A CONTRACTOR OF A CONTRACTOR OFTA CONTRACTOR O
Subtotal (95% CI)		227		229	73.8%	1.28 [0.94, 1.73]	◆
Total events	67		53				
Heterogeneity: Chi <sup>2</sup> =	7.21, df = 5 (F	= 0.21);	I <sup>2</sup> = 31%				
Test for overall effect	Z = 1.57 (P =	0.12)					
5.2.2 NGT reinsertion	1						
Dag 2011	8	88	6	99	7.9%	1.50 [0.54, 4.15]	
El Nakeeb 2009	4	60	5	60	7.0%	0.80 [0.23, 2.83]	
Hartsell1997	8	29	5	29	7.0%	1.60 [0.59, 4.31]	
Stewart 1998	4	40	3	40	4.2%	1.33 [0.32, 5.58]	
Subtotal (95% CI)		217		228	26.2%	1.31 [0.75, 2.31]	-
Total events	24		19				
Heterogeneity: Chi <sup>2</sup> =	0.81, df = 3 (F	<sup>o</sup> = 0.85);	$ ^2 = 0\%$				
Test for overall effect:	Z=0.94 (P=	0.35)					
Total (95% CI)		444		457	100.0%	1.29 [0.98, 1.68]	•
Total events	91		72				
Heterogeneity: Chi <sup>2</sup> =	8.03, df = 9 (F	= 0.53);	$ ^2 = 0\%$				0.05 0.2 1 5 20
Test for overall effect:	Z = 1.83 (P =	0.07)					
Test for subaroup diff			f = 1 (P = 0.93)	$ ^{2} = 0\%$			Favours [experimental] Favours [control]

Figure 4 Analysis of vomiting and NGT reinsertion between the two groups. NGT, nasogastric tube.

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	Early oral fe		Conventional fee	-		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
5.1.1 Wound infection							
da Fonseca 2011	2	24	2	26	0.7%	1.08 [0.17, 7.10]	
Dag 2011	5	99	7	100	2.7%	0.72 [0.24, 2.20]	
El Nakeeb 2009	5	60	5	60	1.9%	1.00 [0.31, 3.28]	
Han-Geurts2007	3	67	4	61	1.6%	0.68 [0.16, 2.93]	
Stewart 1998	0	40	4	40	1.7%	0.11 [0.01, 2.00]	5
Wang DS 2014	1	43	2	45	0.8%	0.52 [0.05, 5.56]	
Zhou T 2006	4	161	3	155	1.2%	1.28 [0.29, 5.64]	
Subtotal (95% CI)		494		487	10.7%	0.74 [0.42, 1.29]	-
Total events	20		27				
Heterogeneity: Chi² = 2.69, c	if = 6 (P = 0.85	5); I² = 0%					
Fest for overall effect: Z = 1.0	06 (P = 0.29)						
6.1.2 Pneumonia	1	2.5	2	24	1.1.1	a tha muli m	
da Fonseca 2011	1	24	0	26	0.2%	3.24 [0.14, 75.91]	
Dag 2011	3	99	3	100	1.2%	1.01 [0.21, 4.88]	
El Nakeeb 2009	2	60	7	60	2.7%	0.29 [0.06, 1.32]	
Han-Geurts2007	5	67	6	67	2.3%	0.83 [0.27, 2.60]	
Stewart 1998	1	40	1	40	0.4%	1.00 [0.06, 15.44]	
Wang DS 2014	1	43	2	45	0.8%	0.52 [0.05, 5.56]	
Zhou T 2006	1	161	7	155	2.8%	0.14 [0.02, 1.10]	
Subtotal (95% CI)		494		493	10.3%	0.55 [0.29, 1.02]	
Total events	14		26				
Heterogeneity: Chi² = 4.89, o Test for overall effect: Z = 1.8		5); I² = 0%					
restilor overall ellect. Z = 1.0	59 (F - 0.00)						
6.1.3 Anastomotic leakage							
da Fonseca 2011	0	24	4	26	1.7%	0.12 [0.01, 2.12]	
Dag 2011	2	99	6	100	2.3%	0.34 [0.07, 1.63]	
El Nakeeb 2009	1	60	2	60	0.8%	0.50 [0.05, 5.37]	
Han-Geurts2007	2	67	2	61	0.8%	0.91 [0.13, 6.27]	
Hartsell1997	0	29	1	29	0.6%	0.33 [0.01, 7.86]	
Lobato Dias Consoli 2010	2	15	1	14	0.4%	1.87 [0.19, 18.38]	
Stewart 1998	1	40	0	40	0.2%	3.00 [0.13, 71.51]	
Zhou T 2006	2	161	4	155	1.6%	0.48 [0.09, 2.59]	
Subtotal (95% CI)		495		485	8.3%	0.53 [0.26, 1.07]	
Total events	10		20				
Heterogeneity: Chi <sup>2</sup> = 4.06, c	if = 7 (P = 0.77)	); I <sup>2</sup> = 0%					
Test for overall effect: Z = 1.7							
5.1.4 Total complications							
da Fonseca 2011	4	24	11	24	4.3%	0.36 [0.13, 0.98]	
Dag 2011	12	99	14	100	5.4%	0.87 [0.42, 1.78]	
El Nakeeb 2009	14	55 60	22	60	8.5%	0.64 [0.36, 1.12]	
Feo 2004	14	50	12	50	4.7%	1.08 [0.55, 2.14]	
Han-Geurts2007	22	67	27	61	11.0%	0.74 [0.48, 1.16]	
Hartsell1997	1	29	1	29	0.4%	1.00 [0.07, 15.24]	
Lobato Dias Consoli 2010	4	15	5	14	2.0%	0.75 [0.25, 2.23]	
	4 10	40	12	40	4.7%	0.83 [0.41, 1.70]	
Stewart 1998	10	40	12	40	4.7%		
Wang DS 2014 Zhou T 2006	8 21					0.84 [0.36, 1.92]	
Zhou T 2006 Subtotal (95% CI)	21	161 588	66	155 578	26.1% 70.7%	0.31 [0.20, 0.48] 0.59 [0.48, 0.73]	
	400	000	100	518	10.1%	0.59 [0.46, 0.75]	•
Total events	109 df = 0 (D = 0.0	S) 12 - 404	180				
Heterogeneity: Chi² = 16.63, Test for overall effect: Z = 5.0			70				
Fotal (95% CI)	1.51	2071		2043	100.0%	0.60 [0.50, 0.71]	◆
Total events	153		253				
Heterogeneity: Chi <sup>2</sup> = 29.02,			%				0.01 0.1 1 10 10
Test for overall effect: Z = 5.8	64 (P < 0.0000	1)					Favours [experimental] Favours [control]
lest for subaroup difference							

Figure 5 Analysis of complications between EOF and COF group. EOF, early oral feeding; COF, conventional oral feeding.

had undergone other GI surgeries rather than colorectal surgery, such as upper GI surgery (31) and small bowel operations (32,33). Secondly, studies of oral feeding and tube feeding were combined in these meta-analyses. Fasttrack colorectal surgery indicates early NGT removal, EOF, and early mobilization rather than early tube feeding (27,28). This is the first updated meta-analysis to evaluate GI function following EOF compared to following COF in patients undergoing colorectal surgery. The meta-analysis shown that EOF was beneficial for patients to recover and can be an available option for clinical treatment.

Almost every patient that underwent GI surgery experienced disorders of GI dysfunction. The major postoperative determinant of GI function is ileus, which is defined as a transient impairment of intestinal motility following abdominal surgery. It has a complex pathogenesis

involving the surgical stress response and inhibitory neural reflexes. Postoperative ileus is thought to influence toleration of oral intake, and vice versa, but reports on possible interactions are controversial (33-35). Diminishing complications and enhancing recovery to allow adequate food intake are the main objectives. A fasting period of 3 to 4 days, or until passage of flatus or defecation after colorectal surgery, has been common practice and is often accompanied by decompression of the stomach with a nasogastric tube and intravenous administration of fluids or nutrition. These procedures have been performed habitually, though controversy still exists. However, recent research on EOF after GI surgery has demonstrated its clinical advantages, especially in the field of colorectal surgery.

The present study followed the recommendations of the PRISMA statement and was strengthened by the stringent inclusion criteria, rigorous search strategy, and avoidance of language limitation. What's more, this metaanalysis was based on 11 RCTs, and 9 of these trials (1,078 patients) were published after 2004. With the development of the surgical and anesthetic practices that have changed over recent years, the results of the present study will be more representative than the previous meta-analyses for current colorectal surgery. The results indicate that EOF is effective and safe for recovery of GI motility after colorectal resection.

There were several limitations to the present metaanalysis. First, the time to first flatus, defecation, and length of hospital stay were presented as median (range), percentage, and time of postoperative complications in some trials which could not be included in our present meta-analysis. In addition, none of the incorporated studies used blinding method for the observers or patients. For feeding protocols, however, they could not lend themselves to double (observers and patients) or single (patients only) blinding, as both would have detected the introduction of food. Second, high statistical heterogeneity was identified in the length of hospital stay. Third, the included studies did not adequately evaluate total hospital costs and quality of life after surgery, which are very important outcomes for patients undergoing elective colorectal surgery. Finally, because only studies of EOF were included in this metaanalysis, our findings may not necessarily be generalized to patients with early postoperative tube feeding.

In conclusion, we found that EOF after elective colorectal resection is optional and safe in improving fast recovery. EOF was associated with a lower incidence of postoperative complications and a reduction in time to first flatus, defecation, and length of hospital stay. Further highquality RCTs of EOF with long-term follow-up and quality of life are necessary to assess hospital costs and quality of life in patients undergoing elective colorectal surgery.

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#### Footnote

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi. org/10.21037/dmr.2019.07.01). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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