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Early Versus Traditional Postoperative Feeding in Patients Undergoing Resectional Gastrointestinal Surgery: A Meta-Analysis

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Background: A meta-analysis evaluating surgical outcomes following nutritional provision provided proximal to the anastomosis within 24 hours of gastrointestinal surgery compared with traditional postoperative management was conducted. *Methods: Databases* were searched to identify randomized controlled trials comparing the outcomes of early and traditional postoperative feeding. Trials involving gastrointestinal tract resection followed by patients receiving nutritionally significant oral or enteral intake within 24 hours after surgery were included for analysis. *Results:* Fifteen studies involving a total of 1240 patients were analyzed. A statistically significant reduction (45%) in relative odds of total postoperative complications was seen in patients receiving early postoperative feeding (odds ratio [OR] 0.55; confidence interval [CI], 0.35 –0.87, *P* = .01). No effect of early feeding was seen with relation to anastomotic dehiscence (OR 0.75; CI, 0.39–1.4, *P* = .39), mortality (OR 0.71; CI, 0.32–1.56, *P* = .39), days to passage of flatus (weighted mean difference [WMD] –0.42; CI, –1.12 to 0.28, *P* = .23), first bowel motion (WMD –0.28; CI, –1.20 to 0.64, *P* = .55), or reduced length of stay (WMD –1.28; CI, –2.94 to 0.38, *P* = .13); however, the direction of clinical outcomes favored early feeding. Nasogastric tube reinsertion was less common in traditional feeding interventions (OR 1.48; CI, 0.93–2.35, *P* = .10). *Conclusions:* Early postoperative nutrition is associated with significant reductions in total complications compared with traditional postoperative feeding practices and does not negatively affect outcomes such as mortality, anastomotic dehiscence, resumption of bowel function, or hospital length of stay. (*JPEN J Parenter Enteral Nutr*. 2011;35:473-487)

Keywords: traditional feeding; early feeding; resectional gastrointestinal surgery; meta-analysis; randomized controlled trials; patient outcome; postoperative complications; hospitalization

Clinical Relevancy Statement

Patients undergoing elective gastrointestinal (GI) surgery are frequently malnourished at presentation because of the underlying conditions for which surgery is sought, the symptoms these create, and/or from side effects of medical management. Traditional approaches to postoperative nutrition care that involve withholding nutrition until passage of flatus or bowel motion have the potential to further jeopardize the nutrition status of these patients and may consequently compromise the postoperative course. Despite more than 30 years of research demonstrating the safety of early feeding practices in this population, change to clinical practice is often slow to be adopted. This current work further adds to the growing body of evidence that supports early postoperative feeding as a safe intervention that has the potential to improve postoperative outcomes, particularly with relation to a reduction in postoperative complications.

Introduction

Traditional nutrition management of patients in the days following GI resectional surgery mandates withholding

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enteral (ie, via oral or tube) nutrition (EN) and providing gastric decompression via a nasogastric (NG) tube. This is maintained until evidence of resumed bowel function is established, after which time a slow progression from fluids to normal diet follows, as tolerance allows. This management has been adopted over the years in the belief that it decreases the risk of nausea, vomiting, aspiration pneumonia, and anastomotic dehiscence.[1] However, a growing number of well-designed, randomized controlled clinical trials (RCTs) suggest that commencing EN within the first day following surgery and abandoning the practice of gastric decompression does not result in adverse clinical incidents and may in fact improve postsurgical outcomes. Moreover, 3 meta-analyses on this topic have been published[2-4] that lend further support to the practice of early postoperative feeding. However, aspects of nutrition provision that may affect surgical outcomes, such as the location of delivery and composition of nutrition provision, have been left largely unaddressed in these previous meta-analyses. Furthermore, additional RCTs on this topic have been published since the completion of the previous meta-analyses. Therefore, the present meta-analysis was undertaken to address these issues and examine the risks and benefits of early feeding compared with the traditional approach following GI resectional surgery.

Methods

Literature Search

Electronic databases (MEDLINE, PubMed, Embase, the Cumulative Index to Nursing and Allied Health Literature, the Cochrane Register of Systematic Reviews, Science Citation Index) were cross-searched using search terms customized to each search engine in an attempt to locate relevant English-language articles comparing the outcomes of early postoperative feeding in resectional surgery with traditional postoperative nutrition management. Reference lists of review articles and existing meta-analyses were hand-searched for further appropriate citations.

Study Selection

All studies comparing early feeding and traditional (nil by mouth) postoperative nutrition management published in the English language were reviewed. Only RCTs with primary comparisons between early and traditional feeding practices were considered for inclusion. Studies were required to have reported clinically relevant outcomes and to have been conducted in adults (>18 years ie, people older than) undergoing elective resectional surgery for whom early feeding was provided proximal to the anastomosis. Unpublished studies and abstracts presented at national and international meetings were excluded. Duplicate publications were also excluded.

Early feeding was defined as the provision of nutritionally significant oral or EN via NG or jejunal feeding tube, given within 24 hours postoperatively. Examples of nutritionally significant oral nutrition include free fluids or standard hospital diet; clear fluids were not included, given their lack of protein and inability to meet nutrition requirements irrespective of volume consumed.[5] Traditional postoperative management was defined as withholding nutrition provision until bowel function had resumed, as evidenced by either passage of flatus or bowel motion. Exclusion criteria included use of immune-modulating enteral feeding products such as Oral Impact (Nestle Healthcare Nutrition, Minneapolis, MN), because these may independently improve postoperative outcomes in some patient populations[6]; early feeding provided distal to the anastomosis; use of parenteral nutrition in either interventional group; patients younger than 18 years; and nonresectional or emergency surgeries. Data extraction and critical appraisal were carried out by 2 authors (E.O. and M.A.M.) for compliance with inclusion criteria and methodological quality. Standardized data extraction forms were used by both of these authors to independently and blindly summarize all the data available in the RCTs meeting the inclusion criteria. The authors were not blinded to the source of the document or authorship for the purpose of data extraction. The data were compared and discrepancies were addressed with discussion until consensus was achieved.

Methodological Quality

Evaluation of methodological quality of identified studies was conducted using the Jadad scoring system.[7] To obtain a maximum score, studies must report that they are randomized (1 point) with an appropriate method of randomization (1 point) and double-blinded (1 point), must report using a suitably robust method to achieve this (1 point), and must report withdrawals or dropouts from the study (1 point).[7] Points can be deducted if inappropriate methods of randomization or double-blinding are used.[7]

Outcomes Assessed

Outcomes assessed were those considered to exert influence over practical aspects of surgical practice and policy decisions within institutions, such as rates of postoperative complications, mortality outcomes, patient tolerance of early feeding, resumption of bowel function, and hospital length of stay (LOS). All studies reporting any number of outcomes of this nature were considered, and final analyses were run on outcome parameters where numbers were sufficient to allow statistical analysis. Where required, authors were contacted for clarification of data or additional information.

Statistical Analysis

Meta-analyses were performed using odds ratios (ORs) for binary outcomes and weighted mean differences (WMDs) for continuous outcome measures. A slightly amended estimator of OR was used to avoid the computation of reciprocal of zeros among observed values in the calculation of the original OR.[8] Random-effects models, developed by using the inverse-variance weighted method approach,[9] were used to combine the data. Heterogeneity among studies was assessed using the Q statistic proposed by Cochran[9-11] and the I^2 index introduced by Higgins and Thompson.[12,13] If the observed value of Q is equal to or larger than the critical value at a given significant level (α), in this case .05, we conclude that the outcome variable is statistically significant. The drawback of Q statistic is that its statistical power depends on the number of studies. The I^2 statistic describes the proportion of variation across studies that is due to between-study heterogeneity rather than chance, and unlike the Q statistic, it does not inherently depend on the number of studies considered.[13]

The issue of heterogeneity was further explored based on year of publication[13] (ie, before or after 2000). Estimates of mean and standard deviation (SD) are required to compute the confidence intervals (CIs). However, some of the published clinical trials did not report the mean and SD, but rather reported the size of the trial, the median, and the range. From these available statistics, estimates of the mean and SD were obtained using formulas proposed by Hozo et al.[14] Funnel plots were synthesized to determine the presence of publication bias in the meta-analysis. Standard error was plotted against the treatment effects (log OR for dichotomous variables and WMD for continuous variables)[9,15,16] to allow 95% CIs to be displayed. All estimates were obtained using computer programs written in *R*.[17] All plots were obtained using the "rmeta" package.[18] In the case of tests of hypotheses, the article reports P values for different study variables. In general, the effect is considered to be statistically significant if the P value is small. If one uses a 5% significance level, then the effect is significant only if the associated P value is $\leq .05$.

Results

Literature Search and Study Selection

Cross-searching of the electronic databases yielded 87 unique abstracts of potential relevance that were retrieved for independent review. Figure 1 presents the results of the study selection following the Quality of Reporting of Meta-Analyses recommendations.[19] The authors of the Han-Geurts et al[20,21] studies were contacted for permission to access information for their intestinal surgery patients (in view of the fact 25% of their sample were vascular patients), which was kindly provided for the 2007 study.

Pooled results yielded 40 patients, with a near-even distribution between feeding interventions (n = 617 traditional postoperative management, n = 623 early postoperative feeding) from 15 studies dating from 1979 to 2007. A summary of the RCTs included in the final meta-analysis is presented in Table 1.

Publication Bias

Publication bias is one of the major criticisms of meta-analysis, as its validity is reliant on a thorough representation of eligible studies being located.[16,22-24] The preferential publishing of studies with statistically significant results, those originating from multicenter trials, and those with government vs private funding has the potential to affect the results of a meta-analysis.[25] Funnel plots are traditionally used as the method of assessing for the presence of publication bias.[26]

The funnel plots displayed in Figure 2 demonstrate symmetry for all outcomes except total complications. This suggests that publication bias occurs within this meta-analysis in the total complications outcome but is absent from the other assessed variables.[11,12] However, the number of studies included in the funnel plots is inadequate to sensitively detect a study bias.[11,13]

Methodological Quality

None of the 15 included studies achieved a modified Jadad score greater than 3 (range 1–3, median 2). Six studies described the method of randomization,[20,21,26-28], 6 reported on withdrawals,[20,26,28-31] and 1 study[33] reported on blinding. Jadad scores are reported in Table 2.

Outcomes Assessed

Sufficient data were available for the analysis for 7 clinically relevant outcomes: total complications (defined as any complication reported within the postoperative period, excluding mortality and nausea/vomiting; Table 3); anastomotic dehiscence; in-hospital mortality; days to passage of bowel motion; days to passage of flatus; hospital LOS; and NG tube reinsertion.

Pooled Data

A statistically significant 45% reduction in relative odds of total postoperative complications was observed in patients receiving early postoperative feeding (OR 0.55; 95% CI, 0.35–0.87, P = .01). Early feeding was

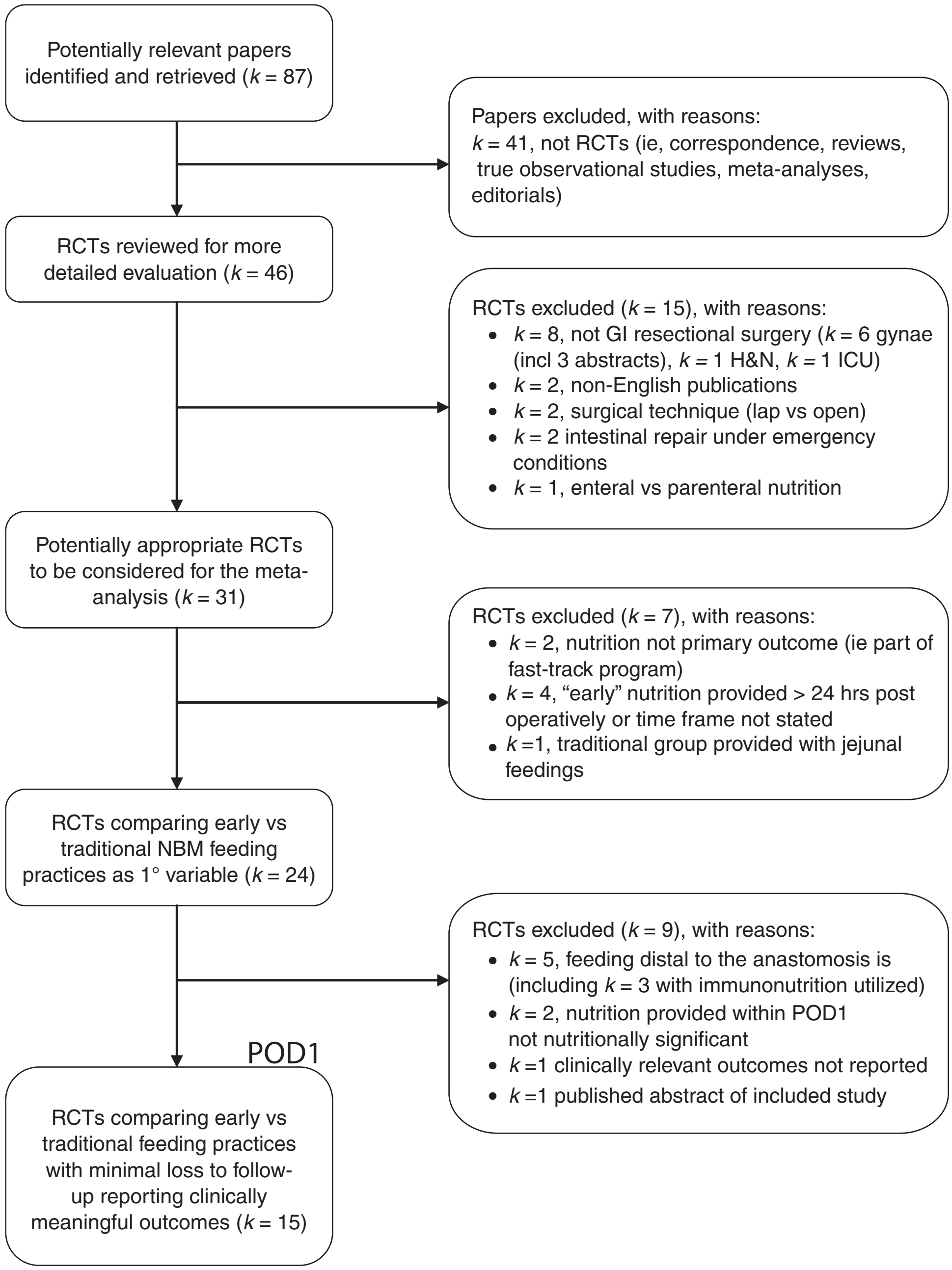

Figure 1. Quality of Reporting of Meta-Analyses statement. GI, gastrointestinal; H&N, head and neck cancer; head and neck; ICU, intensive care unit; NBM, nothing by mouth; POD, postoperative day; RCT, randomized controlled trial.

not associated with significant effects on anastomotic dehiscence (OR 0.75; 95% CI, 0.39–1.4, *P* = .39), mortality (OR 0.71; 95% CI, 0.32–1.56, *P* = .39), resumption of bowel function as evidenced by days to passage of flatus (WMD –0.42; 95% CI, −1.12 to 0.28, *P* = .23) and first bowel motion (WMD –0.28; 95% CI, −1.20 to 0.64, *P* = .55), and reduced LOS (WMD −1.28; 95% CI, −2.94 to 0.38, *P* = .13). A non–statistically significant reduction in the odds of requiring NG tube reinsertion was seen for traditional feeding practices (OR 1.48; 95% CI, 0.93–2.35, *P* = .10).

Stratified Data

The intervention effects of early postoperative feeding were more pronounced in pre-2000 studies compared with those conducted post-2000 for the parameters of postoperative complications, mortality, anastomotic dehiscence, days to passage of flatus and first bowel motion, and hospital LOS. Only pre-2000 studies reported on incidence of nausea and vomiting, with no significant differences observed between intervention groups (OR 0.93; 95% CI, 0.53–1.65, *P* = .8).

Table 1. Summary of Included Studies

Study	Year	Patient Population	n (Traditional/Early)	Early Feeding Protocol
Sagar et al[33]	1979	Major intestinal surgery: esophagogastrectomy (n = 2), gastrectomy (n = 6), colectomy, anterior resection, abdominoperineal resection	15/15	Half-strength Flexical (elemental feeding product) 25 mL/h for 24 h POD1, full-strength Flexical 25 mL/h for 24 h POD2, full-strength Flexical 50 mL/h for 24 h POD3, full-strength Flexical 100 mL/h POD4 via jejunal port of nasogastric/jejunal tube
Ryan et al[30]	1981	Partial colectomy	7/7	Vivonex HN (elemental feeding product) 10% wt/vol 50 mL/h on day of operation, 10% wt/vol @100 mL/h POD1, 10% wt/vol @125 mL/h POD2, 15% wt/vol 125 mL/h POD3, 20% wt/vol 125 mL/h POD4, 20% wt/vol 125 mL/h POD5, 25% wt/vol 125 mL/h POD6 and POD7
Schroeder et al[31]	1991	Small or large bowel resections or reanastomosis: colonic resection, abdominoperineal resection, ileoanal J-pouch, small bowel resection	16/16	50 mL/h Osmolite day of operation, 80 mL/h Osmolite if tolerated thereafter; oral intake POD3
Binderow et al[36]	1993	Laparoscopic-assisted laparotomy with colonic or ileal resection	32/32	Regular diet from POD1
Beier-Holgersen and Boesby[32]	1996	Gastrointestinal disease treated with bowel resection with anastomosis, enterostomy, gastric (n = 5) or esophageal resection (n = 3)	30/30	Clear fluids orally + increasing volumes of Nutridrink via nasojejunal tube from day of surgery
Carr et al[26]	1996	Unspecified intestinal surgery	14/14	Immediate postop nasojenunal feeding: 25 mL/h Fresubin (1 kcal/mL) and increased by 25 mL/h every 4 h until individual caloric goals met
Ortiz et al[29]	1996	Laparotomy for colon or rectal surgery	95/93	Clear fluids on day of surgery (?pre/postop), regular diet from POD1
Hartsell et al[34]	1997	Open colorectal surgery	29/29	Full liquid diet POD1, regular diet once tolerating >1 L in 24 h
Nessim et al[27]	1997	Anorectal reconstructive surgery	27/27	Regular diet from POD1
Stewart et al[28]	1998	Colorectal resection with anastomosis and without stoma formation	40/40	Free fluids from 4 hours postop on day of surgery, regular diet from POD1
Han-Geurts et al[27]	2001	Abdominal surgery (vascular + colonic)	49/56	Regular diet from POD1
Delaney et al[38]	2003	Segmental intestinal or rectal resection by laparotomy, including reoperation or pelvic surgery and those with comorbidities	33/31	Fluid diet D1 post op with regular diet in PM of POD1
Lucha et al[38]	2005	Open colorectal surgery	25/26	Regular diet from 8 h day of surgery
Zhou et al[35]	2006	Excision and anastomosis for colorectal tumor	155/161	Liquid fiberless diet POD–POD3
Han-Geurts et al[20]	2007	Open colorectal surgery	50/46	Regular diet from POD1

POD, postoperative day.

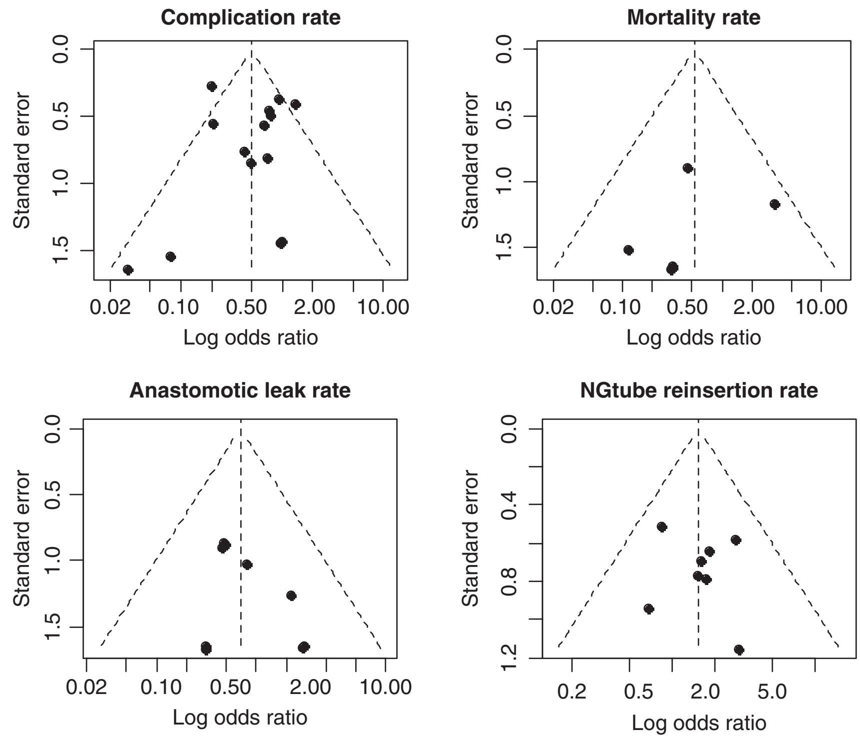

Figure 2. Funnel plots suggesting existence of publication bias. Funnel plots are provided for early feeding vs traditional feeding for rates of complications, mortality, anastomotic leak, and nasogastric (NG) tube reinsertion. The points correspond to the treatment effects (log odds ratio) from 15 individual studies, and the diagonal lines show the expected 95% confidence intervals around the pooled fixed-effect log odds ratio estimate.

Table 2. Jadad Scores of Included Studies

Author	Year/Country	Early	Control	Total	Randomization (out of 2)	Blinding (out of 2)	Withdrawals/ Dropouts (out of 1)	Jadad Total (highest possible total = 5)
Sagar et al	1979/UK	15	15	30	1	0	1	0
Ryan et al	1981/USA	7	7	14	1	0	2	1
Schroeder et al	1991/New Zealand	16	16	32	1	0	2	1
Binderow et al	1993/USA	32	32	64	1	0	1	0
Beier-Holgersen et al	1996/Denmark	30	30	60	1	1	2	0
Carr et al	1996/UK	14	14	28	2	0	3	1
Ortiz et al	1996/Spain	93	95	188	1	0	2	1
Hartsell et al	1997/USA	29	29	58	1	0	1	0
Nessim et al	1997/USA	27	27	54	2	0	3	0
Stewart et al	1998/Australia	40	40	80	2	0	3	1
Hans-Geurts et al	2001/The Netherlands	56	49	105	2	0	2	0
Delaney et al	2003/USA	31	33	64	2	0	2	0
Lucha et al	2005/USA	26	25	51	1	0	1	0
Zhou et al	2006/China	161	155	316	1	0	1	0
Hans-Geurts et al	2007/The Netherlands	46	50	96	2	0	3	1
Total		623	617	1,240				

Results are summarized Table 4, and forest plots are presented in Figures 3–9.

Discussion

This meta-analysis reinforces previous findings that traditional postoperative feeding practices confer no benefit in terms of outcomes following GI resectional surgery.[2-4] Our pooled findings suggest that a statistically significant reduction in total postoperative complications following surgery is associated with the introduction of nutritionally significant food or fluid within 24 hours postoperatively; ours is the first meta-analysis to demonstrate this finding.

We considered it necessary to analyze anastomotic dehiscence as a special outcome subset of the total

Study	Early	Traditional	OR	95% CI Lower	95% CI Upper
Pre-2000					
Sagar	3 of 15	5 of 15	0.53	0.08	3.78
Ryan	2 of 7	7 of 7	0.03	0	0.94
Schroeder	4 of 16	7 of 16	0.46	0.07	2.91
Binderow	0 of 32	0 of 32	1	0.02	61.41
Beier-Holgersen	8 of 30	19 of 30	0.22	0.05	1.08
Carr	0 of 14	4 of 14	0.08	0	2.06
Ortiz	17 of 93	18 of 95	0.96	0.24	3.77
Hartsell	1 of 29	1 of 29	1	0.07	13.42
Nessim	3 of 27	4 of 27	0.75	0.11	5.01
Stewart	10 of 40	12 of 40	0.78	0.17	3.56
Subtotal	**48 of 303**	**77 of 305**	**0.55**	**0.34**	**0.9**
Post-2000					
Han-Geurts	12 of 56	13 of 49	0.76	0.18	3.27
Delaney	7 of 31	10 of 33	0.69	0.14	3.38
Lucha	1 of 26	1 of 25	0.96	0.07	12.99
Zhou	23 of 161	70 of 155	0.21	0.06	0.74
Han-Geurts	22 of 46	20 of 50	1.37	0.33	5.61
Subtotal	**65 of 320**	**114 of 312**	**0.62**	**0.26**	**1.51**
POOLED	**113 of 623**	**191 of 617**	**0.55**	**0.35**	**0.87**

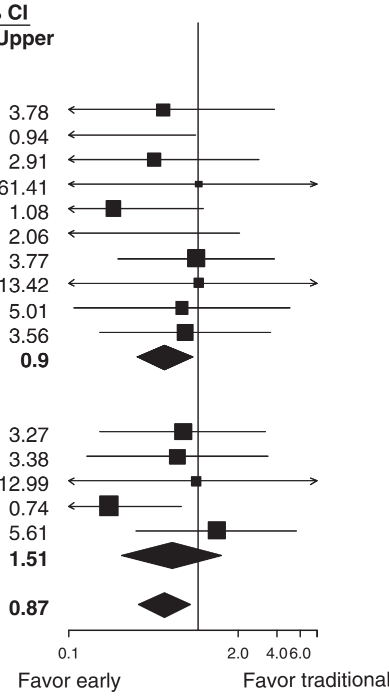

Figure 3. Odds ratio (OR) for complications (nausea and vomiting excluded). Values in the left panel are observed counts for early and traditional feeding, OR, and lower (L) and upper (U) limits of 95% confidence intervals (CIs) for ORs of the outcome variable. In the graph, squares indicate point estimates of treatment effect (OR for early vs traditional groups), with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% CIs for ORs of individual studies. The pooled estimate for the complication rate is the pooled OR, obtained by combining all ORs of the 15 studies using the inverse-variance weighted method. The 95% CI for the pooled estimate is represented by the diamond, and the length of the diamond depicts the width of the CI. Values to the left of the vertical line favor early feeding.

complications in view of the concerns long held by many surgeons that early feeding may increase the incidence of this complication. No difference was seen between interventions in the frequency of this outcome occurring. Similarly, no effect of early feeding was seen in relation to mortality, resumption of bowel function as measured by days to passage of flatus or bowel motion, and hospital LOS compared with traditional management. These results differ from the results obtained in the previously published meta-analyses, which have demonstrated statistically significant reductions in mortality,[2,3] hospital LOS,[2-4] and postoperative infection,[4] and increases in vomiting[2-4] with early feeding. A possible explanation for this may lie in the more specific selection criteria applied to studies for the current analysis, as outlined above.

Another possible reason for these differences may be found on closer examination of the results contained in 2 studies[20,21] that were not included in the previous analyses but that appear to have quite different outcomes to the general trends reported in other studies. A thorough review of the methodology described in these articles was undertaken to elucidate an explanation for these differences, although no significant differences were noted compared with other included articles. Initially, it was suspected that the presence of vascular patients among the study populations might explain the aberrations noted; however, little difference was found in outcomes when these were excluded from the 2007 data set provided through correspondence with the authors. Although it is possible that the remaining vascular patients originating from the 2001 data set[21] may contribute to this finding, we believe it unlikely, as they account for only 2.9% of the total pooled patient data. We further reviewed the methodological quality of these studies, which demonstrated a relatively high quality compared with others included in the analysis (Table 1). Therefore, it is possible that the results from the 2 Dutch studies may represent actual differences in outcomes contrary to those previously published with regard to early feeding.

The evolution of perioperative care throughout the 28 years encompassed by the included studies is a major factor that may influence the conclusions being drawn from the pooled results, and for this reason, studies were stratified for date of publication in an attempt to control for changes in routine clinical practice over time. For most outcomes observed (total complications, mortality, anastomotic dehiscence, days to passage of flatus and bowel

Table 3. List of Complications Contributing to Total Complications

Acute dilatation of the stomach
Allergic drug reaction
Anemia requiring transfusion
Anastomotic breakdown
Aspiration pneumonia
Cardiac arrhythmia
Cardiovascular
Dehydration
Dehydration renal failure
Delirium
Digestive tract complication (unspecified)
Exacerbation of chronic obstructive pulmonary disease
Faintness of vasovagal origin
Fever
Ileostomy necrosis
Ileus
Infected Hickman catheter
Myocardial infarction
Paroxysmal dyspnea
Pelvic abscess
Pharyngolaryngitis
Pneumonia
Postoperative hemorrhage
Pulmonary infection
Readmission to hospital
Repeat laparotomy
Respiratory (unspecified)
Small bowel obstruction
Stroke
Thromboembolic
Urinary tract infection
Venous thrombosis
Wound complication
Wound dehiscence
Wound infection

motion, LOS), results were seen to more strongly favor early feeding in the pre-2000 subgroup than in the post-2000 studies. This may in part be explained by the greater statistical power present in the pre-2000 subgroup because of the larger number of studies ($k = 10$ vs $k = 5$); however, this does not explain the effect for all variables, specifically the measure of bowel function return. Therefore, numbers alone may not account for these differences.

Changes in perioperative practices are likely to play a larger role in explaining the differences seen between stratified subgroups. Nutrition management alone demonstrates a movement over the decades toward providing more physiologically normal nutrition support in the early postoperative period. Sagar et al[33] and Ryan et al[30] commenced early feeding conservatively by present standards through providing diluted elemental formula (protein provided as amino acids; ie, Vivonex HN; Nestlé Healthcare Nutrition, Minneapolis, MN) into the jejunum, which over time progressed to the provision of standard polymeric feed products (intact proteins provided; ie, Jevity; Abbott Laboratories, Zwolle, The Netherlands) into the duodenum or jejunum,[26,31,32] oral fluids,[34,35] and finally full diet[20,21,27-29,36-39] within the first 24 hours postoperatively. There is no indication in the literature whether the diet composition or texture affects surgical outcomes observed in early feeding, though results from the included studies would suggest not.

In addition to the changes in nutrition provision within the time frame encompassed are other aspects of surgical and perioperative care that may affect the results obtained from this analysis. Changes to anesthesia and analgesia prescribing practices have trended toward opioid sparing, which is believed to be associated with reduced nausea, vomiting, sedation, and development of postoperative ileus[40] and thus facilitates the earlier tolerance of EN. The adoption of minimally invasive surgery in preference to open procedures has speeded sped recovery by reducing the size of the surgical incision compared with traditional laparotomy procedures, thus reducing postoperative pain and the cascade of inflammatory responses that lead to catabolism.[40-42] This leads to early mobilization, which has been associated with improved circulation and reduction in postoperative respiratory and thromboembolic complications.[43] Although included studies were not specifically reported as multimodal approaches to postsurgical management (such as "enhanced recovery after surgery" and "fast track"[44-47]), the increasing adoption of these elements in postoperative care over time to overcome the deleterious effects of surgical stress may confer recovery benefits and thus confound the results being attributed in this analysis to early feeding, particularly with a cumulative effect of multiple strategies being embraced. This may be particularly true of the more recent studies in which these philosophies are being more widely accepted as standard practice.

This meta-analysis used inclusion criteria with an increased focus on nutrition parameters, particularly with regard to the location of delivery of nutrition provision and the composition of nutrition provided. This is perhaps the most important difference between this meta-analysis and those previously published.[2-4]

First, we required feeding proximal to the anastomosis for inclusion in this analysis. Up to 12% of patients included in the previous meta-analyses were provided their early nutrition distal to the anastomosis. Fear of anastomotic dehiscence caused by food boluses or vomiting from intolerance of oral diet has been anecdotally purported as a reason for avoidance of early feeding in GI surgery; however, this concept of protecting the anastomosis overlooks that endogenous intestinal secretions of up to 7 L/d continue to be secreted and reabsorbed throughout the GI tract irrespective of

Study	Early	Traditional	OR	95% CI Lower	95% CI Upper
Pre-2000					
Sagar	0 of 15	0 of 15	1	0.02	53.66
Ryan	0 of 7	0 of 7	1	0.02	57.31
Schroeder	0 of 16	0 of 16	1	0.02	53.46
Binderow	0 of 32	0 of 32	1	0.02	51.94
Beier-Holgersen	2 of 30	4 of 30	0.52	0.1	2.65
Carr	0 of 14	1 of 14	0.31	0.01	8.29
Ortiz	0 of 93	0 of 95	1.02	0.02	52.01
Hartsell	0 of 29	1 of 29	0.32	0.01	8.24
Nessim	0 of 27	0 of 27	1	0.02	52.22
Stewart	0 of 40	1 of 40	0.33	0.01	8.22
Subtotal	**2 of 303**	**7 of 305**	**0.58**	**0.22**	**1.54**
Post-2000					
Han-Geurts	0 of 56	3 of 49	0.12	0.01	2.33
Delaney	0 of 31	0 of 33	1.06	0.02	55.24
Lucha	0 of 26	0 of 25	0.96	0.02	50.35
Zhou	0 of 161	0 of 155	0.96	0.02	48.83
Han-Geurts	3 of 46	1 of 50	2.66	0.38	18.77
Subtotal	**3 of 320**	**4 of 312**	**1.03**	**0.27**	**3.88**
POOLED	**5 of 623**	**11 of 617**	**0.71**	**0.32**	**1.56**

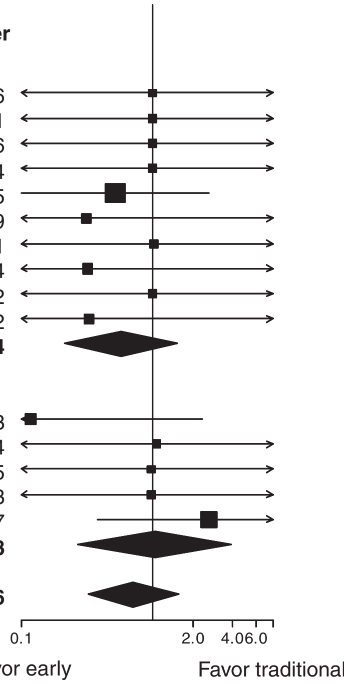

Figure 4. Odds ratios (ORs) for mortality. Values in the left panel are observed counts for early and traditional feeding, ORs, and lower (L) and upper (U) limits of 95% confidence intervals (CIs) for ORs of the outcome variable. In the graph, squares indicate point estimates of treatment effect (ORs for early vs traditional groups), with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% CIs for ORs of individual studies. The pooled estimate for the mortality rate is the pooled OR, obtained by combining all ORs of the 15 studies using the inverse variance weighted method. The 95% CI for the pooled estimate is represented by the diamond, and the length of the diamond depicts the width of the CI. Values to the left of the vertical line favor early feeding.

Study	Early	Traditional	OR	95% CI Lower	95% CI Upper
Pre-2000					
Sagar	0 of 15	1 of 15	0.31	0.01	8.29
Schroeder	0 of 16	0 of 16	1	0.02	53.46
Beier-Holgersen	2 of 30	4 of 30	0.52	0.1	2.65
Carr	0 of 14	0 of 14	1	0.02	53.89
Ortiz	2 of 93	4 of 95	0.56	0.12	2.68
Hartsell	0 of 29	1 of 29	0.32	0.01	8.24
Nessim	0 of 27	0 of 27	1	0.02	52.22
Stewart	1 of 40	0 of 40	3.08	0.12	77.8
Subtotal	**5 of 264**	**10 of 266**	**0.62**	**0.25**	**1.52**
Post-2000					
Han-Geurts	2 of 18	1 of 19	1.87	0.22	15.73
Delaney	0 of 31	0 of 33	1.06	0.02	55.24
Lucha	1 of 26	0 of 25	3	0.12	77.17
Zhou	2 of 161	4 of 155	0.53	0.11	2.52
Han-Geurts	2 of 42	2 of 35	0.83	0.14	5.06
Subtotal	**7 of 278**	**7 of 267**	**0.93**	**0.36**	**2.43**
POOLED	**12 of 542**	**17 of 533**	**0.75**	**0.39**	**1.45**

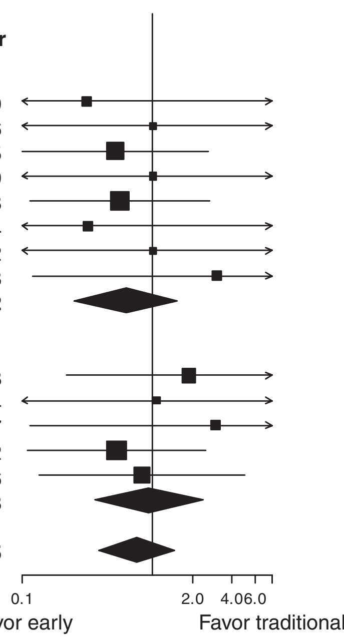

Figure 5. Odds ratios (ORs) for anastomotic leak. Values in the left panel are observed counts for early and traditional feeding, OR, and lower (L) and upper (U) limits of 95% (CIs) for ORs of the outcome variable. In the graph, squares indicate point estimates of treatment effect (ORs for early vs traditional groups), with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% CIs for ORs of individual studies. The pooled estimate for the anastomotic leak rate is the pooled OR, obtained by combining all ORs of the 13 studies using the inverse-variance weighted method. The 95% CI for the pooled estimate is represented by the diamond, and the length of the diamond depicts the width of the CI. Values to the left of the vertical line favor early feeding.

Study	Early	Traditional	OR	95% CI Lower	95% CI Upper
Pre-2000					
Binderow	6 of 32	4 of 32	1.55	0.42	5.78
Hartsell	8 of 27	5 of 27	1.78	0.52	6.11
Stewart	4 of 92	3 of 103	1.46	0.35	6.08
Subtotal	**18 of 151**	**12 of 162**	**1.61**	**0.75**	**3.44**
Post-2000					
Han-Geurts	9 of 56	9 of 49	0.85	0.32	2.3
Delaney	2 of 31	3 of 33	0.74	0.13	4.04
Lucha	5 of 26	3 of 25	1.64	0.38	7.11
Zhou	3 of 161	1 of 155	2.27	0.33	15.6
Han-Geurts	12 of 61	7 of 67	2.68	0.89	8.11
Subtotal	**30 of 320**	**21 of 312**	**1.41**	**0.78**	**2.52**
POOLED	**48 of 471**	**33 of 474**	**1.48**	**0.93**	**2.35**

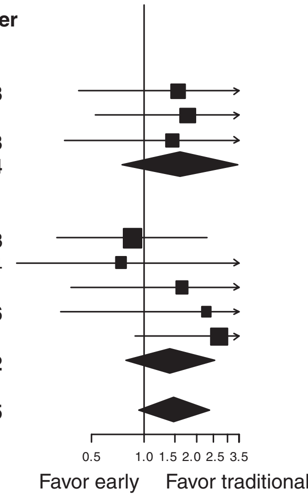

Figure 6. Odds ratios (ORs) for nasogastric (NG) tube reinsertion. Values in the left panel are observed counts for early and traditional feeding, ORs, and lower (L) and upper (U) limits of 95% confidence intervals (CIs) for ORs of the outcome variable. In the graph, squares indicate point estimates of treatment effect (OR for early vs traditional groups), with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% CIs for ORs of individual studies. The pooled estimate for the NG reinsertion rate is the pooled OR, obtained by combining all ORs of the 8 studies using the inverse-variance weighted method. The 95% CI for the pooled estimate is represented by the diamond, and the length of the diamond depicts the width of the CI. Values to the left of the vertical line favor early feeding.

Study	N	Early	N	Traditional	WMD	95% CI Lower	95% CI Upper
Pre-2000							
Schroeder	16	2.41 (1.33)	16	2.91 (1.29)	–0.5	–2.09	1.09
Stewart	40	3.00 (1.20)	40	4.00 (1.20)	–1	–2.41	0.41
Subtotal	**56**		**56**		**–0.87**	**–1.33**	**–0.42**
Post-2000							
Zhou	161	3.00 (0.90)	155	3.60 (1.20)	–0.6	–1.93	0.73
Han-Geurts	43	1.70 (0.20)	49	1.40 (0.10)	0.3	–1.01	1.61
Subtotal	**204**		**204**		**–0.14**	**–1.02**	**0.74**
POOLED	**260**		**260**		**–0.42**	**–1.12**	**0.28**

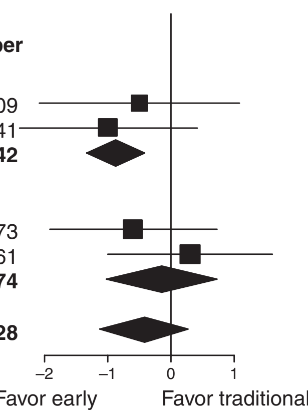

Figure 7. Days to passing flatus. Values in the left panel are sample size (N), mean (standard deviation), weighted mean difference (WMD), and lower (L) and upper (U) limits of 95% confidence interval (CI) for mean of the outcome variable. In the graph, squares indicate point estimates of treatment effect (mean difference, ie, mean for early feeding group of patients minus mean for traditional group of patients), with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% CI for the mean differences of individual studies. The pooled estimate of the days to passing flatus is the WMD. It is obtained by combining all mean differences using the inverse-variance weighted method. The 95% CI for the overall mean based on the pooled estimate is represented by the diamond, and the length of the diamond depicts the width of the CI. Values to the left of the vertical line favor early feeding.

enteral intake in the postsurgical period.[48] Furthermore, the malnutrition and significant weight loss likely to be caused in part by extended postoperative delay in nutrition provision are recognized as more significant risk factors in the development of anastomotic dehiscence.[49] None of the individual studies included in or reviewed for this meta-analysis demonstrated an increase in anastomotic dehiscence with early feeding, regardless of the form in which it was delivered, and indeed, all the published meta-analyses to date suggest a trend toward decreased risk of this adverse outcome being associated with early feeding.

Study	N	Early	N	Traditional	WMD	95% CI Lower	95% CI Upper
Pre-2000							
Schroeder	16	3.21 (1.50)	16	4.16 (1.33)	−0.95	−2.93	1.03
Stewart	40	4.77 (2.15)	40	5.00 (1.80)	−0.23	−2.16	1.7
Subtotal	**56**		**56**		**−0.55**	**−1.25**	**0.15**
Post-2000							
Zhou	161	4.10 (1.10)	155	4.80 (1.40)	−0.7	−2.45	1.05
Han-Geurts	43	4.30 (0.30)	49	3.70 (0.30)	0.6	−1.13	2.33
Subtotal	**204**		**204**		**−0.04**	**−1.32**	**1.23**
POOLED	**260**		**260**		**−0.28**	**−1.2**	**0.64**

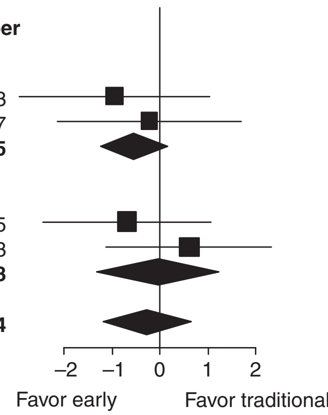

Figure 8. Days to first bowel motion. Values in left panel are sample size (N), mean (standard deviation), weighted mean difference (WMD), and lower (L) and upper (U) limits of 95% confidence interval (CI) for mean of the outcome variable. In the graph, squares indicate point estimates of treatment effect (mean difference, ie, mean for early feeding group of patients minus mean for traditional group of patients), with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% CIs for the mean differences of individual studies. The pooled estimate of the days to first bowel motion is the WMD. It is obtained by combining all mean differences using the inverse-variance weighted method. The 95% CI for the overall mean based on the pooled estimate is represented by the diamond, and the length of the diamond depicts the width of the CI. Values to the left of the vertical line favor early feeding.

Study	N	Early	N	Traditional	WMD	95% CI Lower	95% CI Upper
Pre-2000							
Sagar	15	16.1 (5.27)	15	23.8 (11.86)	−7.67	−15.57	0.23
Schroeder	16	10.0 (4.00)	16	15.0 (10.0)	−5	−11.86	1.86
Binderow	32	6.70 (3.25)	32	8.00 (3.75)	−1.3	−6.01	3.41
Carr	14	9.80 (6.60)	14	9.30 (2.80)	0.5	−5.27	6.27
Hartsell	29	7.20 (3.30)	29	8.10 (2.30)	-0.9	−5.52	3.72
Stewart	40	12.8 (7.25)	40	11.5 (3.61)	1.33	−3.72	6.38
Subtotal	**146**		**146**		**−1.05**	**−2.66**	**0.56**
Post-2000							
Han-Geurts	56	24.5 (21.92)	49	15.6 (8.76)	8.9	1.27	16.53
Delaney	31	5.20 (2.50)	33	5.80 (3.00)	−0.6	−5.19	3.99
Zhou	161	8.40 (3.40)	155	9.60 (5.00)	−1.2	−5.68	3.28
Han-Geurts	46	12.0 (1.80)	49	17.5 (4.20)	−5.5	−10.07	−0.93
Subtotal	**294**		**286**		**−0.93**	**−3.95**	**2.09**
POOLED	**440**		**432**		**−1.28**	**−2.94**	**0.38**

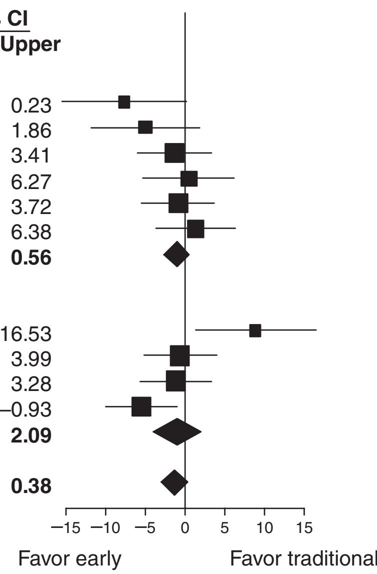

Figure 9. Length of stay (days). Values in the left panel are sample size (N), mean (standard deviation), weighted mean difference (WMD), and lower (L) and upper (U) limits of 95% confidence interval (CI) for mean of the outcome variable. In the graph, squares indicate point estimates of treatment effect (mean difference, ie, mean for early feeding group of patients minus mean for traditional group of patients), with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% CI for the mean differences of individual studies. The pooled estimate of the length of stay (days) is the WMD. It is obtained by combining all mean differences using the inverse-variance weighted method. The 95% CI for the overall mean based on the pooled estimate is represented by the diamond, and the length of the diamond depicts the width of the CI. Values to the left of the vertical line favor early feeding.

Second, we required the provision of nutritionally significant foods or fluids within the first postoperative day for inclusion in this meta-analysis. Clear fluids are regularly chosen as the first oral intake postoperatively,[5] irrespective of whether early feeding or traditional postoperative management is being provided. However, there is little scientific basis for this dietary provision in that it provides little nutrition value[5] and patients have been shown to tolerate the early introduction of solid diet without significant adverse outcomes following a range of

Table 4. Results

Outcome Variables	Year Published	No. of Studies	No. of Patients Evaluated	Pooled OR[a] or WMD[b] (95% CI)	Test for Overall Effect Z	Test for Overall Effect P	Test for Heterogeneity Q	Test for Heterogeneity P	Test for Heterogeneity I^2 Index (95% CI)
Complications (nausea and vomiting excluded)	Pre-2000	10	608	0.55 (0.34 to 0.90)[a]	−2.38	.0173	10.61	.3031	15% (0%–56.5%)
	Post-2000	5	632	0.62 (0.26 to 1.51)[a]	−1.05	.2934	17.78	.0013	77.5% (45.6%–90.6%)
	1979–2007	15	1,240	0.55 (0.35 to 0.87)[a]	−2.55	.0106	29.07	.0102	51.8% (13.2%–73.2%)
Mortality	Pre-2000	10	608	0.58 (0.22 to 1.54)[a]	−1.10	.2729	0.85	.9999	0% (no variation)
	Post-2000	5	632	1.03 (0.27 to 3.88)[a]	0.04	.9695	2.93	.569	0% (0%–71.6%)
	1979–2007	15	1,240	0.71 (0.32 to 1.56)[a]	−0.86	.3902	4.24	.9938	0% (no variation)
Anastomotic leak	Pre-2000	8	530	0.62 (0.25 to 1.52)[a]	−1.04	.2987	1.50	.9822	0% (no variation)
	Post-2000	5	545	0.93 (0.36 to 2.43)[a]	−0.14	.8898	1.44	.8376	0% (0%–42.2%)
	1979–2007	13	1,075	0.75 (0.39 to 1.45)[a]	−0.85	.3932	3.31	.9929	0% (no variation)
Days to passing flatus	Pre-2000	2	112	−0.87 (−1.33 to −0.42)[b]	−3.77	.0002	0.87	.3503	0% (no variation)
	Post-2000	2	408	−0.14 (−1.02 to 0.74)[b]	−0.32	.7512	52.41	<.0001	98.1% (95.2%–99.2%)
	1979–2007	4	520	−0.42 (−1.12 to 0.28)[b]	−1.19	.2355	75.63	<.0001	96% (29.6%–97.8%)
NG tube reinsertion	Pre-2000	3	313	1.61 (0.75 to 3.44)[a]	1.23	.2203	0.05	.9766	0% (no variation)
	Post-2000	5	632	1.41 (0.78 to 2.52)[a]	1.14	.2550	3.12	.5387	0% (0%–73.7%)
	1979–2007	8	945	1.48 (0.93 to 2.35)[a]	1.64	.0990	3.24	.8620	0% (0%–30%)
Days to first bowel motion	Pre-2000	2	112	−0.55 (−1.25 to 0.15)[b]	−1.54	.1230	1.16	.2819	0% (no variation)
	Post-2000	2	408	−0.04 (−1.32 to 1.23)[b]	−0.07	.9463	70.15	.0000	97.1% (96.9%–99.3%)
	1979–2007	4	520	−0.28 (−1.20 to 0.64)[b]	−0.60	.5502	78.99	.0000	96.2% (92.9%–97.9%)
Length of stay	Pre-2000	6	292	−1.05 (−2.66 to 0.56)[b]	−1.28	.2007	10.17	.0704	50.8% (0%–80.5%)
	Post-2000	4	580	−0.93 (−3.95 to 2.09)[b]	−0.60	.5462	47.00	<.0001	93.6% (56.9%–97%)
	1979–2007	10	872	−1.28 (−2.94 to 0.38)[b]	−1.51	.1319	61.19	<.0001	85.3% (74.7%–91.3%)
Nausea and vomiting	Pre-2000	7	532	0.93 (0.53 to 1.65)[a]	−0.25	.8055	10.99	.0886	45% (0%–77%)
	Post-2000	0	0	NA	NA	NA	NA	NA	NA
	1979–2007	7	532	0.93 (0.53 to 1.65)[a]	−0.25	.8055	10.99	.0886	45% (0%–77%)
Days to solid diet	Pre-2000	2	160	−3.28 (−4.46 to −2.10)[b]	−5.45	<.0001	2.96	.0856	66.2% (0%–92.3%)
	Post-2000	2	200	−3.77 (−7.19 −0.35)[b]	−2.16	.0307	12.60	<.0001	92.1% (72.7%–97.7%)
	1979–2000	4	360	−3.48 (−4.72 −2.24)[b]	−5.51	<.0001	15.95	.0012	81.2% (50.9%–92.8%)

CI, confidence interval; NA, not available; NG, nasogastric; OR, odds ratio; WMD, weighted mean difference.
[a]OR.
[b]WMD.

surgical procedures, including upper-GI surgery.[50,51] Furthermore, malnutrition is a common finding in elective GI surgery patients,[52,53] and this has been shown to be independently associated with poor outcomes such as delayed wound healing, development of postoperative complications, and mortality in surgical patients.[52-56] The catabolic effects of the stress response induced by surgery are well recognized,[57,58] as is the ability of adequate nutrition to attenuate the magnitude of the inflammatory responses[59] and nitrogen losses sustained the postoperative period.[60-62] For this reason, we postulate that the early provision of nutritionally significant foods and fluids has a greater potential to positively influence outcomes than indiscriminate provision of food and fluids within the early postoperative period through modulating the body's response to surgical stress and reducing the caloric deficit in the days immediately following surgery, thus reducing the degree of nutrition depletion experienced postoperatively.

Third, studies using immune-enhancing nutrition products as their early feeding intervention were excluded from the present meta-analysis. All previously published meta-analyses on this topic include a large study by Heslin et al[63] that used an immune-modulating enteral formula provided distal to the anastomosis as the early feeding intervention. This study represents 21% of the patients included in the meta-analysis in the 2001 analysis and 16% of the total number of patients in the subsequent meta-analyses.[2-4] In view of the large proportion of patients included and the potential of these specialized nutrition products to affect postoperative outcomes, we believe that the inclusion of this study potentially confounds the results of the previously published meta-analyses. This is particularly so given that the study by Heslin et al[63] is also the largest of the included studies (n = 197) and, as such, will be the most heavily weighted owing to the use of the fixed-effect model in these meta-analyses.[64] As a result of this, the Heslin et al[63] study has the greatest potential to influence the summary estimates of the existing meta-analyses. Vivonex HN contains higher levels of glutamine, an amino acid thought to convey immune-enhancing qualities when provided in pharmacological quantities,[65] than nutrition products of standard composition. Vivonex HN was used as the early feeding intervention in the Ryan et al[30] study that was included in the present meta-analysis; however, this was not considered to be a reason for exclusion, given the dilution of the product used throughout the feeding period.

The absence of reporting on nutrition consumption is perhaps the most disappointing aspect of the studies included in this analysis. Although all the studies that provided small bowel feeding provided data on this subject,[26,30-33] none of the studies that allowed oral intake reported this information.[20,21,27-29,34,36-38] The absence of consumption records requires that we assume the nutrition provision received in early feeding interventions is greater than that received in traditional management. However, this may not be the case, particularly in trials such as those by Han-Geurts et al,[20,21] where the onus for oral consumption was actively placed on the patient. Collection of food consumption records as part of study protocols to allow an estimation of caloric and protein intake in the early postoperative period is a major omission in the clinical trials investigating this topic and needs to be addressed in future studies. Collection of this information in conjunction with anthropometric data may facilitate answering important questions regarding the interaction of quantifiable nutrition provision and postoperative outcomes For example: What level of caloric/nutrition intake is required to reduce LOS or total complications? Does full diet vs nutrient-rich fluid provision in the early period postoperatively result in a greater risk of anastomotic dehiscence? What effect does early vs traditional feeding have on anthropometric outcomes such as weight and lean body mass in the postoperative period and issues such as outcomes and recovery? This information has the potential to revolutionize perioperative nutrition practice and enhance outcomes for patients and the institutions in which they are treated.

A number of limitations are associated with this meta-analysis. First, in an attempt to standardize the differences in reporting between articles, we contacted several authors for clarification of reported data or additional information within their published data. In cases where no response was returned,[28,34,35,37] assumptions relating to the interpretation of various aspects of their published reports were made, such as the composition of the fluid diets reported[34,35,37] or discrepancies in the reporting within the article.[28] For these reasons, although every attempt has been made to ensure that analyzed studies met inclusion criteria and that other data are accurate, there may still be errors that confound the results obtained.

Second, the studies that met inclusion criteria for this meta-analysis consistently yielded poor scores for methodological quality using the Jadad scoring system.[7] Of a possible score of 5, a mean score of 1.9 was achieved, with a maximum score of 3. Although there are limitations of applying traditional methods of assessing methodological quality to nutrition studies because of the often impossible task of blinding for obvious dietary interventions, there should be no impediment to reporting withdrawals or method of randomization. Even with the increasing emphasis on improving the quality of reporting in clinical trials in the medical literature in recent years, no difference was seen in the Jadad score in the average pre-2000 and post-2000 scores (pre-2000 2.0, post-2000 1.8; not significant).

Conclusions

The results of this meta-analysis fail to demonstrate merit in continuing the traditional postoperative feeding practices of withholding nutrition provided proximal to the anastomosis until bowel function is resumed. This is the first meta-analysis to demonstrate statistically significant reductions in total complications in the postoperative course with early feeding. Furthermore, no negative effect of early feeding was demonstrated with regard to in-hospital mortality, anastomotic dehiscence, LOS, and time to recovery of bowel function. For these reasons, surgeons should be confident in adopting early feeding as part of standard practice for elective GI surgery patients.

This analysis also highlights the paucity of data on nutrition and anthropometric parameters and outcomes in studies on this topic. Further studies in this area will require greater multidisciplinary involvement to allow data collection and consideration of these important aspects of postoperative care.

Acknowledgments

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