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BENEFITS OF EARLY FEEDING VERSUS TRADITIONAL NIL-BY-MOUTH NUTRITIONAL POSTOPERATIVE MANAGEMENT IN GASTROINTESTINAL RESECTIONAL SURGERY PATIENTS: A META-ANALYSIS

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ABSTRACT

The objective of the current work was to conduct a meta-analysis of randomized controlled trials evaluating the effect on surgical outcomes of providing nutrition within 24-hours following gastrointestinal surgery compared with traditional postoperative management. A literature search was conducted to identify randomized controlled trials published in English language between1966 and 2007 comparing the outcomes of early and traditional postoperative feeding. All trials involving resection of the portions of the gastrointestinal tract followed by patients receiving nutritionally significant oral or enteral intake within 24-hours after surgery were included for analysis. Random effects meta-analyses were performed. Outcome variables analyzed were complications, mortality, anastomotic dehiscence, nasogastric reinsertion, days to passing flatus, days to first bowel motion, and length of stay. Fifteen studies (n=1240 patients) were analyzed. A statistically significant forty-five percent reduction in relative odds of total postoperative complications were seen in patients receiving early postoperative feeding (OR 0.55 CI 0.35, 0.87, p=0.01). No effect of early feeding was seen with relation to anastomotic dehiscence (OR 0.75, CI 0.39, 1.4, p=0.39), mortality (OR 0.71, CI 0.32,1.56, p= 0.39), resumption of bowel function as evidenced by days to passage of flatus (WMD -0.42, CI -1.12, 0.28, p=0.23) and first bowel motion (WMD -0.28, CI -1.20, 0.64, p=0.55), or reduced length of stay (WMD -1.28, CI -2.94, 0.38, p=0.13). Similarly, nasogastric tube reinsertion was less common in traditional feeding interventions, however this was not statistically significant (OR 1.48, CI 0.93, 2.35, p=0.10). Early provision of nutritionally significant oral or enteral intake is associated with a significant reduction in reported total complications when 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. For these reasons, surgeons should be confident in adopting early feeding as part of standard practice for elective gastrointestinal surgery.

Keywords: Meta-analysis; gastrointesintal surgery; early feeding; surgical complications; human

1. INTRODUCTION

Traditional nil-by-mouth nutritional management of patients in the days following gastrointestinal resectional surgery has been adopted over the years in the belief that it decreases the risk of nausea, vomiting, aspiration pneumonia and anastomotic dehiscence (Nelson, Edwards and Tse, 2008). However, a growing number of well designed randomized controlled clinical trials suggest that it is safe to commence feeding from within 24-hr following surgery. Moreover three meta-analyses on this topic have been published (Andersen, Lewis and Thomas, 2006; Lewis, Andersen and Thomas, 2008; Lewis et al., 2001) which lend further support to the practice of early postoperative feeding. However aspects of nutritional provision that may impact surgical outcomes, such as the location of delivery and composition of nutritional provision, have been left largely unaddressed in these previous meta-analyses. Therefore this present meta-analysis has been undertaken to address these issues and develop a better understanding of the risks and benefits of early feeding when compared to the traditional approach following gastrointestinal resectional surgery.

2. MATERIALS AND METHODS

Electronic databases (Medline, Pubmed, EMBASE, CINAHL, Cochrane Register of Systematic Reviews, Science Citation Index) were cross-searched using search terms customized to each search engine in an attempt to detect relevant English language papers comparing the outcomes of early postoperative feeding in resectional surgery with traditional postoperative nutritional management. Reference lists of review papers and existing meta-analyses were hand searched for further appropriate citations.

All studies comparing early feeding and traditional (nil-by-mouth) postoperative nutritional management published in the English language were reviewed. Only randomized controlled trials with primary comparisons between early and traditional feeding practices were considered for inclusion. Studies must also have reported on clinically relevant outcomes, and have been conducted in adult (>18 years) elective resectional surgical cases in which early feeding was provided proximal to the anastomosis. Unpublished studies and abstracts presented at national and international meetings were excluded. Similarly duplicate publications were also excluded.

Early feeding was defined as the provision of nutritionally significant oral or enteral nutrition via nasogastric or jejunal feeding tube, provided within 24-hours postoperatively. Examples of nutritionally significant oral nutrition include free fluids or standard hospital diet; clear fluids were not included due to their inability to meet nutritional requirements irrespective of volume consumed (Hancock, Cresci and Martindale, 2002). Traditional postoperative management was defined as withholding nutritional provision until bowel function had resumed, as evidenced by either passage of flatus or bowel motion. Exclusion criteria included use of immune modulating enteral feed products such as Oral Impact® (Nestle Healthcare Nutrition, Minneapolis, USA) as these may independently improve postoperative outcomes in some patient populations (Zheng et al., 2007), early feeding provided distal to the anastomosis, use of parenteral nutrition in either interventional group, patients <18 years of age and non-resectional or emergency surgeries. Data extraction and critical appraisal were carried out by two authors (EO and MAM) for compliance with inclusion criteria and methodological quality. Standardized data extraction forms were used by both authors to independently and blindly summarize all the data available in the randomized controlled trials 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.

Evaluation of methodological quality of identified studies was conducted using the Jadad scoring system which provides a numerical quality score based on reporting of randomization, blinding and reporting of withdrawals (Jadad et al., 1996).

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 and mortality outcomes. All studies with reporting on 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.

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 (Agresti, 1996). Random effects models, developed by using the inverse variance weighted method approach (Sutton et al., 2000), were used to combine the data. Heterogeneity among studies was assessed using the Q statistic proposed by Cochran (Cochran, 1954; Hedges and Olkin, 1985; Sutton et al., 2000) and I^2 index introduced by Higgins and Thompson (Higgins and Thompson, 2002; Huedo-Medina et al., 2006). If the observed value of Q is equal to or larger than the critical value at a given significant level (α), in this case 0.05, we conclude that the outcome variable is statistically significant. The drawback of the 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-studies heterogeneity rather than chance and unlike Q statistic it does not inherently depend upon the number of studies considered (Huedo-Medina et al., 2006).

The issue of heterogeneity was further explored based on year of publication i.e. year of publication: before and after 2000. For the computations of the confidence intervals estimates of mean and standard deviation are required. However, some of the published clinical trials did not report the mean and standard deviation, but rather reported the size of the trial, the median and range. From these available statistics, estimates of the mean and standard deviation were obtained using formulas proposed by Hozo et al. (2005). Funnel plots were synthesized in order to determine the presence of publication bias in the meta-analysis. Standard error was plotted against the treatment effects (Log OR for the dichotomous and WMD for continuous variables respectively) (Egger et al., 1997; Sutton et al., 2000; Tang and Liu, 2000) to allow 95% confidence interval limits to be displayed. All estimates were obtained using computer programs written in R (Hornik, 2008). All plots were obtained using the 'rmeta' package (Lumley, 2008). In the case of tests of hypotheses, the paper 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 less than or equal to 5%.

3. RESULTS

Cross searching of the electronic databases yielded 87 unique abstracts of potential relevance which were retrieved for independent review. Figure 1 presents the results of the study selection following the Quality of Reporting of Meta-analyses (QUOROM) recommendations (Moher et al., 1999). Pooled results yielded 1240 patients, with a near even distribution between feeding interventions (n=617 traditional postoperative management, n=623 early post operative feeding) from 15 studies dating from 1979 to 2007. A summary of the randomised controlled trials included in the final meta-analysis are presented in Table 1.

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 (Higgins and Green, 2006; Ng et al., 2006; Sutton and Higgins, 2008; Tang and Liu, 2000). Funnel plots demonstrate symmetry for all outcomes except 'total complications'. This suggests publication bias occur within this meta-analysis in the total complications outcome, but is absent from the other assessed variables (Hedges and Olkin, 1985; Higgins and Thompson, 2002). However the number of studies included in the funnel plots are inadequate to sensitively detect a study bias (Hedges and Olkin, 1985; Huedo-Medina et al., 2006).

None of the 15 included studies achieved a modified Jadad score of over three (range 1 to 3, median 2). Six studies described the method of randomization (Carr et al., 1996; Han-Geurts et al., 2007; Han-Geurts et al., 2001; Nessim et al., 1999; Stewart et al., 1998), six reported on withdrawals (Carr et al., 1996; Han-Geurts et al., 2007; Ortiz, Armendariz and Yarnoz, 1996; Ryan, Page and Babcock, 1981; Schroeder et al., 1991; Stewart et al., 1998), and one study (Beier-Holgersen and Boesby, 1996) reported on blinding. Jadad scores are reported in Table 1.

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

A statistically significant forty-five percent reduction in relative odds of total postoperative complications were observed in patients receiving early postoperative feeding (OR 0.55 CI 0.35, 0.87, p=0.01, Q=29.07, p=0.01, I^2 = 51.8%, CI 13, 73%). Early feeding was not associated with significant effects on anastomotic dehiscence (OR 0.75, CI 0.39, 1.4, p=0.39, Q=3.31, p=0.99 , I^2 = 0%, CI 0, 0%), mortality (OR 0.71, CI 0.32,1.56, p= 0.39, Q=4.24 , p= 0.99, I^2 = 0%, CI 0, 0%), resumption of bowel function as evidenced by days to passage of flatus (WMD -0.42, CI -1.12, 0.28, p=0.23, Q=75.6 , p<0.0001, I^2 = 96%, CI 29, 98%) and first bowel motion (WMD-0.28, CI -1.20, 0.64, p=0.55, Q=79 , p<0.001, I^2 = 96%, CI 93, 98%), and reduced length of stay (WMD -1.28, CI -2.94, 0.38, p=0.13, Q=61 , p<0.001, I^2 = 85%, CI 75, 91%). A non-statistically significant reduction in the odds of requiring nasogastric tube reinsertion was seen for traditional feeding practices (OR 1.48, CI 0.93, 2.35, p=0.10, Q= 3.24, p=0.86, I^2 = 0%, CI 0, 30%).

The intervention effects of early postoperative feeding were more pronounced in pre-2000 studies when 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 length of hospital stay. Only studies pre-2000 reported on incidence of nausea and vomiting, with no significant differences observed between intervention groups (OR 0.93, CI 0.53, 1.65, p=0.8). Sample forest plots are presented in Figures 1 and 2.

Table 1 – Summary of included studies

Study	Patient population	n (trad early)	Jadad Score	Early feeding protocol
Sagar et al. (1979)	Major intestinal surgery – oesophagogastrectomy (n=2), gastrectomy (n=6), colectomy, anterior resection, abdominoperineal resection	15/15	1	½ strength Flexical (elemental feed product) @ 25ml/hr for 24hrs D1 post op, full strength Flexical @ 25ml/hr for 24hrs D2 post op, full strength Flexical @ 50ml/hr for 24hrs D3 post op, full strength Flexical @ 100mL/hr D4 post op via jejunal port of nasogastric/jejunal tube
Ryan et al. (1981)	Partial colectomy	7/7	2	Vivonex HN (elemental feed product) 10% w/v @ 50mL/hr on day of operation, 10% w/v @100mL/hr D1 post op, 10% w/v @125mL/hr D2, 15% w/v @ 125mL/hr D3, 20% w/v @ 125mL/hr D4, 20% w/v @ 125mL/hr D5, 25% w/v @ 125mL/hr D6 & D7
Schroeder et al. (1991)	Small or large bowel resections or reanastomosis – colonic resection, abdominoperineal resection, ileoanal J pouch, small bowel resection	16/16	2	50mL/hr Osmolite day of operation, 80mL/hr Osmolite if tolerated thereafter. Oral intake D3 post op
Binderow et al. (1994)	Laparoscopic assisted Laparotomy with colonic or ileal resection	32/32	1	Regular diet from D1 post op
Beier-Holgersen et al. (1996)	Gastrointestinal disease treated with bowel resection with anastomosis, enterostomy, gastric (n=5) or oesophageal resection (n=3).	30/30	2	Clear fluids orally + increasing volumes of nutridrink via nasojejunal tube from day of surgery

Table 1 (Cont.) – Summary of included studies

Carr et al. (1996)	Unspecified intestinal surgery	14/14	3	Immediate post op nasojenunal feeding – 25ml/hr Fresubin (1kcal/mL) and increased by 25ml/hr q4h until individual caloric goals met
Ortiz et al. (1996)	Laparotomy for colon or rectal surgery	95/93	2	Clear fluids on day of surgery (?pre/post op), Regular diet from D1 post op
Hartsell et al. (1997)	Open colorectal surgery	29/29	1	Full liquid diet D1 post op, regular diet once tolerating >1L in 24hrs
Nessim et al. (1999)	Anorectal reconstructive surgery	27/27	2	Regular diet from D1 post op
Stewart et al. (1998)	Colorectal resection with anastomosis and without stoma formation	40/40	3	Free fluids from 4 hours post op on day of surgery, Regular diet from D1 post op
Han-Geurts et al. (2001)	Abdominal surgery (vascular + colonic)	49/56	2	Regular diet from D1 post op
Delaney et al. (2003)	segmental intestinal or rectal resection by laparotomy, including reoperation or pelvic surgery and those with comorbidities	33/31	2	Fluid diet D1 post op with regular diet in PM of D1 post op
Lucha et al. (2005)	Open colorectal surgery	25/26	1	Regular diet from 8hrs day of surgery
Zhou et al. (2006)	Excision and anastomosis for colorectal tumour	155/161	1	Liquid fibreless diet D1-3 post op
Han-Geurts et al. (2007)	Open colorectal surgery	50/46	3	Regular diet from D1 post op

Values in left panel are observed counts for early and traditional feeding, odds ratio and limits of 95% confidence intervals for odds ratio of the outcome variable. In the graph, squares indicate point estimates of treatment effect (odds ratio for early over traditional groups) with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% confidence interval for odds ratio of individual studies. The pooled estimate for the complication rate is the pooled odds ratio, obtained by combining all odds ratio of the 15 studies using the inverse variance weighted method. The 95% confidence interval for the pooled estimate is represented by the diamond and the length of the diamond depicts the width of the confidence interval. Values to the left of the vertical line favour early feeding.

Figure 1: Odds ratio for complication (nausea and vomiting excluded)

Study	Early	Traditional	OR	L	U
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**

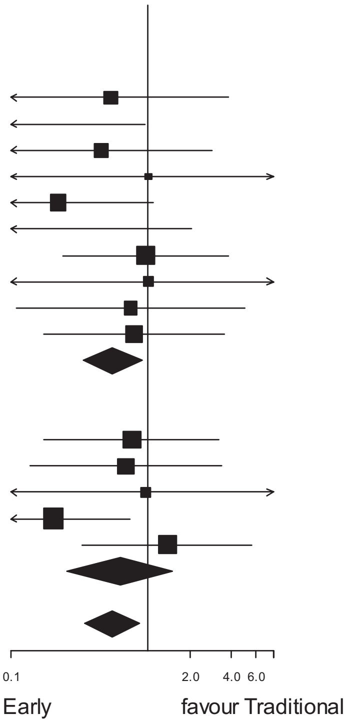
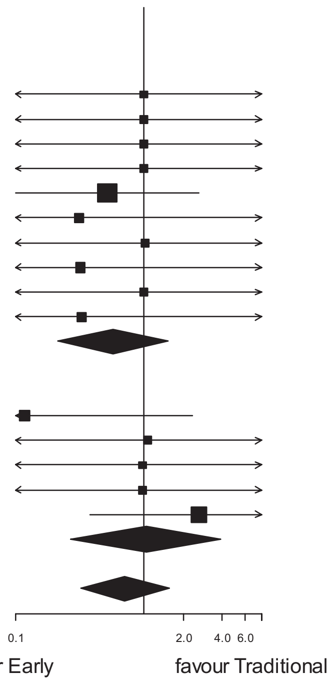


Figure 2: Odds ratio for mortality

Study	Early	Traditional	OR	L	U
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**



Values in left panel are observed counts for early and traditional feeding, odds ratio and limits of 95% confidence intervals for odds ratio of the outcome variable. In the graph, squares indicate point estimates of treatment effect (odds ratio for early over traditional groups) with the size of the squares representing the weight attributed to each study. The horizontal lines represent 95% confidence interval for odds ratio of individual studies. The pooled estimate for the mortality rate is the pooled odds ratio, obtained by combining all odds ratio of the 15 studies using the inverse variance weighted method. The 95% confidence interval for the pooled estimate is represented by the diamond and the length of the diamond depicts the width of the confidence interval. Values to the left of the vertical line favour early feeding.

4. COMMENTS AND CONCLUSION

This meta-analysis re-enforces previous findings that traditional postoperative feeding practices confer no benefit in terms of outcomes following gastrointestinal resectional surgery (Andersen et al., 2006; Lewis et al., 2008; Lewis et al., 2001). 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: this is the first meta-analysis to demonstrate this. In the stratified results most outcomes observed (total complications, mortality, anastomotic dehiscence, days to passage of flatus and bowel motion, length of stay) results were seen to more strongly favour early feeding in the pre-2000 subgroup than in the post-2000 studies. This may be explained by the greater statistical power present in the pre-2000 subgroup due to 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. Other possible explanations include the possibility of a greater quantity of nutrition provided to patients in the pre-2000 by virtue of the higher number of studies utilizing tube feeding rather than voluntary oral intake; differences arising from changes to perioperative practice over the 28 years encompassed by the included studies; or unexplained differences in results from the two Dutch studies included in the post-2000 subgroup.

There are a number of limitations associated with this meta-analysis. Firstly 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 (Delaney et al., 2003; Hartsell et al., 1997; Stewart et al., 1998; Zhou et al., 2006) assumptions relating to the interpretation of various aspects of their published reports were made, such as the composition of the fluid diets reported (Delaney et al., 2003; Hartsell et al., 1997; Zhou et al., 2006), or discrepancies in the reporting within the paper (Stewart et al., 1998). Therefore while every attempt has been made to ensure analysed studies meet inclusion criteria and that other data are accurate, there may still be inconsistencies between the studies included.

Secondly the studies that met inclusion criteria for this meta-analysis consistently yielded poor scores for methodological quality using the Jadad scoring system (Jadad et al., 1996). Out of a possible score of five, a mean score of 1.9 was achieved, with a maximum score of three. 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- and post-2000 scores (pre 2.0, post 1.8, NS).

Thirdly, there currently exist some limitations to the application of meta-analysis to both surgical and nutrition research at the present time. Examples of areas where more statistical research and modelling are required as highlighted by the current work include: (i) improved methods to detect publication bias, particularly when random effects models of meta-analysis are applied, and where the meta-analysis is comprised of a small number of studies, (ii) development of tests for heterogeneity with improved sensitivity to detect between-study variation in circumstances where small numbers of studies are involved, (iii) empirical investigation into the effect of assuming normal distribution during the application of random effects model of meta-analysis, (iv) guidance on investigation of heterogeneity in the circumstances where a small number of studies make subgroup analysis, meta-regression and other methods of sensitivity analysis difficult or invalid, and (v) further investigation on the effect of methodological quality on the influence of effect size in areas of surgery and nutrition.

In conclusion 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, length of stay 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 gastrointestinal surgery.

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