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Review

Enteral vs total parenteral nutrition following major upper gastrointestinal surgery

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ABSTRACT

A best evidence topic in surgery was written according to a structured protocol. The question addressed was in patients undergoing elective major upper gastrointestinal surgery requiring post-operative nutritional support, does enteral feeding as compared to total parenteral feeding confer any clinical benefits. Thirty-two papers were identified by a search of the Medline and Embase databases, of which seven represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group, study group, relevant outcomes and results of these papers were tabulated. All seven of these papers were randomised controlled trials which demonstrated enteral nutrition to be associated with shorter hospital stay, lower incidence of severe or infectious complications, lower severity of complications and decreased cost as compared to parenteral nutrition. For patients undergoing elective major upper gastrointestinal surgery requiring post-operative nutritional support, enteral feeding should be considered as the most desirable form of post-operative feeding.

1. Introduction

A best evidence topic was constructed according to a structured protocol as described in a previous publication.[1]

2. Clinical scenario

You are in a multi-disciplinary meeting discussing a patient scheduled to undergo pancreatic resection for cancer. He has lost approximately one stone in weight over the last two months and it is agreed that he requires post-operative nutritional support. A member of the MDT suggests that this support should be provided by enteral as opposed to the parenteral route. You resolve to check the literature to determine whether or not immediate post-operative enteral feeding confers any clinical benefit as compared to total parenteral nutrition.

3. Three-part question

In patients undergoing major elective upper GI surgery requiring post-operative nutritional support, does immediate post-operative enteral feeding as compared to total parenteral nutrition (TPN) confer any clinical benefits?

4. Search strategy

4.1. Using the Medline and Embase interfaces

Key words – "upper gastrointestinal surgery", esophageal, esophagus, oesophagus, oesophageal, gastric, pancreatic, biliary, hepatic, small bowel, small intestine, enteral feeding, parenteral feeding, enteral nutrition, surgery, resection.

Mesh terms – BILIARY TRACT SURGICAL PROCEDURES *ESOPHAGECTOMY/OR *GASTRECTOMY/OR *GASTROSTOMY/OR *HEPATECTOMY/OR *PANCREATECTOMY *ENTERAL NUTRITION *PARENTERAL NUTRITION, TOTAL.

In addition, the reference lists of relevant papers were searched. The search was current as of August 2011.

5. Search outcome

Thirty-two papers were found using the reported search. From these seven randomised controlled trials comparing TPN and enteral feeding were identified and selected as representing the best evidence to answer this clinical question.

6. Results

The results of these seven papers are summarised in Table 1.

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Table 1
Summary of clinical evidence.

Author, date and country	Study type and level of evidence	Patient group	Outcomes	Key results	Comments
Braga et al. [2] 2001 Italy	Prospective, randomised trial level II	257 pts undergoing gastrectomy ($n = 121$), pancreatectomy ($n = 110$), or oesophagectomy ($n = 26$) were randomized to receive post-operative TPN ($n = 131$) or SEN ($n = 126$)	Length of stay (days)	TPN 20.7 +/−8.8 vs EEN 19.9 +/−8.2 (no significant difference)	Although this study included well-nourished elective surgical patients, a post hoc analysis of the subgroup of malnourished patients showing that overall complication rate was lower in the EEN group as compared with the TPN group (37.1% vs 52.0%; $p = 0.23$).
			Infectious complications	TPN 30 (22.9%) vs EEN 25 (19.8%) (no significant difference)	
			Non infectious complications	TPN 23 (17.5%) vs EEN 20 (15.8%) (no significant difference	
			Mortality	TPN 2 (4.1%) vs EEN 1 (2.3%)	Mean cost per day of EEN was almost four-fold less than TPN ($25 vs $90.60; $p < 0.001$).
			Other outcomes		
			Nutritional goal (achieved within 4 days)	TPN 128/131 (97.7%) vs EEN 100/126 (79.3%) ***p* < 0.001**	Overall they recommended EEN as cheaper and lower complications and length of stay in malnourished subset.
			First flatus post-op (days)	TPN 4.6 +/−2.0 vs EEN 2.4 +/−1.3 ***p* = 0.003**	
			First bowel motion post-op (days)	TPN 6.3 +/−2.1 vs EEN 4.2 +/−1.6 ***p* = 0.001**	
Di Carlo et al. [3] 1999 Italy	Prospective, randomised trial level II	100 pts undergoing pancreaticoduodenectomy (PD) for carcinoma of pancreatic head were randomised into standard enteral nutrition (SEN) $n = 35$, enteral immunonutrition (IEN) $n = 33$, or TPN $n = 32$.	Length of stay (days)	TPN 19.3 +/−8.0 SEN 17.8 +/−6.9	This study had three arms − TPN, standard enteral nutrition and immunonutrition.
			Infectious complications	TPN 8/32 (25%) SEN 6/35 (17.2%)	With respect to TPN vs standard enteral nutrition there was no statistical difference with respect to length of stay, infectious and non infectious complications.
			Non infectious complications	TPN 11/32 (34.3%) SEN 8/35 (22.8%)	
			Mortality	TPN 2/32 (6.2%) SEN 0/35 (0%)	
			Other outcomes		
			Total complications	TPN 19/32 (59.5%) SEN 14/35 (40.0%)	Resumption of normal bowel habit was also statistically quicker in the enterally fed groups compared to the TPN group, however this included the pooled results of the immunonutrition and standard enteral feeding group.
			Severity of complications (sepsis score)	TPN 10.4 SEN 7.9	
			Bowel canalization to gas (days)	TPN 3.8 +/−0.9 SEN/IEN (pooled results) 2.9 +/−1.0 $p < 0.05$	
			Bowel canalization to faeces (days)	TPN 6.5 +/−1.7 SEN/IEN 4.4 +/−1.4 $p < 0.05$	
Braga et al. [4] 1998 Italy	Prospective, randomised trial level II	166 pts undergoing curative surgery for gastric or pancreatic cancer were randomised into standard enteral nutrition (SEN) $n = 55$, enteral nutrition enriched with arginine, RNA and omega-3 (EEN) $n = 55$, or TPN $n = 56$	Length of stay (days)	TPN 17.5 ± 6.1 SEN 16.1 ± 5.9	This study had three arms − TPN, standard enteral nutrition and enriched enteral nutrition.
			Infectious complications	TPN 16/56 (28.5%) SEN 13/55 (23.6%)	Early enteral feeding is a suitable alternative to TPN after major abdominal surgery.
			Non infectious complications	TPN 13/56 (23.2%) SEN 7/55 (12.7%)	
			Mortality	None reported	
			Other outcomes		
			Severity of complications (sepsis score)	TPN 8.6 SEN 6.5 EEN 4.0 ***p* < 0.05** (enriched vs TPN group)	With respect to TPN vs standard enteral nutrition there was no statistical difference with respect to length of stay, infectious and non infectious complications.
			Malnourished patient subgroup: Post-op infection rates	EEN 16.0%, SEN 25.9%, TPN 30.7% $p < 0.05$ (EEN vs TPN)	Subgroup analysis of pre-operatively malnourished patients demonstrated that EEN gave a significant reduction of both severity of infection and length of stay as compared with the TPN group.
			Transfused patient subgroups: Post-op infection rates	EEN 20.0%, SEN 38.4%, TPN 42.8% ***p* < 0.05**	Subgroup analysis of patients receiving homologous blood transfusion demonstrated significant advantage of delivering immunomodulatory nutrition.
Gianotti et al. [5] 1997 Italy	Prospective, randomised trial level II	260 pts undergoing pancreaticoduodenectomy or gastrectomy for cancer were randomised to enteral formula (EN $n = 87$), enteral formula enriched with arginine, omega-3 fatty acids, and RNA (immunonutrition (IEN) group $n = 87$), and TPN ($n = 86$)	Length of stay (days)	EN 19.2 +/−7.9 TPN 21.6 +/−8.9	This study had three arms − TPN, standard enteral nutrition and enteral immunonutrition.
			Infectious complications	EN 20/87 (22.9%) TPN 24/86 (27.9%)	Early post-operative enteral feeding is a valid alternative to parenteral feeding in patients undergoing major surgery.
			Non infectious complications	Not commented on	
			Mortality	Not commented on	
			Other outcomes		
			Immune parameters on day 8 post-op (IL-6 and prealbumin)	IEN group had better recovery of the immune parameters on POD 8 with inverse correlation between IL-6 and preambulin levels ($r = 0.766$)	There was no statistical significant difference demonstrated between EN and TPN for length of stay and infectious complications. Immunonutrition enhances the host response, induces a switch from acute-phase to constitutive proteins, and improves outcome.

(*continued on next page*)

Table 1 (*continued*)

Author, date and country	Study type and level of evidence	Patient group	Outcomes	Key results	Comments
Sand et al. [6] 1997 Finland	Prospective, randomised trial level II	29 pts undergoing curative gastrectomy for cancer were randomised into enteral ($n = 13$) and parenteral feeding ($n = 16$)	Length of stay (days) Infectious complications Non infectious complications Mortality (at 45 days) *Other outcomes* Serum CRP at day 6 post-op (g/L)	Not reported EN 3/13 (23%) TPN 5/16 (31%) $p = 0.7$ EN 3/13 (23%) TPN 4/16 (24%) (no significant difference) EN 0/13 (0%) TPN 1/16 (3%) (no significant difference) EN 32 TPN 61 $\boldsymbol{p = 0.02}$	Enteral nutrition post gastrectomy is safe and well tolerated. Enteral nutrition found to influence significantly lower serum CRP post-operatively. Enteral nutrition is significantly cheaper than parenteral nutrition.
Reynolds et al. [7] 1997 UK	Prospective, randomised trial level II	67 pts undergoing surgery for oesophageal, gastric, or pancreatic malignancy were randomised to post-op enteral ($n = 33$) or parenteral ($n = 34$) feeding	Length of stay (days) Infectious complications Non infectious complications Mortality	Not reported TPN 20/34 (58%) EN 13/33 (39.4%) $p = 0.4$ TPN 17/34 (50%) EN 13/33 (39.4%) $p = 0.3$ TPN 1/34 (2.9%) EN 2/33 (6.1%) $p = 0.6$	Major upper GI surgery increases gut permeability and thus systemic exposure to endotoxin, however this is not influenced by enteral feeding. No reduction in septic morbidity or improvement in clinical outcome observed with EN. EN 10 times cheaper than TPN but this was the only basis on which it could be recommended.
Baigrie et al. [8] 1996 Australia	Prospective, randomised trial level II	97 pts undergoing oesophagectomy or gastrectomy were randomised into TPN started day 1 post-op ($n = 47$) or EN started day 3 post-op ($n = 50$)	Length of stay Infectious complications Non infectious complications Mortality	Not reported TPN 10/47 (21.3%) EN 3/50 (6%) TPN 38/47 (80.8%) EN 33/50 (66%) TPN − 6 (13%): Respiratory failure 3 (6%) MI/arrest 1 (2%) Anastamotic leak (fatal) 1 (2%) CVA 1 (2%) EN group − 4 (8%): Respiratory failure 1 (2%) MI/arrest 1 (2%) Anastamotic leak (fatal) 2 (4%)	EN demonstrated to be safe. Although rates of catheter-related complications were similar, there were 9 cases requiring active intervention. The EN complications were comparatively minor and rarely required intervention. TPN is ten times more expensive than EN, and requires more sophisticated nursing/biochemical monitoring. EN should be preferred to TPN for post-op feeding.

7. Discussion

It is well-established that upper gastrointestinal (GI) resectional surgery for malignancy is associated with considerable post-operative morbidity and mortality. This, in conjunction with the fact that patients undergoing surgery for cancer are frequently per-operatively malnourished, means that early nutritional support is often required. In terms of the technique used to provide post-operative nutritional support, this can be delivered enterally (via a naso–jejunal or percutaneous approach), or parenterally via venous access. Advocates of enteral feeding argue that the small bowel recovers its ability to absorb nutrients almost immediately following surgery, even in the absence of peristalsis.[9,10] Nevertheless, many surgeons traditionally preferred the parenteral as opposed to the enteral route to administer nutrients after surgery, citing the need to protect the newly formed anastomosis. To date seven randomised controlled trials have compared parenteral and enteral feeding post-operatively in patients undergoing major upper GI surgery for a number of pathologies.

Baigrie et al.[8] presented their paper that randomised a cohort of 97 patients into feeding with TPN at day 1 post-op ($n = 47$), and enteral feeding via jejunostomy sited peri-operatively initially with dextrose on day 3, then feeding compound from day 4 ($n = 50$). Their study showed there to be no statistical difference in mortality, or catheter-related complications although the EN catheter-related complications were Less severe than those in the TPN group. The TPN group also encountered significantly more non-catheter-related complications and a higher proportion of life-threatening complications that the EN group. They concluded that EN was ten times cheaper than TPN and was associated with a lower incidence of complications and postulated this reduction in post-operative septic complications may be due conservation of the GI tract lining.

In their study of sixty-seven patients undergoing surgery for oesophageal, gastric, or pancreatic malignancy, Reynolds et al.[7] randomised their cohort to post-operative enteral feeding ($n = 33$) via needle catheter jejunostomy inserted at time of operation and continued for seven days, or parenteral ($n = 34$) feeding started immediately post-operatively and continued for seven days. Their study showed no significant reduction in septic morbidity, non infectious complications, or mortality. They did however note that enteral nutrition was ten times cheaper than parenteral nutrition, and concluded that on this basis alone could it be recommended.

Sand et al.[6] studied a group of twenty-nine patients who underwent curative gastrectomy for cancer. These were randomised into enteral feeding via naso–jejunal tube ($n = 13$) and parenteral feeding ($n = 16$). They came to much the same conclusions as Reynolds et al., finding there to be no statistical difference in infectious complications, non infectious complications, or mortality at 45 days. They did find that the EN group had a significantly lower CRP on six days post-surgery, although did not comment on the significance of this. They felt that enteral nutrition after gastrectomy was both safe and well tolerated, as well as being significantly cheaper than parenteral nutrition.

Ginaotti et al.[5] studied a group of 260 patients undergoing pancreaticoduodenectomy or gastrectomy for cancer. These were randomised to feeding with enteral formula (EN $n = 87$), enteral formula enriched with arginine, omega-3 fatty acids, and RNA

(immunonutrition (IEN) group $n = 87$), and total parenteral nutrition (TPN $n = 86$). They showed no significant statistical difference with respect to length of stay and rates on infectious complications between the enteral nutrition and TPN groups. However they did find that the group receiving immuno-enriched feeding had a significantly shorter hospital stay compared with standard enteral feed and even more so compared with TPN. They also showed that the immunonutrition group had lower rates of post-operative infection, although this did not reach statistical significance. They concluded that early post-operative enteral feeding was a valid alternative to parenteral feeding in patients undergoing major surgery whilst enteral immunonutrition improves outcomes as compared to both standard enteral nutrition and TPN.

Braga et al.[4] studied a group of 166 patients undergoing curative surgery for gastric or pancreatic cancer were randomised into groups similar to Gianotti et al.; those receiving standard enteral nutrition (SEN $n = 55$), enriched enteral nutrition with additional arginine, RNA and omega-3 (EEN $n = 55$), or total parenteral nutrition (TPN $n = 56$). They failed to demonstrate any significant improvement in the length of stay or rates of complications between the TPN and SEN groups. They did however show a statistically significantly lower severity of complications in the enriched enteral nutrition group compared to those receiving TPN, a pattern which was particularly pronounced in patients known to be malnourished pre-operatively and those requiring post-operative transfusion. They concluded that early enteral feeding is a suitable alternative to TPN after major abdominal surgery and that enriched enteral feeding diets should be recommended, particularly in high-risk surgical patients.

Di Carlo et al.,[3] working in the same unit as Braga and Gianotti produced a study looking at 100 patients undergoing pancreaticoduodenectomy (PD) for carcinoma of the pancreatic head. They randomised their cohort into groups receiving standard enteral nutrition (SEN $n = 35$), enteral immunonutrition (IEN $n = 33$), or total parenteral nutrition (TPN $n = 32$). There was no statistical difference with respect to length of stay, infectious and non infectious complications when TPN was compared to standard enteral nutrition. They did however show that patients receiving enteral immunonutrition had a significantly shorter length of stay, a lower rate of infectious complications, and rate of total complications when compared with TPN. In addition, when comparing the pooled results of the groups receiving either standard enteral and immunonutrition vs TPN, they demonstrate a significant decrease in severity of sepsis, and length of time of canalisation to production of flatus and faeces. Their results showed that nutritional goals post pancreaticoduodenectomy can be achieved by enteral feeding, and they concluded that enteral nutrition is feasible and a good alternative to TPN, and TPN should be limited to only patients with severe intolerance to EN.

Finally, a further group led by Braga in 2001[2] looked at 257 patients undergoing gastrectomy ($n = 121$), pancreatectomy ($n = 110$), or oesophagectomy ($n = 26$) who they randomized to receive post-operative TPN ($n = 131$) or early standard enteral nutrition (SEN $n = 126$). They did not demonstrate any statistical benefit of SEN over TPN in length of stay, rate of complications (infectious and non infectious) or mortality. They showed that a greater proportion of patients achieved their nutritional goals within 4 days in the TPN group however the SEN group were significantly quicker to resumption of bowel function. A *post hoc* analysis performed in the subgroup of malnourished patients showed that overall complication rate was lower in the SEN group compared to the TPN group. They concluded that in well-nourished elective surgical patients, artificial nutrition by any route is an auxiliary therapy, although SEN is cheaper and has lower rates of complications and length of stay in the malnourished subset.

8. Clinical bottom line

Enteral feeding immediately following major upper GI surgery is a suitable alternative to parenteral feeding. Although enteral feeding does not seem to offer significant benefit in rates of complications or mortality, it does appear to decrease the length of hospital stay and time to resumption of normal bowel habit. Furthermore it is significantly cheaper than TPN, and in the subset of malnourished patients, its benefits are increased and thus should be considered as the preferred method for delivery of post-operative nutrition.

Conflict of interest
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Not applicable.

Author contribution
George Wheble – Literature search, analysis, writing
William Knight – Literature search, analysis and editing of manuscript
Omar Khan – Analysis and editing of manuscript

References

1. Khan OA, Dunning J, Parvaiz AC, Agha R, Rosin D, Mackway-Jones K. Towards evidence-based medicine in general surgical practice: best BETs. *Int J Surg* 2011;**9**:585–8.
2. Braga M, Gianotti L, Gentilini O, Parisi V, Salis C, Di Carlo V. Early postoperative enteral nutrition improves gut oxygenation and reduces costs compared with total parenteral nutrition. *Crit Care Med* 2001;**29**:242–8.
3. Di Carlo V, Gianotti L, Balzano G, Zerbi A, Braga M. Complications of pancreatic surgery and the role of perioperative nutrition. *Dig Surg* 1999;**16**:320–6.
4. Braga M, Gianotti L, Vignali A, Cestari A, Bisagni P, Di Carlo V. Artificial nutrition after major abdominal surgery: impact of route of administration and composition of the diet. *Crit Care Med* 1998;**26**:24–30.
5. Gianotti L, Braga M, Vignali A, Balzano G, Zerbi A, Bisagni P, et al. Effect of route of delivery and formulation of postoperative nutritional support in patients undergoing major operations for malignant neoplasms. *Arch Surg* 1997;**132**:1222–9.
6. Baigrie RJ, Devitt PG, Watkin DS. Enteral versus parenteral nutrition after oesophagogastric surgery: a prospective randomized comparison. *ANZ J Surg* 1996;**66**:668–70.
7. Reynolds JV, Kanwar S, Welsh FK, Windsor AC, Murchan P, Barclay GR, et al. Does the route of feeding modify gut barrier function and clinical outcome in patients after major upper gastrointestinal surgery? *J Parenter Enter Nutr* 1997;**21**:196–201.
8. Sand J, Luostarinen M, Matikainen M. Enteral or parenteral feeding after total gastrectomy: prospective randomised pilot study. *Eur J Surg* 1997;**163**(10):761–6.
9. Wells C, Tinckler LF, Rawlinson K. Postoperative gastrointestinal motility. *Lancet* 1964;**1**:14–8.
10. Jolliet P, Pichard C, Biolo G, Chioléro R, Grimble G, Leverve X, et al. Enteral nutrition in intensive care patients: a practical approach. *Int Care Med* 1998;**24**: 848–59.