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Prospective, Randomized Trial on the Effect of Cyclic *Versus* Continuous Enteral Nutrition on Postoperative Gastric Function After Pylorus-Preserving Pancreatoduodenectomy

Mark I. van Berge Henegouwen, M.D.,* Louis M. A. Akkermans, Ph.D.,†
Thomas M. van Gulik, M.D.,* A. A. M. Masclee, M.D.,‡ Thybout M. Moojen,*
H. Obertop, M.D.,* and D. J. Gouma, M.D.*

*From the *Department of Surgery, Academic Medical Center, University of Amsterdam; †Department of Surgery, University Hospital, University of Utrecht; and ‡Department of Gastroenterology, Academic Hospital, University of Leiden, The Netherlands*

Objective
The effect of a cyclic *versus* a continuous enteral feeding protocol on postoperative delayed gastric emptying, start of normal diet, and hospital stay was assessed in patients undergoing pylorus-preserving pancreatoduodenectomy (PPPD).

Summary Background Data
Delayed gastric emptying occurs in approximately 30% of patients after PPPD and causes prolonged hospital stay. Enteral nutrition through a catheter jejunostomy is used to provide postoperative nutritional support. Enteral infusion of fats and proteins activates neurohumoral feedback mechanisms and therefore can potentially impair gastric emptying and prolong postoperative gastroparesis.

Methods
From September 1995 to December 1996, 72 consecutive patients underwent PPPD at the Academic Medical Center, Amsterdam. Fifty-seven patients were included and randomized for either continuous (CON) jejunal nutrition (0–24 hr; 1500 kCal/24 hr) or cyclic (CYC) enteral nutrition (6–24 hr; 1125 kCal/18 hr). Both groups had an equal caloric load of 1 kCal/min. The following parameters were assessed: days of nasogastric intubation, days of enteral nutrition, days until normal diet was tolerated orally, and hospital stay. On postoperative day 10, plasma cholecystokinin (CCK) levels were measured during both feeding protocols.

Results
Nasogastric intubation was 9.1 days in the CON group (n = 30) and 6.7 days in the CYC group (n = 27) (not statistically significant). First day of normal diet was earlier for the CYC

group (15.7 *vs.* 12.2 days, $p < 0.05$). Hospital stay was shorter in the CYC group (21.4 *vs.* 17.5 days, $p < 0.05$). CCK levels were lower in CYC patients, before and after feeding, compared with CON patients ($p < 0.05$).

Conclusions

Cyclic enteral feeding after PPPD is associated with a shorter period of enteral nutrition, a faster return to a normal diet, and a shorter hospital stay. Continuously high CCK levels could be a cause of prolonged time until normal diet is tolerated in patients on continuous enteral nutrition. Cyclic enteral nutrition is therefore the feeding regimen of choice in patients after PPPD.

Today, the pylorus-preserving pancreatoduodenectomy (PPPD) is generally accepted as the preferred procedure for pancreatic head cancer. Mortality is reported to be <5%,[1-5] although there still is a substantial morbidity of 20% to 60%.[1-3,6] Morbidity consists mainly of complications such as leakage of the pancreaticojejunal anastomosis, gastrointestinal or intraabdominal hemorrhage, and intraabdominal abscesses.[7-10] It was thought that the incidence of another complication, delayed gastric emptying, was higher after PPPD than after the standard Whipple's procedure,[11,12] but this was not confirmed in later reports.[3,13-15] Delayed gastric emptying occurs in approximately 30% of patients after pancreatoduodenectomy and is a major cause of prolonged hospital stay.[8,13,16] This complication has been related to the occurrence of intraabdominal complications and, according to some reports, to preexisting diabetes mellitus.[17,18]

Several pathophysiologic mechanisms have been proposed to play a role in the occurrence of delayed gastric emptying after pancreatoduodenectomy, including gastroparesis secondary to intraabdominal abscesses or other intraabdominal complications[17,19]; interruption of the gastrointestinal nervous plexus and resection of the duodenal pacemaker[20,21]; ischemia and intraoperative trauma to the pyloric muscle[22,23]; and resection of the duodenum, causing a decrease in gastrointestinal hormone levels and especially motilin, which plays an important role in regulating interdigestive motility. This could give rise to postoperative atony of the gastric antrum.[24,25] Another potential contributor to this complication is the administration of continuous enteral nutrition through a needle catheter jejunostomy. Several randomized studies have reported a benefit of immediate postoperative enteral nutrition in patients undergoing major gastrointestinal surgery.[26-28] Infusion of nutrients causes a delay in gastric emptying through the activation of gastroduodenal feedback mechanisms, as studied extensively in animals and in healthy volunteers.[29-33] These effects are partly mediated by cholecystokinin (CCK). Therefore, we hypothesized that continuous enteral nutrition causes prolonged gastroparesis through continuous activation of jejunogastric feedback mechanisms. This mechanism could be suppressed by administering enteral nutrition in a cyclic pattern—for example, by discontinuing the feeding during the night.

In this randomized study, we investigated two nutritional protocols: a continuous enteral feeding protocol (24 hr/day) and a cyclic feeding protocol in which enteral nutrition was stopped for 6 hours during the night. We evaluated the effects on the incidence of delayed gastric emptying, number of days until normal diet was tolerated orally, and hospital stay. We also investigated gastrointestinal hormone levels (CCK and pancreatic polypeptide [PP]) and small bowel transit time (SBTT) in relation with both enteral feeding protocols.

PATIENTS AND METHODS

Patients

This study was approved by the medical ethics committee of the Academic Medical Center. All patients enrolled in the study had given their signed informed consent preoperatively. All patients were randomized for either continuous or cyclic enteral nutrition on the first postoperative day, before the start of enteral nutritional support. Criteria for inclusion are listed in Table 1.

From September 1995 to December 1996, 72 consecutive patients underwent pancreatoduodenectomy at the Academic Medical Center, Amsterdam. Overall mortality was 1.4%. Only patients who had undergone PPPD were enrolled in the study. Fifteen patients were excluded because of previous gastric resection (n = 3); a standard Whipple's resection (n = 2); early postoperative complications, precluding the start of enteral nutrition on postoperative day 2 (n = 3); or patient refused or not recruited (n = 7).

PPPD was performed using one jejunal loop for restoration of gastrointestinal continuity, with successively the

Address reprint requests to Prof. Dr. D. J. Gouma, Department of Surgery, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands; phone: +31.20.5662166; fax: +31.20.6914858; E-mail: m.i.vanberge-henegouwen@amc.uva.nl

Table 1. CRITERIA FOR THE INCLUSION OF PATIENTS IN THE STUDY

Patients with pancreatic or periampullary malignancies undergoing PPPD
Patients over 18 years of age
Oral and written consent
No prior gastric surgery
No prior chemotherapy/radiotherapy
No direct postoperative complication precluding start of enteral nutrition

PPPD = pylorus-preserving pancreatoduodenectomy.

pancreaticojejunal anastomosis, the biliary anastomosis, and the duodenal anastomosis. The pancreaticojejunal anastomosis was performed in one running layer (PDS 3-0), without drainage of the pancreatic duct. According to some surgeons' preference, a T-tube was placed for external biliary drainage. All patients received perioperative octreotide (Sandostatin; Novartis Pharma B.V., Arnhem, The Netherlands) 100 μg, 3 times daily, from 1 hour before surgery until 6 days after surgery.

Continuous *Versus* Cyclic Enteral Nutrition

All patients received a needle catheter jejunostomy at the end of the operation for postoperative nutritional support. This needle catheter jejunostomy was performed 10 to 30 cm distal to the duodenojejunal anastomosis.

Enteral nutrition was started on the first postoperative day using Nutrison enteral nutrition (Nutricia, Zoetermeer, The Netherlands; contents: 4 g fat, 4 g protein, 12 g carbohydrate, 100 kCal [420 kJ]/100 mL), with a gradual increase during the first 4 days to a maximum of 1500 mL/day.

Patients randomized for continuous enteral nutrition (CON) received 1500 kCal (6300 kJ)/24 hr from day 4 onward; patients randomized for cyclic enteral nutrition (CYC) received nutrition during 18 hours a day, from 6 A.M. to midnight. These patients received a total of 1125 kCal (4725 kJ)/24 hr from day 4 onward. Both groups received an exactly equal caloric load of 1 kCal (4.4 kJ)/min during administration of enteral nutrition.

Both groups were compared with respect to incidence of postoperative delayed gastric emptying, days of nasogastric intubation and jejunal catheter feeding, days until normal diet was tolerated orally, and hospital stay.

The nasogastric tube was removed when gastric retention was <300 mL/24 hr. After removal of the nasogastric tube, patients received a liquid oral diet. Regular diet was started when patients had responded well to the liquid diet during 1 day. This was determined by the ward surgical residents, who were unaware of the nature of the nutritional protocol (continuous or cyclic nutrition). Enteral nutrition was stopped when patients could fulfill their caloric needs orally.

A subanalysis was performed in all patients in whom enteral feeding was completed. A completed feeding protocol was defined as a feeding protocol that was not interrupted because of either technical problems or intraabdominal complications. Patients in whom feeding was stopped were excluded from the subanalysis.

Intraoperative Parameters and Postoperative Complications

Operative time (hours), estimated intraoperative blood loss (milliliters), and transfusions (units of packed red blood cells) were assessed, as well as histopathologic diagnosis and tumor ingrowth into the resection margins in case of malignancy. A microscopically radical resection was defined as both tumor-free resection and dissection margins of the specimen on histopathologic examination.

Overall morbidity and mortality rates were evaluated, including procedure-related complications such as pancreatic leakage, biliary leakage, hemorrhage, and intraabdominal abscesses. General complications that were evaluated were pulmonary, cardiac, and renal complications. Postoperative morbidity was defined as procedure- or

Table 2. PATIENTS' CHARACTERISTICS, PREOPERATIVE FACTORS, AND PREOPERATIVE LABORATORY VALUES*

	Continuous Enteral Nutrition (n = 30)	Cyclic Enteral Nutrition (n = 27)
Patients' characteristics		
M/F	20/10	16/11
Age (yr) [median (range)]	61 (38–76)	67 (37–78)
Preoperative factors		
Preoperative biliary drainage	27 (90%)	22 (81%)
Diabetes mellitus	5 (17%)	7 (26%)
Prior abdominal surgery	7 (23%)	6 (22%)
Preoperative laboratory values		
Bilirubin (mg/dL) [median (range)]	0.8 (0.3–25)	0.7 (0.3–8.2)
Albumin (g/dL) [median (range)]	4.2 (2.5–5.0)	3.2 (2.7–5.9)

* There were no significant differences between the two groups.

Table 3. INTRAOPERATIVE FACTORS, PLACEMENT OF BILIARY T-TUBE, AND HISTOPATHOLOGY

	Continuous Enteral Nutrition (n = 30)	Cyclic Enteral Nutrition (n = 27)
Intraoperative factors		
Operative time (hr) [median (range)]	4.5 (2.7–9.1)	4.3 (2.6–8.3)
Estimated blood loss (mL) [median (range)]	1000 (50–3500)	1100 (300–4500)
Transfusions (units PRBC) [median (range)]	1 (0–4)	1 (0–9)
Placement of biliary T-tube		
Yes	2 (7%)	3 (11%)
No	28 (93%)	24 (89%)
Histopathological diagnosis		
Pancreatic carcinoma	12 (40%)	11 (41%)
Ampullary carcinoma	9 (30%)	9 (33%)
Distal common bile duct carcinoma	3 (10%)	5 (19%)
Other malignancy	3 (10%)	1 (4%)
Chronic pancreatitis	3 (10%)	1 (4%)
Microscopic radicality of resection (in case of malignancy)		
Radical	19/27 (70%)	17/26 (65%)
Nonradical	11/27 (30%)	9/26 (35%)

PRBC = packed red blood cells.
* There were no significant differences between the two groups.

nonprocedure-related complications requiring medical or surgical intervention or readmission to the intensive care unit, causing prolonged hospital stay or leading to postoperative death. Mortality was defined as death during hospital stay. Delayed gastric emptying was defined as gastric stasis, requiring nasogastric intubation for 10 days or more, or the inability to tolerate a regular diet on or before the 14th postoperative day.

Gastrointestinal Hormone Profile

On the 10th postoperative day, gastrointestinal hormone response (CCK and PP) and SBTT were analyzed. Day 10 was chosen to allow a washout period for octreotide, which was administrated until postoperative day 6 and which is known to interfere with gastrointestinal hormone secretion and transit time.[34,35] Hormone assays and SBTT were measured in 22 patients undergoing the two enteral feeding regimens (CON, 11 patients; CYC, 11 patients). All 22 patients had undergone the entire feeding protocol and had no evidence of intraabdominal complications. Measurements commenced at T = −15 min (8 A.M.). At T = 0, enteral feeding was started in the CYC patients; feeding was stopped at T = 300 in these patients. In CON patients, feeding was continued; these patients did not experience any stop in feeding protocol. Blood samples were taken at T = −15, 0, 15, 30, 60, 90, 120, 180, 240, 300, 360, 420, and 480 minutes. Blood was collected in ice-chilled tubes and plasma was stored at −30 C until analysis.

Plasma CCK was determined by a sensitive and specific radioimmunoassay using antibody T_{204}.[36] This antibody binds to all carboxy-terminal CCK peptides containing the sulfated tyrosyl region. The detection limit of the assay is 0.3 pmol/L. The intraassay variation ranges from 4.6% to 11.5%, the interassay variation from 11.3% to 26.1%. Plasma PP concentrations were measured by a sensitive and specific radioimmunoassay as described previously.[37]

Small Bowel Transit Time

On day 10, SBTT was measured by means of the hydrogen breath test. Lactulose (Lactulosum; Centrafarm B.V., Etten-Leur, the Netherlands; 25 mL: 16.8 g lactulose) was added to the enteral nutrition at T = 0; end-expiratory volumes of 30 mL were collected every 10 minutes during 300 minutes, and hydrogen concentrations were measured using a lactometer H_2 breath tester (Lactoscreen; Hoek-Loos, Schiedam, The Netherlands). SBTT was defined as the time to an increase of hydrogen concentration above 10 parts per million compared to baseline values during at least two consecutive readings.

Statistical Analysis and Sample Size

In a recent analysis of 100 patients with PPPD, we found that the mean number of days until normal diet

was started was 13.9.[38] To demonstrate a difference between the two enteral feeding protocols of at least 3 days, we estimated that 25 patients would be required per group when a two-sided test was applied to the data with α = 0.05 and β = 0.2. In an intention-to-treat analysis, the feeding regimens were compared. A subanalysis was performed in patients who completed the feeding protocol.

Data representing days of nasogastric intubation, jejunal catheter feeding, days until normal diet, and hospital stay were expressed as median, mean, and range. Statistical analysis was performed using Mann Whitney U analysis, chi square analysis, and two-sided Fisher's Exact test, where applicable. Gastrointestinal hormone (CCK and PP) levels were expressed as mean (±SEM). Differences in hormone levels in time were assessed using one-way analysis of variance. Differences between the two feeding protocols at the sampling points were assessed using Mann-Whitney U analysis. A p value <0.05 was considered statistically significant.

RESULTS

Patients

Fifty-seven patients were enrolled in the study and randomized for continuous (n = 30) or cyclic (n = 27) enteral nutrition. Median age of the entire study group was 64 (range 37–78) years. Both groups were comparable with respect to patient characteristics, preoperative factors, and preoperative laboratory findings (Table 2). Intraoperative factors, the number of patients who had preoperative placement of a T-tube, and histopathologic diagnosis did not differ between the groups (Table 3).

Overall postoperative morbidity in the entire study group was 35% and did not differ between the groups. Five patients (9%) had leakage of the pancreaticojejunal anastomosis. One patient died as a result of necrotizing pancreatitis, subsequent sepsis, and aspiration. Overall mortality was 1.8% (Table 4).

Continuous *Versus* Cyclic Enteral Nutrition (Intention-to-Treat Analysis)

Number of days of nasogastric intubation and days of enteral nutrition did not differ between the groups (p = 0.82 and p = 0.60, respectively). Number of days until normal diet was shorter for CYC patients (15.7 *vs.* 12.2 days, p = 0.04). Hospital stay was shorter for CYC patients (21.4 *vs.* 17.5 days, p = 0.04). All patients in both groups went home after discharge. The overall incidence of delayed gastric emptying was 25% and did not differ between the groups (p = 0.82) (Table 5).

Table 4. INCIDENCE OF POSTOPERATIVE COMPLICATIONS IN BOTH TREATMENT GROUPS

	Continuous Enteral Nutrition (n = 30)	Cyclic Enteral Nutrition (n = 27)
Surgery related complications		
Pancreatic leakage	3 (10%)	1 (4%)
GI/IA hemorrhage	2 (7%)	2 (7%)
IA abscess	4 (13%)	2 (7%)
Necrotizing pancreatitis	1 (3%)	0
Small bowel obstruction	0	1 (4%)
Prolonged abdominal drainage	0	1 (4%)
Wound infection	1 (3%)	0
General complications		
Pulmonary	1 (3%)	2 (7%)
Cardiac	0	1 (4%)
Urinary tract/renal	2 (7%)	2 (7%)
Total number of complications	14	12
Total number of patients with complications*	11 (37%)	9 (33%)
Mortality*	1 (3%)	0

GI = gastrointestinal; IA = intraabdominal.
* Overall morbidity in the entire study group (n = 57) was 35%; overall mortality was 1.8%. There were no significant differences between the two groups.

Continuous *Versus* Cyclic Enteral Nutrition (Subanalysis)

The subanalysis comprised 37 patients (CON, 19; CYC, 18) after excluding 11 CON patients (technical problem in 3 patients; stopped due to intraabdominal complication in 8 patients) and 9 CYC patients (technical problem in 3 patients; stopped due to intraabdominal complication in 6 patients). Patients with technical problems of enteral feeding had either clogged or kinked feeding catheters, as a result of which enteral feeding became impossible. Enteral nutrition was discontinued in all patients with intraabdominal complications for at least 1 day; therefore, these patients were excluded from the subanalysis.

In the subanalysis, the CYC patients had a similar duration of nasogastric intubation (p = 0.70), a shorter period of enteral nutrition (p = 0.03), an earlier start of normal diet (p = 0.03), and a shorter hospital stay (p = 0.02) (Table 6).

Gastrointestinal Hormone Profile

In CYC patients, fasting plasma CCK levels were 1.7 ± 0.3 pmol/L. After starting the enteral nutrition, plasma CCK levels increased significantly in these patients (p =

Table 5. PARAMETERS FOR GASTRIC FUNCTION AND INCIDENCE OF DGE IN ALL PATIENTS (N = 57)

	Continuous Enteral Nutrition (n = 30)			Cyclic Enteral Nutrition (n = 27)			
	Median	Mean	Range	Median	Mean	Range	p
Nasogastric intubation (days)	5.5	9.1	1–65	4	6.7	1–25	0.82
Enteral nutrition (days)	9	10.3	1–28	8	9.3	0–27	0.60
First day of normal diet	11	15.7	5–68	9	12.2	5–38	0.04
Hospital stay (days)	17	21.4	9–73	14	17.5	10–46	0.04
Number of patients with DGE		7 (23%)			7 (26%)		0.82

DGE = delayed gastric emptying; defined as gastric stasis, requiring nasogastric intubation for 10 days or more, or the inability to tolerate a regular (solid) diet on or before the 14th postoperative day.

0.02). In CON patients, CCK levels did not change during testing (p = 0.99). At T = −15, 0, 15, and 480 minutes, plasma CCK levels between the two feeding regimens were significantly different (p = 0.002, p = 0.003, p = 0.03, and p = 0.02, respectively) (Fig. 1). PP levels were low in both groups and did not change during cyclic or continuous enteral feeding (p = 0.84 for continuous and P = 0.99 for cyclic enteral feeding) (Fig. 2).

Small Bowel Transit Time

In 2 patients, no hydrogen response was measured during testing. These patients (1 CON, 1 CYC) were excluded from further SBTT analysis. Overall median SBTT was 120 (range 60–180) minutes: 110 (70–150) minutes for CON patients (n = 10) and 130 minutes (60–180) for CYC patients (n = 10; p = 0.15).

DISCUSSION

In our department, postoperative enteral nutrition is standard treatment in patients undergoing pancreatoduodenectomy. Postoperative nutrition has been shown to benefit patients undergoing major gastrointestinal surgery. In a recent randomized trial, the early start of enteral nutrition was reported to lower the number of infectious complications after elective gastrointestinal surgery compared to patients who did not receive any nutrition.[28] In a number of studies, enteral nutrition is reported to be superior to parenteral nutrition. Especially in critically ill patients, the number of septic complications is lower in enterally fed patients than in parenterally fed patients.[26,27,39] The early start of enteral feeding is thought to maintain gut mucosal integrity and thus to enhance immunologic competence.[40,41]

Postoperative delayed gastric emptying is probably due to a number of factors secondary to the changed pathophysiology of the gastrointestinal tract after pancreatoduodenectomy. Preoperative factors such as diabetes mellitus and prior abdominal surgery have been reported to be involved in the occurrence of delayed gastric emptying, but probably the most important factor causing this complication is the presence of intraabdominal complications.

Table 6. PARAMETERS FOR GASTRIC FUNCTION AND INCIDENCE OF DGE IN PATIENTS WITHOUT A STOP OF THE ENTERAL NUTRITIONAL PROTOCOL (N = 37)

	Continuous Enteral Nutrition (n = 19)			Cyclic Enteral Nutrition (n = 18)			
	Median	Mean	Range	Median	Mean	Range	p
Nasogastric intubation (days)	4	5.8	1–17	3	4.4	2–12	0.70
Enteral nutrition (days)	11	11.6	5–28	8	8.3	4–12	0.03
First day of normal diet	11	12.2	5–33	8	8.9	5–15	0.03
Hospital stay (days)	17	17.3	9–37	14	13.6	10–23	0.02
Number of patients with DGE		5 (26%)			3 (17%)		0.69

DGE = delayed gastric emptying; defined as gastric stasis, requiring nasogastric intubation for 10 days or more, or the inability to tolerate a regular (solid) diet on or before the 14th postoperative day.

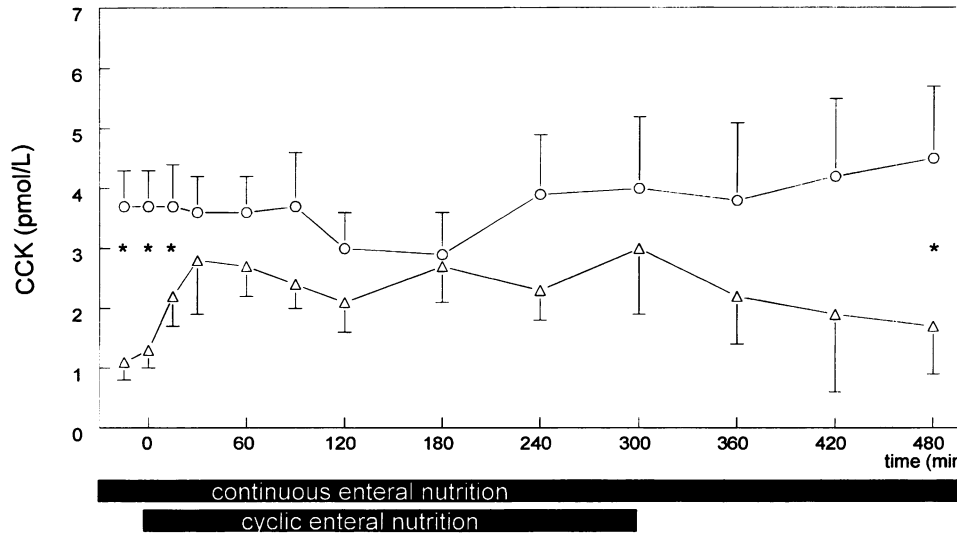

Figure 1. Cholecystokinin (CCK) response to continuous (circles) and cyclic (triangles) enteral nutrition, assessed on the 10th postoperative day. The box indicates the time of infusion of nutrients. Plasma CCK levels did not change with time in patients on continuous enteral nutrition ($p = 0.99$). CCK levels increased in patients on cyclic enteral nutrition after the start of enteral feeding ($p = 0.02$). * indicates a significant difference between the feeding protocols ($p < 0.05$).

In a recent analysis of 200 consecutive patients undergoing pancreatoduodenectomy, we found that the most important factor leading to this complication was the presence of intraabdominal complications ($p < 0.001$).[38] In the present series, the overall incidence of delayed gastric emptying was 25%, comparable to reports by others.[8,13,16] The fact that the incidence of delayed gastric emptying under both nutritional protocols was comparable indicates that the occurrence of this complication was not influenced by nutritional protocol. There was, however, a difference between the two nutritional protocols in number of days until patients tolerated a normal diet. This difference between the two feeding regimens was not influenced by intraabdominal complications, because these patients were excluded in the subanalysis, which showed similar results.

Infusion of nutrients into the intestine slows gastric emptying in healthy volunteers by increasing tonic and phasic pyloric contractions and inhibiting antral contractions. The increase in tonic and phasic pyloric contractions is dose-dependent and correlates with caloric infusion speed and osmotic load.[42,43] In the present study, patients on cyclic enteral nutrition had an exactly equal caloric load per minute of feeding, thus ruling out discrepancies due to differences in infusion speed. We feel this was more important than catching up with total caloric intake per 24 hours in patients receiving cyclic enteral nutrition.

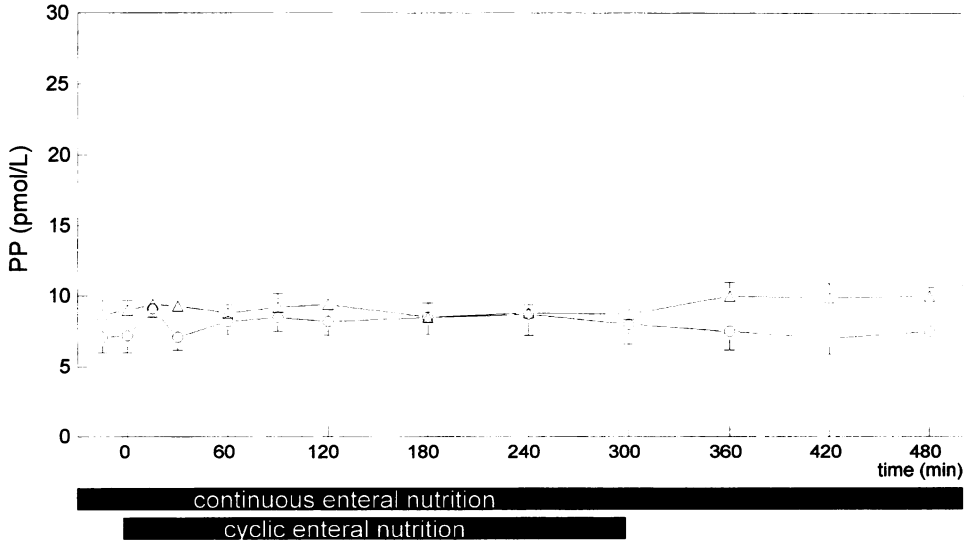

Figure 2. Pancreatic polypeptide (PP) response to continuous (circles) and cyclic (triangles) enteral nutrition, assessed on the 10th postoperative day. The box indicates the time of infusion of nutrients. Plasma PP levels did not change significantly with time in either feeding protocol ($p = 0.84$ for continuous, $p = 0.99$ for cyclic).

A number of factors may be involved in explaining the differences between the two feeding protocols. In a study in patients with Crohn's disease on enteral nutrition, continuously high levels of CCK were measured.[44] High CCK levels are known to cause a delay in gastric emptying.[31,33] Although the primary site of CCK, the duodenum,[45] is resected during pancreatoduodenectomy, postprandial CCK response is only slightly lower after PPPD compared with nonoperated controls. This is not the case after standard Whipple's resection, in which gastrectomy is performed; patients after this type of pancreatic resection show a much lower postprandial CCK response.[46]

In the present study, we found that CCK levels were continuously high in CON patients, whereas CYC patients had significant lower levels of CCK during interruption of feeding. CCK is reported to be an important regulator of nutrient-induced intestinal feedback control.[47] CCK could therefore play an important role in the pathophysiology of the inhibition of gastric emptying during continuous enteral nutrition. Moreover, the fact that this mechanism plays a role in patients on enteral nutrition after pancreatoduodenectomy indicates that a similar gastrointestinal feedback might be a factor after other major surgical procedures in which patients are fed enterally.

Normal plasma levels of PP are reported to be 10 to 30 pmol/L, with a postprandial increase of up to 50 pmol/L.[48] PP levels are low in patients after pancreatoduodenectomy, as shown by others.[49] We found similar results, indicating that PP probably does not play an important role in postoperative gastric motility.

There was no significant difference in median SBTT between the two feeding regimens. Adaptive changes of intestinal transit time to diets of differing fat composition have been described previously in healthy volunteers,[50] but these results are hard to extrapolate to the present study.

In conclusion, cyclic enteral nutrition after pancreatoduodenectomy reduces the number of days until patients tolerate a normal diet, thereby reducing hospital stay. These effects are probably partly due to an inhibition of humoral (CCK-mediated) feedback mechanisms. Cyclic enteral nutrition is therefore the feeding regimen of choice in these patients.

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Discussion

PROF. R. SHIELDS (Edinburgh, United Kingdom): Can I first thank you, Mr. Chairman, for inviting me to comment on this paper. We must congratulate the authors of the paper for the low mortality and their good immediate results following this major operation. There were three points I would like to bring up.

The first is the very important physiologic information that is provided. We have known for more than 40 years from Hunt's work on gastric emptying that there is a duodenal "brake" to gastric emptying related to the fat and caloric content of the meal. We have never been sure if there are similar brakes lower in the intestine because, when tubes were inserted into the gastrointestinal tract in the intact patient, there was often the possibility that there was retrograde perfusion of the duodenum when fluid was instilled into the jejunum. In the absence of the duodenum, you have shown clearly that there is in fact a jejunal brake. This important study shows this for the first time. The hormone studies that you have reported clearly bear this out, particularly as far as CCK is concerned.

The second point is that in your analysis, you study clinical parameters that are really all time-related. I am not sure what objective factors determined these criteria. For example, who decided that intubation should cease? Who decided that enteral nutrition should cease? Was it a doctor, or a nurse? Were the criteria objective or not, or just a hunch? How did you eliminate bias—for example, the decision to commence a normal diet, or the time a patient should leave hospital? If I had been doing a study like this, I would have had a third group of patients who did not have any enteral nutrition at all. I am quite sure that they may have had even a shorter period of intubation and perhaps even a shorter duration before normal diet was commenced, and they may have even left hospital earlier.

I would like to know what was the cost benefit of enteral