Clinical aspects of postoperative enteral feeding in the surgical patient

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The printing of this thesis was financially supported by:

Nutricia Nederland B.V.
Nycomed Nederland B.V.
Fresenius Kabi Nederland B.V.
Guerbet B.V.

Clinical aspects of postoperative enteral feeding in the surgical patient
Thesis, Erasmus University Rotterdam
ISBN 90-8559-147-3

Cover: K.M. Han

Printed by Optima Grafische Communicatie, Rotterdam

Clinical Aspects of Postoperative Enteral Feeding in the Surgical Patient

Klinische aspecten van postoperatieve enterale voeding in de chirurgische patient

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de rector magnificus

Prof.dr. S.W.J. Lamberts

en volgens besluit van het College voor Promoties
De openbare verdediging zal plaatsvinden op

woensdag 1 maart 2006 om 11.45 uur

door

Ingrid Johanna Maria Geurts

Geboren te Utrecht

PROMOTIECOMMISSIE

Promotoren:	Prof.dr. J.Jeekel
	Prof.dr. H.W. Tilanus
Overige leden:	Prof.dr. D. Tibboel
	Prof.dr. H. Obertop
	Prof.dr. E.J. Kuipers

Aan mijn ouders
Voor Ming en Antonie

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1 General introduction and outline of the thesis

GENERAL INTRODUCTION

Introduction

Prognosis of patients undergoing surgery does not merely depend on surgery alone. There is a preoperative phase in which a risk calculation may be made and patients are prepared for the operation and anaesthesia. Then, there is the operation phase and finally the postoperative phase. In this last phase, many customs have been developed to optimise clinical outcome and keep complications down to a minimum. As knowledge increased, some customs have been abandoned or adapted. One of these, is management of postoperative ileus and postoperative feeding. In this thesis, several customs regarding postoperative enteral feeding are evaluated and compared with alternatives in order to determine the most effective way of optimising postoperative nutritional status and clinical outcome. The next section addresses (postoperative) gastrointestinal tract function and traditional approaches of postoperative management. This section is followed by an outline of this thesis.

Principles of gastrointestinal motility

A major function of the gastrointestinal tract is the passage and storage of food. Not only surgery itself, but also anaesthetic procedure and postoperative factors may affect its good functioning. Normal physiology is described first, followed by mechanisms responsible for impaired perioperative function.

Motor function of the gastrointestinal tract is preceded by electrophysiologic changes in smooth muscle bundles in the muscularis mucosae of the intestinal wall. These bundles conduct action potentials; changes in this membrane potential determine the state of contraction. Two types of electrical activity can be distinguished: slow waves and spikes. Slow wave activity in particular evokes the rhythmic contractions. Frequency differs in different parts of the gastrointestinal tract. Spikes appear when the voltage of the slow waves rises above 40 millivolt. Frequency is determined by the level of slow wave potential. Changes in voltage level of the resting membrane potential will either depolarise or hyperpolarise the membrane, making the smooth muscle fibers more or less excitable, respectively[1]. Several factors – including the parasympathetic and sympathetic nerve system, gastrointestinal hormones, transmitters and epi- and norepinephrine – influence the membrane potential changes and thus muscle contraction. Acetylcholine and other transmitters are secreted by the myenteric plexus fibers which together with the submucosal plexus form the enteric nervous system. In addition, the parasympathetic and sympathetic nerve systems influence gastrointestinal tract motor function[2]. In general, parasympathetic stimulation increases motoric activity, whereas sympathetic stimulation has the adverse effect. Connections between the myenteric plexus and the parasympathetic and sympathetic nervous system induce several gastrointestinal reflexes. These reflexes

control gastrointestinal peristaltic movement, gastrointestinal secretion, evacuation of the colon, stomach motility and defecation. Pain reflexes may initiate gastrointestinal tract dysfunction.

Gastrointestinal motility is governed by gastrointestinal hormones as well. Secretin and gastric inhibitory peptide both have an inhibitory effect. The role of cholecystokinin is still controversial, with some studies demonstrating an inhibiting effect on gastric and colonic motility, and others observing no effect on colonic motility [3,4]. Gastrin, produced by the antral mucosa, has a positive effect on gastric motility.

Passage of food is achieved by peristaltic contractions and local contractions stimulated by distension of the bowel wall. The nature of motoric activity differs between the fed and fasting states. The fed pattern is characterized by irregular phasic contractions, determined by consistency and nature of the meal. Full liquid meals inhibit motoric activity whereas solid food induces strong antral contractions [5]. Fasting produces a cyclic reproducible pattern of contractions, alternating with periods of inactivity. This pattern, called the interdigestive migrating motor complex (MMC), was first described by Szurszewski in 1969, and later by Sarna et al. and Malagelada et al. [6-8]. Three phases of motor activity can be distinguished. Phase I shows motor quiescence, phase II irregular contractions and phase III continuous phasic propulsive contractions. Lasting from 1-2 hours, MMC migrates from the lower esophageal sphincter to the ileum at 100 minutes intervals.

Food intake induces a variety of reactions. The stomach relaxes so that it can expand without an increase in intragastric pressure [9]. This mechanism is partially vagus mediated. The antrum and the distal part of the corpus reduce food particles to a smaller size by peristaltic waves resulting in propulsion and retropulsion. Finally the food particles are emptied into the duodenum, controlled by gastrin, volume and hormonal and nervous feedback from the duodenum [10]. The food is then mixed in the small intestine and propelled forward by contractions induced by slow waves, as mentioned before. Peristaltic activity greatly increases after food intake. This is partly caused by the gastroenteric reflex, initiated by distension of the stomach and conducted from the myenteric plexus from the stomach to the wall of the small intestine. Frequency of the peristaltic waves decreases in caudal direction. Contractile activity after food intake lasts from 2.5-8 hours [11]. Ileal motility, increased by the gastroenteric reflex, allows passage of contents into the cecum. Further passage in the colon is effected by contractions of circular and longitudinal muscles called haustrations. Mass peristaltic movements, occurring after food intake, are initiated by gastrocolic and duodenocolic reflexes and further move faeces distally. Proximal and distal colon differ in motoric response to food: the proximal colon has a reservoir function in contrast to the distal colon which functions more as a conduit [12,13]. Finally defecation occurs as a result of the intrinsic defecation reflex and the parasympathetic defecation reflex.

Postoperative ileus

As stated before: gastrointestinal surgery will impair intestinal motility. Recovery of intestinal motility takes a few hours to 24 hours for the small intestine, 24-48 hours for the stomach and 48-72 hours for the colon [14,15].

Postoperative ileus is defined as a transient impairment of intestinal motility occurring after abdominal surgery, as manifested by the absence of bowel sounds and intestinal distension. Various factors are known to be involved in the mechanism. Neural reflexes, humoral and inflammatory agents have been identified as ileus-inducing factors [16]. In 1872 it was first observed that bowel contractions were enhanced by dividing of the spinal cord at the level of the medulla [17]. Many more studies followed implicating a central role for the sympathetic pathway in postoperative ileus. The parasympathetic nervous system increases intestinal motility. The sympathetic nervous system on the other hand inhibits motility, and is believed to predominate [18]. Sympathetic hyperactivity induced by surgical stress especially inhibits colonic motility, contributing to the onset and persistence of ileus [19]. The magnitude of intestinal inflammatory response correlates with the extent and duration of postoperative ileus [20]. Intestinal manipulation increases mucosal permeability; the resulting bacterial translocation possibly enhances inflammatory response [21,22]. Mediators thought to be involved are nitric oxide, substance P, opioid agonists, vasoactive intestinal peptide and prostanoids. Increased cyclooxygenase-2 (COX-2) expression after laparotomy with resultant elevated levels of prostaglandins decreases intestinal contractility and may in this way contribute to postoperative ileus [23].

Abdominal surgery exerts a complex effect on gastrointestinal motility. Animal studies demonstrated disturbance of myoelectrical activity in the immediate postoperative period [24,25]. Migrating Motor Complex (MMC) activity is also diminished following laparotomy but increases in the postoperative course [26]. It still remains unclear how this is related to postoperative ileus.

As postoperative ileus has no evident favourable effects, great efforts are still being made to diminish its severity and duration. Several options are available depending on the different mechanisms involved in the origin of postoperative ileus. Firstly, inhibitory sympathetic reflexes can be effectively blocked by epidural local anaesthetics [27,28]. Continuous epidural analgesia with local anaesthetics was shown to have a positive effect on reducing ileus [29,30]. Secondly, minimal invasive surgery – which minimises gastrointestinal manipulation and surgical trauma – is also thought to diminish postoperative ileus. Its reduced inflammatory response indicates less surgical stress compared to open surgery, but convincing differences are in duration of postoperative ileus were not found [31-33]. Thirdly, early enteral nutrition possibly has a reducing effect on ileus. Since it takes only a few hours for small bowel motility to recover, enteral feeding can be started soon after operation. Early enteral feeding further stimulates bowel motility and is in this

way thought to diminish ileus [34]. Findings from clinical trials in this field are however controversial.

In summary, postoperative ileus serves no purpose and can lead to complications and longer hospital stay.

Nasogastric decompression

Postoperative nasogastric intubation for prophylactic purposes became popular in the thirties and has been routinely used until only a few years ago [35]. This practice was based on the concept that abdominal surgery is followed by paralytic ileus with bowel distension as a consequence. Intubation intended to decrease gastric and enteric distension, and to prevent vomiting, pulmonary aspiration and wound or fascial dehiscence. The tube was left into place until bowel sounds could be heard and flatulency appeared. This regimen was questioned as bowel motility became better understood. The total amount of fluid removed by a nasogastric tube is disproportionate to the amount secreted by the intestinal tract. Furthermore, gastric distension is also known to be related to the swallowing of air which cannot be prevented by the use of a nasogastric tube. In a large trial Wolff et al. showed that the absence of a nasogastric tube postoperatively did not increase morbidity [36]. Also, there was no increase in the incidence of incisional hernia [37]. Disadvantages of nasogastric tubes became evident [38,39]. Many clinical trials were undertaken and finally a review in 1995 concluded that routine nasogastric decompression in elective abdominal surgery is not associated with earlier recovery of bowel function, and may lead to a higher incidence of pneumonia and atelectasis [40-42]. This review was recently updated to include 28 randomised controlled trials encompassing 4194 patients randomised to either prophylactic postoperative nasogastric tube use or no routine use [43]. Anastomotic leakage did not differ between groups; bowel function recovered earlier in the non-intubated patients.

Thus, routine use of a postoperative nasogastric tube apparently has no advantages.

History of postoperative feeding policy

Postoperative routines increasingly acknowledge the importance of feeding. Studley was one of the first clinicians who became aware of the importance of nutritional status on postoperative outcome. Patients who had lost substantial weight had poorer outcomes in terms of higher mortality [44]. Since then, further evidence was provided relating malnutrition to poor clinical outcome in surgical patients [45-51]. Approximately 9 - 44% of surgical, hospitalized patients were found to be malnourished [52-55]; this finding fully underlines the significance of preoperative feeding.

Total parenteral nutrition (TPN) given prior to operation was thought to improve nutritional status and therefore to reduce postoperative morbidity and mortality. This theory was supported by findings from nonrandomized studies [56,57]. Its use declined how-

ever when clinical randomized studies reported inconclusive results and TPN-related complications [58]. TPN was also found to be associated with an exaggerated acute phase and metabolic response after injury or endotoxin release.

Effects from surgery on nitrogen balance, immune response, host defence and protein loss became gradually clear [59-61]. Intestinal mucosa acts as a defence barrier against pathogens, preventing the release of immunosuppressive agents. Enteral nutrition seems to be vital for maintenance of intact intestinal mucosa. Withholding enteral feeding was shown to lead to mucosal atrophy and to exert a negative influence on stress responses and postoperative morbidity [62]. Soop et al. in a prospective randomized trial found insulin resistance and nitrogen loss to be diminished after postoperative enteral feeding [63]. Enteral feeding was also demonstrated to enhance wound healing and increase anastomotic strength [46,61]. Duration of ileus is shortened by early resumption of enteral intake [64]. The positive effects of enteral feeding on clinical outcome and complications were first established in trauma patients and patients with severe burns [59,65-69]. Meanwhile, knowledge on postoperative gastrointestinal tract motility increased; enteral feeding was demonstrated to be tolerated within 24 hours after laparotomy [70,71].

In conclusion, there is ample evidence that enteral feeding is superior to parenteral feeding following gastrointestinal surgery.

Early postoperative oral feeding

The traditional approach to resumption of oral intake following abdominal surgery is based on the belief that postoperative ileus must be completely resolved before a solid diet can be consumed. Underlying fear of persistent ileus and anastomotic leakage is the reason for this belief. Thus, patients are kept sober until bowel movement and the passage of flatus. Wara and Hessov were the first to question the necessity of this conservative postoperative diet regimen [72].

Laparoscopic abdominal surgery has several advantages over open abdominal surgery, one of which is resumption of oral feeding within 48 hours after operation [73-77]. Several prospective cohort studies assessing the feasibility of early oral feeding in open abdominal surgery showedthat most patients tolerated it well and could be discharged earlier [77-81]. In addition, several prospective, randomized trials were conducted concerning conventional gastrointestinal surgery [64,82-88]. Groups did not significantly differ in vomiting, reinsertion of a nasogastric tube and duration of hospitalization. Limitations of these studies were however heterogenous population, use of nasogastric drainage and varying resumption times of oral feeding.

A recent meta-analysis reviewing 11 prospective controlled trials in which enteral feeding was started within 24 hours after operation, demonstrated a reduction in septic complications [89]. Length of hospital stay was reduced in eight of eleven studies assessed, resulting in an overall statistically significant reduction of 0.84 day ($p < 0.001$). Even early

enteral feeding by a nasogastric tube in patients with a generalised peritonitis due to enteric perforation may be safe [90].

We may conclude that postoperative fasting lacks a scientific foundation.

Enteral access routes

Of the various possibilities to gain enteral access for feeding purposes, the main distinction is between invasive and non-invasive methods. Nasogastric and nasoenteric tubes are non-invasive tools that can be easily placed and are effective for short-term feeding. However, as complications can occur such as esophageal perforation, variceal bleed and malposition, they are considered unsuitable for long-term feeding purposes. Tube clogging and dislocation is another issue resulting in reluctance of placement for long term purposes [91,92]. Therefore, when prolonged feeding is expected, gastrostomy or jejunostomy is performed using a percutaneous, endoscopic or operative technique. Recent developments of softer and self-propelling tubes might result in increased catheter efficacy and less of the former described complications [93].

Percutaneous endoscopic gastrostomy (PEG) is generally preferred in patients with inability to eat but who have a functional gastrointestinal tract, for example patients with central nervous system disorder [94,95]. Contraindications for the use of percutaneous endoscopic devices are ascites and impossibility of passage of an endoscope. However, a mortality rate of up to 22% has been described, making this a hazardous procedure necessitating a stringent patient selection [96]. One of the reasons that PEG is considered to be more suitable for long-term feeding purposes is that PEG is associated with less reflux and a lower risk of aspiration compared to nasogastric tube feeding [97]. In a recent paper the results of three clinical trials and a metaanalysis were discussed, comparing early enteral feeding by PEG and by nasogastric tube in dysphagic stroke patients [98]. Patients with a PEG had a higher incidence of pressure sores; patients with a nasogastric tube a higher incidence of haemorrhage. Interestingly, PEG was associated with a significantly poorer outcome and a higher mortality rate compared to nasogastric tube. In this patient category, enteral feeding by nasogastric tube is therefore preferred to PEG.

To minimise risk of aspiration, jejunostomy is preferred to gastrostomy in patients who have gastroparesis or gastric outlet obstruction. Still, jejunostomy minimises the risk of aspiration but does not totally prevent it [99]. In addition, jejunostomy can be performed concomitant to upper digestive surgery and in trauma patients to enable early postoperative feeding [100,101]. Complication rates of 0 – 26% are reported, warranting strict patient selection [102-105]. A feeding jejunostomy can be performed open or laparoscopically [106]. Laparoscopic placement is obviously less invasive and would have the same benefits as other minimally invasive types of surgery [107-109]. A total laparoscopic technique or a laparoscopic aided technique can be used depending on the surgeon's expertise and preference [110]. Conversion rate is acceptable, and morbidity rate is comparable to open

surgery. This makes laparoscopic feeding jejunostomy a viable method to obtain enteral access with the advantages of minimal invasive surgery.

In view of recent developments and literature, it is in order to reconsider currently used guidelines on usage of the diverse enteral access routes.

Nutritional assessment

Terminology

The term malnutrition is usually associated with inadequate food intake. Actually, malnutrition is the sum of reduced food intake due to the effect of underlying disease, increased nutrient requirement, or altered ability to utilise or absorb nutrients. All of these result in body composition changes, characterized by macro- and/or micronutrient deficiencies. Nutritional status describes not only disease determined body composition but also the normal situation. Nutritional assessment intends to measure this body composition. Malnutrition can be diagnosed by means of nutritional assessment and the extent of nutritional depletion can be estimated. Nutritional assessment can also be used to identify patients at risk for malnutrition. In surgical patients nutritional status may also be considered a prognostic factor for postoperative complications.

Nutritional parameters

Malnutrition and clinical outcome are strongly related. This is why national societies for parenteral and enteral nutrition recommend nutritional support [111,112] for malnourished patients. Proposed cut-off points for assessing malnourished state are:

BMI < 18.5 kg/m^2 and/or percentage of weight loss > 10%:

Nutritional assessment in surgical patients first aims at identifying patients who are malnourished or are at risk for developing malnourishment, and second at improving nutritional status. Nutritional treatment aims to diminish the number and/or severity of postoperative complications, to enhance postoperative recovery, to shorten length of hospital stay and to improve quality of life and feeling of well-being.

The ESPEN guidelines for nutritional screening published in 2003 comprised an action plan for identifying patients at nutritional risk so that adequate nutritional intervention is possible [113]. This plan includes screening, nutritional assessment and monitoring, as well as clinical outcome.

There is, however, no gold standard for measuring nutritional status. Nutritional assessment considers both subjective and objective parameters. Various questionnaires have been developed for screening purposes. Frequently used, the subjective global assessment questionnaire (SGA) is recommended by the ASPEN board of directors [111,114-117]. It includes physical examination and features of patient history as well. Other question-

naires are summarized in Table 1. A short nutritional assessment questionnaire was recently developed in the Dutch language for easy in-hospital application [118].

Objective parameters include laboratory methods and measurement of body composition (Table 2). The most sensitive parameters for assessment of protein nutritional status are albumin, pre-albumin and retinol-binding protein levels. Albumin level, especially, has proven its correlation with postoperative complications [119,120]. Although albumin level, like other biochemical parameters, is influenced by acute factors and co-morbidity, its measurement is an inexpensive and simple prognostic tool. Bioelectrical impedance analysis (BIA) measures the opposition of body cells and tissues to the flow of a radiofrequency alternating electrical current [121]. In this way, total body impedance is obtained and body composition can be assessed. Several estimations can be made from BIA such as phase angle, an indicator based on reactance and resistance. Phase angle was demonstrated to have prognostic value for occurrence of postoperative complications [122]. Dual-energy x-ray absorptiometry (DEXA) is another method for measuring body

Table 1. Questionnaires used for nutritional assessment

questionnaire	purpose
subjective global assessment (SGA) [114]	screening
malnutrition universal screening tool (MUST) [125]	screening
nutritional risk score (NRS-2002) [126]	screening, risk assessment
short nutritional assessment questionnaire (SNAQ) [118]	screening

Table 2. Nutritional assessment tools

tool		parameter	purpose
anthropometry		hand grip, weight loss, %ideal weight, TSF, BSF, BMI	screening, prediction of complications
biochemical assessment		albumin, pre-albumin, transferrin, retinol binding protein, CRP, nitrogen balance, lymphocyte count	Prediction of complications
immune function		delayed cutaneous hypersensitivity	
BIA			
DEXA		FFM, PA	research
indirect calorimetry			
isotope dilution methods			research
combined nutritional indices	Prognostic Nutritional Index (PNI) [53]	albumin, transferrin, delayed type skin hypersensitivity, TSF	prediction of complications
	modified PNI [127]	albumin, lymphocyte count	prediction of complications
	Nutritional Risk Index (NRI) [128]	albumin, %usual weight	identification of patients at risk for complications
	Nutritional index of Maastricht (NMI) [129]	albumin, prealbumin, lymphocyte count, %ideal weight	assessment of nutritional status

TSF = triceps skin fold, BSF = biceps skin fold, BMI = body mass index, CRP = C - reactive protein, BIA = bioelectrical impedance analysis, DEXA = dual energy x-ray absorptiometry, FFM = fat free mass, PA = phase angle

composition, based on the concept that tissue attenuates energy beams differentially as they pass through [123,124]. Use of these modern methods of body composition assessment is limited in that they have not been validated in a healthy population. In addition, DEXA is an expensive method, limitating its use for clinical purposes. Combined nutritional indices use different individual parameters. Results are, however, difficult to interpret since these indices, too, have not been validated in a healthy population and are influenced by disease and co-morbidity. This makes interpretation of the results difficult. Aims of different assessment methods differ: some are developed as a screening tool, others for predicting mortality. This makes them difficult to compare and to interpret.

Despite a clear relation between malnourishment and clinical outcome, it has proven to be difficult to relate postoperative outcome to enteral feeding in well nourished patients. This is partly due to heterogeneity of clinical trials and partly due to the fact that postoperative morbidity is multifactorial. A meta-analysis of trials comparing early enteral feeding with temporary postoperative fasting indicated a reduction of any infection in the early fed group [89]. This was independent of preoperative nutritional status. Preoperative nutritional status, however, was poorly defined or not mentioned at all in several of the trials. Other factors that could have influenced duration of ileus and the effects of enteral feeding on outcome, such as anaesthesia and analgesia, differed between studies and were not standardised.

As no single screening tool has been validated with respect to clinical outcome, combinations of questionnaires and biochemical parameters are recommended. Prior stratification of patients by nutritional status is necessary for valid interpretation of the results.

Nutritional assessment is essential for predicting clinical outcome and identifying patients at risk for complications. Practical tools are needed for clinical application.

OUTLINE OF THE THESIS

Although there is growing evidence that surgical patients may benefit from early enteral feeding, controversies remain in whom, when en how to feed. This thesis analyses the influence of enteral feeding on postoperative outcome and provides guidelines for post-operative enteral feeding management iaimed at optimising clinical outcome.

In a prospective randomized trial presented in *chapter 2* an early postoperative oral feeding regimen is compared with a gradually expanding feeding regimen. The chapter addresses several questions related to postoperative patient-controlled feeding: is early postoperative oral feeding feasible; can a full diet be reached earlier using an early oral feeding regimen; does an early oral feeding policy lead to faster recovery and shorter hospital stay. In short, is there still a reason to keep patients 'nil by mouth'? *Chapter 3* contains the results of another prospective trial aiming to assess the influence of early introduction of an oral diet on postoperative ileus and quality of life.

Access techniques for enteral feeding in patients who cannot start an oral diet within days after operation, include nasoenteral tube or jejunostomy placement. Several aspects of these techniques are described in *chapters 4, 5 and 6*. In *chapter 4* a large group of esophagectomised patients receiving a feeding jejunostomy is studied. What kinds of complications are associated with placement and usage of a feeding jejunostomy and is an alternative access method in order? An alternative is then presented in *chapter 5*, a prospective randomized trial comparing feeding jejunostomy with nasoduodenal tube in a similar patient population. Answers are sought to questions like: what kinds of complications occur with each method? Which method is associated with the least morbidity?; and: is nasoduodenal tube feeding an effective method? *Chapter 6* presents an extensive literature review on different features of laparoscopic jejunostomy. This systematic review aims to classify current surgical techniques and to assess evidence on safety of laparoscopic feeding jejunostomy.

Preoperative risk assessment increasingly makes use of nutritional status. Patients in whom adequate food intake is compromised pre- or postoperatively are at risk for malnutrition and may be prone to more postoperative morbidity. A clinically feasible method is needed to identify these patients, after which they can be given adjuvant feeding. *Chapter 7* aims to relate preoperative nutritional status in a potentially compromised patient population to postoperative complications. Assessment tools using easy available parameters are used in an attempt to identify a subgroup of patients who would benefit from adjuvant feeding.

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2 Randomized clinical trial of patient-controlled versus fixed regimen feeding after elective abdominal surgery

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British Journal of Surgery 2001 88:1578-82

ABSTRACT

Background: Although studies have shown that early oral feeding after abdominal surgery is feasible, many surgeons still advocate a careful, slow introduction of postoperative feeding. This study was conducted to investigate whether patient-controlled postoperative feeding is possible in patients undergoing colonic or aortic surgery.

Methods: A randomised clinical trial compared patient-controlled postoperative oral feeding (PC group) with a fixed regimen (FR group). Patients in the PC group (n = 56) received oral feeding when they requested it; patients in the FR group (n = 49) started a normal diet on day 5. Endpoints were time to tolerance of a diet similar to the preoperative diet, reinsertion of a nasogastric tube, complications and duration of hospitalization.

Results: Median time to resumption of a normal diet was 3 days in the PC group and 5 days in the FR group ($p < 0.001$). Reinsertion of a nasogastric tube was required in nine patients in each group (p not significant). The incidence of complications was similar in both groups: 12 of 56 in the PC group and 13 of 49 in the FR group. There was no significant difference in duration of hospital stay between the groups.

Conclusion: Most patients tolerate a normal diet on the third day after operation. Patient-controlled postoperative feeding is safe and leads to an earlier resumption of a normal diet.

INTRODUCTION

Postoperative nutritional status is a major factor in clinical outcome [1-5]. Most surgeons use a regimen in which oral feeding is gradually introduced following the resumption of bowel sounds and the passage of flatus. This policy is based mainly on fear of anastomotic leakage and persisting ileus. Postoperative paralytic ileus is due to inhibitory neural reflexes in the gastrointestinal tract and to local release of inflammatory agents [6,7]. Various factors influence the duration of postoperative ileus, the most important being the nature of the surgery [8]. There are indications that resumption of enteral feeding is one of the factors that diminishes the duration of ileus [9].

Several small prospective clinical trials have questioned the policy of a gradual introduction of postoperative diet and have concluded that early oral feeding is feasible [10-14]. In these studies resumption of eating took place either after the nasogastric tube had been removed or on the second day after operation, as desired by the patient.

Patient-controlled feeding after operation may lead to a better nutritional status and to an earlier feeling of well being than feeding according to a fixed regimen. The former may thus promote earlier hospital discharge. This hypothesis was investigated in a prospective randomized trial comparing postoperative patient-controlled feeding with a fixed regimen.

PATIENTS AND METHODS

In a 1-year period 105 patients awaiting elective abdominal surgery were randomized to participate in the trial (Table 1). Randomization took place in the operating theatre preceding operation. All 105 patients were enrolled in the study and underwent elective abdominal surgery including open colonic surgery and transabdominal central vascular reconstruction procedures. They were all above the age of 18 years and were not participating in another study at that time. Furthermore, all patients were mentally competent, able to speak and understand the Dutch language, and gave written informed consent. The study was approved by the medical ethics committee.

Table 1. Baseline patient characteristics

	PC group (n = 56)	FR group (n = 49)
Sex ratio (M:F)	25:31	32:17
Age (years)*	68 (12)	65 (12)
Type of surgery		
vascular	38	30
colonic	18	19

* Values are mean (s.d.). PC, patient controlled; FR, fixed regimen

Patients were assigned randomly to a patient-controlled diet after operation (PC group) or a fixed postoperative feeding regimen (FR group). Randomization was by the use of sequentially numbered, sealed envelopes. Patients in the PC group chose when to start an oral diet. The feeding regimen for the FR group was as follows: 25 ml water per h on the day of operation (day 0); 50 ml water per h on day 1; liquid diet consisting of water, tea, coffee and lemonade on day 2; liquid diet on day 3; easily digestible diet on day 4; and normal diet on day 5.

All operations were performed by a consultant surgeon or a senior resident supervised by a consultant surgeon. All patients underwent mechanical bowel preparation before operation. A nasogastric tube was inserted before surgery and was removed immediately after the operation in each patient.

Outcome measures were the time span between operation and the tolerance of a normal diet, reinsertion of a nasogastric tube, complications and duration of hospital stay. Postoperative complications related to the type of surgery were defined and registered. Anastomotic leakage was assessed by clinical symptoms or radiological examination. Ileus was assessed by clinical examination. The length of hospitalization, defined as the number of days in the hospital after the day of the operation, was recorded. Patients were discharged when able to tolerate a normal diet, had had a bowel movement and had no complications preventing hospital discharge. During their admission, patients were asked several questions concerning nausea, vomiting, flatus, bowel movement and diet, and their responses were recorded in a diary. Reinsertion of a nasogastric tube was recorded. Two clinical investigators examined the patients daily, listened for bowel sounds and supervised completion of the diaries. In addition, patients noted their preferences on standard hospital dietary forms. The clinician responsible for the clinical decisions regarding treatment also examined the patients.

Statistical analysis

All randomized patients were analysed on an intention-to-treat basis. Continuous, normally distributed data are expressed as mean (s.d.) and other quantitative data as median (range). The Mann-Whitney *U* test was used to compare non-normally distributed data between study groups. The X^2 test was used to compare proportions. P-values reported are two-tailed. $P < 0.05$ was considered to be statistically significant.

RESULTS

Over 1 year 105 patients were randomized and included in the trial. Patient characteristics were comparable between the two groups (Table 1).

Table 2. Number and type of complications

	PC group (n = 56)	FR group (n = 49)
Relaparotomy		
- Anastomotic leakage*	2	1
- Postoperative haemorrhage	1	1
- Other[§]	3	1
Pelvic abscess	0	1
Myocardial infarction	1	1
Cerebral vascular accident	0	1
Pneumonia	1	1
Urinary tract infection	2	4
Wound infection	0	2
Exacerbation COPD	1	0
Asthma cardiale	1	0
Total	12	13

No patients had more than one complication; * Colonic surgery only; [§]prolonged ileus, colitis. PC, patient controlled; FR, fixed regimen; COPD, chronic obstructive pulmonary disease

There were two cases of anastomotic leakage in the PC group, both in patients who had a colonic resection. One anastomotic leak occurred in the FR group. These three patients required re-operation. Other complications occurred in ten patients in the PC group and 12 patients in the FR group (Table 2). There were three deaths, all in the PC group ($p < 0.05$). One patient died 3 days after operation from a myocardial infarction; another patient developed fatal acute respiratory distress syndrome 2 days after operation. There were no signs of aspiration. Neither patient had resumed a solid diet at that time and it is improbable that these deaths were related to food intake. The third patient developed postoperatively ischaemic colitis following aortic surgery. The patient underwent a Hartmann's procedure but died from multiple organ failure.

Nine patients in each group required reinsertion of a nasogastric tube because of repeated vomiting. In each case the tube was withdrawn the next day and oral feeding was resumed according to randomization. All other patients tolerated their diet well. Median duration to resumption of a normal diet was 3 days in the PC group compared with 5 days in the FR group ($P < 0.001$). The median duration of hospital stay was 11 days in both groups (P not significant) (Table 3).

Table 3. Primary outcome measures

	PC group	FR group
Time to normal diet (days)	3 (1-12)	5 (4-13)*
Hospital stay (days)	11 (3-72)	11 (6-34)

Values are median (range). PC, patient controlled; FR, fixed regimen. *$P < 0.001$ *versus* PC group (Mann-Whitney *U* test)

Table 4. Time to resumption of normal diet and hospital stay in patients who underwent aortic and colonic surgery

	PC group		FR group	
	Aortic	Colonic	Aortic	Colonic
Time to normal diet (days)	5 (2-12)	4 (1-11)	6 (4-9)	6 (4-13)
Hospital stay (days)	13 (7-35)	15 (3-72)	12 (6-34)	12 (6-27)

Values are mean (range). PC, patient controlled; FR, fixed regimen. There were no significant differences between patients who had aortic or colonic surgery in either group

A comparison was made between patients undergoing aortic surgery and patients undergoing colonic surgery with respect to hospital stay and time to resumption of a normal diet. In neither group was a significant differences found (Table 4).

There were no significant differences between the FR and the PC groups in the incidence of nausea and vomiting, and time to passage of flatus and faeces. All patients in both groups had bowel movement on the first day after operation.

DISCUSSION

Several aspects of postoperative management in general surgery are more empirical than evidence based. One example is the standard use of a nasogastric tube preoperatively and after surgery. In several studies it has been shown that this does not contribute to a better recovery and often leads to complications such as aspiration [15-17]. Another example is the belief that patients should not eat until a few days after surgery, in order to avoid anastomotic leakage or ileus. Several small prospective randomized studies have demonstrated that this strict feeding regimen is not necessary. Bufo *et al.* [10] concluded that most patients tolerated immediate postoperative feeding without developing major complications; these findings were confirmed by several others [12-15,18-21]. However, in most of these latter studies the nasogastric tube was only removed following bowel movement [11,12,14,18], or a regular diet was started only several days after surgery [10,13,19,20].

In the present study a normal diet was tolerated in nearly all patients in the PC group 3 days after operation. In all cases the nasogastric tube was removed directly after surgery. Reinsertion occurred nine times in both groups; these results are similar to those of previous reports [11,13,22,23]. In contrast to the aforementioned studies, patients were given the opportunity to start a normal diet on the first postoperative day. In other studies a regular diet was resumed a few days after surgery on the assumption that postoperative ileus takes 24-48 hours to resolve. However, Avrahami *et al.* [24], studying gastric emptying after transabdominal vascular surgery, concluded that a normal diet may be started on the second day after operation. In the present study all patients started fluids on the first postoperative day. The median time to resumption of a normal diet in the PC group was 3 days in contrast to 5 days in the FR group. There was no difference between the groups in

the need for reinsertion of a nasogastric tube. These findings justify the conclusion that patients are able to judge their own food tolerance adequately.

There was no difference in time to resumption of a normal diet between patients who underwent aortic surgery and those who had colonic surgery in either group. Although the number of patients was small, these results are in accordance with other reports [24,25].

The incidence of anastomotic leakage and overall complications did not differ from that in other reports. The size of the group was too small to relate anastomotic leakage to a feeding regimen. Experimental studies have shown that anastomotic healing in rats is improved by early postoperative enteral feeding [26]; clinical studies, however, lacked sufficient patient numbers to confirm these findings. Duration of recovery may be influenced positively by an early feeding regimen and may lead to earlier discharge from hospital. The duration of hospitalization was not shorter in the PC group in the present study, whereas a trend towards a shorter hospital stay has been observed previously when an early feeding regimen is followed [27-29]

Secondary endpoints did not differ between groups. The importance of bowel movement as an indicator for regaining bowel function is questionable as it also represents activity of the small bowel. Passage of flatus and stool is often used as a measure of resolving postoperative ileus. However, both are non-specific since they may only indicate distal bowel emptying. Furthermore, duration of postoperative ileus is influenced by many different factors. The present findings confirm the assumption that these subjective measures of bowel function cannot indicate when to start or expand an oral diet.

It is concluded that patient-controlled postoperative feeding is safe and is started significantly earlier than the fixed regimen imposed by the physician.

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3

The impact of early enteral feeding on postoperative ileus duration and postoperative recovery: a prospective randomized multicentre trial

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ABSTRACT

Background: Postoperative convalescence is mainly determined by extent and duration of postoperative ileus. We conducted a prospective, randomized trial evaluating the effects of early oral feeding on functional gastrointestinal recovery and quality of life.
Methods: 128 patients undergoing elective open colorectal and open abdominal vascular surgery participated in the trial. 67 were randomized to a conventionally expanding diet, and 61 to a regimen providing for resuming an oral diet as fast as tolerated.
Results: Reinsertion of a nasogastric tube was necessary in 20 percent of the fast expanding group and in 10 percent of the conventional group ($p = 0.213$). Complication rate was similar for both groups, as well as return of gastrointestinal function. A normal diet was tolerated after 2 days in the fast expanding group versus 5 days in the conventional group ($p < 0.001$). Quality of life scores were similar in both groups.
Conclusion: Early resumption of oral intake does not diminish duration of postoperative ileus, nor does it increase complications like reinsertion of the nasogastric tube or aspiration. Tolerance of an oral diet is not influenced by gastrointestinal functional recovery. There is therefore no reason to withhold oral intake following open colorectal or abdominal vascular surgery.

INTRODUCTION

Perioperative care is aimed to obtain optimum postoperative outcome and quality of life. Restoration of normal gastrointestinal function to allow adequate food intake and quick recovery is one of the main objectives. The major postoperative determinant of gastrointestinal function is ileus, defined as a transient impairment of intestinal motility following abdominal surgery. It has a complex pathogenesis involving mechanisms such as surgical stress response and inhibitory neural reflexes [1-3]. The pathogenesis being multifactorial implies that attempts to influence the mechanism of postoperative ileus should also be multifactorial. This concept has indeed led to successful introduction of a multimodal approach to perioperative care.

Postoperative ileus may be a significant factor delaying early resumption of an oral diet. However, conversely, early resumption of oral feeding has been suggested to reduce duration of postoperative ileus [4]. Although early postoperative resumption of an oral diet was found to be feasible, the precise effect on ileus duration and gastrointestinal convalescence still remains unclear [5,6]. Likewise, the correlation between dietary intake and quality of life is unclear. We report a trial aimed at assessing the effects of an early oral diet on gastrointestinal function and quality of life in patients undergoing elective, open, colorectal or abdominal vascular surgery.

MATERIALS AND METHODS

In order to obtain a representative cross-section of the Dutch population, two teaching and one non-teaching hospitals participated. Altogether 128 patients awaiting elective open colorectal or aortic aneurysm surgery were enrolled in the trial (Table 1). Patients were all above the age of 18 years and were not participating in another study at that time. Furthermore, all patients were mentally competent, able to speak and understand the Dutch language and gave written informed consent. The study was approved by the medical ethical committees of the three hospitals. Patients were randomly assigned to either a conventional expanding diet or a diet of their own choice.

Randomisation took place in the operating theatre preceding operation and was carried out by telephone according to a computer-generated list with blocked sequences. To ensure equal distribution of vascular and colorectal operative procedures as well as hospital, patients were stratified accordingly. Patients in the patient-controlled diet group started an oral diet on any chosen postoperative day. The feeding regimen for the conventional group was as follows: operating day (day 0): 25 cc of water per hour; day 1: 50 cc of water per hour; day 2: liquid diet consisting of water, tea, coffee and lemonade; day 3: liquid diet; day 4: easy digestible diet; day 5: normal diet. All operations were

performed by a staff surgeon or a resident supervised by a staff surgeon. All patients underwent bowel preparation and received prophylactic antibiotics preoperatively. A nasogastric tube was inserted prior to surgery and was removed on the first postoperative day at the latest. Postoperative complications were defined and registered. Complications were categorized as surgical or non-surgical (Table 2). Duration of operation was defined as length of time between the first incision and placement of the last suture. Patients were discharged when they showed no complications, passage of stool had occurred and recovery was well enough in relation to the home situation. Daily during admission, patients were asked to report on nausea, vomiting, flatus, bowel movement and diet in a diary. Two clinical investigators daily examined the patients, listened for bowel movement and checked diary reporting. The physician responsible for the clinical decisions regarding treatment also examined the patients.

The primary endpoint was reinsertion of a nasogastric tube. The decision to proceed to reinsertion was left to the responsible physician. Other outcome measures were time span between operation and the tolerance of a normal diet, duration of hospitalisation and complications. Bowel function was assessed by time to first bowel movement, flatulence and time to first defecation.

Quality of Life and pain scores

Patients completed a visual analogue pain score (VAS) once preoperatively, daily for 1 week postoperatively, and next at 6 weeks and 3 months postoperatively. To assess whether rate of resumption of diet differentially impacted on health related quality of life (HRQoL), the Short Form-36 (SF-36) was administered 1 day preoperatively and at 1 week, 6 weeks and 3 months postoperatively. The SF-36 includes one multi-item scale measuring each of eight health concepts: (1) physical functioning, (2) role limitations due to physical health problems, (3) bodily pain, (4) general health, (5) vitality, (6) social functioning, (7) role limitations due to emotional problems, and (8) mental health[7]. Scores per dimension range from 0-100. Higher scores indicate a better QOL.

The Multidimensional Fatigue Inventory-20 (MFI-20) determines the level of fatigue and was administered together with the SF-36[8]. It consists of 20 items divided into five scales: general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue. Scores per item range from 1 to 5. Accordingly, the total score per scale may range from 4 (no fatigue) to 20 (exhausted).

Cost-effectiveness of either surgical modality was evaluated using the EuroQol-5D (EQ-5D) measured preoperatively, daily for the first postoperative week, and next at 1 week, 6 weeks and 3 months postoperatively. The EQ-5D describes health status by five attributes: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each attribute has three response categories, i.e. 'no problems', 'some problems' or 'se-

vere problems'[9]. From these EQ-5D scores Quality Adjusted Life Years (QALY's) were derived[10,11].

Statistical analysis

Power calculation had shown that 150 patients were needed in each group. As accrual was much slower than expected, the trial was stopped after three years. This decision was not based on the accumulated outcome. All randomised patients were analysed on an intention-to-treat basis. Continuous, normally distributed data are expressed as mean values with their standard deviation. Other quantitative data were noted as median values with their range. The Mann-Whitney U test was used in not-normally distributed data for comparisons of both study groups. The chi-square test was used to compare proportions. The reported p-values are two-tailed. A p-value less than 0.05 was considered to be statistically significant. Repeated measurements Anova was used to evaluate the longitudinal QOL scores.

RESULTS

Of 136 eligible patients from April 2002 until October 2004, 4 refused participation and 4 were unable to comprehend (Fig. 1). Characteristics of the remaining 128 patients are given in Tables 1 and 2. These characteristics as well as perioperative data did not differ between patient groups. The primary outcome measure was not influenced by location of hospital. Quality of life data were obtained from 69 patients.

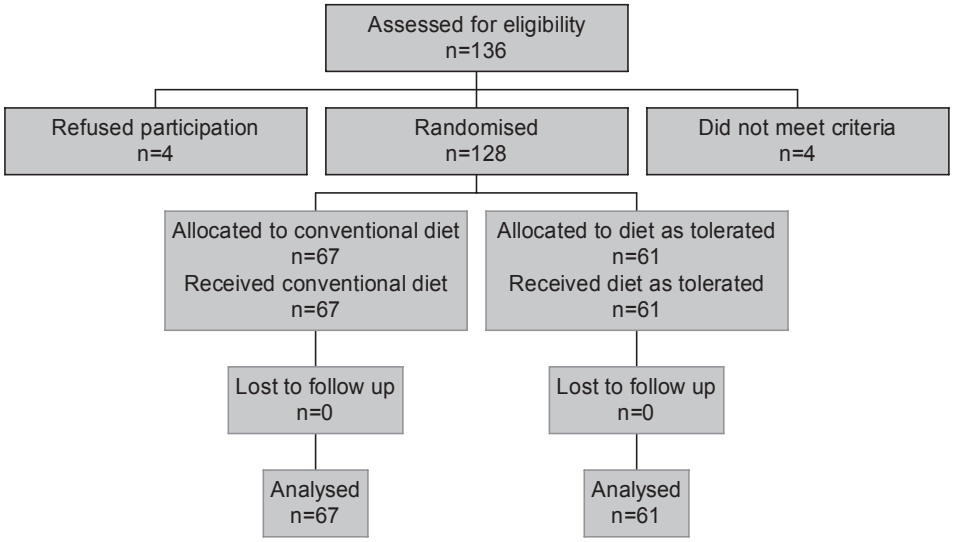

Fig. 1. Flow diagram of trial participants

Table 1. Patient characteristics and baseline data

	Conventional group N=67	Fast group N=61	P
Sex M	32 (48)	36 (59)	
F	35 (52)	25 (41)	
Median (range) age (years)	67 (33-87)	63 (18-82)	0.126
BMI (range)	26.1 (18.4-56.8)	25.8 (17.5-38.8)	0.340
Type of surgery			
Vascular	17 (25)	15 (25)	
Abdominal	50 (75)	46 (75)	
Epidural anaesthesia	33 (57)	34 (57)	0.718
Operating time (minutes, range)	120 (46-345)	120 (60-338)	0.739
Blood loss (ml, range)	560 (100-3500)	400 (50-2070)	0.042
Cardial history	21 (31)	12 (20)	0.159
Pulmonal history	11 (16)	13 (21)	0.505
Diabetes	5 (8)	8 (13)	0.387

Values in parentheses are percentages unless stated otherwise.

Table 2. Operative procedures

Surgical procedure	Conventional group N=67	Fast group N=61
Vascular operation	17 (25)	15 (24)
Hemicolectomy	19 (28)	14 (23)
Ileocoecal resection	2 (3)	6 (10)
Low anterior resection	10 (15)	14 (23)
Total mesorectal excision	2 (3)	1 (2)
Restoring continuity	9 (14)	6 (10)
Hartmann's procedure	5 (8)	5 (8)
Total mesorectal excision with stoma	3 (4)	0

Values in parentheses are percentages

Gastrointestinal recovery is summarized in Table 3. Reinsertion of a nasogastric tube was needed in 20 percent of the patients in the fast group versus 10 percent in the conventional group, due to repeated vomiting (n.s.; $p = 0.213$). In each case the tube could be withdrawn within the next few days and oral feeding was resumed according to prior randomization. There were no significant differences between groups for return of bowel function. Patients in the fast group tolerated a diet containing solid foods the second postoperative day; patients expanding gradually started a normal diet the fifth postoperative day ($p < 0.001$). Duration of hospitalisation was similar for both groups.

Table 4 gives an overview of complications and in-hospital mortality. Complications occurred in 20 patients (33 percent) in the fast group and in 14 (21 percent) in the conventional group ($p = 0.162$). Complication rates did not differ between patients having

Table 3. Convalescence of gastrointestinal function

	Conventional group N=67	Fast group N=61	P
Reinsertion nasogastric tube (%)	7 (10)	12 (20)	0.213
Days to normal bowel sounds (range)	1 (1-4)	1 (1-7)	0.212
Days to flatus passage (range)	2 (1-7)	2 (1-10)	0.604
Days to first defecation (range)	3 (1-10)	4 (1-9)	0.175
Days to tolerance of solid diet (range)	5 (2-19)	2 (1-13)	<0.001
Days to reinsertion gastric tube	0	0	0.789
Hospital stay (days, range)	8 (5-160)	9 (4-81)	0.979

Table 4. Complications and in-hospital mortality

Complications	Conventional group N=67	Fast group N=61	P
Anastomotic leakage*	2 (3)	3 (5)	ns
Wound dehiscence	2 (3)	3 (5)	ns
Ileus	3 (4)	5 (8)	ns
Abdominal abscess	0	1 (2)	ns
Digestive tract	0	1 (2)	ns
Haemorrhage	2 (3)	0	ns
Wound infection	3 (5)	4 (7)	ns
Pneumonia	5 (7)	6 (10)	ns
Urinary tract infection	2 (3)	2 (3)	ns
Cardial	0	1 (2)	ns
Thromboembolic	1 (1)	0	ns
Mortality	2 (3)	3 (5)	ns

Values in parentheses are percentages. Patients may have more than one complication. * applies only to patients having undergone digestive tract surgery, receiving an enteral anastomosis.

undergone a vascular procedure or digestive tract surgery. Three patients from the fast group died in hospital. One was a woman who died from cardiac complications 5 days following total mesorectal resection. The other two were men each with a cardiopulmonary history. They both developed anastomotic leakage after hemicolectomy and died of multiple organ failure 52 and 16 days, respectively, after surgery. Two patients from the conventional group died in hospital. One was a 75-year-old woman who developed pneumonia and died of respiratory insufficiency three weeks after hemicolectomy. The other was a man with a cardiac history who died following vascular surgery complicated by haemorrhage and wound dehiscence.

Quality of life scores assessed by the SF36 and MFI-20 are shown in Table 5. No significant differences were found between the groups. Median health scores (VAS) and EuroQol-5D scores are plotted in Figures 2 and 3, respectively, and show similar measures for both groups.

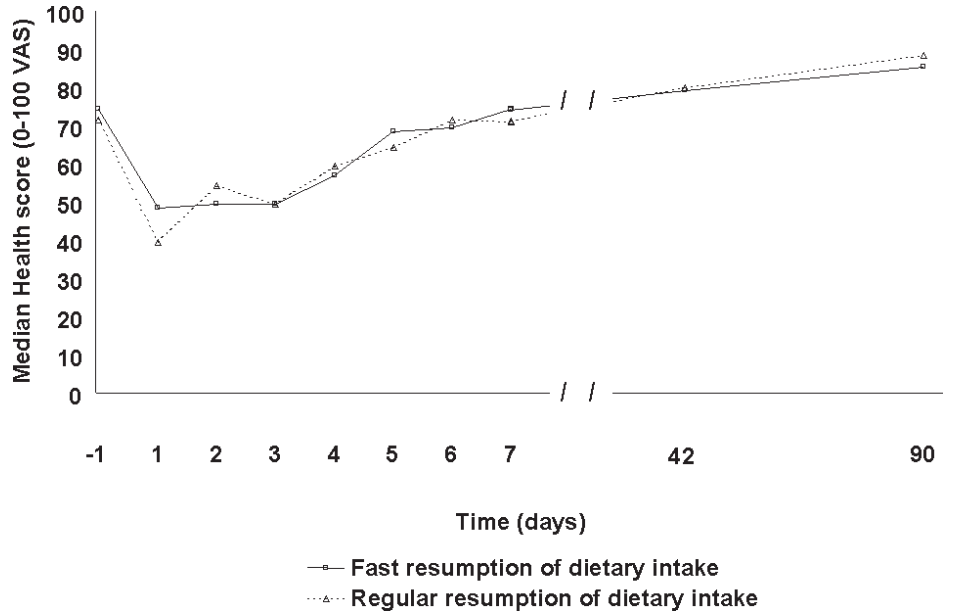

Fig. 2. Median VAS score in time after surgery for both groups

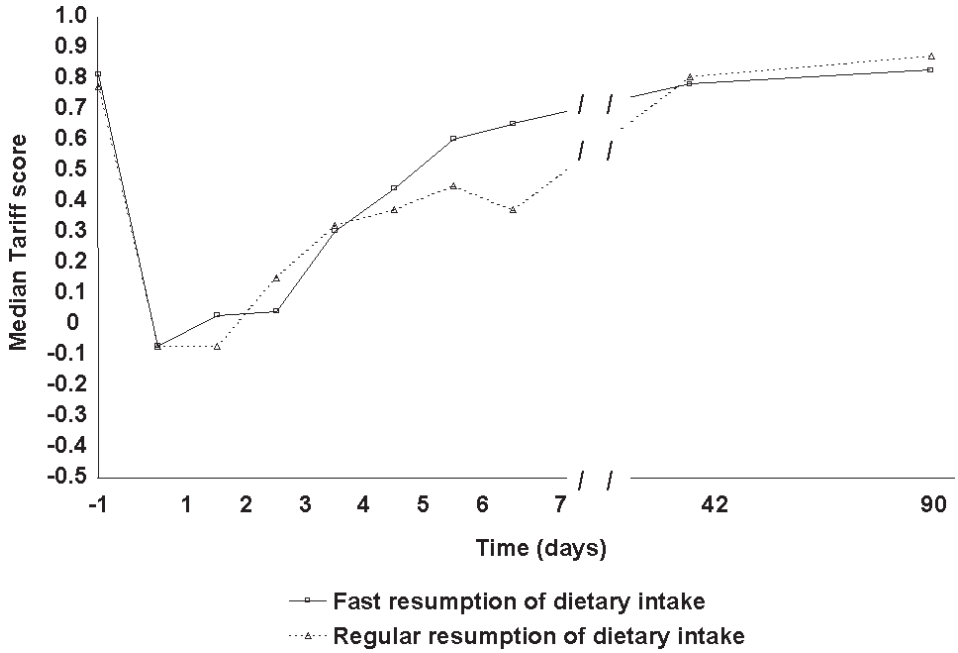

Fig. 3. Tariff (EuroQol) scores at baseline and in time after surgery for both groups

Table 5. Quality of Life following fast versus conventional resumption of dietary intake. Estimated differences, 95% confidence intervals and P-values at the dimensions of the SF-36 and MFI-20 scales during follow-up. Positive estimated differences at the SF-36 dimensions indicate that fast dietary resumption results in higher quality of life scores (i.e. better QOL). Positive estimated differences at the MFI-20 dimensions indicate that fast dietary resumption results in higher fatigue scores (i.e. more fatigue).

Dimension	Estimated difference	95% Confidence Interval	P
SF-36			
Physical functioning	0.575	-11.0 to 12.2	0.921
Role physical	-3.46	-17.7 to 10.7	0.626
Bodily pain	-0.19	-11.4 to 11.0	0.973
General health	0.88	-6.2 to 8.0	0.805
Vitality	6.02	-4.2 to 16.2	0.241
Social functioning	4.1	-6.3 to 14.6	0.433
Role emotional	12.9	-2.0 to27.7	0.087
Mental health	-0.20	-6.1 to 5.8	0.947
MFI-20			
General fatigue	-0.30	-1.1 to 0.5	0.449
Physical fatigue	-0.18	-1.0 to 0.7	0.672
Reduced activities	0.04	-1.5 to 1.6	0.96
Reduced motivation	-0.57	-1.5 to 0.4	0.228
mental fatigue	-0.43	-1.8 to 0.9	0.515

DISCUSSION

Postoperative ileus is an important factor contributing negatively to postoperative convalescence. Perioperative care is therefore aimed at minimizing the extent and duration of postoperative ileus. Early resumption of an oral diet is suggested to diminish ileus duration but results from trials are inconclusive [5,6,12,13]. Most studies still used a prophylactic nasogastric tube, despite consensus on this specific item [14].

Management in our study did not include routine nasogastric drainage. Frequency of reinsertion of a nasogastric tube did not differ significantly between patients with an early resumption of oral intake and patients expanding their diet gradually. This finding is in accordance with other studies [6,15]. Total duration of days in situ of a nasogastric tube did not differ between groups. Functional recovery of the digestive tract also did not differ between groups. However, patients in the fast group tolerated a meal containing solid food significantly earlier than the regular expanding group. This clearly suggests that oral feeding is tolerated independently of the presence of postoperative ileus. Introduction of an early oral feeding protocol does not seem to reduce duration of postoperative ileus. This finding casts doubt on the assumption that ileus contributes negatively to tolerance of a normal diet.

Although a systematic review concludes that there seems to be no clear advantage of keeping patients nil by mouth for any amount of time postoperatively, a recent survey

among European surgeons showed that only from 5 to 50% had implemented an early oral feeding regimen [16,17]. In recent years multiple fast track regimes combining surgical and anaesthetic techniques, analgesia, diet and mobilisation, have been introduced [18-21]. Although the concept of multimodal treatment seems to work, the contribution of each separate item remains unclear. This is probably due to inconsistency in the diverse fast track protocols. In order to arrive at a definite protocol with maximum effect on recovery, we need to evaluate the separate items in a further standardised perioperative regime. As little is known of the effects of early introduction of oral feeding and nutritional status, these issues in particular warrant clarification.

Complications and mortality in our study did not differ between groups. The two deaths in the fast group because of anastomotic leakage cannot be attributed to the feeding regimen. In both cases leakage occurred before a diet containing solid food had been resumed. Group size is also too small to attribute anastomotic leakage to diet. Furthermore, the literature gives evidence that an adequate oral intake has a strengthening effect on intestinal anastomoses and does not lead to anastomotic complications [19,22]

Quality of life is perhaps the most important endpoint to the patient. Very few studies have assessed quality of life after gastrointestinal surgery, is and these compare laparoscopic colonic resection with open resection [23,24]. Schwenk et al. in a review article demonstrated similar quality of life scores in patients undergoing either laparoscopic or open colonic surgery [25]. Studies analysing multimodal treatment aimed at enhancing postoperative recovery have, until now, not assessed quality of life. In the present study, we found no quality of life benefits for the group with early resumption of oral intake. This finding would seem to indicate that early oral feeding as a sole enhancing factor in postoperative management, does not influence feeling of well being. It would therefore be interesting to know the effect of multimodal treatment on quality of life.

In conclusion, the large majority of postoperative patients tolerate early resumption of oral intake well, and it does not seem to lead to a higher postoperative complication rate. In addition, it is suggested an oral diet is well tolerated despite incomplete recovery of gastrointestinal function. There is therefore no reason to withhold oral intake following open colorectal or abdominal vascular surgery.

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4 Relaparotomy following complications of feeding jejunostomy in esophageal surgery

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Digestive Surgery 2004; 21:192-6

ABSTRACT

Background: After recognition of the importance of early postoperative enteral feeding, placement of a feeding jejunostomy as an adjunct to gastrointestinal surgery has become widely accepted. However, little attention has been paid to surgical complications and their consequences. Feeding jejunostomy as an adjunct to esophageal resection and reconstruction can lead to serious surgical complications.

Methods: Between 1978 and 2000, 1,387 patients underwent esophageal resection and reconstruction. Of these, 1,166 patients received a needle catheter feeding jejunostomy at the end of the operation. All postoperative complications were prospectively evaluated in a database including surgical complications related to the feeding jejunostomy.

Results: Overall, surgical complications occurred in 36%. There were 13 (1.1%) feeding jejunostomy related complications leading to relaparotomy. Of these, intraperitoneal leakage was the most common complication (n = 5). Other jejunostomy-related complications included dislodgement (n = 4), herniation (n = 3) and torsion (n = 1). Five patients (0.4%) died despite relaparotomy.

Conclusions: Feeding jejunostomy as an adjunct to esophageal resection and reconstruction can lead to serious surgical complications. Preventive measures have not resulted in a decrease in complication rate. Complications of leakage necessitating relaparotomy are associated with a high mortality rate. Therefore, other means of enteral access should be considered.

INTRODUCTION

The importance of early postoperative enteral feeding in trauma patients and in critically ill patients has become increasingly evident [1,2,3], leading to renewed interest in access routes for nutritional support. Many access routes to the gastrointestinal tract for enteral feeding purposes have been described, of which the feeding jejunostomy tube is most often advised [4]. The concept of feeding jejunostomy was first introduced in 1973 by Delany et al. [5].

Placement of a tube or needle catheter jejunostomy as an adjunct to upper gastrointestinal tract surgery is now widely accepted [6,7,8,9]. Although the different techniques for inserting a feeding catheter have been well described, surgical complications related to the jejunostomy feeding tube are seldom reported. To develop a responsible policy regarding this specific feeding access it is important to specify the technical complications that can occur.

Therefore, this study reviewed the complications of feeding jejunostomy after esophagogastric surgery in a series of 1,166 patients.

METHODS

Between 1978 and 2000, a total of 1,387 patients underwent elective esophagogastric surgery in our hospital. All patients were prospectively entered into the Esophageal Surgery Database.

Of these 1,387 patients, 1,166 (84%) underwent a needle catheter jejunostomy as part of the primary operative procedure for early postoperative enteral feeding.

In this study, only complications resulting in relaparotomy were taken into consideration.

The technique for placement of the needle catheter was the same in all patients following the technique described by Delaney et al. [5]. Approximately 20 cm distal to the ligament of Treitz the jejunostomy site is selected. Through the anterior abdominal wall a hollow needle containing a silicone catheter (ch 10, Cystofix®, B. Braun Melsungen AG) is brought into the peritoneal cavity. The catheter is first inserted intramurally for a distance of 5 cm into the wall of the jejunum and is then brought intraluminal. A purse-string suture of absorbable material is used to fixate the catheter to the jejunum and the jejunum is then fixated to the abdominal wall by two more interrupted sutures.

On the first postoperative day the correct position of the catheter is tested by an X-ray after contrast material given into the catheter. After confirming the position of the catheter, enteral feeding is started directly, following a standard feeding protocol, beginning on the first postoperative day. Nutritional support consisted of Nutrison standard

solution, 1.0 Kcal/ml (Nutricia Nederland B.V.) as a continuous infusion commencing at 30 cm^3/hr increasing to 84 cm^3/hr on the third day as tolerated. The nasogastric tube is removed on either the first or the second postoperative day. Patients are allowed to drink 25 cm^3 of water per hour. Approximately 10 days after operation an esophagogram is obtained and if no anastomotic leakage is present, the patient starts an oral diet and, if this is tolerated, intrajejunal feeding is discontinued. Patients are discharged when no visible leakage is evident and when oral intake is adequate. Three weeks after discharge, at the first visit at the outpatient clinic, the jejunostomy catheter is removed if adequate intake is achieved. In selected cases such as leakage of the cervical anastomosis the catheter is left in place until adequate intake is possible.

RESULTS

Of 1,387 patients undergoing esophageal resection, 1,166 (84%) received a needle catheter jejunostomy. Table 1 presents data on the patients at baseline. The jejunostomy catheter was placed without complications in all patients. The enteral nutrition protocol was tolerated by all patients until after the contrast study.Overall, there were 571 complications with a surgical cause (table 2) in 422 patients receiving a jejunostomy catheter. Thirteen of these complications were related to the jejunostomy catheter (1.1%) all requiring relaparotomy (table 3). In one patient there was torsion of the jejunostomy catheter; it was removed and replaced by another, which unfortunately obstructed 3 days later. In 3 patients a herniation of small bowel behind the jejunostomy occurred. In 4 patients complete dislodgement of the jejunostomy catheter occurred which resulted

Table 1. Patient characteristics, surgical interventions and diagnosis at baseline.

	n = 1,166
Sex ratio (M:F)	875 (75%) : 291(25%)
Age, years	62 (31-86) SD 10.08
Type of surgery	
Esophagogastric resection and stomach tube reconstruction	956 (82%)
Esophagogastric resection and colonic interposition	154 (13.2%)
Diagnosis	
Malignant disease	901 (77.3%)
Caustic esophageal stricture	4 (0.3%)
Radiotherapy	10 (0.9%)
Achalasia	15 (1.3%)
Gastroesophageal reflux	80 (6.9%)
Barrett esophagus	97 (8.3%)
Miscellaneous	95 (8.1%)

in intraperitoneal leakage in 3 of them. All 4 patients were reoperated and received a new jejunostomy. Intraperitoneal leak of enteral contents without catheter dislodgement occurred five times.

Overall, mortality rate was 3.1%. There were five deaths (0.4%) as a direct consequence of jejunostomy related complications. Onset of complications ranged from 14 to 93 days after the primary operation (table 4). One patient, who had a prior history of cardiac dysfunction, was reoperated because of abdominal wall dehiscence. At exploration, intraperitoneal leakage of jejunal contents at the jejunostomy site was found. This patient developed a septic shock and died a few days later due to myocardial infarction. In the second patient the cervical gastroesophageal anastomosis was disconnected because of an anastomotic leak. A few days later tube feed leakage from the abdominal wound was observed. Because of a poor prognosis this patient was not reoperated and died shortly

Table 2. Surgical complications in the patient group

Complications	**n = 1,166**
Anastomotic dehiscence	115
Postoperative bleeding	50
Chylothorax	44
Pareses n. recurrens	171
Complications of jejunostomy	13
Necrosis of the neo esophagus	23
Wound infection	25
Other	120
Total	571

Table 3. Complications related to catheter jejunostomy

Complication	**relaparotomy**	**death**
Torsion	1	0
Herniation	3	2
Dislodgement	4	0
Intraperitoneal leakage	5	3
Total	13 (1.1%)	5 (0.4%)

Table 4. Data on the deceased patients.

Age of patients years	Operation	Day of onset	Complication	Cause of death
♂ 69 yrs	A	14	Leakage	cardiac
♂ 74 yrs	A	25	Leakage	sepsis
♂ 74 yrs	B	40	Leakage	sepsis
♂ 67 yrs	A	93	Herniation	ARDS
♂ 73 yrs	B	21	Herniation	sepsis

A = esophagogastric resection and tube stomach reconstruction; B = esophagogastric resection and colonic interposition; day of onset = number of days after the primary operation.

afterward. Autopsy confirmed intra-abdominal leak of tube feeding. A 74-year-old man developed a visible leak of the feeding jejunostomy at the skin site approximately 1 month after the primary operation without abdominal symptoms. Ultrasonography suggested intra-abdominal fluid. At exploratory laparotomy enteric leakage at the former jejunostomy site was demonstrated. This patient died of sepsis a few days later. The fourth patient was readmitted to the hospital (3 months after his primary operation) with severe abdominal pain. At admittance he was resuscitated and intubated. A relaparotomy was performed demonstrating an internal herniation around an adhesion of the former feeding jejunostomy that had resulted in an ischemic small bowel. The small bowel was partially resected; a few hours later he died in the ICU of septic shock. The last patient presented with abdominal pain and vomiting and was readmitted nearly 1 month after the esophagogastric resection. At laparotomy, a strangulation of the small bowel around the feeding jejunostomy was found. Reposition with removal of the catheter was performed. Postoperatively, this patient developed a respiratory distress due to pulmonary aspiration from which he did not recover.

COMMENT

The beneficial role of early enteral nutrition in recovery from elective and acute abdominal surgery has been assessed [1,2,3,10]. This has led to an increased use of different types of enteral access routes such as the gastrostomy catheter, needle catheter jejunostomy and the tube jejunostomy. Jejunostomy feeding tubes can be placed as a primary procedure or used as an adjunct to major abdominal operations. In esophageal surgery oral intake is delayed until healing of the anastomosis is adequate; this usually takes up to 7 days. The advantages of postoperative enteral feeding on stress response in this specific kind of surgery have recently been clarified [11]. Enteral nutrition seems to provide a better regulation of inflammatory cytokine response and reduces endotoxin translocation. Nutritional

Table 5. Overview of studies and complications attributed to placement of feeding catheter jejunostomy

Author/year	Patients	Complications	
		n	%
Myers et al.[14] 1995	2,022	34	1.5
Gore et al.[17] 1996	92	14	15.2
Sonawane et al.[16]1997	96	15	15.2
Zapas et al.[18] 1998	92	34	37
De Gottardi et al.[9]1999	100	26	26
Sarr[12] 1999	500	3	0.6
Yagi et al.[13] 1999	78	3	3.8
Holmes et al.[15] 1999	222	37	10

support by a feeding jejunostomy is regarded as safe and functional [7,8,9].

Nevertheless, despite the advantages of feeding jejunostomy, serious complications do occur and can be life threatening. Previous studies report major complication rates of 0 – 3% [9,12,13,14], whereas smaller series describe higher complication rates of 4 – 26% [15,16,17,18]. Table 5 presents an overview of the most important series dealing with the feeding jejunostomy.

In the current series major complications were defined as those requiring relaparotomy; this was necessary in 13 patients (1.1%). Myers et al. [14] report 1% jejunostomy-related reoperations in a large series of 2,002 applications. The authors claim that securing the catheter and confirming the correct catheter position by a contrast study could have prevented approximately half of these reoperations. In the present series, a contrast study was obtained routinely postoperatively in all patients. In all patients with jejunostomy related complications, correct intraluminal position and catheter patency were confirmed by postoperative roentgenogram. Hence, in the present series we did not find a contrast study to have a preventive effect on the reported complications. Furthermore, an analysis of the role of postinsertion jejunograms showed that there were no changes in management following a contrast study, making the use of a routine postinsertion jejunogram unwarranted [19]. Only one other prospective, non-randomized study evaluating complications of needle catheter jejunostomy has been published [20]. In 80 oncology patients, a needle catheter jejunostomy was placed at the end of their operation. There were no major complications; obstruction of the catheter occurred only once, which was managed conservatively. However, this is a small study excluding patients older than 75 years.

Major complications directly related to feeding jejunostomy resulted in death in 5 patients (0.4%). This is a mortality rate of 40% in patients requiring relaparotomy. These findings are in accordance with findings in other large series which report mortality rates ranging from 0 to 1.4% [12,13,14,15]. In all cases, intraperitoneal leakage and herniation with resulting bowel necrosis were the main intraoperative findings.

Considering these results it seems justified to consider other means of enteral access in esophagogastric surgery, for example, the nasoduodenal feeding tube. Page et al. [21] conducted a clinical trial in which patients undergoing esophagectomy were started on enteral feeding by a nasojejunal tube, which was well-tolerated in this way. A prospective, randomized trial comparing feeding by jejunostomy versus a nasoduodenal tube is necessary to further establish the optimal method of postoperative enteral feeding and is in progress.

Complications after placement of a feeding jejunostomy requiring relaparotomy are associated with a high mortality rate. Because preventive measures such as meticulously securing the catheter and use of postoperative contrast studies do not seem efficient, other means of enteral access for feeding purposes should be considered.

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5 Feeding jejunostomy versus nasoduodenal tube in esophagogastric surgery: a prospective randomized trial

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Accepted for publication British Journal of Surgery

ABSTRACT

Background: In esophageal surgery, feeding jejunostomy is often performed but can be accompanied by serious complications.The aim of this prospective randomized trial is to compare feeding jejunostomy and nasoduodenal feeding tube regarding complications and efficacy in esophageal surgery.

Method: In an 18-month period, 150 consecutive patients undergoing esophageal resection were randomized to participate in the trial. In 79 patients enteral access was obtained by a jejunostomy whereas 71 patients received a nasoduodenal tube. Enteral feeding was started the first postoperative day.

Results: In the jejunostomy group there were minor catheter-related complications in 32 (41%) patients versus 23 (32%) in the nasoduodenal group. Leakage of the jejunostomy requiring reoperation occurred once. Enteral feeding was given for a median duration of 11 days in the jejunostomy group and 10 days in the nasoduodenal group. In total, 5 patients in the jejunostomy group and 9 patients in the nasoduodenal group did not tolerate full enteral feeding. The time period between operation and full enteral feeding was 3 days in both groups.

*Conclusions:*The nasoduodenal tube is a safe and efficient method for postoperative enteral feeding in esophageal resection and is preferred to jejunostomy.

INTRODUCTION

Patients undergoing gastrointestinal surgery are often prone to starvation both preoperatively and postoperatively and are therefore at risk for malnutrition. Patients with an esophagogastric tumor often present with weight loss and feeding problems due to obstruction. Indeed, a significant proportion of patients having undergone digestive surgery were found to be malnourished[1]. A prohibited postoperative intake will add to this problem. Because early enteral feeding is considered to have a beneficial effect on postoperative morbidity in these patients, early enteral feeding is promoted[2]. Enteral access is usually obtained by a feeding jejunostomy placed concomitant with the primary operative procedure. Although a feeding jejunostomy is considered to be safe, serious complications with its use have been described[3-9]. An alternative access route may be through a nasoduodenal feeding tube. A prospective randomized trial was conducted to compare the feeding jejunostomy and the nasoduodenal feeding tube with regard to complications and efficacy.

PATIENTS AND METHODS

A total of 150 consecutive patients undergoing esophageal resection were randomized to participate in the trial. Randomization took place in the operating theater after esophageal resection had been performed. The study was approved by the Medical Ethical Committee. All patients gave written informed consent prior to operation.

Patients were randomly assigned to receive either a nasoduodenal feeding tube or a jejunostomy catheter. Randomization took place using sequentially numbered, sealed envelopes. All patients were operated by two staff surgeons.

In 79 patients enteral access was obtained by placing the needle catheter following the technique first described by Delany et al.[10]. Approximately 20 cm distal to the ligament of Treitz the jejunostomy site is selected. Through the anterior abdominal wall a hollow needle containing a silicone catheter (ch 10, Cystofix®, B. Braun Melsungen AG) is brought into the peritoneal cavity. The catheter is first inserted intramurally for a distance of 5 cm into the wall of the jejunum and is then brought intraluminal. A purse-string suture of absorbable material is used to fixate the catheter to the jejunum and the abdominal wall.

On the first postoperative day the correct position of the catheter is tested by an X-ray after contrast material given into the catheter. After confirming the position of the catheter, enteral feeding is started directly following a standard feeding protocol, beginning on the first postoperative day.

In 71 patients a radiopaque, polyurethane self-propelling nasoduodenal tube was utilised, measuring 145 cm (ch 10 Bengmark, Nutricia Nederland b.v., manufacturer:

Châtel Medical Devices SA). The tube is placed using a guide wire, just before completing the cervical anastomosis and brought into position into the proximal jejunum. The guide wire is kept near the patient so that in case of dislodgement the tube can be replaced without the need of a gastroscopy. Enteral feeding is started the first postoperative day following the same feeding protocol as in the jejunostomy group. In both groups a transabdominal urinary catheter is placed at the end of the operation.

Nutritional support consisted of Nutrison standard solution (Nutricia Nederland B.V.) 1.0 Kcal/ml as a continuous infusion commencing at 30 cc/h increasing to 84 cc/h on the third day as tolerated. The nasogastric decompression tube is removed on either the first or the second postoperative day. Patients are allowed to drink 25 cc of water per hour. Approximately 10 days after operation an esophagogram is obtained and, if no anastomotic leakage was present, the patient is allowed to start an oral diet. Intrajejunal feeding is then discontinued and in the nasoduodenal feeding patient group the tube is removed. Patients are discharged from hospital when there is no visible leakage and when oral intake is possible. The jejunostomy catheter is removed at the first visit at the outpatient clinic approximately 3 weeks postoperatively.

The primary outcome measure was catheter-related complications. Surgical and non-surgical complications were identified and registered. The time period between operation and the tolerance of full enteral feeding and the time at which both catheters were removed was also recorded.

Statistical analysis

All randomized patients were analysed on an intention-to-treat basis. The Mann-Whitney U test was used to compare quantitative outcomes. The chi-square test/Fisher's exact test was used to compare proportions. A two-sided p-value less than 0.05 was considered statistically significant.

RESULTS

Over a period of 18 months 150 consecutive patients having undergone esophageal resection and reconstruction were randomized for participation. Table 1 presents base line characteristics of the study group. There were 79 patients in the jejunostomy group and 71 patients in the nasoduodenal tube group. Age, gender distribution and types of operative procedures were similar in the two groups. All patients were operated through a midline abdominal incision. Twelve patients also received a thoracotomy because of proximal localisation of the tumor.

Patients were classified into three groups on the basis of morbidity: catheter-related, surgical and non-surgical complications (Table 2). There were 8 deaths in total; 6 in the

Table 1. Patient characteristics and surgical interventions at baseline

	jejunostomy group n = 79	**nasoduodenal group n = 71**
sex (M/F)	64 (81%) : 15 (19%)	56 (79%) : 15 (21%)
age (yrs)	61 (28-89)	61 (39-85)
THE*	73 (92%)	65 (92%)
TTER**	6 (8%)	6 (8%)

*THE: transhiatal esophageal resection;

**TTER: transthoracic esophageal resection, data shown are numbers of patients (%) or median (range)

Table 2. Complications according to randomized group

complications	**jejunostomy group n = 79**	**nasoduodenal group n = 71**	**p-value**
surgical	17 (22%)	23 (32%)	0.195
non-surgical	41 (52%)	33 (46%)	0.518
catheter-related	32 (41%)	23 (32%)	0.315
death	6 (8%)	2 (3%)	0.281
total	54 (68%)	53 (75%)	0.470

Data shown are numbers of patients (%)

Table 3. Catheter-related complications

complications	**jejunostomy group n = 79**	**nasoduodenal group n = 71**
obstruction	5 (6%)	2 (3%)
removal by patient	4 (5%)	2 (3%)
dislocation	5 (6%)	16 (23%)
infection insertion site*	13 (16%)	
leakage*	3 (4%)	
relaparotomy	1 (1%)	0 (0%)

* Only applies to the jejunostomy group;

jejunostomy group and 2 in the nasoduodenal group; none of these deaths could be attributed to catheter-related complications.

The incidence of catheter-related complications was 41% (95% confidence interval: 30%-52%) in the jejunostomy group and 32% (95% CI: 22%-45%) in the nasoduodenal group ($p = 0.315$, Table 3). One patient underwent relaparotomy 10 days after his primary operation due to leakage of the jejunostomy. Symptoms in this case were fever, increasing infection parameters and small bowel contents at the catheter insertion site. During exploratory laparotomy no intraabdominal leakage was found; the catheter was removed and the jejunostomy closed.

Occurrence of surgical-related complications was 22% in the jejunostomy group versus 32% in the nasoduodenal group (Table 4).

Table 4. Surgical complications

complications	jejunostomy group n=79	nasoduodenal group n=71
leakage of cervical anastomosis	5 (6%)	8 (11%)
splenectomy	4 (5%)	4 (6%)
hemorrhage	3 (4%)	3 (4%)
wound dehiscence	2 (3%)	3 (4%)
chylous leakage	0 (0%)	2 (3%)
mediastinitis	2 (3%)	2 (3%)
recurrent nerve pareses	0 (0%)	4 (6%)

Table 5. Non-surgical complications

complications	jejunostomy group n=79	nasoduodenal group n=71
wound infection	5 (6%)	4 (6%)
urinary tract infection	4 (5%)	1 (1%)
pneumonia	27 (34%)	29 (41%)
aspiration	1 (1%)	2 (3%)
cardiac events	3 (4%)	4 (6%)
thrombo-embolic events	7 (9%)	4 (6%)
delirium	3 (4%)	2 (3%)

Patients can have more than one complication

Non-surgical complications were similar in both groups, of which pneumonia was the most common (Table 5).

Catheter efficacy

Median time between operation and toleration of full enteral feeding was 3 days in both groups (Table 6). Enteral feeding was given for a median duration of 11 days in the jejunostomy group and 10 days in the nasoduodenal group. Total duration of enteral feeding was 7 days in both groups. Five patients did not attain full enteral feeding via jejunostomy due to nausea and abdominal distension, this was also the case in 9 patients

Table 6. Catheter efficacy

	jejunostomy group n=79	nasoduodenal group n=71	p-value
time to reach target nutrition rate	3 (2-9)	3 (1-12)	0.110
duration of full enteral support	7 (1-123)	7 (1-53)	0.406
total duration of enteral support	11 (2-126)	10 (2-55)	0.210
intolerance of enteral nutrition	9 (11%)	5 (7%)	0.411

Data shown are median days (range) or number of patients (%)

with a nasoduodenal tube. A switch to parenteral infusion was needed in 1 patient with a jejunostomy catheter and in 3 with a nasoduodenal tube. In all cases this was due to removal of the catheter within 3 days after operation. Two patients initially received a nasoduodenal tube but, due to cervical anastomosis leakage and reoperation, had to convert to feeding jejunostomy. Four patients with a feeding jejunostomy converted to a nasoduodenal tube because of early accidental removal of the jejunostomy catheter.

Five patients were discharged whilst still using the jejunostomy catheter and four patients went home still using the nasoduodenal tube.

Median duration of hospitalisation was 14 days in each group.

DISCUSSION

Patients undergoing esophagogastric surgery are often in a suboptimal condition due to tumor effects and physiological status. A significant proportion is found to be malnourished[11]. Esophagogastric surgery is accompanied by high morbidity influenced by the patient's condition and an extensive operation field with strong impact on pulmonary function. Postoperative enteral feeding has been shown to have a beneficial effect on postoperative morbidity in patients undergoing gastrointestinal surgery. In a recent meta-analysis of controlled trials comparing early enteral feeding with postoperative starvation a reduction of infectious complications was found in patients who were enterally fed[12]. Enteral feeding resulted in a decrease in complication rate in malnourished patients undergoing gastrointestinal surgery compared to parenteral feeding[13]. A similar trial in esophagogastric surgery indicated a reduced postoperative morbidity in the enteral group[14,15]. Immediate postoperative enteral feeding has thus become common practice[4,5]. Usually this is achieved by placing a jejunostomy concomitant with the primary procedure. However, this procedure is associated with complications described in 1.5% to 37% of patients[7,16-21]. Since feeding jejunostomy has reduction of postoperative morbidity as primary goal, complications induced by this procedure are undesirable.

The present study describes complications related to administration of enteral feeding. Catheter-related complications were frequent and similar in both groups: in the jejunostomy group the incidence was 41%. Other studies on usage of a feeding jejunostomy in esophageal surgery describe variable complication rates (Table 7). This can be attributed to the fact that most studies only consider major complications and have a retrospective study design.

In the present study infection at the insertion site was the most common complication followed by catheter dislocation. Leakage of the jejunostomy necessitating relaparotomy occurred in one patient and was considered a major complication. These results are in accordance with findings in other recent series which report mortality rates up to 50%

Table 7. Overview of the usage of feeding jejunostomy in esophageal surgery

year	author	study design	number of patients	complications
1988	Brandmair[3]	RCT	40	45%
1994	Gerndt[4]	retrospective	523	2.1%
1995	Wakefield[5]	retrospective	58	14%
1996	Mercer[6]	RCT	32	13%
1999	Yagi[7]	RCT	78	3.8%
2004	Date[8]	retrospective	42	21.4%
2004	Han-Geurts[9]	prospective	1166	1.1%

RCT = randomized controlled trial

following relaparotomy for catheter-related complications. Myers et al. report 1% jejunostomy-related relaparotomies in a large series of 2002 applications[16]; the authors claim that securing the catheter and confirming correct position by a postoperative roentgenogram could have prevented half of these reoperations. In the present series, despite a similar policy followed in each patient, we were unable to prevent the reported complications.

The catheter-related complication rate in our nasoduodenal group was 32% and consisted mainly of tube dislocation. Dislocation is a frequently described phenomenon with nasoduodenal tubes and special attention must be paid to firm nasal fixation with plaster. Despite its common occurrence, in the present study it did not lead to intergroup differences in duration of tube feeding. No major nasoduodenal catheter-related complications were found. Two prospective studies described the use of a nasoduodenal feeding tube in esophagic and gastrointestinal surgery[22,23]; complication rates of 3.5% and 0% respectively, were found with complications consisting of tube dislodgement. However, patient numbers in that study were small. This problem may be reduced in the future since feeding catheters are continuously improved.

Tolerance of enteral feeding was comparable in both groups with the majority commencing to a full diet within three days after operation. Only 7% in the jejunostomy group and 11% in the nasoduodenal group did not reach the full nutritional regimen due to feeding-related abdominal symptoms. This indicates a good enteral tolerance, in accordance with other studies[6,22,24].

To our knowledge, this is the first prospective randomized trial comparing jejunostomy and nasoduodenal tube as means of feeding access. The results show that the nasoduodenal tube is an effective means of administering enteral feeding. In this trial one major complication regarding jejunostomy was found; minor complications were comparable to those accompanying the nasoduodenal tube. Major complications related to feeding jejunostomy are regarded unacceptable since the initial purpose is to reduce postoperative complications. Therefore, it may be concluded that for postoperative enteral feeding purposes in esophagogastric surgery the nasoduodenal tube is preferred to a jejunostomy catheter.

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6 Laparoscopic feeding jejunostomy: a systematic review

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Surgical Endoscopy 2005; 19:951-7

ABSTRACT

Background: Enteral feeding devices have gained popularity since the beneficial effects of enteral nutrition have been clarified. Laparoscopic placement of a feeding jejunostomy is the most recently described enteric access route. In order to classify current surgical techniques and assess evidence on safety of laparoscopic feeding jejunostomy a systematic review was performed.
Methods: The electronic databases Medline, Cochrane and Embase were searched. Reference lists were checked and requests for additional or unpublished data were send to authors. Outcome measures were surgical technique and catheter-related complications.
Results: Enteral access for feeding purposes can be effectively achieved by laparoscopic jejunostomy. Laparoscopic jejunostomy can be accomplished either total laparoscopic or laparoscopic aided. The most experience was obtained with total laparoscopic placement. Which technique to apply should depend on the surgeon's expertise. Conversion rate is similar to other laparoscopic procedures. Complications can be serious and therefore strict patient selection should be warranted.
Conclusion: Laparoscopic feeding jejunostomy is a viable method to obtain enteral access with the advantages of minimal invasive surgery.

INTRODUCTION

The enteral route is the preferred route for nutrition administration in malnourished or oncologic patients and for patients in the postoperative period [1-4]. Various access routes for enteral nutrition are available but for the purpose of long-term tube feeding preference is given to percutaneous endoscopic gastrostomy or operative gastrostomy or jejunostomy. Since minimally invasive techniques have many advantages, increasing attention is paid to laparoscopic or laparoscopic-assisted placement of a feeding jejunostomy [5-9]. Laparoscopic feeding jejunostomy was first described 1990 [10]. After several failed attempts to perform a percutaneous endoscopic gastrostomy in a quadriplegic patient on ventilatory support, the authors succeeded in placing a laparoscopic feeding jejunostomy. Following this primary report many others started to apply this technique and describe their personal experience. Feeding jejunostomy is, however, associated with serious and less-serious complications [11,12]. The laparoscopic technique is regarded as a safe procedure and an alternative to open feeding jejunostomy [13].

Following an extensive literature search to identify relevant literature and their references, this systematic review aims to classify current surgical techniques and assess evidence on safety of laparoscopic feeding jejunostomy.

METHODS AND TECHNIQUES

The Embase, Medline and Cochrane databases from 1981 through April 2004 were searched by two independent reviewers, using the keywords: "laparoscopic" and "jejunostomy" with the boolean operators "and" and "or". The search was restricted to titles and abstracts. There were no language restrictions. Authors were contacted for additional data on outcomes not reported in publications. Both independent reviewers extracted data. Discrepancies were resolved by discussion and consensus. From each study data were collected on indication for placement, surgical technique and catheter-related complications. Surgical technique was categorised as total laparoscopic and laparoscopic aided. Outcomes potentially related to placement and usage of feeding jejunostomy included woundinfection, dislodgement, obstruction, leakage, bowel perforation, volvulus and reoperation.

RESULTS

Twenty three studies were identified [10,13-34]. Two studies were excluded because only a technique description was given without patient characteristics [32,33]. Attempts to obtain

unpublished data from the authors were unsuccessful. One study was excluded since both laparoscopic gastrostomy and jejunostomy were described and no distinction was made in groups regarding results [34]. Sixteen studies had a prospective study design [10,14,15,17,18,21-24,26-31]. The earliest study dated from 1990 [10]. Additional unpublished data were obtained for two of the studies [14,31].

Underlying pathology

Indications for placement of a feeding jejunostomy differed between studies (Table 1). Nine studies included upper digestive carcinoma. Eight studies included neurologic deficit and seven studies trauma resulting in neurologic damage. Malnutrition was an indication in four studies. Motility disorders of the digestive tract was mentioned in two studies and gastropareses of different origins in three. In three studies a laparoscopic jejunostomy was placed as an adjunct to surgery and postoperative recovery. Four studies mentioned diverse reasons for applying a feeding jejunostomy.

Technique

Several techniques for placement of feeding jejunostomy were used. One study does not describe method of placement in the jejunostomy group but uses T-fasteners in the gastrostomy group making it likely the same technique was used in the jejunostomy group [20]. An overview is given in Table 2. The techniques were classified into two groups: the total laparoscopic method and the laparoscopic aided method which includes exteriorizing of the small bowel.

Feeding jejunostomy using a total laparoscopic approach was applied in the majority of the studies [10,13,15,17,19-21,24-27,29,31]. A further distinction was made into three different methods of retracting and anchoring the jejunum to the anterior abdominal wall (Table 2).

The first technique uses transabdominal sutures [10,15,19,24,29,31]. After the usual establishment of a pneumoperitoneum and placement of three trocars, three or four transabdominal sutures are placed in a diamond configuration incorporating seromuscular jejunal wall and anterior abdominal wall. A feeding tube or a needle catheter is inserted through the centre of the array of sutures. In one study one of the transabdominal sutures is used [10] to attain a seal around the feeding catheter to prevent leakage. In another study adjacent intracorporeal sutures were placed around the catheter [24,31]. In the remaining studies, no fixation is used. The transabdominal sutures are tied over bolsters to prevent skin damage. After two weeks the jejunum is expected to be adherent to the abdominal wall and the bolsters and sutures are removed. Sangster et al. applied the transabdominal suturing technique only in the beginning of his study [19]. Allen in his study used transabdominal sutures but tied them at fascie level [29].

In four studies T-fasteners are employed which were originally developed for fixation of the anterior gastric wall in percutaneous gastrostomy [17,20,21,25]. The T-fastener consists of

Table 1. [1]diverse: a: esophageal rupture, b: Heller myotomie (2), esophageal perforation (4), gastric perforation (1), c: head and neck carcinoma (NR), pancreatic carcinoma (NR), aspiration (NR), d: benign disease

author	year	design	n	neurologic	trauma	upper digestive carcinoma	head & neck carcinoma	gastroparesis	motility disorder	malnutrition	adjunctive	diverse[1]
O'Regan [10]	1990	prosp	1		1							
Morris [14]	1991	prosp	3	2	1							
Albrink [15]	1992	prosp	1		1							
Ellis [16]	1992	retro	17			3					14	
Duh [17]	1993	prosp	5							5		
Eltringham [18]	1993	prosp	3		1				2			
Sangster [19]	1993	retro	23	4	16		2				1	
Edelman [20]	1994	retro	2	1	1							
Duh [21]	1995	prosp	36	11		13	12					
Ramesh [22]	1995	prosp	1				1					
Gedaly [23]	1996	prosp	9	6	3							
Hotokezaka [24]	1996	prosp	32	10		5		16	1	2		
Murayama [25]	1996	retro	5	2	1					2		
Senkal [26]	1998	prosp	18			13	1					3[a]
Nguyen [27]	1999	prosp	66			11		2			46	7[b]
Rosser [28]	1999	prosp	38			26						35[c]
Allen [29]	2002	prosp	35	4		7		23		1		
Duzgun [30]	2002	prosp	7			2	5					
Nicolau [31]	2003	prosp	2			2						
Senkal [13]	2004	retro	80			68	18					8[d]
total			**384**	**40**	**25**	**150**	**39**	**41**	**3**	**26**	**61**	**49**

Table 2. Numbers are patient numbers; NR = not reported

author	n	method	fixation	wound infection	bleeding	removal	pain	dislodgment	obstruction	leakage	perforation	volvulus	re operation	conversion	mortality
O'Regan [10]	1	tot lap	transabd	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0	0
Albrink [15]	1	tot lap	transabd	0	0	0	0	0	0	0	0	0	0	0	NR
Duh [17]	5	tot lap	Tfastener	0	0	0	0	0	0	1	0	0	0	0	1
Sangster [19]	23	tot lap	transabd	3	0	0	0	0	0	0	0	0	0	0	1
Edelman [20]	2	tot lap	Tfastener	0	0	0	0	1	0	0	0	0	0	0	NR
Duh [21]	36	tot lap	Tfastener	3	0	0	0	5	0	0	3	1	3	3	4
Hotokezaka [24]	32	tot lap	transabd	4	0	0	0	4	2	0	1	0	1	4	3
Murayama [25]	5	tot lap	Tfastener	0	0	0	0	4	0	0	0	0	0	0	5
Senkal [26]	18	tot lap	pursestr	1	0	0	0	0	0	0	0	0	0	0	NR
Nguyen [27]	66	tot lap	pursestrg	2	0	0	0	0	1	0	1	0	2	0	NR
Allen [29]	35	tot lap	transabd	2	0	2	2	0	0	0	0	0	1	0	NR
Nicolau [31]	2	tot lap	transabd	0	0	0	0	0	0	0	0	0	0	0	NR
Senkal [13]	80	tot lap	pursestg	3	0	2	0	0	3	0	0	0	0	0	NR
Morris [14]	3	lap aided	extracorp	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0	NR
Ellis [16]	17	lap aided	witzel	0	0	NR	NR	NR	NNR	0	0	0	0	0	NR
Eltringham [18]	3	lap aided	extracorp	0	0	0	0	2	0	0	0	0	0	0	0
Ramesh [22]	1	lap aided	pursestr	0	0	0	0	0	0	0	0	0	0	0	0
Gedaly [23]	9	lap aided	extracorp	2	0	1	0	0	0	1	0	0	0	0	NR
Rosser [28]	38	lap aided	transabd	0	1	0	0	0	0	0	0	0	0	0	NR
Duzgun [30]	7	lap aided	extracorp	0	0	0	0	0	0	2	0	0	0	0	0
total	**384**			**20**	**1**	**5**	**2**	**16**	**6**	**4**	**5**	**1**	**7**	**7**	**9**

a T-bar with a suture attached to its centre. It is inserted by a slotted needle and dislodged into the jejunal lumen by a stylet. Four T-fasteners are introduced percutaneously into the jejunum serving to retract and anchor the small bowel to the abdominal wall (Fig. 1A-E). They are placed in a diamond-like configuration. A needle catheter can be placed

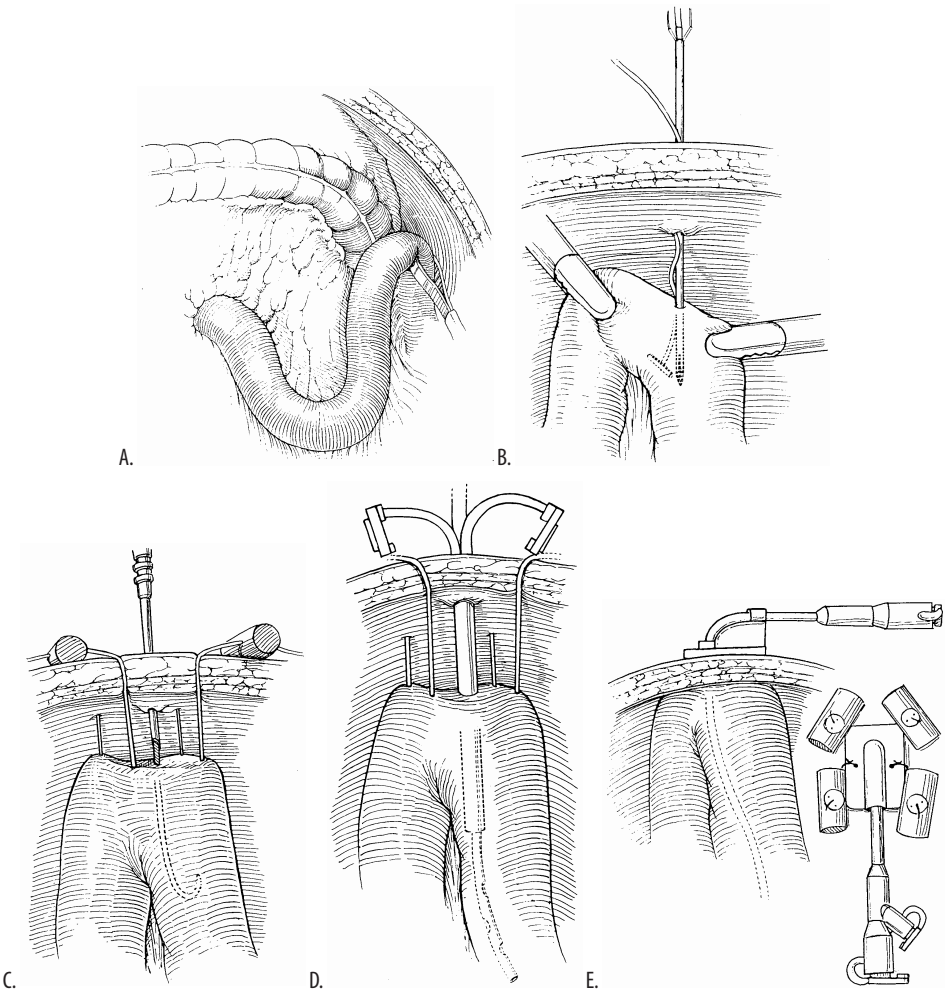

Fig. 1A-E. (A) The proximal jejunum and the ligament of Treitz are identified by lifting the transverse mesocolon and running the small bowel with the graspers. (B) The T-fastener is introduced percutaneously and discharged into the lumen from the slotted needle by the stylet. (C) Four T-fasteners are used to retract the antimesenteric jejunal wall. A J-wire is introduced into the lumen of the jejunum through an 18-gauge needle. (D) The jejunostomy catheter is placed through the peel-away introducer, which is then removed. (E) The T-fasteners and the jejunostomy catheter are secured to the abdominal wall. The T-fastener sutures are cut 2 weeks later, and the metal T-bars are allowed to pass in the stool. (by permission of BMJ Publishing Group: Duh QY, Senokozlieff-Englehart AL, Siperstein AE. Prospective evaluation of the safety and efficacy of laparoscopic jejunostomy. WJM 1995; 162:117-122).

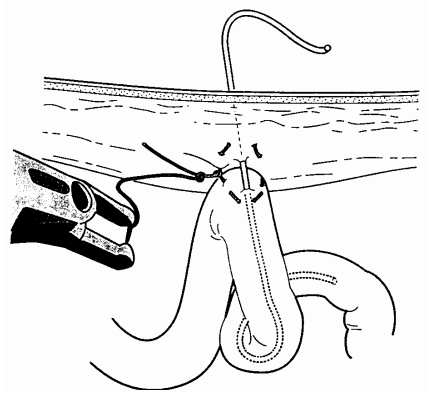

Fig. 2. Schematic view showing the position of the purse-string sutures to create a seal around the jejunal catheter using intracorporeal suturing. (by permission of Blackwell Publishing. Nguyen NT, Schauer PR, Wolfe BM. Laparoscopic needle catheter jejunostomy. BJS 2000; 87: 482-483).

through the centre of the sutures. The authors do not describe if and how they secure the catheter to the jejunum. After two weeks the T-fasteners are removed.

Senkal et al. and Nguyen et al. use three trocars performing jejunostomy [26,27]. The jejunum is fixated to the abdominal wall by an intracorporeal placed pursestring suture and additional anchoring sutures between jejunum and abdominal wall (Fig. 2).

In laparoscopic aided feeding jejunostomy, placement of the catheter is established extracorporeal by means of a small abdominal incision through which the jejunum is retracted [14,16,18,22,23,28,30]. Ellis et al. advocate use of a 4-cm wide abdominal midline incision allowing extraction of the chosen catheter entry site on the jejunum [16]. They propose serosal tunnelling of the feeding catheter to minimise the risk of an enterocutaneous fistula. The jejunum is then fixed to the abdominal wall by interrupted sutures. Rosser and colleagues also use a 4-cm skin incision but the abdominal fascia is left intact [28] (Fig. 3A-E). With the aid of endoclose and endostitch instruments four sutures are placed in a diamond configuration fixating the small bowel to the fascia. A needle catheter is placed using the Seldinger technique from the centre of the fixation points into the jejunum. The sutures are then tightened and tied to the abdominal wall. Several other authors describe a technique using one of the trocar openings through which the jejunum is exteriorised [14,18,22,23]. An enterotomy is then performed and a Foley catheter is inserted and fixated by a purse-string suture. The bowel is fixated to the anterior abdominal wall by several seromuscular sutures.

Complications

Complications were registered in 17 studies. One study does not give any data on complications in that study but additional information from the author states that there were a few umbilical leaks and they abandoned this technique [14].

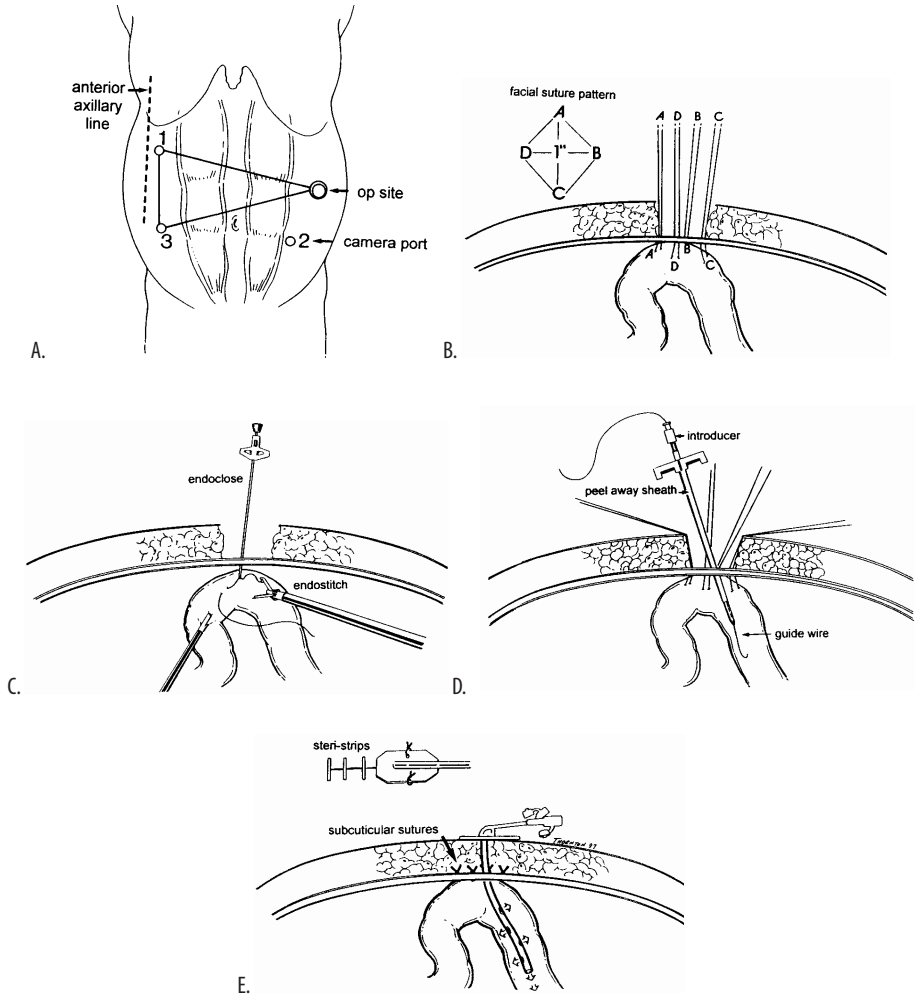

Fig. 3A-E. (A) Port placement. (B) Diamond-shaped suture placement on small bowel. (C) Initial suture placement. (D) Guidewire, introducer, and peel-away sheath. (E) Jejunostomy tube in place (by permission of Exerpta Medica Inc. JC Rosser, Rodas EB, J Blancaflor. A simplified technique for laparoscopic jejunostomy and gastrostomy tube placement. The American Journal of Surgery 1999;177:61-65).

In all but three studies jejunostomy catheter related complications were found [15,22,31]. Woundinfection was the most frequent complication and occurred in 8 studies. Intraabdominal bleeding requiring packed cells occurred once. Reoperation due to catheter-related complications was needed in 4 studies [21,24,27,29,]. In the study by Duh et al. relaparotomy was performed because of a volvulus of the jejunum, and twice a relaparoscopy for reinsertion of a dislodged catheter [21]. In the group of Hotokezaka et al. replacement took place by a relaparotomy [24]. Small bowel perforation was corrected by a second laparoscopy and an obstructed catheter was replaced by a new one during

second laparoscopy in the study by Nguyen et al.[27]. One patient was reoperated because of persistent pain, but no catheter problems were found[29]. Conversion of the laparoscopic procedure to an open procedure is mentioned in two studies[21,24,]. Conversion was necessary because of perforation of the jejunum by instruments and catheter or because of severe adhesions[21,24]. Length of operating time was estimated in 11 studies.

Mortality is reported in nine studies but deaths occurred only in four studies[17,19,21,24]. One patient died of aspiration pneumonia[24]; the other deaths were not related to placement or usage of feeding jejunostomy.

CONCLUSION

This is a meta-analysis of studies dealing with laparoscopic jejunostomy. Many of these studies contain small patient numbers and are mainly concerned with technique description. Also a clinical heterogenousity was present. However, we were interested in giving an overview of indications, techniques and results.

When feeding for a period of exceeding 6 weeks is expected, gastrostomy or jejunostomy is indicated. This can be accomplished by using a percutaneous, endoscopic or operative technique.

Since its introduction, percutaneous endoscopic gastrostomy is, considered the procedure of choice in patients with impaired eating ability but who have a functional gastrointestinal tract[35,36]. Contraindications for the use of percutaneous endoscopic devices are esophageal disorders, and head and neck malignancies.

Furthermore, in patients prone to aspiration or who have gastroparesis or gastric outlet obstruction jejunostomy is generally preferred to gastrostomy[37]. In addition, jejunostomy can be performed during upper digestive surgery to enable early postoperative feeding[38-40]. In this meta-analysis upper digestive malignancy was indeed the most common underlying pathology.

Laparoscopic placement has the same advantages as other minimally invasive types of surgery and has a beneficial effect on postoperative recovery[5-9]. Minimal invasive access for feeding jejunostomy can be accomplished by a total laparoscopic technique or a laparoscopic aided technique. Advantage of the laparoscopic aided procedure is the direct visualisation and placement of the catheter and avoidance of intracorporeal suturing. Advantage of the total laparoscopic method is the avoidance of mini-laparotomy. Fixation of the jejunum to the abdominal wall can be performed using transabdominal sutures, intracorporeal sutures or T-fasteners. From this meta-analysis it can only be concluded that the most experience is obtained with the total laparoscopic operative technique. Therefore, which method to use depends on the surgeons' expertise and the availability of materials.

A variety of complications is associated with placement and usage of a postoperative feeding jejunostomy including mortality [11,12]. Complication rates of 0–26% are reported [41-47]. In a large study reviewing more than 2000 applications 1% jejunostomy-related reoperations are reported [43]; the authors claim that securing the catheter and confirming the correct catheter position by a contrast study could have prevented approximately half of these reoperations but others could not confirm this statement [12]. In the current meta-analysis 69 complications were found (17%). This is comparable to complication rates of open surgery. Two studies report higher rates of 36-50% [21,24]. This was explained by the fact that these complications were largely related to complications of preexisting disease. Woundinfection and catheter dislodgement were the most common. Major complications necessitating relaparotomy occurred in 1.8%.This is in accordance with rates found in open surgery for feeding jejunostomy [11,12].

Conversion rate was high in the studies by Duh and Hotokezaka due to adhesions and accidental enterotomies [21,24]. In other studies there was no need for conversion but this can be largely explained by the fact that patients whom severe adhesions were expected from previous operations were excluded [21]. Conversion rate in laparoscopic jejunostomy is comparable to conversion rates reported in other laparoscopic procedures.

Laparoscopic jejunostomy can be adequately performed in different ways of which the total laparoscopic method is the most frequent described. The surgeon's expertise should determine the appropriate operative technique. Conversion rate is acceptable. The morbidity rate of laparoscopic feeding jejunostomy is comparable to open surgery. Still, serious complications do occur and strict patient selection is therefore warranted. Laparoscopic feeding jejunostomy is a viable method to obtain enteral access with the advantages of minimal invasive surgery.

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7 Nutritional status as a risk factor in esophageal surgery

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Submitted

ABSTRACT

Background: Nutritional condition is one of the factors determining postoperative outcome in esophageal surgery. This study explored the relation between preoperative nutritional status and postoperative infectious complications in order to identify a subgroup of patients who would benefit from preoperative feeding.

Methods: From a prospective database 400 patients who underwent esophageal resection for malignancy were selected. Preoperative nutritional status was assessed by body mass index (BMI), prognostic nutritional index (PNI), nutritional risk index (NRI) and weight loss. The association between nutritional parameters and postoperative complications and mortality, gender, age and hospitalization was assessed.

Results: PNI and NRI differed between the patients with and without postoperative infectious complications (resp. $p = 0.031$ and $p = 0.009$). No difference in nutritional parameters or age was found in the patients who died in hospital. Although nutritional parameters were significantly higher in patients without neoadjuvant treatment, no difference in incidence of complications was found. A correlation was found between age and nutritional parameters; patients older than 70 years did not have more complications, although there was a trend towards increasing incidence of complications with increasing age. A receiver operating characteristic (ROC) curve showed PNI and NRI to have a low predictive value for postoperative complications.

Discussion: Preoperative nutritional status established by PNI, NRI, BMI and weight loss has limited value in predicting complications following esophageal resection. Therefore, based on these parameters the value of preoperative support seems questionable.

INTRODUCTION

Esophageal surgery in patients with esophageal cancer is accompanied by high morbidity. Patients are often cachectic at presentation due to tumor effect and tumor obstruction. Because the preoperative physiological status of the patient is known to influence postoperative morbidity and mortality, much effort is made to optimise this condition to diminish postoperative complications [1,2]. Several risk scores have been developed to identify high-risk patients in order to individualise optimal treatment [3,4]. Preoperative nutritional condition has only received minor attention in risk-analysis [3-7]. Not much is known about the effect of preoperative feeding on postoperative clinical outcome in gastrointestinal surgery. Pretreatment nutritional support to maintain body weight throughout treatment could possibly decrease postoperative complications. Currently all patients undergoing esophageal surgery receive enteral feeding postoperatively. There is also no consensus on preoperative feeding. No clinical study has been able to demonstrate the beneficial effect of routine postoperative enteral feeding on morbidity in esophageal surgery. To establish a responsible pre-and postoperative feeding policy in patients receiving multimodality treatment for esophageal carcinoma, it is important to identify which patients would benefit from pre- and postoperative nutritional support.

The aim of the current study is to establish the relation between preoperative nutritional condition assessed by body mass index (BMI), prognostic nutritional index (PNI), nutritional risk index (NRI) and weight loss and postoperative morbidity. In this way, it is attempted to select a subgroup of patients in whom additional preoperative feeding is beneficial.

MATERIALS AND METHODS

In total 400 patients with an esophageal malignancy undergoing esophageal resection and gastric tube reconstruction between 1996 and 2003 were examined. All patients were prospectively entered into the Esophageal Surgery Database. All operations were performed or supervised by the last two authors (HWT, TCT). Mode and extent of resection were standardized and determined by the location [8]. An abdominal transhiatal resection was performed for distal esophageal tumors. A combined transthoracic and abdominal procedure was performed for proximal tumors.

Preoperative neoadjuvant chemotherapy or chemoradiation therapy was given in 174 patients in the context of a clinical trial.

Preoperative nutritional status was assessed using the PNI, NRI, BMI (weight/size^2) and percentage of weight loss [4]. PNI is calculated from the formula 10 × serum albumin – (0.005 × absolute lymphocyte count) [5,6]. The nutritional risk index developed by Buzby

et al. is calculated using the formula NRI = (1.519 × serum albumin) + (41.7 × present weight/usual weight) [9]. NRI determines the degree of malnutrition as follows: borderline mild (> 97.5), moderate (83.5-97.5) and severe (< 83.5). Weight loss over the previous 3 months was recorded as a percentage of the normal body weight. Patients were categorized in four groups regarding percentage of weight loss: none, < 5%, 5-10% and > 10% of usual bodyweight. BMI was classified into four groups indicating ideal body weight: < 18.5 indicating underweight, 18.5-24.9 indicating normal weight, 25-29.9 indicating overweight and > 30 indicating obesity.

Data were obtained on postoperative infectious complications, stage of the resected specimen, length of hospital stay, postoperative mortality and tumor-related death. Postoperative mortality was defined as death in the hospital after surgery. The follow-up period ranged from 2 weeks to 91 months.

Data analysis

Comparison of categorical and continuous data was done using the Chi-square test or Mann-Whitney's test, respectively. Multivariate analysis of various factors regarding the probability of infectious complications was done using logistic regression. P = 0.05 (two-sided) was considered the limit of significance.

RESULTS

Data on patient demographics at baseline are given in Table 1.

Postoperative complications and mortality are presented in Table 2. Complications are categorized as infectious and non-infectious. A total of 171 patients had one or more infectious complications; in these patients mean PNI was significantly higher, 42.5 versus 41.7 in patients without infectious complications (p = 0.031) (Table 3). The predictive value however, is low as demonstrated by a low area under the ROC curve (Fig. 1). Degree

Table 1. Data on patient demographics at baseline

	n = 400
gender (m:f)	314:86 (79%:21%)
age (yrs)	62 (28-89)*
reconstruction type:	
stomach tube reconstruction:	
- cervical anastomosis	384 (96%)
- intrathoracic anastomosis	5 (1.2%)
Roux-en-Y esophagojejunostomy	11 (2.8%)
neoadjuvant treatment	226 (56.5%)

*Numbers are median (range), data are patient numbers (%), unless otherwise stated

Table 2. Data on postoperative complications and mortality rate

complications	**n = 400**
infectious	
anastomotic leakage	32 (8%)
leakage feeding jejunostomy	8 (2%)
woundinfection	17 (4%)
urinary tract infection	9 (2%)
pneumonia	130 (32%)
sepsis	
non-infectious	
postoperative hemorrhage	15 (4%)
chylothorax	14 (4%)
recurrent nerve paresis	60 (15%)
embolic	
mortality	22 (6%)

Data are numbers of patients (%).

of malnutrition described by NRI in patients with and without infectious complications is given in table 4. The mean value of BMI was 24.9 in patients with infectious complications and 24.5 in those without (p = ns). Of the patients without any preoperative weight loss, 39% developed postoperative infectious complications; 49% of the patients with a weight loss < 5% of usual bodyweight, 41% of the patients with a weight loss of 5 to 10%, and 47% of the patients with > 10% weight loss of their usual body weight developed

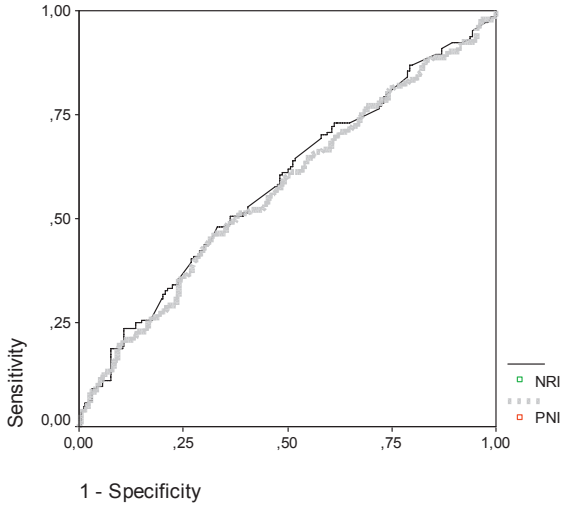

Fig. 1. ROC curve for the prediction of infectious complications by PNI and NRI.

For all possible cut-off levels of PNI and NRI, the sensitivity and specificity are calculated and plotted against each other. The Area under the curve is 0.57 for PNI and 0.58 for NRI. The diagonal dotted line represents an imaginary test without any predictive value. A useful test would have a ROC-curve which is located in the upper-left corner with a large Area under the curve (> 0.8).

Table 3. Data on nutritional parameters

	complication group n = 171	control group n = 229	p-value
mean PNI (%)	42.1	42.8	0.031
mean BMI (kg/m^2)	24.5	24.9	0.490
weight loss			
no	60 (35%)	93 (40.6%)	
0-5%	36 (21%)	38 (16.6%)	
5-10%	30 (17.5%)	44 (19.2%)	
>10%	40 (23.4%)	45 (19.7%)	0.456
unknown	5 (2.9%)	9 (3.9%)	

Data are numbers of patients (%) unless otherwise stated

Table 4. Degree of malnutrition assessed by NRI in patients with infectious complications versus patients without.

complications	severe	moderate	borderline mild	normal	total
yes	1	28	18	97	144
(percentage within NRI)	(50%)	(58.3%)	(48.6%)	(38.8%)	
no	1	20	19	153 (61.2%)	193
(percentage within NRI)	(50%)	(41.7%)	(51.4%)		337

Data are numbers of patients unless otherwise stated

Table 5. BMI values in patients with (yes) and without (no) postoperative infectious complications

complications	BMI < 18.5	BMI 18.5-24.9	BMI 25-29.9	BMI >29.9	p-value
yes	6 (35%)	98 (45%)	57 (42%)	10 (34%)	0.577
no	11 (65%)	122 (55)%	77 (58%)	19 (66%)	

Data are numbers of patients (%).

Table 6. Multivariate analysis of infectious complications according to various factors.
Data given are odds ratios (OR) for complications with 95% Confidence Intervals (CI).

risk factor	OR	P-value	95% CI
PNI (%)	0.96#	0.078	0.91-1.01
gender	1.71*	0.083	1.05-2.85
chemo/radiation	1.29†	0.217	0.86-1.95
obesitas	0.85‡	0.432	0.56-1.28

per unit (%), * males versus females, † yes versus no, ‡ BMI ≥25 versus < 25 kg/m^2

postoperative infectious complications. Table 5 shows the complication rates of patients in different weight categories.

Postoperative complications did not occur more often in patients receiving neoadjuvant chemotherapy and/or radiotherapy. All nutritional parameters were significantly higher in patients without neoadjuvant treatment. Patients older than 70 years did not have more complications, although there was a trend towards increasing incidence of

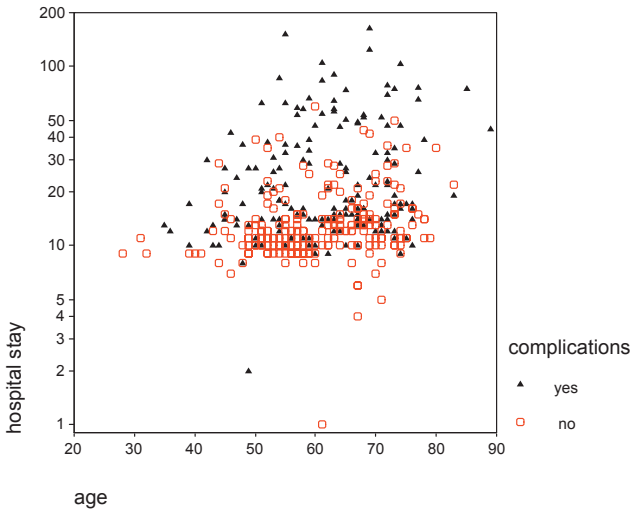

Fig. 2. Relationship between hospital stay, age and complications

complications with increasing age. There was relationship between age and nutritional parameters, as shown in Fig. 2. Patients with complications and patients older than 70 years were hospitalized for a longer time.

More complications were observed in males. There was no difference in nutritional parameters between males and females.

No difference in nutritional parameters or age was found in the patients who died in hospital versus those who survived.

Multivariate analysis of infectious complications according to various factors was performed and identified the male gender as a risk factor (Table 6), but adjusted for this PNI lost its significance ($p = 0.10$). This is in line with the low predictive value in univariate analysis. The same analysis with NRI instead of PNI gave similar results.

CONCLUSION

Much effort is made to optimise postoperative outcome in patients with esophageal malignancy. One way to accomplish this is by careful patient selection; another is to optimise the preoperative condition. Risk factors for postoperative complications have been identified and various scoring systems to predict mortality have been proposed [3,4,5,7]. Since malnutrition is associated with an increase of postoperative infectious complications in gastrointestinal surgery, improvement of preoperative nutritional status seems important. In the current study nutritional status expressed as PNI, BMI and percentage of preoperative weight loss were evaluated in order to predict clinical outcome in patients

with esophageal malignancy. An attempt was also made to identify a patient subgroup who would benefit most from preoperative feeding.

PNI was developed by Buzby et al.[6] in 1984 and modified by Onodera et al.[10]; a preoperative PNI < 40 was associated with a high risk for postoperative complications. A later study by Nozoe et al. demonstrated a significant difference in PNI in patients with and without complications[11]. The current study indeed demonstrated a significant difference in PNI between patients with complications and those without ($p = 0.031$); however, the ROC curve shows that this does not make it a sensitive test for predicting infectious complications. Because mean PNI values in the current study were comparable to that of Nozoe et al., this cannot explain the different outcome. Care was taken in the current study to establish a homogenous and a large patient group with regard to operative procedure; these factors may be in part responsible for the difference between the studies.

No correlation was found between degree of malnutrition established by NRI and incidence of postoperative infectious complications. Also, the degree of preoperative weight loss and BMI did not influence the postoperative complication rate. A striking finding in this study, as in other studies, is the low incidence of malnutrition in patients with esophageal malignancy assessed by these parameters[12]. One explanation may be that despite considerable weight loss, patients still remain overweight. Albumin is in a normal range in the majority of the patients. Albumin however, has a long half-life making it less suitable for detecting early protein deficiency. Other studies evaluating preoperative nutritional condition in esophageal malignancy show variable results[7,13-15]. Kunisaki et al. did not find weight loss and BMI to be correlated with the occurrence of postoperative pulmonary complications[13]; they did, however, find preoperative disrupted nutritional dynamics.

In the present study both PNI and BMI were lower in patients receiving preoperative chemoradiation therapy, but no relation was found with the occurrence of complications. This outcome confirms the findings of a recent prospective trial[16]. Takagi et al. evaluated the relationship between preoperative immunosuppression and morbidity and demonstrated a higher BMI in patients with postoperative complications; they concluded that not the nutritional state but depression of cell-mediated immunity was related to the complication rate in patients who received preoperative nutritional support[15]. Parenteral support for patients undergoing chemotherapy before esophageal surgery is not recommended[18]. Although nutritional status improves, this effect is counteracted by the high incidence of catheter-related complications. The role of enteral support in this patient category, remains unclear.

In the present study PNI, BMI and complication rate did not differ between patients older and younger than 70 years of age.

No correlation was found between age, gender, preoperative chemoradiation therapy and weight on the one hand and nutritional state assessed by PNI, NRI, BMI and weight

loss on the other. Our study also showed that PNI and NRI are not useful tests for predicting postoperative complications in this specific patient population.

Besides the limitations of the retrospective character of this study, it may be concluded that preoperative nutritional status established by PNI, NRI, BMI and weight loss has no predictive value on postoperative infectious complications in patients with an esophageal malignancy.

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8 General discussion, future perspectives and recommendations

GENERAL DISCUSSION

Complications after gastrointestinal surgery have been found to occur in from 17-43% of cases (1-7). Surgical intervention induces various host responses, including fever, immunologic and metabolic changes, and wound repair. These mechanisms can lead to postoperative complications. In order to minimise postoperative morbidity efforts were directed towards identifying factors that might influence postoperative outcome. Malnutrition was identified as an important factor associated with incidence of postoperative complications (8,9). This relation led to the concept of nutrition-associated complications. Optimising nutritional status became an important issue.

Current policy regarding preoperative preparation includes a fasting period for at least twenty-four hours after operation. This obviously contributes negatively to nutritional condition. Postoperative metabolic responses such as insulin resistance are exacerbated by prolonged fasting or inadequate diet (10-11). Early enteral feeding was shown to have a positive effect on postoperative outcome and should therefore be propagated to minimise metabolic response (12). Another reason for early involvement of the intestinal tract is that even a short period of fasting leads to mucosal atrophy (13).

Another important issue in optimising postoperative care, is to determine the most appropriate and safe enteral access route. The oral route is the most natural one but not always accomplishable. Gastric paresis or upper digestive surgery where a high anastomosis is performed prohibit early oral intake. In these cases enteral access can be obtained by a nasoduodenal tube or a feeding jejunostomy.

Difficult is the identification of patients who would benefit from postoperative or even preoperative additional nutritional support. Malnutrition describes a situation of underlying illness resulting not only in diminished food intake but also in metabolic consequences of this illness. Preoperative nutritional assessment attempts to single out patients who are prone to complications due to malnutrition.

In this thesis we investigated current practices in postoperative feeding. The above discussed new insights were implemented to obtain optimal postoperative feeding policy. The next section addresses the questions formulated in the aims of the thesis. Future perspectives are discussed and recommendations are made.

Is there a reason to keep patients "nil by mouth" postoperatively?

Traditionally, patients undergoing a laparotomy are kept in a fasted state after the operation. The nasogastric tube is kept in place until ileus has resolved, that is, when peristaltic movements are heard at physical examination. Finally, when passage of bowel has occurred, the patient is allowed to resume oral feeding. This policy is based on fear for complications as a result of abdominal distension (vomiting, incisional hernia) and for burdening the gastrointestinal tract in presence of ileus and a fresh wound (anas-

tomotic leakage). Nevertheless, there is increasing evidence that enteral feeding has a beneficial effect on the intestinal mucosa. Withholding enteral feeding leads to atrophy and compromises the function of the mucosa as a defense barrier. So there must be a good reason not to give enteral feeding. The study described in *chapter 2* demonstrates that early resumption of oral feeding is well tolerated, with a full diet achieved two days earlier. Nasogastric tube reinsertion was not needed more often. These findings suggest that early enteral feeding does not prolong duration of postoperative ileus, but may indeed shorten this period. Although it is difficult to relate solely early enteral feeding to shortening of ileus duration, several clinical studies seem to confirm this hypothesis. In a large trial Bozetti et al. found an earlier passage of faeces in patients receiving enteral feeding compared to parenteral (14). Patient numbers were too small to draw conclusions on anastomotic leakage. However, as we feel the question should be whether there is any benefit in postoperative fasting rather than whether early resumption of enteral feeding leads to complications, we did not consider this a primary endpoint. Lewis et al., in a review summarizing 11 studies, did however not find a higher incidence of anastomotic dehiscence (15). From the data presented in chapter 2 and from the perspective of the literature we may conclude that there is no rationale for maintaining a routine postoperative fasting period.

Does early oral feeding affect duration of postoperative ileus and quality of life?

Ileus is thought to influence toleration of oral intake, and vice versa. Reports on possible interactions are controversial, however [14,59,60]. This interaction should be further clarified before adequate multimodal postoperative recovery regimes can be introduced. While several studies, including the one presented in chapter 2, demonstrated that most patients will tolerate early oral feeding, a considerable proportion of European surgeons are reluctant to allow patients to start a diet containing solid food before ileus has resolved [61]. One of the considerations for this attitude is the existing variety of interpretations and definitions of postoperative ileus. Each different aspect influencing postoperative recovery should be investigated therefore, and consensus on its place in multimodal regimes should be reached. Defining ileus as a transient impairment of intestinal motility following abdominal surgery, it can be assumed that this is a self-limitating process. Indeed, in patients managed by a multimodal approach, the incidence of ileus persisting for more than 72 hours after surgery was found to be as infrequent as 5% [62]. Findings from the study described in *chapter 3* also confirm that most patients will tolerate oral feeding before complete resolvance of ileus. This not only suggests that patients themselves are able to indicate the time of eating, but also that ileus does not influence food tolerance. The positive influence of enteral feeding on postoperative recovery probably must be sought in fewer complications and better regulation of immune function, with greater effect from combining early feeding with other factors influencing ileus. Quality of life is

expected to improve with quicker recovery and shorter hospitalization. We were not able to prove this assumption in the study presented in chapter 2; patient numbers were too small to make a statement on incidence of complications and hospital stay was the same in both study groups. This probably explains the fact that no differences were found in outcome of quality of life scores. However, since this is the one factor that is important from a patient's point of view, quality of life should be assessed in future clinical trials concerning postoperative management and recovery. With respect to the findings of the clinical trials described in chapters 2 and 3, it seems safe to state that since ileus does not negatively contribute to tolerance of an early oral diet, patients are free to start eating when they feel like it.

What are the complications of a feeding jejunostomy and is a less invasive access method in order?

When oral feeding following surgery is impossible but the gastrointestinal tract is still functioning, another enteral access method is indicated. Nasoduodenal tubes and jejunostomy are appropriate access routes in patients requiring nutritional support for around one month or less, which is usually the case. Patients who have undergone esophageal surgery patients require nutritional support until the anastomosis has healed (between 7 and 10 days postoperatively). Also, they are at risk for substantial morbidity and even mortality despite recent technical developments. Seeing that the incidence of complications was found to vary from 18-50% (16-19), there is reason enough to put all efforts in decreasing this rate. Malnutrition is a common problem in these patients due to disease-related factors. As it contributes to increased postoperative morbidity, ongoing malnutrition must be avoided. One of the aims of postoperative enteral feeding is to minimise effects from surgery and disease. However, partly depending on the route of access, this in itself may cause complications. Routine postoperative nutritional support and usage of a jejunostomy catheter inserted concomitant to the primary operation have been recommended after esophageal surgery (20-24). Application of a feeding jejunostomy may show minor complications, such as bloating, diarrhea and tube blockage, but also major ones, such as leakage, intestinal herniation, and dislodgment (25-27). As minor complications only slightly affect patients, *chapter 3* concentrated on the major complications related to feeding jejunostomy. It describes a large population of 1387 esophagectomized patients, of whom 84% underwent simultaneous insertion of a feeding jejunostomy catheter. Of the latter, 1.1% showed jejunostomy related complications, a proportion in accordance with those reported in other studies (25,28-31). These complications all necessitated relaparotomy, leading to death in 40% of the patients needing exploration. The outcomes of our study demonstrate that a feeding jejunostomy is potentially hazardous. Although these patients are routinely given enteral feeding, evidence on better outcome compared to withholding food is lacking. A better outcome has only been described in malnourished patients (14). Further studies are needed to

establish effects of routine nutritional intervention in this patient category. So far, we can indeed question the rationale of routine enteral feeding. We feel it is undesirable to routinely add a potential risk factor to an already risky surgical procedure with an often complicated postoperative period. Since there are other, non-invasive methods available for obtaining enteral access, these should be taken into consideration.

Which enteral access method is associated with the least morbidity and is a nasoduodenal tube an effective feeding method for postoperative use?

The results described in the previous section justify the search for an alternative, less-invasive enteral access method. Preferably, this should be non-invasive, easy to place, and equally effective for administration of enteral feeding as a jejunostomy. The improved polyurethane nasoenteric tubes seem to be an effective means for enteral feeding with an expected duration of days to several weeks (32). Intraoperative placement of a nasoduodenal tube is easily accomplished (33). *Chapter 4* describes the results from a trial comparing the polyurethane Bengmark nasoduodenal tube as a non-invasive access route with jejunostomy. Minor catheter-related complications were equally common. Progressing deterioration in the presence of a jejunostomy catheter gave reason for exploratory laparotomy once, which was considered a major complication. Both groups tolerated the enteral diet similarly well. A large study by Braga et al. comparing feeding through a jejunostomy versus nasojejunal tube, demonstrated equal efficacy of both access routes (34). More than 90% of patients reached their nutritional goal. Intolerance in 9% necessitated a switch to parenteral feeding. The results from our own prospective study are consistent with those reported by Braga et al., with 11% switch-over in the jejunostomy group and 7% in the nasoduodenal group. Mean duration of enteral feeding in our study was ten days in both groups. Since this is only a short period of time, one can argue if routine performance of an invasive additional procedure is justified when an equally effective non-invasive procedure is available.

A jejunostomy is indicated in patients requiring additional enteral feeding for a longer period of time. In non-surgical patients this is performed in a separate operative procedure and a minimally invasive procedure is therefore preferred. Although laparoscopic procedures are considered minimally invasive, they are not entirely without risk. Possible risks need to be assessed before introducing laparoscopic jejunostomy as common practice. *Chapter 5* gives an overview of different techniques for performing a laparoscopic feeding jejunostomy in 384 patients and discusses complications and conversion rate. It is concluded that laparoscopic jejunostomy is a viable way of gaining enteral access. Still, complications do occur and patient selection is therefore important.

Is it possible to identify a subgroup of esophageal surgery patients prone to nutrition-related complications using PNI, NRI, BMI and weight loss? Is routine nutritional assessment useful in esophageal surgery?

There are many different methods for evaluating nutritional risk in patients undergoing digestive surgery but no gold standard. In esophageal surgery, weight loss, albumin level, lymphocyte count, anthropometric measurements and rapid turnover proteins are the most commonly used parameters. The prognostic nutritional risk index developed by Buzby and Mullen is a multiparameter model predicting risk of postoperative complications in patients undergoing gastrointestinal surgery (35). Its complexity, however, forms an important drawback for clinical routine application. The modified prognostic risk index developed by Onodera et al. is an easier way of assessing nutritional status and was therefore preferred in the study presented in *chapter 6* (36). Onodera et al. found patients with a preoperative PNI below 40 to be prone to postoperative complications after gastrointestinal surgery. Another study found low PNI-values to be associated with a higher complication rate in esophageal surgery as well (37). Our study described in chapter 6 did indeed show lower PNI-values in patients with complications but as suggested by the ROC-curve PNI has a low predictive power.

Serum albumin has repeatedly proven to be an important independent predictor of postoperative outcome (38,39). In most studies however patients were not stratified to type of surgery. Kudsk et al. suggested that different serum albumin levels apply to different sites of surgery, or in other words, esophageal surgery has a different serum albumin cut-off point for developing complications than for example colorectal surgery (40). Furthermore, patients with esophageal malignancy often present with normal albumin levels although being malnourished (41,42). This may be explained by the fact that these patients experience acute weight loss and that albumin has limited ability to detect early protein deficiency due to its relatively long half-life. In our study, mean serum albumin was 42.2 g/l.

Reports on weight loss as a prognostic factor for postoperative complications are controversial (43-45). ROC-curve analysis demonstrated weight loss >10% of usual body weight to be the only index with a moderate prognostic performance that is worth evaluating in the preoperative nutrition assessment in patients undergoing gastrointestinal surgery (8). A nonsignificant improvement of predictive ability was obtained by the combination of serum albumin, total lymphocyte count, total iron-binding capacity, and serum cholinesterase activity. Barbosa-Silva in a recent study, found weight loss > 10% at first to be associated with morbidity but after adjusting for confounders the association disappeared (46). In patients undergoing esophageal surgery weight loss could also not be identified as a significant predictor of morbidity (47). We found a 22% proportion of malnourished patients based on > 10% weight loss. Mean BMI of this patient group was 23, which is within normal range, suggesting that these patients were overweight prior to their weight loss. The results from *chapter 7* indicate that significant weight loss in

esophageal surgery is not associated with a poorer clinical outcome. Our results are consistent with the results obtained by Weimann et al. and Brandmair et al. (42,48). Patients with preoperative weight loss of > 10% were found to have similar metabolic responses to surgery as patients without any weight loss. Energy expenditure and substrate oxidation rates were within normal range; weight loss was therefore most likely to occur from tumour related dysphagia. Most patients had a relative normal nutritional status, as in our own study. Risk assessment of esophageal surgery therefore, does not seem to be possible on the ground of nutritional parameters solely.

In view of this outcome it could be hypothesized that patients with esophageal cancer must be considered a different entity within cancer patients. Their malnutrition has an acute character and is mainly caused by inability of nutritional intake due to tumour obstruction. Protein energy depletion due to the occurrence of tumour cachexia seems to be of less importance. Although preoperative nutritional additives may very well have a positive influence on occurrence of postoperative complications and clinical outcome, patient selection based on nutritional assessment has no use. A prospective clinical trial randomising between patients fed or non-fed preoperatively may finally put an end to the discussion.

CONCLUSIONS AND RECOMMENDATIONS

A fasting period following gastrointestinal surgery is not useful. A nasogastric tube should be removed at the end of surgery. Patients can be started on an oral diet the first postoperative day and expand as quickly as they wish.

When oral feeding is impossible after esophageal surgery, enteral feeding can be administered through a peroperatively placed jejunostomy catheter. Note that this can be associated with major complications.

A nasoduodenal tube is an equally effective, non-invasive means for feeding purposes in the same patient category.

The role of preoperative nutritional status in patients with esophageal malignancy in relation to postoperative outcome remains unclear. A clinically easy to use and reliable tool for assessment of nutritional status in these patients seems not available as yet. Therefore, identification of a patient subgroup who would benefit from adjuvant feeding remains difficult. For now, no recommendations can be made concerning preoperative adjuvant feeding.

FUTURE PERSPECTIVES

Fast track surgery

The main goal of postoperative early enteral feeding is to stimulate postoperative recovery. Or in other words, to shorten the duration of postoperative ileus and to limit complications. As pointed out solely relating enteral feeding to postoperative outcome is very diffult. Gastrointestinal motility is determined through a complex ensemble of neural and hormonal factors. Surgical trauma, anaesthesia, pain, surgery induced catabolism, starvation and immobilisation all lead to a stress response determining postoperative convalescence. Responses may be neuroendocrine or inflammatory (49,50). There are several ways to intervene with these mechanisms. Epidural anaesthesia inhibits afferent neural stimuli and could in this way modify neuroendocrine and stress responses and enhance recovery. Several studies undertaken to establish the effect of epidural anaesthesia on postoperative convalescence, demonstrated that continuous epidural anaesthesia with local anaesthetics reduced postoperative ileus (51,52,53). This effect also has implications for tolerance of early enteral feeding. Furthermore, side effects of anaesthetics such as nausea and vomiting are reduced, enabling food intake and early mobilisation. Surgical trauma can be diminished by using minimal invasive techniques or horizontal incisions (54,55).

A perioperative policy combining these factors in a multimodal rehabilitation programme, would lead to the most optimal recovery.

This principle of fast track postoperative care – consisting of epidural analgesia, early enteral feeding and early mobilisation – has recently been advocated with good results (56,57). Still, there are wide variations in composition of fast-track programs. Recently, a consensus review by the ESPEN group was presented, standardising the various aspects of multimodal rehabilitation in patients undergoing colonic surgery (58). This is especially of importance for interpretation of results of future trials and further refinement of pre- and postoperative policies.

Future investigations should further analyse standardised fast track regimens on postoperative rehabilitation;

Future trials should include preoperative preparation of the patient. Careful patient selection is needed to individualise preoperative measures. Nutritional assessment with easy accessable tools is important to identify patients who would benefit from pre- and postoperative additional feeding.

Future trials concerning early introduction of enteral feeding and fast track rehabilitation are needed in the pediatric population as well. Adequate enteral feeding in children might be of even more importance than in the adult group.

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9 Summary

SUMMARY

Chapter 1

Improving postoperative clinical outcome is one of the main issues in surgical patient treatment. Improved insight into peri-operative physiology has revealed several intrinsic mechanisms potentially influencing recovery after surgery. Postoperative ileus is such a mechanism in patients who have undergone gastrointestinal surgery, leading to discomfort, delayed food intake, immobilisation and impaired convalescence. Minimising duration of ileus is a primary goal of peri- and postoperative management and has led to several changes in current anaesthetic and postsurgical policy. An important factor influencing ileus is enteral feeding. This thesis aims to give further insights and directions in postoperative feeding management intending to optimise postoperative outcome. Chapter 1 gives an overview of physiology of gastrointestinal motility and postoperative ileus. It further describes traditional postoperative policy, insights in adjuvant feeding and enteral access routes, as well as clinical value and methods of nutritional assessment.

Chapter 2

Patients undergoing a laparotomy are traditionally kept sober for some time after operation, and diet is not expanded to solid food until ileus resolves and gastrointestinal tract function has recovered. This chapter reports a prospective, randomized trial investigating the feasibility of immediate postoperative oral feeding. The traditional, gradually expanding feeding regimen is compared to a patient-controlled diet involving start of oral diet on the first postoperative day. We found that early oral feeding is well-tolerated. Frequency of necessity to reinsert a nasogastric tube did not differ between groups. Furthermore, the group on a patient-controlled diet reached a full diet in 3 days versus 5 days in the group on the traditional diet. Complication rate was the same in both groups. These findings indicate that early introduction of oral feeding is feasible, thus undermining the necessity of a postoperative fasting period.

Chapter 3

Although early postoperative resumption of an oral diet was found to be feasible, as discussed in the former chapter, the effect on ileus duration and gastrointestinal convalescence remains unclear. Likewise, the correlation between dietary intake and quality of life is unclear. In chapter 3 a prospective, multicenter trial is reported aimed at assessing the effects of an early oral diet on gastrointestinal function and quality of life in patients undergoing elective, open, colorectal or abdominal vascular surgery. Patients were randomized to a conventionally expanding diet, and to a regimen providing for resuming an oral diet as fast as tolerated. No differences were found between groups in postoperative quality of life. We found no difference in frequency of reinsertion of a nasogastric tube;

time to toleration of a solid food containing diet was 2 days in the fast expanding group versus 5 days in the conventional group. Return of bowel function was the same in both groups; these findings confirm the results presented in chapter 2. Furthermore, although patient numbers are small, it seems that an oral diet is well tolerated despite an incomplete postoperative recovery of gastrointestinal function.

Chapter 4

When oral feeding is impossible, for example after esophagectomy, other access methods for postoperative enteral feeding are needed. Access in patients undergoing upper digestive surgery is often obtained by performing a feeding jejunostomy concomitantly. Although enteral feeding is provided effectively in this way, it is important to realise that this is an invasive method of enteral feeding access with risk of complications. Chapter 4 presents a large series of esophagectomized patients receiving a jejunostomy for feeding purposes. Enteral feeding and the use of feeding tubes may give rise to minor side-effects and complications such as bloating, diarrhoea, and clogging of the tube. These are considered acceptable, and have little or no consequences. Of more importance are complications leading to morbidity and delayed postoperative convalescence. Therefore, the study described in chapter 4 focussed on major complications. Ranging from intraperiotoneal leakage to torsion of the jejunostomy site, major jejunostomy-related complications occurred in 1.1% of the cases. Exploratory laparotomy was needed in every case; half of the patients died due to septic complications. In conclusion, our findings show feeding jejunostomy to be a potentially hazardous surgical procedure.

Chapter 5

A prospective, randomized trial embedded in the study presented in chapter 4, compared an invasive enteral access method with a non-invasive one in terms of complications and efficacy. 150 patients having undergone esophagectomy, were randomized to receive either a feeding jejunostomy or a nasoduodenal feeding tube. Minor catheter-related complications were found in 32 (40.5%) patients in the jejunostomy group versus 22 (31.4%) in the nasoduodenal group. One patient needed an exploratory laparotomy due to intraperiotoneal leakage of the jejunostomy catheter. Catheter efficacy measured as tolerance of enteral feeding and time needed to achieve full enteral feeding did not differ between groups. We therefore concluded that a nasoduodenal tube is an effective means of enteral feeding as a jejunostomy. A rationale for preference for a nasoduodenal tube over a jejunostomy is given.

Chapter 6

Laparoscopic jejunostomy is a novel technique for performing feeding jejunostomy. In a systematic review, various surgical techniques are classified and evidence on safety is

assessed. Laparoscopic placement of a feeding jejunostomy offers the same advantages of other minimal-invasive procedures. Conversion rate is similar to other laparoscopic procedures. This makes it an applicable method for patients who otherwise would need open surgery for placement of a jejunostomy catheter. Still, complications do occur and patient selection is therefore warranted.

Chapter 7

Additional pre- and/or postoperative feeding may result in a better postoperative outcome in some groups of patients. Preoperative nutritional assessment may serve to select such patient groups. Obviously, malnourished patients or patients at risk for malnourishment will benefit most from additional feeding. Nutritional assessment should be easy to perform and use simple parameters, making it applicable for clinical use. Chapter 7 reports a study attempting to identify a subgroup of patients with oesophageal cancer who might benefit from adjuvant feeding. In 400 patients nutritional status was assessed by BMI, weight loss, PNI and NRI. Nutritional status was compared in patients with and without infectious complications. Although PNI and NRI differed significantly between patient groups ($p = 0.031$ and $p = 0.009$, respectively), ROC curve analysis showed a low predictive value for both tests. No correlation was found between BMI and weight loss, and complications. Remarkably, the incidence of malnutrition in patients with oesophageal malignancy assessed by these parameters was found to be low. Possible explanations for this finding are discussed. We concluded that nutritional assessment with these specific parameters in patients with oesophageal malignancy is not suited for identifying a subgroup of patients in whom additional feeding would be beneficial. There is a need to develop nutritional assessment tools specific for patient category and surgical site.

10 Samenvatting

SAMENVATTING

Hoofdstuk 1

Eén van de belangrijkste doelen van de behandeling en zorg rond en na een operatie, is het verbeteren van het postoperatieve herstel en het verminderen van het optreden van complicaties. Er zijn verschillende mechanismen die het herstel van de patiënt kunnen beïnvloeden. Een goed voorbeeld daarvan is het optreden van ileus na gastrointestinale chirurgie. Dit geeft een onbehaaglijk gevoel, misselijkheid en verminderde eetlust, en leidt tot immobilisatie en vertraagd herstel. Een primair doel van peri- en postoperatieve zorg is dan ook de duur van het optreden van ileus te verkorten; dit heeft geleid tot een aantal veranderingen binnen het huidige anaesthesiologische en chirurgische beleid. Ileus wordt o.a. beïnvloed door enterale voeding. Dit proefschrift heeft tot doel inzicht te geven in het huidige beleid rondom een operatie en richtlijnen te geven voor het voedingsbeleid na een operatie om op die manier het postoperatieve herstel te optimaliseren. In het eerste hoofdstuk wordt een overzicht gegeven van de fysiologie van de tractus digestivus en postoperatieve ileus. Het huidig postoperatieve beleid wordt beschreven, alsmede verschillende aspecten van aanvullende voeding en toegangswegen, en tenslotte de klinische waarde van de voedingstoestand en methoden om deze te bepalen.

Hoofdstuk 2

Na een laparotomie is het gebruikelijk patiënten nuchter te houden en het dieet pas naar vaste voeding uit te breiden op het moment dat de gastrointestinale functie hersteld is. In dit hoofdstuk wordt een prospectieve, gerandomiseerde studie besproken waarin de tolerantie en effecten van het direct na operatie starten van orale voeding wordt onderzocht. Het huidige traditionele beleid, waarbij voeding langzaam volgens vastgesteld schema wordt uitgebreid, wordt vergeleken met een dieet waarbij de patiënt vanaf de eerste dag na operatie zelf het tijdstip van eten bepaalt, evenals wat hij eet. De primaire uitkomstmaat was het inbrengen van een maagsonde in geval van braken. De meeste patiënten verdroegen het snelle dieet goed. Bij beide groepen was het in gelijke mate nodig om een maagsonde in te brengen. De patiënten in de snelle groep verdroegen een normaal dieet op dag 3 na operatie versus dag 5 in de traditionele groep. De incidentie van complicaties was hetzelfde in beide groepen. Uit deze bevindingen kan geconcludeerd worden dat het goed mogelijk is om direct na operatie een normaal dieet te introduceren en dat het in acht houden van een nuchtere periode niet nodig is.

Hoofdstuk 3

Uit het vorige hoofdstuk bleek dat een snelle hervatting van een normaal dieet na operatie goed mogelijk is. Echter, het effect van orale voeding op de duur van ileus en het herstel van de gastrointestinale functie blijft onduidelijk. Ook de relatie tussen dieet en kwaliteit

van leven is niet duidelijk. In dit hoofdstuk wordt een prospectieve, gerandomiseerde studie beschreven die als doel had de relatie in kaart te brengen tussen het snel hervatten van normale voeding en gastrointestinale functie en kwaliteit van leven. De patiënten werden, net als in de vorige studie, verdeeld in een groep die zelf het tijdstip van hervatten, en de inhoud van orale voeding bepaalt, en in een groep die het traditionele, langzaam uitbreidende dieet volgt. De patiënten in de snelle groep bereikten een normaal dieet op dag 2 na operatie en de patiënten in de traditionele groep op dag 5. Herstel van gastrointestinale functie werd in beide groepen op dag 4 bereikt. Kwaliteit van leven was hetzelfde in beide groepen. Samenvattend, ondanks de kleine patiëntenaantallen in dit onderzoek is het aannemelijk dat een normaal dieet direct na operatie goed verdragen wordt, niettegenstaande het feit dat de tractus digestivus op dat moment nog niet volwaardig functioneert.

Hoofdstuk 4

Wanneer het onmogelijk is om te eten, bijvoorbeeld na oesophagusresectie, is een andere voedingsmethode nodig. Meestal wordt bij patiënten die een operatie aan het bovenste deel van de tractus digestivus ondergaan, een voedingsjejunostomie tijdens dezelfde ingreep aangelegd. Alhoewel toediening van enterale voeding op deze wijze goed mogelijk is, is het belangrijk zich te realiseren dat dit een invasieve methode is met de daaraan verwante risico's op complicaties. In hoofdstuk 4 wordt een grote serie patiënten beschreven die een oesophagusresectie hebben ondergaan en die een voedingsjejunostomie kregen. Enterale voeding en het gebruik van voedingssondes gaan gepaard met bijeffecten en complicaties zoals diarree en verstopping van de sonde. Dit zijn acceptabele complicaties, die weinig of geen consequenties voor de patiënt hebben. Van belang zijn de complicaties die leiden tot morbiditeit en vertraagd postoperatief herstel. Het onderzoek dat in hoofdstuk 4 wordt beschreven concentreert zich dan ook op dit soort complicaties. Bij 1,1% van de patiënten ontstond een jejunostomie-gerelateerde complicatie variërend van intraperitoneale lekkage tot torsie ter plaatse van de jejunostomie. Bij elke patiënt vond een relaparotomie plaats; de helft van de patiënten overleed ten gevolge van septische complicaties. Concluderend tonen deze bevindingen aan dat een voedingsjejunostomie een niet te onderschatten ingreep is met potentiele gevaren.

Hoofdstuk 5

Een prospectieve, gerandomiseerde studie in dezelfde patiëntencategorie als die beschreven in hoofdstuk 4, vergelijkt een invasieve enterale toegangsweg met een non-invasieve wat betreft effectiviteit en complicaties. 79 patiënten krijgen een voedingsjejunostomie en 71 een nasoduodenale voedingssonde. Minimale sonde-gerelateerde complicaties traden op bij 32 patiënten met een jejunostomie en bij 22 met een nasoduodenale sonde. Eén patiënt met een jejunostomie onderging een relaparotomie in verband met intra-

peritoneale lekkage van de jejunostomie-catheter. De effectiviteit bepaald als tolerantie van enterale voeding en tijdsduur tot het bereiken van volledige enterale voeding, was hetzelfde in beide groepen. Er kan op grond van deze bevindingen geconcludeerd worden dat het voeden via een nasoduodenale sonde even effectief is als via een jejunostomie. De voorkeur voor het gebruik van een nasoduodenale sonde wordt besproken.

Hoofdstuk 6

Het laparoscopisch aanleggen van een voedingsjejunostomie is een nieuwe methode. Een systematische review werd verricht waarin de verschillende technieken worden geclassificeerd en de veiligheidsaspecten worden besproken. Het laparoscopisch aanleggen van een voedingsjejunostomie heeft dezelfde voordelen als andere minimaal invasieve ingrepen. Dit maakt het een goed toepasbare methode om enterale voeding toe te dienen aan patiënten die anders een laparotomie hiervoor zouden moeten ondergaan. Complicaties kunnen zich echter voordoen en patiënten dienen dan ook streng geselecteerd te worden.

Hoofdstuk 7

Aanvullende pre- en/of postoperatieve voeding zou bij bepaalde patiënten kunnen leiden tot een beter postoperatief herstel. Het vaststellen van de voedingstoestand zou zinvol kunnen zijn om deze te selecteren. Ondervoede patiënten of zij die de kans lopen om ondervoed te raken zullen het grootste voordeel hebben van adjuvante voeding. De methode om de voedingsconditie te bepalen moet bij voorkeur gemakkelijk zijn, zodat deze klinisch toepasbaar is, en dus gebruik maken van eenvoudige parameters. In hoofdstuk 7 wordt een studie gepresenteerd waarin een poging wordt gedaan een subgroep van patiënten met oesophaguscarcinoom te identificeren die mogelijk gebaat zijn bij adjuvante voeding. Bij 400 patiënten werd de voedingsconditie bepaald met behulp van de BMI, mate van gewichtsverlies, PNI en NRI. De voedingsstatus van patiënten met en zonder complicaties werd met elkaar vergeleken. PNI en INR waarden vertoonden significante verschillen tussen beide groepen maar een ROC-curve-analyse toonde een lage voorspellende waarde voor beide onderzoeksmethoden. Er werd geen correlatie gevonden tussen BMI en gewichtsverlies, en complicaties. Opmerkelijk was de bevinding dat de incidentie van ondervoeding bij patiënten met oesophagus carcinoom vastgesteld met deze bepalingen, laag was. Mogelijke verklaringen hiervoor worden besproken. Concluderend kan gesteld worden dat bepaling van de voedingsstatus met behulp van deze parameters bij patiënten met een oesophaguscarcinoom, niet geschikt is om een subgroep te identificeren die baat zou hebben bij adjuvante voeding. Het is nodig om eenvoudige methoden te ontwikkelen voor het bepalen van de voedingsconditie toegespitst op patiëntencategorie en operatiegebied.

11 Appendices

DANKWOORD

Het is er dan toch van gekomen. Ik had mij voorgenomen niet met dit soort tekst te eindigen want het leek me altijd een beetje overdreven, maar ik kan niets anders zeggen. Zonder hulp van velen was het allemaal niet gelukt, en een aantal daarvan wil ik in het bijzonder bedanken.

Prof.dr J. Jeekel, ik ben erg blij en vereerd om bij u te mogen promoveren. Het is onbegrijpelijk hoe iemand zoveel energie kan hebben en dat werkt bijzonder motiverend. De interesse voor het doen van klinische trials heb ik aan u te danken en met mij, de patiënten. Dank voor alle steun, adviezen, correcties en ideeen. Ik zou u graag eens vergezellen naar China.

Prof.dr H.W. Tilanus, ik kon altijd te pas en te onpas bij u binnen vallen met wat dan ook. Vooral de laatste maanden was het nodig dat er weer wat orde in de chaos werd geschapen. Altijd geinteresseerd en enthousiast, optimistisch en altijd tijd. Veel heb ik van u geleerd en veel zou ik nog van u willen leren; u bent een chirurg zoals ik graag zou willen zijn. Dank voor het vertrouwen.

Dr. K.J. Brouwer, mijn opleider uit de Zuiderziekenhuis periode, dankzij een artikeltje uit Leiden, besproken tijdens de vrijdagmiddag 'journalclub' ontstond de basis voor dit proefschrift. Eerst gestart met de pilot trial waarbij u er als geen ander op toe zag dat ook alle patienen werden geincludeerd, zoals u dat trouwens voor alle lopende trials deed; bijzonder stimulerend. Dank voor de uitstekende no-nonsense opleidingsjaren waar ik nog steeds, en daar ben ik niet de enige in, met een warm hart en nostalgie aan terug denk.

Prof.dr H. Obertop, prof.dr D. Tibboel en prof.dr E.J. Kuipers: hartelijk dank voor de interesse in dit proefschrift en de beoordeling daarvan.

Dr. W.C.J. Hop, na uren doorgebracht te hebben op jouw kamer werd langzaam duidelijk hoe hard ik je nodig had. Dank voor je eindeloze geduld als de database toch weer eens niet bleek te kloppen of onvolledig bleek te zijn. Ik ben blij dat je 'achter de tafel' wilt zitten.

Anastasia Lim, je hebt er vele fietsuurtjes opzitten, op weg naar bijna verloren gegane gegevens en nog te includeren patienten. Ik hoop dat je het leuk vond en dat je er wat aan hebt voor je verdere toekomst. Je hebt mij in ieder geval een hoop kopzorgen ontnomen en vele plezierige uurtjes en kopjes koffie.

Niels Kok, dank voor al je 'op het laaste nippertje werk' wat je allemaal belangeloos deed. Je moet met het allemaal nog maar eens precies uitleggen.

H. Lont, J. van Essen, KJ Brouwer, dank voor de begeleiding van de trials, waarvan het verloop valt of staat met het enthousiasme en inzet van de coordinatoren.

Mijn paranymfen, C.M.E. Contant en C.J. Meeussen. Caroline, ik ben blij dat je me wilt ondersteunen in deze tijd. Je bent een goede vriendin, en een voorbeeld van iemand met tomeloze energie die het onmogelijke weer voor elkaar krijgt. Binnenkort maar weer eens een congresje in een leuke (winkel)stad?

Conny, ik ben vereerd dat je deel wilt zijn van 'onze' gewoontes en naast me wil staan. Ik zal nooit vergeten dat je, toen ik je vroeg, begon te lachen en zei "ja, leuk, maar wat is dat dan?" Behalve de ideale collega ben je ook een ideale vriendin. Binnenkort eindelijk dat weekendje Antwerpen en niet te vergeten Barcelona.

Mijn collega's in het Sophia Kinderziekenhuis, G. Madern, Th. van de Hoonaard, K. van de Ven, Gerda Zijp, Sigrid Nijs, Conny Meeussen en Shareen Idu en de arts-assistenten: dank voor de tijd en ruimte die ik gekregen heb om dit boekje tot een goed einde te brengen. Ik hoop nog vele jaren met jullie dit prachtige vak te kunnen uitoefenen.

Mijn kamergenoot, Sebas Eijsbouts, die altijd weer een oprecht luisterend oor had en menig computer probleem heeft opgelost.

Het verpleegkundig personeel van alle aan de trials deelnemende ziekenhuizen wil ik bijzonder bedanken. Dankzij jullie inzet, stimulans en enthousiasme is het gelukt de trials goed te laten verlopen. Ook alle arts-assistenten ben ik veel dank verschuldigd voor het includeren en randomiseren van alle patienten.

Conny Vollebregt en Anneke van Duuren, datamanagers van het trialbureau heelkunde, waren een bron van informatie en schiepen orde in de chaos van gegevens. Dank voor de stimulerende woorden.

Ko Hagoort en Laraine Visser hebben van alles een leesbaar geheel gemaakt en de puntjes op de i gezet, en dat ook nog op het laatste moment.

Mijn lieve ouders, niet te geloven hoe jullie het konden opbrengen steeds weer naar me te luisteren en steeds weer voor me klaar stonden. Van jullie heb ik geleerd door te zetten en dat niets onmogelijk is. Ik weet nog dat ik vroeger zei dat ik operatiezuster wilde worden; die bekentenis werd onmiddellijk gecorrigeerd met een vriendelijk "nee, je bedoelt

operatie dokter". En jullie hadden, uiteraard, gelijk. Dank voor de kansen die jullie me geboden hebben en die mij tot een gelukkig mens hebben gemaakt.

Lieve Ming, ik ben ongelooflijk blij en gelukkig dat jij mijn man en beste vriend bent. Een optimistischer en behulpzamer mens bestaat niet. Het leven is een feest met jou en altijd een verrassing. Van jou heb ik geleerd te doen wat je leuk vindt. Je bent de ideale vader voor Antonie en …… (wij weten het!).

Lieve Antonie, mijn lieve grote jongen, ik hou van je en blijf altijd bij je. Je bent samen met pappa, mijn alles en we maken er een leuke dag van.

CURRICULUM VITAE

Ingrid Han-Geurts werd geboren op 6 augustus 1969 te Utrecht. Zij doorliep de middelbare school op het Christelijk Lyceum te Zeist en behaalde het VWO examen in 1987. In dat jaar begon de studie Geneeskunde aan de Universiteit van Utrecht, welke in 1995 beëindigd werd. Daarna begon zij haar eerste baan als AGNIO chirurgie in het Zuiderziekenhuis (nu Medisch Centrum Rijnmond West geheten) te Rotterdam. Daar werd het idee geboren om een trial te starten naar snelle postoperatieve voeding. In 1996 vertrok zij naar Maastricht, om daar verder te gaan als AGNIO, met de bedoeling haar horizon te verbreden in een academisch ziekenhuis. In 1997 startte zij met de opleiding heelkunde te Rotterdam. De eerste 3 jaar werden doorgemaakt in wederom het toenmalige Zuiderziekenhuis onder toeziend oog van dr. K. Brouwer. Van 2000-2003 werd het tweede deel van de opleiding gevolgd in het toenmalige Academisch Ziekenhuis Rotterdam-Dijkzigt (opleiders prof. dr. H.A. Bruining en prof.dr. H.J. Bonjer). Vervolgens bekwaamde zij zich verder in de gastrointestinale chirurgie bij prof.dr. H.W. Tilanus, en de oncologische chirurgie bij prof.dr. A.M.M. Eggermont. In 2005 werd gestart met een chirurg in vervolg opleiding in de kinderchirurgie in het Erasmus MC Sophia Kinderziekenhuis bij prof.dr. F.W.J. Hazebroek. Gedurende de opleidingsperiode, en ook nog een tijdje daarna, werkte zij aan promotie onderzoek naar 'postoperatieve enterale voeding'.

Zij is getrouwd met Kuo-Ming Han en samen hebben zij een zoon: Antonie. Antonie krijgt bijna aansluitend aan de verdediging van dit proefschrift een broertje of zusje.