

Immediate Postoperative Oral Nutrition Following Esophagectomy: A Multicenter Clinical Trial

Teus J. Weijs, MD, PhD, Gijs H. K. Berkelmans, MD, Grard A. P. Nieuwenhuijzen, MD, PhD, Annemarie C. P. Dolmans, MANP, Ewout A. Kouwenhoven, MD, PhD, Camiel Rosman, MD, PhD, Jelle P. Ruurda, MD, PhD, Frans van Workum, MD, Marc J. van Det, MD, PhD, Luis C. Silva Corten, MD, Richard van Hillegersberg, MD, PhD, and Misha D. P. Luyer, MD, PhD

Department of Surgery, Catharina Hospital, Eindhoven; Department of Surgery, ZGT Hospital, Almelo; Department of Surgery, Canisius-Wilhelmina Hospital, Nijmegen; and Department of Surgery, University Medical Center Utrecht, Utrecht, the Netherlands

Background. Immediate start of oral intake is beneficial following colorectal surgery. However, following esophagectomy the safety and feasibility of immediate oral intake is unclear, thus these patients are still kept nil by mouth. This study therefore aimed to determine the feasibility and safety of oral nutrition immediately after esophagectomy.

Methods. A multicenter, prospective trial was conducted in 3 referral centers between August 2013 and May 2014, including 50 patients undergoing a minimally invasive esophagectomy. Oral nutrition was started postoperatively immediately (clear liquids on postoperative day [POD] 0, liquid nutrition on POD 1 to 6, solid food from POD 7). Nonoral enteral nutrition was started when <50% of caloric need was met on postoperative day POD 5 or when oral intake was impossible. A comparison was made with a retrospective cohort (n = 50) with a per-protocol delayed start of oral intake until POD 4 to 7.

Results. The median caloric intake at POD 5 was 58% of required. In 38% of the patients nonoral nutrition was

started, mainly due to complications (36%). The pneumonia rate was 28% following immediate oral intake and 40% following delayed oral intake ($p = 0.202$). The aspiration pneumonia rate was 4% in both groups. The anastomotic leakage rate was 14% after immediate oral intake versus 24% following delayed oral intake ($p = 0.202$). The 90-day mortality rate was 2% in both groups. Hospital stay and intensive care unit stay were significantly shorter following immediate oral intake.

Conclusions. Immediate start of oral nutrition following esophagectomy seems to be feasible and does not increase complications compared to a retrospective cohort and literature. However, if complications arise an alternative nutritional route is required. This explorative study shows that a randomized controlled trial is needed.

(Ann Thorac Surg 2016;■:■-■)

© 2016 by The Society of Thoracic Surgeons

Patients are routinely kept nil by mouth during a variable period [1] following an esophagectomy. This nutritional regimen differs from other types of gastrointestinal surgery, in which immediate oral feeding enhances recovery and reduces morbidity [2, 3]. Although the exact mode of action is not fully understood, activation of the autonomic nervous system may play a role in reducing postoperative complications and inflammation [4, 5]. Based on these beneficial effects, immediate start of oral intake is a crucial part of enhanced recovery protocols [6].

Accepted for publication April 20, 2016.

Presented at the Thirteenth Annual World Conference of The World Organization for Specialized Studies on Diseases of the Esophagus, Monaco, Aug 31–Sept 3, 2015.

Presented at The Congress of the European Society for the Diseases of the Esophagus, Stockholm, Sweden, Nov 5–7, 2015.

Address correspondence to Dr Luyer, Department of Surgery, Catharina Hospital, Michelangelolaan 2, Eindhoven, the Netherlands; email: misha.luyer@cze.nl.

The main reasons to keep patients orally fasted following esophagectomy are a hypothetically increased risk of (aspiration) pneumonia and anastomotic leakage. However, despite oral fasting, anastomotic leakage and pneumonia rates remain high, at 0% to 35% and 2% to 39%, respectively, depending on the definition [7]. Another argument is that patients undergoing an esophagectomy are at short- and long-term nutritional risk [8]. To ensure adequate intake and overcome the fasting period, a nasojejunal or jejunostomy tube is often used for feeding, as enteral nutrition is preferred [9, 10]. Nonetheless these feeding routes have their own minor and major complications. A randomized controlled trial (RCT) showed that a jejunostomy is accompanied by 16% insertion site infection, 11% dislocation, 6% obstruction, and 4% leakage and reported a 26% nasojejunal tube dislocation rate [11]. In the largest cohort the relaparotomy rate for jejunostomy related complications was 1% and the mortality rate was 0.4% [12].

It is unknown at this moment whether immediate start of oral intake following esophagectomy is safe and if

nutritional requirements can be adequately met [10]. Therefore, the present explorative study was designed to investigate whether immediate (from postoperative day [POD] 0) start of oral feeding following esophagectomy is feasible and safe.

Patients and Methods

Design and Patients

This study was an exploratory single-arm multicenter trial to investigate the hypothesis that immediate oral nutrition, starting clear liquids on POD 0 and liquid nutrition on POD 1, following esophagectomy is feasible and safe. The medical ethical committee approved the protocol [12]. An independent data and safety monitoring board evaluated the data of every 5 included patients and then determined if study continuation was justified, to ensure patient safety [12].

Patients 18 years of age or older undergoing minimally invasive Ivor Lewis esophagectomy were enrolled in the Catharina Hospital, Canisius-Wilhelmina Hospital and ZGT Hospital, following informed consent. Exclusion criteria were preoperative weight loss >15%, mental retardation, or a preexistent inability for oral intake [13].

Surgical Procedures

Three teams of 2 experienced surgeons, each performing >30 minimally invasive esophagectomies yearly, performed the surgery. Laparoscopy with lymphadenectomy and intracorporeal gastric conduit formation was followed by thoracoscopy in prone position [14]. An end-to-side or side-to-side intrathoracic anastomosis was made with staplers or hand-sewn with V-loc sutures (Medtronic, Dublin, Ireland). During the creation of the anastomosis a 34Ch nasogastric tube was used as aid for suturing and removed at the end of the operation. Pyloric drainage was not performed because recent reviews and meta-analysis show that significant complications do occur but anastomotic leakage or pneumonia are not reduced [1, 15, 16]. Two participating centers preferred creation of a jejunostomy. In these patients the jejunostomy was sealed and only used if predefined indications for nonoral nutrition were met [13].

Nutritional Regimen

Oral liquids were started immediately postoperatively, meaning starting clear liquids on POD 0 and liquid nutrition on POD 1. According to Dutch Guidelines and enhanced recovery after surgery (ERAS) recommendations assessments for leakage, aspiration, gastric dilatation or delayed gastric emptying were performed only in case of clinical suspicion [1, 15]. Routine contrast swallow studies following Ivor Lewis esophagectomy are ineffective because most anastomotic leaks are clinically beforehand [17], and routine assessments for the other conditions have not been investigated in Ivor Lewis esophagectomy. Solid food was started 1 week postoperatively, if recovery was good (decreasing C-reactive protein, good mobilization, independence of intravenous fluids, and intravenous analgesics). Dieticians supervised

the patients, monitored nutritional goals, and calculated caloric requirements with the modified Harris-Benedict formula +30% for postoperative energy expenditure.

The indications for nonoral nutrition were caloric intake <50% of required on POD 5 and complications prohibiting oral intake [13]. When nonoral nutrition was indicated, enteral nutrition was preferred, either via an endoscopically placed nasojejunal tube or via a peroperatively placed jejunostomy catheter. Total parenteral nutrition (TPN) was reserved for severe chyle leakage or other conditions prohibiting enteral nutrition.

Outcome

Primary outcomes were the incidence and severity of anastomotic leakage and pneumonia [13]. Anastomotic leakage was defined as any sign of leakage of the esophago-gastric anastomosis at endoscopy, reoperation, radiographic investigations, postmortal examination or when gastrointestinal contents were found in drain fluid. Anastomotic leakage was graded based on the treatment given according to Price and colleagues [18]: A) treated by antibiotics and nil-by-mouth; B) treated by endoscopic or radiologic reinterventions; C) treated surgically; and D) conduit necrosis requiring conduit resection and esophageal diversion). Patients with a clinically suspected leakage (eg, increased C-reactive protein/leukocyte counts, fever, and respiratory decline) were routinely evaluated by a computed tomography scan and endoscopy.

Pneumonia was defined according to the Uniform Pneumonia Score [19]. This registration system assigns points for temperature, leucocyte count and radiography findings. Pneumonia is defined as ≥ 2 points, of which at least 1 point is based on radiography. Aspiration pneumonia was scored separately, being defined as pneumonia following clinical aspiration of saliva, liquid, solid food, or vomit. Oral intake was halted in patients with clinical signs of aspiration (eg, coughing after oral intake) or suspected recurrent nerve injury (eg, hoarseness) and they were evaluated by an ENT (ear, nose, and throat) physician.

Dietary outcomes were the total caloric intake on POD 5, the percentage of calorie and protein requirements that were met on POD 5 and the need for nonoral nutrition [13].

Other clinical outcomes were the occurrence of vomiting, nasogastric tube reinsertion, total length of intensive care unit (ICU) admission, length of hospital stay, hospital readmission within 30 days after discharge, complications during initial hospital admission classified according to the Clavien-Dindo classification [20], chyle leakage, and in-hospital, 30-day, and 90-day mortality. Chyle leakages <2 L/day were treated with a medium chain trichlyceride diet or TPN and chyle leakages >2 L/day were candidates for surgery.

Retrospective Comparison

A comparison was made with a cohort of 50 consecutive patients undergoing minimally Ivor Lewis esophagectomy prior to the prospective trial. Patient data was collected at the 3 participating centers in proportion to the

number of patients that were locally included in the prospective arm. These patients were kept nil by mouth for 4 to 7 days postoperatively depending on the clinical course and fed via a jejunostomy or a nasojejunal tube when a jejunostomy was not possible. At surgeon's preference nasogastric drainage was performed for the first postoperative days or not.

Statistical Analyses

No formal power calculations were performed because this was an explorative trial. The aim was to include 50 patients in the prospective arm; well above the size of 20 to 30 patients advised by idea, development, exploration, assessment, and long-term study recommendations [21]. Intention-to-treat analysis was performed using SPSS 22.0 (IBM, Armonk, NY). Categorical data are presented as frequency (percentage) and continuous data as median (interquartile range). The Mann-Whitney *U* test was used to compare continuous data or ordinal data, and chi-square and Fisher exact tests were used to compare all other categorical data. A *p* value <0.05 was considered to be statistically significant.

Results

The prospective, immediate oral intake arm was conducted between August 1, 2013, and May 28, 2014. Two patients were excluded since preoperative weight loss exceeded 15% and 4 patients declined to participate. The remaining 50 patients were included. All patients were extubated on the day of surgery and started oral intake immediately postoperatively. The retrospective delayed oral intake arm consisted of 50 consecutive patients prior to the prospective arm. This group had a significantly longer duration of surgery, slightly increased blood loss and a higher proportion receiving a jejunostomy and postoperative nasogastric drainage (Table 1).

Dietary Outcome

In the immediate oral intake group, 35 (70%) patients had oral intake on POD 5 (Table 2). Their median caloric intake was 1,205 (956 to 1,405) kcal, 58% (46% to 70%) of required. Regarding proteins 44% (35% to 51%) of the requirements were met. Median weight 1 month postoperatively was a median of 4 (3 to 7) kg lower compared to the weight at the moment of surgery.

In the immediate oral intake group, 19 (38%) patients required nonoral nutrition during hospital admission. At POD 5, 15 (30%) patients were fed nonorally due to complications prohibiting the oral route. After POD 5 nonoral feeding was started in 3 (6%) patients due to complications prohibiting the oral route, and in 1 (2%) patient due to insufficient caloric intake on POD 5. The routes used for nonoral feeding were a nasojejunal tube or jejunostomy in 15 (30%) patients and TPN in 4 (8%) patients. TPN was started due to chyle leakage (2), delayed gastric emptying and concomitant ileus after failed attempts for enteral feeding (1), and aspiration pneumonia with hemodynamic instability precluding endoscopic guided nasojejunal tube placement (1).

In the immediate oral intake group, 2 (4%) patients had complications of nonoral nutrition; a jejunostomy insertion site abscess requiring radiologic guided drainage (1) and a jejunostomy leakage requiring repositioning (1). In the delayed oral intake group 8 (16%) patients developed complications of nonoral nutrition; an intraabdominal abscess requiring relaparotomy (1), insertion site abscess requiring drainage under local anesthesia (2), insertion site abscess requiring computed tomography-guided drainage (1), insertion site abscess requiring drainage and jejunostomy removal under general anesthesia (2), insertion site infiltrate requiring antibiotics (1), and jejunostomy tube dislocation requiring start of TPN (1).

Anastomotic Leakage

The (clinically manifesting) anastomotic leakage rate was 14% with immediate oral intake versus 24% with delayed oral intake (*p* = 0.202) (Table 3). Anastomotic leakage required surgery in 3 (6%) patients with immediate oral intake and in 7 (14%) patients with delayed oral intake (*p* = 0.319). Other leaks with immediate oral intake were a leakage of the gastric tube staple line at the level of the diaphragm (1) and a leakage through localized conduit necrosis (1). Another leak with delayed oral intake was a tracheo-oesophageal fistula.

Pneumonia

The pneumonia rate was 28% with immediate oral intake versus 40% with delayed oral intake (*p* = 0.205) (Table 3). No significant differences were observed regarding aspiration pneumonia and pneumonia requiring ICU management. Both aspirations in the immediate oral intake group occurred on POD 2. Subsequently 1 (2%) patient developed bilateral pulmonary embolism causing persistent pulmonary problems. After 112 days, of which 110 days of mechanical ventilation, the treatment was ceased and the patient died. The other patient required mechanical ventilation for 8 days and recovered. In the delayed oral intake group 2 (4%) aspirations occurred; 1 (2%) at POD 2 despite nasogastric decompression and 1 (2%) at POD 3 during a reoperation for a colonic herniation through the diaphragm, of which both patients recovered. In the delayed oral intake group 1 (2%) patient developed respiratory failure due to a fulminant bilateral pneumonia and died on POD 6.

Nasogastric Drainage

Nasogastric drainage during the first 3 to 4 postoperative days was applied in 32 (64%) patients with delayed oral intake versus 0 patients with immediate oral intake (*p* = 0.000). Nasogastric drainage during the first postoperative days, compared to no nasogastric drainage, did not significantly affect the nasogastric tube reinsertion rate (22% versus 34%; *p* = 0.224), anastomotic leakage rate (22% versus 18%; *p* = 0.617), pneumonia rate (32% versus 38%; *p* = 0.612), or aspiration pneumonia rate (6% versus 3%; *p* = 0.767).

The nasogastric tube reinsertion rate was 32% with immediate oral intake and 28% with delayed oral intake (*p* = 0.663). Indications for nasogastric tube reinsertion

Table 1. Demographic Data

Variable	Immediate Oral Nutrition (n = 50)	Delayed Oral Nutrition (n = 50)	p Value
Sex			
Male/Female	42 (84)/8 (16)	40 (80)/10 (20)	0.603 ^a
Age	67 (60–71)	65 (58–71)	0.576 ^b
Nicotine user	7 (14)	11 (22)	0.362 ^a
Preoperative % weight loss	4.1 (0–8.4)	3.3 (0.0–7.1)	0.811 ^b
ASA class	II (II–II)	II (II–II)	0.786 ^b
Immunosuppressive drugs	3 (6)	2 (4)	0.646 ^a
Comorbidity	41 (82)	40 (80)	0.799 ^a
Malignancy	7 (14)	8 (16)	0.779 ^a
Cardiovascular	16 (32)	15 (30)	0.829 ^a
Diabetes	10 (20)	8 (16)	0.603 ^a
Pulmonary	15 (30)	12 (24)	0.499 ^a
Thoracic/abdominal surgery	14 (28)	14 (28)	1.000 ^a
Histology			0.273 ^a
High-grade dysplasia	1 (2)	0 (0)	
Non-small cell carcinoma	0 (0)	1 (2)	
Squamous cell carcinoma	4 (8)	1 (2)	
Adenocarcinoma	45 (90)	48 (96)	
Clinical TNM			
T-stage	3 (3–3)	3 (3–3)	1.000 ^b
N-stage	1 (0–2)	1 (0–2)	0.980 ^b
Neoadjuvant therapy			0.068 ^a
None	1 (2)	2 (4)	
Chemotherapy	1 (2)	7 (14)	
Chemo radiotherapy	48 (96)	41 (82)	
Duration of surgery, min	243 (217–297)	313 (280–383)	0.000 ^b
Blood loss, mL	100 (100–200)	213 (100–500)	0.037 ^b
Intraoperative complications	1 (2) ^c	1 (2) ^d	1.000 ^e
Conversion to open surgery	0 (0)	2 (4)	0.153 ^e
Jejunostomy created	14 (28)	47 (94)	0.000 ^a
Nasogastric tube postoperative	0 (0)	32 (64)	0.000 ^a

^a Chi-square test. ^b Mann-Whitney *U* test. ^c Bleeding of pulmonary vein managed without conversion. ^d Splenic laceration treated with splenectomy. ^e Fisher exact test.

Values are n (%) or median (interquartile range).

ASA = American Society of Anesthesiologists; TNM = tumor, node, metastasis.

after immediate oral intake were leakage (9), suspected leakage (4), aspiration (2), and vomiting (1). With delayed oral intake, the indications for nasogastric tube reinsertion were leakage (11) and suspected leakage (3). Vomiting occurred in 1 (2%) patient with immediate oral intake and in 1 (2%) patient with delayed oral intake ($p = 1.000$).

Other Clinical Data

There were no statistically significant differences regarding complication severity, chyle leakage, or mortality (Table 4). All chyle leakages were closed successfully. Hospital and ICU stay were significantly shorter in the immediate oral intake group. The causes of 90-day mortality were pneumonia after developing a broncho-oesophageal fistula in the immediate oral intake group

(1) and a fulminant bilateral pneumonia in the delayed oral intake group (1).

The readmission rate was 24% with immediate oral intake versus 14% with delayed oral intake ($p = 0.205$). With immediate oral intake the most frequent indications for readmission were pneumonia (5) and gastrointestinal complaints (4); with delayed oral intake these were empyema (3) and pneumonia (1).

Comment

The current study shows that it is feasible to start an oral liquid diet immediately in most patients following minimally invasive esophagectomy. Pneumonia rates and severity of anastomotic leakage were not increased compared to a retrospective cohort and other studies [18, 22–24]. However, oral nutrition was not feasible in

Table 2. Postoperative Dietary Data in the Immediate Oral Nutrition Group

Postoperative Dietary Data	Values
Oral intake in kilocalories (n = 35)	
Energy need, kcal	2141 (1917–2349)
Oral intake on POD 5, kcal	1205 (956–1405)
Proportion of energy need achieved	58 (46–70)
Oral intake in proteins (n = 35)	
Protein need, g	116 (104–131)
Oral protein intake on POD 5, g	50 (39–59)
Proportion of protein need achieved, %	44 (35–51)
Reasons to start nonoral nutrition	
Insufficient oral intake on POD 5	1 (2)
Complications prohibiting oral intake	18 (36)
Anastomotic leakage	7 (14)
Chyle leakage	4 (8)
Pneumonia	4 (8)
Gastric staple line leakage	1 (2)
Ileus	1 (2)
Empyema	1 (2)
Total	19 (38)
Route for nonoral nutrition	
Nasojejunal tube	10 (20)
Jejunostomy	5 (10)
Parenteral nutrition	4 (8)
Total	19 (38)

Values are n (%) or median (interquartile range).

POD = postoperative day.

38% of patients, in which tube feeding or parenteral nutrition was started.

Some data suggest that immediate start of oral intake following esophagectomy might be beneficial [10]. In animal experiments, enteral feeding passing an esophagogastric anastomosis improved anastomotic healing [25]. Next, animal experiments and RCTs in colorectal surgery show that immediate oral intake and even sham

feeding via chewing gum triggers the autonomic nervous system, reducing inflammatory-based complications and length of stay [4, 5, 26]. In upper gastrointestinal surgery, immediate oral intake reduced the length of stay and complications compared to immediate jejunostomy tube feeding [2]. Furthermore, complications and discomfort related to nonoral nutrition may be avoided. A feeding jejunostomy is associated with many minor complications (13% to 38%), and occasionally (0% to 3%) severe complications that require a reoperation [10]. Another nonoral route for enteral nutrition is a nasojejunal tube, however these dislocate frequently (20% to 35%) and are uncomfortable [10].

An increased incidence and severity of anastomotic leakage is the most feared potential risk of immediate oral intake, but its definition is unclear, resulting in a variable incidence of 0% to 35% [7]. In a recent systematic review, only 28 publications defined anastomotic leakage, using 22 different definitions [7]. Anastomotic leakages that require surgery represent the most severe leakages and are objectified by surgeons. Therefore this was deemed to be the most reliable definition for interstudy comparisons. The most contemporary and largest state-of-the-art studies were sought that conformed to the current practice to delay the start of oral nutrition at least until POD 5 to 7 following esophagectomy with intrathoracic anastomosis. In these studies, anastomotic leakage required a surgical reintervention in 5% to 6% of the patients, comparable to the results obtained with immediate oral intake in the present study [22–24]. There are 2 comparative studies in which the effects of a 5- to 7-day nil-by-mouth regimen were compared to a prolonged nil-by-mouth regimen (even up to 1 month). Significantly reduced anastomotic leakage rates were observed when the start of oral intake was further delayed [27, 28]. It is unclear, however, if the reduced anastomotic leakage rate was a consequence of a further delay in the start of oral intake, or should be attributed to the retrospective design with patient selection and multiple factors differing between groups.

Table 3. Anastomotic Leaks and Pneumonia

Variable	Immediate Oral Nutrition (n = 50)	Delayed Oral Nutrition (n = 50)	p Value
Esophagogastric anastomotic leakage			
Antibiotics and nil per os	1 (2)	1 (2)	
Endoscopic or radiologic intervention	3 (6)	4 (8)	
Surgery			
Thoracoscopy	2 (4)	6 (12)	
Thoracotomy	1 (2)	1 (2)	
Total	7 (14)	12 (24)	0.202 ^a
Pneumonia	14 (28)	20 (40)	0.205 ^a
Requiring ICU management	3 (6)	4 (8)	0.999 ^b
Following clinical aspiration	2 (4)	2 (4)	1.000 ^b

^a Chi-square test. ^b Fisher exact test.

Values are n (%).

ICU = intensive care unit.

Table 4. Other Clinical Data

Variable	Immediate Oral Nutrition (n = 50)	Delayed Oral Nutrition (n = 50)	p Value
Surgical complications (Clavien-Dindo)			0.073 ^a
Grade 1	3 (6)	1 (2)	
Grade 2	11 (22)	9 (18)	
Grade 3a	5 (10)	5 (10)	
Grade 3b	2 (4)	5 (10)	
Grade 4a	8 (16)	11 (22)	
Grade 4b	0	2 (4)	
Grade 5 (in-hospital mortality)	1 (2)	2 (4)	
Chyle leakage			1.000 ^b
Medium-chain triglyceride diet	2 (4)	2 (4)	
Total parenteral nutrition	1 (2)	1 (2)	
Surgery	1 (2)	1 (2)	
Total	4 (8)	4 (8)	
Length of stay			
Hospital admission, days	12 (8–20)	13 (10–30)	0.050 ^a
Intensive care unit admission, days	1 (1–5)	3 (1–9)	0.020 ^a
Mortality			
In hospital	1 (2)	2 (4)	1.000 ^c
30-day	0	1 (2)	1.000 ^c
90-day	1 (2)	1 (2)	1.000 ^c
Combined in hospital/90-day mortality	2 (4)	2 (4)	1.000 ^c

^a Mann-Whitney *U* test. ^b Chi-square test. ^c Fisher exact test.

Values are n (%) or median (interquartile range).

A second reason to delay the start of oral intake following esophagectomy, is a potentially increased incidence of (aspiration) pneumonia. Pneumonia rates following esophagectomy vary widely (2% to 39%) in literature due to a significant variation in definitions [7]. Using the only published objective registration method for pneumonia showed a somewhat lower pneumonia rate with immediate oral intake (28%) compared to the delayed oral intake group (40%) and the 2 only other cohorts using this definition (36% to 40%) [19]. The pneumonia rate also lies within the 2% to 39% range of pneumonia rates using other definitions [7]. Data regarding aspiration pneumonia are scarce. Following Ivor Lewis esophagectomy the reported aspiration pneumonia rate is 4.4%, with 50% mortality [29], similar to the current study (4%). Others reported a 4% to 10% incidence of radiologically or endoscopically detected aspiration following esophagectomy [30, 31]. However, it is unclear whether or not this caused pneumonia in all these cases.

To overcome the problematic variety in definitions for pneumonia and anastomotic leakage we also graded the severity of surgical complications using the widely accepted and validated Clavien-Dindo classification [20]. The rate of severe complications (grade 3 to 5) was 32% with immediate oral intake, compared to 40% with delayed oral intake in the present study and 30% to 36% in other, recently published studies [32–34].

Finally, applying oral intake only after esophagectomy may result in insufficient caloric intake. In the current

study the median caloric intake achieved with oral nutrition on POD 5 was substantially lower than the calculated requirements, and significant weight loss occurred. Jejunostomy tube feeding can meet 46% to 100% of the postoperative nutritional requirements [10]. The amount of caloric intake reported in the current study is at the lower end of that range, and intuitively reaching calculated nutritional requirements should be preferred. However, a high amount of (jejunostomy) tube feeding might impair respiration [35] and evidence is lacking that the amount of postoperative enteral feeding influences outcome [36]. In ERAS protocols a mean oral intake of 1200 kcal/day postoperatively is accepted, which is similar to the intake in the current study [6]. In colorectal surgery the median protein intake was 32 g at POD 4, less than achieved in the current study (50 g) [37]. It is known that an esophagectomy induces weight loss, and that this is not regained even at 3 years postoperatively [38]. With routine jejunostomy tube feeding a median weight loss up to 6.2 kg is reported; higher than the weight loss with immediate oral intake in the current study [10]. It is debatable whether weight loss is acceptable early postoperatively, or if this should be postponed.

A drawback of immediate oral intake following esophagectomy is the frequent occurrence of complications that prohibit oral intake. Subsequently 38% of patients required nonoral nutrition, compared to 11% to 21% of patients following colorectal or upper abdominal surgery. Another limitation is the retrospective, non-randomized comparison with significant differences

regarding duration of surgery, blood loss, number of jejunostomies created, and use of postoperative nasogastric decompression. The increased duration of surgery in the retrospective cohort may be explained by the routine creation of a jejunostomy, which was only performed in a minority of the immediate oral intake group. The difference in blood loss was small and postoperative nasogastric decompression was not associated with pneumonia or anastomotic leakage, therefore it is unlikely that these have influenced the results. However, these issues underline the need for a RCT.

This explorative trial shows that immediate start of oral intake following esophagectomy is feasible in most patients with a complication rate that is comparable to a retrospective cohort and other studies using a nil-by-mouth regimen. For patients without complications it is hypothesized that immediate oral intake might improve recovery. However, when complications occur that preclude oral intake an alternative route for feeding is needed.

The authors wish to thank Fanny Heesakkers, Carlijn Hermans, and Maartje Kroes for their valuable contribution through data collection. The authors wish to acknowledge the contributions of the dietitians Chantal Koppens-Donkers and Lisette de Craen-Kat in calculating nutritional need and intake. (Dutch Trial Register, NTR4136.)

References

- Findlay JM, Gillies RS, Millo J, et al. Enhanced recovery for esophagectomy. A systematic review and evidence-based guidelines. *Ann Surg* 2014;259:413-31.
- Lassen K, Kjaeve J, Fetveit T, et al. Allowing normal food at will after major upper gastrointestinal surgery does not increase morbidity: a randomized multicenter trial. *Ann Surg* 2008;247:721-9.
- Pragatheeswarane M, Muthukumarassamy R, Kadambari D, et al. Early oral feeding vs. traditional feeding in patients undergoing elective open bowel surgery: a randomized controlled trial. *J Gastrointest Surg* 2014;18:1017-23.
- van den Heijkant TC, Costes LM, van der Lee DG, et al. Randomized clinical trial of the effect of gum chewing on postoperative ileus and inflammation in colorectal surgery. *Br J Surg* 2015;102:202-11.
- Boelens PG, Heesakkers FF, Luyer MD, et al. Reduction of postoperative ileus by early enteral nutrition in patients undergoing major rectal surgery: prospective, randomized, controlled trial. *Ann Surg* 2014;259:649-55.
- Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Clin Nutr* 2012;31:783-800.
- Blencowe NS, Strong S, McNair AG, et al. Reporting of short-term clinical outcomes after esophagectomy: a systematic review. *Ann Surg* 2012;255:658-66.
- Baker A, Wooten LA, Malloy M. Nutritional considerations after gastrectomy and esophagectomy for malignancy. *Curr Treat Options Oncol* 2011;12:85-95.
- Fujita T, Daiko H, Nishimura M. Early enteral nutrition reduces the rate of life-threatening complications after thoracic esophagectomy in patients with esophageal cancer. *Eur Surg Res* 2012;48:79-84.
- Weijs TJ, Berkelmans GH, Nieuwenhuijzen GA, et al. Routes for early enteral nutrition after esophagectomy. A systematic review. *Clin Nutr* 2015;34:1-6.
- Han-Geurts IJ, Hop WC, Verhoef C, et al. Randomized clinical trial comparing feeding jejunostomy with nasoduodenal tube placement in patients undergoing oesophagectomy. *Br J Surg* 2007;94:31-5.
- Han-Geurts IJ, Verhoef C, Tilanus HW. Relaparotomy following complications of feeding jejunostomy in esophageal surgery. *Dig Surg* 2004;21:192-6.
- Weijs TJ, Nieuwenhuijzen GA, Ruurda JP, et al. Study protocol for the nutritional route in oesophageal resection trial: a single-arm feasibility trial (NUTRIENT trial). *BMJ Open* 2014;4:e004557.
- Biere SS, van Berge Henegouwen MI, Maas KW, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet* 2012;379:1887-92.
- Oesofagus Carcinoom: Landelijke Richtlijn, versie 3.1. Utrecht, the Netherlands: Vereniging van Integrale Kankercentra, 2010. Available at <http://www.oncoline.nl/oesofaguscarcinoom>. Accessed December 18, 2015.
- Arya S, Markar SR, Karthikesalingam A, et al. The impact of pyloric drainage on clinical outcome following esophagectomy: a systematic review. *Dis Esophagus* 2015;28:326-35.
- Jones CM, Clarke B, Heah R, et al. Should routine assessment of anastomotic integrity be undertaken using radiological contrast swallow after oesophagectomy with intra-thoracic anastomosis? Best evidence topic (BET). *Int J Surg* 2015;20:158-62.
- Price TN, Nichols FC, Harmsen WS, et al. A comprehensive review of anastomotic technique in 432 esophagectomies. *Ann Thorac Surg* 2013;95:1154-60.
- Weijs TJ, Seesing MF, van Rossum PS, et al. Internal and external validation of a multivariable model to define hospital-acquired pneumonia after esophagectomy. *J Gastrointest Surg* 2016;20:680-7.
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-13.
- McCulloch P, Altman DG, Campbell WB. No surgical innovation without evaluation: the IDEAL recommendations. *Lancet* 2009;374:1105-12.
- Luketich JD, Pennathur A, Awais O, et al. Outcomes after minimally invasive esophagectomy: review of over 1000 patients. *Ann Surg* 2012;256:95-103.
- Rutegard M, Lagergren P, Rouvelas I, et al. Intrathoracic anastomotic leakage and mortality after esophageal cancer resection: a population-based study. *Ann Surg Oncol* 2012;19:99-103.
- Shewale JB, Correa AM, Baker CM, et al. Impact of a fast-track esophagectomy protocol on esophageal cancer patient outcomes and hospital charges. *Ann Surg* 2015;261:1114-23.
- Tadano S, Terashima H, Fukuzawa J, et al. Early postoperative oral intake accelerates upper gastrointestinal anastomotic healing in the rat model. *J Surg Res* 2011;169:202-8.
- Lubbers T, de Haan JJ, Luyer MD, et al. Cholecystokinin/cholecystokinin-1 receptor-mediated peripheral activation of the afferent vagus by enteral nutrients attenuates inflammation in rats. *Ann Surg* 2010;252:376-82.
- Bolton JS, Conway WC, Abbas AE. Planned delay of oral intake after esophagectomy reduces the cervical anastomotic leak rate and hospital length of stay. *J Gastrointest Surg* 2014;18:304-9.
- Tomaszek SC, Cassivi SD, Allen MS, et al. An alternative postoperative pathway reduces length of hospitalisation following oesophagectomy. *Eur J Cardiothorac Surg* 2010;37:807-13.
- Cerfolio RJ, Bryant AS, Bass CS, et al. Fast tracking after Ivor Lewis esophagogastrectomy. *Chest* 2004;126:1187-94.
- Puri V, Hu Y, Guthrie T, et al. Retrograde jejunogastric decompression after esophagectomy is superior to nasogastric drainage. *Ann Thorac Surg* 2011;92:499-503.

31. Atkins BZ, Shah AS, Hutcheson KA, et al. Reducing hospital morbidity and mortality following esophagectomy. *Ann Thorac Surg* 2004;78:1170-6.
32. Xia BT, Rosato EL, Chojnacki KA, et al. Major perioperative morbidity does not affect long-term survival in patients undergoing esophagectomy for cancer of the esophagus or gastroesophageal junction. *World J Surg* 2013;37:408-15.
33. Goldberg RF, Bowers SP, Parker M, et al. Technical and perioperative outcomes of minimally invasive esophagectomy in the prone position. *Surg Endosc* 2013;27:553-7.
34. Lerut T, Moons J, Coosemans W, et al. Postoperative complications after transthoracic esophagectomy for cancer of the esophagus and gastroesophageal junction are correlated with early cancer recurrence: role of systematic grading of complications using the modified Clavien classification. *Ann Surg* 2009;250:798-807.
35. Watters JM, Kirkpatrick SM, Norris SB, et al. Immediate postoperative enteral feeding results in impaired respiratory mechanics and decreased mobility. *Ann Surg* 1997;226:369-77.
36. Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24 h of intestinal surgery versus later commencement of feeding: a systematic review and meta-analysis. *J Gastrointest Surg* 2009;13:569-75.
37. Carli F, Trudel JL, Belliveau P. The effect of intraoperative thoracic epidural anesthesia and postoperative analgesia on bowel function after colorectal surgery: a prospective, randomized trial. *Dis Colon Rectum* 2001;44:1083-9.
38. Martin L, Lagergren P. Long-term weight change after oesophageal cancer surgery. *Br J Surg* 2009;96:1308-14.