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Early Oral Feeding After Surgery for Upper Gastrointestinal Malignancies: A Prospective Cohort Study

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ABSTRACT

Objectives: Poor nutritional status following abdominal surgeries for esophageal and gastric cancers remains a major challenge in postoperative care. Our study aimed to investigate the efficacy of starting early oral feeding (EOF) in patients undergoing surgical resection of upper gastrointestinal malignancies. ***Methods:*** A total of 180 consecutive patients with a diagnosis of esophageal or gastric malignancies undergoing elective surgical resection between January 2008 and February 2011 were enrolled in this prospective cohort study. Seventy-two patients were assigned to the EOF group, and 108 patients received late oral feeding (LOF). Postoperative endpoints were compared between the two groups. ***Results:*** Nasogastric tubes were removed from patients on average 3.3±1.6 days after the surgery in the EOF group and 5.2±2.5 days in the LOF group ($p < 0.001$). The soft diet regimen was started and tolerated significantly sooner in the EOF group (5.8±1.2 days) than the LOF group (9.5±5.5 days). Hospital stay was significantly shorter in the EOF group compared to the LOF group (6.7±3.1 days vs. 9.1±5.8 days, $p < 0.001$). Surgical complications and rehospitalization occurred less in EOF group compared with the LOF group. However, the differences were not significant ($p > 0.050$). ***Conclusions:*** EOF is safe following esophageal and gastric cancer surgery and results in faster recovery and hospital discharge.

Poor nutritional status following abdominal surgeries remains a major challenge in postoperative care.[1–4] Malnutrition may worsen outcomes of patients undergoing resection of gastrointestinal (GI) tumors by increasing postoperative complications.[4,5] Previously, gas passage and audible bowel sounds were safety indicators to initiating oral feeding.[6] However, in modern postoperative care, early feeding is considered key to shortening the length of hospital stay and improving patient outcomes.[1–4,6,7]

Esophageal and gastric cancers are common malignancies reported all over the world causing a remarkable number of deaths annually.[8,9] Patients with tumors of the upper GI tract often suffer from malnourishment, too.[5,10,11] Moreover, on the one hand, malignancy evokes catabolic status and, on the other hand, interferes with appetite and eating habits.[11–13] Chemoradiation therapy before and after surgical resection of tumors may worsen existing malnourishment.[13,14] Despite the existence of a variety of nutritional support methods, enteral feeding provides the most physiologic route and at the same time avoids other complications and adverse events associated with parenteral feeding.[1–3,7,15] However, due to the theoretical concerns regarding the possibility of leakage and anastomosis rupture in patients with operative resection of upper GI tumors (including the esophagus and stomach) delayed postoperative oral feeding and the application of a nasogastric (NG) tube for gastric decompression along with intravenous (IV) fluid administration have been common practice in such surgeries.[6]

Recent studies do not support the traditional concept of delayed oral feeding after gastrointestinal surgeries,[16,17] but have shown promising benefits to early feeding following operations on the colon and rectum.[1-4,7,12,15] However, there is a lack of evidence comparing the risks and benefits of early and late feedings in patients undergoing surgeries for upper GI malignancies. This is due to the fear of early contact of surgical anastomosis sites with passing substances and consequently increasing the chance of leakage.

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Our study aimed to investigate the safety of early oral postoperative feedings in patients undergoing resection of esophageal and gastric tumors. We sought to establish a protocol for early oral feeding (EOF) following surgical resection of upper GI tumors.

METHODS

This prospective, non-randomized clinical trial took place between January 2008 and February 2011 at the Cancer Institute of Tehran University of Medical Sciences. Patients enrolled were diagnosed with esophageal or gastric malignancies and due to undergo elective surgical resection.

Diagnosis of malignancy was made based on a preoperative endoscopic biopsy. Histological specimens were evaluated by a clinical pathologist to confirm the diagnosis and determine tumor grade. Of the 180 patients included in this study, 72 were treated by EOF while the remaining 108 patients received traditional methods of postoperative oral feeding.

The study was in accordance with the tenets of the Declaration of Helsinki and the institutional review board and the ethics committee of our hospital approved the study protocol.

Patients received general anesthesia by a single team of anesthetists. All surgeries were performed by experienced attending surgeons (two surgeons in the patient group and three surgeons in the control group) via laparotomy with thoracotomy (in transthoracic esophagectomies). Esophagectomy was performed with regional lymph node dissection in patients diagnosed with esophageal cancer. Neoadjuvant chemotherapy was performed in indicated cases. Resected esophagus was reconstructed using a gastric tube via posterior mediastinum. Gastric tumors were resected with radical lymph node dissection while reconstruction was made by the Billroth II method or esophagojejunostomy in subtotal and total gastrectomy, respectively. All the anastomoses were hand sewn in two layers with separate sutures using 3-0 absorbable thread in the inner layer and 3-0 silk thread in the outer layer. Prophylactic antibiotics metronidazole and ceftriaxone were administered intravenously (IV).

In patients in the EOF group (the case group), a liquid regimen was started 24 to 48 hours after surgery depending on the possibility of extubation and tolerance. The regimen contained 50 cc of black tea combined with two sugar cubes (total 8 g) orally every eight hours while the patient still had the NG tube. The NG tube was flushed every eight hours to avoid blockage. It was removed when its secretion decreased to less than 500 cc per day. The liquid regimen increased in volume and, depending on the patient's tolerance, a soft diet was started after 24 hours of liquid initiation. In the traditional oral feeding group (the control group), feeding was started following five postoperative days if audible bowel sounds, the passage of flatus, or bowel habits were observed.

In both groups, no prokinetic agent was used, and a diclofenac suppository and IV morphine were administered for pain control. No epidural analgesia was performed in any patient. Patients were visited daily by attending physicians who evaluated any progress or deterioration of general conditions and surgical site complications. Laboratory tests or imaging studies (X-radiography, contrast studies, and CT scanning) were requested based on clinical impression (presence of fever, GI secretions from the wound, signs of peritoneal irritation, or sepsis). All patients were referred to the oncology clinic for adjuvant treatments and later follow-up. We compared clinical outcomes of patients in the EOF group with patients of the traditional late oral feeding (LOF) group. Data regarding demographic and clinicopathologic characteristics of the patients were collected from patients' medical records. This included medical comorbidities (diabetes, chronic obstructive pulmonary disease (COPD), cardiac disease or presence of a New York Heart Association (NYHA) class I or II, and renal dysfunction), and events arising during the postoperative periods including oral feeding tolerance and complications. Duration of decompressing NG tube, time needed to initiate oral intake along with solid diet tolerance, and duration of IV fluid (more than 1 liter per day), were compared between the two groups.

Postoperative complications considered in the analysis included generalized peritonitis, abscesses, fistulas formation, vomiting after initiation of oral feeding, rehospitalization or reoperation, and mortality. Complications were defined according to the clinical findings and laboratory and imaging studies.

Data were presented as mean ± standard deviation (SD) or number and percentage. Data were analyzed

Table 1: Demographics and primary clinicopathological characteristics of patients.

Variables	EOF (n = 72)	LOF (n = 108)	*p*-value
Age, years	61.4±10.3	61.6±11.8	0.933
Sex			0.831
Male	35 (48.6)	55 (50.9)	
Female	37 (51.4)	53 (49.1)	
Weight, kg	56.0±11.4	55.0±12.6	0.707
Tumor site			0.161
Esophagus	38 (52.8)	47 (43.5)	
Stomach	34 (47.2)	61 (56.5)	
Tumor anatomical level			0.340
Upper esophagus	1 (1.4)	0 (0.0)	
Middle esophagus	19 (26.4)	23 (21.3)	
Lower esophagus	20 (27.8)	25 (23.1)	
Cardia	22 (30.6)	32 (29.6)	
Fundus	1 (1.4)	1 (0.9)	
Body	4 (5.6)	7 (6.5)	
Antrum	5 (6.9)	20 (18.5)	
Staging			0.466
I	6 (8.3)	9 (8.3)	
II	27 (37.5)	34 (31.5)	
III	39 (54.2)	65 (60.2)	
Anastomosis site			0.339
Neck	38 (52.8)	46 (42.6)	
Thorax	9 (12.5)	14 (13.0)	
Abdomen	25 (34.7)	48 (44.5)	

EOF: early oral feeding; LOF: late oral feeding.

using SPSS Statistics (SPSS Statistics Inc., Chicago, US) version 17. The chi-square and Student's *t*-test for qualitative and quantitative normal variables, and Mann-Whitney U test for non-parametric continuous variables were applied, and the values were considered statistically significant at $p < 0.050$.

RESULTS

Medical records of 180 patients with a diagnosis of esophageal or gastric cancer were reviewed. Of these, 72 patients (40%) were treated with EOF while the remaining 108 patients (60%) were received LOF. The demographic and primary clinicopathologic characteristics of patients are summarized in Table 1. No significant difference was present between the two groups in age, gender, diagnosis of upper GI tumors, and other clinical or pathological features.

There was no statistically significant difference ($p = 0.922$) between the EOF (4.1%, 3 of 72 patients) and LOF (2.7%, 3 of 108 patients) groups in term of vomiting after starting oral feeding [Table 2]. Four patients (5.5%) in the EOF group required fasting (repeated nil per os [NPO]) following the initiation of oral feeding compared with two patients (1.8%) in the LOF group ($p = 0.821$). Time to gas passage was 3.0±0.8 and 4.3±1.2 days in the EOF and LOF groups, respectively, which occurred significantly earlier in the EOF group ($p < 0.001$). The NG tube was removed 3.3±1.6 days after the surgery in the

Table 2: Postoperative feeding outcomes.

Outcome	EOF (n = 72)	LOF (n = 108)	*p*-value
Vomiting, n	3 (4.1)	3 (2.7)	0.922
Repeated NPO, n	4 (5.5)	2 (1.8)	0.821
Time to NG tube removal, days	3.3±1.6	5.2±2.5	< 0.001
Time to gas passage, days	3.0±0.8	4.3± 1.2	< 0.001
Time to starting soft diet, days	5.8±1.9	9.6±5.6	< 0.001

EOF: early oral feeding; LOF: late oral feeding; NPO: nil per os; NG: nasogastric.

Table 3: Postoperative clinical outcomes.

Outcome	EOF (n = 72)	LOF (n = 108)	*p*-value
Hospital stay, days	6.7±3.1	9.1±5.9	< 0.001
Rehospitalization			
Anastomosis leakage	2 (2.7)	5 (4.6)	0.417
Nausea and vomiting	2 (2.7)	1 (0.9)	0.351
Peritonitis	1 (1.4)	1 (0.9)	0.641
Abscess formation	0 (0.0)	1 (0.9)	0.600
Fistula	1 (1.4)	0 (0.0)	0.400
Total	**6 (8.3)**	**8 (7.4)**	**0.516**

EOF: early oral feeding; LOF: late oral feeding.

EOF group and after 5.2±2.5 days in the LOF group ($p < 0.001$). The soft diet regimen was started and tolerated significantly sooner ($p < 0.001$) after surgery by patients in the EOF group (5.8±1.9 days) than in patients of the LOF group (9.6±5.6 days). Similarly, the average duration of IV fluid administration (> 1000 cc per day) was significantly shorter in the EOF group (6.7±3.1 days) compared to the LOF group (9.1±5.9 days) ($p = 0.003$).

The average length of hospital stay was 6.7±3.1 days in the EOF group and 9.1±5.8 days in the LOF group ($p < 0.001$). Moreover, in total, six patients (8.3%) in EOF group and eight patients (7.4%) in the LOF group had rehospitalization due to postoperative complications ($p = 0.516$). Anastomosis leakage was the most prevalent reason for rehospitalization in both groups followed by nausea and vomiting, and peritonitis [Table 3]. There was no statistically significant difference between both groups regarding different types of postoperative complications ($p > 0.050$).

DISCUSSION

Tumors of upper GI are still among the most prevalent malignancies worldwide causing a remarkable burden on the health care system.[8,9,18] Moreover, gastric and esophageal cancers are more prevalent in developing countries.[9,19] The method of choice for treating patients with upper GI malignancies has been surgical resection of tumors and extensive lymphadenectomy.[20] However, surgeons have started to pay more attention to the patient's quality of life and postoperative recovery time.[2] For this purpose, multimodal or fast-track programs have been developed aiming to provide early enteral feeding and ambulation while avoiding IV volume overload.[17] However, EOF has not become common practice in surgical oncology since its safety is not documented by sufficient evidence.[1–4,7,15]

Hur and colleagues[3] studied the safety and surgical outcomes of starting EOF on the second postoperative day followed by a soft diet regimen on the third day in 35 patients undergoing curative surgical resection for distal gastric tumors and compared it with 31 patients receiving a conventional diet schedule as the control group. The authors found that the duration of hospitalization was shorter in the EOF group compared to the control group. Moreover, lymphocyte count recovered faster in the EOF group than in the control group. Two years later, Hur et al,[2] showed again that EOF after surgery for gastric cancer was feasible and could result in shorter hospitalization and improve several aspects of patients postoperative quality of life. In their randomized control trial, enrolling 58 patients with gastric cancer, the duration of hospitalization and time to the first flatus along with the quality of life scores for fatigue, nausea and vomiting decreased significantly following the surgery in the EOF group compared to the control group. There was not such a significant difference observed between the two groups in terms of morbidity, costs of hospitalization, and postoperative pain or complications.

On the other hand, Fujita et al,[21] showed that starting early feeding via enteral routes in patients who had undergone esophagectomy for the cancer of thoracic esophagus had reduced life-threatening surgical complications, which facilitated clinical recovery. The authors randomly assigned 88 patients into a parenteral group and 76 patients to an enteral feeding group. Life-threatening surgical complications including anastomosis leakage (due to tension and ischemia at the anastomosis site) and pneumonia occurred in 19.3% and 11.3% of patients in the enteral group and 10.5% and 5.2% patients in

the parenteral group, respectively. Furthermore, the enteral group showed a significantly higher success rate of recovery than the parenteral group (77.6% and 63.6%, respectively) and a much shorter hospital stay (16 and 19 days, respectively).

Other studies assessing EOF following colorectal procedures are also in favor of this component of fast track program.[1,12] Kawamura et al,[12] proposed appetite as a reliable indicator for starting postoperative oral feeding in patients with elective colon cancer surgery while El Nakeeb and colleagues[1] focused on the duration of the operation and amount of blood loss as a determinant of oral feeding tolerability in candidates of colonic anastomosis.

In line with existing evidence, our study showed that EOF leads to earlier removal of NG tube. EOF also helps resolve postoperative ileus and start gas passage. Also, patients in the EOF group had a shorter duration of IV fluid administration and earlier initiation of a soft diet. The satisfactory outcomes in association with EOF could occur due to the surgical technique we employed in the majority of our patients.

However, even minimal complications or compromised recovery may result in fear of practicing this method of EOF in postoperative patients. Heslin et al,[22] in 1997 studied 195 patients undergoing surgical resection for upper GI malignancy and randomly assigned them to a group receiving immune-enhanced formula (IEF) via jejunostomy on the first day or the control group who received conventional IV crystalloid solutions. There was no significant difference between the two groups in the number of minor and major wound complications and duration of hospital stay or postoperative mortality. One patient in the IEF group had bowel necrosis that required reoperation. The authors concluded that early enteral feeding with an IEF was not safe and should not be routine in surgeries for upper GI tumors. On the contrary, surgical complications and rehospitalization occurred less in the EOF group compared to the LOF group and overall/postoperative duration of hospitalization was shorter in the patients who received EOF. The life-threatening complications that led Heslin to forbid colleagues to use EOF in surgical oncology for upper GI malignancy may be due to the nature of their IEF regimen.[22] It may be that immune-enhancing supplements consisting of arginine, RNA, and omega-3 fatty acids are not tolerated so early by a resting bowel on the first postoperative day. However, in our study, we started liquid on the first day and then gradually advanced the diet. Also, we preferred the oral pathway over the NG tube not only due to greater patients' satisfaction (a more physiological approach) but also for the benefits of stimulating patients' appetite.

However, the findings of our study should be interpreted in light of its limitations including our relatively small sample size. The non-randomized feature of our investigation may also limit its results. Also, our inclusion criteria may limit extrapolation of results to a wider surgical setting. Our study included two different surgical entities (i.e.; esophageal and gastric malignancies), although these tumors are both categorized as upper GI tumors and have similar natures, a discrete grouping of each tumor with attention to one particular tumor type at a time would make interpretation of our results more reliable. To answer these questions, we need randomized controlled trials to enroll patients into different modalities of EOF to find the most feasible one and to let this method of nutritional management be adopted as standard postoperative care.

CONCLUSION

EOF is safe and is a physiologic stimulant for the bowel, and would resolve postoperative ileus. This would expedite enteral feeding with nutritional and immunologic benefits. The patient would also feel a higher level of recovery, and be more motivated to be independent, ambulate, and be discharged. Starting EOF is safe in patients undergoing surgery for upper GI tumors and results in earlier recovery and hospital discharge.

Disclosure
The authors declared no conflicts of interest. No funding was received for this study.

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