

Original Paper

Comparison between the Effects of Early and Late Nourishing by Jejunal Feeding in Patients with Esophageal Cancer after EsophagectomySamad Beheshti Rouy¹, Farzad Kakaei², Mehran Rahimi^{3*}¹Department of Cardiothoracic Surgery, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran²Department of General & Vascular Surgery, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran³Students' Research Committee, Tabriz University of Medical Sciences, Daneshgah Street, Tabriz, Eastern Azerbaijan, Iran**Corresponding Author:** Mehran Rahimi, E-mail: rahimimehran95@gmail.com**ARTICLE INFO***Article history*

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Esophageal Cancer**ABSTRACT**

Background: Esophageal cancer has become one of the most common cancers in the last decade and multiple treatment methods can be prescribe based on its extent and grade. It has been proven that nutritional states are very important to tolerance surgery. **Aim:** The aim of this study was to evaluate the efficacy and safety of early (6 hours) starting of jejunal feeding comparing with late (72 hours) nourishing by jejunal feeding in patients with esophageal cancer after esophagectomy. **Methods:** In this prospective-randomized study, 50 patients undergoing esophagectomy for esophageal cancer were randomly divided into two groups. Then patients underwent surgery. In case group (n=25) nourishing by jejunostomy was started 6 hours after surgery and in control group (n=25) as a conventional method, nourishing by jejunostomy was started 72 hours after surgery. **Results:** There were no significant differences between two groups in term of age, type of tumor and grade of tumor. In case and control group; ICU stay time, hospitalization, transfusion rate, preoperative serum albumin level were 2.2±0.32 and 1.76±0.14 days, 9.28±0.56 and 9.12±0.14 days, 0.24±0.11 and 0.28±0.1 unites, 3.93±0.09 and 3.8±0.07, respectively. The albumin serum levels 6 hours and 72 after surgery in case and control group were 3.74±0.07 and 3.6±0.08, 3.66±0.08 and 3.54±0.07, respectively. **Conclusion:** Based on the results, the transfusion rate, ICU stay and hospitalization days in case group was lower than control group. But there were no significant differences between two groups. In general, it seems that early start of nutrition via jejunal tube in patients undergoing esophagectomy have no more complications comparing conventional method. Its benefits need additional studies.

INTRODUCTION

The incidence of esophageal cancer is globally on a growing trend. This type of cancer is relatively uncommon in many countries and is still seriously fatal. The incidence of esophageal cancer is very diverse in different parts of the world (1). Prognosis of patients with esophageal cancer is not satisfactory; hence five-year survival rate is less than 5% among these patients; thus, the main goal of surgical treatment of esophageal cancer is to improve symptoms, and if possible, to treat the disease completely. Unfortunately, most of the patients who undergo surgery for this purpose die of disease recurrence or its metastasis to other parts of the body (2). Therefore, improving the quality of life of patients after surgery should be considered as a top priority, and the factors deteriorating the quality of life of these patients should be eliminated (2,3). Quality of life of these patients, in addition to the mental status and pain reduction in the patients, includes improved nutritional status and faster return to normal oral diet at the patient's level of need.

According to recent studies, the complications and mortality of esophageal cancer are directly related to the nutritional

status of patients (4-6). This issue contains preoperative and postoperative nutritional status and support. Over the past decades, the Glasgow Prognostic score (GPS), based on serum albumin and C reactive protein (CRP) levels, has been considered the most extensively validated tool, and is thus used in routine clinical assessment for cancer patients (7). Preoperative nutritional deficiencies can be corrected by parenteral nutrition or by oral intake. Correcting nutritional disorders can reduce the complications rate of the surgery.

The most important point in these patients is the time of enteral onset after the surgery. Traditionally, most surgeons oppose the onset of nutrition on the first day in these patients due to the possibility of opening anastomosis and pneumonia (8). According to various studies, it has been reported that the onset of nutrition within the first 24 hours after surgery or burned patients can reduce the rate of infection and mortality (9-11). Enteral feeding can started via naso-gastric or naso-enteric tube or via jejunal feeding tube.

According to the above, the main purpose of this study was to prove the safety of early enteral feeding and comparison between the effects of early and late nourishing by jejunostomy feeding in patients with esophageal cancer after esophagectomy.

MATERIALS AND METHODS

In this prospective randomized comparative study, 50 patients with distal esophageal cancer candidate for esophagectomy were studied at Tabriz Imam-Reza hospital since 2015 to 2017. All the patients had distal esophagus cancer proved by endoscopic biopsy and pathologic report. All the patients planned to underwent transhiatal esophagectomy with no contraindication for general anesthesia and surgery. Study was approved by the Ethics Committee of the Tabriz Azad University of Medical Sciences and every patient was entered in the study after receiving the informed consent form. During the study, all stages were explained to the patients and patients have the right to withdraw from the study.

Patients enrolled into the study were randomly assigned into two groups (Case and Control groups) using a random number table. Then patients underwent transhiatal esophagectomy. In control group, as usual method, the nourishing by jejunostomy was started 72 hours after surgery. In the case group, 6 hours after surgery 30 milliliter of dextrose 5% drip per hour was started via jejunostomy tube, then 12 hours after operation dextrose 5% was converted to dextrose 10%. Feeding with the formula, based on a diet designed by a dietitian was started 24 hours after surgery. He calculated energy and protein needs for the patients, and brings it to the level of energy needed by the patient during 72 hour.

Why dextrose 5%?

Jejunum feeding should start with iso-osmol fluid and then gradually converted to hyper osmol fluid. Iso-osmol fluid can be dextrose 5% or normal saline. We selected dextrose because of its energy.

All patients were admitted to ICU after surgery. Routine lab tests and arterial blood gas analysis were done every morning during ICU admission. Serum albumin level was analyzed in three time intervals (before operation, 6 hours after operation and 72 hours after operation) in the two groups.

The data were collected using a questionnaire prepared by the researcher. Data were analyzed using SPSS v.17 software. An analysis was made for quantitative variables using descriptive statistics (mean \pm standard deviation), frequency and means difference for independent groups; and for qualitative variables using Chi-square test and Fisher's exact test. In this study, p value less than 0.05 were considered for significantly correlations

RESULTS

At all, 29 patients (58%) were male and 21 (42%) were female. In case group, 19 (76%) patients were male and 6 (24%) were female; in control group, 10 patients (40%) were male and 15 (60%) were female. There was a significant relationship between gender differences in two groups ($p = 0.01$).

Mean age of the patients was 58.86 ± 1.49 years, with the highest age of 81 and the lowest of 36 years. Mean age of patients in case group was 64.16 ± 1.78 years and in the control group, was 56.63 ± 1.37 years. According to the results, no significant relationship was found in the mean age difference between the two groups ($p = 0.84$).

The results of the hospitalization and ICU admission rates, as well as the transfusion rate in the two groups, are shown in Table 1.

According to the results of postoperative systemic and topical complications, shown in Table 2, the major complications include: pneumonia, chylothorax and atelectasis. There was no significant correlation between systemic complications in both groups ($p = 0.63$).

According to the results from the tumor type, the incidence of adenocarcinoma was the alike in both groups and was equal to 11 (44%). Furthermore, the incidence of SCC (squamous cell carcinoma) in both groups was the same and equal to 14 (56%). No significant correlation was found between the two groups in the incidence of adenocarcinoma and SCC ($p = 0.61$). The highest rates of tumor stage in both groups were stage 3a, which were 11 patients (44%) in the case group and 10 patients (40%) in the control group. There was no significant correlation between the incidence of tumor stage in the two groups ($p = 0.64$). The pathologic tumor stage of the two groups after surgery were shown in Table 3.

Regarding the results of mortality in patients, under two different starting regimens after surgery, in the case group, which was started after 6 hours post-operative nourishing by jejunostomy, there was no mortality, but in the control group with onset of nourishing 72 hours postoperative by jejunostomy, one patient died after pneumonia, and 24 patients (96%) were alive ($p = 0.5$).

The serum albumin levels measurements in three time intervals (before operation, 6 hours after operation and 72 hours after operation) in the two groups did not show any significant relationship between the two groups. The results for albumin levels of the two groups in three time intervals are shown in Table 4.

There was no overall complication arising from the use of this method.

DISCUSSION

The prevalence of esophageal cancer, in particular adenocarcinoma, is increasing during recent years among the worldwide population. In different parts throughout the world, the incidence of this cancer varies (1). The incidence of esophageal cancer in the southern shores of the Caspian Sea is 93 per 100,000 in male and 110 per 100,000 in women (12).

In this study, 50 patients were evaluated in two groups of 25 patients based upon the onset of post-operative nutritional regimens. Patients in two groups were alike in age, type

Table 1. Results of the hospitalization and ICU admission rates and transfusion rate in the two groups

| | Case Group | Control Group | P value |
|--------------------------------------|-----------------|-----------------|---------|
| ICU admission rates ^(day) | 2.2 \pm 0.32 | 1.76 \pm 0.14 | 0.21 |
| Hospitalization ^(day) | 9.28 \pm 0.56 | 9.12 \pm 0.41 | 0.81 |
| Transfusion rate | 0.24 \pm 0.11 | 0.28 \pm 0.1 | 0.8 |

Result were in Mean \pm SD

Table 2. Results of systemic and topical complications in the two groups

| | n(%) | | P value |
|------------------------|------------|---------------|---------|
| | Case Group | Control Group | |
| Systemic complications | | | 0.63 |
| No complications | 21 (84%) | 22 (88%) | |
| Pneumonia | 2 (8%) | 1 (4%) | |
| Chylothorax | 1 (4%) | 0 (0%) | |
| Atelectasis | 1 (4%) | 2 (8%) | |
| Topical complications | | | - |
| No complications | 21 (84%) | 21 (84%) | |
| Wound infection | 1 (4%) | 1 (4%) | |
| Neck anastomosis leak | 3 (12%) | 3 (12%) | |

Table 3. Phathologic stage of the two groups after surgery

| | n(%) | | P value |
|-------------|------------|---------------|---------|
| | Case Group | Control Group | |
| Tumor stage | | | 0.64 |
| 1a | 2 (8%) | 0 (0%) | |
| 1b | 2 (8%) | 2 (8%) | |
| 2a | 2 (8%) | 2 (8%) | |
| 2b | 6 (24%) | 10 (40%) | |
| 3a | 11 (44%) | 10 (40%) | |
| 3b | 2 (8%) | 1 (4%) | |

Table 4. Results for albumin levels of the two groups in three time intervals

| | Case Group | Control Group | P value |
|--------------------------|-------------|---------------|---------|
| Serum Albumin | | | |
| Before Surgery | 3.39±0.09 | 3.8±0.07 | 0.29 |
| 6 hours after operation | 3.74±0.07 | 3.6±0.08 | 0.22 |
| 72 hours after operation | 3.66 ± 0.08 | 0.54 ± 0.07 | 0.31 |

Results were in Mean±SD

of tumor and tumor grade in pathology examination, and there was no significant difference between the two groups. In related studies, variable times have been reported with different outcomes about the early onset of postoperative nourishment in patients with esophageal cancer underwent esophagectomy.

In the study of Lim and colleagues in 2014, it has been reported that the routine method used in Seoul Hospital in patients undergoing esophagectomy is to start nourishing 16 hours after the operation and brings it to the level of energy needed by the patient within 6 to 7 days. In their study, the researchers examined the effects of timely onset of nourishing in these patients within 1 day-after surgery and continued during 24 hours in 3 patients. According to the study of Lim

and colleagues, starting early nutrition in these patients in the first 24 hours after the operation reduced the time needed to reach the patient's nutritional energy level to less than 5 days without any side effects in patients (13). However, in our study early onset of nourishing in patients undergoing esophagectomy does not have significant and threatening complications in these patients relative to the late onset of jejunostomy nourishment.

In the study of Kobayashi and colleagues in 2013, 103 patients underwent esophagectomy because of esophageal cancers. The patients from this study were divided to two groups. Group 1: Starting a diet in less than 3 days after surgery and Group 2: Starting a diet after 3 days after surgery. In this study, like the other similar studies, the patients' clinical variables after surgery were compared to the start of the diet. Based on the results from this study, the group 1 had fewer days in terms of first fecal excretion ($p < 0.01$), lower dose of postoperative albumin prescription ($p < 0.01$), less use of TPN ($p < 0.01$), and the duration of symptoms in group 1 was inferior than the group 2 ($p < 0.01$). There was no significant difference in postoperative complications between the two groups. Kobayashi and colleagues therefore, pointed out that early onset of nourishing in patients undergoing esophagectomy in less than 3 days after surgery reduced the rate of albumin infusion and the use of TPN. Early onset jejunostomy nourishing also causes the onset of early intestinal movements and reduces the recovery time of symptoms associated with systemic infections in these patients (14). In a study by Gabor and colleagues, it was noted that early onset of nutrition even when intestinal peristalsis has failed, can maintain intestinal integrity and immunity (15).

However, some studies have opposed results about early-onset nutrition, including Studies by Manba and Wheble and their colleagues (16, 17). In a study by Monebo and colleagues in 2013, 103 patients underwent esophagectomy due to esophageal cancer. Of the 103 patients, 42 patients were nourished in the first 72 hours after surgery. Therefore, 42 patients under study were divided into two groups according to the goals of the study: Group 1 (D1) (15 patients): underwent jejunostomy nourishing within first 24 hours after surgery. Group 2 (D2-3) (27 patients) underwent jejunostomy nourishing within 24 to 72 hours after surgery. Then, clinical findings including the time of first

fecal excretion, the amount of received albumin after surgery, the level of serum albumin concentration in patients before and after surgery, and the overall rate of venous intake were compared. Based on the results, pneumonia in group 1 (D1) was significantly higher than group 2 (D2-3) ($p = 0.03$). However, other clinical findings, including systemic and topical complications in group 1 (D1) were less than group 2 (D2-3) and there was no significant difference in any of the clinical findings within the two groups. In the study of Manba and colleagues from 42 patients, one death was reported in group 1 (D1) (6.66%), in which case the difference between the two groups was not statistically significant ($p = 0.66$). So, the researchers reported at the end that early onset of nutrition in patients in less than 24 hours had no clinical benefit for patients, and starting feeding at 24 to 72 hours was recommended based upon the status of each patient (16). The results from the study conducted by Wheble and colleagues in 2012, are consistent with the results from the study by Manba and colleagues (17).

Among the studies in this area, our study has reported the fastest start of jejunostomy nourishing among patients underwent esophagectomy. In our study, the case group started jejunostomy nourishing within 6 hours after surgery, and the results were compared with the start of jejunostomy nourishing in 72 hours after surgery. Based on the results obtained during our study, there was no significant difference in the hospitalization rate, ICU addition rate and transfusion rates ($p = 0.81, 0.21, 0.8$; respectively).

In the case of systemic and topical complications, in the case group, 21 patients (84%) and in the control group, 22 patients (88%) had no complications. 2 patients (1%) in the case group and 1 patient (1%) in the control group had pneumonia; and only 1 patient (1%) had chylothorax in the case group, which was not statistically significant between two groups ($P = 0.63$). In the case of topical complications, including wound infection and opening anastomosis, the findings were similar in the two groups. There was no significant difference in serum albumin level between the two groups in the three measurement intervals, and the measured values were similar between the two groups.

After surgery, no cases of mortality were reported in case group which underwent jejunostomy nourishing in 6 hours after surgery, but in control group, starting with feeding by jejunostomy nourishing 72 hours after surgery, 1 case (4%) of mortality was recorded, and 24 patients (96%) were alive ($p = 0.5$).

CONCLUSION

According to the results of this study, despite the lower level of transfusion and mortality in patients of the case group, however, there was no significant difference between two groups even in these cases and in both hospitalized and ICU admitted cases and postoperative complications. Overall, it seems that early onset of nourishing in patients undergoing esophagectomy does not have significant and threatening complications and can be considered as an option for starting enteral nutrition.

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