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Peripheral vein infusions of amino acids facilitate recovery after esophagectomy for esophageal cancer: Retrospective cohort analysis

Masafumi Konosu [a, *], Takeshi Iwaya [a], Yusuke Kimura [b], Yuji Akiyama [a], Yoshihiro Shioi [a], Fumitaka Endo [a], Hiroyuki Nitta [a], Koki Otsuka [a], Keisuke Koeda [a], Akira Sasaki [a]

[a] Department of Surgery, Iwate Medical University, Morioka, Iwate 020-8505, Japan
[b] Department of Palliative Care Medicine, Iwate Medical University, Morioka, Iwate 020-8505, Japan

HIGHLIGHTS

- Radical resection for esophageal cancer is a highly invasive procedure.
- Enteral feeding has been used in postoperative period for esophagectomy.
- Peripheral vein infusion of amino acids is effective for post esophagectomy.

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ABSTRACT

Background: To investigate the efficacy of amino acid administration via peripheral veins in addition to conventional enteral feeding following esophagectomy.
Materials and methods: Retrospective analysis of data pertaining to 33 patients with esophageal cancer who underwent radical esophagectomy and satisfied the required nutrition control. Patients were divided into the amino acid group (n = 17) and control group (n = 16). Primary outcomes were albumin (Alb) and prealbumin (PreAlb) levels, urinary 3-methylhistidine/creatinine (3-MeHis/Cre) ratios, nitrogen balance, and weight; postoperative complications were noted as secondary outcomes.
Results: Alb levels were significantly higher in the amino acid group on postoperative day (POD)-14 (3.4 ± 0.3 vs. 3.1 ± 0.4 mg/dL in the control group, $p = 0.018$) and at 1 month after surgery (3.8 ± 0.4 vs. 3.5 ± 0.3 mg/dL, $p = 0.045$). No significant differences were observed in PreAlb and urinary 3-MeHis/Cre rates between the treatment groups. Body weights at 3 months postoperatively were decreased by 6% and 3% in the control and amino acid groups, respectively.
Conclusion: Peripheral venous administration of amino acids soon after surgical stress is an effective method for nutritional control.

1. Introduction

Radical resection for esophageal cancer involves extensive dissection and lymphadenectomy in the neck, chest, and abdomen. The procedure is invariably associated with damage to the mediastinum [1]. Optimal perioperative respiratory and circulatory management and proactive nutritional control during the early postoperative period can reduce the incidence of complications.

Highly invasive procedures, such as esophagectomy, tend to alter the energy dynamics in the body [1], i.e., endogenous energy is consumed from the breakdown of skeletal muscle induced by stress hormones and cytokines. In addition, the requirement of extracorporeal energy is reduced, including that from enteric and intravenous nutrition [2]. Therefore, excessive nutritional administration during the early postoperative period frequently induces adverse events (AEs), such as infections due to increased blood sugar, immunocompromised patients [3]. Guidelines from the American Society for Parenteral and Enteral Nutrition (ASPEN), published in 2009 [4], recommend initiation of enteral nutrition within 24–48 h of the start of intensive care with gradual increase in dose to reach the target dose over the next 48–72 h [4]. Under conditions of insufficient enteral nutrition by day 7 from the start of

* Corresponding author. Department of Surgery, Iwate Medical University, 19-1 Uchimaru, Morioka, Iwate 020-8505, Japan.
E-mail address: masafumi.konosu@nifty.com (M. Konosu).

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care, ASPEN also recommends initiation of intravenous feeding [4]. The guidelines from The European Society for Clinical Nutrition and Metabolism (ESPEN), published in 2009 [3], recommends initiation of intravenous feeding within 24–48 h in cases where normal nutrient intake is not achieved for at least 3 days because of intolerance or the presence of contraindications to enteral feeding [3]. Although the total recommended energy doses are similar in ASPEN and ESPEN, ASPEN recommends enteral feeding, whereas ESPEN recommends intravenous feeding, despite being predicated on enteral feeding.

In recent years, enteral feeding has primarily been used in the early postoperative period after esophagectomy [5,6]. Postoperative enteral feeding through jejunostomy or gastrostomy after esophagectomy with gastric tube reconstruction is known to reduce the incidence of postoperative complications, such as infection and malnutrition [6]. Although postoperative weight loss is unavoidable in the long term because of lack of oral feeding, an improvement in nutritional intake during the early postoperative period may minimize malnutrition in the first few months postoperatively. Nutritional intake that does not fully meet the requirement for carbohydrate-based energy due to intravenous feeding is acceptable during the early postoperative period [3,4]. However, there is no consensus regarding the doses of proteins and amino acids, which are essential for maintenance of skeletal muscle and for *in vivo* energy production.

In this study, we assessed the changes in nutritional indicators during transvenous administration of amino acids via conventional enteral feeding during perioperative and early postoperative periods in esophagectomy patients.

2. Materials and methods

2.1. Materials

Data from consecutive 110 esophageal cancer patients who received radical esophagectomy with two or three field lymphadenectomy from 2008 to 2012 were collected. Inclusion criteria were as follows: (1) histological diagnosis of esophageal cancer; (2) Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) of 0–2, and (3) provision of written consent. Exclusion criteria were preoperative factors which had need for increase or decrease of volume of infusion and enteral feeding as follows: (1) active infection prior to surgery, (2) 85 years or older, (3) congestive heart failure, (4) demonstrated abnormal electrolyte metabolism, (5) obstructive uropathy, (6) high degree of hepatorenal failure, (7) severe diabetes, (8) allergy to cow's milk protein, (9) active double cancer.

2.2. Surgical procedure

The surgical procedure consisted of subtotal esophagectomy, two or three-field lymph node dissection in the chest and abdomen or in the neck, chest, and abdomen, and gastric tube reconstruction via the posterior mediastinum route using right-sided thoracoscopic or right thoracotomy, laparotomy, and bilateral cervical approaches.

2.3. Nutritional control

1) Preoperative nutrition control

Food was withheld from all patients from 2 days prior to the operation, and fasting (no food or liquid) was initiated from 21 h prior to the operation. Two days prior to the operation, subjects were administered a 5% sugared acetic acid Ringer's solution (30–40 mL/kg/day). No immune-enhancing diets were given during the preoperative period.

2) Postoperative nutrition control

Patients were divided into two groups by postoperative peripheral venous infusion solutions; Subjects who were administered vitamin B1, sugar, electrolytes, and amino acid solutions were assigned to the amino acid group, whereas those with a 10% sugar maintenance solution were assigned to the control group (Compositions of infusion solutions are presented in Supplementary Table 1).

Enteral feeding was administered with a 5% glucose solution from the jejunostomy on postoperative day 1. After confirming the absence of issues with jejunostomy, subjects were administered a semidigestion nutrition agent at 5 kcal/kg on postoperative day 2, 10 kcal/kg on postoperative day 3, and 25 kcal/kg on postoperative days 4–7 (Supplementary Fig. 1).

In addition, peripheral venous nutrition was administered to a total energy intake of 15 kcal/kg on postoperative days 1–3 and 10 kcal/kg on postoperative days 4–7. Furthermore, amino acids were administered to patients of the amino acid group at 1.0 g/kg on postoperative days 1–3 and at 0.7 g/kg on postoperative days 4–7. All Subjects started ingestion after postoperative day 8 and peripheral venous nutrition was discontinued concomitantly.

Table 1
Patient characteristics.

		Intervention group (n = 17)	Control group (n = 16)	*p* value
Age[a]		62	64.5	0.40[b]
Gender	male	14	13	0.64[c]
	female	3	3	
Preoperative weight [kg][d]		60.6	58.8	0.67[e]
Body mass index[d]		21.9	22.2	0.82[e]
Location of the lesion	Ut	3	1	0.51[b]
	Mt	10	10	
	Lt	3	5	
	Ae	1	0	
Depth of tumor invasion	T1	5	7	0.33[b]
	T2	3	3	
	T3	8	6	
	T4	1	0	
Lymph node metastasis	N0	10	8	0.43[c]
	N1	7	8	
Distant organ metastasis	M0	17	16	–
	M1	0	0	
Stage	IA	4	5	0.98[b]
	IB	1	1	
	IIA	5	2	
	IIB	3	4	
	IIIA	6	4	
Preoperative therapy		8	9	0.85[c]
Operative technique	thoracotomy	4	4	0.75[c]
	thoracoscopic	13	12	
Operative time [min][d]		649	639.5	0.92[e]
Operative bleeding [ml][d]		199	176.5	0.44[e]
% ideal body weight[d] (range)		99.7 (79.8–115.9)	100.9 (70.4–139.8)	0.82[e]
malnutrition	normal	13	11	0.79[b]
	mild	3	3	
	moderate	1	2	
	severe	0	0	

Ut, upper thoracic esophagus; Mt, middle thoracic esophagus; Lt, lower thoracic esophagus; Ae, abdominal esophagus.
[a] Median.
[b] Mann–Whitney's test.
[c] Yates-corrected c-square.
[d] Mean.
[e] Student's *t*-tt.