ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

Effect of Swallowing Training on Swallowing Function and Quality of Life of Patients after Esophageal Cancer Surgery: A Randomized Controlled Clinical Trial

Xiaoqiong Wu[1,†,a], Shen Ling[1,†,b], Jian Zhang[1,2,c], Lin Wang[3,d], Jinkang Tu[1,e], Yuejun Lin[1,f], Yiming Wu[1,g], Tengfei Fu[1,h], Qing Yu[1,*,i], Jun Chen[1,*,j]

[1]Department of Rehabilitation Medicine, Zhongshan Hospital, Fudan University, Shanghai, 200000, China
[2]Orthopedics Department, Zhongshan Hospital, Fudan University, Shanghai, 200000, China
[3]Thoracic Surgery Department, Zhongshan Hospital, Fudan University, Shanghai, 200000, China
[a]wu.xiaoqiong@zs-hospital.sh.cn, [b]lingshen1112@163.com, [c]zhang.jian@zs-hospital.sh.cn, [d]wang.lin3@zs-hospital.sh.cn, [e]tu.jinkang@zs-hospital.sh.cn, [f]lin.yuejun@zs-hospital.sh.cn, [g]wu.yiming@zs-hospital.sh.cn, [h]fu.tengfei@zs-hospital.sh.cn, [i]yu.qing@zs-hospital.sh.cn, [j]chen.jun2@zs-hospital.sh.cn
[†]These authors contributed equally to this work and share first authorship.
[*]Corresponding author

Abstract: *To investigate the impact of swallowing training on swallowing function and quality of life in postoperative patients with esophageal cancer. We recruited 79 patients scheduled for esophageal surgery and randomly assigned them to one of three groups: Group A (conventional nursing measures), Group B (conventional nursing measures and respiratory exercises), and Group C (conventional nursing measures, respiratory exercises, and swallowing training). The EAT-10 scale and quality of life questionnaire were administered to all three groups 1 day before, 10 days after, and 30 days after surgery. The swallowing function of all three groups was evaluated 1 day before and 10 days after surgery using the standardized swallowing assessment, and the incidence of postoperative problems was calculated. The intragroup assessment showed that all groups had significantly higher the standardized swallowing assessment, EAT-10, dysphagia and eating difficulties scores ($p<0.05$), and significantly lower physical and role function scores 10 days after surgery ($p<0.05$). The intergroup assessment revealed that Group C had significantly lower EAT-10, dysphagia and eating difficulties scores ($p<0.05$), and significantly higher emotional functioning score than the other two groups ($p<0.05$). Additionally, the incidence of complications was decreased in Group B and C compared to Group A. Patients with esophageal cancer will struggle with swallowing and have a decline in quality of life after surgery. Swallowing training during the preoperative period may accelerate the recovery of swallowing function and quality of life in patients.*

Keywords: *Esophageal cancer surgery; Quality of life; Swallowing training; Respiratory exercise; Enhanced recovery after surgery (ERAS)*

1. Introduction

Esophageal cancer (EC) is one of the most prevalent malignant tumors in the world, ranking eighth in incidence and sixth in mortality [1]. According to data presented in 2020, China has a high incidence of EC, accounting for 53.70 % new cases and 55.35 % deaths of the global total [2], [3]. Currently, the primary treatment for esophageal cancer consists of surgical intervention with chemotherapy/radiotherapy [4]. However, the influences of surgery are prone to induce complications, including reflux esophagitis, pulmonary infection, chylothorax and difficulty in swallowing [5]. Injuries to the recurrent laryngeal nerve during surgical procedures are a common cause of difficulty in swallowing [6], which could increase the risk of pneumonia, malnutrition, and possibly mortality following esophagectomy [7], [8].

With the advancement of endoscopic technology in recent years, the widespread application of thoracoscopic surgery is progressively minimizing patient damage from esophagectomy [9], [10]. The

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

adoption of the enhanced recovery after surgery (ERAS) concept has also contributed greatly to the control of postoperative complications, hence decreasing the recovery period and enhancing patients' quality of life [11]. The efficacy and safety of ERAS has been supported by numerous randomized controlled trials, particularly in patients with gastric [12], [13], colorectal [14], and gynecologic cancers [15]. The availability of standardized recommendations on ERAS following esophagectomy did not occur until 2018, hence the evidence on the use of ERAS after EC surgery is still inadequate [16].

The most important aspect of ERAS for EC is to solve two problems: firstly, to allow patients to walk early and recover coughing ability, to reduce the incidence of pulmonary complications, and to avoid prolonging the time to return to daily life after surgery; secondly, to resume oral feeding early, to shorten the use time of routinely applied nasogastric tube and gastrointestinal tube, and to avoid the risk of swallowing disuse symptoms. Respiratory and swallowing rehabilitation have the potential to become essential ERAS components and effective treatments to the challenges. The majority of current research focuses on perioperative rehabilitative management of respiratory function following EC surgery [17]–[19]. These findings demonstrated that postoperative patients might benefit from respiratory training by reducing their risk of developing lung infections and atelectasis, decreasing their intubation length, and shortening their hospital stay. Although swallowing rehabilitation has received less attention following esophageal cancer surgery, its usefulness for post-stroke dysphagia has been confirmed [20]. Takatsu et al. reported that swallowing interventions were advantageous for postoperative patients with EC in terms of early beginning of transoral feeding and shorter hospitalization [21]. Additionally, the increased risk of postoperative pneumonia in EC (6.5-27.8%) [22] is partially attributable to poor swallowing function leading to aspiration (0-81%) [23] and pharyngeal residues (22-62.5%) [24]. Therefore, swallowing rehabilitation are anticipated to play an important role in the ERAS program following esophagectomy [25]. It is necessary to perform additional research on the clinical benefits of swallowing interventions.

Thus, we hypothesized that swallowing intervention combined with respiratory training in postoperative patients with EC is more beneficial than respiratory training individually. The aim of our study was to investigate the effects on swallowing performance, perception, and quality of life in postoperative patients with EC of combining training relevant to swallowing and respiratory function.

2. Method

2.1 Trial design

This clinical study is designed to be prospective and randomized. The research was performed at Zhongshan Hospital, Fudan University. The research protocol was approved by the Ethics Committee of Zhongshan Hospital of Fudan University (institutional review board approval no: B2021-410, chairperson: Xin-Yu QIN, date:2021-06-15). According to the Declaration of Helsinki, the research was conducted. Prior to their participation in the study, all patients offered their informed consent.

2.2 Subjects

From March 2021 to March 2022, 90 patients were recruited and treated at Department of Thoracic Surgery in Zhongshan Hospital. The eligibility criteria are as follows: (1) In line with diagnostic criteria for esophageal cancer [26], categorized as squamous cell carcinoma, and experienced combined thoracoscopic and laparoscopic radical esophagectomy for first time; (2) 25-80 years old. The exclusion criteria: (1) Serious postoperative complications (anastomotic fistula, chyle leakage, severe pneumothorax, etc.); (2) history of severe respiratory disease; (3) previous surgical impaired swallowing function; (4) important blood vessels or organs were infiltrated by the tumor, or it spread to distant sites, rendering radical surgery unfeasible; (5) incision infection.

The participants were randomized into one of three intervention groups (ratio 1:1:1) using random numerical table method: Group A (n=30), Group B (n=30), and Group C (n=30) (Figure 1).

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

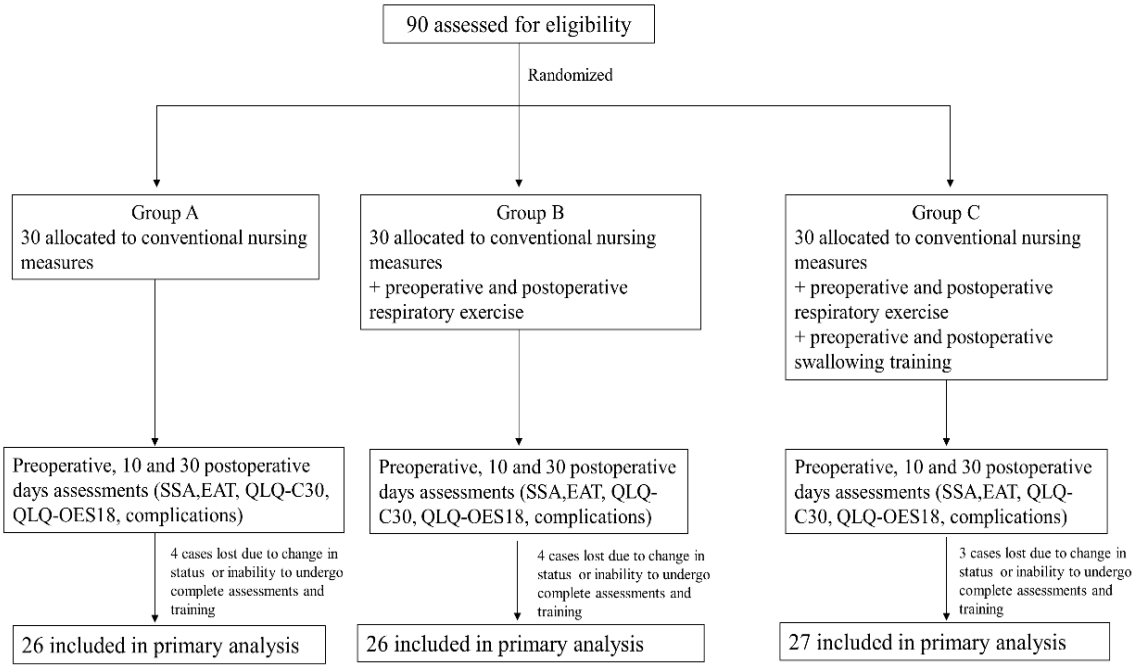


Figure 1: Diagram of enrollment and follow-up.

2.3 Sample size calculation

Using G*Power version 3.1.9.7, a sample size of 69 participants was determined for repeated measures analysis of variance. A power of 80%, a 95% confidence interval and a medium effect size of 0.25 (based on SSA) were considered (number of groups was 3 and number of measurements was 3). Considering of possible dropouts, the minimum sample was estimated as 90 individuals. The final 79 participants who finished the trial successfully underwent analysis.

2.4 Interventions

Group A: The patients received conventional postoperative treatment, which included pain management, early postoperative bedside extremity activities and postural shifts, and psychological support. Specific early limb exercises comprised (1) ankle pumping, (2) alternating knee flexion and extension of both legs, and (3) double upper limb supination. Specific postural transfer included: (1) bedside sitting on the first postoperative day; (2) gradual transition to bedside sitting, bedside standing, and in-room walking once cardiac monitoring discontinued.

Group B: Based on the intervention in group A, the patients received 1 day of preoperative and 10 days of postoperative respiratory training. Preoperative training included: (1) abdominal breathing: instructed the patient to place one hand on the upper belly, the other hand on the chest, and half flexion of both knees in order to relax the abdominal muscles. The ratio of inhalation to expiration was 1:2 and breathing frequency was 8-9 times per minute. Training was maintained for 10 minutes a day; (2) balloon blowing: frequency was 3-4 times per minute, and daily exercise was maintained for 5 minutes; and (3) aerobic exercise was stair climbing until mild shortness of breath, with a Borg score of 3. Postoperative treatment comprised of: (1) respiratory pattern correction and respiratory rhythm modification; (2) exhalation training: instructed the patients to inhale the maximum amount of air through the nose, hold the breath for 2 seconds, and mobilized the abdominal muscles to complete 3 exhalations quickly and briefly; (3) thoracic mobility training: raised the hands to the maximum degree during inhalation and slowly lowered them during exhalation; (4) respiratory muscle strength training: clasped hands together and stretched them to the maximum angle, executed chest breathing training, with breathing frequency 8-9 times per minute; (5) coughing technique instruction: instructed the patient to take a seated position, inhaled deeply through the nose, held their breath for 3 seconds, then bent their body forward and tensed their abdominal muscles to perform a successful cough.

Group C: The patients underwent 1 day of preoperative and 10 days of postoperative swallowing function training in addition to treatments in group B. Preoperative training included: (1) active tongue

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

and lip movements: cheek puffing, tongue extension to lick both corners of the mouth, gum sweeping, and tongue rolling training; (2) 30 repetitions of Shaker exercise [27]. On the basis of preoperative training, postoperative training consisted of: (1) deep sensation training: the therapist placed the vibrator's head on the regions of the mouth that require stimulation, such as the cheeks, lips, tongue, and posterior pharyngeal wall; (2) pharyngeal muscle ice stimulation: the therapist applied an ice swab on the soft palate and center of the tongue for vertical temperature tactile stimulation, lateral stimulation at the posterior root of the tongue, and stimulation on the sides of the tongue; (3) mastication training: chewed the chewing stick for 50 repetitions on each side; (4) sub-chin muscle exercise: inserted a tiny ball between the chin and collarbone, compressed the ball slightly downward, held for 5 seconds, and then released, 15 repetitions; (5) vocal cord training: yawn, mild hum training, vowel pronunciation in turn, 2 minutes of training time; (6) supraglottic swallowing: instructed the patients to inhale and hold the breath, force the breath downward, and held the breath while swallowing; (7) 5 repetitions of Masako swallowing [28]; (8) swallowing and breathing coordination training: employed physiological breathing control to coordinate the respiratory pause when swallowing, completed the sequential process of inhalation, breath holding, swallowing, and coughing 5 times. The above interventions are based on a synthesis of the findings of previous research [7].

2.5 Outcome measures

In the three groups, the proportion of surgical complications (pulmonary infection, pulmonary atelectasis, and pneumothorax) was calculated. Objective swallowing performance was evaluated before and 10 days after treatment. The efficacy of subjective impression and quality of life were evaluated in the three groups of patients before treatment, 10 days after treatment, and 30 days after treatment, respectively.

Objective assessment of swallowing: the standardized swallowing assessment (SSA) [29] was utilized to evaluate swallowing function in three groups of patients, which comprised of three components: (1) clinical examination; (2) swallowing 5 milliliters of water 3 times; (3) swallowing 60 milliliters of water if the preceding steps are normal. The range of available scale scores was between 18 and 46. The worse swallowing function, the higher the score.

Subjective assessment of swallowing: the subjective swallowing perception of the three patient groups were evaluated using the eating assessment tool (EAT-10) [30]. The questionnaire consisted of 10 items, each of which received a score of 4 out of 40, with a score of 3 or above indicating likely swallowing difficulties.

Quality of life: The Chinese version of the European Organization for Research and Treatment of Cancer (EORTC) Core Quality Of Life Questionnaire [31], [32], the QLQ-C30 (version 3.0), including its esophageal cancer-specific questionnaire (EORTC QLQ-OES18) [33], [34], was applied to evaluate. The QLQ-C30 contained 5 multi-item function scales, 3 multi-item symptom scales, 6 single-item symptom scales, and a two-item global quality of life measure. Higher functional scores suggested a higher quality of life. The QLQ-OES18 scale consisted of 4 symptom domains and 6 single symptom entries that describe esophageal cancer-specific symptoms. Due to the overlap between the symptom sections of the two scales, only the functional section of the QLQ-C30 was chosen for final analysis. All scores were transformed linearly to a 0 to 100 scale.

2.6 Data analysis

Using analysis of variance (ANOVA) for continuous data and the chi-square test of independence for categorical data, the randomization adequacy was determined by comparing baseline demographic data between groups. The measurement variables adopting a mixed-model repeated-measures ANOVA, with treatment group (Group A, B, and C) as the between-subject component and time (before, 10 days after, and 30 days after surgery) as the within-subject factor. The assumptions for using repeated-measures ANOVA were verified, including normality, homogeneity of variance, and sphericity. Bonferroni correction was utilized for post hoc comparisons.

Effect sizes (ES) for post hoc test were estimated by calculating the Hedge's g. According to Cohen, ES of 0.2, 0.5, and 0.8 were categorized as small, moderate, and large, respectively [35], [36]. Eta squared (η_g^2) was the ES for ANOVA. The interpretation of these squared ES results in the following: 0.01 = small effect, 0.06 = moderate effect, and 0.14 = large effect [37]. Data analyses were performed in the RStudio (R version 4.1.2). $p < 0.05$ was selected as the cutoff for statistical significance in all tests.

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

3. Results

3.1 Demographic and clinical characteristics

Table 1 was the demographic and clinical characteristics of the 79 participants in the final analysis. There was no statistically significant difference among the three groups (p>0.05).

Table 1: Demographic and clinical characteristics.

Variables	Group A (n=26)	Group B (n=26)	Group C (n=27)	F/χ^2	p value
Age (mean±sd)	62.73±6.89	63.54±8.34	65.63±6.05	1.167	0.317[a]
Gender, No.(%)				0.126	0.939[b]
Male	21(80.8%)	20(76.9%)	21(77.8%)		
Female	5(19.2%)	6(23.1%)	6(22.2%)		
Tumor site, No.(%)					0.796[c]
Upper	2(7.7%)	1(3.8%)	1(3.7%)		
Middle	10(38.5%)	8(30.8%)	7(25.9%)		
Lower	14(53.8%)	17(65.4%)	19(70.4%)		
Preoperative chemotherapy, No.(%)				0.575	0.750[b]
Yes	4(15.4%)	6(23.1%)	6(22.2%)		
No	22(84.6%)	20(76.9%)	21(77.8%)		
Preoperative dysphagia, No.(%)				0.589	0.745[b]
Yes	21(80.8%)	20(76.9%)	23(85.2%)		
No	5(19.2%)	6(23.1%)	4(14.8%)		
Recurrent laryngeal nerve lymph node dissection, No.(%)					0.954[c]
Not exist	3(11.5%)	2(7.7%)	4(14.8%)		
Unilateral	8(30.8%)	9(34.6%)	9(33.3%)		
Bilateral	15(57.7%)	15(57.7%)	14(51.9%)		

a: One-way Anova. b: Chi-square test. c: Fisher exact test.

3.2 Assessment of dysphagia comparison

The group-by-time interaction for the mixed-model repeated measure ANOVA was statistically significant between the three groups in SSA and EAT (Table S1). After 10 days, the intragroup evaluation revealed that the SSA score was improved significantly in all groups (p<0.05). In addition, the EAT score was significantly higher in all groups after 10 days (p<0.05). Compared to baseline, the EAT score was significantly higher in group A (p=0.002) and significantly lower in the group C (p=0.014) after 30 days (Table 2).

Table 2: Comparison of SSA and EAT within group.

Assessment	Baseline mean±sd	10-day mean±sd	Hedges' g	p^a	30-day mean±sd	Hedges' g	p^b	η_g^2	p^c
SSA								0.64	2.66×10^{-35}
Group A	18.15±0.46	26.69±3.13	3.75	4.75×10^{-13}	-	-	-		
Group B	18.15±0.54	24.77±3.79	2.41	3.64×10^{-9}	-	-	-		
Group C	18.11±0.32	20.41±2.33	1.36	2.06×10^{-5}	-	-	-		
EAT								0.68	2.39×10^{-57}
Group A	7.11±4.11	24.77±4.32	4.12	2.21×10^{-14}	13.42±7.65	1.01	2.0×10^{-3}		
Group B	6.62±4.53	23.35±4.13	3.80	4.89×10^{-15}	6.04±2.76	0.15	1		
Group C	6.48±4.58	13.63±2.95	1.83	1.95×10^{-6}	3.00±2.94	0.89	1.4×10^{-2}		

p^a indicated a statistically significant difference from baseline to after 10 days (paired sample t-test). p^b indicated a statistically significant difference from baseline to after 30 days (paired sample t-test). p^c indicated a statistical significance from the baseline, to after 10 days and to after 30 days (repeated measures ANOVA).

After 10 days, the intergroup assessments inferred that SSA and EAT score was significantly lower in the group C (p<0.0001) than group A and B. After 30 days, significant differences existed between all groups in EAT score (p<0.001) (Figure 2).

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

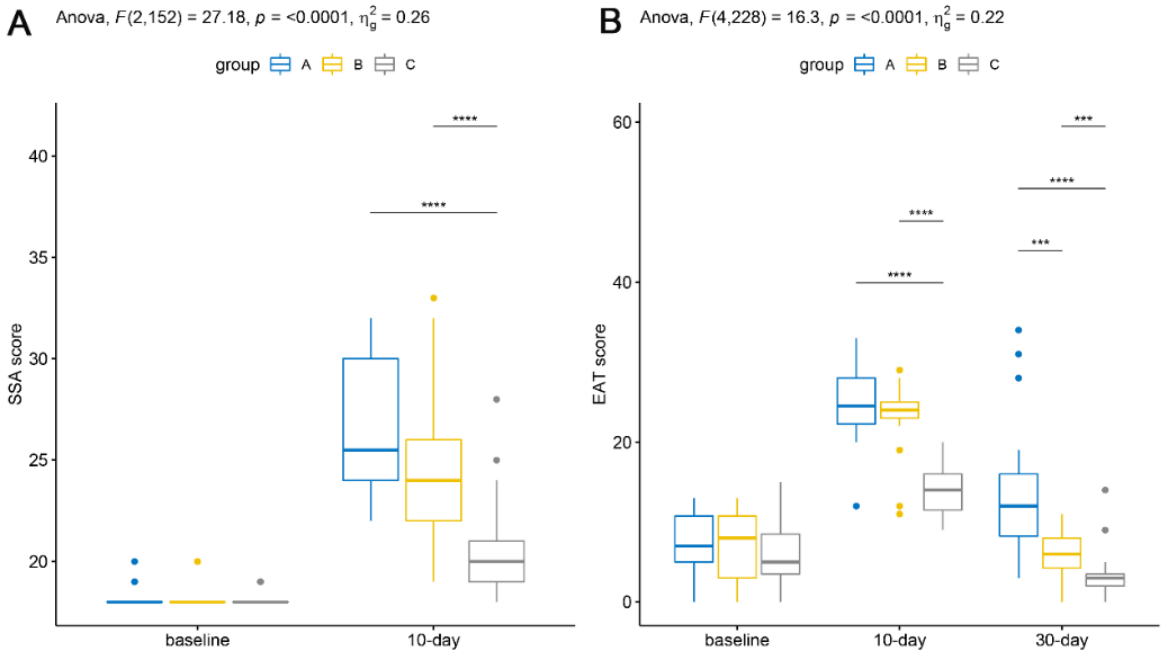


*Figure 2: Comparison of SSA and EAT between group. The p value and effect size of the group-by-time interaction were displayed above the graph. *** represents p<0.001, **** represents p<0.0001.*

3.3 Quality of life comparison

Table 3: Comparison of QLQ-C30 within group.

Assessment	Baseline mean±sd	10-day mean±sd	Hedges' g	p^a	30-day mean±sd	Hedges' g	p^b	η_g^2	p^c
Physical functioning								0.63	1.48×10^{-50}
Group A	96.67±4.32	49.62±14.50	4.33	1.51×10^{-14}	79.49±20.99	1.12	2.00×10^{-3}		
Group B	98.46±4.74	61.03±17.96	2.81	7.56×10^{-10}	94.10±5.44	0.84	3.00×10^{-2}		
Group C	97.78±4.13	72.59±16.26	2.09	1.09×10^{-8}	97.47±5.01	0.07	1		
Role functioning								0.67	2.58×10^{-55}
Group A	96.15±9.78	20.51±21.24	4.50	9.33×10^{-15}	58.97±27.58	1.77	1.02×10^{-6}		
Group B	98.07±7.19	32.05±27.05	3.28	2.19×10^{-11}	82.69±13.73	1.38	1.02×10^{-4}		
Group C	95.68±9.91	54.94±21.59	2.39	4.38×10^{-9}	87.04±11.63	0.79	2.40×10^{-2}		
Emotional functioning								0.31	2.45×10^{-19}
Group A	88.46±8.52	68.27±14.72	1.65	3.87×10^{-5}	83.01±12.80	0.49	0.33		
Group B	87.18±9.78	71.15±13.17	1.36	1.21×10^{-5}	92.63±8.61	0.58	0.07		
Group C	86.48±9.33	82.78±15.70	0.28	0.65	99.07±3.53	1.76	1.67×10^{-6}		
Cognitive functioning								0.21	1.30×10^{-12}
Group A	98.72±6.54	85.90±15.42	1.07	3.00×10^{-3}	96.80±6.70	0.29	0.98		
Group B	99.36±3.27	85.86±13.08	1.39	1.61×10^{-4}	98.08±5.43	0.28	0.98		
Group C	97.53±6.03	93.83±12.36	0.38	0.33	99.38±3.21	0.38	0.55		
Social functioning								0.43	3.24×10^{-28}
Group A	66.03±19.14	31.41±13.60	2.05	1.07×10^{-6}	63.46±21.09	0.13	1		
Group B	71.15±19.75	42.31±18.99	1.47	5.04×10^{-5}	81.41±17.84	0.54	0.05		
Group C	74.07±18.10	56.79±14.81	1.03	4.00×10^{-3}	88.27±11.15	0.93	9.00×10^{-3}		

p^a indicated a statistically significant difference from baseline to after 10 days (paired sample t-test). p^b indicated a statistically significant difference from baseline to after 30 days (paired sample t-test). p^c indicated a statistical significance from the baseline, to after 10 days and to after 30 days (repeated measures ANOVA).

The group-by-time interaction was also statistically significant in QLQ-C30 and QLQ-OES18 (Table S2 and Table S3). After 10 days, the intragroup comparisons in QLQ-C30 showed that, with the exception of emotional and cognitive functioning in group C, all five functioning scores were significantly lower in all groups ($p<0.05$). After 30 days, physical and role functioning score differed significantly in group

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

A (p=0.002, p=1.02×10-6) and B (p=0.03, p=1.02×10-4), whereas social (p=0.009), emotional (p=1.67×10-6), and role functioning scores (p=0.024) differed significantly in group C (Table 3).

There were no cognitive function differences in QLQ-C30 between the groups, hence it was not displayed. Refer to Figure 3 for particular differences between groups.

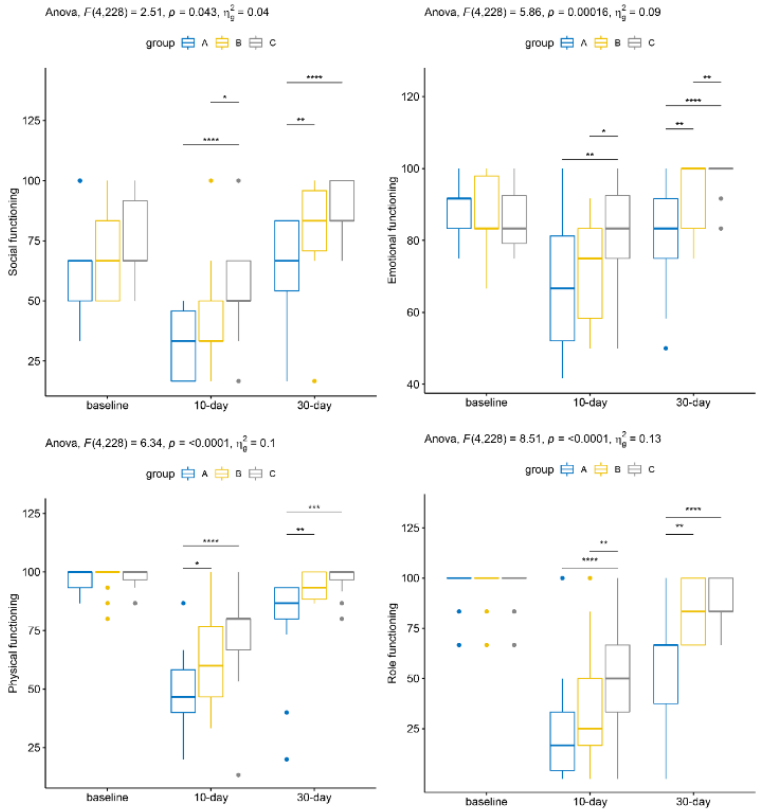
Table 4: Comparison of QLQ-OES18 within group.

Assessment	Baseline mean±sd	10-day mean±sd	Hedges' g	p^a	30-day mean±sd	Hedges' g	p^b	η_g^2	p^c
Dysphagia								0.67	1.76×10^{-54}
Group A	20.94±13.45	74.36±12.87	4.00	9.12×10^{-15}	35.47±24.35	0.73	0.05		
Group B	15.81±12.24	72.65±15.47	4.01	2.46×10^{-13}	17.95±17.80	0.14	1		
Group C	19.34±11.36	41.56±13.98	1.72	6.54×10^{-7}	5.76±7.78	1.37	6.51×10^{-6}		
Eating difficulties								0.57	1.57×10^{-42}
Group A	14.74±12.09	49.36±11.53	2.89	6.18×10^{-10}	32.69±16.65	1.21	2.53×10^{-4}		
Group B	11.22±7.80	52.89±9.41	4.75	2.31×10^{-15}	22.12±13.32	0.98	4.00×10^{-3}		
Group C	14.51±9.97	29.32±12.74	1.28	1.00×10^{-4}	6.17±7.16	0.95	3.00×10^{-4}		
Reflux								0.03	0.02
Group A	3.21±8.19	1.92±5.43	0.18	1	2.56±7.74	0.08	1		
Group B	2.56±7.74	0.00±0.00	0.46	0.31	4.49±7.54	0.25	1		
Group C	4.32±8.76	0.00±0.00	0.69	0.03	0.00±0.00	0.69	0.03		
Esophageal pain								0.08	8.07×10^{-5}
Group A	8.97±12.97	14.53±14.32	0.40	0.47	7.27±6.24	0.17	1		
Group B	6.41±10.50	14.10±11.14	0.70	0.08	1.28±3.62	0.64	0.11		
Group C	11.11±13.43	13.58±13.55	0.58	0.18	2.06±4.40	0.67	0.07		
Trouble swallowing saliva								0.06	8.72×10^{-4}
Group A	0.00±0.00	7.69±17.15	0.62	0.09	5.13±12.26	0.58	0.13		
Group B	0.00±0.00	8.97±17.78	0.69	0.05	1.28±6.54	0.27	0.98		
Group C	0.00±0.00	2.47±8.90	-	-	0.00±0.00	-	-		
Choking								0.06	9.79×10^{-4}
Group A	5.13±15.47	21.79±24.84	0.79	0.04	6.41±21.12	0.07	0.81		
Group B	7.69±14.32	12.82±21.24	0.28	0.77	1.28±6.54	0.57	0.17		
Group C	4.94±12.07	14.81±21.35	0.56	0.05	1.23±6.42	0.85	0.02		
Dry mouth								0.33	2.54×10^{-20}
Group A	21.79±20.96	56.41±29.47	1.33	4.32×10^{-4}	28.20±27.80	0.26	1		
Group B	14.10±19.26	64.10±28.16	2.04	1.49×10^{-6}	6.41±13.40	0.46	0.25		
Group C	18.52±21.35	27.16±22.71	0.39	0.39	3.70±10.67	0.46	0.33		
Tasting problems								0.01	0.25
Group A	0.00±0.00	1.28±6.54	0.01	1	2.56±9.06	0.16	1		
Group B	0.00±0.00	2.56±9.06	0.39	0.48	2.56±9.06	0.39	0.48		
Group C	0.00±0.00	0.00±0.00	-	-	1.23±6.41	0.27	0.65		
Coughing								0.34	1.29×10^{-21}
Group A	2.56±9.06	30.77±24.81	1.49	7.14×10^{-5}	15.38±23.53	0.55	0.21		
Group B	1.28±6.54	15.38±19.39	2.07	6.42×10^{-7}	1.28±6.54	0.27	0.98		
Group C	3.70±10.68	14.81±23.27	0.60	0.11	1.23±6.41	0.28	0.98		
Speech difficulties								0.10	1.14×10^{-5}
Group A	0.00±0.00	11.54±18.72	0.86	1.30×10^{-2}	10.26±15.69	0.49	0.25		
Group B	0.00±0.00	7.69±14.32	0.75	0.02	3.85±10.86	-	-		
Group C	0.00±0.00	1.23±6.41	0.27	0.98	1.23±6.41	0.27	0.98		

p^a indicated a statistically significant difference from baseline to after 10 days (paired sample t-test). p^b indicated a statistically significant difference from baseline to after 30 days (paired sample t-test). p^c indicated a statistical significance from the baseline, to after 10 days and to after 30 days (repeated measures ANOVA).

Intragroup comparisons in QLQ-OSE18 demonstrated that there was no difference in reflux, esophageal pain, trouble swallowing saliva, and tasting problems. After 10 days, dry mouth and coughing score was no significant change in group C. After 30 days, dysphagia (p=6.51×10-6) and eating difficulties (p=3.00×10-4) score was significantly lower in group C (Table 4).

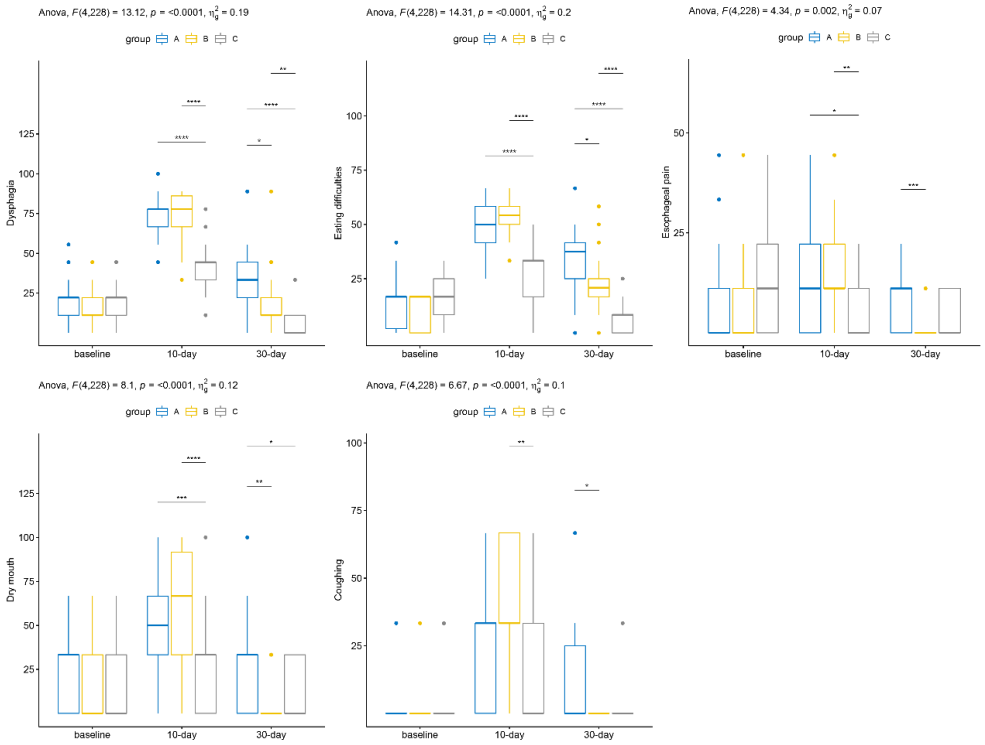
ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610



** represents p<0.05, ** represents p<0.01, *** represents p<0.001, **** represents p<0.0001.*

Figure 3: Comparison of QLQ-C30 within group. The p value and effect size of the group-by-time interaction were displayed above the graph.

In QLQ-OSE18, there were no differences in reflux, trouble swallowing saliva, choking, tasting problems, and speech difficulties between the groups, so they were not shown. See Figure 4 for details.



** represents p<0.05, ** represents p<0.01, *** represents p<0.001, **** represents p<0.0001.*

Figure 4: Comparison of QLQ-OES18 within group. The p value and effect size of the group-by-time

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

interaction were displayed above the graph.

3.4 Proportion of complications

Patients in group B and C were less probable than group A to suffer complications (Table 5).

Table 5: Proportion of complications after surgery.

Complications	Group A(n=26)	Group B(n=26)	Group C(n=27)
pneumothorax	11(42.3%)	3(11.5%)	3(11.1%)
pulmonary infection	13(50.0%)	3(11.5%)	3(11.1%)
pulmonary atelectasis	20(76.9%)	9(34.6%)	8(29.6%)

4. Discussion

ERAS is a multidisciplinary rehabilitation program that covers preoperative, intraoperative, and postoperative periods to expedite patient recovery. It is widely utilized in the treatment of a variety of malignancies, including EC. The recovery of swallowing function is strongly associated with nutritional assessment and intervention, feeding, and prevention of pulmonary complications. Our study demonstrated that combined swallowing and respiratory training was more effective than respiratory training alone in enhancing the swallowing function and quality of life. This impact was still significant 30 days after surgery.

All participants' SSA and EAT score were significantly lower 10 days after surgery compared to preoperatively, indicating that the surgical procedure had a larger detrimental effect on swallowing function (Table 2). Common sites of esophageal cancer metastases are the paraglottic lymph nodes of the recurrent laryngeal nerve [38]. Identification of the recurrent laryngeal nerve and lymph node clearing along the distribution of the recurrent laryngeal nerve by thoracoscopic are challenging and can result in nerve injury easily. This results in overt and silent aspiration and pharyngeal residue in individuals [7]. 10 days later, the EAT and SSA scores of the combined intervention group were significantly lower than those of the other two groups, but significantly higher than their baseline. As indicated by expert standards [39], patients at this stage continue to be fed mainly through tube feeding for nutrition support benefits.

At 30 days postoperatively, the EAT scores in the non-rehabilitation group were remained significantly higher than at baseline, whereas the scores in the combined training group were significantly lower than at baseline (Table 2). Moreover, the combined intervention group's EAT scores were significantly lower than those of the other two groups at the same period (Figure 2). The findings clearly highlight the role of swallowing rehabilitation, which obtained satisfactory outcomes one month after the treatments. Training in swallowing decreased postoperative swallowing dysfunction and alleviated swallowing discomfort caused by tumor progression. The research conducted by Takatsu [21] also demonstrated that early swallowing interventions expedite the commencement of transoral feeding and shorten hospital stays. The difficulty of patients without training to regain swallowing function after surgery may be due to nerve injury or scarring of the anastomosis, which inhibited the contraction of pharyngeal muscles and the opening of the upper esophageal sphincter [40]–[42].

In our study, the functional scale scores in QLQ-C30 declined 10 days after surgery and recovered 30 days after surgery. In QLQ-OSE18 scale, opposing changes occurred in dysphagia, eating difficulties, dry mouth, and coughing. These modifications suggest a temporary decrease in postoperative quality of life. Similar to the findings of earlier studies, the quality of life worsened in almost all aspects within six weeks postoperatively [43], [44]. In this study, however, the time to recovery of quality of life was shorter in the combined treatment group than in earlier research. Particularly, emotional and cognitive functioning reached baseline levels 10 days after surgery in the combined treatment group, whereas the other two groups reached normal levels 30 days after surgery. We speculated that swallowing training expedited the enhancement of cognitive and emotional functioning. At 30 days after surgery, it is noteworthy that none of the groups' role functioning scores had returned to their preoperative levels. The role conflict after surgery, the psychological anxiety connected with physical healing, and the pressure of returning to work have a negative effect on the patients' mental health [45]. Therefore, psychological intervention may be necessary in addition to swallowing training [46].

Dysphagia and eating difficulties were the two most significant symptoms the participants had after surgery. EC surgery resulted in a number of structural alterations, including reduced blood supply to the gastrointestinal system, decreased esophageal peristalsis, and shortened food retention time in the

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

gastrointestinal tract [47]. 30 days after surgery, patients who did not received swallowing training have not completely recovered from their eating difficulties. Nasal tube feeding merely satisfied the need for food intake and does not relieve the symptoms of dysphagia and eating difficulties. Swallowing rehabilitation is indispensable for the treatment of postoperative swallowing-related symptoms.

Pulmonary complications are the leading cause of death following surgery. Pneumonia has been demonstrated to be a risk factor for hospitalization and long-term survival [48]. In our research, there was no difference in the occurrence of complications between the combined swallowing training and respiratory training groups. Although swallowing training had no effect on reducing postoperative respiratory complications, swallowing saliva during training did not increase the incidence of complications, proving the protocol's safety.

The strengths of this study consist of its longitudinal design, well-established scale evaluation, and particular swallowing training procedures. There are also several challenges in our study: (1) This study consisted of a modest sample size and a single-center design. Multicenter trials with larger samples will be required in the foreseeable future. Stratification according to clinical characteristics, such as smoking and nerve injury, is also advantageous. (2) Future research should employ more objective measures of swallowing function, such as electronic laryngoscopy and videofluoroscopic study of swallowing. (3) In the future, additional complications, such as anastomotic leakage and malnutrition, should be added to the statistics of postoperative complications.

5. Conclusion

After surgery, patients with EC will experience swallowing difficulties and a decline in quality of life, and swallowing training could expedite their recovery. Swallowing training has the potential to become an integral aspect of ERAS.

Data availability

The Department of Rehabilitation Medicine, Zhongshan Hospital, Fudan University, offers patient data checking. Documentation paper associated with patient data are not publicly available. The corresponding author can be contacted if raw materials or patient data are required. After receiving approval, the file could be supplied in electronic form.

Author contributions

All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization, Qing YU and Jun CHEN; Methodology, Jun CHEN; Investigation, Lin WANG and Xiao-Qiong WU; Formal Analysis, Shen LING and Jian ZHANG; Resources, Lin WANG and Teng-Fei FU; Writing - Original Draft, Xiao-Qiong WU and Shen LING; Visualization, Yi-Ming WU and Shen LING.

Acknowledgement

We would like to express our sincere gratitude to Dr. Chen-Guang WANG, for his expert advice and friendly support with language improvements.

References

[1] D. J. Uhlenhopp, E. O. Then, T. Sunkara, and V. Gaduputi, "Epidemiology of esophageal cancer: update in global trends, etiology and risk factors," Clin. J. Gastroenterol., vol. 13, no. 6, pp. 1010–1021, Dec. 2020, doi: 10.1007/s12328-020-01237-x.
[2] Cao Wei, Chen Hongda, Yu Yiwen, Li Ni, Chen Wanqing, and Ni Jing, "Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020," Chin. Med. J. (Engl.), vol. 134, no. 07, pp. 783–791, Apr. 2021, doi: 10.1097/CM9.0000000000001474.
[3] H. Sung et al., "Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries," CA. Cancer J. Clin., vol. 71, no. 3, pp. 209–249, May 2021, doi: 10.3322/caac.21660.
[4] C. T. Demarest and A. C. Chang, "The Landmark Series: Multimodal Therapy for Esophageal Cancer," Ann. Surg. Oncol., vol. 28, no. 6, pp. 3375–3382, Jun. 2021, doi: 10.1245/s10434-020-09565-5.

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

[5] Q.-L. Xu, H. Li, Y.-J. Zhu, and G. Xu, "The treatments and postoperative complications of esophageal cancer: a review," J. Cardiothorac. Surg., vol. 15, no. 1, p. 163, Jul. 2020, doi: 10.1186/s13019-020-01202-2.

[6] M. G. Scholtemeijer, M. F. J. Seesing, H. J. F. Brenkman, L. M. Janssen, R. van Hillegersberg, and J. P. Ruurda, "Recurrent laryngeal nerve injury after esophagectomy for esophageal cancer: incidence, management, and impact on short- and long-term outcomes," J. Thorac. Dis., vol. 9, no. S8, pp. S868–S878, Jul. 2017, doi: 10.21037/jtd. 2017.06.92.

[7] A. Kaneoka et al., "Presentation of oropharyngeal dysphagia and rehabilitative intervention following esophagectomy: a systematic review," Dis. Esophagus, vol. 31, no. 8, Aug. 2018, doi: 10. 1093/ dote/ doy050.

[8] R. Momosaki, "Rehabilitative management for aspiration pneumonia in elderly patients," J. Gen. Fam. Med., vol. 18, no. 1, pp. 12–15, Mar. 2017, doi: 10.1002/jgf2.25.

[9] H. Kikuchi and H. Takeuchi, "Future Perspectives of Surgery for Esophageal Cancer," Ann Thorac Cardiovasc Surg, p. 4, 2018.

[10] M.-L. Qiu, J.-B. Lin, X. Li, R.-G. Luo, B. Liu, and J.-W. Lin, "Current state of esophageal cancer surgery in China: a national database analysis," BMC Cancer, vol. 19, no. 1, p. 1064, Nov. 2019, doi: 10.1186/s12885-019-6191-2.

[11] T. D. Martin et al., "Newly implemented enhanced recovery pathway positively impacts hospital length of stay," Surg. Endosc., vol. 30, no. 9, pp. 4019–4028, Sep. 2016, doi: 10.1007/s00464-015-4714-8.

[12] S. H. Kang et al., "Multimodal Enhanced Recovery After Surgery (ERAS) Program is the Optimal Perioperative Care in Patients Undergoing Totally Laparoscopic Distal Gastrectomy for Gastric Cancer: A Prospective, Randomized, Clinical Trial," Ann. Surg. Oncol., vol. 25, no. 11, pp. 3231–3238, Oct. 2018, doi: 10.1245/s10434-018-6625-0.

[13] Y. Lee, J. Yu, A. G. Doumouras, J. Li, and D. Hong, "Enhanced recovery after surgery (ERAS) versus standard recovery for elective gastric cancer surgery: A meta-analysis of randomized controlled trials," Surg. Oncol., vol. 32, pp. 75–87, Mar. 2020, doi: 10.1016/j.suronc.2019.11.004.

[14] X. Ni, D. Jia, Y. Chen, L. Wang, and J. Suo, "Is the Enhanced Recovery After Surgery (ERAS) Program Effective and Safe in Laparoscopic Colorectal Cancer Surgery? A Meta-Analysis of Randomized Controlled Trials," J. Gastrointest. Surg., vol. 23, no. 7, pp. 1502–1512, Jul. 2019, doi: 10. 1007/ s11605-019-04170-8.

[15] S. P. Bisch et al., "Outcomes of enhanced recovery after surgery (ERAS) in gynecologic oncology – A systematic review and meta-analysis.," Gynecol. Oncol., vol. 161, no. 1, pp. 46–55, Apr. 2021, doi: 10. 1016/ j.ygyno.2020.12.035.

[16] A. Ashok et al., "The enhanced recovery after surgery (ERAS) protocol to promote recovery following esophageal cancer resection," Surg. Today, vol. 50, no. 4, pp. 323–334, Apr. 2020, doi: 10. 1007/ s00595-020-01956-1.

[17] J. Inoue et al., "Prevention of postoperative pulmonary complications through intensive preoperative respiratory rehabilitation in patients with esophageal cancer," Dis. Esophagus, vol. 26, no. 1, pp. 68–74, Jan. 2013, doi: 10.1111/j.1442-2050.2012.01336.x.

[18] K. H. Tukanova, S. Chidambaram, N. Guidozzi, G. B. Hanna, A. H. McGregor, and S. R. Markar, "Physiotherapy Regimens in Esophagectomy and Gastrectomy: a Systematic Review and Meta-Analysis," Ann. Surg. Oncol., vol. 29, no. 5, pp. 3148–3167, May 2022, doi: 10.1245/s10434-021-11122-7.

[19] I. Yamana et al., "Randomized Controlled Study to Evaluate the Efficacy of a Preoperative Respiratory Rehabilitation Program to Prevent Postoperative Pulmonary Complications after Esophagectomy," Dig. Surg., vol. 32, no. 5, pp. 331–337, 2015, doi: 10.1159/000434758.

[20] P. M. Bath, H. S. Lee, and L. F. Everton, "Swallowing Therapy for Dysphagia in Acute and Subacute Stroke," Stroke, vol. 50, no. 3, pp. e46–e47, Mar. 2019, doi: 10.1161/STROKEAHA.118.024299.

[21] J. Takatsu et al., "Clinical benefits of a swallowing intervention for esophageal cancer patients after esophagectomy," Dis. Esophagus, vol. 34, no. 5, p. doaa094, May 2021, doi: 10.1093/dote/doaa094.

[22] S. Ozawa, K. Koyanagi, Y. Ninomiya, K. Yatabe, and T. Higuchi, "Postoperative complications of minimally invasive esophagectomy for esophageal cancer," Ann. Gastroenterol. Surg., vol. 4, no. 2, pp. 126–134, Mar. 2020, doi: 10.1002/ags3.12315.

[23] S. Y. Lee, H.-J. Cheon, S. J. Kim, Y. M. Shim, J. I. Zo, and J. H. Hwang, "Clinical predictors of aspiration after esophagectomy in esophageal cancer patients," Support. Care Cancer, vol. 24, no. 1, pp. 295–299, Jan. 2016, doi: 10.1007/s00520-015-2776-8.

[24] P. Koh, G. Turnbull, E. Attia, P. LeBrun, and A. G. Casson, "Functional assessment of the cervical esophagus after gastric transposition and cervical esophagogastrostomy," Eur. J. Cardiothorac. Surg., vol. 25, no. 4, pp. 480–485, Apr. 2004, doi: 10.1016/j.ejcts.2003.12.034.

[25] M. Rubinkiewicz, J. Witowski, M. Su, P. Major, and M. Pędziwiatr, "Enhanced recovery after surgery (ERAS) programs for esophagectomy," J. Thorac. Dis., vol. 11, no. S5, pp. S685–S691, Apr. 2019, doi: 10.21037/jtd.2018.11.56.

[26] V. Meves, A. Behrens, and J. Pohl, "Diagnostics and Early Diagnosis of Esophageal Cancer," Visc.

ISSN 2618-1584 Vol. 5, Issue 6: 55-66, DOI: 10.25236/FMSR.2023.050610

Med., vol. 31, no. 5, pp. 315–318, 2015, doi: 10.1159/000439473.
[27] J. A. Logemann et al., "A Randomized Study Comparing the Shaker Exercise with Traditional Therapy: A Preliminary Study," Dysphagia, vol. 24, no. 4, pp. 403–411, Dec. 2009, doi: 10.1007/s00455-009-9217-0.
[28] J. A. Logemann, "Treatment of Oral and Pharyngeal Dysphagia," Dysphagia, vol. 19, no. 4, pp. 803–816, Nov. 2008, doi: 10.1016/j.pmr.2008.06.003.
[29] Park Yeon-Hwan, Han Hae-Ra, Oh Seieun, and Chang HeeKyung, "Validation of the Korean Version of the Standardized Swallowing Assessment Among Nursing Home Residents.," J. Gerontol. Nurs., vol. 40, no. 2, pp. 26–35, Feb. 2014, doi: 10.3928/00989134-20131220-08.
[30] P. C. Belafsky et al., "Validity and Reliability of the Eating Assessment Tool (EAT-10)," Ann. Otol. Rhinol. Laryngol., vol. 117, no. 12, pp. 919–924, Dec. 2008, doi: 10.1177/000348940811701210.
[31] C. Wan et al., "Validation of the simplified Chinese version of EORTC QLQ-C30 from the measurements of five types of inpatients with cancer," Ann. Oncol., vol. 19, no. 12, pp. 2053–2060, Dec. 2008, doi: 10.1093/annonc/mdn417.
[32] H. Zhao and K. Kanda, "Translation and validation of the Standard Chinese version of the EORTC QLQ-C30," Qual. Life Res., vol. 9, no. 2, pp. 129–137, Mar. 2000, doi: 10.1023/A:1008981520920.
[33] W.-C. Chie, C.-J. Tsai, C. Chiang, and Y.-C. Lee, "Quality of life of patients with oesophageal cancer in Taiwan: validation and application of the Taiwan Chinese (Mandarin) version of the EORTC QLQ-OES18: a brief communication," Qual. Life Res., vol. 19, no. 8, pp. 1127–1131, Oct. 2010, doi: 10.1007/s11136-010-9675-8.
[34] Z. Dai et al., "Validation of EORTC QLQ-OES18 for Chinese patients with esophageal cancer," Esophagus, vol. 30, no. 10, pp. 1–7, Oct. 2017, doi: 10.1093/dote/dox046.
[35] J. Cohen, Statistical power analysis for the behavioral sciences. New York: Routledge, 2013. [Online]. Available: https://doi.org/10.4324/9780203771587
[36] I. Turner Herbert M. and Bernard Robert M., "Calculating and Synthesizing Effect Sizes," Contemp. Issues Commun. Sci. Disord., vol. 33, no. Spring, pp. 42–55, Mar. 2006, doi: 10.1044/cicsd_33_S_42.
[37] J. Khalilzadeh and A. D. A. Tasci, "Large sample size, significance level, and the effect size: Solutions to perils of using big data for academic research," Tour. Manag., vol. 62, pp. 89–96, Oct. 2017, doi: 10.1016/j.tourman.2017.03.026.
[38] T. Okumura, Y. Shimada, T. Watanabe, N. Nakamichi, T. Nagata, and K. Tsukada, "Functional outcome assessment of swallowing (FOAMS) scoring and videofluoroscopic evaluation of perioperative swallowing rehabilitation in radical esophagectomy," Surg. Today, vol. 46, no. 5, pp. 543–551, May 2016, doi: 10.1007/s00595-015-1203-6.
[39] M.-J. Chen et al., "Nutrition therapy in esophageal cancer—Consensus statement of the Gastroenterological Society of Taiwan," Dis. Esophagus, vol. 31, no. 8, Aug. 2018, doi: 10. 1093/ dote/ doy016.
[40] H. KATO et al., "Videofluoroscopic Evaluation in Oropharyngeal Swallowing after Radical Esophagectomy with Lymphadenectomy for Esophageal Cancer," Anticancer Res., vol. 27, no. 6C, p. 4249, Nov. 2007, [Online]. Available: http://ar.iiarjournals.org/content/27/6C/4249.abstract
[41] R. E. Martin, P. Letsos, D. H. Taves, R. I. Inculet, H. Johnston, and H. G. Preiksaitis, "Oropharyngeal Dysphagia in Esophageal Cancer Before and After Transhiatal Esophagectomy," Dysphagia, vol. 16, no. 1, pp. 23–31, Jan. 2001, doi: 10.1007/s004550000044.
[42] W. G. Pearson, S. E. Langmore, L. B. Yu, and A. C. Zumwalt, "Structural Analysis of Muscles Elevating the Hyolaryngeal Complex," Dysphagia, vol. 27, no. 4, pp. 445–451, Dec. 2012, doi: 10. 1007/ s00455-011-9392-7.
[43] J. R. Jung and J. H. Kim, "Changes in Psychological Distress and Quality of Life After Esophageal Cancer Surgery: A Prospective Study," Asian Oncol Nurs, vol. 22, no. 1, pp. 21–28, Mar. 2022, [Online]. Available: https://doi.org/10.5388/aon.2022.22.1.21
[44] P. Lagergren et al., "Health-related quality of life among patients cured by surgery for esophageal cancer," Cancer, vol. 110, no. 3, pp. 686–693, Aug. 2007, doi: 10.1002/cncr.22833.
[45] Q. Cheng, C. Kong, S. Chang, and A. Wei, "Effects of psychological nursing intervention on personality characteristics and quality of life of patients with esophageal cancer," Clin. Res. Hepatol. Gastroenterol., vol. 37, no. 3, pp. 283–288, Jun. 2013, doi: 10.1016/j.clinre.2012.08.009.
[46] E. Pinto, F. Cavallin, and M. Scarpa, "Psychological support of esophageal cancer patient?" J. Thorac. Dis., vol. 11, no. S5, pp. S654–S662, Apr. 2019, doi: 10.21037/jtd. 2019.02.34.
[47] S. Däster, S. D. Soysal, L. Stoll, R. Peterli, M. von Flüe, and C. Ackermann, "Long-Term Quality of Life after Ivor Lewis Esophagectomy for Esophageal Cancer," World J. Surg., vol. 38, no. 9, pp. 2345–2351, Sep. 2014, doi: 10.1007/s00268-014-2576-1.
[48] M. Chevallay, M. Jung, S.-H. Chon, F. R. Takeda, J. Akiyama, and S. Mönig, "Esophageal cancer surgery: review of complications and their management," Ann. N. Y. Acad. Sci., vol. 1482, no. 1, pp. 146–162, Dec. 2020, doi: 10.1111/nyas.14492.