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Timing of Using Exercise-Based Dysphagia Boot Camp (DBC) Impacts Functional Swallowing Outcomes after Surgical Management of Oropharyngeal Cancer

Laishyang Melody Ouyoung[1], Margaret Nurimba[1], Mark Swanson[2], Franklin Wu[1], Ryan Zilter[1], Susie Nam[3], Brenda Caprobres Villegas[3] and Uttam Sinha[2]*

[1]Keck School of Medicine of the University of Southern California, USA

[2]Department of Otolaryngology - Head and Neck Surgery, Keck School of Medicine of the University of Southern California, USA

[3]Department of Speech Pathology, Keck Medical Center of the University of Southern California, USA

Abstract

Objectives: To evaluate the impact of Dysphagia Boot Camp (DBC) swallowing intervention timing on functional swallowing outcomes after treatment of oropharyngeal cancer.

Study Design: Retrospective cohort study at a single academic tertiary care center between 2007 to 2018.

Methods: Patients who underwent dysphagia therapy after treatment of oropharyngeal cancer were identified on retrospective chart review and stratified into three cohorts based on tumor management: (1) primary Chemoradiation (CRT), (2) Transoral Robotic Surgery with adjuvant CRT (TORS), (3) free tissue transfer and Flap reconstruction with adjuvant CRT (Flap). The timing of dysphagia therapy intervention was defined as "early" if less than, or "late" if greater than 26 weeks after primary resection date or completion of chemoradiation. The primary outcome of the study was to assess the impact of Dysphagia Boot Camp (DBC) intervention timing on differences in Functional Oral Intake Scores (FOIS) after dysphagia boot camp therapy.

Results: A total of 32 patients (TORS, n=10; Flap, n=12; CRT, n=10) were included in the analysis. There were significant differences in pre-therapy FOIS (p=0.010) between cohorts, with TORS patients having greater FOIS than flap and CRT patients prior to DBC therapy. DBC therapy alone resulted in significant improvements in FOIS score regardless of primary treatment arm (TORS, p=0.002; Flap, p=0.027; CRT, p=0.019). When adjusting for timing of therapy, early DBC therapy was associated with significant improvement in FOIS score for the TORS (Z=2.060, p=0.039) and flap (Z=2.205, p=0.027) cohorts.

Conclusion: While primary chemoradiation and extensive surgical resection of oropharyngeal cancers are associated with poorer functional swallowing outcomes, early DBC therapy is associated with increased improvement in FOIS scores. This highlights the need for early referral and engagement in swallow rehabilitation after treatment of oropharyngeal cancers.

Keywords: Oropharyngeal cancer; FOIS; Swallow intervention; Rehabilitation

Introduction

Patients with oropharyngeal cancer are at risk for developing multifactorial dysphagia from treatment effects of Chemoradiation (CRT) and surgical management [1,2]. While advances in surgical and radiation therapy have drastically improved oncologic outcomes, these are not without risks. In surgical resections of oropharyngeal cancer, resections of the base of the tongue are associated with worse functional swallowing outcomes due to increased pharyngeal transit time, penetration, and aspiration [1]. Radiation-induced fibrosis of the pharynx and esophagus can lead to significant morbidity including aspiration pneumonia, feeding tube dependence, and malnutrition [3,4]. Similarly, other therapy-induced toxicities including mucositis, xerostomia, odynophagia, trismus, and progressive neuropathy can have significant impact on swallow function and quality of life [5-9].

Due to increased awareness of the importance of early dysphagia management, a multitude

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Correspondence:
Laishyang Melody Ouyoung, Keck School of Medicine of the University of Southern California, 1975 Zonal Ave, Los Angeles, CA 90033, USA, Tel: 3234428928;
E-mail: lai.ouyoung@med.usc.edu

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of studies have shown that exercise-based swallowing therapy before [10,11], during [12], and after CRT has been demonstrated to have varying degrees of efficacy in regards to functional outcomes. Patients who adhered to exercise-based swallowing therapy during and/or after CRT had improved oral diet, shorter duration of gastrostomy tube use and higher quality of life scores [10-16].

Studies focusing on rehabilitation of swallow function after surgical management of head and neck cancers are less well defined. Surgical resection of head and neck cancer is associated with moderate but persistent deficits in swallowing function and quality of life [17-19]. Similarly, there are significant associations between the extent of surgical resection and postoperative swallow function [1,20]. Of surgical options, Transoral Robotic Surgery (TORS) is generally associated with better long-term functional and quality of life outcomes compared to extensive surgical resections requiring free flap reconstruction. While these modalities are often associated with decreased dose requirements of chemoradiation, the addition of adjuvant CRT is associated with poorer long-term functional and quality of life outcomes and persistent dysphagia [21]. Studies on dysphagia in patients who undergo surgical management such as TORS or free flap reconstruction surgery with adjuvant CRT are lacking. Additionally, there is a relative paucity of data on the impact of swallowing intervention in these patients, with only one study suggesting that earlier initiation of swallow therapy in surgically managed patient's results in improved functional outcomes [20]. As such, the purpose of this current study is to quantitatively evaluate the impact of swallowing intervention timing on functional swallowing outcomes in oropharyngeal cancer patients who undergo surgical management with adjuvant chemoradiation.

Methods

Patient Selection

After approval by the Institutional Review Board at the University of Southern California, Health Sciences Campus, patients who underwent exercise-based Dysphagia Boot Camp (DBC) therapy between 2008 through 2017 after surgical or medical management of oropharyngeal cancer were identified on retrospective chart review. Patients were stratified into three cohorts based on tumor management. The TORS cohort was defined as patients who underwent transoral robotic surgery with adjuvant chemoradiation. The flap cohort was defined as patients who underwent free tissue transfer and flap reconstruction with adjuvant chemoradiation. Lastly, the Chemoradiation (CRT) cohort was defined as patients who underwent primary chemoradiation of the primary tumor alone. Criteria for patients who underwent swallow therapy are listed below.

Dysphagia boot camp therapy

Inclusion for candidacy for DBC therapy was multifactorial and made in conjunction by the surgeon and Speech-Language Pathologist (SLP) based on their Modified Barium Swallow (MBS), dysphagia severity, level of patient satisfaction with current swallowing, and ability to understand and cooperate with the program. At the start of therapy, evaluation consisted of baseline Functional Oral Intake Scores (FOIS), gastrostomy tube status, and bedside swallowing examination. All patients underwent exercise-based swallow therapy (DBC) targeting hyolaryngeal excursions, cricopharyngeal opening, and tongue base retraction against resistance, in conjunction with Neuromuscular Electrical Stimulation (NMES) applied to the cervical strap muscles throughout each swallow therapy session. All patients need to come to DBC 2 times per week for 8 weeks. The DBC therapy program included the ABCLOVE voice therapy program previously established by our institution which was designed specifically for head and neck cancer patients with components of breathing, counseling [22], laryngeal manipulation, oral resonance, vocal function exercises, and elimination of bad habits.

Data collection

Surgical and pathologic data were abstracted from medical records. Functional Oral Intake Scores (FOIS) and timing of DBC intervention after cancer treatment was abstracted from swallow therapy records. Timing of DBC intervention was defined as "early" if less than, or "late" if greater than 26 weeks after primary resection date or completion of chemoradiation. The primary outcome of the study was differences in FOIS after swallowing therapy. Secondary outcomes of the study were ability to achieve G-tube independence after dysphagia therapy and need for esophageal dilation after dysphagia therapy.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics Version 24 (IBM, Chicago, IL). Chi-squared tests, Fisher exact tests, and independent samples t-test were used for bivariate statistical analysis. Two-way repeated measures ANOVA was conducted to evaluate the impact of intervention timing on pre- and post-therapy FOIS. The Wilcoxon signed-rank test was used for non-parametric paired samples assessment of pre- and post-therapy FOIS scores. Univariate binomial analysis was performed to identify risk factors for gastrostomy tube dependence and esophageal dilation requirement after therapy. Significant risk factors were adjusted for confounders using stepwise multivariate analysis, with a maximum of two variables included in the analysis due to small sample size. Statistical significance was set at an alpha of 0.05.

Results

Patient demographics as stratified by treatment cohort are presented in Table 1. A total of 32 patients were included in the study, of whom 10 underwent TORS resection followed by adjuvant chemoradiation, 12 underwent free flap reconstruction and adjuvant chemoradiation, and 10 underwent primary chemoradiation. There were no significant differences in age (p=0.919), gender (p=0.351), tumor stage (p=0.245), or extent of distant metastatic disease (p=0.625) between patient cohorts. TORS patients had a greater burden of regionally metastatic disease compared to Flap and CRT patients (TORS, 90% *vs.* Flap, 66.7% and CRT, 40, p=0.045).

Outcomes after DBC therapy are presented in Table 2. There were significant differences in pre-therapy FOIS (p=0.010) between treatment cohorts, with TORS patients having greater FOIS than flap and CRT patients prior to DBC therapy. Similarly, a greater percentage of flap (83.3%) and CRT (60%) patients had gastrostomy tubes in place at the initiation of DBC therapy compared to TORS patients (p=0.011). There were significant differences in secondary outcomes, as 90% of TORS patients achieved gastrostomy tube independence after swallow therapy, compared to only 41.7% of flap, and 40% of CRT patients (p=0.043). There were no differences in gastrostomy tube dependence between DBC therapy patients (TORS, p=0.300; Flap, p=0.576; CRT, p=0.133). However, a greater percentage of flap patients who underwent late DBC therapy required esophageal dilation after DBC therapy compared to those who underwent early DBC therapy (75% *vs.* 0%, p=0.013).

Table 1: Patient demographics stratified by DBC swallowing intervention timing.

	TORS			Flap			CRT			
Intervention	**Early**	**Late**	**p-value[a]**	**Early**	**Late**	**p-value[a]**	**Early**	**Late**	**p-value[a]**	**p-value[b]**
	n=7	**n=3**		**n=8**	**n=4**		**n=2**	**n=8**		
Age										
Mean	58.8 ± 6.9	60.0 ± 6.3	0.819	57.9 ± 6.8	64.5 ± 18.1	0.52	57.1 ± 7.0	58.8 ± 9.2	0.799	0.919
Gender										
Male	7 (100)	2 (66.7)		5 (62.5)	4 (100)		2 (100)	8 (100)		0.351
Female	0	1 (33.3)	0.3	3 (37.5)	0	0.491	0	0	NA	
TNM Staging Tp, n (%)										
T1	3 (42.9)	0		1 (12.5)	1 (25)		1 (50)	0		0.245
T2	3 (42.9)	2 (66.7)		2 (25)	1 (25)		1 (50)	1 (12.5)		
T3	1 (14.3)	1 (33.3)		2 (25)	1 (25)		0	1 (12.5)		
T4	NA	NA		A	0		0	2 (25)		
TX	NA	NA	0.5	A	1 (25)	0.673	0	4 (50)	0.244	
Np, n (%)										
N0/NX	1 (14.3)	0		1 (12.5)	3 (75)		0	6 (75)		0.045*
N1	1 (14.3)	2 (66.7)		5 (62.5)	1 (25)		0	0		
N2b	1 (14.3)	0		1 (12.5)	0		1 (50)	1 (12.5)		
N2c	3 (42.8)	1 (33.3)	0.85	1 (12.5)	0	0.269	1 (50)	1 (12.5)	0.133	
Mp, n (%)										
M0/MX	7 (100)	3 (100)		8 (100)	4 (100)		1 (50)	8 (100)		0.625
M1	0	0	NA	0	0	NA	1 (50)	0	0.2	

[a] p-values calculated within treatment cohorts between early and late swallow intervention groups
[b] p-values calculated between primary treatment cohorts. Abbreviations: NA, not applicable

Table 2: Outcomes after DBC swallow therapy, stratified by primary treatment and swallow intervention timing.

	TORS			Flap			CRT			
Intervention	**Early**	**Late**	**p-value[a]**	**Early**	**Late**	**p-value[a]**	**Early**	**Late**	**p-value[a]**	**p-value[b]**
	n=7	n=3		n=8	n=4		n=2	n=8		
FOIS										
Before Therapy Mean ± SD	4.7 ± 1.0	3.7 ± 2.3	0.518	2.4 ± 1.4	2.3 ± 1.9	0.912	4	2.4 ± 1.8	0.035*	0.010*
After Therapy Mean ± SD	6.1 ± 0.4	5 ± 1.7	0.371	4.6 ± 1.8	3.5 ± 1.7	0.331	5 ± 1.4	3.9 ± 2.4	0.458	0.064
Difference in FOIS Mean ± SD	1.4 ± 1.1	1.3 ± 0.6	0.865	2.3 ± 2	1.3 ± 0.5	0.213	1 ± 1.4	1.5 ± 1.5	0.711	0.610
Gastrostomy tube prior to swallow therapy, n (%)										
Yes	1 (14.3)	1 (33.3)		6 (75)	4 (100)		0	6 (75)		0.011*
No	6 (85.7)	2 (66.7)	1.000	2 (25)	0	0.515	2 (100)	2 (25)	0.133	
Gastrostomy tube independent after swallow therapy, n (%)										
Yes	7 (100)	2 (66.7)		4 (50)	1 (25)		2 (100)	2 (25)		0.043*
No	0	1 (33.3)	0.300	4 (50)	3 (75)	0.576	0	6 (75)	0.133	
Required esophageal dilatation after swallow therapy, n (%)										
Yes	0	0		0	3 (75)		0	4 (50)		0.121
No	7 (100)	3 (100)	NA	8 (100)	1 (25)	0.018*	2 (100)	4 (50)	0.467	

[a] p-values calculated within treatment cohorts between early and late swallow intervention groups
[b] p-values calculated between primary treatment cohorts

A two-way repeated measure ANOVA between early- and late-initiation groups was performed to determine the specific impact of DBC intervention timing on the post-therapy difference in FOIS (Table 3). DBC therapy alone resulted in significant improvements in FOIS score regardless of primary treatment arm (TORS, p=0.002; Flap, p=0.027; CRT, p=0.019). Intervention timing alone did exert a strong effect size in the TORS cohort ($F(1,9)=2.148$; $p=0.181$; $\eta^2_p=0.192$); moderate effect size in the CRT cohort ($F(1,9)=0.900$; $p=0.370$; $\eta^2_p=0.091$) and mild effect size in the flap cohort ($F(1,11)=0.504$; $p=0.495$; $\eta^2_p=0.044$). The combined impact of both intervention timing and therapy resulted in a moderate effect in the flap cohort ($F(1,12)=0.94$, $p=0.355$, $\eta^2_p=0.072$) and small effect in the CRT cohort

Table 3: Comparison of intervention timing on improvements in FOIS, stratified by treatment arm.

Study Arm	Effect	SS	df	MS	F	p-value	η^2_p
TORS	Timing	5.04	1,9	5.04	2.148	0.181	0.192
	Therapy	9.8	1,10	9.8	18.85	0.002	0.653
	Therapy x Timing	0.01	1,10	0.01	0.02	0.891	0.005
Flap	Timing	2.08	1,11	2.08	0.504	0.495	0.044
	Therapy	22.04	1,12	22.04	15.63	0.027	0.566
	Therapy x Timing	1.33	1,12	1.33	0.94	0.355	0.072
CRT	Timing	6.05	1,9	6.05	0.900	0.371	0.091
	Therapy	9.8	1,10	9.8	8.67	0.019	0.464
	Therapy x Timing	0.2	1,10	0.2	0.18	0.682	0.018

Table 4: Impact of intervention timing on pre and post DBC therapy improvement in FOIS.

Study Arm	Swallow Intervention	FOIS, Pre-(Mean ± SD)	FOIS, Post- (Mean ± SD)	Z-Score	Effect Size (r)	p-value
TORS	Any	4.4 ± 1.4	5.8 ± 1.0	2.565	0.573	0.010
	Early	4.7 ± 1.0	6.1 ± 0.4	2.060	0.551	0.039
	Late	3.7 ± 2.3	5 ± 1.7	1.633	0.667	0.102
Flap	Any	2.3 ± 1.5	4.3 ± 1.8	2.732	0.558	0.006
	Early	2.4 ± 1.4	4.6 ± 1.8	2.205	0.551	0.027
	Late	2.3 ± 1.9	3.5 ± 1.7	1.890	0.668	0.059
CRT	Any	2.7 ± 1.7	4.1 ± 2.2	2.266	0.507	0.023
	Early	4	5 ± 1.4	1.000	0.053	0.317
	Late	2.4 ± 1.8	3.9 ± 2.4	1.208	0.247	0.040

Table 5: Factors significantly associated with gastrostomy tube dependence and esophageal dilation requirements after DBC swallow therapy.

	Univariate				Multivariate			
Variable	**OR**	**95%**	**CI**	**p-value**	**OR**	**95%**	**CI**	**p-value**
Esophageal Dilation								
G-tube dependence after therapy								
Yes	12.000	1.226	117.412	0.033				
No	1-REF							
Gastrostomy Tube Dependence								
Intervention Timing								
Late	6.500	1.377	30.682	0.018	5.232	0.727	37.641	0.100
Early	1-REF							
Gastrostomy tube prior to swallow therapy								
Yes	33.800	3.455	330.622	0.002	29.554	2.726	320.366	0.005
No	1-REF							
Treatment				0.079				
Flap	12.600	1.186	133.892	0.036				
CRT	13.500	1.197	152.211	0.035				
TORS	1-REF							

($F(1,10)=0.18$, $p=0.682$; $\eta^2_p=0.018$).

To better evaluate the impact of DBC swallow intervention and its timing on improvements in FOIS, Wilcoxon signed rank tests are presented in Table 4. Regardless of the timing of intervention, DBC swallow therapy resulted in significant improvements in FOIS score in the TORS ($Z=2.565$, $p=0.010$), flap ($Z=2.732$, $p=0.006$) and CRT ($Z=2.266$, $p=0.023$) cohorts. When adjusting for timing of therapy, early DBC swallow therapy was associated with significant improvement in FOIS score for the TORS ($Z=2.060$, $p=0.039$) and flap ($Z=2.205$, $p=0.027$) cohorts. In contrast, in CRT patients, late initiation of DBC swallow therapy resulted in significant post-therapy FOIS improvements ($Z=1.208$, $p=0.040$) while early DBC swallow therapy did not significantly improve FOIS ($Z=0.053$, $p=0.317$). Overall, DBC swallow therapy was associated with large effect sizes, $r \geq 0.50$ in all surgically managed patients, regardless of timing of therapy. In CRT patients, early initiation of therapy exerted a small effect ($r<0.10$) on FOIS while late initiation resulted in a moderate effect ($0.10 \leq r <0.30$) on improvements in FOIS score. Figure 1 summarizes the impact of therapy timing on improvements in FOIS.

Risk factors for gastrostomy tube dependence and post-therapy esophageal dilation requirement are presented in Table 5. On univariate analysis, the most important risk factor for continued esophageal dilation requirements was gastrostomy tube dependency after swallow therapy. (OR=12.000, 95% CI 1.226 to 117.412). The strongest risk factors for gastrostomy tube dependence were pre-therapy gastrostomy tube (OR=33.800, 95% CI 3.455 to 330.622), late swallow intervention (OR=6.500, 95% CI 1.377 to 30.682), and primary treatment with free flap reconstruction (OR=12.600, 95% CI 1.186 to 133.892) or chemoradiation (OR=13.500, 95% CI 1.197 to 152.211). On multivariate analysis, the presence of gastrostomy tube prior to therapy contributed the highest risk for post-therapy dependence (OR=29.554, 95% CI 2.726 to 320.366). Late intervention was associated with a greater than five-time risk of gastrostomy tube dependence (OR=5.232, 95% CI 0.727 to 37.641).

Discussion

Swallowing dysfunction after treatment of oropharyngeal cancer contributes to reduced patient quality of life and increased morbidity. Thus, swallow rehabilitation after treatment for oropharyngeal cancer is crucial for restoration of baseline swallowing function. However, the optimal timing to start swallowing therapy has yet to be well established. While most studies on swallowing rehabilitation in head and neck cancer patients focus on those treated with primary chemoradiation, our study is the first to examine the effect of timing on these outcomes in patients managed with both surgery and adjuvant chemoradiation.

The results of this study demonstrate that early exercise-based Dysphagia Boot Camp (DBC) intervention is significantly associated with improvements in FOIS compared to late intervention, especially in oropharyngeal cancer patients who undergo primary surgical management with adjuvant chemoradiation. At baseline, patients who underwent early DBC swallow therapy had increased FOIS scores, compared to the late DBC swallow therapy groups. Similar to the study by Denk et al. [20], we also show that swallowing rehabilitation, regardless of timing, significantly improves functional oral intake in oropharyngeal cancer patients who undergo surgical management of their tumors [20]. Additionally, late intervention was associated with an increased risk of post-therapy gastrostomy tube dependence, which itself was the strongest predictive factor for esophageal dilation requirements after swallow therapy. Taken together, this supports a role for early swallow intervention in all oropharyngeal cancer patients, regardless of primary tumor management.

Interestingly, while CRT patients who received early swallow therapy had higher baseline FOIS compared to the late therapy group, we found that late initiation of swallow therapy in the CRT cohort was associated with significantly improved FOIS and greater effects compared to those who received early swallow therapy. These findings contrast with other findings in the literature that suggest that prophylactic or early speech and swallow interventions are preferable due as acute toxicities from CRT often present early in the course of care [11,12,20,23]. However, this observed difference may be attributable to selection bias at our institution. As a tertiary care center, CRT patients are often referred to speech and swallow therapy at our department from outside providers after these toxicities are made apparent in the form of severe dysphagia, malnutrition, and failure to thrive. Thus, the proportion of CRT patients who received early swallow therapy was much smaller than those who received late swallow therapy and the detected differences may not adequately represent the benefits of early swallow rehabilitation.

Limitations of this study include those inherent to a retrospective cohort study, including small sample size and selection bias. Other limitations include the inclusion of heterogeneous tumor stages and diversified adjuvant radiotherapy and chemotherapy regimens, which could not be adequately controlled for due to the small sample size of this analysis. Lastly, we acknowledge that while the functional oral intake scale has been validated as a measure of physiologic swallow function, it may not be in accordance with patient reported quality of life. A recent study by Kirsch et al. demonstrated that while physiologic swallow function declines with time after chemoradiation, patient reported QOL did not [24]. Due to the retrospective nature of this study, we noted that a range of QOL surveys were used throughout the study period. Because of the inconsistent evaluation of our cohort's QOL patients, our study excluded QOL as a parameter of study. As such, larger studies that evaluate both physiologic swallow function and qualitative assessments of swallowing-related quality of life are further warranted.

Conclusion

While primary chemoradiation and extensive surgical resection of oropharyngeal cancers are associated with poorer functional swallowing outcomes, early exercise-based dysphagia boot camp therapy is associated with significant improvement in FOIS scores. This highlights the need for early referral and engagement in swallow rehabilitation after treatment of oropharyngeal cancers.

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