

# Functional and Patient-reported Changes in Swallowing and Voice After Combined Chemotherapy and Radiotherapy for Limited Stage Small Cell Lung Cancer

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## Research

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# Abstract

*Purpose:* To describe the nature and impact of dysphagia (difficulty swallowing) and dysphonia (impaired voice) in patients with limited-stage small cell lung cancer (SCLC) before and after chemoradiation.

*Methods:* A prospective cohort study was conducted on patients receiving chemoradiotherapy for limited-stage SCLC. Patients received either 40Gy in 15 fractions, 45Gy in 30 fractions (delivered BD) or 50Gy in 25 fractions, commencing the second cycle of carboplatin/etoposide or cisplatin/etoposide chemotherapy. Outcomes included: videofluoroscopy swallowing studies (VFSS) to investigate aspiration, swallowing function, and oesophageal motility disorders; limitations to oral intake; patient-reported swallowing problems; and patient-reported voice problems. Data were collected before treatment and at one, three and six months post-treatment.

*Results:* Twelve patients were enrolled. The oropharyngeal swallow was safe and functional at all time points. Three patients exhibited oesophageal motility disorders before treatment, while a further three exhibited disorders post-treatment. Oral intake was most compromised one month post-treatment with five patients being either tube dependent or eating only very limited diets. At all other times patients were eating a normal or near-normal diet. Despite normal oropharyngeal swallowing on VFSS, three patients reported moderate or severe swallowing difficulties one month post-treatment. Three additional patients reported moderate or severe difficulties three and six months post-treatment. Patients who reported swallowing difficulties one month post-treatment had all received a mean and maximum radiation dose to the oesophagus of  $\geq 15.7$ Gy and  $\geq 42$ Gy respectively. Dose-response relationships were no longer apparent three and six-months post treatment. Voice problems were variable, with the worst scores reported one month post-treatment.

*Conclusions:* Although patient numbers are small, this study identified discordance between observed swallowing function and patient-reported problems, which has clinical implications for the management of patients with SCLC, as well as identifying areas for future research. Ongoing efforts to reduce mucosal toxicity in lung cancer patients are essential.

## Introduction

Lung cancer remains the most common cancer in the world, with over 2 million estimated new cases and 1.7 million deaths worldwide in 2018<sup>1</sup>. Mortality and morbidity – both from the disease as well as its treatment(s) – remain significant challenges for clinicians, and it has been identified that patients with lung cancer experience more symptom distress than those with other types of cancer<sup>2</sup>. Dysphagia (difficulty swallowing) and dysphonia (impaired voice) have been identified in patients with lung cancer as being significant problems, which may be caused by direct tumour invasion (from mediastinal disease or cervical lymphadenopathy), nerve compression (causing unilateral vocal-cord palsy), age, dyspnoea or deconditioning, and these problems may be further compounded by the treatment itself, which often

comprises intensive chemoradiotherapy<sup>3,4</sup>. Dysphagia can result in malnutrition, aspiration pneumonia, associated hospital admissions, anxiety and depression, and a significant reduction in Quality of Life (QOL)<sup>5-8</sup>.

Acute dysphagia has been recognised as a dose-limiting toxicity in patients with lung cancer receiving concurrent chemoradiotherapy, with reports that between 30–51% of patients develop moderate (Grade 2) dysphagia, while 11–13% develop severe (Grade 3) dysphagia during the acute phase of treatment<sup>9,10</sup>. However, the data is limited by the somewhat crude measurement of 'dysphagia', using the NCI Common Terminology Criteria for Adverse Events (CTCAE) scoring system which is based on subjective symptoms and does not identify the actual cause or nature of the swallowing problem. 'Dysphagia' may refer to swallowing difficulties as a result of oesophagitis-related pain, aspiration of fluids or a physical inability to clear solid food through the pharynx or oesophagus. These varying presentations have vastly different management strategies and impacts on patients, so an accurate appraisal of the nature of the problem using a variety of tools that measure all aspects of dysphagia is essential.

The need for well-designed, prospective research on the nature of dysphagia and dysphonia in lung cancer patients has been previously identified<sup>4,11</sup>. Understanding exactly what types of swallowing and voice problems patients develop and when, ensures accurate information can be provided to patients prior to treatment and allows clinicians to provide more timely preventative or therapeutic intervention, potentially avoiding dysphagia-related malnutrition or aspiration pneumonia, or the daily challenges resulting from dysphonia.

Most studies investigating symptoms in patients with lung cancer only include those with non-small cell lung cancer (NSCLC)<sup>2</sup>. Although small cell lung cancer (SCLC) makes up only about 13–15% of all lung cancers<sup>12,13</sup>, management of limited stage disease often involves a hyperfractionated radiotherapy schedule delivered twice daily; a schedule typically associated with increased rates of oesophagitis<sup>14</sup>. Those with SCLC also have a poor prognosis with a 5-year relative survival rate of 31–34%<sup>12,15</sup>. This higher morbidity and mortality profile highlights the importance of maximising QOL at all stages of treatment planning and delivery, so accurate data on the outcomes and risks of this vulnerable patient group is urgently required.

There are currently no studies that have reported on swallowing or voice outcomes in patients with SCLC, and the use of instrumental measures of swallowing function for any lung cancer patients is also lacking. The purpose of this prospective study therefore was to investigate the nature and impact of dysphagia and dysphonia in patients with limited-stage SCLC before and after treatment, using a range of measures to examine potential associations between post-treatment outcomes and treatment-related characteristics.

## **Methods And Materials**

### **Study Design and Participants**

This was a prospective longitudinal cohort study, using repeated measures on a convenience sample of newly diagnosed patients with SCLC from [removed for blind review]. The study was approved by the [removed for blind review] ethics committee prior to commencement (HREC approval: [removed for blind review]) and all participants provided written informed consent prior to participation.

Patients with newly diagnosed limited-stage SCLC were recruited prior to receiving chemoradiotherapy at one of [removed for blind review]'s three radiotherapy sites across [city, country; removed for blind review]. Patients were eligible for inclusion if they were: over 18 years of age; had limited stage disease (defined as no known distant metastatic disease and appropriate for radical chemoradiotherapy); able to read English; no previous radiotherapy to the head or neck; and no previous conditions or treatment that could cause swallowing or voice impairment.

Chemotherapy consisted of either carboplatin and etoposide or cisplatin and etoposide, given every 3 weeks for 4 cycles. Radiotherapy commenced with the second cycle of chemotherapy and was delivered using one of the following established protocols: 40 Gy in 15 fractions over 3 weeks (1 fraction per day); 45 Gy in 30 fractions over 3 weeks (2 fractions per day); or 50 Gy in 25 fractions over 5 weeks (1 fraction per day).

## Data Collection

Data were collected on patients at four time points: prior to commencement of radiotherapy; 1 month post-completion of radiotherapy; 3 months post-completion of radiotherapy; and 6 months post-completion of radiotherapy.

At each time point data were collected on: swallowing function, limitations to oral intake, patient-reported swallowing and voice problems, health-related quality of life (QOL) and nutritional outcomes. Study data were entered into and managed using the REDCap electronic data capture tool hosted at [removed for blind review]<sup>16,17</sup>.

Videofluoroscopic swallowing studies (VFSS; also referred to as the modified barium swallow) were used to analyse swallowing function. Swallowing images were recorded using the Philips Allura FD20 X-ray system and converted to .avi format for later analysis. During the VFSS participants completed the following with the patient seated in the lateral position: three swallows of 5 ml and one swallow of 10 ml liquid, three swallows of 5 ml semi-solid (pureed fruit), and a piece of solid food (½ cracker). All boluses were mixed or coated with barium to allow clear visualisation of the bolus through the oral cavity, pharynx and upper oesophagus. An anterior-posterior view was also taken while the participant swallowed 5 ml bolus of semi-solid, to allow observation of the presence of oesophageal motility disorder(s). Measures taken from the VFSS images were: (i) aspiration of liquids, using the Penetration-Aspiration Scale<sup>18</sup>, an 8-point scale ranging from 1 (material does not enter the airway) to 8 (material enters the airway, passes below the vocal folds, and no effort is made to eject), (ii) overall swallow function of liquids, semi-solids and solids, using the Swallowing Performance Status Scale (SPSS)<sup>19</sup>, a 7-point rating scale which takes a number of different swallowing features into account, including how

safely and effectively the bolus moves through the oral cavity and pharynx, and (iii) oesophageal motility disorder(s), rated as present or absent.

Oral intake was measured using the Functional Oral Intake Scale (FOIS) which rates the degree to which a person needs to modify the consistency/texture of food they eat and/or requires tube feeding. The scale ranges from 7 (total oral intake with no restrictions) to 1 (nothing by mouth) and has demonstrated validity and reliability<sup>20</sup>.

Patient-reported swallowing and voice problems were measured using the Dysphagia Handicap Index (DHI)<sup>21</sup> and the Voice Handicap Index (VHI)<sup>22</sup> respectively. These are questionnaires which, for the DHI, comprise 25 items with three response options (never; sometimes; always) and one global item, and for the VHI, comprises 30 items rated on a 5-point Likert-type scale.

The University of Washington QOL questionnaire (UW-QOL)<sup>23</sup> was used to measure health-related QOL. It includes 16 questions regarding pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder, taste, saliva, mood and anxiety.

Demographic and treatment-related data were collected from the medical records. Data of interest included: gender, age, nutritional status (using the Patient-Generated Subjective Global Assessment [PG-SGA]<sup>24,25</sup>), radiotherapy regimen, chemotherapy agent, mean radiation dose to the oesophagus, maximum radiation dose to the oesophagus, oesophagitis (worst CTCAE score recorded and duration of worst CTCAE score recorded) and required admission for neutropenia.

## Statistical Analysis

Descriptive statistics were used to summarise the demographic and clinical characteristics of the participants. These included counts and percentages for nominal valued variables; and means and standard deviations or medians, interquartile ranges and ranges for continuous valued variables.

For the purposes of analysis, the global item scores of the DHI were rated as normal (score of 1), mild (score of 2 or 3), moderate (score of 4 or 5) or severe (score of 6 or 7)<sup>26</sup>.

## Results

Figure 1 shows the patient flow and data availability from recruitment to final data collection at 6 months post treatment. From a potential cohort of 34 patients diagnosed with limited-stage SCLC, complete – or near complete – data were collected on 12. Figure 1 outlines the reasons for non-participation or dropout and highlights the challenges of recruiting to studies with cancer types, as well as recruiting to supportive care research, particularly in the period immediately following diagnosis and prior to commencing treatment. Although we had intended to recruit 30 participants in total, the study was closed early as time and financial limitations did not allow for ongoing recruitment. Table 1 outlines the demographic and treatment characteristics for the 12 study participants.

Table 1  
Patient and treatment characteristics

Characteristic	n	%
Gender		
Male	5	42
Female	7	58
Age		
Median (range)	67.5 (51–79)	
Radiotherapy treatment		
40 Gy / 15 fractions	7	58
45 Gy / 30 fractions <sup>#</sup>	3	25
50 Gy / 25 fractions	2	17
Chemotherapy		
Carboplatin/etoposide	10	83
Cisplatin/etoposide	2	17
Mean dose to oesophagus (Gy)		
Median (range)	18 (10–32)	
Maximum dose to oesophagus (Gy)		
Median (range)	42 (25–46)	
Admission for neutropenia during treatment		
Yes	5	
No	7	
<sup>#</sup> BD treatment		

## Swallow Function

No patient was observed to aspirate on VFSS either before or after treatment. Swallowing Performance Status Scale (SPSS) scores were 1 (normal) or 2 (within functional limits) at all times, for all liquid, semi-solid and solid boluses (see Appendix A).

Three patients exhibited oesophageal motility disorders before treatment. These problems persisted post-treatment for those three patients, and there were an additional three patients who also exhibited these

disorders at various times post-treatment – one patient at 3 months post-treatment only, one patient at 1 and 3 months post-treatment and one patient at all three post-treatment time points (see Appendix A).

## Oral Intake

Table 2 outlines the oral diet that patients were managing at each time point. All patients were managing a normal or near normal diet consistency pre-treatment. The most marked limitations occurred at 1 month post-treatment when one patient remained feeding tube dependent (score 3), two managed an oral diet of a single consistency only (score 4), and two managed an oral diet with multiple consistencies, but requiring special preparation (for example, only eating food that was pureed or very soft with extra sauces; score 5). Oral intake returned to a normal or near normal consistency at 3 and 6 months post-treatment with the exception of one patient who remained limited to a special preparation diet (score 5).

Treatment-related toxicity data revealed that all five patients who required a significant modification of their diet at 1 month post-treatment (scores 3–5) had experienced Grade 3 oesophagitis and required hospital admission for neutropenia during treatment. Nevertheless, pain had completely resolved for all patients at 1 month post-treatment, other than the one who remained feeding tube dependent due to persistent pain. Of the seven patients who were eating a normal or near-normal diet consistency at 1 month post-treatment (scores 6–7) all had experienced a maximum of Grade 1–2 oesophagitis during treatment and were not diagnosed with neutropenia at any time. There were no relationships readily apparent between FOIS scores and treatment data at 3 and 6 months post-treatment.

Table 2  
Functional Oral Intake Scale scores by timepoint

	Timepoint							
	Baseline (n = 12)		1 month (n = 12)		3 months (n = 12)		6 months (n = 10)	
FOIS rating	n	%	n	%	n	%	n	%
Tube dependent								
1 Nothing by mouth								
2 Tube dependent with minimal attempts of food or liquid								
3 Tube dependent with consistent oral intake of food or liquid			1	8				
Total oral intake								
4 Total oral diet of a single consistency			2	17				
5 Total oral diet with multiple consistencies, but requiring special preparation			2	17	1	8	1	10
6 Total oral diet with multiple consistencies, without special preparation, but with specific food limitations	3	25	3	25	3	25	3	30
7 Total oral diet with no restrictions	9	75	4	33	8	67	6	60

## Patient-Reported Swallowing Problems

For all domains – physical, functional and emotional – scores were worst at 1 month post-treatment and had improved by 6 months but not back to baseline (pre-treatment) levels (see Table 3). Scores from the global item of the DHI (a rating that “best describes the severity of your swallowing problem”) identified that two patients reported moderate or severe swallowing difficulties at baseline, three patients reported moderate or severe swallowing difficulties 1 month post-treatment, but these difficulties were reported as no more than mild at follow-up assessments for those patients, and three different patients reported a new onset of moderate or severe swallowing difficulties at 3 and 6 months post-treatment (see Fig. 2).

Table 3  
Dysphagia Handicap Index scores by subscale for patient-reported swallowing problems

Subscale/Statistic	Timepoint			
	Baseline (n = 12)	1 month (n = 10)	3 months (n = 10)	6 months (n = 10)
Physical (max 36)				
Median	1.6	3.8	5	2
Interquartile range	0 to 6.4	2.5 to 6.8	1.5 to 6.3	1 to 5
Range	0 to 9	0 to 10	1 to 9	0 to 10
Functional (max 36)				
Median	0	8	3	2
Interquartile range	0 to 5.5	0.8 to 10.3	0.5 to 5	0 to 4.4
Range	0 to 11	0 to 18	0 to 7	0 to 9
Emotional (max 28)				
Median	0.5	3	2	1
Interquartile range	0 to 4.5	0 to 7.3	0 to 2	0 to 2.7
Range	0 to 6	0 to 10	0 to 5	0 to 7
Lower scores represent better outcomes				

Exploration of treatment-related toxicity data revealed that patients who reported any swallowing difficulties at 1 month post-treatment (mild, moderate or severe) had all received a mean radiation dose to the oesophagus of 15.7 Gy or more, and a maximum dose of 42 Gy or more. In contrast, those who reported no swallowing difficulties at 1 month all received mean and maximum radiation doses to oesophagus less than these doses. The relationship between DHI scores and treatment data was no longer apparent at 3 and 6 months post-treatment and there were no obvious relationships between oesophagitis or neutropenia and DHI scores.

## Patient-Reported Voice Problems

Patient-reported voice problems were minimal, with median scores of 0 or 1 ('never' or 'almost never' experience the problem) at all time points for the functional, physical and emotional domains (see Appendix B). The most frequent or highest scores were provided in response to questions rating the statements: "My voice sounds creaky and dry", "I run out of air when I talk" and "The sound of my voice varies throughout the day". The greatest spread of scores occurred at 1 month post-treatment although

patients continued to report problems (though to a lesser degree) across voice-related physical, functional and emotional domains at 3 and 6 months post-treatment.

## Health-Related Quality of Life (QOL)

Scores for all QOL domains varied at all time points with no clear patterns evident. See Appendix C for the scores for each symptom scale presented as per UW-QOL v4 guidelines.

## Nutritional Outcomes

PG-SGA scores were worst at 1 month post-treatment with a median point score of 8, indicating the need for nutrition intervention, bordering on a 'critical need for improved symptom management and/or nutrition intervention' (see Table 4). Scores at 1 month post-treatment also identified that 50% of patients were moderately malnourished (PG-SGA category B), with the remaining 50% being well nourished (PG-SGA category A). No patient was identified as being severely malnourished (PG-SGA category C) at any point. Exploration of treatment-related toxicity data revealed that patients who were moderately malnourished and in need of nutrition intervention at 1 month post-treatment had all received a mean radiation dose to oesophagus of 15.7 Gy or more, and a maximum dose of 42 Gy or more.

Table 4  
PG-SGA scores indicating nutritional status by timepoint

	Timepoint							
	Baseline (n = 12)		1 month (n = 12)		3 months (n = 10)		6 months (n = 8)	
	n	%	n	%	n	%	n	%
Total PG-SGA score								
Median	5		8		3.5		4.5	
Interquartile range	3 to 9		3 to 11		2 to 6		2 to 10	
Range	1 to 10		2 to 15		2 to 10		2 to 11	
Global PG-SGA rating								
A (well nourished)	8	73	6	50	8	80	6	75
B (mod malnourished)	3	27	6	50	2	20	2	25
PG-SGA scores indicate level of intervention required: 0–1, no intervention; 2–3, education required; 4–8, requires intervention; >9, critical								

## Discussion

This study is the first time that detailed functional and patient-reported data on swallowing and voice outcomes in patients with SCLC has been reported. Although patient numbers were small due to challenges recruiting from this uncommon patient cohort, the prospectively collected data is comprehensive and has implications for the multidisciplinary management of these complex patients.

Detailed assessment of swallowing function using VFSS identified that in our cohort swallowing was safe and effective at all times. There is limited data in the literature regarding the prevalence of dysphagia in patients with lung cancer. In a study of 72 patients with advanced lung cancer (8% of whom had SCLC) receiving palliative chemotherapy, 18% identified as having dysphagia on the self-rated EAT-10 tool<sup>27</sup>. This could represent an over-estimation, as some patients had neurological co-morbidities or a history of radiotherapy to the head and neck, or it could be an under-estimation, as only outpatients undergoing palliative chemotherapy were recruited. A small number of subsequent studies have attempted to identify the prevalence of dysphagia in heterogeneous cohorts of cancer patients (including those with lung cancer). Kenny et al.<sup>5</sup> found that of the 59 lung cancer patients in their cohort of 385 cancer patients, 25% had dysphagia as confirmed through clinical evaluation. In a recent study from our centre, 78% of lung cancer patients reported dysphagia for solids and 33% reported dysphagia for liquids<sup>28</sup>. While these symptoms were usually rated as mild, responses to the statement “I have trouble eating certain solid foods” were often severe. The low prevalence of oropharyngeal dysphagia in the current study may be an artefact of the small sample and selection bias; in particular, our careful exclusion of patients with dysphagia-associated comorbidities.

Oral intake limitations, patient-reported swallowing function and nutritional status were most compromised at 1 month post-treatment, even though oropharyngeal swallow function was safe and normal (or near normal) at this time. For the patient with the most significant swallowing issues at this time their UW-QOL pain score was ‘moderate’, but for all other participants there was no clear association between swallowing complaints and reported levels of pain, indicating an alternative cause to their issues. It is possible that residual sensory changes following the resolution of treatment toxicities contributed to these patients’ limitations to their diet, reports of dysphagia symptoms and compromised nutritional status. The relationship between radiation dose to the oesophagus and acute oesophagitis is well-established<sup>29</sup>, as is the relationship between oesophageal dose and nutritional status<sup>30</sup>. More recently, neutropenia has also been identified as a risk factor for higher grades of acute oesophagitis<sup>10,31</sup>. In the current study, limitations in oral intake, patient-reported dysphagia and compromised nutritional status at 1 month post-treatment were only observed in patients who had received a higher oesophageal dose, as well as those who had experienced Grade 3 oesophagitis and neutropenia. It therefore seems plausible that more severe toxicities and mucosal damage contribute to residual sensory changes, even after those toxicities have resolved, and this hypothesis warrants further investigation. Reducing this risk requires ongoing efforts to optimise mucosal protection during radiotherapy, and approaches such as IMRT that keep the oesophageal dose as low as reasonably achievable are essential.

At 3 and 6 months post-treatment, the potential influencing factors to patients' perceptions of swallowing problems are less clear. Indirect factors such as prophylactic cranial irradiation (PCI), associated de-conditioning and sarcopenia, functional decline and fatigue could all contribute<sup>4,5,32-34</sup>.

The discordance between observed and reported dysphagia has been well-documented in the head and neck cancer literature<sup>35-37</sup>. Across all cancer types, a modest agreement at best has been shown between NCI CTCAE ratings and patient-reported outcomes<sup>38</sup>. In lung cancer patients specifically, a discrepancy between clinician-rated dysphagia (based on the NCI CTC) and patient-reported QOL and pain measures has also been reported<sup>39</sup>. This is the first time that a discrepancy has been identified between physiological swallow function (using VFSS) and patient-reported dysphagia in lung cancer. The value of instrumental assessment – specifically VFSS – cannot be understated. These tools can identify functional problems but they can also differentiate between a physiological problem and other issues, such as residual sensory changes. These findings highlight the importance of measuring different aspects of swallowing in research that attempts to investigate the nature or extent of dysphagia in a given population, including lung cancer. There are also implications for the clinical management of patients following chemoradiotherapy, as identifying the nature and extent of dysphagia will be highly dependent on the tools used. The subsequent management of dysphagia relies on this accurate classification of the problem, and assists in patient education and support approaches such as speech pathologists and dietitians working together to optimise oral intake and nutritional status.

Voice problems in our cohort were minimal overall. Previous research investigating lung cancer patients reported that 90% of them were perceptually dysphonic, however only 27.5% were concerned about their voice<sup>40</sup>. This again highlights the discrepancy between observed and reported problems; indicating an application to dysphonia as well as dysphagia. The minimal problems found in our study may reflect this discrepancy as we only collected data on patient-reported voice problems without any instrumental or clinician-rated validation.

The small numbers in this study presented a number of limitations. We were unable to characterise the prevalence of dysphagia in SCLC or to robustly explore the potential associations between dysphagia and radiation treatment factors. Nevertheless we were able to demonstrate the feasibility of objective dysphagia assessment using VFSS and the ability to collect data across a variety of functional and patient-reported domains. Further research is now required to better understand the apparent discrepancy between observed and reported dysphagia in this population, and to investigate the potential link between mucosal damage and its impact on swallowing function or sensory changes.

## Conclusions

This study is the first time that patient-reported dysphagia following chemoradiation for SCLC has been reported, and it has been identified despite an absence of impaired swallow function. Patient-reported dysphagia is multi-factorial, and our findings suggest that treatment factors such as radiation dose to the oesophagus and oesophagitis may all have an impact. Despite our best efforts, side effects from

intensive treatment are often unavoidable, so clinicians must acknowledge and identify the potential for patient-reported dysphagia in lung cancer patients, so that appropriate and timely support and intervention can be provided.

## Declarations

*Consent for publication:*

Not applicable

*Availability of data materials:*

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

*Competing interests:*

The authors declare that they have no competing interests

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*Author contributions:*

JF was a major contributor to study design, data collection, data analysis and interpretation, and manuscript writing.

KG assisted with study design, statistical analysis and was a major contributor in writing the manuscript.

RH assisted with data collection, data interpretation and manuscript writing.

AD assisted with study design and data analysis.

MD assisted with data collection and interpretation.

NK assisted with study design, data interpretation and manuscript writing.

JP-N assisted with study design and manuscript writing.

SS assisted with study design, data collection and manuscript writing.

BS assisted with study concept and design.

DB assisted with study concept and design, data collection, data interpretation and manuscript writing.

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## References

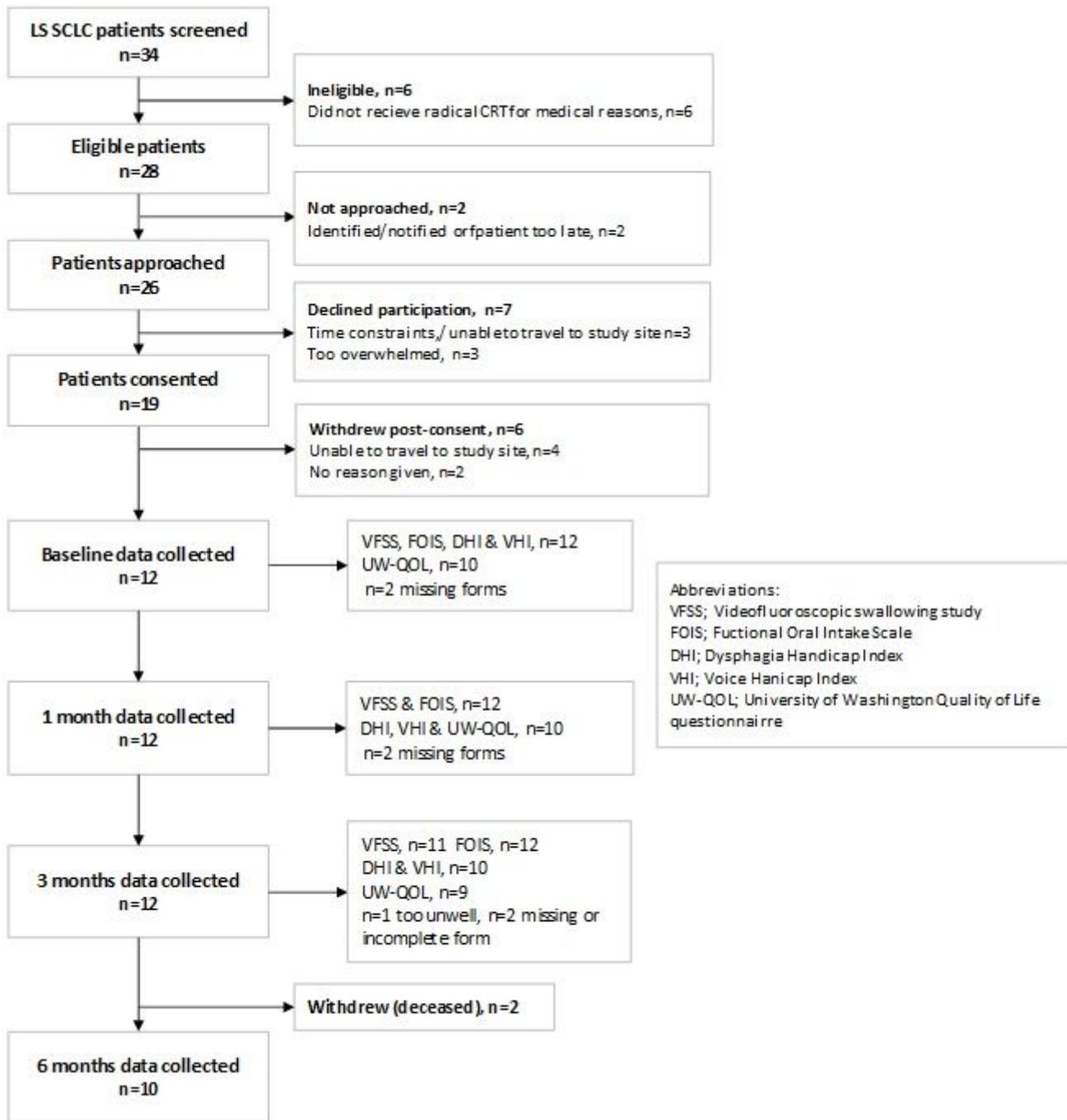
1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*. 2018;68(6):394-424.
2. Cooley ME. Symptoms in adults with lung cancer: a systematic research review. *Journal of pain and symptom management*. 2000;19(2):137-153.
3. Camidge D. The causes of dysphagia in carcinoma of the lung. *Journal of the Royal Society of Medicine*. 2001;94(11):567-572.
4. Brady GC, Carding PN, Bhosle J, Roe JW. Contemporary management of voice and swallowing disorders in patients with advanced lung cancer. *Current opinion in otolaryngology & head and neck surgery*. 2015;23(3):191-196.
5. Kenny C, Regan J, Balding L, et al. Dysphagia prevalence and predictors in cancers outside the head, neck, and upper gastrointestinal tract. *Journal of Pain and Symptom Management*. 2019;58(6):949-958. e942.
6. Clavé P, Shaker R. Dysphagia: current reality and scope of the problem. *Nature Reviews Gastroenterology & Hepatology*. 2015;12(5):259.
7. Verdonshot RJ, Baijens LW, Serroyen JL, Leue C, Kremer B. Symptoms of anxiety and depression assessed with the Hospital Anxiety and Depression Scale in patients with oropharyngeal dysphagia. *Journal of psychosomatic research*. 2013;75(5):451-455.
8. Carrión S, Cabré M, Monteis R, et al. Oropharyngeal dysphagia is a prevalent risk factor for malnutrition in a cohort of older patients admitted with an acute disease to a general hospital. *Clinical nutrition*. 2015;34(3):436-442.
9. Dehing-Oberije C, De Ruyscher D, Petit S, et al. Development, external validation and clinical usefulness of a practical prediction model for radiation-induced dysphagia in lung cancer patients. *Radiotherapy and Oncology*. 2010;97(3):455-461.
10. De Ruyscher D, Dehing C, Bremer R, et al. Maximal neutropenia during chemotherapy and radiotherapy is significantly associated with the development of acute radiation-induced dysphagia in lung cancer patients. *Annals of oncology*. 2007;18(5):909-916.
11. Raber-Durlacher JE, Brennan MT, Verdonck-de Leeuw IM, et al. Swallowing dysfunction in cancer patients. *Supportive Care in Cancer*. 2012;20(3):433-443.
12. American Cancer Society. *Cancer Facts & Figures 2020*. Atlanta: American Cancer Society; 2020.

13. Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. *Journal of clinical oncology*. 2006;24(28):4539-4544.
14. Turrisi AT, Kim K, Blum R, et al. Twice-daily compared with once-daily thoracic radiotherapy in limited small-cell lung cancer treated concurrently with cisplatin and etoposide. *New England Journal of Medicine*. 1999;340(4):265-271.
15. Faivre-Finn C, Snee M, Ashcroft L, et al. Concurrent once-daily versus twice-daily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): an open-label, phase 3, randomised, superiority trial. *The Lancet Oncology*. 2017;18(8):1116-1125.
16. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *Journal of biomedical informatics*. 2019;95:103208.
17. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics*. 2009;42(2):377-381.
18. Rosenbek JC, Robbins J, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. *Dysphagia*. 1996;11(2):93-98.
19. Karnell MP, MacCracken E. A database information storage and reporting system for videofluorographic oropharyngeal motility (OPM) swallowing evaluations *American Journal of Speech-Language Pathology*. 1994;3:54-60.
20. Cray MA, Mann GDC, Groher ME. Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. *Archives of physical medicine and rehabilitation*. 2005;86(8):1516-1520.
21. Wallace KL, Middleton S, Cook IJ. Development and validation of a self-report symptom inventory to assess the severity of oral-pharyngeal dysphagia. *Gastroenterology*. 2000;118(4):678-687.
22. Jacobson BH, Johnson A, Grywalski C, et al. The Voice Handicap Index (VHI) Development and Validation. *American Journal of Speech-Language Pathology*. 1997;6(3):66-70.
23. Weymuller Jr EA, Alsarraf R, Yueh B, Deleyiannis FW-B, Coltrera MD. Analysis of the performance characteristics of the University of Washington Quality of Life instrument and its modification (UW-QOL-R). *Archives of Otolaryngology–Head & Neck Surgery*. 2001;127(5):489-493.
24. Ottery F. Patient-generated subjective global assessment. In: McCallum P, Polisena C, eds. *The clinical guide to oncology nutrition*. Chicago: American Dietetic Association; 2005.
25. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. *European journal of clinical nutrition*. 2002;56(8):779-785.
26. Silbergleit AK, Schultz L, Jacobson BH, Beardsley T, Johnson AF. The dysphagia handicap index: development and validation. *Dysphagia*. 2012;27(1):46-52.
27. Brady GC, Roe JW, O'Brien M, Boaz A, Shaw C. An investigation of the prevalence of swallowing difficulties and impact on quality of life in patients with advanced lung cancer. *Supportive Care in*

*Cancer*. 2018;26(2):515-519.

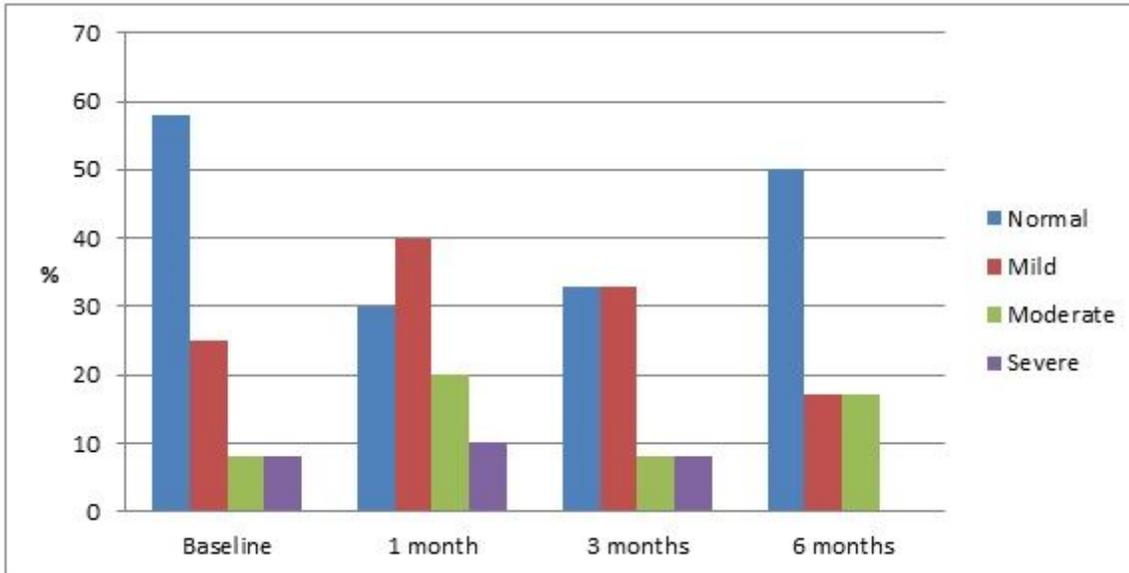
28. Frowen J, Hughes R, Skeat J. The prevalence of patient-reported dysphagia and oral complications in cancer patients. *Supportive Care in Cancer*. 2020;28(3):1141-1150.
29. Everitt S, Callahan J, Obeid E, Hicks RJ, Mac Manus M, Ball D. Acute radiation oesophagitis associated with 2-deoxy-2-[18F] fluoro-d-glucose uptake on positron emission tomography/CT during chemo-radiation therapy in patients with non-small-cell lung cancer. *Journal of Medical Imaging and Radiation Oncology*. 2017;61(5):682-688.
30. Kiss N, Krishnasamy M, Everitt S, Gough K, Duffy M, Isenring E. Dosimetric factors associated with weight loss during (chemo) radiotherapy treatment for lung cancer. *European journal of clinical nutrition*. 2014;68(12):1309-1314.
31. Everitt S, Duffy M, Bressel M, et al. Association of oesophageal radiation dose volume metrics, neutropenia and acute radiation oesophagitis in patients receiving chemoradiotherapy for non-small cell lung cancer. *Radiation Oncology*. 2016;11(1):20.
32. De Ruyscher D, Dingemans AMC, Praag J, et al. Prophylactic cranial irradiation versus observation in radically treated stage III non–small-cell lung cancer: A randomized phase III NVALT-11/DLCRG-02 study. *Journal of Clinical Oncology*. 2018;36(23):2366-2377.
33. Frowen J. Dysphagia in patients with non-head and neck cancer. *Current opinion in otolaryngology & head and neck surgery*. 2019;27(3):162-167.
34. Zhao W-T, Yang M, Wu H-M, Yang L, Zhang X-m, Huang Y. Systematic review and meta-analysis of the association between sarcopenia and dysphagia. *The journal of nutrition, health & aging*. 2018;22(8):1003-1009.
35. Jensen K, Lambertsen K, Torkov P, Dahl M, Jensen A, Grau C. Patient assessed symptoms are poor predictors of objective findings. Results from a cross sectional study in patients treated with radiotherapy for pharyngeal cancer. *Acta Oncologica*. 2007;46(8):1159-1168.
36. Logemann JA, Pauloski BR, Rademaker AW, et al. Xerostomia: 12-Month changes in saliva production and its relationship to perception and performance of swallow function, oral intake, and diet after chemoradiation. *Head and Neck*. 2003;25(6):432-437.
37. Pedersen A, Wilson J, McColl E, Carding P, Patterson J. Swallowing outcome measures in head and neck cancer–How do they compare? *Oral oncology*. 2016;52:104-108.
38. Atkinson TM, Ryan SJ, Bennett AV, et al. The association between clinician-based common terminology criteria for adverse events (CTCAE) and patient-reported outcomes (PRO): a systematic review. *Supportive Care in Cancer*. 2016;24(8):3669-3676.
39. Sarna L, Swann S, Langer C, et al. Clinically meaningful differences in patient-reported outcomes with amifostine in combination with chemoradiation for locally advanced non–small-cell lung cancer: an analysis of RTOG 9801. *International Journal of Radiation Oncology\* Biology\* Physics*. 2008;72(5):1378-1384.
40. Lee CF, Carding PN, Fletcher M. The nature and severity of voice disorders in lung cancer patients. *Logopedics Phoniatrics Vocology*. 2008;33(2):93-103.

# Figures



**Figure 1**

Participant flow and data availability at all time points



**Figure 2**

Dysphagia Handicap Index global score for patient-reported swallowing problems

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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