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Measurement and clinical evaluation of oropharyngeal dysphagia; a multidimensional approach

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Citation

Heijnen, B. J. (2018, November 14). *Measurement and clinical evaluation of oropharyngeal dysphagia; a multidimensional approach*. Retrieved from <https://hdl.handle.net/1887/66614>

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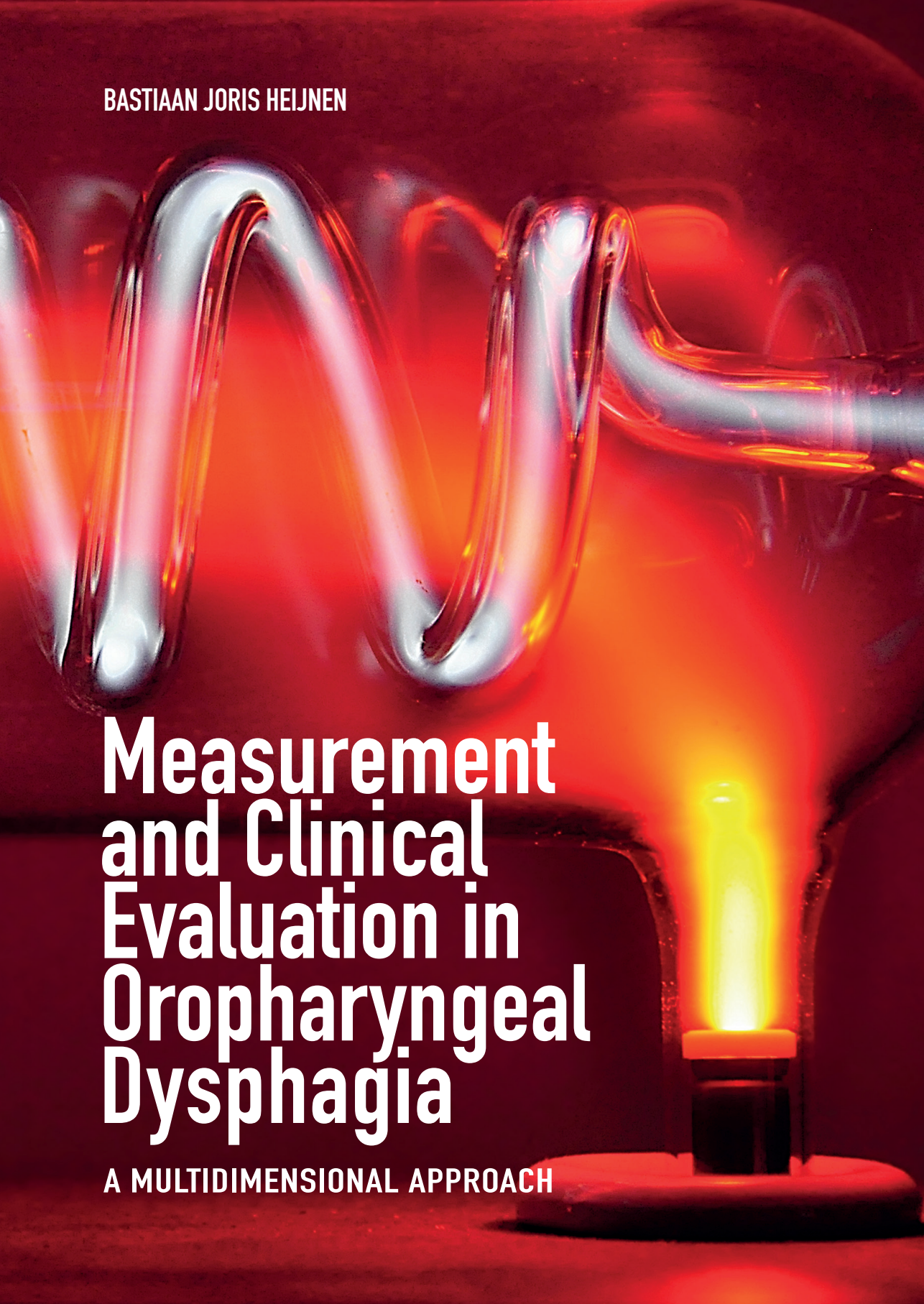


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Author: Heijnen, B.J..

Title: Measurement and clinical evaluation of oropharyngeal dysphagia; a multidimensional approach

Issue Date: 2018-11-14



BASTIAAN JORIS HEIJNEN

Measurement and Clinical Evaluation in Oropharyngeal Dysphagia

A MULTIDIMENSIONAL APPROACH

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Measurement and evaluation in oropharyngeal dysphagia

A multidimensional approach

PhD thesis, Leiden University Medical Centre, Leiden 2018

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ISBN: 978-94-930-1979-9

Picture cover ©2010, Ken Lee. Museum of Neon Art, Los Angeles, U.S.A.

Graphic design by Wendy Schoneveld || wenz iD.nl

Printed by ProefschriftMaken || ProefschriftMaken.nl

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Financial support for the publication of this thesis has been provided by MDS B.V. and Pentax Medical.

Measurement and Clinical Evaluation in Oropharyngeal Dysphagia

A MULTIDIMENSIONAL APPROACH

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van de Rector Magnificus prof.mr. C.J.J.M. Stolker,
volgens besluit van het College voor Promoties
te verdedigen op woensdag 14 november 2018
klokke 15.00 uur

door

Bastiaan Joris Heijnen

geboren te Eindhoven
in 1984

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Prof. dr. I.M. Verdonck – de Leeuw

(Amsterdam UMC & Vrije Universiteit, Amsterdam)

For my grandmother

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1



General Introduction



This first chapter explains the main topic of the thesis, oropharyngeal dysphagia, and the aspects related to its assessment. The chapter presents the research questions addressed in the thesis and briefly introduces the contents of each chapter.

Deglutition

Swallowing, or rather deglutition, is a highly organized sequence of movements and sensory processes that involves fine coordination regulated by both cortical and brainstem processes.[1, 2] Figure 1 shows the various anatomical structures that are involved in swallowing: the lips(1), teeth(2), oral cavity(3), tongue(4), palate(5), pharynx(6), epiglottis(7), larynx(8), esophagus(9), and vocal folds(10).[2] Muscle innervation and sensory feedback are provided by the cranial nerves V, VII, IX, X, XI, and XII.[2, 3]

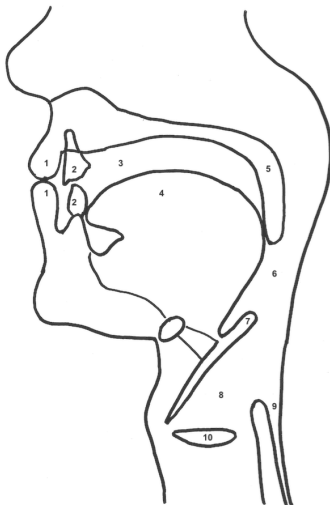


Figure 1. Anatomical structures involved in swallowing.

Swallowing occurs in four phases, starting with the oral preparatory phase (Figure 2A). This phase consists of voluntary actions required before a swallowing reflex is initiated, e.g. mastication and bolus placement. The second is the oral phase (Figure 2B), comprising the oral transport of the bolus to the pharynx, which is the last voluntary act before the swallowing reflex is initiated. The third is the pharyngeal phase (Figure 2C). In this phase, the bolus is transported through the pharynx, the larynx is elevated, the vocal folds are closed, and the tongue and the pharyngeal muscles transport the bolus towards the esophagus. In the fourth and last phase, the esophageal phase

(Figure 2D), the bolus enters the esophagus and is transported towards the stomach by peristaltic movements.[2, 4]

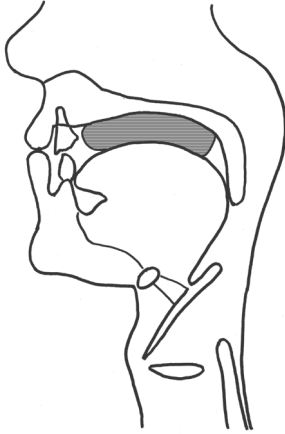


Figure 2A. Oral preparatory phase.

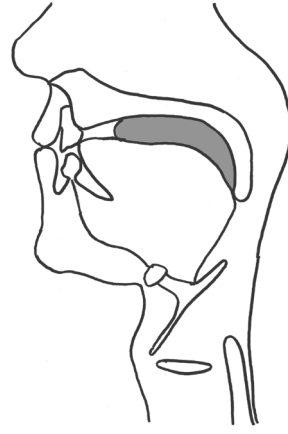


Figure 2B. Oral phase.

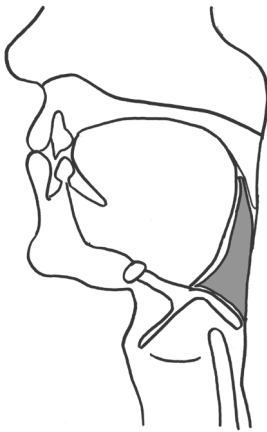


Figure 2C. Pharyngeal phase.



Figure 2D. Esophageal phase.

Swallowing disorders (dysphagia)

The concept of oropharyngeal dysphagia (OD) captures the arduous disruption of the process of transporting solids or liquids from the mouth to the esophagus.[5] This concept includes penetration into the larynx or aspiration of the bolus below the vocal fold level into the trachea[6]. OD can also take the form of oropharyngeal residue or pooling after swallowing.[7] It is associated with malnutrition, dehydration, aspiration

pneumonia, and sudden death. [8-11] Dysphagia is also known to have severe negative impacts on the quality of life. [12, 13].

Prevalence and patient populations

OD is often secondary to iatrogenic, metabolic, myopathic, neurogenic, or structural conditions. The most common causes are neurological, due to stroke or neurodegenerative diseases; the second most common ones are iatrogenic, resulting from surgery or radiation. [7] The prevalence of OD, as reported in the literature, varies from 2 to 16% in a normal population, and older age is associated with higher prevalence.[14] The prevalence of OD varies by medical condition: a prevalence of 8-80% was found after stroke, of 11-81% in Parkinson's disease, and of 27-30% after head trauma.[15]

Screening for dysphagia

The aim of screening for dysphagia is to identify at-risk patients. According to the World Health Organization a screening tool is a simple test to identify a subject with a disease or complaint but without the symptoms. [16] The screening methods should be easy to administer and quick, avoiding burden and invasiveness for the patients. [17] An important feature of a screening tool is that it strikes the right balance between sensitivity and specificity. Sensitivity refers to the proportion of positive-tested subjects who actually have the disease. Specificity is the opposite, referring to the proportion of negative-tested subjects in whom the disease is absent. A sensitivity of 70% and a specificity of 60% is considered a minimal requirement for an OD screening tool. [18]

In everyday medical practice a clinician often starts to investigate the presence of dysphagia by asking the patient whether there are swallowing complaints.[19] In addition, patients can be subjected to a (bedside) dysphagia screening, of which there are several types. Clinical features of aspiration can be noted with or without using a standardized form to determine whether a patient is at risk for dysphagia. Also a trial swallow using water or a substance in different viscosities can be combined with testing oxygen desaturation to detect patients at risk for OD.[17, 18, 20] Examples of evidence-based screening methods are the 3-oz. water swallow test[21], a V-VST (volume-viscosity swallowing test)[22, 23], a TOR-BSST (Toronto Bedside Swallowing Screening Test)[23], and a cough test[24]. A positive result indicates that further assessment for dysphagia is needed. To illustrate, consider the procedure of the 3-oz. water swallow test. A patient is instructed to drink a glass of water (90 cc) all at once. Meanwhile, the patient is observed for signs of aspiration; those may take the form of coughing, choking, clearing the throat, watery eyes, or shortness of breath.

When the subject undergoing screening test scores positive on one of the signs, further assessment for dysphagia is needed.

Assessment for dysphagia

After failing the initial screening, the patient should undergo further dysphagia assessment.[17] The two gold standards are fiberoptic endoscopic evaluation of swallowing (FEES) and videofluoroscopy (VFS). The latter is a radiographic examination of the swallowing act, which allows the investigator to visualize the complete trajectory of the swallowing act from mouth to stomach. VFS may show abnormal structures, pathological muscle activity, penetration, aspiration, and passage problems (Figure 3A). A disadvantage of VFS is the X-ray load for the patient.[2] The other gold standard, FEES, is the observation of swallowing in real time with a flexible nasendoscope introduced via the nose into the pharynx. By showing the swallowing act in motion, FEES gives information about the occurrence of penetration, aspiration, or passage problems (Figure 3B). In contrast to VFS, however, it only shows the swallowing act in the pharyngeal phase, not after passing through the upper esophageal sphincter and below. Another disadvantage derives from the short interval during swallowing in which there is a white-out due to muscle contractions.[25]

Patient-perceived aspects of dysphagia

Functional Health Status (FHS) is the ability to perform tasks in multiple domains [26] and it serves as an indicator of the influence of a given disease on particular functional

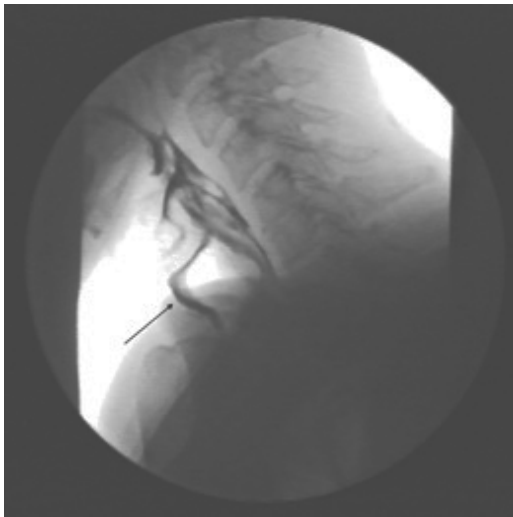


Figure 3A. VFS shows aspiration of thin liquids.

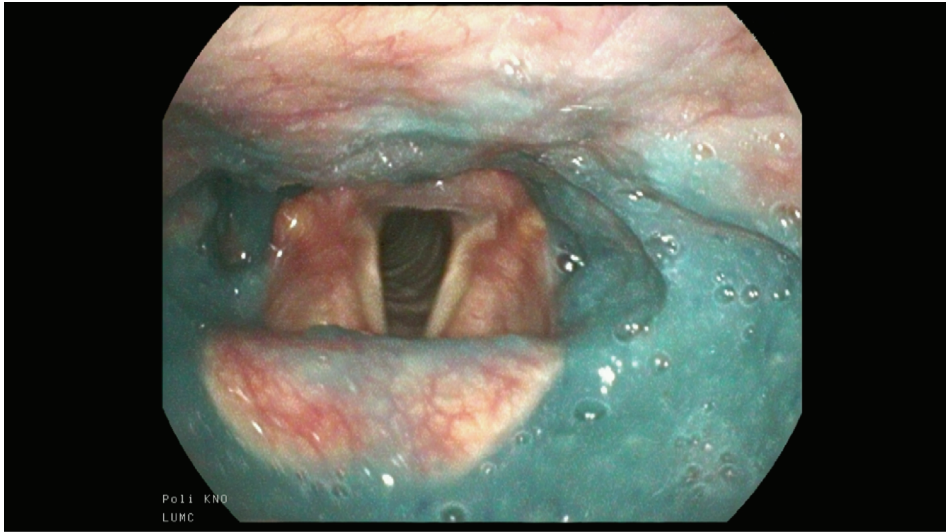


Figure 3B. FEES shows residue after swallowing with penetration of blue-dyed thick liquids. The residue creates the risk of aspiration.

aspects of a person. In dysphagia, FHS assessment quantifies the severity of the symptoms. This measure is complemented by Health-Related Quality of Life (HRQoL), which refers to the unique perception individuals may have of their health, taking into account social, functional, and psychological issues.[26] HRQoL can be divided into generic HRQoL and disease-specific HRQoL. The latter evaluates HRQoL in patients with a specific diagnosis and takes the characteristics and conditions of a disease into account. It has to be sensitive to measure the effects of a condition or intervention. [27] Generic HRQoL is able to measure a wide variety of characteristics, including clinical and sociodemographic features.

The severity that the consequences of dysphagia may have on different aspects of a patient's life, as measured in terms of either FHS or HRQoL, is usually ascertained from patient self-report questionnaires. Before a questionnaire can be used in everyday clinical practice or for research purposes, however, its measurement properties (its reliability, validity, and responsiveness) should be evaluated and be judged sufficient. [28, 29] These aspects are, among other characteristics, described in psychometrics.

Psychometrics

Psychometrics refers to the construction and validation of measurement instruments. [30] The main domains for checking whether a questionnaire is a reliable and valid form of measurement, as determined by the COSMIN taxonomy of measurement

properties and definitions for health-related patient-reported outcomes (HR-PRO), are reliability, validity, and responsiveness.[28] Reliability is the degree to which a measure is free from measurement error. Validity is the degree to which an HR-PRO instrument measures the construct it purports to measure. Responsiveness is the ability of an HR-PRO instrument to detect change over time in the construct to be measured.[28] Only measures or questionnaires with psychometric properties that are deemed sufficient should be used to evaluate a patient's status or treatment outcome.

Treatment of dysphagia

When the assessments show significant abnormalities, treatment is indicated. There are six categories of treatment modalities for OD.[31] The first is bolus modification and management, which includes adjusting the viscosity, volume, temperature, and/or acidity of the bolus. The second comprises behavioral techniques such as oral motor exercises. The third is sensory and neurophysiologic stimulation, for example taste or temperature adaptation or electrical stimulation. The fourth is postural adjustment, e.g. chin-tuck or head-turn maneuvers. The fifth consists of swallow maneuvers such as effortful swallow or Mendelsohn maneuver, the latter referring to prolonging the larynx in a high position to prevent aspiration. And the last is adjunctive biofeedback, which gives a patient visual information on the swallowing act.[2, 31-33]

AIM AND SCOPE

The aim of this thesis is to improve the measurement and evaluation of OD, focusing on the use of patient self-report measures.

The first study, presented in chapter 2, investigates the effects of radiochemotherapy on dysphagia, voice, speech, and trismus in patients with head and neck cancer (HNC). HNC patients suffer from various functional, physical, and emotional impairments due to both the primary illness and the secondary consequences of the tumor treatment [34]. Head and neck oncological treatments can have a severe impact on the anatomical structures, organ function, and quality of life [35].

A systematic review was conducted to study the effects of radiotherapy or chemotherapy on functions of the upper aerodigestive tract, including swallowing, in HNC patients. Data on patient characteristics, interventions, outcome measures, and treatment effects were summarized. Furthermore, the available evidence on interventions by speech pathologists was examined.

In chapter three, therapy effects are compared to determine the effects of traditional therapy and neuromuscular electrical stimulation (NMES) on patient self-reported

HRQoL in patients with Parkinson's disease and OD. NMES may be a therapeutic adjunct to known interventions in the treatment of OD [36-38]. The rationale underpinning NMES is that stimulation of muscle fibers by stimulating the nerve and the motor end plate would result in a re-education of the functional muscle-contraction patterns[38, 39].

In a randomized controlled trial the effects of adjunctive NMES in dysphagic Parkinson's disease patients were compared to traditional speech language therapy for dysphagia treatment with HRQoL as the primary outcome measure. It was hypothesized that NMES would not only lead to significant improvement of the swallowing function but would also contribute to an increased HRQoL in these patients.

Chapter 4 makes a comparison between daily clinical practice and the use of screening tools. It determines the diagnostic performance of daily clinical practice versus patient self-report tools in patients with OD. In daily clinical practice, a single question such as 'What about swallowing?' is frequently used without any additional standardized testing. The purpose of this study was to compare the diagnostic performance of a single question on swallowing with the FHS questionnaire EAT-10[40] as reference test. It was hypothesized that a single question, 'What about swallowing?', would show poor diagnostic performance when compared to the EAT-10. It was expected that the single question would have insufficient sensitivity and specificity to identify patients at risk of dysphagia.

In chapter 5 the reliability and validity of common self-report measures in OD are determined. Quality of life is considered to be an important patient-reported outcome measure in objectifying the current health status or therapy effects in patients with OD. In this study, the validity and reliability of the Dutch version of the Deglutition Handicap Index (DHI) and the MD Anderson Dysphagia Inventory (MDADI) were determined in oncological patients with OD.

Chapter 6 explores the predictive value of self-report measures for aspiration. The presence of aspiration is the most critical clinical sign of OD. Screening for and detecting OD may be done in several ways, but the gold standard is FEES or VFS. Unfortunately, the gold standard is often not available when dysphagia has to be assessed. The purpose of this study was to build a model to forecast aspiration in patients with OD using common patient self-evaluation questionnaires and oral intake status. Logistic regression was used to build a model to predict aspiration. Performance of the model was evaluated by constructing receiver operating characteristic (ROC) curves and computing the area under the curve (AUC).

Chapter 7 provides a general summary and draws some conclusions. On that basis, a number of recommendations for future research are made.

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2



Dysphagia, speech, voice and trismus following radiotherapy and/or chemotherapy in patients with head and neck carcinoma: a review of literature

Published in: Biomed Res Int. 2016;2016:6086894.

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ABSTRACT

Introduction

Patients with head and neck cancer suffer from various impairments due to the primary illness, as well as secondary consequences of the oncological treatment. This systematic review describes the effects of radiotherapy and/or chemotherapy on the functions of the upper aerodigestive tract in patients with head and neck cancer.

Methods

A systematic literature search was performed by two independent reviewers using the electronic databases PubMed and Embase. All dates up to May 2016 were included.

Results

Of the 947 abstracts, sixty articles met the inclusion criteria and described one or more aspects of the sequelae of radiotherapy and/or chemotherapy. Forty studies described swallowing-related problems, 24 described voice-related problems, seven described trismus and 25 studies described general quality of life. Only 14 articles reported that speech pathologists conducted the interventions, of which only six articles described in detail what the interventions involved.

Conclusion

In general, voice quality improved following intervention, whereas quality of life, dysphagia and oral intake deteriorated during and after treatment. However, as a consequence of the diversity in treatment protocols and patient characteristics, the conclusions of most studies cannot be easily generalised. Further research on the effects of oncological interventions on the upper aerodigestive tract is needed.

INTRODUCTION

Head and neck oncological patients suffer from various functional, physical, and emotional impairments due to both the primary illness and the secondary consequences of the tumor treatment [1]. The oncological treatment of head and neck tumors depends on the location and the stage of the tumor, as well as the treatment preferences of the individual patient. Head and neck oncological treatment can include surgery, radiotherapy, chemotherapy or combinations of these. The impact of head and neck oncological treatments on the anatomical structures, organ function and the quality of life (QoL) should not be underestimated [2]. For instance, the implications of loss of function for people treated non-surgically for head and neck cancer (HNC) and its detrimental effects on functioning and QoL are well documented [3].

In order to assist people with dysphagia to adjust to, and live successfully with the sequelae of the primary condition, speech pathologists managing this caseload need to ensure post-treatment services are available [4] that address not only the physical but also the emotional and psychosocial needs. A qualitative study by Nund et al. [5] exploring dysphagia management by speech pathologists suggests that care givers generally feel ill-prepared for their role. Furthermore, this study suggests that clinicians should provide adequate and timely training and support to carers. Furthermore, Krisciunas et al. [6] concluded that within speech pathology there is no standardised therapy for HNC patients and scant evidence to support any particular protocol. As a result, institutions and individual speech pathologists need to develop their own protocols based on 'standard' practices or anecdotal evidence.

Evidence-based practice (EBP) is hailed to be paramount in the practice of speech pathology [7]. The American Speech-Language-Hearing Association (ASHA) defines evidence-based practice as, "...an approach in which current, high-quality research evidence is integrated with practitioner expertise and client preferences and values, into the process of making clinical decisions" [8]. Essentially, EBP involves moving the foundation for clinical decisions from clinical protocols centered solely on expert opinion to the integration of clinical expertise, the best current research evidence, and individual client values. To facilitate EBP in healthcare, clinical practice guidelines can be developed to summarise clinically relevant evidence [9].

Several reviews have been published about the outcomes after radiotherapy and/or chemotherapy in HNC patients (e.g., Frowen et al. [10]; Jacobi et al. [11]; van der Molen et al. [12]; Paleri et al. [13]; Roe et al. [14]). Most of the reviews focused on selected functional domains in populations with HNC: health-related QoL [15], swallowing [13, 14, 16], and voice and speech [11]. Only the review by van der Molen et al. [12] covered a wider range of functional outcomes in patients with advanced HNC, including

swallowing, mouth opening, nutrition, pain and QoL. Further, the purpose of some studies was to provide evidence-based clinical guidelines (e.g., Paleri et al. [13]) and did not perform systematic literature searches in line with the PRISMA guidelines [17]. As such, even though a number of reviews have been published over the last ten years, a comprehensive updated systematic review is needed that includes all functional domains affected by radiotherapy and/or chemotherapy in patients with head and neck carcinoma.

A systematic review was conducted to describe the effects of radiotherapy and/or chemotherapy on functions of the upper aerodigestive tract in patients with HNC and examined the evidence of interventions by speech pathologists.

METHODS

A systematic literature search was performed by two independent reviewers. The electronic biomedical databases PubMed and Embase were used (search period from start of database until 5 May 2016). The searches were limited to English language publications. In Pubmed the MeSH terms *larynx* or *hypopharynx* were combined with all MeSH terms related to head and neck neoplasms (Table 1). Next, the results were linked to all MeSH terms for chemotherapy or radiotherapy, after which the outcome was combined with all MeSH terms found for dysfunctions of the upper aerodigestive tract and limited with adults +19 years. The exact syntax of the literature search is presented in Table 1.

In Embase the thesaurus terms *larynx* or *hypopharynx* were linked to *neoplasm* and *radiotherapy* or *chemotherapy*. Next, the search outcome was combined with the following terms: *dysphagia*, *speech*, *speech disorder*, *voice*, *dysphonia*, *xerostomia*, *quality of life*, *dysarthria* or *trismus* (see Table 1).

To identify the most recent publications, the search was complemented by free-text words in PubMed and Embase (for the period after April 2015 until May 2016). Truncation symbols and wildcards were used to search for variant forms of words or word extensions. *Laryn**, *pharyn** or *hypopharyn** were combined with *cancer**, *neoplasm**, *tumour** or *carcinoma**. Furthermore, these free text words were combined with *radiation**, *radiotherap**, *chemotherap**, *adjuvant therap** or *radiochemotherap** and, finally, combined with *deglut**, *swallow**, *dysphag**, *speech**, *voic**, *articulat**, *dysphon**, *quality of life**, *xerostom**, *dysarthr** or *anarthr**.

Only articles presenting both pre- and post-intervention data of the upper aerodigestive tract functions of the participants were included. Review articles and studies with a population sample of less than 20 patients were excluded, as well as experiments on

Table 1. Search strategies per literature database

Database and Search Terms	Limits	Number of records
Subject Headings Embase: (larynx/ OR pharynx/ OR hypopharynx/) AND (neoplasm/ OR larynx disorder/ OR pharynx disorder/ OR larynx cancer/ OR larynx carcinoma/ OR pharynx cancer/ OR pharynx carcinoma/) AND (radiotherapy/ OR chemotherapy/ OR chemoradiotherapy/ OR adjuvant therapy/ OR drug therapy/) AND (speech sound disorder OR speech/ or speech disorder/ OR swallowing/ OR dysphagia/ OR dysphonia/ OR voice disorder/ OR aphonia/ OR speech intelligibility/ OR xerostomia/ OR dysarthria/ OR esophagus speech/ OR larynx prosthesis/ OR trismus/ OR "quality of life"/)	English	201
PubMed: ("Larynx"[Mesh] OR "Pharynx"[Mesh] OR "Hypopharynx"[Mesh]) AND ("Neoplasms"[Mesh] OR "Head and Neck Neoplasms"[Mesh] OR "Neoplasms, Second Primary"[Mesh] OR "Pharyngeal Neoplasms"[Mesh] OR "Oropharyngeal Neoplasms"[Mesh] OR "Tonsillar Neoplasms"[Mesh] OR "Nasopharyngeal Neoplasms"[Mesh] OR "Mouth Neoplasms"[Mesh] OR "Laryngeal Neoplasms"[Mesh] OR "Tongue Neoplasms"[Mesh] OR "Thyroid Neoplasms"[Mesh] OR "Salivary Gland Neoplasms"[Mesh] OR "Jaw Neoplasms"[Mesh] OR "Lip Neoplasms"[Mesh] OR "Thyroid Carcinoma, Anaplastic"[Mesh] OR "Neoplasms, Squamous Cell"[Mesh] OR "Neoplasms, Basal Cell"[Mesh] OR "Otorhinolaryngologic Neoplasms"[Mesh] OR "Hypopharyngeal Neoplasms"[Mesh] OR "Laryngeal Diseases"[Mesh] OR "Pharyngeal Diseases"[Mesh]) AND ("Radiotherapy"[Mesh] OR "Radiotherapy, Adjuvant"[Mesh] OR "Radiotherapy, High-Energy"[Mesh] OR "Radiotherapy, Image-Guided"[Mesh] OR "Radiotherapy, Intensity-Modulated"[Mesh] OR "Radiotherapy, Conformal"[Mesh] OR "Radiotherapy, Computer-Assisted"[Mesh] OR "Radiotherapy Planning, Computer-Assisted"[Mesh] OR "Radiotherapy Dosage"[Mesh] OR "Brachytherapy"[Mesh] OR "Radiosurgery"[Mesh] OR "Radiation Oncology"[Mesh] OR "Dose-Response Relationship, Radiation"[Mesh] OR "Consolidation Chemotherapy"[Mesh] OR "Induction Chemotherapy"[Mesh] OR "Maintenance Chemotherapy"[Mesh] OR "Chemotherapy, Adjuvant"[Mesh] OR "Chemotherapy, Cancer, Regional Perfusion"[Mesh] OR "Drug Therapy"[Mesh] OR "Drug Therapy, Combination"[Mesh] OR "Radiotherapy"[Mesh] OR "Radiation Dosage"[Mesh]) AND ("Articulation Disorders"[Mesh] OR "Speech"[Mesh] OR "Speech Sound Disorder"[Mesh] OR "Speech, Esophageal"[Mesh] OR "Speech, Alaryngeal"[Mesh] OR "Speech Intelligibility"[Mesh] OR "Speech Disorders"[Mesh] OR "Deglutition Disorders"[Mesh] OR "Deglutition"[Mesh] OR "Dysphonia"[Mesh] OR "Voice Disorders"[Mesh] OR "Hoarseness"[Mesh] OR "Aphonia"[Mesh] OR "Xerostomia"[Mesh] OR "Dysarthria"[Mesh] OR "Larynx, Artificial"[Mesh] OR "Speech, Esophageal"[Mesh] OR "Trismus"[Mesh] OR "Quality of Life"[Mesh])	Adult: 19+ years English	304
Free Text Embase: (larynx* OR pharynx* OR hypopharynx* OR laryngo* OR larynge*) AND (cancer OR cancers OR neoplasm* OR tumour* OR tumor OR tumors OR carcinoma*) AND (radiation* OR radiotherap* OR chemotherap* OR adjuvant therap* OR radiochemotherap*) AND (deglut* OR swallow* OR dysphag* OR speech* OR voic* OR hoarse* OR aphon* OR rough* OR articul* OR dysphon* OR (quality AND life) OR xerostom* OR dysarthr* OR anarthr* OR trismus)	Publication date: last year	397
PubMed: <i>As per Embase Free Text</i>	Publication date: from 2015/05/05 to 2016/05/05	148

animals or articles not published in English. Furthermore, studies published before 1990, case reports, expert opinions, and articles describing combinations of therapy including surgical interventions were excluded.

Final decisions on inclusion were made based on the original articles by consensus between two expert reviewers in accordance with the PRISMA statement [17]. The reference lists of all the included articles were searched for additional literature. Next, the standard quality assessment QualSyst as described by Kmet et al. [18] was performed in order to evaluate the methodological strength and weaknesses of the included studies. All ratings were performed by two independent reviewers. After consensus, studies with poor methodology scores (<50%) were excluded. All included articles were classified according to the Australian National Health and Medical Research Council (NHMRC) Evidence Hierarchy [19]. Data were retrieved from all studies and tabulated; further details on selected speech pathology interventions were summarised separately.

RESULTS

Using MeSH or thesaurus terms, 304 articles were located in PubMed and 201 in Embase. Free-text word searches resulted in another 148 articles in PubMed and 397 in Embase. The combination of these searches, without overlap, yielded 947 articles. Figure 1 outlines the PRISMA reviewing process according to Moher et al. [20]. Sixty articles met all inclusion criteria.

Table 2 shows the outcomes of the QualSyst critical appraisal tool by Kmet et al. [18]. As all studies had sufficient methodological quality, no further studies were excluded; the overall methodological quality ranged from adequate to good with 0 studies ranked as poor, 3 studies as adequate, 3 studies as good, and 54 studies as strong. Based on the NHMRC Evidence Hierarchy [19], 6 studies were classified as level II evidence and 54 studies as level III evidence.

All 60 studies focussed on different functions of the upper aerodigestive tract following radiotherapy and/or chemotherapy for HNC. The following constructs were evaluated across the different studies: communication (voice and speech), functions of the digestive tract (oral intake, weight loss, dysphagia, trismus, xerostomia and tube dependency), QoL and overall survival rates.

Table 3 provides a summary of the 60 retrieved observational and intervention studies that met the inclusion criteria. The first column presents the reference of the author(s). The second column represents the number of subjects, the third column the etiology of the head and neck malignancies and the 4th column displays the staging of the

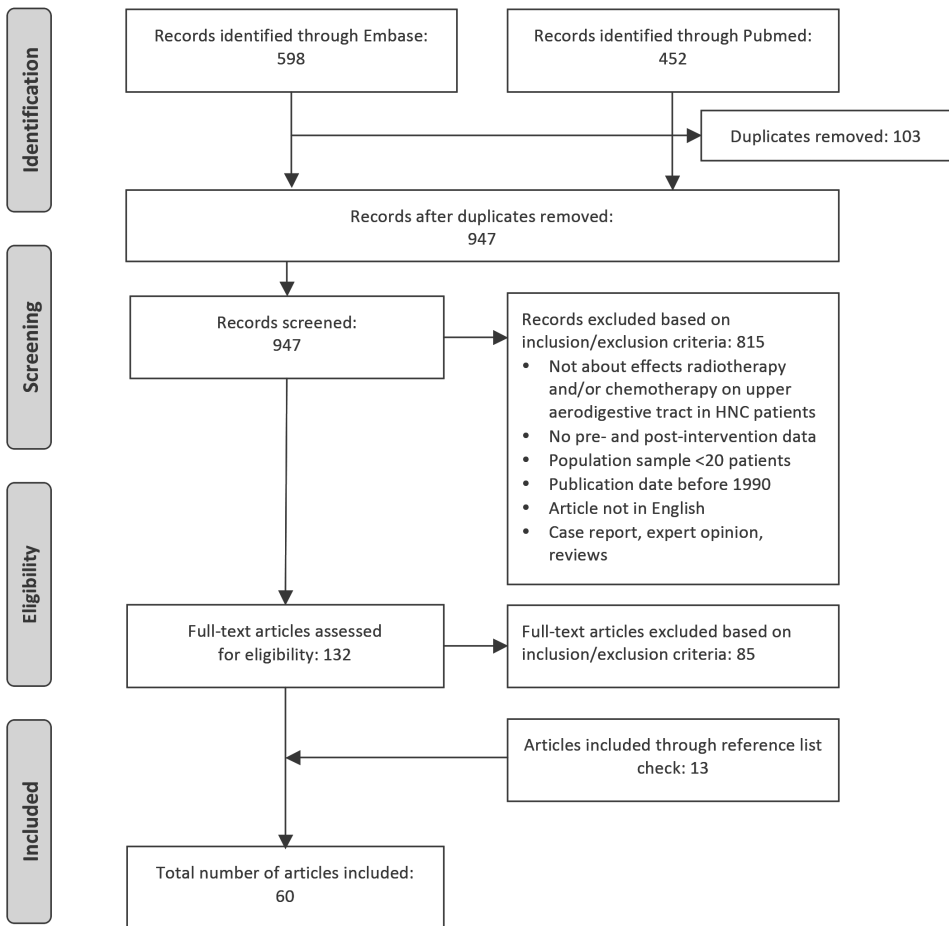


Figure 1. PRISMA Flow chart

malignancies. The 5th column shows whether voice and/or speech, digestive tract and QoL were studied. The 6th and 7th columns show the evaluation techniques and the treatment, respectively. The 8th column present the follow-up and the last column describes the author's key findings.

Voice and/or speech function

Twenty-four studies evaluated voice and/or speech function [21-43] with a follow-up time ranging from 1 month follow-up [42] to ten years follow-up [43]. Most studies included patients with laryngeal tumors only, however 11 studies [22, 25, 30, 31, 34-38,

44] also included non-laryngeal tumors. Seventeen studies [21, 23, 24, 26, 28, 29, 31-33, 35, 36, 38-43] included patients with low-grade tumors (i.e., T1, T2), 15 studies included patient with advanced tumors [22, 23, 25, 27, 30-38, 42, 44].

Table 2. Methodological quality based on QualSyst critical appraisal tool by Kmet et al. 2004 [18] and NHMRC 1999 [19] evidence level of included articles

Reference	Kmet score (%)	Methodological Quality ¹	NHMRC level of evidence ²
Aaltonen et al. 2014 [24]	25 / 28 (89%)	Strong	II
Ackerstaff et al. 2009 [25]	22 / 28 (79%)	Good	II
Agarwal et al. 2009 [26]	19 / 24 (79%)	Good	III-2
Agarwal et al. 2011 [45]	17 / 20 (85%)	Strong	III-3
Akst et al. 2004 [46]	17 / 20 (85%)	Strong	III-3
Al-Mamgani et al. 2012 [27]	19 / 20 (95%)	Strong	III-3
Al-Mamgani et al. 2012 [47]	21 / 22 (95%)	Strong	III-3
Al-Mamgani et al. 2013 [28]	21 / 22 (95%)	Strong	III-3
Al-Mamgani et al. 2015 [29]	21 / 22 (95%)	Strong	III-3
Arraras Urdaniz et al. 2005 [77]	18 / 20 (90%)	Strong	III-2
Bansal et al. 2004 [30]	14 / 24 (58%)	Adequate	III-3
Bibby et al. 2008 [21]	18 / 22 (82%)	Strong	III-2
Bottomley et al. 2013 [78]	24 / 28 (86%)	Strong	II
Buchbinder et al. 1993 [48]	14 / 26 (54%)	Adequate	III-1
Caudell et al. 2010 [49]	21 / 22 (95%)	Strong	III-3
Christianen et al. 2015 [50]	21 / 22 (95%)	Strong	III-3
Cohen et al. 2006 [74]	19 / 20 (95%)	Strong	III-3
Dornfeld et al. 2007 [22]	17 / 22 (77%)	Strong	III-3
Dijkstra et al. 2007 [51]	19 / 22 (86%)	Strong	III-3
Feng et al. 2007 [52]	19 / 22 (86%)	Strong	III-3
Feng et al. 2010 [53]	20 / 20 (100%)	Strong	III-3
Frowen et al. 2009 [16]	22 / 22 (100%)	Strong	III-2
Haderlein et al. 2013 [54]	17 / 20 (85%)	Strong	III-3
Hutcheson et al. 2014 [55]	18 / 20 (90%)	Strong	III-3
Jacobi et al. 2016 [31]	17 / 18 (94%)	Strong	III-3
Karlsson et al. 2015 [32]	26 / 28 (93%)	Strong	II
Karlsson et al. 2016 [33]	18 / 20 (90%)	Strong	III-3
Kazi et al. 2008 [34]	17 / 20 (85%)	Strong	III-2
Kerr et al. 2015 [35]	19 / 20 (95%)	Strong	III-2
Kotz et al. 2012 [56]	24 / 28 (86%)	Strong	II

Table 2. *Continued*

Reference	Kmet score (%)	Methodological Quality ¹	NHMRC level of evidence ²
Kraaijenga et al. 2015 [36]	19 / 20 (95%)	Strong	III-3
Kumar et al. 2014 [57]	19 / 20 (95%)	Strong	III-2
Lazarus et al. 2014 [38]	19 / 20 (95%)	Strong	III-3
List et al. 1999 [75]	15 / 18 (83%)	Strong	III-3
McLaughlin et al. 2009 [58]	19 / 20 (95%)	Strong	III-3
Mittal et al. 2001 [37]	16 / 20 (80%)	Strong	III-3
Murry et al. 1998 [59]	11 / 20 (55%)	Adequate	III-3
Niedzielska et al. 2010 [39]	17 / 20 (85%)	Strong	III-2
Nourissat et al. 2010 [60]	23 / 26 (88%)	Strong	III-3
Ottoson et al. 2014 [61]	19 / 22 (86%)	Strong	III-3
Pauli et al. 2012 [62]	19 / 22 (86%)	Strong	III-3
Pauloski et al. 2006 [63]	18 / 20 (90%)	Strong	III-3
Rademaker et al. 2003 [64]	17 / 20 (85%)	Strong	III-3
Remmelts et al. 2013 [40]	18 / 20 (90%)	Strong	III-3
Salama et al. 2008 [65]	17 / 20 (85%)	Strong	III-3
Sanguineti et al. 2014 [23]	19 / 20 (95%)	Strong	III-3
Scrimger et al. 2007 [66]	18 / 20 (90%)	Strong	III-3
Spector et al. 1999 [41]	17 / 22 (77%)	Good	III-3
Starmer et al. 2014 [67]	18 / 20 (90%)	Strong	III-3
Stenson et al. 2009 [68]	16 / 20 (80%)	Strong	III-3
Strigari et al. 2010 [69]	17 / 20 (85%)	Strong	III-3
Tuomi et al. 2015 [42]	18 / 20 (90%)	Strong	III-2
Vanshtein et al. 2015 [70]	20 / 24 (83%)	Strong	III-3
van der Molen et al. 2010 [76]	24 / 26 (92%)	Strong	II
van der Molen et al. 2012 [44]	16 / 20 (80%)	Strong	III-3
van der Molen et al. 2013 [71]	19 / 20 (95%)	Strong	III-3
Verdonck-de Leeuw et al. 1999 [43]	18 / 20 (90%)	Strong	III-2
Verdonck-de Leeuw et al. 2014 [79]	16 / 20 (80%)	Strong	III-2
Vlachich et al. 2014 [72]	18 / 20 (90%)	Strong	III-3
Wilson et al. 2011 [73]	18 / 20 (90%)	Strong	III-3

¹ Methodological quality: strong >80%; good 60 – 79%; adequate 50 – 59; poor <50.

² NHMRC Evidence Hierarchy designates the following hierarchy: Level I (evidence obtained from a systematic review of all relevant RCTs), level II (evidence obtained from at least one properly designed RCT), level III-1 (evidence obtained from well-designed pseudo-RCTs [alternate allocation or some other method]), level III-2 (evidence obtained from comparative studies with concurrent controls and allocation not randomised [cohort studies], case control studies, or interrupted time series with a control group), level III-3 (evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group), and level IV (evidence obtained from case series, either post-test or pre-test and post-test).

Nine studies [21, 26, 31, 33, 34, 36, 39, 42, 44] used acoustic analysis to evaluate voice quality, six studies [27-29, 35, 36, 40] used the Voice Handicap Index and three studies [24, 39, 43] used videolaryngostroboscopy. In several studies, either descriptions of how voice quality was evaluated were missing or non-validated tools were used (e.g., patients self-reporting or trial-specific questionnaires). Only four studies [23, 26, 32, 44] reported whether the patient received any voice therapy.

All the studies reported good to excellent outcomes for voice quality at long term follow-up. Some studies specifically reported pre- to post-treatment improvements of voice or speech quality following radiotherapy and/or chemotherapy [21, 25, 26]. However, other studies [23, 38, 42, 44] reported a deterioration after therapy at long term follow-up. Al-Mamgani et al. [29] found a better voice outcome in case of single vocal cord irradiation compared with irradiation of the whole larynx. Mittal et al. [37] concluded that radiation with tissue/dose compensation (TDC) improved articulatory outcome compared to radiation without TDC.

Functions of the digestive tract

Forty studies [16, 22, 25, 35-38, 42, 45-76] describe the effects of radiotherapy and/or chemotherapy on the functions of the digestive tract and used a variety of outcome measures. Of these 40 studies, 16 studies [16, 36, 37, 45, 49, 52, 53, 55, 57, 61, 63, 65, 67, 68, 71, 76] used videofluoroscopy to measure physiological changes in swallowing function. Eight studies [22, 36, 46, 47, 49, 54, 58, 72] used feeding tube dependency as a (dichotomous) outcome, whereas seven studies [36, 46, 56, 63, 64, 67, 76] described the level of oral intake in more detail. Only four studies [36, 38, 55, 73] used a condition specific validated measure for swallowing disorders (e.g. MDADI).

With regard to nutritional status, five studies [22, 58, 60, 61, 76] used the body mass index as an outcome or reported specifically on weight gain or loss. Seven studies [36, 38, 48, 51, 62, 71, 76] used the presence of trismus as an outcome by reporting on the maximum distance of mouth opening. Saliva flow (as a measure of xerostomia) was used in four studies [37, 38, 66, 69].

Follow-up times in these studies range from immediately post-therapy [60] to 6 years post-therapy [36], describing both low stage tumors and more advanced tumors. Thirty-two studies used the TNM-classification system, stage was described in six other studies and the remaining two studies did not report on tumor stage or grade. However, it was unclear whether the clinical TNM-score or the pathological TNM-score was used to describe the severity of the disease. Eight studies [16, 36, 46, 48, 51, 55, 56, 67, 71, 76] described whether the patients received functional treatment (by a speech pathologist); the remainder of the articles did not mention whether the patient received any additional treatment.

Table 3. Overview of included observational and intervention studies (N = 60) that met eligibility criteria

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Aaltonen et al. 2014 [24]	N=56	Glottic = 56 (100%)	T1a = 56 (100%)	V	Videolaryngostroboscopy Expert rating (GRBAS) Patient self-rating (VAS) hoarseness and impact on everyday life	Group 1: laser surgery (n=31) Group 2: RT (n=25)	6, 24 months	Similar overall voice quality for both groups. Laser surgery yielded more breathiness compared to RT.
Ackerstaff et al. 2009 [25]	N=207	Oral cavity = 40 (19%) Oropharyngeal = 129 (62%) Hypopharyngeal = 38 (19%)	T3 = 65 (31%) T4 = 142 (69%)	V D QoL	EORTC QLQ-C30 EORTC QLQ-H&N35 Trial-specific questionnaires	Group 1: intra-arterial cisplatin 4 weekly (n=104) + RT Group 2: intravenous cisplatin 3 weekly (n=103) + RT	7 weeks; 3 months; 1, 2, 5 years	Both groups showed improved oral intake and voice quality, at 1 year follow-up often better compared to baseline.
Agarwal et al. 2009 [26]	N=50	Glottic = 50 (100%)	T1 = 33 (66%) T2 = 17 (34%)	V	Voice analysis Acoustic parameters: frequency, intensity, perturbation Patient-reported improvement in voice quality	RT	3-6 months	A trend for improvement in voice quality following RT was found.
Agarwal et al. 2011 [45]	N=47	Oropharyngeal Hypopharyngeal Laryngeal (No details provided)	T1 T2 T3 T4 (No details provided)	D	Videofluoroscopy PSSHN	CRT	2, 6, 12 months	Significant impairment of swallowing and aspiration.
Akst et al. 2004 [46]	N=196	Oral cavity = 12 (6%) Base of tongue = 41 (21%) Tonsil = 41 (21%) Other oropharyngeal = 15 (8%) Hypopharyngeal = 34 (17%) Laryngeal = 50 (26%) Unknown = 3 (1%)	T1 = 15 (8%) T2 = 42 (21%) T3 = 65 (33%) T4 = 70 (36%) Unknown = 4 (2%)	D	Presence of feeding tube Presence of tracheotomy Level of oral diet	CRT	3, 6, 12, 24 months	A majority of patients did not need a tracheotomy but need a feeding tube during treatment. At 1 year follow-up most patients had a (nearly) normal oral intake. Patients with tumor stage IV and age ≥ 60 had prolonged feeding tube use and slower recovery.
Al-Mangani et al. 2012 [27]	N=170	Supraglottic = 121 (71%) Glottic = 49 (29%)	T3 = 170 (100%)	V QoL	EORTC QLQ-C30 EORTC QLQ-H&N35 VHI	Group 1: CRT (n=48) Group 2: RT (n=122)	2, 4, 6 weeks; 3, 6, 12 months	Adding chemotherapy to RT did not diminish QoL or voice handicap.
Al-Mangani et al. 2012 [47]	N=176	Hypopharyngeal = 176 (100%)	T1 = 18 (10%) T2 = 55 (31%) T3 = 56 (32%) T4a = 35 (20%) T4b = 12 (7%)	D QoL	Tube dependency EORTC QLQ-C30 EORTC QLQ-H&N35	Group 1: CRT (n=102) Group 2: RT (n=74)	2, 4, 6 weeks; 3, 6 months; 1, 2 years	CRT significantly improved functional outcome. Acute toxicity increased but late radiation side effects did not increase.

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Al-Mangami et al. 2013 [28]	N=1050	Glottic = 1050 (100%)	T1a = 551 (52%) T1b = 168 (16%) T2a = 209 (20%) T2b = 122 (12%)	V QoL	EORTC QLQ-C30 EORTC QLQ-H&N35 VHI	RT	4, 6 weeks; 3, 6, 12, 18, 24, 36, 48 months	Excellent outcome with good QoL and VHI scores.
Al-Mangami et al. 2015 [29]	N=30	Glottic = 30 (100%)	T1a = 30 (100%)	V	Laryngoscopy VHI	Single vocal cord RT	4, 6, 12 weeks; 6, 12, 18 months	Single vocal cord RT showed better voice quality compared to whole larynx RT.
Arraras Urdaniz et al. 2005 [77]	N=60	Paranasal sinuses = 3 (5%) Nasopharyngeal = 3 (5%) Oral cavity = 2 (3%) Oropharyngeal = 25 (42%) Hypopharyngeal = 9 (15%) Laryngeal = 18 (30%)	T2 = 2 (3%) T3 = 20 (33%) T4 = 38 (64%)	QoL	EORTC QLQ-C30 EORTC QLQ-H&N35	Group 1: hyperfractionated concomitant boost RT + cisplatin (n=30) Group 2: hyperfractionated conventional RT + cisplatin (n=30)	1 month	QoL in both groups was relatively good. QoL improved in the follow-up period.
Bansal et al. 2004 [30]	N=45	Base of tongue = 20 (44%) Tonsil = 10 (22%) Unknown = 15 (33%)	Stage III = 17 (38%) Stage IV = 23 (51%) Not reported = 5 (11%)	V QoL	Acute and late morbidity scoring of skin, oropharyngeal mucosa, salivary glands, larynx and oesophagus (LENT/SOMA) EORTC QLQ-C30	RT	1, 4 months	During RT a decline in all QoL domains was found. QoL improved after 1 month, but did not reach pre-RT levels.
Bibby et al. 2008 [21]	N=30	Glottic = 30 (100%)	T1 = 21 (70%) T2 = 9 (30%)	V QoL	Voice analysis Patient self-rating voice quality VR-QoL	RT	3, 6, 12 months	After RT expert-rated perceptual auditory outcomes, patient self-rated VAS and all subscales of VR-QoL showed significant improvement.
Bottomley et al. 2013 [78]	N=450	Laryngeal Hypopharyngeal (No details provided)	T2 T3 T4 (No details provided)	QoL	EORTC QLQ-C30 EORTC QLQ-H&N35	Group 1: sequential CRT (n=224) Group 2: alternating CRT (n=226)	6, 12, 18, 24, 36, 48 months	The HRQoL scores of the majority of patients returned to baseline after therapy. No group differences were found.
Buchbinder et al. 1993 [48]	N=21	No details provided	No details provided	D	MIO	Group 1: RT + unassisted exercise Group 2: RT + stacked tongue depressors combined + unassisted exercise Group 3: RT + TheraBite® system combined + unassisted exercise	2, 4, 6, 8, 10 weeks	The highest increase in MIO was reached in group 3.
Caudell et al. 2010 [49]	N=83	Nasal cavity = 3 (4%) Nasopharyngeal = 7 (8%) Oral cavity = 1 (1%) Oropharyngeal = 44 (53%) Hypopharyngeal = 6 (7%) Laryngeal = 17 (21%) Unknown = 5 (6%)	Tx-2 = 28 (34%) T3-14 = 55 (66%)	D	Videofluoroscopy PEG dependency	Group 1: CRT (n=70) Group 2: RT (n=13)	12 months	Mean dose to the larynx greater than 41 Gy and a receiving volume greater than 24% showed association with increased PEG dependency and aspiration.

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Christianen et al. 2015 [50]	N=238	Nasopharyngeal = 8 (3%) Oral cavity = 11 (5%) Oropharyngeal = 71 (30%) Hypopharyngeal = 12 (5%) Laryngeal = 136 (57%)	T1-T2 = 161 (68%) T3-T4 = 77 (32%)	D	Grade of swallowing dysfunction according to the RTOG/EORTC Late Radiation Morbidity Scoring Criteria	Group 1: conventional RT (n=33) Group 2: accelerated RT (n=155) Group 3: CRT (n=50)	6, 12, 18, 24 months	Patterns of swallowing dysfunction may be caused by radiobiological mechanisms of radiation induced damage and recovery. No group differences were found.
Cohen et al. 2006 [74]	N=53	Oral cavity = 14 (26%) Oropharyngeal = 11 (21%) Hypopharyngeal = 3 (6%) Laryngeal = 9 (17%) Supraglottic = 13 (24%) Unknown = 3 (6%)	T0 = 3 (6%) T1 = 3 (6%) T2 = 17 (32%) T3 = 30 (56%)	D QoL	PSS-HN Head and Neck RT Questionnaire (selected questions) FACT-H&N	CRT	3, 6, 12, 18, 24, 36, 48, 60 months	Most patients returned to pre-treatment function (QoL and performance) by 12 months.
Dornfeld et al. 2007 [22]	N=27	Oral cavity = 1 (4%) Oropharyngeal = 16 (59%) Hypopharyngeal = 1 (4%) Laryngeal = 6 (22%) Unknown = 3 (11%)	Tx = 2 (7%) T1 = 6 (22%) T2 = 7 (26%) T3 = 5 (19%) T4 = 7 (26%)	V D QoL	Weight Type of diet Type of speech Presence of PEG tube HNCI	CRT	1 year	Speech, diet and QoL outcomes showed an inverse relationship with the delivered radiation dose to the larynx.
Dijkstra et al. 2007 [51]	N=29	Parotid = 4 (14%) Maxilla = 4 (14%) Gingiva = 2 (7%) Floor of mouth = 3 (10%) Trigonum retromolare = 4 (14%) Oropharyngeal = 8 (27%) Other localization = 4 (14%)	No details provided	D	MIO	RT	12-48 weeks	Increase in mouth opening was significantly less in the group of patients with trismus related to head and neck cancer and is difficult to treat with exercise therapy.
Feng et al. 2007 [52]	N=36	Base of tongue = 19 (53%) Tonsil = 12 (33%) Nasopharyngeal = 5 (14%)	T1 = 2 (5%) T2 = 11 (31%) T3 = 9 (25%) T4 = 14 (39%)	D QoL	Videofluoroscopy Esophagogram HNQoL UWQoL EORTC Late Radiation Morbidity Scale	CRT	3 months	Statistically significant dose-volume effect relationships for dysphagia and aspiration were found. Reducing the doses to the swallowing structures may improve swallowing.
Feng et al. 2010 [53]	N=73	Base of tongue = 38 (52%) Tonsil = 35 (48%)	T1 = 9 (12%) T2 = 29 (40%) T3 = 17 (23%) T4 = 18 (25%)	D	Videofluoroscopy UWQoL (swallowing question) HNQoL (eating domain) Observer rated dysphagia	CRT	3, 6, 12, 18, 24 months	Long-term measures of swallowing were slightly worse than pre-therapy measures.
Frowen et al. 2009 [16]	N=81	Base of tongue = 19 (24%) Soft palate = 7 (2%) Tonsil = 26 (32%) Supraglottic = 8 (10%) Hypopharyngeal = 8 (10%) Laryngeal = 18 (22%)	T1 = 11 (14%) T2 = 27 (33%) T3 = 31 (38%) T4 = 12 (15%)	D	Videofluoroscopy	Group 1: CRT (n=23) Group 2: CT (n=58)	3, 6 months	Swallowing in both groups was best at baseline, a decline at 3 months and an improvement at 6 months post-therapy was shown. Baseline levels were not reached. Predictors for swallowing outcome were: intoxications, tumor size, RT technique and baseline level of swallowing. Patients who received conformal RT had a very low risk of penetration and aspiration of liquids by 6 months post-treatment.

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Haderlein et al. 2013 [54]	N=45	Oropharyngeal = 3 (7%) Hypopharyngeal = 18 (40%) Laryngeal = 24 (53%)	T2 = 15 (33%) T3 = 17 (38%) T4 = 13 (29%)	D QoL	PEG dependency EORTC QLQ-C30	CRT	3-6 months intervals	Almost 50% of patients had deterioration of swallowing function after CRT.
Hutchesson et al. 2014 [55]	N=47	Nasopharyngeal = 1 (2%) Oral cavity = 1 (2%) Oropharyngeal = 41 (88%) Hypopharyngeal = 2 (4%) Supraglottic = 2 (4%)	T1 = 16 (34%) T2 = 14 (30%) T3 = 12 (25%) T4 = 5 (11%)	D	Videofluoroscopy PSS-HIN MDADI	Group 1: RT (n=23) Group 2: CRT (n=23) Group 3: surgery (n=1)	6, 12, 24 months	Two years post-therapy, mild deterioration of swallowing without chronic aspiration was found.
Jacobi et al. 2016 [31]	N=34	Nasopharyngeal = 6 (18%) Oral cavity/oropharyngeal = 15 (44%) Hypopharyngeal = 13 (38%)	T1 = 6 (18%) T2 = 13 (38%) T3 = 11 (32%) T4 = 4 (12%)	V	Speech analysis	CRT	10 weeks; 1 year	Received dose to tongue and velopharynx were most relevant for speech and voice quality.
Karlsson et al. 2015 [32]	N=74	Laryngeal = 74 (100%)	T0 = 1 (1%) T1 = 44 (60%) T2 = 22 (30%) T3 = 6 (8%) T4 = 1 (1%)	V QoL	EORTC QLQ-C30 EORTC QLQ-H&N35 S-SECEL	Group 1: CRT + voice rehabilitation (n = 37) Group 2: CRT only (n = 37)	1, 6 months	Patients treated with voice rehabilitation experienced benefits of therapy on communication and HRQoL.
Karlsson et al. 2016 [33]	N=40	Laryngeal = 40 (100%)	T1s = 2 (5%) T1 = 20 (50%) T2 = 13 (33%) T3 = 5 (12%)	V QoL	EORTC QLQ-C30 EORTC QLQ-H&N35 S-SECEL Perceptual and acoustic voice analysis	RT (1 subject received concomitant chemotherapy)	1, 6, 12 months	One year after treatment most outcomes showed no significant improvements compared to baseline measurements.
Kazi et al. 2008 [34]	N=21	Hypopharyngeal = 8 (38%) Laryngeal = 10 (48%) Supraglottic = 3 (14%)	Stage III Stage IV No details provided	V	Voice analysis Electrolottography	CRT	1, 6, 12 months	Patients treated with CRT had a better voice quality compared to patients after total laryngectomy.
Kerr et al. 2015 [35]	N=200	Tongue base = 77 (38%) Tonsil / soft palate = 123 (62%)	T0-T1 = 42 (21%) T2 = 72 (36%) T3 = 48 (24%) T4 = 38 (19%)	V D	KPS ECOG toxicity and response criteria scale PSS-HIN RBHOMS VHI-10 Edmonton Self-Assessment Scale (Self-rated Xerostomia)	Group 1: 3DCRT (n = 83) Group 2: IMRT (n = 117)	3, 6, 12, 24 months	IMRT showed better functional outcomes compared to 3DCRT, both 3-6 and 12-24 months post-treatment.
Kotz et al. 2012 [56]	N=26	Nasopharyngeal = 1 (4%) Tongue base = 11 (42%) Tonsil = 11 (42%) Oropharyngeal = 1 (4%) Glottic = 1 (4%) Unknown = 1 (4%)	T2 = 1 (4%) T3 = 5 (19%) T4 = 20 (77%)	D	PSS-HIN (Eating in public and Normalcy of diet) FOIS	Group 1: CRT + prophylactic swallowing therapy (n=13) Group 2: CRT (n=13)	3, 6, 9, 12 months	Prophylactic swallowing therapy improves swallowing at 3 and 6 months, later there were no group differences.

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Kraaijenka et al. 2015 [36]	N=22	Nasopharyngeal = 4 (18%) Oral cavity/oropharyngeal = 10 (46%) Hypopharyngeal/laryngeal = 8 (36%)	T1 = 5 (23%) T2 = 9 (41%) T3 = 7 (32%) T4 = 1 (4%)	V D QoL	Videofluoroscopy Acoustic analysis Presence of feeding tube FOIS Pain (VAS) Trismus QoL aspects (based on EORTC QLQ-C30 and EORTC QLQ-H&N35) SWAL-QoL VHI	CRT	2, 6 years	Functional swallowing and voice problems at 6 years post-treatment were minimal, possibly due to preventive swallowing rehabilitation programs.
Kumar 2014 [57]	N=46	Tonsil = 19 (41%) Base of tongue = 22 (47%) Pharyngeal wall = 3 (7%) Unknown = 2 (5%)	T0 = 2 (4%) T1 = 15 (33%) T2 = 14 (30%) T3 = 12 (26%) T4 = 3 (7%)	D	Videofluoroscopy	CRT	From <6 to >18 months	Aspiration and penetration was associated with dose and volume delivered to the floor of mouth muscles.
Lazarus et al. 2014 [38]	N=29	Nasopharyngeal = 3 (10%) Oropharyngeal = 18 (63%) Pharyngeal = 1 (3%) Hypopharyngeal = 1 (3%) Laryngeal = 5 (18%) Unknown primary = 1 (3%)	Stage I = 2 (7%) Stage II = 1 (4%) Stage III = 5 (17%) Stage IVa = 21 (72%)	D V QoL	Tongue strength, jaw ROM and tongue ROM Saliva weight Eating Assessment Tool MDADI Speech Handicap Index EORTC QLQ-H&N35 PSS-HN (Normalcy of Diet, Eating in Public and Understandability of Speech) KPS	CRT	3, 6 months	Patients performed worse in oral outcomes, performance status and QoL after treatment.
List et al. 1999 [75]	N=64	Nasopharyngeal = 1 (2%) Oral cavity = 6 (9%) Oropharyngeal = 34 (53%) Hypopharyngeal = 10 (16%) Laryngeal = 9 (14%) Other = 4 (6%)	Stage III = 4 (6%) Stage IV = 60 (94%)	D QoL	KPS PSS-HN McMaster University Head and Neck RT Questionnaire (selected questions) FACT-H&N	CRT	1, 3, 6, 9, 12 months	Decline of QoL and functional aspects resolved 1 year after treatment, however, oral intake stayed restricted.
McLaughlin et al. 2009 [58]	N=91	Nasopharyngeal = 9 (10%) Oral cavity = 19 (21%) Oropharyngeal = 32 (35%) Hypopharyngeal = 7 (8%) Laryngeal = 12 (13%) Unknown = 4 (4%) Other = 8 (9%)	Stage II = 1 (1%) Stage III = 21 (23%) Stage IV = 69 (76%)	D	Weight loss Aspiration Overall nutritional status Duration G-tube placement Treatment-related complications	CRT	6, 12 months	Patients treated with CRT could be managed without nutritional support via G-tube. Dysphagia at baseline and advanced tumor stage are associated with increased risk of longer G-tube dependency.
Mittal et al. 2001 [37]	N=39	Nasopharyngeal = 4 (10%) Oropharyngeal = 17 (44%) Hypopharyngeal = 7 (18%) Laryngeal = 5 (13%) Unknown = 6 (15%)	Stage III = 5 (13%) Stage IV = 34 (87%)	D V	Videofluoroscopy Saliva production PSS-HN FACT-H&N Fisher-Logemann Test of Articulation Competence	Group 1: CRT with TDC (n=18) Group 2: CRT without TDC (n=21)	3 months	Patients treated with TDC had better oral intake, swallowing function and articulation.

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Murry et al. 1998 [59]	N=37	Oropharyngeal = 19 (52%) Hypopharyngeal = 6 (16%) Laryngeal = 12 (32%)	T3 T4 (No details provided)	D	HNHQ Questionnaire on swallowing	CRT	6 months	During treatment QoL and swallowing function decreased acutely and significantly. Six months post-therapy QoL exceeded pre-treatment level. Recovery was site-specific: oropharyngeal tumor patients had poorest outcome, whereas hypopharyngeal tumor patients showed most rapid recovery. Physical recovery followed psychosocial recovery. Organ preservation treatment may improve swallowing after treatment.
Niedzielska et al. 2010 [39]	N=45	Laryngeal = 45 (100%)	T1 = 24 (53%) T2 = 21 (47%)	V	Videolaryngostroboscopy Acoustic analysis	RT	1-3 years	All irradiated patients showed reduced vibration of the vocal cords. Except for some of the acoustic parameters, most data were comparable to a healthy control group (N=24).
Nourissat et al. 2010 [60]	N=535	Oral cavity = 63 (12%) Oropharyngeal = 17 (3%) Hypopharyngeal = 8 (1%) Supraglottic = 100 (19%) Glottic = 347 (65%)	T1 = 329 (61%) T2 = 206 (39%)	D QoL	Weight KPS EORTC QLQ-C30 Structured general questionnaire	RT	Direct post-therapy	The occurrence of adverse effects of RT appeared to be one of the main reasons for weight loss. Correlations were found between genetic factors associated with the adverse effects of cancer treatments.
Ottoson et al. 2014 [61]	N=101	Oral cavity = 20 (20%) Oropharyngeal = 62 (61%) Hypopharyngeal = 8 (8%) Laryngeal = 11 (11%)	T1 = 11 (10%) T2 = 16 (16%) T3 = 28 (28%) T4 = 46 (46%)	D	Videofluoroscopy BMI	RT	5 years	Dysphagia with aspiration was related to unintentional weight loss and a lower BMI.
Pauli et al. 2012 [62]	N=75	Sinus, nose = 6 (8%) Salivary gland = 10 (13%) Gingiva, buccal = 6 (8%) Tongue, floor of mouth = 15 (20%) Tonsil = 24 (32%) Base of tongue, oropharyngeal = 11 (15%) Other = 3 (4%)	T0 = 5 (7%) T1 = 13 (17%) T2 = 29 (39%) T3 = 9 (12%) T4 = 18 (24%) Unknown = 1 (1%)	D QoL	MIO Patient reported outcome Gothenburg Trismus Questionnaire EORTC QLQ-C30 EORTC QLQ-H&N35 HAUS	Group 1: surgery (n=8) Group 2: surgery + RT (n=15) Group 3: surgery + CRT (n=6) Group 4: RT (n=16) Group 5: CRT (n=29) Group 6: no treatment (n=1)	3, 6, 12 months	Trismus was a major side-effect of the treatment of head and neck cancer and deteriorates HRQoL.
Pauloski et al. 2006 [63]	N=170	Nasopharyngeal = 8 (5%) Oral cavity = 15 (9%) Oropharyngeal = 80 (47%) Hypopharyngeal = 14 (8%) Laryngeal = 42 (25%) Unknown = 11 (6%)	Stage IV = 122 (72%) Other = 48 (28%)	D	Videofluoroscopy Oral intake	Group 1: CRT (n=147) Group 2: RT (n=22) Unknown (n=1)	1, 3, 6, 12 months	In both groups limitations in oral intake and diet after cancer treatment were significantly related to reduced laryngeal elevation and reduced cricopharyngeal opening due to treatment.

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Rademaker et al. 2003 [64]	N=255	Nasopharyngeal = 13 (5%) Oral cavity = 25 (10%) Oropharyngeal = 118 (46%) Hypopharyngeal = 22 (9%) Laryngeal = 59 (23%) Unknown = 18 (7%)	Stage II = 16 (6%) Stage III = 48 (19%) Stage IV = 187 (73%) Unknown = 4 (2%)	D	Percentage of oral intake Food consistencies	CRT	1, 3, 6, 12 months	Eating ability decreased during treatment and improved 12 months after treatment to near pretreatment levels.
Remmelts et al. 2013 [40]	N=248	Glottic = 248 (100%)	T1s = 26 (10%) T1a = 103 (42%) T1b = 42 (17%) T2 = 77 (31%)	V	VHI (physical subscale) 5-item questionnaire	Group 1: RT (n=159) Group 2: laser surgery (n=89)	12 months	VHI scores were comparable for both groups. Regarding laryngeal preservation surgery is the treatment of first choice.
Salama et al. 2008 [65]	N=95	Nasopharyngeal = 4 (4%) Oral cavity = 8 (9%) Oropharyngeal = 49 (52%) Hypopharyngeal = 5 (5%) Laryngeal = 22 (23%) Other = 7 (7%)	Tx = 7 (7%) T1 = 15 (15%) T2 = 19 (20%) T3 = 16 (17%) T4 = 38 (40%)	D	Videofluoroscopy SPS	CRT	1-2 months	Improvement of swallowing ability compared to baseline was associated with advanced tumor stage.
Sanguineti et al. 2014 [23]	N=124	Base of tongue = 54 (43%) Soft palate = 2 (2%) Tonsil = 59 (48%) Pharyngeal wall = 1 (1%) Unknown = 8 (6%)	T0 = 8 (6%) T1 = 37 (30%) T2 = 49 (40%) T3 = 14 (11%) T4 = 16 (13%)	V	CTCAE FACT-HN (items HN4 and HN10)	Group 1: CRT (n=108) Group 2: RT (n=16)	3, 6, 12, 18, 24, 36, 48, 60 months	Mild voice changes were common and strictly correlated to mean dose to larynx and should be kept under 50 Gy.
Scrimger et al. 2007 [66]	N=47	Nasopharyngeal = 10 (21%) Oral cavity = 20 (43%) Oropharyngeal = 9 (19%) Hypopharyngeal/laryngeal = 6 (13%) Unknown primary = 2 (4%)	T0 = 2 (4%) T1 = 7 (15%) T2 = 20 (42%) T3 = 12 (25%) T4 = 6 (13%)	D QoL	Mouth saliva flow UW-QoL RTOG late-toxicity scale XQoL	Group 1: RT (n=5) Group 2: RT (n=12) Group 3: surgery +RT (n=30)	3, 6, 12 months	Non-surgery resulted in better QoL questionnaire scores compared to surgery. Patients with good saliva production did not exhibit better QoL after RT than patients with less saliva production.
Spector et al. 1999 [41]	N=659	Glottic = 659 (100%)	T1 = 659 (100%)	V	Voice preservation	Group 1: low-dose RT (n=90) Group 2: high-dose RT (n=104) Group 3: conservation surgery (n=404) Group 4: endoscopic resection (n=61)	5 years	Groups 2-4 had similar unaided laryngeal voice preservation rates, however group 1 had significant lower unaided laryngeal voice preservation.
Stamler et al. 2014 [67]	N=71	Oropharyngeal = 71 (100%)	T1 = 24 (34%) T2 = 19 (27%) T3 = 13 (18%) T4 = 12 (17%) Unknown = 3 (4%)	D	Videofluoroscopy FOIS	Group 1: CRT (n=65) Group 2: RT (n=6)	1-18 months	Patients undergoing nonsurgical treatment for oropharyngeal tumors were at risk for post-treatment dysphagia.

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Stenson et al. 2009 [68]	N=111	Buccal = 4 (3%) Alveolus/gingivae = 7 (6%) Floor of mouth = 32 (29%) Tongue = 50 (45%) Palate/oral cavity NOS = 4 (4%) Trigonum retromolare = 13 (12%) Unknown = 1 (1%)	T1 = 9 (8%) T2 = 15 (14%) T3 = 20 (18%) T4 = 67 (60%)	D	Videofluoroscopy SPS	Group 1: CRT (n=84) Group 2: surgery + CRT (n=27)	2, 4, 6, 8, 10, 12, 16, 20, 24, 30, 36 months	Ninety-two % of all patients were able to maintain weight via oral route. Both groups showed comparable overall survival. Ninety-two % of all patients had a sufficient oral intake.
Strigari et al. 2010 [69]	N=63	Nasopharyngeal = 44 (70%) Floor of mouth/oral cavity = 2 (3%) Oropharyngeal = 11 (17%) Hypopharyngeal = 4 (7%) Unknown primary = 2 (3%)	T1-T2 = 17 (23%) T3-T4 = 46 (73%)	D	Saliva flow Xerostomia related questionnaires RTOG late-toxicity scale	RT	3, 6, 12, 18, 24 months	The mean score on the xerostomia related questionnaire increased (worsened) after RT and decreased (improved) over time in all patients.
Tuomi et al. 2015 [42]	N=67	Supraglottic = 13 (19%) Glottic = 54 (81%)	T1s = 2 (3%) T1 = 41 (61%) T2 = 17 (25%) T3 = 6 (9%) T4 = 1 (2%)	V D QoL	Acoustic analysis EORTC QLQ-C30 EORTC QLQ-H&N35 S-SECEL	RT	1 month	Patients treated for supraglottic tumors experienced more problems in eating and swallowing prior to therapy compared to glottic tumors and demonstrated significant HRQoL reduction after treatment. In contrast, glottic tumors presented with inferior voice quality.
Vainshtein et al. 2015 [70]	N=40	Base of tongue = 18 (45%) Tonsil = 22 (55%)	T1 = 8 (20%) T2 = 20 (50%) T3 = 8 (20%) T4 = 4 (10%)	D QoL	HNQoL UWQoL XQoL	CRT	1, 3, 6, 12, 18, 24 months	At 6.5 years post-therapy patients showed a stable or improved HRQoL in most domains comparable with baseline and 2 years post-therapy.
van der Molen et al. 2010 [76]	N=49	Nasopharyngeal = 7 (14%) Oral cavity/oropharyngeal = 24 (49%) Hypopharyngeal/laryngeal = 18 (37%)	T1 = 8 (16%) T2 = 15 (31%) T3 = 19 (39%) T4 = 7 (14%)	D	Videofluoroscopy MIO BMI FOIS VAS pain	Group 1: standard rehabilitation (n=28) Group 2: experimental rehabilitation (n=27)	10 weeks	(Preventive) rehabilitation in head and neck cancer patients, was feasible and improved functional outcomes post-therapy.
van der Molen et al. 2012 [44]	N=55	Non-laryngeal = 36 (65%) Laryngeal = 19 (35%)	T1 = 8 (15%) T2 = 15 (27%) T3 = 21 (38%) T4 = 11 (20%)	V QoL	Acoustic analysis Study-specific QoL questionnaire	CRT	10 weeks; 1 year	CRT effects 10 weeks post-therapy were worse than 1 year post-therapy, and both were worse than baseline.
van der Molen et al. 2013 [71]	N=55	Nasopharyngeal = 7 (13%) Oral cavity/oropharyngeal = 29 (53%) Hypopharyngeal/laryngeal = 19 (34%)	T1 = 8 (15%) T2 = 15 (27%) T3 = 21 (38%) T4 = 11 (20%)	D	Videofluoroscopy MIO Study-specific structured questionnaire	CRT	10 weeks; 1 year	A correlation between dose to structures was found for dysphagia and trismus.
Verdonck-de Leeuw et al. 1999 [43]	N=60	Glottic = 60 (100%)	T1 = 60 (100%)	V	Videolaryngostroboscopy Voice quality rating Self-rating of vocal performance and quality	RT	0.5-10 years	Voice and its characteristics improved after treatment but did not reach pre-treatment levels in half of the patients.

Reference	Subjects	Carcinoma	Staging	Topic	Evaluation technique	Treatment(s)	Follow-up	Key findings / author's conclusions
Verdonck-de Leeuw et al. 2014 [79]	N=164	Oral/oropharyngeal = 95 (58%) Hypopharyngeal/laryngeal = 69 (42%)	No details provided Stage III = 42 (30%) Stage IVa = 81 (57%) Stage IVb = 18 (13%)	QoL	EORTC QLQ-C30 EORTC QLQ-H&N35	CRT	6 weeks; 6, 12, 18, 24 months	Significant difference in HRQoL between survivors and non-survivors in favor of survivors was found.
Viacich et al. 2014 [72]	N=141	Sinus/nasal cavity = 2 (1%) Nasopharyngeal = 12 (9%) Oral cavity = 5 (4%) Oropharyngeal = 82 (58%) Hypopharyngeal = 6 (4%) Laryngeal = 30 (21%) Unknown = 4 (3%)	Stage III = 42 (30%) Stage IVa = 81 (57%) Stage IVb = 18 (13%)	D	PEG requirement	CRT	12 months	IMRT dose to the inferior constrictor correlated with persistent dysphagia requiring prolonged PEG use.
Wilson et al. 2011 [73]	N=167	Nasopharyngeal = 5 (3%) Oropharyngeal = 66 (39%) Hypopharyngeal = 21 (13%) Laryngeal = 63 (38%) Unknown primary = 12 (7%)	T1 = 37 (22%) T2 = 37 (22%) T3 = 37 (22%) T4 = 44 (27%) Unknown = 12 (7%)	D QoL	MDADI UWQoL	Group 1: CRT (n=104) Group 2: RT (n=63)	3, 6, 12 months	HRQoL deteriorated significantly post-treatment. Little improvement may be expected 3 to 12 months post-treatment.

3DCRT: 3D conformal radiotherapy; BMI: body mass index; CRT: chemoradiotherapy; CTCAE: Common Terminology Criteria for Adverse Events; D: digestive tract; EOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; EORTC QLQ-H&N35: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire module Head and Neck cancer; FACT-HN: Functional Assessment of Cancer Therapy-Head and Neck; FOIS: Functional Oral Intake Scale; GRBAS: Grade, Roughness, Breathiness, Asthenicity, Strain scale; HADS: Hospital Anxiety and Depression Scale; HNCI: Head and Neck Cancer Inventory; HNQoL: Head and Neck quality of life; HNRQ: Head and Neck Radiotherapy Questionnaire; HRQoL: Health-related quality of life; IMRT: intensity modulated radiation therapy; KPS: Karnofsky Performance Status scale; LENT/SOMA: Late Effects Normal Tissue-Subjective, Objective, Management, Analytic scales; MDADI: MD Anderson Dysphagia Inventory; MIO: maximum incisional opening; NOS: not otherwise specified; PEG: percutaneous endoscopic gastrostomy; PSS-HN: Performance Status Scale for Head & Neck cancer patients; QoL: quality of life; RBHOMS: Royal Brisbane Hospital Outcome Measure for Swallowing; ROM: range of motion; RT: radiotherapy; RTOG: Radiation Therapy Oncology Group; S-SECEL: Swedish version of the Self-Evaluation of Communication Experiences after Laryngeal Cancer; SPS: Swallowing Performance Status scale; TDC: tissue/dose compensation; UWQoL: University of Washington Quality of Life Questionnaire; V: voice and/or speech; VAS: Visual Analog Scale; VHI: Voice Handicap Index; VHI-10: Voice Handicap Index-10; VR-QoL: Voice Related Quality of Life; XQoL: Xerostomia Questionnaire.

Nine studies reported impaired swallowing function following radiotherapy and/or chemotherapy [38, 45, 50, 53-55, 67, 72, 73].

Five studies [16, 59, 64, 74, 75] showed that swallowing was least affected at baseline, worst immediately following post-treatment (0-3 months post-treatment), and improved by 6-12 months post-treatment and later. However, swallowing usually did not return to pre-treatment functioning level. In four studies [49, 52, 57, 71], a relation between dose-volume, dysphagia and aspiration was found. Caudell et al. [49] showed that a mean radiation dosage >41 Gy with >24% volume of the larynx being radiated, was associated with increased percutaneous endoscopic gastrostomy (PEG) dependency and aspiration. Akst et al. [46] correlated advanced tumor stage and age >60 years with a deterioration of swallowing.

Ackerstaff et al. [25] demonstrated improved oral intake post-radiotherapy and/or chemotherapy. Stenson et al. [68] stated that weight remained unchanged after treatment (via oral route), whereas Nourissat et al. [60] described a mean weight loss of 2.2 kg post-treatment.

QoL

Twenty-five studies [21, 22, 25, 27, 28, 30, 32, 33, 36, 38, 42, 44, 47, 52, 54, 60, 62, 66, 70, 73-75, 77-79] described the short- and long-term effects of treatment for HNC on patients' general QoL. The European Organization for Research and Treatment of Cancer (EORTC) C30-questionnaire was used in fifteen studies [25, 27, 28, 30, 32, 33, 36, 42, 47, 54, 60, 62, 77-79] and the more HNC specific EORTC H&N35 was used in thirteen studies [25, 27, 28, 32, 33, 36, 38, 42, 47, 62, 77-79]. Other questionnaires that were used included the University of Washington QoL Questionnaire (UWQoL) [52, 66, 70, 73], the Head and Neck QoL or HNQoL [52, 70] and the Xerostomia Related QoL or XQoL [66, 70]. Follow-up time for QoL was up to six years post-treatment [36], including patients with tumors that were early staged and patients with advanced tumors.

Although three studies [21, 70, 77] demonstrated improvements in QoL, four studies [25, 38, 42, 53] reported a decrease in general QoL as a result of radiotherapy and/or chemotherapy. Bansal et al. [30] found a significant decline in physical, social and emotional functioning as well as in global health scores following a course of radiotherapy. However, the patients' functional scores improved one month post-treatment, but did not reach pre-treatment levels. The health-related QoL (HRQoL) scores of the majority of patients in the Bottomley et al. [78] study returned to baseline at 48 months follow-up. These findings support the findings of Ackerstaff et al. [25], Cohen et al. [74], Karlsson et al. [33], List et al. [75] and Wilson et al. [73], who suggested that HRQoL deteriorates significantly immediately post-treatment, with variable degrees of improvement 3-72 months post-treatment.

Reported (efficacy of) speech pathology interventions

We assessed the speech pathology interventions against the following criteria: a) whether a detailed description of the intervention was provided; b) whether the authors provided a description of treatment duration and intensity; and c) what the speech pathology intervention outcomes were. The reported efficacy of 14 speech pathology intervention studies aimed at addressing problems in dysphagia, speech, voice and trismus are summarised in Table 4.

Of the 60 articles included in this review, 14 studies [16, 22, 23, 26, 32, 36, 44, 46, 48, 55, 56, 67, 71, 76] reported whether there was any treatment for the sequelae of radiotherapy and/or chemotherapy. Of these intervention studies, five focused on voice-related problems [23, 26, 32, 36, 44], two focused on trismus [48, 51], seven focused on swallowing disorders [16, 36, 46, 55, 56, 67, 76] and one study reported on both swallowing disorders and trismus [71].

The three studies that investigated the treatment of trismus [48, 51, 71] presented the most detailed information on what the interventions involved. The study by Dijkstra et al. [51] described a wide variety of trismus-specific therapies, suggesting that most patients received a combination of therapies. The patients in the Van der Molen et al. [44] and Kraaijenga et al. [36] studies did not receive any speech therapy. The remainder of the studies reported that patients received speech therapy; however, most of these studies did not provide specific data on treatment duration or intensity. None of the voice-related studies provided information on the specific exercises prescribed to patients except Karlsson et al [32].

Of the eight studies on swallowing disorders, only Kotz et al. [56] and van der Molen et al. [76] described the prescribed exercises in detail. The aim of the latter study was to compare the effectiveness of experimental rehabilitation to standard rehabilitation in 49 advanced HNC patients. The authors concluded that preventive rehabilitation is feasible and effective in reducing the extent and/or severity of various functional short-term effects of chemoradiotherapy [71]. This finding is supported by the 6 years follow-up study by Kraaijenga et al. [36]. Kotz et al. [56] described a temporary improvement. These are the only studies that provided detailed information about the speech pathology intervention and reported on the effectiveness of the intervention.

Table 4. Overview of speech pathology interventions aimed at addressing problems in dysphagia, speech, voice and trismus (n = 14)
HNC: head and neck cancer; HRQoL: health-related quality of life; MIO: maximum incisal opening; ROM: range of motion.

Reference	Topic	General description of intervention and treatment intensity/duration	Description of specific exercises	Conclusions specific to therapy
Agarwal et al. 2009 [46]	Voice	All patients received counseling and voice therapy by a trained speech pathologist. No specific data provided on treatment frequency/intensity	No description of exercises provided	Forty-seven of 50 patients showed compliance to the therapy. No specific conclusions of influence of provided therapy on primary outcomes described.
Akst et al. 2004 [46]	Swallowing	Swallowing evaluation and intervention when clinically indicated.	No description of exercises provided	No specific conclusions of influence of provided therapy on primary outcomes described.
Buchbinder et al. 1993 [48]	Trismus	Six to 10 exercise sessions per day for a 10-week period.	Group 1: unassisted exercises: reach maximum MIO and closing, jaw motion to left, right and protrusively.	The first four weeks no differences between groups were found. After week 4 minimal improvements in group 1 and 2 were found and group 3 still improved. The highest increment in MIO was reached in group 3.
			Group 2: unassisted exercises: reach maximum MIO and closing, jaw motion to left, right and protrusively. Stacked tongue depressors, to mechanically increase MIO (5x30 seconds per session).	
			Group 3: unassisted exercises: reach maximum MIO and closing, jaw motion to left, right and protrusively. Combined with the TheraBite® System (5x30 seconds per session).	
Dijkstra et al. 2007 [51]	Trismus	Physical therapy for trismus, median of 4 sessions.	Physical therapy consisting of: -Active range of motion -Hold and relax -Manual stretching -Joint distraction Following therapeutic tools used in described cohort: -Rubber plugs -Tong blades -Dynamic bite opener -TheraBite® System	MIO increases significantly after physical therapy. History of HNC decreases the effect of physical therapy, compared to other trismus patients.
Frowen et al. 2009 [16]	Swallowing	All patients were seen by a speech pathologist as an aspect of regular care.	No description of exercises provided	No specific conclusions of influence of provided therapy on primary outcomes described.
Hutchesson et al. 2014 [55]	Swallowing	All patients received prophylactic swallowing therapy to avoid nothing by mouth periods during treatment. No specific data provided on treatment frequency/intensity	Targeted swallowing exercises	No specific conclusions of influence of provided therapy on primary outcomes described.

Reference	Topic	General description of intervention and treatment intensity/duration	Description of specific exercises	Conclusions specific to therapy
Karlsson et al. 2015 [32]	Voice	Group 1: voice therapy group received 10 x 30 minutes sessions over 10 weeks. Group 2: vocal hygiene group: 1 session for vocal hygiene advice.	Group 1: voice therapy consisting of: relaxation, respiration, posture and phonation exercises. Group 2: vocal hygiene advice	Patients treated with voice therapy experienced greater improvements compared to patients that only received vocal hygiene advice. Group 1 showed a significant better functional communication and HRQoL.
Kotz et al. 2012 [56]	Swallowing	Group 1: weekly treatment by speech pathologist and daily 3x10 home sessions of exercises. Group 2: swallowing assessment and treatment if necessary after treatment.	Group 1: prophylactic swallowing therapy consisting of effortful swallow, tongue base retraction exercises, super supraglottic swallow and the Mendelsohn maneuver Group 2: control group only receive symptomatic dysphagia treatment.	Prophylactic swallowing therapy improves swallowing at 3 and 6 months, later there were no group differences found.
Kraaijenka et al. 2015 [36]	Swallowing and voice	Daily practice from the start of the treatment until 1 year post-treatment.	Two combined groups: TheraBite® System and standard logopedic swallowing exercises (same cohort as van der Molen et al. 2010 [76])	Minimal voice and swallowing difficulties were found 60 months after treatment in patients treated with prophylactic swallowing exercises.
Sanguinetti et al. 2014 [23]	Voice	75.8% of the patients received speech therapy. No therapy was provided to 30 patients. No specific data provided on treatment frequency/intensity	No description of exercises provided	No specific conclusions of influence of provided therapy on primary outcomes described.
Starmer et al. 2014 [67]	Swallowing	Patients received prophylactic swallowing and trismus exercises.	No description of exercises provided	No specific conclusions of influence of provided therapy on primary outcomes described.
Van der Molen et al. 2010 [76]	Swallowing	Patients received instructions in advance of their oncological treatment. Three times daily exercises.	Group 1: range-of-motion exercises and three strengthening exercises, i.e., the effortful swallow, the Masako maneuver, the super-supraglottic swallow. Stretch holding for 10-30 seconds at a point of mild discomfort. Group 2: Stretch of the mouth using the TheraBite® System and a strengthening exercise: swallowing with the tongue elevated to the palate while maintaining mouth opening at 50% of its maximum. Stretch holding for 10-30 seconds at a point of mild discomfort.	Similar outcome in both groups were found. Preventive rehabilitation can improve early post-treatment functional outcomes.
Van der Molen et al. 2012 [44]	Voice	No specific speech or voice therapy.	N/A	N/A
Van der Molen et al. 2013 [71]	Swallowing and trismus	Study was aimed at describing dose-effect relationships in two treatment groups described in earlier study. References to other published study where treatment regime is described.	Group 1: standard exercises Group 2: experimental exercises	Any possible difference between the two included treatment groups is not described, nor possible influence of the respective treatments

DISCUSSION

In total, 60 studies met the inclusion criteria. The studies described the effects of radiotherapy and/or chemotherapy on the functions of the upper aerodigestive tract in patients with HNC. The articles yielded by this systematic review vary in their findings regarding tumor characteristics and treatment modalities. As a result of this variability, no statistical pooling was possible. We also set out to investigate the involvement of speech pathologists in treating patients with HNC.

When considering treatment outcomes, voice quality worsened at the start of radiotherapy and/or chemotherapy, but eventually improved after therapy finished. Dysphagia can be a major side-effect of HNC and its treatment. The high incidence of dysphagia in this study population can cause serious secondary consequences, such as: malnutrition, dehydration, an increased risk of aspiration and, at worst, death [80]. As dysphagia is a common sequelae to oncological treatment, early detection and treatment is needed to avoid, or minimise serious secondary complications [81].

The general description of the study population in Table 3 shows that there was great variability in both the location of the tumor, and the grading/staging, making comparisons of these studies difficult. As the follow-up times varied in each study, the outcomes may be non-comparable. Thus, this review shows that there is a need for a more standardised approaches to research in this field.

Additionally, a large range of outcome measures were used - some of which are not validated. This calls into question the reliability of results reported in some of the studies. The use of validated and standardised assessments in future research would provide more robust findings.

When considering the functional outcomes of radiotherapy and/or chemotherapy, one of the most important factors is whether the patient had received voice or swallowing therapy. Interestingly, only 14 of the 60 included studies reported whether the patients received any speech therapy. Thus, in 46 articles functional results, such as voice quality, are presented with no specification of whether the patient received therapy. As some of these studies have a follow-up of >2 years, it is fair to assume that patients sought help for voice or swallowing problems. Therefore, the involvement of speech therapy may be underreported, suggesting that the presented outcomes in these studies are biased and raise questions about their reliability.

When information was provided about treatment, only six articles [32, 48, 51, 56, 71, 76] described in detail both the treatment intensity as the actual treatment. Furthermore, these studies are the only five that include conclusions about the efficacy of speech therapy in this specific population. In the context of EBP, this finding demonstrates the need for more research into the efficacy of speech pathology

interventions for patients with HNC receiving radiotherapy and/or chemotherapy. To enable the objective reporting of the effectiveness of radiation and/or chemotherapy, baseline measurements of different aspects of voice quality and swallowing are required. To manage expectations, health care professionals and patients need to be made aware that some aspects of both voice and swallowing commonly do not recover to the level prior to the oncological intervention [16]. Regarding effectiveness of voice treatments, the following multidimensional assessment is recommended [82]: a videolaryngostroboscopy recording of the laryngeal structures and the vocal fold vibration; an acoustic and a perceptual analysis of voice; a voice-related questionnaire on QoL (e.g., the Voice Handicap Index) [83], and a functional health status questionnaire. Such a protocol would be in line with the recommendations for functional assessment of voice pathology as described by the Committee on Phoniatrics of the European Laryngological Society [84].

When describing aspects of swallowing function, both fiberoptic endoscopic evaluation of swallowing and videofluoroscopy are considered to be the gold standard in dysphagia assessment [85]. In addition to these tools, questionnaires on HRQoL and functional health status are recommended and should be integrated in the overall swallowing assessment protocol. Repeated measurements of outcome measures should be performed in order to monitor for any side-effects of the oncological intervention, to detect spontaneous recovery and to measure the effects of the speech pathology interventions. Apart from baseline measurements, post-treatment and follow-up measurements should be used to monitor functional and QoL outcomes. Additional research is needed to develop clinical practice guidelines to support evidence-based practice in the area of dysphagia, speech, voice and trismus following radiotherapy and/or chemotherapy in patients with head and neck carcinoma. These practice guidelines should bring together the best available current evidence within a specific clinical area, formulating evidence-based recommendations for clinicians and present choices between different interventions that have an impact on health and use of resources [86]. This systematic review summarised the effects of radiotherapy and/or chemotherapy on the function of the upper aerodigestive tract in patients with head and neck cancer. However, because of the marked variation in treatment protocols and patient characteristics, outcome data from the included studies cannot easily be generalised. Recommendations for future studies advocate the use of a multidimensional assessment protocol, using well validated measures and standardised pre, post and follow up measurements, thus allowing for future meta-analysis of homogeneous outcomes.

CONCLUSION

The studies included in this systematic review described a wide variety of outcomes in patients with HNC following radiotherapy and/or chemotherapy. The findings about the long-term functional implications of radiotherapy and/or chemotherapy in patients with HNC are inconclusive as a result of the wide range of outcome measures used and the possible influence of underreported speech therapy.

Future researchers need to consider targeting more homogeneous groups using standardised treatment protocols to improve the treatment outcomes, thereby decreasing the side effects of the oncological treatments. Findings of these studies need to inform the decision-making process in the treatment of HNC so complications can be better predicted with due consideration of the possible negative side effects to the upper aerodigestive tract. Although the main objective of most studies was to determine curing rates, the importance of the functional implications of the side effects of oncology treatments should not be overlooked, particularly their impact on QoL. Finally, more research is needed to gain a full understanding of the complexity and variety in the effects of effects of radiotherapy and/or chemotherapy on the functions of the upper aerodigestive tract following for HNC.

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3



Neuromuscular electrical stimulation versus traditional therapy in patients with Parkinson's disease and oropharyngeal dysphagia: Effects on quality of life

Published in: Dysphagia. 2012 Sep;27(3):336-45.

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ABSTRACT

This study compares the effects of traditional logopedic dysphagia treatment versus NMES as adjunct to therapy on quality of life in patients with Parkinson's disease and oropharyngeal dysphagia. Eighty-eight patients were randomized over three treatment groups. Traditional logopedic dysphagia treatment or traditional logopedic dysphagia treatment combined with NMES at sensor or motor level stimulation were compared. Three times (pre-, posttreatment, and three months following treatment), two quality of life questionnaires (Swal-QOL MD Anderson Dysphagia Inventory) and a single item Dysphagia Severity Scale were scored. The Functional Oral Intake Scale (FOIS) was applied to assess the dietary intake.

After therapy all groups showed significant improvement on the Dysphagia Severity Scale and restricted positive effects on quality of life. Minimal group differences were found. These effects remained unchanged three months following treatment. No significant correlations were found between the dietary intake and quality of life. Logopedic dysphagia treatment results in a restricted increased quality of life in patients with Parkinson's disease. In this randomized controlled trial, all groups showed significant therapy effects on the Dysphagia Severity Scale, as well as restricted improvements on the SWAL-QoL and the MDADI. However, only slight non-significant differences between groups were found.

INTRODUCTION

Oropharyngeal dysphagia is a common finding in patients with Parkinson's disease. It is estimated that up to 80% of all patients will suffer from oropharyngeal dysphagia during the first stages of the disease. In advanced stages of the disease, the incidence of dysphagia can increase up to 95%. [1,2]. Literature describes the main phenomena of dysphagia in patients with Parkinson's disease in terms of rigidity and bradykinesia of swallowing. Incomplete cricopharyngeal relaxation, reduced cricopharyngeal opening, and delayed initiation of the swallowing reflex have been suggested as possible mechanisms of dysphagia in this patient population [3,4]. Furthermore, delayed oropharyngeal transition time, reduced muscle strength, as well as aspiration are common findings in dysphagic Parkinson patients. [4,5,6].

Dysphagia is associated with malnutrition, dehydration, aspiration pneumonia, and sudden death [7,8,9]. Dysphagia is also associated with severe consequences for the quality of life of [10,11]. In patients with Parkinson's disease these consequences become more prominent when the disease becomes more invalidating and the ability to enjoy oral foods becomes less evident [12,13].

Currently, the treatment of dysphagia in patients with Parkinson's disease exists of traditional logopedic dysphagia treatment by a speech therapist. Usually, this treatment is provided once or twice a week, for several months or years. Oral motor exercises, airway protecting maneuvers, postural correction to facilitate bolus transition, and thermotactile stimulation are included in this therapy [14]. The literature regarding randomized controlled trials on the outcomes of speech therapy for swallowing dysfunction in patients with Parkinson's disease is scarce. Baijens et al., Nagaya et al. and Sharkawi et al. [15,4,16] describe a positive effect of speech therapy on patients with Parkinson's disease and dysphagia, but methodological issues may arise [15]. No information is provided about blinding of pre versus posttreatment condition [4] or the reliability of measurements using a single assessor or rater [16]. Furthermore, most studies base their conclusion on rather small subject populations ($N \leq 10$ subjects).

Neuromuscular electrical stimulation (NMES) can be a therapeutic adjunct to known interventions in the treatment of dysphagia [17,18,19]. The rationale of NMES is the stimulation of muscle fibres by stimulating the nerve and the motor-end-plate of the nerve, resulting in a re-education of the functional muscle-contraction-patterns [19,20]. NMES has not been investigated in Parkinson patients with oropharyngeal dysphagia yet.

The aim of this randomized controlled trial is to investigate the effects of adjunctive NMES in dysphagic Parkinson patients compared to traditional logopedic dysphagia treatment with Health Related Quality of Life (HRQOL) as primary outcome measure.

It was hypothesized that NMES would not only contribute to a significant improvement of the swallowing function, but would also contribute to an increased quality of life in these patients.

METHODS

Patients and design

A three-arm open randomized trial was set-up to evaluate the hypotheses. Patients from diverse hospitals all over the Netherlands, with a diagnosis of idiopathic Parkinson's disease and dysphagic complaints, underwent a standardized clinical examination by a laryngologist as well as a clinical observation of the oral intake of various food consistencies and volumes by a speech and language pathologist at the outpatient clinic of dysphagia in the Maastricht University Medical Center. Only after objectifying the presence and severity of oropharyngeal dysphagia, patients were admitted to this study. The degree of dysphagic complaints ranged from mild to severe: For example, problems of bolus-forming, slow eating, oropharyngeal passage disorder, coughing while drinking, abnormal amounts of residue or, severe aspiration. The severity of the Parkinson's disease was assessed using the Hoehn and Yahr (H&Y) disability score [21]. The neurological diagnosis was confirmed by the patient's neurologist. Written informed consent was obtained from all patients prior to participation. The study protocol was approved by the medical ethical committee of the university medical center.

Inclusion and exclusion criteria

For inclusion in this study the following criteria had to be met:

1. Diagnosis of idiopathic Parkinson's disease as confirmed by a neurologist;
2. Patient's physical condition considered as in a 'stable' course of Parkinson's disease;
3. Unaltered protocol of antiparkinsonian medication for at least two months;
4. Age between 40-80 years old;
5. Presence of oropharyngeal dysphagia with preservation of the swallowing reflex;

Excluded were the following patients:

1. Patients with known other neurological diseases (such as Amyotrophic Lateral Sclerosis or Multiple Sclerosis);
2. Patients with severe mental depression or severe cognitive degeneration (Mini Mental State Examination < 23);
3. Patients with deep brain stimulation or malignancies, extensive surgery or radiotherapy of the head and neck region;

4. Patients with severe cardiopulmonary diseases, epilepsy, carotid sinus syndrome or dermatological diseases of the head and neck;
5. Patients who received dysphagia treatment during the past six months prior to randomization.

Sample size and randomization

After a conservative sample size calculation, three intervention groups were formed of at least thirty patients per treatment group. Parkinson patients were randomly assigned to one of the three treatment groups. Randomization was performed by assigning each consecutive patient to the next treatment group; Thus, the first patient was assigned to group 1, the second patient to group 2, the third patient to group 3, the fourth again to group 1, etc.

Treatment groups and treatment protocol

Group 1 received traditional logopedic dysphagia treatment (Group TT) by an experienced speech therapist. This treatment consisted of oral motor exercises, airway protecting maneuvers, and postural compensation based on the dysphagic findings as well as the therapist's individual preference and experience. Group 2 and Group 3 received the same treatment as Group 1 combined with neuromuscular electrical stimulation of the suprahyoid musculature. In this study, Vitalstim® equipment was used (VitalStim® Therapy; frequency 80 Hz, pulse width 700 microseconds; Chattanooga Group, Chattanooga, TN, USA). The VitalStim stimulator cycles automatically off for one second every minute because of fixed settings by the manufacturer. NMES consisted of transcutaneous electrical stimulation by positioning electrodes bilaterally on the neck in order to facilitate contraction of the suprahyoid muscles (Fig 1). Group 2 and 3 differed in the applied electrical current intensity of the NMES. The neuromuscular electrical stimulation of Group 2 (Group NMES-M) was set to stimulate at a motor level, to an extent that contractions of the underlying musculature were visible in combination with the subjective 'grabbing sensation' of the patient. Spasm of the musculature was avoided. Group 3 (Group NMES-S) received NMES on a sensory level [22]. Therapists received additional training and information on NMES by an experienced laryngologist certified to use surface electrical stimulation. The training was given according to the manual of the manufacturer, the VitalStim certification course (<http://www.vitalstim.com>) and the study of Ludlow et al. [20,22]. All patients were familiarized with the application of the electrical stimulator by their speech therapist during training sessions before the onset of the experiment. The therapists performed test treatment sessions with NMES on their Parkinson patients in the presence of the laryngologist and speech and language pathologist to ensure

standardized application of NMES. The correct placement of the electrodes, the application of the NMES unit, and the correct setting of the motorical and sensory electrical current thresholds were trained.

Therapies were administered at the patient's residence by experienced speech therapists trained in dysphagia management. In total, eighty-five speech therapists were involved in the study. All groups received 13 to 15 dysphagia treatment sessions of half an hour each, on five consecutive days per week within a period of three to five weeks. All patients were treated within 34 days (median = 23; 25th perc. = 21 and 75th perc. = 25 days). The variation in the number of treatment sessions and period duration, resulted from daily logistics in clinical practice.

EVALUATION MEASUREMENTS

Baseline characteristics

The following tools (or scales) were used to describe the patient characteristics; The Mini Mental State Examination (MMSE) was scored to assess the cognition [23]. The MMSE is scaled from 0 to 30, respectively. The Hoehn and Yahr Scale was used to judge the severity of Parkinson's disease [21]. The Hoehn and Yahr Scale ranges from 0 to 5, where 0 refers to absence of motor disabilities and 5 indicates bedridden or wheelchair dependant motor behavior. All baseline characteristics were determined by an experienced laryngologist trained to perform these tests.

Pre-, Post-, and Follow-up treatment evaluation

As dietary evaluation, the Functional Oral Intake Scale (FOIS) [24] was used (Table 6). Two questionnaires on quality of life related to oropharyngeal dysphagia were applied in this study: The SWAL-QOL [13] and the MD Anderson Dysphagia Inventory (MDADI) [25]. The Dutch translation of the SWAL-QOL, translated and validated by Bogaardt et al.[26], was used to determine the quality of life in dysphagic Parkinson patients. This 44-item questionnaire is a highly valid instrument in evaluating the quality of life concerning dysphagia and has a very reliable short-term reproducibility [13]. Its eleven subscales represent the different aspects of quality of life. The minimum and maximum score range per subscale from 0 to 100, indicating extremely impaired quality of life versus no impairment as experienced by the individual. The MDADI consists of 20 items and is composed of a global assessment (a single question) and three subscales: The emotional, the functional, and the physical subscale. It uses a five-point item scale, resulting in a minimum total score of 20 and maximum of 100. The original scoring uses a reversed coding in two items. In the Dutch consensus translation and validation

[27] all items are rated the same, thus, rewriting two questions. All three measurement tools were used to evaluate swallowing function at three time points: pretreatment, posttreatment, and at a three months follow-up. In addition, a visual analogue scale, the Dysphagia Severity Scale (DSS), was administered. Using the DSS, the patient self-reports his swallowing function with a score from 0 to 100 by rating a single question: 'How do you qualify your swallowing today?' Scores can vary from 0 ('Can't swallow at all') to 100 ('Normal swallow'). The DSS was filled in after every treatment session. Therefore, the DSS had a maximum of 15 measurement moments. The first two measurements were averaged as a baseline and the last two as a posttherapy result. The treatment sessions as well as all examinations were performed during the "on" motor phase of the Parkinson's disease [28]. All scales and questionnaires with the exception of the DSS, were rated during a patient's visit at the outpatient clinic for dysphagia in presence of a speech and language pathologist. Apart from the above-mentioned evaluation tools, data were gathered on swallowing function using videofluoroscopy of the swallowing act and fiberoptic endoscopic evaluation of swallowing (FEES).

Statistical analysis

All data were formally tested for normality with the Kolmogorov-Smirnoff test prior to further analysis. The distribution of the data was not sufficiently normal to allow parametric statistics. Descriptive statistics of baseline data, effect data (post minus pretreatment data), and follow-up minus posttherapy data, were determined. Differences between posttherapy and baseline data were tested for significance by a Wilcoxon Signed Rank Test. Group differences were tested using a Mann-Whitney *U* test. All statistical analyses were performed using SPSS 15.0 (SPSS Inc., Chicago, IL).

RESULTS

Patient characteristics

After applying inclusion and exclusion criteria, a total of 109 subjects were included in this study. All patients were diagnosed with idiopathic Parkinson's disease having oropharyngeal dysphagia. All patients were assigned to one of the three treatment groups as described previously. During the period of intervention, 21 subjects were excluded because of diverse methodological reasons (change of antiparkinson medication $N=17$, dental surgery $N=2$, other reasons $N=2$). The excluded subjects did not experience adverse effects from therapy. Furthermore, no significant differences in baseline data were present between the group of excluded subjects and the group

of included subjects. Finally, 88 patients (65 males, 23 females) did accomplish the full period of therapy. The mean age was 68 years, with a range of 42 to 81 years. The MMSE ranged from 23 to 30 points (median 28), whereas the Hoehn and Yahr scores ranged from 1 to 4 (median 2). No differences were found between the baseline characteristics of the three treatment groups. In Table 1 the patients' characteristics for each treatment group separately as well as for all groups combined, are presented.

Table 1. Patient characteristics.

Descriptive statistics of patient characteristics for each group separately as well as for all groups combined.

Group ^a	Gender (N _{Male} ^c , N _{Female})	Age (years)		MMSE		H&Y scale	
		Median	25';75' perc.	Median	25';75' perc.	Median	25';75' perc.
Group TT (N=28)	22;7	69	62;74	28,0	26,0;29,0	2	1,0;4,0
Group NMES-M (N=27)	20;9	65	60;74	28,0	26,0;29,5	2	1,0;3,0
Group NMES-S (N=30)	23;9	66	60;69	28,0	26,5;29,0	2	1,5;3,0
Total Group (N=85)	65;25	68	60;73	28,0	26,0;29,0	2	1,0;3,0

^a TT = traditional therapy, NMES-M = neuromuscular electrical stimulation at a motor level, NMES-S = neuromuscular electrical stimulation at a sensory level.

Treatment effects

The median and the interquartile range of the stimulation intensities in the NMES-M and the NMES-S group were, respectively, 9,5 (7 to 13,75) and 3,25 (2,75 to 4,25) mA. Improvement on the Dysphagia Severity Scale during the treatment period is presented in Table 2. Table 2 presents the descriptive statistics of the baseline and the effect data (post- minus pretreatment data) of the Dysphagia Severity Scale: the median, the 25th, and the 75th percentile of a patient's self-evaluation of dysphagia. The median progress on the DSS is 14 points (range -33 to 70). The effect data have been tested for significance (Wilcoxon Signed rank test) resulting in a significant positive therapeutically effect for all groups. However, no statistically significant differences in effect data were found between the three treatment groups (Mann-Whitney *U* test).

Table 3 to 5 show the descriptive statistics of both quality of life measurement tools: The SWAL-QOL and the MDADI. For each group separately as well as for the total group, data are presented. Table 3 and 4 contain, respectively, descriptive statistics of the

Table 2. Dysphagia Severity Scale (DSS).

Descriptive statistics of the baseline data and the effect data (post- minus pretreatment data), the number of patients per treatment group, and the level of significance of the difference between posttherapy data compared to baseline data for all groups (Wilcoxon Signed rank test).

Group ^a	Baseline data ^b			Effect data			
	Median	25';75'perc.	N	Median	25';75'perc.	N	P-value
Group TT	59	41;88	28	19	3;44	28	0,000
Group NMES-M	72	52;88	27	10	0;31	27	0,000
Group NMES-S	74	49;87	30	6	-2;24	30	0,005
Total Group	67	49;88	85	14	0;30	85	0,000

^a TT = traditional therapy, NMES-M = neuromuscular electrical stimulation at a motor level, NMES-S = neuromuscular electrical stimulation at a sensory level.

^b The maximum score of the scale is 100.

baseline data, the effect data, and the follow-up minus posttherapy data of the SWAL-QOL. A Wilcoxon signed rank test was used to test for significant changes between baseline and posttherapy measurements (Table 4). In table 4, only dysphagia-concerning subscales of the SWAL-QOL are given. Applying a Bonferoni correction, both the total group and the TT group showed a significant change on the Symptom Index. The total group also presented a significant effect on the Burden scale. No other statistically significant results were found. Because of the minimally increased medians during the period following therapy (Table 4), no tests were performed to test for significant differences between the post- and follow-up data.

Table 5 shows the descriptive statistics of the baseline data, the effect data, and the follow-up data minus the posttherapy data for the MDADI and its subscales. To test for significant changes between baseline and posttherapy measurements, a Wilcoxon signed rank test was used. Following Bonferoni correction, significant therapy effects were found for the total group on the total score, the global assessment, and both the physical and emotional subscales. None of the groups reached significance on the functional subscore. The only other significant effects were found for the TT group and the NMES-M group on, respectively, the global assessment score and the total score. No significant group differences were found. After three months, the follow-up measurement showed ignorable median changes in all treatment groups. Only total group changes were tested for significance and indicated at a minor deterioration of the global assessment score.

Descriptive statistics of baseline data and of the effect data, and follow-up minus posttherapy data of the Functional Oral Intake Scale, are given in Table 7. The range of scores of the FOIS is one to seven, indicating nothing by mouth to total oral diet with no restrictions.

Table 3. SWAL-QOL.
Descriptive statistics of the baseline data and the number of patients per treatment group.

Base-line		Food selection		Eat duration		Eat desire		Fear		Sleep		Fatigue		Communication		Mental Health		Social effects		Symptom	
SWAL-QOL ^a	Data	Burden	Median	25;75 ^c perc.	Median	25;75 ^c perc.	Median	25;75 ^c perc.	Median	25;75 ^c perc.	Median	25;75 ^c perc.	Median	25;75 ^c perc.	Median	25;75 ^c perc.	Median	25;75 ^c perc.	Median	25;75 ^c perc.	
Group ^b	N																				
Group TT	30	57	38;75	75	75;100	50	25;75	83	67;100	100	81;100	75	38;88	67	33;77	63	38;75	80	68;86	75	54;81
NMES-M	29	50	25;88	75	75;94	38	13;69	83	54;100	88	75;100	50	38;82	58	46;75	63	44;88	75	60;95	75	58;95
NMES-S	29	63	31;82	75	50;88	38	25;63	88	63;100	88	75;100	75	25;94	75	46;79	63	38;75	75	65;85	75	65;85
Total group	88	63	38;75	75	66;88	44	25;63	83	67;100	94	81;100	69	38;88	67	42;75	63	38;75	80	60;90	75	60;90

^a The maximum score of each scale is 100.

^b TT = traditional therapy, NMES-M = neuromuscular electrical stimulation at a motor level, NMES-S = neuromuscular electrical stimulation at a sensory level.

Table 4. SWAL-QOL

	N	SWAL-QOL Subscale ^a																		
		Burden			Food selection			Eat duration			Eat desire			Social effects			Symptom			
		Median	25;75 ^b perc.	P-Value	Median	25;75 ^b perc.	P-Value	Median	25;75 ^b perc.	P-Value	Median	25;75 ^b perc.	P-Value	Median	25;75 ^b perc.	P-Value	Median	25;75 ^b perc.		
Effect data	Group TT	14	0	-13;9	N.S.	0	0;25	N.S.	6	-15;12	N.S.	0	-8;0	N.S.	0	0;6	N.S.	10	1;19	0.004
	NMES-M	17	0	0;25	N.S.	0	-6;13	N.S.	12	0;25	N.S.	0	-8;4	N.S.	0	-3;15	N.S.	4	-2;10	N.S.
	NMES-S	18	6	0;37	N.S.	0	-16;0	N.S.	12	-3;37	N.S.	0	-8;17	N.S.	0	-8;16	N.S.	4	-5;11	N.S.
	Total group	49	0	0;25	0.009	0	-12;6	N.S.	12	0;25	N.S.	0	-8;8	N.S.	0	0;15	N.S.	5	0;11	0.001
Follow-up minus posttreatment	Group TT	6	19	9;53	N.A.	-13	-31;6	N.A.	-12	-19;3	N.A.	0	-2;2	N.A.	0	-9;6	N.A.	10	-22;14	N.A.
	NMES-M	6	0	-12;6	N.A.	-19	-38;0	N.A.	0	-16;25	N.A.	0	0;6	N.A.	0	-4;5	N.A.	-4	-12;-2	N.A.
	NMES-S	7	0	-25;0	N.A.	0	0;12	N.A.	-13	-25;0	N.A.	0	-41;0	N.A.	0	-25;5	N.A.	0	-42	N.A.
	Total group	19	0	0;12	N.A.	0	-25;0	N.A.	-12	25;0	N.A.	0	0;0	N.A.	0	-10;5	N.A.	-2	-1;-7	N.A.

Descriptive statistics of the effect data (post- minus pretreatment data), the number of patients per treatment group, and the level of significance of the difference between posttherapy data compared to baseline data for all groups (Wilcoxon Signed rank test).

^a The maximum score of each scale is 100.

^b TT = traditional therapy, NMES-M = neuromuscular electrical stimulation at a motor level, NMES-S = neuromuscular electrical stimulation at a sensory level.

Table 5. MD Anderson Dysphagia Inventory (MDADI).

Descriptive statistics of the baseline data, the effect data (post- minus pretreatment data), and the follow-up minus posttherapy data, the number of patients per treatment group, and the level of significance of the difference between posttherapy data compared to baseline data for all groups as well as the level of significance of the difference between follow-up data compared to posttherapy data for all groups combined.

Baseline data			Effect data			Follow-up minus posttherapy data						
MDADI ^a	Group ^b	Median	25;75 perc.	N	Median	25;75 perc.	N	P-value	Median	25;75 perc.	N	P-value
Global assessment	Group TT	3	2;4	29	0	0;2	29	0,012	0	-1;0	17	N.A.
	NMES-M	4	2;4	29	0	0;1	28	N.S.	0	0;0	13	N.A.
	NMES-S	4	2;5	27	0	0;1	27	N.S.	0	-1;0	13	N.A.
Functional subscale	Total Group	4	2;4	85	0	0;1	84	0,000	0	-1;0	43	0,011
	Group TT	21	19;22	27	0	-2;3	25	N.S.	0	-1;3	16	N.A.
	NMES-M	21	18;22	29	0	-2;4	27	N.S.	0	-5;0	11	N.A.
	NMES-S	20	18;24	25	0	-1;2	25	N.S.	1	-2;2	13	N.A.
Physical subscale	Total Group	21	18;23	81	0	-2;4	77	N.S.	0	-2;2	40	N.S.
	Group TT	28	24;31	28	2	-1;5	24	N.S.	0	-5;3	15	N.A.
	NMES-M	26	22;30	29	1	-2;7	28	N.S.	0	-3;2	13	N.A.
	NMES-S	28	22;32	25	2	-5;6	25	N.S.	-2	-5;1	12	N.A.
Emotional subscale	Total Group	28	23;30	82	2	-1;6	77	0,000	-1	-4;2	40	N.S.
	Group TT	21	18;24	27	1	-3;3	27	N.S.	0	-3;2	16	N.A.
	NMES-M	21	17;24	28	2	0;4	26	N.S.	-1	-4;2	13	N.A.
	NMES-S	20	18;24	27	1	-1;3	26	N.S.	-2	-5;2	12	N.A.
Total score	Total Group	21	18;24	82	1	-1;3	79	0,002	-1	-3;2	41	N.S.
	Group TT	72	63;80	26	2	-4;8	22	N.S.	1	-4;6	13	N.A.
	NMES-M	69	63;81	28	7	2;13	25	0,007	-3	-10;3	11	N.A.
	NMES-S	74	65;82	24	4	-1;9	23	N.S.	-2	-11;3	11	N.A.
	Total Group	72	64;81	78	4	-1;11	70	0,000	0	-10;3	35	N.S.

^a The range of the Total Score, the Global Assessment, and the Emotional, Functional, and Physical subscale is, respectively, 20 to 100, 1 to 5, 6 to 30, 5 to 25 and, 8 to 40. ^b TT = traditional therapy, NMES-M = neuromuscular electrical stimulation on a motor level, NMES-S = neuromuscular electrical stimulation on a sensory level.

Table 6. Functional Oral Intake Scale (FOIS)

Functional Oral Intake Scale for Dysphagia (Crary et al.)	
Level 1	Nothing by mouth
Level 2	Tube dependent with minimal attempts of food or liquid
Level 3	Tube dependent with consistent oral intake of food or liquid
Level 4	Total oral diet of a single consistency
Level 5	Total oral diet with multiple consistencies, but requiring special preparation or compensations
Level 6	Total oral diet with multiple consistencies without special preparation, but with specific food limitations
Level 7	Total oral diet with no restrictions

Table 7. Functional Oral Intake Scale (FOIS).

Descriptive statistics of baseline data and effect data (differences in post- minus pretherapy) and follow-up minus posttherapy data.

Functional Oral Intake Scale ^a	Baseline Data			Post- minus pretreatment data			Follow-up minus post data		
	Median	25';75' perc.	N	Median	25';75' perc.	N	Median	25';75' perc.	N
Group TT	7	6;7	29	0	0;0	29	0	0;0	17
Group NMES-M	7	6;7	29	0	0;0	29	0	-1;0	13
Group NMES-S	7	6;7	29	0	0;0	29	0	0;0	13
Total group	7	6;7	87	0	0;0	87	0	0;0	43

^aThe maximum score of the scale is 7.

^b TT = traditional therapy, NMES-M = neuromuscular electrical stimulation on a motor level, NMES-S = neuromuscular electrical stimulation on a sensory level.

No significant correlations were found between the dietary intake and the quality of life questionnaires or the Dysphagia Severity Scale (all $R < .2$). This finding was also observed in the study of Plowman-Prine et al. [11].

DISCUSSION

The aim of this study is to investigate the effects of NMES in patients with Parkinson's disease and oropharyngeal dysphagia compared to traditional logopedic dysphagia treatment with Health Related Quality of Life (HRQOL) as primary outcome measure. This study provides positive effects of dysphagia therapy in patients with Parkinson's disease as found in other studies [15]. One hundred nine subjects have been randomly assigned to one of three different treatment groups. All groups show significant therapy effects on the Dysphagia Severity Scale, as well as restricted improvements on the SWAL-QoL and the MDADI. Using the SWAL-QoL, both the total group and the TT group display a significant improvement on the Symptom Index. The total group also presents a significant effect on the Burden scale. Using the MDADI, significant therapy effects are found for the total group on the total score, the global assessment, and both the physical and emotional subscales. For the TT group and the NMES-M group, improvements are found on, respectively, the global assessment score and the total score. However, only slight non-significant differences between groups are found. Additionally, in this study oral-intake related clinical scales do not correlate significantly (all $R < 0.2$) with HRQOL related scales. The question arises if the FOIS scale is a satisfactory measure for dysphagia severity in this patient population, given the normal scores in the present study. The discrepancy between symptoms of dysphagia in daily life and oral intake versus the dysphagic findings using swallowing assessment tools like FEES or VFS, are known in Parkinson's disease [29]. The hypothesis that electrical stimulation would provide a better outcome on HRQOL can not be confirmed. Remarkably is the fact that irrespective of the applied quality of life measurement tool, no group differences are found regarding effect data nor follow-up minus posttherapy data, thus suggesting the lack of any adjunct therapy effect of NMES.

However, these findings might be explained by other causes as well. One concern might lie in the sample size (power). However, according to the sample size calculation, the total group ($N=88$) used for statistical analyses is sufficient. For several, mainly logistic reasons, only few patients with severe Parkinson disease ($H\&Y>3$) have been included. Usually, this group of patients is admitted to nursing homes, thus not visiting outpatient clinics. The moderate severity of Parkinson's disease in our patient population ($H\&Y$ scale: median = 2) might have contributed to less significant group differences. If

patients would have shown more severe impairments at the beginning of therapy, therapy outcome might have been more evident; Theoretically, severely impaired subjects can show more improvement on a questionnaire or rating scale than subjects who show minor impairments prior to therapy. However, based on literature, it is unclear which treatment group would have gained the most benefit in case of a group of patients with more severe symptoms of Parkinson's disease. Furthermore, the population of included patients is a realistic representation of Parkinson patients consulting speech therapists for dysphagic complaints. Another explanation for the absence of group differences can be the treatment period of three weeks. Probably, this treatment period is not long enough to observe significant group differences in therapy outcome, in spite of the high treatment intensity. Furthermore, the fixed stimulation variables (frequency and pulse width) of the VitalStim electrical stimulator might not have been optimal for treatment of deglutition disorders in Parkinson's disease. Different stimulation variables can cause different effects in oropharyngeal excitability [31]. In Parkinson's disease swallowing problems can be due to loss of neurological control of swallowing rather than muscle weakness or peripheral sensory dysfunction [5]. Although sensory and motor effects of this type of electrical stimulation have been reported [32,22], this adjunct to traditional logopedic dysphagia treatment can be less appropriate for these patients compared to other patient groups. The possible effect of electrical stimulation on dysphagia in these patients might be too small to be detected at a HRQOL-level. In this study, no adverse effects were observed; Ludlow et al. [22] observed that aspiration and pooling were significantly reduced in chronically dysphagic patients during surface electrical stimulation with low sensory threshold levels of stimulation, whereas almost all subjects showed depression of the hyoid bone during motor-level stimulation at rest. The authors hypothesized a higher risk of further decreased hyolaryngeal elevation during electrical stimulation in dysphagic patients who were already suffering from reduced hyolaryngeal elevation. Finally, the lack of significance can not be explained by incompetence of a restricted number of speech therapists, since eighty-five speech therapists experienced in dysphagia treatment have been involved in this study.

The application of statistical analyses has been rather conservative in the present study; The large number of statistical tests has led to a major impact of the Bonferroni-correction on the data.

Summarizing, no convincing arguments or evidence have been found in favor of any of the three treatment options studied. Possibly, the use of larger patient groups may have revealed minor differences in therapy effects. However, based on our preliminary data, no further conclusions can be made.

CONCLUSION

This study is one of the first attempts to evaluate the effects of adjunct NMES in the treatment of Parkinson patients with oropharyngeal dysphagia. In this randomized controlled trial, all groups (TT, NMES-S, and NMES-M) show significant therapy effects on the Dysphagia Severity Scale, as well as restricted improvements on the SWAL-QoL and the MDADI. However, only slight non-significant differences between groups have been found. Although some methodological and clinimetric issues might arise, most of these can be explained by ethical or logistical restrictions. In future, a larger study might be needed to clarify these preliminary findings.

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4



‘What about swallowing?’ Diagnostic performance of daily clinical practice compared with the Eating Assessment Tool – 10

Published in: *Dysphagia*. 2016 Apr;31(2):214-22.

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ABSTRACT

Introduction

In daily clinical practice, patients are frequently asked about their swallowing as part of the patient-clinician interview. This study compares the diagnostic performance of a single open question 'What about swallowing?' (usual care) with the Eating Assessment Tool (EAT-10) as reference test in screening for oropharyngeal dysphagia (OD).

Materials and methods

303 outpatients at risk of OD were recruited at three university hospitals: 162 men and 141 women with a mean age of 70 years. All data were retrieved by phone.

Results

To identify patients at risk of dysphagia, two different cut-off scores for the EAT-10 total score were retrieved from the literature. The diagnostic performance of the single question was determined by comparing dichotomized answers to the single question (no problems versus difficulties in swallowing) with the EAT-10 as reference test. Sensitivity, specificity, positive and negative predictive values ranged between 0.75-0.76, 0.75-0.84, 0.93-0.97 and 0.38-0.43, respectively.

Discussion and Conclusion

Mostly, the results of this exploratory study indicate a sufficient diagnostic performance of the single question in identifying patients who are at risk of dysphagia when using the EAT-10 questionnaire as a reference test. Further research, is, however, necessary to provide additional psychometric data on Functional Health Status (FHS) questionnaires including the single question using either FEES or VFS as gold standard or reference test.

INTRODUCTION

Oropharyngeal dysphagia (OD) is associated with malnutrition, dehydration, aspiration pneumonia, and sudden death [1, 2]. It is known to affect social life[3]: patients may no longer enjoy eating and drinking, and may avoid social activities. OD may, therefore, have a major impact on a patient's Health-Related Quality of Life (HR-QoL)[2-4].

HR-QoL is the effect of (chronic) medical conditions and their treatment on daily functioning and quality of life (QoL)[5], which is "a state of complete physical, mental and social well-being, not merely the absence of disease or infirmity"[6], as defined by the World Health Organization (WHO) in 1946[6]. A recent systematic review by Timmerman et al.[7] gives an overview of HR-QoL questionnaires regarding dysphagia. Examples of these questionnaires are the Dysphagia Handicap Index (DHI)[8], the M.D. Andersen Dysphagia Inventory[9] and the SWAL-QOL[10-12].

The gold standard for detecting dysphagia is fibre optic endoscopic evaluation of swallowing (FEES)[13] or video fluoroscopy of the swallowing act (VFS)[13, 14]. The importance of detecting OD at an early stage is being recognized more frequently. Most examinations can, however, be burdensome, time-consuming and costly [15], and therefore, not performed as routine clinical practice in every patient visiting an otorhinolaryngology department.

Another way of screening for OD is the use of a Functional Health Status (FHS) questionnaire., which quantifies the influence of a given disease on particular functional aspects as experienced by the patient[4]. In OD, FHS questionnaires quantify the severity of the swallowing problem [4, 16]. A recent systematic review by Speyer et al.[4] retrieved three English-language questionnaires on FHS in adults with OD: the Eating Assessment Tool (EAT-10)[17], the Swallowing Outcome after Laryngectomy (SOAL)[18], and the Self-report Symptom Inventory. The Sydney Swallow Questionnaire (SSQ)[19] proved to be identical to the Modified Self-report Symptom Inventory.

The Eating Assessment Tool (EAT-10) by Belafsky et al.[17] is a short 10-item, easy to use, self-administered questionnaire[4]. Although the EAT-10 is considered to be predominantly a questionnaire on FHS, some items on HR-QoL are also included. The sum score of this 10-item questionnaire ranges from 0 to 40[17]. Belafsky et al.[17] found that a sum score ≥ 3 indicates that a patient is at risk of dysphagia and warrants further examination. In a recent study by Rofes et al.[20], however, it was determined that a cut-off score ≥ 2 would be optimal. Rofes et al. [20] calculated the sensitivity and specificity of the EAT-10 using VFS as a reference test (golden standard[21]). By using a cut-off score of ≥ 2 , the sensitivity and specificity for OD was 89% and 82%, respectively. Lately Cheney et al. [22] evaluated the ability of the EAT-10 to screen for aspiration risk in patients with dysphagia describing a cutoff score of > 15 : sensitivity 71% and

specificity 53%. As Cheney et al. used the EAT-10 not just to screen for OD but to screen for aspiration in selected patients with OD, cut-off points differed highly from earlier data by Belafsky et al. [17] and Rofes et al. [20]

In daily clinical practice, however, a single question such as 'What about swallowing?' is frequently used without any additional standardized testing. For example, general practitioners may restrict their patient history on swallowing to a single question, whereas clinicians in specialized dysphagia clinics will include standardized questionnaires such as the EAT-10 as part of the assessment and management of dysphagia. The diagnostic performance of a single question has not been explored until now. If a patient's answer was negative, it is possible that no further swallowing screening or assessment would be performed. As symptoms like coughing, choking, feeling the food sticking (in the throat) after swallowing and respiration problems may all be aspects of OD, a single question might expect a patient to have preliminary knowledge about the concept of dysphagia. Therefore, the use of a single question on swallowing instead of a more detailed questionnaire such as the EAT-10, might lead to an under-diagnosis of those patients at risk of dysphagia.

The purpose of the current study is to compare the diagnostic performance of a single question on swallowing (usual care) with the FHS questionnaire EAT-10 as reference test. Two different EAT-10 cut-off scores for patients at risk of dysphagia will be used: a sum score ≥ 3 as suggested by Belafsky et al. [17] and ≥ 2 as defined by Rofes et al. [20]. We hypothesize that a single question, 'What about swallowing?', which is part of everyday clinical practice, will show poor diagnostic performance when compared to the EAT-10. It is expected that the single question will have insufficient sensitivity and specificity to identify patients at risk of dysphagia.

METHODS

Subjects

We studied a consecutive series of new patients who visited the outpatient clinics for dysphagia or otorhinolaryngology of the Leiden University Medical Centre (LUMC), Maastricht University Medical Centre (MUMC) and Skane University Hospital Malmö (SUS Malmö). Included were participants aged at least 18 years of age who might be at risk of OD. Patients with severe cognitive problems were excluded. Within six months of their initial visit to the clinics, patients were contacted by telephone. All data was collected during that call.

Protocol

First, patients were invited to participate when contacted by phone. After informed consent and during that same phone call, data on the current status of the patients were collected. Subject characteristics including age, gender and actual oral intake were registered. The latter was assessed using the Functional Oral Intake Scale (FOIS) which ranges from 1 (i.e., nothing by mouth) to 7 (i.e., no restrictions)[23]. Subsequently, a single question was posed, representing clinical daily practice: 'What about swallowing?'. All answers were written down and at a later stage dichotomized, to normal (i.e., no complaints) and abnormal (i.e., at least mild complaints). For example, participants responded 'I can eat and drink everything' (normal) or 'Sometimes meat gets stuck in my throat' (abnormal). Finally, the EAT-10 was administered. The EAT-10 consists of ten questions which can be scored from 0 (no problem) to 4 (severe problem). The range of the sum score is 0 to 40[17].

Statistics

Apart from descriptive data analysis, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the single question 'What about swallowing?' were calculated. The EAT-10 was used as a reference test. A sensitivity of $\geq 70\%$ and a specificity of $\geq 60\%$ was considered as minimum requirement for screening instruments[24]. Both cut-off scores by Belafsky et al.[17] and Rofes et al.[20] were used to identify patients at risk of dysphagia.

RESULTS

The LUMC, MUMC and SUS Malmö included 303 patients (78, 122 and 103 patients, respectively). Patient characteristics are provided in Table 1. One hundred and sixty-two patients (53%) were male with a median age of 70 years (IQR, 60-77 years), and 141 were female with a median age of 69 years (IQR, 57-76 years). Medical diagnoses included head and neck cancer (15%) and neurological diseases such as stroke, Parkinson's disease, multiple sclerosis or myotonic dystrophy (46%). A third group of patients suffered from a variety of diseases such as general weakness due to other diseases, cricopharyngeus hypertrophy, epiglottitis etc.(39%). Most patients followed an oral intake without any restrictions: The median FOIS score was 7 (IQR, 5-7).

Figure 1A shows the FOIS levels in relation to the dichotomized EAT-10 scores using a cut-off score of ≥ 3 points according to Belafsky et al.[11] to distinguish patients at risk of dysphagia and those demonstrating normal swallowing. The data in the figure indicates that 36.0% of the total population obtained an abnormal EAT-10 score, thus

being at risk of dysphagia, while oral intake was normal, whereas 2.3% of the total population obtained a normal EAT-10 score while their oral intake was restricted. This may suggest that a cut-off point of ≥ 3 misses 2.3% of participants who seem at risk of dysphagia. When using the cut-off score of ≥ 2 points by Rofes et al. [20], the following data are found (see Figure 1B): 38.9% of the total population producing an abnormal EAT-10 score have a normal oral intake, whereas 1.0% of those with a normal EAT-10 score have an oral intake with restrictions.

Figure 2A displays the answer to the single question 'What about swallowing?' in relation to the EAT-10 outcome using the cut-off score by Belafsky and underlines the previous findings shown in Figure 1A. A total of 200 (66.1%) patients report having swallowing problems when answering the single question. Two-hundred and forty-four of these patients were at risk of dysphagia according to the EAT-10. In 103 patients (34.0%) the single question was scored as normal; however, 59 (19.5%) of these patients were at risk of dysphagia according to the EAT-10. Figure 2B shows similar data using the cut-off score by Rofes et al.[20]. In 103 patients (34%), the single question was scored as normal; however, 64 (21.1%) of these patients were at risk of dysphagia according to the EAT-10.

In Figure 3, the distribution is displayed of the answers to the single question versus the EAT-10 total score. The histogram shows that the patients who report having no swallowing problem on the single question can score ≥ 3 points on the EAT-10, with some patients having EAT-10 sum scores up to 32.

Table 1. Subject characteristics (number of subjects, gender, age, FOIS and medical diagnoses per center.

Subject characteristics		Patient recruitment (Centre)			Total
		LUMC	SUS Malmö	MUMC	
Number of subjects		78	103	122	303
Gender (M;F)		34 M; 44 F	50 M; 53 F	78 M; 44 F	162 M; 141 F
Age in yrs (Med; IQR)	All	67; 53-76	74; 64-79	69; 62-74	70; 60-77
	Male	67; 56-71	75; 66-79	69; 64-75	70; 63-77
	Female	69; 50-76	73; 62-79	68; 55-73	69; 57-76
FOIS (Med; IQR)		7; 6-7	6; 5-7	6; 5-7	7; 5-7
Medical diagnoses (N; %)	Head and Neck cancer	27; 35	3; 3	16; 13	46; 15
	Neurological disorder	16; 20	28; 27	95; 78	139; 46
	Other	35; 45	72; 70	11; 9	118; 39

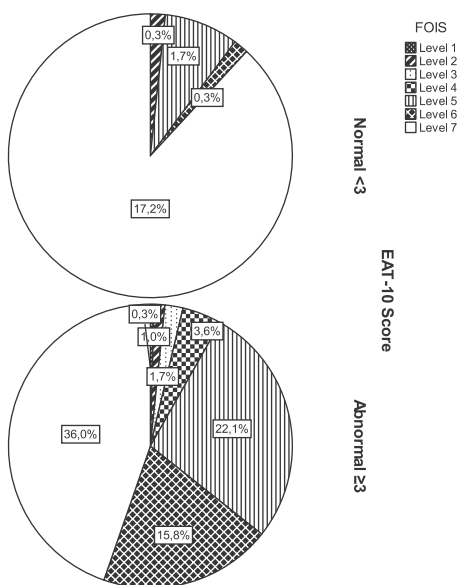


Figure 1A.
FOIS levels in percentages by dichotomized EAT-10 scores (cut-off score ≥ 3) [17]

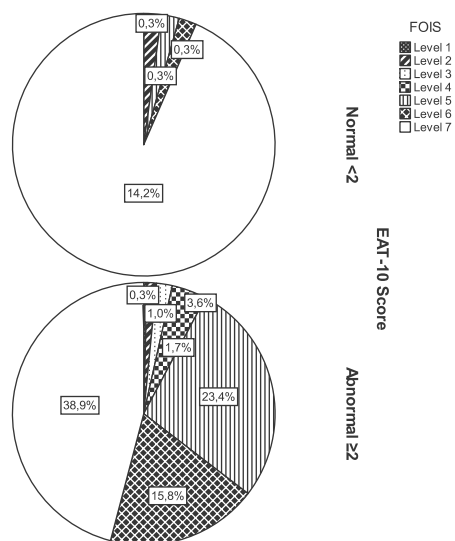


Figure 1B.
FOIS levels in percentages by dichotomized EAT-10 scores (cut-off score ≥ 2) [20]

Table 2 shows the frequencies of the EAT-10 scores per item for three groups: all participants (N=303), subjects with normal swallowing (N=103) and those with abnormal swallowing (N=200) according to the single question. In addition, Figure 4 illustrates the sum of all total scores per EAT-10 item for the same three groups; higher scores were obtained for items 2, 4 and 8 and lower scores for items 1 and 6. All three groups showed similar tendencies.

The diagnostic performance of the single question was determined using the EAT-10 as reference test and the single question as index test (Table 3). Table 3A and 3B present cross-tabs based on the cut-off sum score according to Belafsky et al.[17] and Rofes et al. [20], respectively. Using a cut-off score of ≥ 3 , the following data are found: sensitivity of 76%, specificity of 75%, PPV of 93% and NPV of 43% (Table 3A). Changing the EAT-10 cut-off score to ≥ 2 points increases specificity to 84% and PPV to 97%, and decreases the sensitivity to 75% and NPV to 38% (Table 3B).

Table 2. Frequencies of the EAT-10 scores per item for three groups: all participants (N=303), subjects with normal swallowing (N=103) and abnormal swallowing (N=200) according to the single question.

EAT-10	Group	EAT-10 Item score				
		0 (No problem)	1	2	3	4 (Severe problem)
1. My swallowing problem has caused me to lose weight	All (N= 303)	219(72,2%)	28(9,2%)	28(9,2%)	13(4,2%)	16(5,2%)
	Single Question Normal (N=103)	82(79,7%)	13(12,6%)	6(5,8%)	0(0%)	2(1,9%)
	Single Question Abnormal (N=200)	136(68%)	15(7,5%)	22(11%)	13(6,5%)	14(7%)
2.My swallowing problem interferes with my ability to go out for meals	All (N= 303)	161(53,0%)	35(11,5%)	30(9,9%)	39(12,8%)	39(12,8%)
	Single Question Normal (N=103)	75(72,8%)	14(13,6%)	4(3,9%)	6(5,8%)	4(3,9%)
	Single Question Abnormal (N=200)	85(42,5%)	21(10,5%)	26(13,0%)	33(16,5%)	35(17,5%)
3. Swallowing liquids takes extra effort	All (N= 303)	167(55,0%)	50(16,5%)	35(11,4%)	41(13,5%)	11(3,6%)
	Single Question Normal (N=103)	86(83,5%)	9(8,7%)	4(3,9%)	4(3,9%)	0(0%)
	Single Question Abnormal (N=200)	80(40,0%)	41(20,5%)	31(15,5%)	37(18,5%)	11(5,5%)
4. Swallowing solids takes extra effort	All (N= 303)	106(34,8%)	52(17,1%)	45(14,8%)	71(23,4%)	30(9,9%)
	Single Question Normal (N=103)	64(62,1%)	20(19,5%)	8(7,8%)	9(8,7%)	2(1,9%)
	Single Question Abnormal (N=200)	41(20,5%)	32(16,0%)	37(18,5%)	62(31,0%)	28(14,0%)
5. Swallowing pills takes extra effort	All (N= 303)	146(48,1%)	39(12,8%)	51(16,8%)	36(11,8%)	32(10,5%)
	Single Question Normal (N=103)	69(67,0%)	15(14,6%)	15(14,6%)	2(1,9%)	2(1,9%)
	Single Question Abnormal (N=200)	76(38,0%)	24(12,0%)	36(18,0%)	34(17,0%)	30(15,0%)
6. Swallowing is painful	All (N= 303)	220(72,6%)	32(10,5%)	19(6,2%)	18(5,9%)	15(4,8%)
	Single Question Normal (N=103)	85(82,6%)	8(7,7%)	8(7,7%)	1(1,0%)	1(1,0%)
	Single Question Abnormal (N=200)	134(67,0%)	24(12,0%)	11(5,5%)	17(8,5%)	14(7,0%)
7. The pleasure of eating is affected by my swallowing	All (N= 303)	155(51,1%)	35(11,5%)	43(14,1%)	38(12,5%)	33(10,8%)
	Single Question Normal (N=103)	81(78,7%)	11(10,7%)	4(3,9%)	5(4,8%)	2(1,9%)
	Single Question Abnormal (N=200)	73(36,5%)	24(12,0%)	39(19,5%)	33(16,5%)	31(15,5%)
8. When I swallow food sticks in my throat	All (N= 303)	120(39,6%)	49(16,1%)	51(16,7%)	49(16,1%)	35(11,5%)
	Single Question Normal (N=103)	68(66,0%)	22(21,4%)	9(8,7%)	1(1,0%)	3(2,9%)
	Single Question Abnormal (N=200)	51(25,5%)	27(13,5%)	42(21,0%)	48(24,0%)	32(16,0%)
9. I cough when I eat	All (N= 303)	138(45,5%)	55(18,0%)	51(16,8%)	39(12,8%)	21(6,9%)
	Single Question Normal (N=103)	59(57,3%)	26(25,2%)	13(12,6%)	3(3,0%)	2(1,9%)
	Single Question Abnormal (N=200)	78(39,0%)	29(14,5%)	38(19,0%)	36(18,0%)	19(9,5%)
10. Swallowing is stressful	All (N= 303)	148(48,7%)	45(14,8%)	47(15,5%)	41(13,5%)	23(7,5%)
	Single Question Normal (N=103)	66(64,0%)	16(15,6%)	10(9,7%)	8(7,8%)	3(2,9%)
	Single Question Abnormal (N=200)	81(40,5%)	29(14,5%)	37(18,5%)	33(16,5%)	20(10,0%)

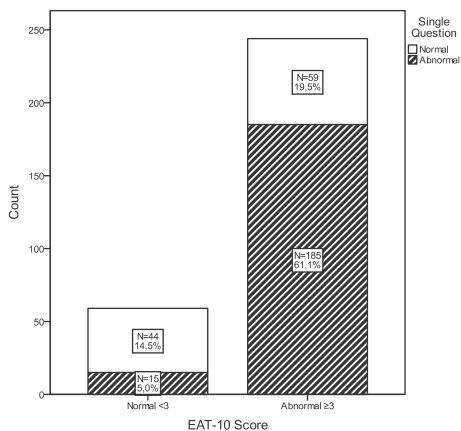


Figure 2A. Subjects at risk of OD: Data on single question by dichotomized EAT-10 scores (cut-off score ≥ 3) [17].

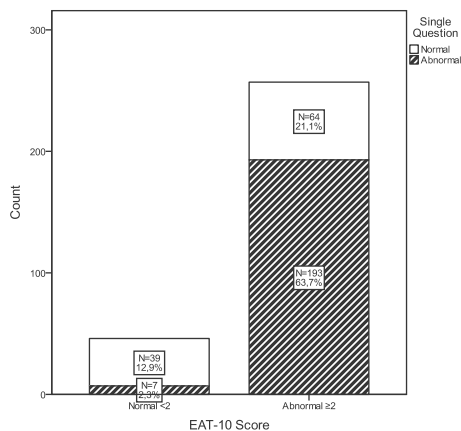


Figure 2B. Subjects at risk of OD: Data on single question by dichotomized EAT-10 scores (cut-off score ≥ 2) [20].

Table 3A Cross-tabs of the EAT-10 using a cut-off score of ≥ 3 [11] (Reference test) and the single question “What about swallowing?” (Index test). Diagnostic performance of the single question: Se=0.76, Sp=0.75, PPV=0.93 and NPV=0.43.

		EAT-10 (Reference test)		Total
		+	-	
		(At risk of OD)	(Not at risk)	
Single question “What about swallowing?” (Index test)	+	185	15	200
	(Abnormal)			
	-	59	44	103
	(Normal)			
Total		244	59	303

Table 3B Cross-tabs of the EAT-10 using a cut-off score of ≥ 2 [12] (Reference test) and the single question (Index test). Diagnostic performance of the single question: Se=0.75, Sp=0.84, PPV=0.97 and NPV=0.38.

		EAT-10 (Reference test)		Total
		+	-	
		(At risk of OD)	(Not at risk)	
Single question “What about swallowing?” (Index test)	+	193	7	200
	(Abnormal)			
	-	64	39	103
	(Normal)			
Total		257	46	303

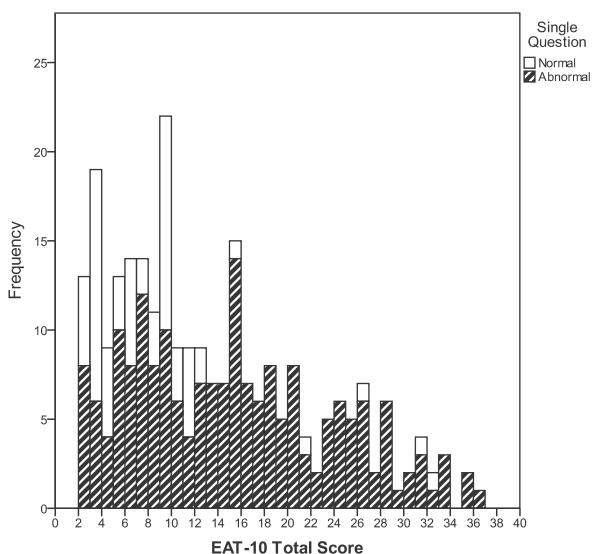


Figure 3. Distribution of data on single question by EAT-10 total score.

DISCUSSION

The purpose of the current study was to compare the diagnostic performance of a single question on swallowing with the FHS questionnaire EAT-10 as a reference test to identify patients who are at risk of dysphagia. Although it may be hypothesized that a validated questionnaire may have a higher sensitivity and specificity, a single question is still part of everyday clinical practice and, therefore, its diagnostic performance should be known. For example, most general practitioners may restrict their patient history on swallowing to a single question, whereas clinical experts in OD will ask for more detailed information and will usually include standardized assessments on OD such as the EAT-10.

The use of a measurement tool in clinical practice can only be justified by its validity and reliability. When validating questionnaires, different psychometric characteristics should be taken in account as shown by Terwee et al.[25] and Aaronson et al.[26] such as content validity, internal consistency, criterion validity, construct validity, reproducibility, responsiveness, floor and ceiling effects, and interpretability. In 2010, Mokkink et al.[27] published the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN)[28]: a taxonomy of measurement properties and definitions for health-related patient reported outcomes.

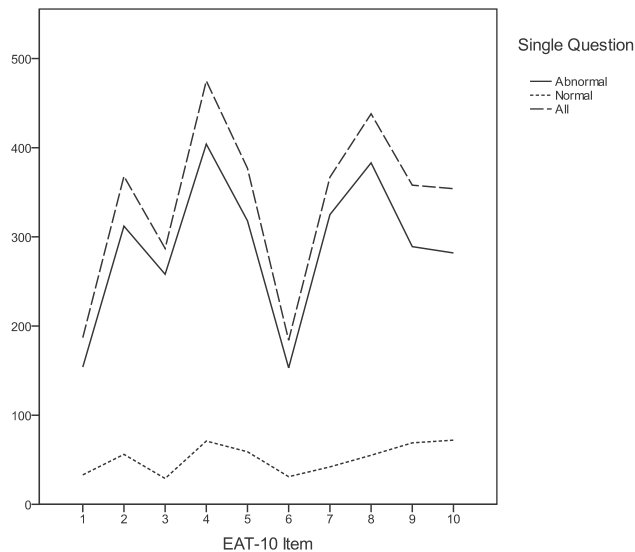


Figure 4. Sum of all total scores per EAT-10 item for all subjects (N=303) and subjects with abnormal swallowing (N=200) and normal swallowing (N=103) according to the single question.

In a psychometric review by Speyer et al. [4] on FHS in OD, three FHS questionnaires were retrieved whose measurement properties were determined using the COSMIN checklist[29] and the 4-point rating scale according to Terwee et al.[30]. All three FHS questionnaires obtained poor overall methodological quality scores for most psychometric properties and, therefore, psychometric re-assessment of all FHS questionnaires was advised. In a more recent publication, Rofes et al.[20] provided additional information on the diagnostic performance of the EAT-10 compared with VFS. The EAT-10 showed an ROC AUC of 0.89 for OD with an optimal cut-off score at two instead of the proposed cut-off at three by Belafsky et al.[17]. The sensitivity and specificity were 0.89 and 0.82, respectively.

In this study, we demonstrated that a single question has sufficient sensitivity and specificity to screen for patients at risk of dysphagia when using the EAT-10 as reference test; depending on the EAT-10 cut-off point, sensitivity and specificity of the single question ranged between 75 to 76% and 75 to 84%, respectively. These values fall within the minimum norms for sensitivity and specificity of $\geq 70\%$ and $\geq 60\%$ as suggested by Bours et al.[21] or Kertscher et al.[24]. This leads to the rejection of our initial hypothesis that a single question 'What about swallowing?' would show poor diagnostic performance when compared to the EAT-10.

However, despite of the sufficient sensitivity and specificity, the low NPV of the single

question (ranging between 0.38 and 0.43 depending on the cut-off point) remains a concern and may restrict the use of the single question in screening for dysphagia; a high percentage of subjects (false negatives) will not be considered for further dysphagia assessment even though they are actually at risk for dysphagia. In contrast to the NPV, the PPV (ranging between 0.93 and 0.97) is adequate and only very few subjects (false positives) will be referred for further assessment while not being at risk for dysphagia.

Some methodological remarks can be made, however. First of all, in this study, a Swedish and Dutch consensus translation by dysphagia experts of the EAT-10 was used. These translations were not validated. Furthermore, all data were gathered by phone, whereas the EAT-10 was developed as a patient self-report. Another aspect is the possible priming of patients using a standardized protocol order: the single question was asked first, directly followed by the EAT-10. Finally, the subject population in general showed limited restrictions in oral intake as measured by FOIS, indicating a mild severity of OD. It cannot be ruled out that in the case of patients with more severe swallowing problems, data might have been slightly different from those presented in this manuscript. In our opinion, however, none of these matters is expected to be of significant influence on the reported outcome.

Nonetheless, even though the single open question showed sufficient diagnostic performance, the use of a standardized questionnaire may have advantages. Using a standardized set of questions warrants the retrieval of similar information from all patients and prohibits the omission of essential information. Furthermore, in contrast to the single question, patients do not need to have preliminary knowledge about the concept of dysphagia. A questionnaire could list all associated issues such as coughing, history of pneumonia, etc. Still, in case of the availability of multiple screening tools with sufficient diagnostic performance, different clinical work settings may require different screening tools depending on factors such as number of trained staff, workload per staff member, availability of FEES or VFS in the setting itself, and possible time constraints[24].

Currently, research is being carried out to determine the diagnostic performance of FHS questionnaires including the single question using either FEES or VFS as reference test. This study will provide additional psychometric data on FHS questionnaires as a screening instrument for patients at risk of OD and the validity and reliability of a single question representing daily clinical practice.

CONCLUSION

Because OD is associated with malnutrition, dehydration, aspiration pneumonia, sudden death[1, 2], decreased HR-QoL[7] and is often a complication of other medical problems[31], early detection and adequate screening are important. A single open question 'What about swallowing?' is often part of daily clinical practice.

Even though the NPV was rather low, this study found high sensitivity, specificity and PPV data for this single question in identifying patients who are at risk of dysphagia when using the EAT-10 questionnaire as a reference test. Ongoing research will provide additional psychometric data on FHS questionnaires such as the single question using either FEES or VFS as gold standard or reference test. Once the measurement properties of all FHS questionnaires, including daily clinical practice or the single open question, are known, an optimal choice between FHS questionnaires can be justified.

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5



Quality of life in oncological patients with oropharyngeal dysphagia: Validity and reliability of the Dutch version of the Deglutition Handicap Index (DHI) and the MD Anderson Dysphagia Inventory (MDADI)

Published in: Dysphagia. 2011 Dec;26(4):407-14.

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ABSTRACT

Quality of life is considered to be an important outcome measurement in objectifying the current health status or therapy effects in patients with oropharyngeal dysphagia. In this study, the validity and reliability of the Dutch version of the Deglutition Handicap Index (DHI) and the MD Anderson Dysphagia Inventory (MDADI) have been determined in oncological patients with oropharyngeal dysphagia. 76 consecutive patients were selected at the Medical University Hospital Maastricht and were asked to fill in three questionnaires on quality of life related to oropharyngeal dysphagia (the Swal-Qol, the MDADI, and the DHI) and a simple one-item visual analogue Dysphagia Severity Scale. None of the quality of life questionnaires showed any floor or ceiling effects. The test retest reliability of the MDADI and the Dysphagia Severity Scale proved to be good. The test retest reliability of the DHI could not be determined because of insufficient data. However, the intraclass correlation coefficients were rather high. The internal consistency proved to be good. However, when applying confirmatory factor analysis, the underlying constructs as defined by the subscales per questionnaire could not be distinguished. When considering the criterion validity, the MDADI as well as the DHI showed satisfactory associations with the Swal-Qol (reference or gold standard) after having removed its less relevant subscales.

INTRODUCTION

Patients with advanced head and neck cancer often suffer from oropharyngeal dysphagia as a result of the disease itself or its treatment¹. Dysphagia can lead to malnutrition and dehydration as well as an increased risk of aspiration². When objectifying a patient's current health status as well as the effects of a therapeutic intervention, quality of life is considered to be an important evaluation tool³.

In the literature, a few questionnaires on health related quality of life can be found that focus on oropharyngeal dysphagia: The Swal-Qol⁴, the MD Anderson Dysphagia Inventory (MDADI)⁵, and the Deglutition Handicap Index (DHI)⁶. When using a questionnaire in research, its psychometric characteristics must be well-known and of sufficient high quality, otherwise, the study results cannot be interpreted or be given any clinical relevance. Although the reliability and validity of the Swal-Qol has been described⁴, hardly any data are available on the psychometric quality of the MDADI or the DHI. The Swal-Qol is an elaborated 44-item questionnaire containing eleven subscales. Although the Swal-Qol is a commonly used instrument in research, its application in daily clinical practice may be limited. Clinicians need a short, easy-to-handle questionnaire for clinical screening.

In this study, the validity and the reliability of the Dutch version of the DHI and the MDADI in oncological patients with oropharyngeal dysphagia will be determined.

METHODS

Subjects

Patients were selected consecutively at the outpatients' clinic for dysphagia at the Department of Otorhinolaryngology, Head and Neck Surgery and at the MAASTRO clinic at the Medical University Hospital in Maastricht (MUMC). Patient recruitment took place during outpatients' visits at the outward patient clinic. A small sample of included patient was recruited by phone after having studied their medical records. All included patients had to meet the following criterion; the patients had to be diagnosed by a laryngologist as having oropharyngeal dysphagia based on oncological disorders. Furthermore, a patient's general condition had to be considered as stable during repeated measurements. Lastly, included patients may not show any cognitive restrictions. Patients received oral information about the study and were only included after informed consent.

In total, 76 patients were included in the study. There were 57 (75%) men and 19 (25%) women in this study, with an age ranging from 45 to 83 years. The mean age for men

and women was, respectively, 64 and 61. The status of the oral feeding restrictions was scored, using the Functional Oral Intake Scale or FOIS by Crary et al.⁷ Two subjects were tube dependent, while all other subjects were on a total oral diet varying from a diet with a single consistency (N=7), with multiple consistencies and special preparation or compensation (N=30), without any special preparation but with some food limitations (N=28), to a normal oral diet (N=9).

Questionnaires

Four questionnaires have been used in this study; Three questionnaires on quality of life related to oropharyngeal dysphagia, namely, the Swal-Qol⁴, the MD Anderson Dysphagia Inventory (MDADI)⁵, the Deglutition Handicap Index (DHI)⁶, plus a simple one-item visual analogue scale (Dysphagia Severity Scale). Both the MDADI and the DHI were translated into Dutch by three independent researchers and combined into one final translation by mutual consensus. The Dysphagia Severity Scale needed no translation and the Swal-Qol had already been translated by Bogaardt et al.⁸.

The first questionnaire, the Swal-Qol, is considered to be the golden standard for determining quality of life in oropharyngeal dysphagia. This 44-item tool exhibits good internal-consistency reliability and short-term reproducibility⁴. It consists of eleven subscales (see Table 1). The minimum and maximum score per subscale are zero and 100, indicating extremely impaired quality of life versus no impairment as experienced by the individual. The DHI is a 30-item questionnaire on deglutition related aspects in daily life (5 point-rating scale: 0-4). The questionnaire is subdivided in three domains of ten items: emotional (psychosocial consequences), functional (nutritional and respiratory consequences) and, physical (symptoms related to swallowing), The minimum score is zero points (indicating no handicap) and the maximum score is 120 points (indicating maximum handicap)⁶. The MDADI consists of 20 items. It is composed of a global assessment (a single question) and three subscales, namely, the emotional subscale (eight items), the functional subscale (five items), and the physical subscale (six items). The global assessment refers to the individual's swallowing difficulty affecting the overall daily routine. The emotional, functional, and physical subscales refer to the individual's affective response to the swallowing disorder, the impact of the disorder on daily activities, and the self-perceptions of the swallowing difficulties, respectively⁵. Using five-point scales (1-5), the minimum total score is 20 and the maximum total score is 100. In the original version of the MDADI, all but two items were scored in a way that higher scores referred to higher functioning. In the Dutch translation, it was decided to use a uniform way of scoring. Thus, by adjusting the scoring of two items, low scores refer to low functioning, whereas high scores refer to high functioning. The Dysphagia Severity Scale is a self-designed evaluation tool,

Table 1. Descriptive analysis of the MD Anderson Dysphagia Inventory (MDADI), the Deglutition Handicap Index (DHI), the Dysphagia Severity Scale, and the Swal-Qol.

Quality of Life Scale		Range of Scale	Median (25';75' percentiles)	N
Swal Qol ^a	Burden	0 – 100	63 (6;75)	73
	Food Selection	0 – 100	75 (25;88)	71
	Eating Duration	0 – 100	25 (0;63)	71
	Eating Desire	0 – 100	75 (27;100)	72
	Fear	0 – 100	88 (69;100)	71
	Sleep	0 – 100	75 (44;88)	73
	Fatigue	0 – 100	58 (33;83)	73
	Communication	0 – 100	63 (50;88)	71
	Mental Health	0 – 100	65 (30;90)	71
	Social Functioning	0 – 100	65 (25;92)	73
	Symptoms	0 – 100	63 (44;77)	73
DHI ^b	Total Score	0 – 120	36 (20;46)	42
	Emotional Subscore	0 – 40	10 (2;22)	46
	Functional Subscore	0 – 40	12 (8;19)	44
	Physical Subscore	0 – 40	10 (6;16)	44
MDADI ^{ac}	Total Score	20 – 100 ²	66 (51;77)	74
	Global Assessment	1 – 5	4 (2;4)	76
	Emotional Subscore	6 – 30	20 (15;25)	75
	Functional Subscore	5 – 25	17 (13;21)	75
	Physical Subscore	8 – 40	25 (19;29)	75
Dysphagia Severity Scale ^a		0 – 100	49 (34;71)	57

^a Lower scores indicate more severely impaired quality of life or ability to swallow (MDADI, Dysphagia Severity Scale, Swal-Qol). ^b Higher scores indicate more severely impaired quality of life (DHI). ^c According to Chen et al. (2001) the range of scores is zero to 100, while using a scale of 1 to 5. In this study the range of scores has been adjusted.

consisting of one visual analogue scale, quantifying the severity of the swallowing disorder and the extent of impairment experienced by the patient. A score of 100 (the maximum) indicates normal swallowing abilities, while a score of zero indicates extreme swallowing impairment or inability to swallow.

Protocol

Patients were asked to fill in all four questionnaires during their outpatients' visit or when recruited by phone, at home. Within two weeks after the first measurement⁹, all patients received by post the MDADI, the DHI and the Dysphagia Severity Scale for repeated measurements purposes. The researchers made sure that all repeated

measurements were sent back in time for adequate retest interval analysis⁹, reminding patients if necessary by phone.

Statistical analysis

Table 2 presents a glossary of psychometric and statistical terminology as used in this study. Measurement properties of the MDADI and the DHI were determined and compared to the quality criteria as defined by Terwee et al.¹⁰.

Firstly, both questionnaires were examined for possible **floor and ceiling effects** by objectifying the number of respondents achieving the lowest or highest possible scores. Next, the **test retest reliability** was assessed by determining intraclass correlations coefficients (two-way random effects model, ICC) between repeated measurements on the MDADI, the DHI and the Dysphagia Severity Scale. Confirmatory Maximum Likelihood (ML) factor analyses were performed to determine the number of (homogeneous) (sub)scales of each questionnaire. In addition, by computing Cronbach's α coefficients, the **internal consistency reliability** of the MDADI and the DHI was estimated. The associations among the four administered questionnaires plus the FOIS, and among the subscales per instrument have been determined by nonparametric Spearman's correlation coefficients. (Sub)scales from the MDADI and the DHI that were supposed to measure the same concept were compared, thus, defining **construct validity (convergent validity)**. Finally, the **criterion validity** was determined by computing nonparametric Spearman's correlations between the Swal-Qol (reference or gold standard) and both the MDADI and the DHI. All statistical analyses were performed using SPSS 15.0.

RESULTS

Table 1 presents the descriptive statistics for all four questionnaires. To examine possible **floor or ceiling effects**, the total score of the MDADI, the total score of the DHI, and the Dysphagia Severity Scale have been visualized by means of histograms (Figure 1A, 1B, and 1C), thus, objectifying the number of respondents achieving the lowest or highest possible scores. As less than 15% of the respondents achieved the lowest or highest possible score, no floor or ceiling effects are considered to be present¹⁰.

To assess the **test retest reliability**, intraclass correlation coefficients (two-way random effects model, ICC) have been determined between repeated measurements on the total scores of the MDADI and the DHI, as well as on the Dysphagia Severity Scale. The ICC's were respectively, .96, .94, and .87. A positive rating for reliability can

Table 2. Glossary of psychometric and statistical terminology.

Terminology	Definition
Construct validity	The extent to which a measurement corresponds to theoretical concepts (constructs) concerning the phenomenon under study ¹⁵ .
Convergent validity	Convergent validity refers to the degree to which a measure is correlated with other measures that it is theoretically predicted to correlate with. In contrast, discriminant validity describes the degree to which the measure is not similar to (diverges from) other measures that it theoretically should not be similar to. Convergent validity and discriminant validity are variants of construct validity ¹⁵ .
Correlation coefficient	An index that quantifies the linear relationship between a pair of variables (range -1 to 1) with the sign indicating the direction of the relationship and the numerical magnitude its strength. Values of -1 or 1 indicate that the sample values fall on a straight line, whereas a value of zero indicates the lack of any linear relationship between the two variables ¹⁶ .
Criterion validity	The extent to which the measurement correlates with an external criterion of the phenomenon under study ¹⁵ .
Cronbach's alpha	The estimate of the correlation between the total score across a series of items from a rating scale and the total score that would have been obtained had a comparable series of items been employed. ¹⁵ Cronbach's alpha is an index of internal consistency of a psychological test ranging from 0 to 1. (Guidelines for interpretation: < 0.60 unacceptable, 0.60-0.65 minimally acceptable, 0.70-0.80 respectable, 0.80-0.90 very good, and > 0.90 consider shortening the scale by reducing the number of items ¹⁷ .)
Factor analysis	A set of statistical methods (e.g. maximum likelihood estimation), for analyzing the correlations among several variables in order to estimate the number of fundamental dimensions that underlie the observed data and to describe and measure those dimensions ¹⁵ . These underlying, unobservable, latent variables, are usually know as the common factors ¹⁷ . Using exploratory factor analysis, no hypothesis about the number and kind of common factors exists prior to analysis. In case of confirmatory factor analysis, the number of common factors has been predetermined.
Floor or ceiling effect	The number of respondents who achieved the lowest or highest possible score ¹⁰ .
Goodness of fit	The degree of agreement between an empirically observed distribution and a mathematical or theoretical distribution ¹⁵ .
Internal consistency	The extent to which items in a (sub)scale are intercorrelated, thus measuring the same construct ¹⁰ .
Intraclass correlation	The proportion of variance of an observation due to between-subject variability in the 'true' scores of a measuring instrument ¹⁶ .
Test retest reliability	An index of score consistency over a brief period of time (typically several weeks), usually the correlation coefficient determined between administration of the test twice with a certain amount of time between administrations ¹⁶ .

only be given when the ICC is at least 0.70 in a sample size of at least 50 patients¹⁰. Because of missing values, the actual sample sizes used for ICC computation were 64 (MDADI), 35 (DHI) and, 49 (Dysphagia Severity Scale). Therefore, in case of the DHI, the reliability could not be determined appropriately, as a consequence of too few data. Both other two instruments are considered to have good test retest reliability.

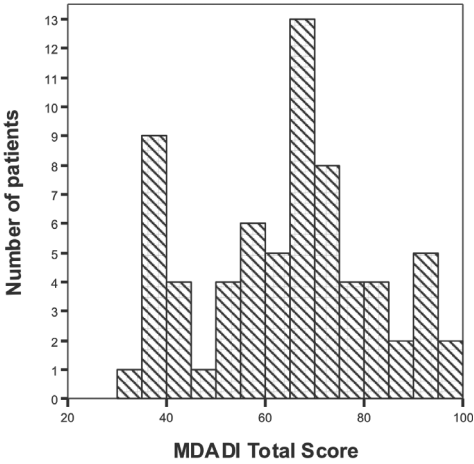


Figure 1A. Data distribution on the MDADI

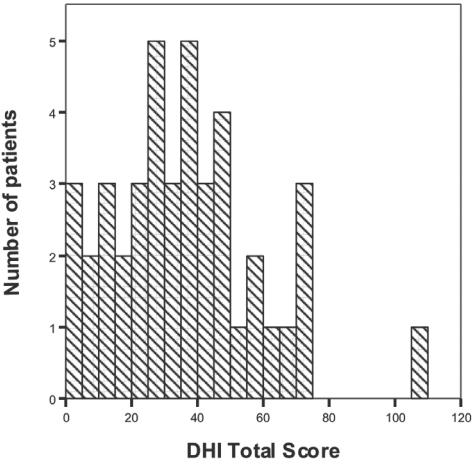


Figure 1B. Data distribution on the DHI

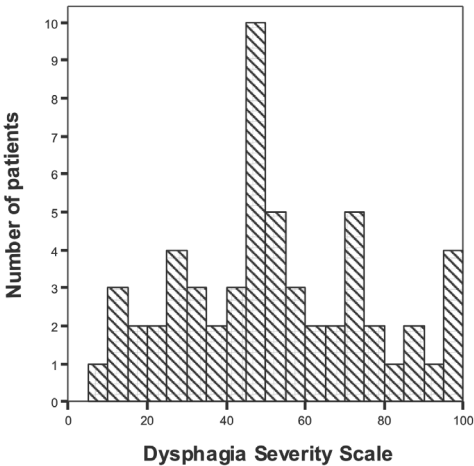


Figure 1C. Data distribution on the Dysphagia Severity Scale

Internal consistency is an important measurement property for questionnaires and describes the extent to which items in a questionnaire (sub)scale are correlated, thus measuring the same concept. In case of an existing theoretical model or because the factor structure has been determined previously, confirmatory factor analysis should be applied in order to determine the number of (homogeneous) (sub)scales. Therefore, a confirmatory Maximum Likelihood (ML) factor analysis has been performed using all items of the MDADI to test whether three factors could be distinguished (namely, the three subscales). However, this three-factor model was rejected (goodness-of-fit test,

$p < .000$). A four-factor model referring to the global assessment as possible fourth factor, was rejected as well ($p = .003$). A confirmatory ML factor analysis using all items of the DHI and a three-factor model resulted too in rejection of the possibility of three underlying constructs or subscales (goodness-of-fit test, $p < .000$).

Still, as the subject population was rather limited, further analysis was performed to gather more information about the questionnaires' psychometric properties. Cronbach's alpha has been determined as it is considered an adequate measure of internal consistency reliability. Low Cronbach's alpha's suggest lack of correlation ($\alpha \leq 0.70$)⁹, whereas high Cronbach's alpha's indicate redundancy of one or more items ($\alpha > 0.90$)^{9,11}. Cronbach's alpha's have been calculated for each (sub)scale separately of the MDADI and the DHI (see Table 3). All Cronbach's alpha's are between .76 and .94, thus indicating good internal consistency, although some redundancy may be present. Considering the outcome of the factor analyses without any obvious homogeneous (sub)scales detected as well as the adequate Cronbach's alpha's per (sub)scales, the internal consistency of both questionnaires might be described as yet unclear¹⁰.

Table 3. Cronbach's alpha per (sub)scale of the MD Anderson Dysphagia Inventory (MDADI) and the Deglutition Handicap Index (DHI).

Quality of Life Scale		Cronbach's alpha
MDADI	Total Score	.94
	Global Assessment	n.a.
	Emotional Subscore	.86
	Functional Subscore	.82
	Physical Subscore	.87
DHI	Total Score	.93
	Emotional Subscore	.94
	Functional Subscore	.84
	Physical Subscore	.76

The associations among the four patient administered questionnaires plus the FOIS, and among the subscales per instrument were determined by nonparametric Spearman's correlation coefficients as well (Table 4 and 5). For the correlations coefficients (R), a minimum value for a strong correlation was set at 0.7 and above^{12,13,14}. Correlation coefficients between 0.3 and 0.7 were considered to be a substantial correlation only and R-values < 0.3 were considered to be a weak correlation. Negative correlations are expected as all questionnaires but the DHI, associate lower scores

Table 4. Associations among the MDADI, the DHI, the Dysphagia Severity Scale, and the FOIS (nonparametric Spearman's correlation coefficients).

MDADI			DHI				Dysphagia Severity Scale		FOIS ^a
	Total Score	Global Assessment	Emotional Subscore	Functional Subscore	Physical Subscore	Total Score	Emotional Subscore	Functional Subscore	Physical Subscore
MDADI	Total Score	.75** (74)	.94** (74)	.92** (74)	.91** (74)	-.87** (41)	-.89** (44)	-.70** (43)	-.57** (42)
	Global Assessment		.68** (75)	.72** (75)	.66** (75)	-.72** (42)	-.65** (46)	-.64** (44)	-.65** (44)
	Emotional Subscore			.81** (74)	.82** (74)	-.85** (41)	-.93** (45)	-.63** (43)	-.52** (43)
	Functional Subscore				.77** (75)	-.82** (41)	-.86** (45)	-.65** (44)	-.54** (43)
DHI	Physical Subscore					-.82** (41)	-.75** (45)	-.78** (44)	-.62** (43)
	Total Score						.89** (42)	.84** (42)	.78** (42)
	Emotional Subscore							.60** (44)	.54** (44)
	Functional Subscore								.66** (42)
Dysphagia Severity Scale	Physical Subscore								
FOIS									

* Correlation is significant at the .01 level (2-tailed). ** Correlation is significant at the .05 level (2-tailed). ^a Lower scores indicate more severely impaired oral intake.

with more severely impaired quality of life or restricted functional oral intake. Correlations between the quality of life instruments and the functional feeding status proved rather low ($-.013 \leq R \leq .53$). **Construct validity** could be determined by comparing (sub)scales from the MDADI and the DHI that were supposed to measure the same concept. Associations between similar subscales from both questionnaires as well as both total scores demonstrated whether or not they defined the same target construct (**convergent validity**). Correlation coefficients between both emotional, functional and physical subscales from the MDADI and the DHI were, respectively, $-.93$, $-.65$, and $-.62$. The correlations between the Dysphagia Severity Scale and both total scores from the MDADI and the DHI were rather low (respectively, $.45$ and $-.52$), whereas the correlation between both total scores of the MDADI and the DHI was strong ($R = -.87$). The mean correlation coefficients between the subscales of the MDADI and between the subscales of the DHI, were respectively, $.80$ ($.66 \leq R \leq .82$) and $.60$ ($.54 \leq R \leq .66$). When considering the Swal-Qol as the reference standard or gold standard, the extent to which the MDADI and the DHI agreed or correlated with the Swal-Qol could be defined as the questionnaires' **criterion validity**. Table 5 presents the associations among the Swal-Qol versus the MDADI, the DHI, the Dysphagia Severity Index and the FOIS (nonparametric Spearman's correlation coefficients). The mean correlation coefficients between subscales from the Swal-Qol versus the total score of the MDADI, the total score of the DHI, and the Dysphagia Severity Scale were, respectively, $.67$ ($.39 \leq R \leq .86$), $-.61$ ($-.38 \leq R \leq -.80$), and $.36$ ($.30 \leq R \leq .73$). Next, based on the authors' clinical experience, subscales that were considered to be of lesser importance to oropharyngeal dysphagia, were excluded by mutual consensus. Thus, when excluding the subscales Fear, Sleep, Fatigue, and Communication, the mean correlation coefficients were, respectively, $.76$ ($.62 \leq R \leq .86$), $-.71$ ($-.60 \leq R \leq -.80$), and $.42$ ($.31 \leq R \leq .73$). According to Terwee et al. (2007), the correlation with the reference standard needs to be at least $.70$. Only after having excluded the less relevant subscales of the Swal-Qol, the MDADI as well as the DHI show satisfactory associations with the reference standard.

DISCUSSION & CONCLUSIONS

In this study the psychometric characteristics have been determined for the MDADI as well as the DHI. The Dysphagia Severity Scale was introduced to reveal any advantages or disadvantages of using elaborated questionnaires compared to a simple visual analogue scale, while the Swal-Qol was considered the reference or gold standard. None of the quality of life questionnaires showed any floor or ceiling effects. The test retest reliability of the MDADI and the Dysphagia Severity Scale proved to be good. However,

Table 5. Associations among the Swal-Qol versus the MDADI, the DHI, the Dysphagia Severity Scale, and the FOIS (nonparametric Spearman's correlation coefficients).

Swal-Qol	MDADI			DHI			Dysphagia Severity Scale			FOIS ^a
	Total Score	Global Assessment	Emotional Subscore	Functional Subscore	Physical Subscore	Total Score	Emotional Subscore	Functional Subscore	Physical Subscore	
Burden	.84** (71)	.69** (73)	.79** (72)	.79** (72)	.78** (72)	-.68** (39)	-.77** (43)	-.54** (41)	-.46** (41)	.50** (73)
Food Selection	.77** (69)	.67** (71)	.68** (70)	.80** (70)	.78** (70)	-.69** (38)	-.68** (42)	-.69** (40)	-.51** (40)	.40** (71)
Eating Duration	.70** (69)	.57** (71)	.63** (70)	.66** (70)	.72** (70)	-.70** (39)	-.63** (43)	-.69** (41)	-.40* (41)	.41** (71)
Eating Desire	.71** (70)	.56** (72)	.66** (71)	.68** (71)	.73** (71)	-.70** (39)	-.70** (43)	-.64** (41)	-.31* (41)	.38** (72)
Fear	.57** (69)	.58** (71)	.52** (70)	.49** (70)	.59** (70)	-.38* (37)	-.42** (41)	-.32* (39)	-.30 (39)	.31** (71)
Sleep	.39** (71)	.36** (73)	.31** (72)	.47** (72)	.42** (72)	-.47** (39)	-.47** (43)	-.40** (41)	-.35* (41)	.26* (73)
Fatigue	.46** (71)	.43** (73)	.36** (72)	.46** (72)	.53** (72)	-.42** (39)	-.30* (43)	-.58** (41)	-.41** (41)	.25 (55)
Communication	.63** (69)	.63** (71)	.52** (70)	.61** (70)	.61** (70)	-.48** (37)	-.46** (41)	-.36* (39)	-.47** (39)	.42** (71)
Mental Health	.86** (69)	.72** (71)	.82** (70)	.83** (70)	.80** (70)	-.80** (37)	-.85** (41)	-.63** (39)	-.49** (39)	.48** (71)
Social Functioning	.85** (71)	.73** (73)	.76** (72)	.90** (72)	.75** (72)	-.78** (39)	-.84** (43)	-.62** (41)	-.49** (41)	.61** (73)
Symptoms	.62** (71)	.66** (73)	.53** (72)	.58** (72)	.61** (72)	-.60** (39)	-.54** (43)	-.51** (41)	-.73** (41)	.33** (73)

* Correlation is significant at the .01 level (2-tailed). ** Correlation is significant at the .05 level (2-tailed). ^a Lower scores indicate more severely impaired oral intake.

because of too many missing data in case of the DHI, the test retest reliability of the DHI could not be determined even though the intraclass correlation coefficients were rather high. The internal consistency using Cronbach's alpha's seemed to be good. However, when applying confirmatory factor analysis, the underlying constructs as defined by the subscales per questionnaire could not be distinguished. Probably, because of unclear constructs, only both emotional subscales were strongly correlated, whereas the associations between the other corresponding subscales were just moderate. Overall, the Dysphagia Severity Scale, showed rather low correlations with the other three questionnaires. It seemed that a detailed questionnaire could not be replaced by a single one item scale, quantifying the severity of the swallowing disorder. The concepts being measured proved to be different. When considering the criterion validity, the MDADI as well as the DHI showed satisfactory associations with the Swal-Qol after having removed its less relevant subscales.

In conclusion, when considering the validity and reliability of the Dutch version of the MDADI and the DHI, not all psychometric characteristics have been met sufficiently. In general, the importance of determining these psychometric characteristics and of objectifying concepts such as validity and reliability, must be stressed when developing a questionnaire. If a questionnaire's characteristics prove to be poor, the study results cannot be interpreted correctly nor can any clinical relevance be determined. Therefore, it is recommended that in future outcome studies, only quality of life questionnaires will be used that show sufficiently good psychometric characteristics.

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6



Prediction of aspiration in dysphagia using logistic regression: oral intake and self-evaluation

Submitted in: Clinical Otolaryngology

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ABSTRACT

Objectives

Oropharyngeal dysphagia (OD) has a major influence on health in general and health-related quality of life (HR-QoL) in particular. The gold standard assessments for OD, especially for aspiration in OD, are fiberoptic endoscopic evaluation of swallowing (FEES) and videofluoroscopy (VFS), but not all patients have access to such procedures. Therefore, the current study built a prediction model to forecast aspiration in patients with OD on the basis of common self-evaluation questionnaires and oral intake status.

Methods

A consecutive series of 111 patients with confirmed diagnosis of OD was measured according to a standardised protocol using the following tools: the Swallowing Quality of Life Questionnaire (SWAL-QOL), the Dysphagia Handicap Index (DHI), two self-report visual analogue scales which measure the severity and the impairment of the swallowing problem on everyday social life as experienced by the patient, the Eating Assessment Tool 10 (EAT-10), the Functional Oral Intake Scale (FOIS) and subsequently FEES (the gold standard). Penalised logistic regression was carried out to predict aspiration. The performance of the resulting models was evaluated by constructing receiver operating characteristics (ROC) curves and computing areas under the curve (AUC).

Results

The final model showed an AUC of 0.92, indicating excellent performance.

Conclusion

This study shows that it may be possible to accurately predict aspiration in oropharyngeal dysphagia by a non-invasive and non-instrumental assessment protocol including oral intake status and self-report questionnaires on functional health status and HR-QoL.

INTRODUCTION

Oropharyngeal dysphagia (OD) has a major influence on health in general and notably on health-related quality of life (HR-QoL)[1-3]. OD is known to negatively influence social life; patients may no longer enjoy eating and drinking, and may avoid social activities[1]. In turn, OD can cause dehydration and malnutrition[2, 4]. Moreover, OD has economic consequences; Bonilha et al.[5] calculated that the costs for OD in stroke patients were \$ 4510 per patient per year. For all of these reasons, detecting OD and optimising its care is increasingly important.

Aspiration or silent aspiration in severe OD can cause aspiration pneumonia and, when accompanied by malnutrition and dehydration, can lead to hospitalization, IC admission or even death[2, 4]. The gold standards for detecting aspiration and silent aspiration are videofluoroscopic (VFS) and fiberoptic endoscopic evaluation of swallowing (FEES). While both have a high sensitivity and specificity[6], they are invasive, may be burdensome for the patient and are expensive. Moreover, these gold standards are not generally available in clinical settings such as a nursing home or general practice. Screening for OD can be performed in various ways such as by trial swallows using water or substances with different viscosities, by oxygen desaturation or by cough elicitation[7, 8]. Screening should be sufficiently sensitive and specific but also easy to administer without extensive training[7]. When patients fail the screening, further assessment of OD is recommended. Numerous assessments are available to evaluate OD in further detail. Each one is focussed on certain domains such as functional health status (FHS), health-related quality of life (HR-QoL) or oral intake. Two commonly used FHS questionnaires are the Eating Assessment Tool (EAT-10)[9] and the Sydney Swallow Questionnaire (SSQ)[10], and a common HR-QoL questionnaire is the Swallowing Quality of Life questionnaire (SWAL-QOL)[11]. Self-evaluation questionnaires such as the Dysphagia Handicap Index (DHI)[12] include items on both HR-QoL and FHS. Some measures have several subscales and over 40 items (e.g., SWAL-QOL), whereas others consist of a single visual analogue scale on swallowing function[13] or a single ordinal scale on oral intake (e.g., Functional Oral Intake Scale or FOIS)[14].

The presence of aspiration is the most critical clinical sign in patients with OD. However, the literature[15, 16] reveals a moderate to low correlation between self-evaluation questionnaires and aspiration as determined by FEES or VFS. Also, oral intake as assessed by the FOIS shows weak correlations with aspiration[14].

Predictive modelling entails developing a mathematical tool that generates an accurate prediction[17]. Several studies on dysphagia have used predictive modelling to forecast swallowing problems based on various criteria: for example, dosimetric parameters in radiotherapy[18, 19], tumour size and location[19], VFS parameters[20] or cervical

auscultation[21]. The predicted outcome of the models ranged from radiotherapy-induced dysphagia[18, 19] to persistent dysphagia after stroke[20] and presence of aspiration[21]. The predicted outcome of most studies was dysphagia, though not differentiating between dysphagia with or without aspiration. To the best of our knowledge, no models thus far have used individual or combined self-evaluation questionnaires on FHS and/or HR-QoL in OD for predicting aspiration.

Clinicians often employ patient self-evaluation in daily clinical practice and recognise the importance of early detection of aspiration when working with patients with OD. With their co-operation, predictive modelling using questionnaires as predictors and aspiration as the outcome becomes an option. The possibility of collaboration led to the design for the current study: the purpose was to build a predictive model that could forecast aspiration in patients with OD using oral intake status and commonly used self-evaluation questionnaires on FHS and HR-QoL.

METHODS

Patients

The study included a consecutive series of patients with OD who visited the outpatient clinic of the department of Otorhinolaryngology and Head and Neck Surgery of the Leiden University Medical Centre. Patients were included if they (1) were at least 18 years old and (2) were not suffering from severe cognitive problems. All had a confirmed diagnosis of OD based on FEES examination by an experienced ENT specialist or speech-language pathologist (SLP). This study was approved by the local Medical Ethical Committee.

Measures

As part of standard care at the outpatient clinic of the department of Otorhinolaryngology and Head and Neck Surgery, all patients completed several self-evaluation questionnaires during the week prior to their FEES exam. The following standardised protocols were used (listed in order of administration).

1. The *SWAL-QOL*[11, 22, 23] is a 44-item questionnaire on HR-QoL. It is considered to be the gold standard for measuring HR-QoL in OD[24]. The *SWAL-QOL* consists of ten subscales (Burden, Eating duration, Eating desire, Food selection, Communication, Fear, Mental health, Social functioning, Fatigue and Sleep) and one symptom scale (14 items, among which coughing, choking, gagging and drooling)[25]. The minimum and maximum scores on each subscale range from

- 0 to 100: not impaired to extremely impaired HR-QoL, respectively.
2. The *DHI*[12] measures FHS as well as HR-QoL. This 25-item questionnaire concerns the effect of OD on Physical (9 items), Functional (9 items) and Emotional (7 items) aspects of patients' lives. Each item is scored as 0, 2 or 4, with higher scores meaning more severe disability. The total score ranges from 0 to 100. The DHI has one additional question about the severity of a patient's swallowing problem ranging from 1-7 (Severity question: 1 normal, 7 severe problem).
 3. Each of two concise self-report 100-mm *Visual Analogue Scales (VAS)*[13] measures a certain aspect of swallowing. One concerns the severity of the swallowing problem as experienced by the patient (Severity: FHS), whereas the other measures the perceived impact of the swallowing problem on everyday social life (Impairment: HR-QoL). Higher scores indicate greater impairment (range 0 - 100).
 4. The *EAT-10*[9] is a short 10-item self-administered questionnaire[8]. Although predominantly regarding FHS, it also includes some HR-QoL items [26]. Each one is rated on a five-point scale (0-4); the summed score ranges from 0 to 40 (higher scores are more abnormal). A sum of ≥ 2 [27] or ≥ 3 [9] is considered abnormal.
 6. The *Functional Oral Intake Scale (FOIS)*[14] registers actual oral intake. The scores range from 1 (nothing by mouth) to 7 (total oral diet with no restrictions). During a patient's visit to the outpatient clinic, the FOIS was completed by the clinician.

Subsequently, FEES was performed according to a standardised protocol[28]. Patients were offered three swallow trials of three different consistencies (nine trials maximum): methylene blue dyed water (thin) or applesauce (thick) in portions of 10 mL and three bite-sized crackers with a fixed weight of 3.3 g (solid). In the event of aspiration, the trial of that particular consistency was stopped. FEES examinations were performed with a XION chip-on-the-tip flexible nasendoscope (Berlin, Germany). Results were recorded with RVC Clinical Assistant (Baarn, the Netherlands), a medical archive and image viewer. Recordings were rated by consensus among two SLPs using the Penetration Aspiration Scale (PAS)[29]. FEES results were dichotomised into no aspiration (PAS score 1-3) or aspiration (PAS scores 4-8)[30]. If the patient aspirated during any of the (maximum of) nine trials with any of the three consistencies, he or she was considered an aspirator in this study. All patients were categorised either as aspirating or not.

Statistical analysis

Logistic regression was used to predict the outcome (dichotomous variable: aspiration present/absent). Model performance was evaluated by constructing receiver operating characteristics (ROC) curves and computing areas under the curve (AUC). In order to

objectively evaluate whether individual questionnaire items contributed to prediction, a penalised version of logistic regression was used on all items. To that end, a variant of the LASSO regression was applied, namely the elastic net. LASSO allows to simultaneously perform model selection and estimation, whereby variables not contributing to prediction are removed from the model. A penalty parameter determines how many variables are retained. This parameter is chosen automatically by a cross-validation procedure. AUC and *glmnet* packages in R version 3.4.0 were used for all analyses[31].

RESULTS

Patient characteristics

One-hundred-eleven patients were included from June 2014 till November 2015 (Table 1). Sixty-seven subjects (60%) were male with a median age of 65 years (IQR 58-71) compared to 44 (40%) female subjects with a median age of 67 years (IQR 52-74). Medical diagnoses included head and neck cancer (36%) and neurological disorders (37%) such as stroke, Parkinson's disease, multiple sclerosis and myotonic dystrophy. The remaining patients (27%) had diagnoses like general weakness due to other diseases, cricopharyngeal muscle hypertrophy or epiglottitis. The median FOIS score for the total group was 6 (IQR 4-7), so most patients had an oral intake with some restrictions.

Descriptive statistics

Table 2 displays the descriptive statistics for the SWAL-QOL, DHI, VAS and EAT-10. The median scores on the SWAL-QOL subscales were Burden 38 (IQR 13-75), Eating duration 38 (IQR 0-75), Eating desire 67 (IQR 33-92), Food selection 63 (IQR 25-75), Communication 75 (IQR 38-88), Fear 75 (IQR 56-94), Mental health 55 (IQR 35-85), Social functioning 55 (IQR 30-85), Fatigue 58 (IQR 33-75) and Sleep 75 (IQR 38-88). The median SWAL-QOL symptom score was 61 (IQR 46-71). The median DHI total score was 48 (IQR 28-64) and the additional DHI Severity question showed a median of 5 (IQR 4-6). The median VAS scores on Severity and Impairment were 51 (IQR 30-80) and 55 (IQR 30-85) mm, respectively. The EAT-10 had a median score of 15 (IQR 8-23).

FEES showed no aspiration in any of the nine trials using three different viscosities (thin, thick, solid consistency) in 90 (81%) patients. A group of 21 (19%) patients aspirated on at least one swallow trial.

Table 1. Subject characteristics

	Total group	111
Number of subjects [n (%)]	Male (%)	67 (60)
	Female (%)	44 (40)
Age in years [Med (IQR)]	Total group	66 (56-72)
	Male	65 (58-71)
	Female	67 (52-74)
Medical diagnosis [n (%)]	Head and neck cancer	40 (36)
	Neurological disorder	41 (37)
	Other	30 (27)
FOIS ¹ [Med (IQR)]		6 (4-7)

1 Range 1 – 7: 'Nothing by mouth' to 'Total oral diet with no restrictions'.

Prediction modelling

To build prediction models, first two sets of variables (A and B) were specified a-priori (Table 3). In a second, exploratory step, automatic variable selection was used to choose the prediction model.

Pre-specified variables

The first set of variables (A) in the logistic regression model was selected on the basis of the literature and clinical experience. Six subscales of the SWAL-QOL (HR-QoL) were considered of lesser importance to oropharyngeal dysphagia and, therefore, excluded: Communication, Fear, Mental health, Social functioning, Fatigue and Sleep[32]. The remaining subscales, namely Burden, Food selection, Eating duration and Eating desire, and the Symptom scale of the SWAL-QOL were included, as were the DHI total subscale scores (Functional, Physical and Emotional subscales) and both VAS scales on swallowing (Severity and Impairment)[13]. As coughing is considered a clinically relevant symptom of aspiration, item 9 of the EAT-10 (I cough when I eat) was also listed [33]. Lastly, the FOIS was added to include information about oral intake. This prediction model yielded an AUC of 0.862.

The second set (B) included fewer variables: the subscale Food selection of the SWAL-QOL, the DHI subscales (Functional, Physical and Emotional), item 9 of the EAT-10 and the FOIS. Both VAS scales and the remaining SWAL-QOL subscales were excluded. This reduced model obtained an AUC of 0.852.

The first analysis using set A identified a non-linear association between the gold standard and the Symptom scale of the SWAL-QOL, which led to the inclusion of a quadratic term for the Symptom scale score. Based on this second model, an AUC of

0.874 was found. Because the Symptom scale score was not included in set B, this prediction model remained unchanged.

Score X =

$$\begin{aligned}
 &18.6591708 + (0.0007031 * \text{SWAL-QOL Burden}) + (0.0326739 * \text{SWAL-QOL Food Selection}) \\
 &- (0.0219832 * \text{SWAL-QOL Eat duration}) + (0.0081344 * \text{SWAL-QOL Eat desire}) - \\
 &(0.2093808 * \text{SWAL-QOL Symptom}) + (0.0020425 * \text{SWAL-QOL Symptom Squared}) + \\
 &[(0.6740265 * \text{DHI item 1p score 2}) + (3.5526187 * \text{DHI item 1p score 4})] - [(19.2522260 * \text{DHI} \\
 &\text{Severity Question score 2}) - (36.8925068 * \text{DHI Severity Question score 3}) - (19.3098857 * \\
 &\text{DHI Severity Question score 4}) - (19.9454640 * \text{DHI Severity Question score 5}) - \\
 &(18.4990410 * \text{DHI Severity Question score 6}) - (15.9065488 * \text{DHI Severity Question score} \\
 &7)] - (0.0363491 * \text{VAS Severity}) + (0.0428708 * \text{VAS Impairment}) + [(4.6092903 * \text{EAT10 item} \\
 &9 \text{ score 1}) + (4.3063001 * \text{EAT10 item 9 score 2}) + (3.6040778 * \text{EAT10 item 9 score 3}) + \\
 &(1.8982514 * \text{EAT10 item 9 score 4})] - (0.4016869 * \text{FOIS})
 \end{aligned}$$

The inverse logistic function of the final score X indicates the chance of aspiration:

$$P_{\text{aspiration}} f(x) = 1 / (1 + \exp(-x))$$

Automatic variable selection

The first penalised logistic regression included all available variables. Based on this regression, certain variables were added to sets A (model 2) and B (model 1). For the first set of variables (A), the DHI additional question on severity (Severity question) and the DHI item 1p ('I cough when I drink') were added. For the second set (B), the squared Symptom scale score was added in addition to the two DHI items (Severity question and item 1p). This yielded AUCs of 0.922 for set A and 0.915 for set B.

Table 3 provides an overview of the included variables and the results per prediction model by showing per item the odds ratio, 95% confidence interval and p-value. Figure 1a-e presents ROC figures and AUC outcomes per model. The following formula predicts the presence of aspiration in an individual subject based on the penalised logistic regression model (model 3) using the first set of variables A with an AUC of 0.922:

Thus, to determine the chance of aspiration in an individual with OD, the following scores need to be entered in the formula:

- SWAL-QOL: subscales Burden, Food Selection, Eat Duration, Eat Desire and Symptom score (ranging from 0 to 100);
- DHI: Item 1p and Severity question. In the formula variables are included per score

Table 2. Descriptive analysis of patient self-evaluation questionnaires (n=111): SWAL-QOL, Dysphagia Handicap Index (DHI), Visual Analogue Scales (VAS), EAT-10.

Questionnaire ¹	(Sub)scale	Range scale	Median (IQR)
SWAL-QOL	Burden	0-100	38 (13-75)
	Eating duration	0-100	38 (0-75)
	Eating desire	0-100	67 (33-92)
	Food selection	0-100	63 (25-75)
	Communication	0-100	75 (38-88)
	Fear	0-100	75 (56-94)
	Mental health	0-100	55 (35-85)
	Social functioning	0-100	55 (30-85)
	Fatigue	0-100	58 (33-75)
	Sleep	0-100	75 (38-88)
	Symptom score	0-100	61 (46-71)
DHI	Physical	0-36	16 (10-22)
	Functional	0-36	20 (10-28)
	Emotional	0-28	10 (4-18)
	Total score	0-100	48 (28-64)
	Severity question	1-7	5 (4-6)
VAS	Severity (FHS)	0-100	51 (30-80)
	Impairment (HR-QoL)	0-100	55 (30-85)
EAT-10	Total score	0-40	15 (8-23)

¹ Higher scores indicate higher degree of disability.

for item 1p (score 0, 2 or 4) and for Severity question (score 2 to 7; not 1). These variables include binary numbers (present = 1; absent = 0); For example, if item 1p is scored 2, the section of the formula relating to item 1p is completed as follows: $(0.6740265 \times 1) + (3.5526187 \times 0)$;

- VAS: Severity and Impairment (score 0-100);
- EAT10: item 9. In the formula variables are included per score for item 9 (score 1, 2, 3 or 4). These variables are expressed as binary numbers (present = 1; absent = 0);
- FOIS (score 0-7).

Next, to determine the chance of aspiration, the inverse logistic function of the final score X needs to be calculated.

Table 3. Overview of included variables and results per prediction model.

	Model 1				Model 2				Model 3 (LASSO)			
	Set A (figure 1a) AUC 0.862				Set B (figure 1b) AUC 0.852				Set A (figure 1c) AUC 0.874			
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
(Intercept)	NA	NA	0.40	NA	NA	0.07	NA	NA	0.52	NA	NA	1.00
SWAL-QOL Burden	0.99	0.96-1.02	0.39	0.99	0.96-1.01	0.31	1.00	0.97-1.03	0.96	1.00	0.97-1.03	0.96
SWAL-QOL Food selection	1.02	0.99-1.05	0.14	1.02	1-1.04	0.06	1.03	1.00-1.05	0.08	1.03	1.00-1.07	0.05
SWAL-QOL Eating duration	1.01	0.98-1.03	0.67				1.00	0.97-1.03	0.97	0.98	0.94-1.01	0.21
SWAL-QOL Eating desire	1.00	0.98-1.02	0.96				1.00	0.98-1.02	0.98	1.01	0.98-1.04	0.57
SWAL-QOL Symptom	0.99	0.94-1.03	0.57				0.82	0.66-1.01	0.06	0.81	0.61-1.07	0.14
SWAL-QOL Symptom squared							1.00	1.00-1.00	0.06	1.00	1.00-1.00	0.10
DHI Subscale Physical	0.95	0.86-1.05	0.33	0.96	0.87-1.05	0.34	0.95	0.86-1.05	0.31			0.90
DHI Subscale Functional	1.04	0.94-1.16	0.41	1.05	0.96-1.15	0.29	1.04	0.94-1.16	0.44			1.11
DHI Subscale Emotional	1.03	0.91-1.15	0.67	1.07	0.97-1.18	0.17	1.01	0.89-1.13	0.92			1.02
DHI item 1p ¹ score 2										1.96	0.28-13.98	0.50
DHI item 1p ¹ score 4										34.90	1.91-638.76	0.02
DHI Severity Question ² score 2										0.00	0.00-INF	1.00
DHI Severity Question ² score 3										0.00	0.00-INF	1.00
DHI Severity Question ² score 4										0.00	0.00-INF	1.00
DHI Severity Question ² score 5										0.00	0.00-INF	1.00
DHI Severity Question ² score 6										0.00	0.00-INF	1.00

DHI Severity Question ² score 7	0.99	0.96-1.03	0.76	0.99	0.95-1.03	0.73	0.96	0.91-1.02	0.21	0.00	0.00-INF	1.00	0.00	0.00-INF	1.00
VAS Severity	0.99	0.96-1.03	0.76	0.99	0.95-1.03	0.73	0.96	0.91-1.02	0.21						
VAS Impairment	1.01	0.98-1.05	0.45	1.02	0.98-1.06	0.44	1.04	0.99-1.10	0.14						
EATI0 item 9 ³ score 1	33.87	3.70-310.01	0.00	30.25	3.78-241.77	0.00	51.78	4.74-565.29	0.00	100.41	3.05-3300.58	0.01	93.39	2.88-3026.65	0.01
EATI0 item 9 ³ score 2	15.92	1.62-154.72	0.02	16.05	1.86-138.56	0.01	28.15	2.29-346.29	0.01	74.17	1.67-3289.54	0.03	90.10	2.08-3899.97	0.02
EATI0 item 9 ³ score3	47.62	4.42-513.04	0.00	51.11	5.42-481.70	0.00	80.10	5.83-1100.82	0.00	36.75	0.98-1380.57	0.05	68.33	1.78-2621.67	0.02
EATI0 item 9 ³ score 4	26.80	2.41-298.47	0.01	33.04	3.39-321.76	0.00	35.89	2.75-469.06	0.01	6.67	0.16-280.41	0.32	6.48	0.21-200.31	0.29
FOIS	0.72	0.49-1.07	0.11	0.70	0.48-1.02	0.06	0.69	0.45-1.06	0.09	0.67	0.43-1.03	0.07	0.81	0.52-1.26	0.35

¹DHI item 1p: cough when I drink (score 1-3: never, sometimes, always). ²DHI: Patient self-rated severity of dysphagia (score: 0-7; normal to severe problem).³³EAT-10 item 9: I cough when I drink (score: 0-4; no problems - severe problems).

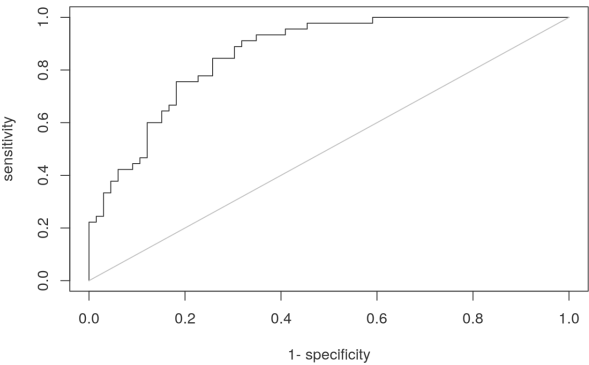


Figure 1a. ROC Model 1 Variable set (A) included the following variables: SWAL-QOL subscales Burden, Food selection, Eat duration, Eat desire and Symptom scale, DHI subscales (Functional, Physical and Emotional), VAS scales (Severity and Impairment), EAT-10 item 9 ('I cough when I eat') and FOIS. AUC 0.862.

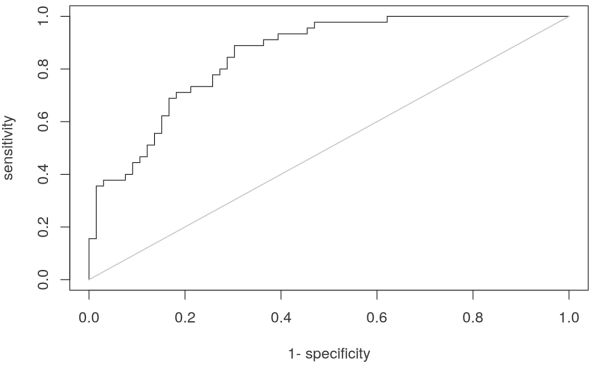


Figure 1b. ROC Model 1 Variable set (B). Reduced model to SWAL-QOL Food Selection, DHI subscales (Functional, Physical and Emotional), EAT-10 item 9 ('I cough when I eat') and FOIS. AUC 0.852.

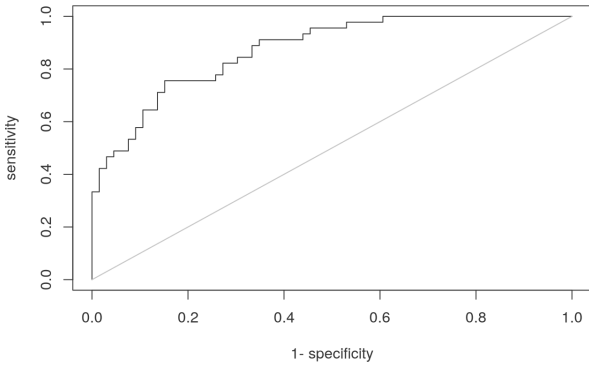


Figure 1c. ROC Model 2 Variable set (A), included the following variables: SWAL-QOL subscales Burden, Food selection, Eat duration, Eat desire, Symptom scale and Symptom scale squared, DHI subscales (Functional, Physical and Emotional), VAS scales (Severity and Impairment), EAT-10 item 9 ('I cough when I eat') and FOIS. AUC 0.874

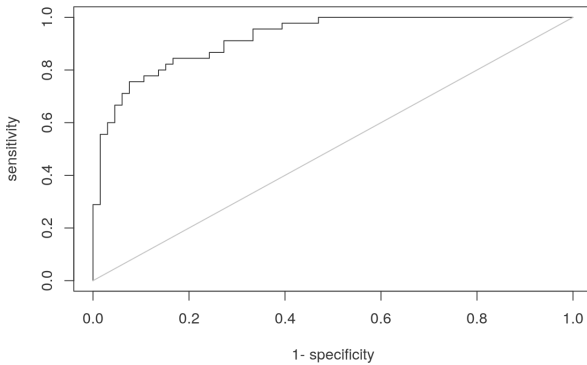


Figure 1d. ROC Model 3 Variable set (A) included the following variables: SWAL-QOL subscales Burden, Food selection, Eat duration, Eat desire, Symptom scale and Symptom scale squared, DHI item 1p ('I cough when I drink'), DHI Severity Question, VAS scales (Severity and Impairment), EAT-10 item 9 ('I cough when I eat') and FOIS. AUC 0.922

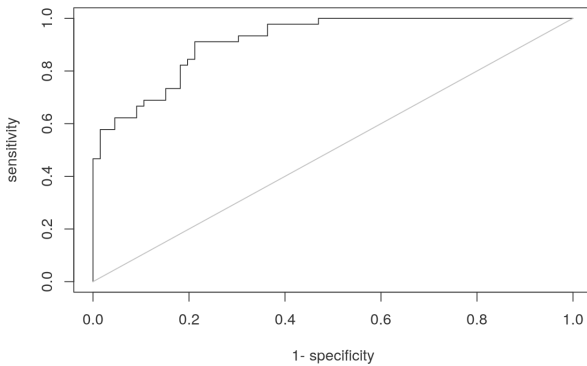


Figure 1e. ROC Model 3 Variable set (B) included the following variables: SWAL-QOL subscales Food selection and the Symptom scale squared, DHI subscales (Functional, Physical and Emotional), DHI item 1p ('I cough when I drink'), DHI Severity question, EAT-10 item 9 ('I cough when I eat') and FOIS. AUC 0.915

DISCUSSION

The purpose of this study was to build a prediction model for aspiration in patients with OD using common self-evaluation questionnaires and patients' oral intake status. Logistic regression modelling is the preferred method for this[34]. Herein, the number of parameters tested determines the size of the study population needed[35]. Both clinical experience and prior knowledge from the literature may be used to limit the number of predictors in such models. The variable selection was based on these assumptions. Good accuracy was found [36], i.e. AUC of 0.86 and 0.85 for variable sets A and B, respectively. Subsequently, LASSO regression showed excellent accuracy, i.e. AUC of 0.92 for selection of variables from both sets A and B. The resulting formula may be used in the future as a guide to predict aspiration in patients with OD. This study has some limitations. Firstly, the subjects had high FOIS scores, i.e. no functional impairments in oral intake or only mild impairments. This may have influenced our findings and the generalisability of the results. In view of that possibility,

a consecutive series of patients was included to avoid selection bias. As such, our population forms a representative sample of persons visiting an outpatient clinic for dysphagia in an academic hospital setting. Secondly, only details on the LASSO regression model using the set of variables A are presented here. However, as the AUCs were almost equal for both sets (A and B) when using LASSO regression modelling, the option of using set B in daily clinics might be considered as well. Clinicians may prefer to use DHI subscales rather than adding the SWAL-QoL subscales and VAS scales on Severity and Impairment. Future studies may consider such clinical preferences when building regression models. Thirdly, external validation of the findings in another group of patients with OD was not performed. Nonetheless, all predictive models showed good to excellent accuracy with all $AUC \geq 0.85$ and AUC exceeding 0.92 when using LASSO regression. Even though no great differences are expected when other groups of patients with OD are included, it may be interesting to compare the current results with those from future studies in other populations with OD. Casting the net wider might reveal similarities or discrepancies in study outcomes; to what degree our predictive model can be generalised to other patient populations remains to be evaluated in follow-up research. Our model can be considered a first step towards the assessment of aspiration risk in patients with OD using oral intake and self-report questionnaires only. The high accuracy of the final prediction model seems to make this a very promising avenue.

These findings are relevant for clinical practice and underscore the importance of self-reported evaluations in the clinical assessment of patients with OD. Until now, these questionnaires were used to measure concepts such as FHS and HR-QoL. They were not used for decision-making; specifically, they were not used to determine whether a patient with dysphagia was at risk for aspiration. The current study suggests that in the absence of gold standard measures, an accurate risk assessment can be performed on the grounds of combined oral intake and self-reported FHS and HR-QoL. Possibly, future studies may address the usefulness of the current assessment protocol in clinical settings such as nursing homes or general practices where access to VFS or FEES may still be limited, in contrast to the widespread availability in tertiary centres nowadays. Furthermore, the use of a non-instrumental assessment protocol to identify aspiration in patients with OD may reduce costs in healthcare.

CONCLUSIONS

This study shows that aspiration in patients with OD may be predicted by a cost-effective, simple and non-invasive assessment protocol including oral intake status

and patient self-evaluation questionnaires on FHS and HR-QoL. A predictive model was built using data from a consecutive series of patients at an outpatient clinic of a tertiary care centre. This model may be used to predict aspiration in patients with OD.

Acknowledgements

We would like to acknowledge the contribution of Vivienne A.H. van de Kamp and Ellen L. van den Akker, SLPs at the department of Otorhinolaryngology and Head and Neck Surgery of the Leiden University Medical Centre, who assisted with and performed the FEES examinations.

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7



Summary, general discussion and conclusions



OD is the disturbance in the process of transporting solids or liquids from the mouth to the esophagus. OD can cause major complications such as dehydration, malnutrition, aspiration pneumonia, and even death. Because OD is often a secondary expression of another primary cause, it is underdiagnosed, with consequences such as aspiration pneumonia and negative effects on FHS and HRQoL.

The effects of OD may impact domains such as a patient's health or FHS, HRQoL, and social functioning. Also the burden it places on the caregiver should not be underestimated.

Over the last two decades, there has been a huge increase in publications on OD, as objectified by electronic database searches. Recent studies on the reliability and validity of commonly used instruments show insufficient psychometric robustness. Despite the availability of FEES and VFS as the gold standard for the assessment of OD, in practice the screening and measuring of HRQoL and FHS show room for improvement. An analysis of studies reporting on OD revealed that outcomes are often not comparable due to substantial differences in measurement techniques and study designs. Despite the increase in publications and attempts to improve OD care, the low quality of the study designs and the use of measurement instruments with insufficient psychometric properties hamper the comparison of results between studies. When the tools are insufficiently robust, the interpretation of outcomes in all published studies using these instruments remains unclear and possibly flawed.

To improve their robustness, the questionnaires should be redesigned and re-evaluated. Until then, investigators should use only the best available ones, basing their choice on the psychometric properties of the tools. Despite known shortcomings, the questionnaires used in this thesis were the best ones available at the time they were administered.

The scope of this thesis spanned several issues in the measurement and evaluation of OD. The screening, assessment, and treatment effect for OD have been covered, with a special emphasis on patient self-evaluation. The need for further research is, however, evident.

When reviewing the literature on a specific clinical diagnosis, such as HNC, it was observed that the attention traditionally given to a primary disease or illness and its treatment, both in general practice and in research settings, has shifted in the course of the decade toward functional outcomes. Although reports on functional outcomes have appeared more frequently, their usability leaves much to be desired. One reason is that assessing functional outcomes is seldom the first priority of these studies but rather a secondary aspect. Another reason is that the outcomes are often uncomparable

due to methodological, measurement, and evaluation differences between the studies. Consequently, the amount of meta-data being generated is insufficient for meta-analysis, which makes it impossible to obtain outcomes for large cohorts or draw conclusions for functional outcomes of specific interventions. In line with the previous shortcomings the effects of speech language therapy, among others, would need to be studied and the results of those studies should be carefully reported.

In light of the literature review in chapter 2 and the gaps mentioned above, there is a clear need for consensus on methods and minimum requirements for research and reporting on functional outcomes. In particular, the following needs should be addressed:

- Consensus on which measurement or evaluation technique is appropriate for each functional outcome: e.g. voice, speech, swallowing, trismus, and HRQoL.
- Consensus on measurement moments, with a minimal requirement of measuring pre-therapy and preferably long-term post-therapy.

When shifting the focus of attention from HNC to a chronic disease, for instance Parkinson's disease (PD), with a wide variety of functional impairments, a review of the literature reveals an extensive range of treatment results. In contrast, there are fewer reports on the outcomes of swallowing therapy. Since dysphagia in PD can cause major complications, it would be important to evaluate existing, new, and additional therapies. In this thesis it was shown, in chapter 3, how to systematically evaluate the effect of a new treatment modality for dysphagia in PD. In a randomized clinical trial both pre- and post-therapy outcomes were taken into account when evaluating the participants' HRQoL and functional outcomes with reference to the dietary intake. Although all groups showed lasting improvement in HRQoL and severity scores after therapy, no correlation was found between those scores and dietary intake.

A large share of diagnostics in dysphagia care consists of determining whether a patient is at risk for dysphagia before deciding to subject that individual to further assessment. Although many screening tools are available to identify patients who need further dysphagia assessment, there is a need for short, fast, and easy screening options. A common starting point is just asking whether a patient has a swallowing complaint instead of using a questionnaire or screening instrument. Until now, to the best of our knowledge, no research has been done on the value of asking that straightforward question. Determining the sensitivity and specificity of a single question could make everyday clinical practice more evidence-based. Moreover, a simple technique could lead to time and cost savings without disrupting the course of activity or progress in the outpatient clinic. As mentioned in chapter 4, further research is necessary to

provide additional psychometric data on Functional Health Status (FHS) questionnaires, including the single question, and how the resulting information can be combined with the results from either fiberoptic endoscopic evaluation of swallowing (FEES) or videofluoroscopy (VFS) as the gold standard or reference test. With the knowledge of recent studies on the reliability and validity of commonly used instruments this study shows that the use of a simple question has also a potential share in screening for OD. The advantages of a screening questionnaire versus a screening question should be weighed up in order to determine the advantages and disadvantages e.g. burden for the patient or time consumption. Innovation requires looking at what is already there with different eyes. Thus, a single question can be as good as a questionnaire.

From the starting point of screening for dysphagia, it is usual to continue on to further assessment. At that point, QoL is considered an important outcome measurement, as it objectifies the current health status or therapy effects in patients with OD. Measuring HRQoL requires instruments that are reliable and valid, however. To that end this thesis assessed two questionnaires, the M.D. Anderson dysphagia inventory and the Deglutition Handicap Index, in terms of their reliability and validity. It was shown how to evaluate their reliability and validity in a structured and constructive manner in chapter 5.

Not every health professional has access to the gold standard procedures to evaluate the presence of aspiration in dysphagia. In most nursing homes, for example, there is absence of the equipment to execute FEES or VFS. To avoid unnecessary diagnostic procedures, innovative options should be given due consideration. These novel techniques should be easy to administer, put less burden on the patient and health professional, be reliable, and yield consistent results. In an attempt to fill that need, we built a prediction model to forecast aspiration in patients at risk for OD on the basis of common self-evaluation questionnaires and oral intake status. Using commonly available instruments, it was shown that it is possible to accurately predict aspiration in oropharyngeal dysphagia by a non-invasive and non-instrumental assessment protocol including oral intake status and self-report questionnaires on FHS and HRQoL. The performance of the final model was excellent. On the basis of findings in chapter 6, we conclude that every health professional can determine, after further evaluation of this technique, whether aspiration is present in a patient or not.

FUTURE STUDIES

The measurement and evaluation of OD may improve significantly when new FHS and HRQoL questionnaires are developed in line with item response theory (IRT) such as Rasch analysis. By departing from the classical approach to questionnaire development and applying newer methods, the methodological issues that have arisen over the past years can be resolved. Consequently, measurement and evaluation would become more accurate and informative, thereby improving the care for OD. Second, a more uniform way of evaluating OD and its treatment can facilitate quantitative and qualitative comparisons, which in turn could lead to better treatment choices and more pertinent outcome knowledge. There is still a need to raise awareness of underdiagnosed OD as a consequence of other more prominent diseases. Attention to comorbidity is warranted not only to manage the health-related consequences and their implications for the patient's FHS or HRQoL but also to reduce the carer's burden. All multi-dimensional aspects of OD should be taken into account when characterizing a patient.

With innovations and novel perspectives, new avenues may open to connect applied research and evidence-based clinical practice with the field providing dysphagia care. The first step in that direction is to make evidence-based methods of diagnosing OD more accessible to health professionals with no access to the gold standard. The outcomes and recommendations presented in this thesis may give some useful guidance for this development.

8



Summary, general discussion and conclusions in Dutch



Orofaryngeale dysfagie (OD) is een probleem in het proces van het transporteren van voeding van de mond naar de oesophagus. OD kan grote gevolgen hebben zoals dehydratie, ondervoeding, aspiratie, longontsteking en zelfs overlijden. OD is vaak een secundaire uiting van een onderliggend probleem, waardoor het ondergediagnosticeerd is, met mogelijk aspiratiepneumonieën, overlijden, negatieve gevolgen voor de functionele gezondheidstoestand en gezondheidsgerelateerde kwaliteit van leven als gevolg.

OD kan invloed hebben op verschillende aspecten van het leven van de patiënt, zoals de algemene gezondheid, functionele gezondheidstoestand, gezondheidsgerelateerde kwaliteit van leven en het sociaal functioneren. Ook de belasting voor de mantelzorger moet niet onderschat worden.

De laatste twee decennia is er een forse toename van studies naar OD en publicaties over OD. Recente studies naar betrouwbaarheid en validiteit van vaak gebruikte instrumenten laten onvoldoende kwaliteit zien van de psychometrische kenmerken. Ondanks de beschikbaarheid van een gouden standaard voor het onderzoek naar OD, laat de dagelijkse praktijk ruimte voor verbetering van het screenen naar OD en het meten van gezondheidsgerelateerde kwaliteit van leven en functionele gezondheidstoestand middels vragenlijsten.

Een analyse van studies die over OD rapporteren laat resultaten zien die niet goed met elkaar te vergelijken zijn. Dit wordt veroorzaakt door substantiële verschillen in evaluatietechnieken en studie opzet. Ondanks het stijgende aantal onderzoeken en pogingen om de zorg voor OD te verbeteren, maakt de lage methodologische kwaliteit van studies, het gebruik van instrumenten met psychometrische kenmerken van onvoldoende kwaliteit, de vergelijking van resultaten tussen studies lastig. Het gebruik van meetinstrumenten die onvoldoende kwaliteit hebben, heeft grote invloed op de interpretatie van resultaten uit deze studies.

Om deze kwaliteit te verbeteren moeten de vragenlijsten opnieuw ontwikkeld en gevalideerd worden. Tot dat moment moeten onderzoekers alleen de best beschikbare vragenlijsten gebruiken en desbetreffende psychometrische kenmerken in acht nemen. De vragenlijsten die gebruikt zijn in deze thesis waren op dat moment, ondanks de tekortkomingen, de best beschikbare voor het betreffende doel.

De scope van dit proefschrift omvat verschillende problemen in het meten en evalueren van OD. Screening, onderzoek en het effect van de therapie voor OD worden behandeld, met de nadruk op zelfevaluatie. De noodzaak naar verder onderzoek is evident.

Kijkend naar een specifiek ziektebeeld zoals hoofd-halskanker, wordt duidelijk dat er naast aandacht voor het primaire ziektebeeld en de behandeling ervan zowel in de

praktijk als in verschenen publicaties er de laatste tien jaar een verschuiving gaande is naar de functionele uitkomsten. Hoewel deze uitkomsten meer gerapporteerd worden, laat de bruikbaarheid ervan nog te wensen over. Bijvoorbeeld doordat functionele uitkomsten niet de primaire uitkomstmaat van de studie zijn. En als gevolg van methodologische, meet- en evaluatie verschillen tussen studies kunnen uitkomsten vaak niet met elkaar vergeleken worden. Dit resulteert in een te kleine hoeveelheid meta-data waardoor het niet mogelijk is om een meta-analyses uit te voeren. Hierdoor is het niet mogelijk om uitkomsten van grote cohorten te gebruiken en om conclusies te trekken voor de functionele uitkomsten van specifieke behandelingen met behulp van een meta-analyse. Daarbij moeten effecten van therapieën, zoals die van logopedie onderzocht worden en de uitkomsten dienen nauwkeurig gerapporteerd te worden. In het kader van het systematische review in hoofdstuk 2 en de bovengenoemde hiaten is het nodig een consensus van minimale vereisten voor het onderzoeken van functionele uitkomsten vast te stellen.

De volgende studie eigenschappen zouden vastgesteld moeten worden:

- consensus over welke meet- of evaluatietechniek gebruikt dient te worden voor elke functionele uitkomst zoals stem, spraak, slikken, trismus en gezondheidsgerelateerde kwaliteit van leven.
- aanvullend zou er een consensusbesluit genomen moeten worden over de meetmomenten met als minimale vereiste een meting voor de behandeling en bij voorkeur een meting (lange termijn) na de behandeling.

Als de focus verschuift van hoofd- halskanker naar een chronisch ziektebeeld zoals de ziekte van Parkinson (ZvP) met een verscheidenheid aan functionele gevolgen is er een grote hoeveelheid aan onderzoeksresultaten beschikbaar. Daarentegen zijn er minder uitkomsten van therapie voor het slikken beschikbaar. Omdat OD bij patiënten met de ZvP grote gevolgen kan hebben is er behoefte aan het evalueren bestaande, nieuwe en aanvullende therapieën. Dit proefschrift laat in hoofdstuk 3 zien hoe het effect van een nieuwe behandelmodaliteit systematisch geëvalueerd kan worden bij patiënten met de ZvP. In een gerandomiseerde klinische trial worden zowel de uitkomsten van voor als na de behandeling meegenomen in het bepalen van het effect van de behandeling door gebruik te maken van vragenlijsten over de gezondheidsgerelateerde kwaliteit van leven en de functionele uitkomsten. Hoewel alle groepen een langdurig therapie effect laten zien op het gebied van gezondheidsgerelateerde kwaliteit van leven en in de ernst scores na de therapie werd er geen correlatie met de orale intake gevonden.

Het is belangrijk een patiënt eerst te kunnen screenen op mogelijke OD, alvorens de patiënt te onderwerpen aan verder onderzoek. Hoewel er een ruime keuze is aan screeningstools om te bepalen welke patiënt verder onderzoek nodig heeft is er behoefte aan korte, snelle en makkelijke manieren van screenen. Een veel gebruikte techniek is het simpelweg vragen aan de patiënt of hij slikklachten heeft in plaats van het gebruiken van een vragenlijst of screeningstool. Tot nu toe, voor zover we weten, is er geen onderzoek gedaan naar de waarde van de uitkomst van een dergelijke vraag. In hoofdstuk 4 werd de sensitiviteit en specificiteit van dergelijke technieken bepaald, hierdoor wordt de werkwijze in de dagelijkse praktijk meer evidence-based en worden tijd- en kostenbesparingen gemaakt zonder het gebruik van buitensporige instrumenten die de dagelijkse gang van zaken in de spreekkamer verstoren.

Aanvullende psychometrische gegevens moeten nog verkregen worden om deze functionele gezondheidstoestand vragenlijsten, waarbij ook deze anamnestiche vraag met FEES of VFS (gouden standaard) als referentie test, geëvalueerd wordt. Met de huidige kennis van betrouwbaarheid en validiteit van vaak gebruikte vragenlijsten laat deze studie zien dat een simpele vraag een potentieel aandeel kan hebben in het screenen naar OD. De voordelen van een screenende vragenlijst of één screeningsvraag moeten tegen elkaar afgewogen worden wat betreft de voor- en nadelen, zoals de belasting voor de patiënt of de hoeveel tijd die het gebruik van een instrument kost. Innovatie vraagt hier om beschikbare middelen met andere ogen te bekijken. Concluderend, een enkele vraag kan net zo informatief zijn als een lijst met vragen.

Screening wordt vaak logisch opgevolgd door verder onderzoek. Kwaliteit van leven wordt beschouwd als een belangrijke uitkomstmaat in het objectiveren van de huidige gezondheidstoestand of therapie-effecten bij patiënten met OD. Het meten van gezondheidsgelateerde kwaliteit van leven moet uitgevoerd worden met betrouwbare en gevalideerde instrumenten. Twee vragenlijsten, de M.D. Anderson dysphagia inventory en de Deglutition Handicap Index, zijn geëvalueerd op betrouwbaarheid en validiteit in dit proefschrift. Hoofdstuk 5 laat zien hoe een vragenlijst op een structurele en constructieve manier geëvalueerd kan worden.

Niet iedere hulpverlener die met OD te maken heeft, heeft toegang tot de gouden standaard om de aanwezigheid van aspiratie te onderzoeken. Bijvoorbeeld in een verpleeghuis zijn meestal geen faciliteiten voor het uitvoeren van een FEES of een VFS. Om onnodige diagnostiek te voorkomen moeten innovatieve opties overwogen en onderzocht worden. Deze opties dienen makkelijk in het gebruik te zijn, niet belastend voor de patiënt en hulpverlener en dienen daarnaast betrouwbaar en consistent te zijn. In dat kader is er een voorspellend model gebouwd om de aanwezigheid van

aspiratie te voorspellen bij patiënten met het risico op OD op basis van gebruikelijke zelfevaluatie vragenlijsten en de huidige orale intake. Met deze instrumenten is het mogelijk om accuraat de aanwezigheid van aspiratie te voorspellen door gebruik te maken van een niet invasief, niet instrument gebonden onderzoeksprotocol. Het uiteindelijke model heeft een excellente prestatie. Met de bevindingen in hoofdstuk 6, kan elke gezondheidsprofessional, na verdere evaluatie van deze techniek, snel, makkelijk en zeker bepalen of een patiënt aspireert of niet.

TOEKOMSTIGE STUDIES

Onderzoek en evaluatie van OD zal waarschijnlijk significant verbeteren wanneer er nieuwe functionele gezondheidstoestand en kwaliteit van leven vragenlijsten ontwikkeld worden die gebruik maken van de item response theory (IRT) zoals Rasch analyse. Door afscheid te nemen van de klassieke vragenlijstontwikkeling en nieuwe ontwikkelmethodes toe te passen, zullen de methodologische problemen die de laatste jaren aan het licht zijn gekomen worden opgelost. Dit zal als gevolg hebben dat onderzoek en evaluatie van OD meer accuraat en informatief worden. Hiermee zal tevens de zorg voor OD verbeterd worden. Daarbij is er een meer uniforme werkwijze in de evaluatie van OD nodig om zo kwantitatieve en kwalitatieve vergelijking te kunnen maken tussen studies. Dit zal leiden tot betere behandelkeuzes en zekerdere resultaten. Er is nog steeds behoefte aan een grotere alertheid op ondergediagnosticeerde OD, als consequentie van andere, meer prominente, ziektebeelden. Aandacht voor comorbiditeit is nodig om de gevolgen voor de gezondheidsgerelateerde consequenties te reguleren en om de belasting van de mantelzorgers te verminderen. OD moet mulidimensioneel in kaart gebracht worden tijdens de zorg voor patiënten met slikproblemen.

Vernieuwingen en nieuwe perspectieven zullen nieuwe mogelijkheden creëren om toegepast onderzoek en evidence-based patiëntenzorg met elkaar te verbinden. De eerste stap is het toegankelijk maken van methoden voor het diagnosticeren van OD zonder de beschikking te hebben over de gouden standaard. De uitkomsten en aanbevelingen uit dit proefschrift kunnen voor deze ontwikkeling de eerste stap zijn.

Abbreviations
List of publications
Curriculum Vitae
Acknowledgements



ABBREVIATIONS

3DCRT	Three dimensional Conformal Radiotherapy
ASHA	American Speech-Language Hearing Association
AUC	Area Under the Curve
BMI	Body Mass Index
COSMIN	Consensus-based Standards for the Selection of Health Measurement Instruments
CRT	Chemoradiotherapy
CTCAE	Common Terminology Criteria for Adverse Events
D	Digestive tract
DHI	Deglutition Handicap Index
	Dysphagia Handicap Index
DSS	Dysphagia Severity Scale
EAT-10	Eating Assessment Tool-10
EBP	Evidence-Based Practice
ECOG	Eastern Cooperative Oncology Group
ENT	Ear, Nose and Throat
EORTC	The European Organization for Research and Treatment of Cancer
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
EORTC QLQ-H&N35	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire module Head and Neck cancer
FACT-HN	Functional Assessment of Cancer Therapy-Head and Neck
FEES	Fiberoptic Endoscopic Evaluation of Swallowing
FHS	Functional Health Status
FOIS	Functional Oral Intake Scale
GRBAS	Grade, Roughness, Breathiness, Asthenicity, Strain scale
HNC	Head and Neck Cancer
HNCI	Head and Neck Cancer Inventory
HNRQ	Head and Neck Radiotherapy Questionnaire
HNQoL	Head and Neck quality of life
H&Y scale	Hoehn and Yahr scale
HR-PRO	Health-Related Patient-Reported Outcomes
HRQoL	Health-Related Quality of Life
IC	Intensive Care
ICC	Intraclass Correlations Coefficients

ABBREVIATIONS

IMRT	Intensity Modulated Radiation Therapy
IQR	Interquartile Range
IRT	Item Response Theory
KPS	Karnofsky Performance Status
LASSO	Least Absolute Shrinkage and Selection Operator
LENT/SOMA	Late Effects Normal Tissue Subjective, Objective, Management, Analytic Scales
LUMC	Leiden University Medical Center
MDADI	MD Anderson Dysphagia Inventory
MeSH	Medical Subject Headings
MIO	Maximum Incisal Opening
ML	Maximum Likelihood
MMSE	Mini Mental State Examination
MUMC	Maastricht University Medical Center
NHMRC	National Health and Medical Research Council
NMES	Neuromuscular Electrical Stimulation
NMES-M	Neuromuscular Electrical Stimulation at a Motor level
NMES-S	Neuromuscular Electrical Stimulation at a Sensory level
NOS	Not Otherwise Specified
NPV	Negative Predictive Value
OD	Oropharyngeal Dysphagia
PAS	Penetration Aspiration Scale
PD	Parkinson's Disease
PEG	Percutaneous Endoscopic Gastrostomy
PPV	Positive Predictive Value
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta Analyses
PSS-HN	Performance Status Scale for Head & Neck cancer patients
QOL	Quality of Life
ROC	Receiver Operating Characteristic
RBHOMS	Royal Brisbane Hospital Outcome Measure for Swallowing
ROM	Range of Motion
RT	Radiotherapy
RTOG	Radiation Therapy Oncology Group
SOAL	Swallowing Outcome after Laryngectomy
S-SECEL	Swedish version of the Self-Evaluation of Communication Experiences after Laryngeal Cancer
SPS	Swallowing Performance Status

SSQ	Sydney Swallow Questionnaire
SUS Malmö	Skane University Hospital Malmö
SWAL-QOL	Swallowing Quality of Life Questionnaire
TDC	Tissue/Dose Compensation
TOR-BSST	Toronto Bedside Swallowing Screening Test
TT	Traditional Therapy
UWQoL	University of Washington Quality of Life Questionnaire
V	Voice or Speech
VAS	Visual Analogous Scale
VFS	Videofluoroscopy
VHI	Voice Handicap Index
VHI-10	Voice Handicap Index-10
VR-QoL	Voice Related Quality of Life
V-VST	Volume-Viscosity Swallowing Test
WHO	World Health Organization
XQoL	Xerostomia Quality of Life Questionnaire

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CURRICULUM VITAE

Bastiaan Joris Heijnen was born in Eindhoven, The Netherlands, on February 3rd, 1984. He attended the Eckart College for pre-university education and graduated in 2002. In the same year he started studying Speech and Language Pathology on the Fontys University of Applied Sciences in Eindhoven. He obtained his Bachelor of Health degree in 2005. After his graduation he started working at the Catharina Hospital, Department of Otorhinolaryngology as a speech language pathologist with a specific focus on voice disorders. In 2006 he started his own Speech Language Therapy practice, treating professional voice users. Both ended in 2009.

In 2007 he moved to Leiden and started studying Clinical Language Speech and Hearing Sciences on the faculty of Medicine at Utrecht University. In 2010 he obtained his Master of Science degree. During this period, he worked at the Jacob Clinic, center for rehabilitation and Nieuw Unicum, Multiples Sclerosis Expertise Center. From december 2009 until november 2010 he started his scientific career as a researcher at the department of Otorhinolaryngology, Head and Neck surgery at Maastricht University Medical Center.

From November 2010 to the present, he started working as a member Laryngological team at the Department of Otorhinolaryngology, Head and Neck surgery of the Leiden University Medical Center in a combined function of Speech Language Pathologist and PhD candidate.

Bastiaan is a son of Hendrikus Petrus Heijnen and Nancy Audrey Dees, he has two brothers Geert Alexander and Pim Jasper.

He has a relationship with Alexander Munts and they live together in Heemstede.

ACKNOWLEDGMENTS (IN DUTCH)

Luctor et emergo. Het is volbracht. Volbracht omdat het een lange weg is geweest met kuilen, bergen en dalen. Met meestal licht aan het einde van de tunnel. Soms in het donker hebben anderen mij geholpen, hebben zij een stukje meegelopen of even licht gemaakt. Ondanks dat je een promotietraject voornamelijk alleen doet, wil ik een aantal mensen bedanken voor hun kennis, hulp, vriendschap, steun en liefde.

Geachte Professor Speyer, Beste Renée, Zonder jou zaten we hier niet. Jouw taak als een van de twee promotoren mag niet onderschat worden. Je kennis van de dysfagie, wetenschap, flexibiliteit en veerkracht heeft dit traject mede tot een goed einde gebracht. Samen hebben we heel wat valkuilen omzeild en hebben we elkaar, maar meestal jij mij, uit de put geholpen. Als ik er echt even doorheen zat wist je me weer te motiveren, relativeerde je het probleem en lukte het weer om door te gaan. Bedankt!

Geachte Professor Frijns, Beste Johan, Als mijn promotor wil ik je bedanken voor je inhoudelijke en logistieke ondersteuning de afgelopen periode. Nooit heb ik getwijfeld aan je geloof in mij en je geloof in een succesvolle afronding van mijn promotietraject, je ervaring in de wetenschap en in het begeleiden van promovendi is van onschatbare waarde.

Beste Elisabeth, Ton, Professor van Benthem en Professor Fleuren, dank voor de vrijheid om naast de patiëntenzorg, die altijd doorgaat, mijn promotie vorm te geven en af te ronden.

Beste Collega's, Staf, Assistenten, Verpleegkundigen, Secretariaresses, Ondersteuners en Onderzoekers, dank dat jullie er zijn geweest en voor jullie collegialiteit. Even niet met onderzoek bezig zijn is essentieel in het doen van onderzoek. Ellen en Christa, je zal maar een promoverende collega hebben... Bedankt voor jullie geduld, humor en samenwerking.

Vivienne, jij valt bijna niet te bedanken. Naast collega ook vriendin en onvervangbaar. Je scherpe analytische blik en je hulp bij het concretiseren van oplossingen op verschillende momenten over verschillende onderwerpen is fantastisch en waardevol. We hebben gelachen en gehuild maar met jou ben ik steeds een stap verder gekomen. Dat je mijn paranimf wilde zijn betekent veel voor me.

Birgit, onze geschiedenis gaat ver terug. Wat we ook mee maakten in ons leven, bleven we met elkaar in contact. Dank voor onze vriendschap en dat je nu mijn paranimf bent!

Willem, Jeroen en Tineke, los van de afstand na mijn vertrek uit Eindhoven startte ik ook nog met een eindeloos project dat vergeleken met reistijd van en naar Eindhoven nog veel meer tijd kostte. Ik ben blij dat het fundament van onze vriendschap zo stevig is, dat het overeind blijft onder de zwaarste omstandigheden.

Daan, Ronald & Maarten, Rob, Marieke, Berit, Jan & Hein. Dank voor de afleiding en gezelligheid! Nu de S eraf is, is er hopelijk meer tijd!

Geert, Linda, Oda & Ask, Pim & David en natuurlijk ook ooms, tantes, neven en nichten. Familie staat vast. Fijn dat jullie er zijn of waren. Hetzelfde geldt voor Gerard† & Corry, Edwin & Ilona, Daphne, Jeroen & Jade.

Lieve Pap en Mam, terugkijkend zat dit er natuurlijk altijd al aan te komen. Als kind wilde ik de meest onmogelijke (technische) projecten al uitvoeren. Die systematisch nèt iets te hoog gegrepen waren. Jullie lieten me en stimuleerden me om het te proberen maar ook om door te gaan. Als je het kan, moet je het doen. En zie hier het is gelukt. Dank voor jullie opvoeding, steun, liefde en stabiele basis.

Lieve Oma, dit boekje is ook voor jou. Alle telefoontjes, logeerpartijen, quatre-mains van jongs af aan tot nu, bevestigen onze speciale band. Je trots, als ik iets gepubliceerd had en je vriendinnen de manuscripten verplicht moesten lezen, is geweldig.

Lieve Alex, zonder jou was ik er niet aan begonnen en had ik het niet afgemaakt. Bij jou zag ik dat wetenschap leuk was. Naast dat, ben je als mijn man, in ons drukke leven onmisbaar. Je liefde, humor, geduld, luisterend oor, kritische blik en stabiliteit zijn zo belangrijk geweest afgelopen periode, dat ik weer bijteken!

