



Review article

Affective symptoms in patients with oropharyngeal dysphagia: A systematic review[☆]

Rob J.C.G. Verdonshot^{a,b,*}, Laura W.J. Baijens^{a,c}, Sophie Vanbelle^d, Ilona van de Kolk^a, Bernd Kremer^{a,c}, Carsten Leue^e

^a Department of Otorhinolaryngology, Head and Neck Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

^b Emergency Department, Erasmus Medical Center, Rotterdam, The Netherlands

^c GROW-School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht, The Netherlands

^d Department of Methodology and Statistics, CAPHRI, Maastricht University, Maastricht, The Netherlands

^e Department of Psychiatry and Psychology, Maastricht University Medical Center, Maastricht, The Netherlands

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ABSTRACT

Objective: Affective disorders are prevalent in different somatic conditions and influence somatic symptom bother and quality of life. Mood and anxiety disorders impact patients' compliance and adherence to treatment. This systematic review summarizes published studies on affective complaints in patients with oropharyngeal dysphagia (OD) in order to determine the quality of studies concerning any association of OD with symptoms of depression and/or anxiety.

Methods: A literature search was carried out using electronic databases Embase, Medline, Web-of-science, PsycINFO, Cochrane Library, and Google scholar. Two reviewers made the preselecting cut by screening all articles on title and abstract and independently screened the full texts of this initial set of articles. Methodological quality of the studies that met the inclusion criteria was assessed independently.

Results: Twenty-six articles were included in the analysis after full-text screening and by applying the inclusion and exclusion criteria. All studies concluded that symptoms of depression were associated with impaired swallowing function, and 9 out of 12 studies concluded that symptoms of anxiety were associated with functional impairment of swallowing. The reviewers found heterogeneous outcomes and methodological limitations, which prevented data from pooling.

Conclusion: Although no meta-analytic conclusions can be drawn, it appears that symptoms of anxiety and depression are common in OD. Caregivers have to be aware of this in order to detect affective comorbidity. Given that affective conditions influence patients' treatment adherence and compliance, integrated care approaches should be advocated in case of comorbidity. Studies on treatment effect are lacking and well-designed prospective research is needed.

1. Introduction

Oropharyngeal dysphagia (OD) is commonly seen in the otorhinolaryngology outpatient clinic, and is defined as 'difficulty to transport bolus from the mouth, via the pharynx, to the entrance of the esophagus' [1]. The etiology of OD is diverse: stroke; chronic neurological diseases (e.g., multiple sclerosis, Parkinson's disease, myasthenia gravis); head and neck cancer or its oncological treatment effects (e.g., surgery, radiation); inclusion body myositis; Zenker's diverticulum; cervical spine abnormalities (e.g., degenerative, osteophytes); rising age (presbyphagia), etc. [1–3]. The prevalence of OD is high. For

instance, it affects > 30% of patients who had a stroke, and 52%–82% of patients with Parkinson's disease. The prevalence of OD is increasing with age, and up to 40% of the elderly aged 65 years and older have OD. This frequency is even higher in institutionalized elderly [4]. It is estimated that OD affects 40 million people in Europe [5]. The complications of OD can be severe: aspiration pneumonia; dehydration; malnutrition; or even sudden death [1,6–8]. Furthermore, it affects health-related quality of life. Patients with OD often have feelings of shame, embarrassment, and social isolation [7–11]. Because of the complexity of the etiology, and a high incidence of mental health related comorbidity, a multidisciplinary strategy including mental

[☆] Department where work was done: Department of Otorhinolaryngology, Head and Neck Surgery, Maastricht University Medical Center, Maastricht, The Netherlands.

* Corresponding author at: Department of Otorhinolaryngology, Head and Neck Surgery, Maastricht University Medical Center, PO Box 5800, 6202 AZ Maastricht, The Netherlands.
E-mail address: RJCG.Verdonschot@alumni.maastrichtuniversity.nl (R.J.C.G. Verdonshot).

health care is essential [12,13]. In general, psychiatric symptoms of anxiety and depression are common in patients with chronic conditions (chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), irritable bowel syndrome (IBS), overactive bladder (OAB) etc.) [14–19], and OD is also associated with clinically relevant affective complaints [20]. However, little is known about the strength and the direction of this association and investigations on the pathophysiology, risk factors, and treatment effect are scarce.

The aim of this systematic review is to summarize published studies on affective symptoms in patients with OD and to analyze the quality of the literature. The broader objective was to elucidate how affective comorbidities may impact on symptom bother and treatment compliance in order to advocate integrated or collaborative care approaches.

2. Method

2.1. Identification and selection of studies

This review was conducted by following the Cochrane Collaboration criteria for systematic reviews. One of the authors and an experienced university library information specialist carried out a literature search using the electronic biomedical databases Embase, Medline, Web-of-Science, PsycINFO, Cochrane Library, and Google scholar. Search terms were related to dysphagia and to affective conditions (see Table 1 for the complete syntax). The entire search was performed on the 1st of June 2016. Two independent reviewers made the first preselecting cut by screening all articles on title and abstract. Then they independently screened full texts of this initial set of articles. Furthermore, the reference lists of the selected articles were screened for additional literature. If an article was not electronically available, the authors were contacted to obtain the full text. All studies that examined swallowing function and affective conditions were included. However, reviews, studies without use of validated assessment tools on affective symptoms, expert opinions, conference papers, studies with a sample size below 10, and studies in patients with eating disorders or other psychiatric disorders (not being affective conditions) were excluded.

2.2. Data analysis and assessment of study quality

The included studies were assessed for methodological quality using a 12-item critical appraisal tool derived from the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) (Table 2). The QUADAS is a tool to assess the diagnostic accuracy of studies included in systematic reviews [21]. Two independent reviewers used its critical appraisal criteria to analyze all included articles, scoring each criterion with a ‘yes’, ‘no’, or ‘unclear’. Internal validity was rated with items 3, 4, 5, 6, 9, 10, 11, and 12, and external validity with items 1, 2, 7, and 8. The reviewers resolved any differences between assigned scores through discussion.

Table 1
Literature search.

Embase	(dysphagia/de OR (dysphag* OR ((swallow* OR deglutit*) NEAR/3 (disorder* OR problem*)):ab,ti) AND(psychiatry/exp OR psychiatrist/de OR 'psychiatric diagnosis'/de OR 'mood disorder'/exp OR 'anxiety disorder'/exp OR 'mental patient'/exp OR (psychiatr* OR depressi* OR (mood OR anxi* OR Affective) NEAR/3 disorder*) OR neuropsych*) :ab,ti) NOT ([Conference Abstract]/lim OR [Letter]/lim OR [Note]/lim OR [Conference Paper]/lim OR [Editorial]/lim)
Medline	(Deglutition Disorders/ OR (dysphag* OR ((swallow* OR deglutit*) ADJ3 (disorder* OR problem*)):ab,ti.) AND (exp psychiatry/ OR exp mood disorders/ OR exp anxiety disorders/ OR Mentally Ill Persons/ OR (psychiatr* OR depressi* OR ((mood OR anxi* OR Affective) ADJ3 disorder*) OR neuropsych*) :ab,ti.) NOT (letter OR news OR comment OR editorial OR congresses OR abstracts).pt.
Web-of-science	TS = (((dysphag* OR ((swallow* OR deglutit*) NEAR/3 (disorder* OR problem*))) AND ((psychiatr* OR depressi* OR ((mood OR anxi* OR Affective) NEAR/3 disorder*) OR neuropsych*))) AND DT = (Article)
PsycINFO	(Dysphagia/ OR (dysphag* OR ((swallow* OR deglutit*) ADJ3 (disorder* OR problem*)):ab,ti.) AND (exp psychiatry/ OR exp Affective Disorders/ OR exp anxiety disorders/ OR (psychiatr* OR depressi* OR ((mood OR anxi* OR Affective) ADJ3 disorder*) OR neuropsych*) :ab,ti.) NOT (letter OR news OR comment OR editorial OR congresses OR abstracts).pt.
Cochrane	((dysphag* OR ((swallow* OR deglutit*) NEAR/3 (disorder* OR problem*)):ab,ti) AND ((psychiatr* OR depressi* OR ((mood OR anxi* OR Affective) NEAR/3 disorder*) OR neuropsych*) :ab,ti)
Google scholar	Dysphagia "swallowing deglutition disorder disorders problem problems" psychiatry psychiatrist psychiatric "mood affective anxiety disorders" depression depressive

Table 2
Criteria for quality assessment.

1.	Was the spectrum of patients representative of the patients who will receive the test in practice?
2.	Were the selection criteria clearly described?
3.	Was the diagnostic swallowing tool (e.g. questionnaire, FEES) likely to correctly classify the swallowing condition?
4.	Was the psychiatric screening tool a validated screening tool?
5.	Is the time period between the diagnostic swallowing test and the psychiatric screening test short enough to be reasonably sure that the target conditions did not change between the two tests?
6.	Did all patients receive the same diagnostic tests?
7.	Was the execution of the swallowing test described in sufficient detail to permit replication of the test?
8.	Was the execution of the psychiatric test described in sufficient detail to permit replication of the test?
9.	Were the psychiatric test results interpreted without knowledge of the results of the swallowing test?
10.	Were the swallowing test results interpreted without knowledge of the results of the psychiatric test?
11.	Were withdrawals from the study explained?
12.	Method of data analyses. Were appropriate statistical methods applied?

3. Results

A total of 3586 articles were identified, and 2528 remained after removing duplicates. All articles were screened for title and abstract, which left 60 potentially eligible for inclusion. The level of agreement between the two reviewers for this first selection was 91%. The level of agreement between the two reviewers for eligibility after full text screening was 75%. After discussion full consensus was achieved. Finally 24 articles were included in the analysis after full-text screening and by applying the inclusion and exclusion criteria [9–11,20,22–41]. All of the articles included were written in English (see Fig. 1 for the flowchart of the literature search process). Fifteen articles reported on cross-sectional studies [9,10,20,23–28,30–33,36,41], 5 on prospective cohort studies [22,29,37,39,40], 2 on retrospective cohort studies [11,38], and 2 on case-control studies [34,35]. The studies were too heterogeneous in outcome and not of sufficient quality to carry out a meta-analysis. Instead, a qualitative analysis was performed. Table 3 provides an overview of the included articles, summarizing study design, sample size, population characteristics, and measurement tools. The included articles are segregated by type of assessment tools used for OD (single swallowing questions, clinical evaluation of swallowing, swallowing-related questionnaires, videofluoroscopic swallowing studies and fiber-optic endoscopic evaluation of swallowing), and discussed below.

3.1. Quality of studies

The quality assessment is presented in Table 4. The level of agreement between the two reviewers for quality assessment was

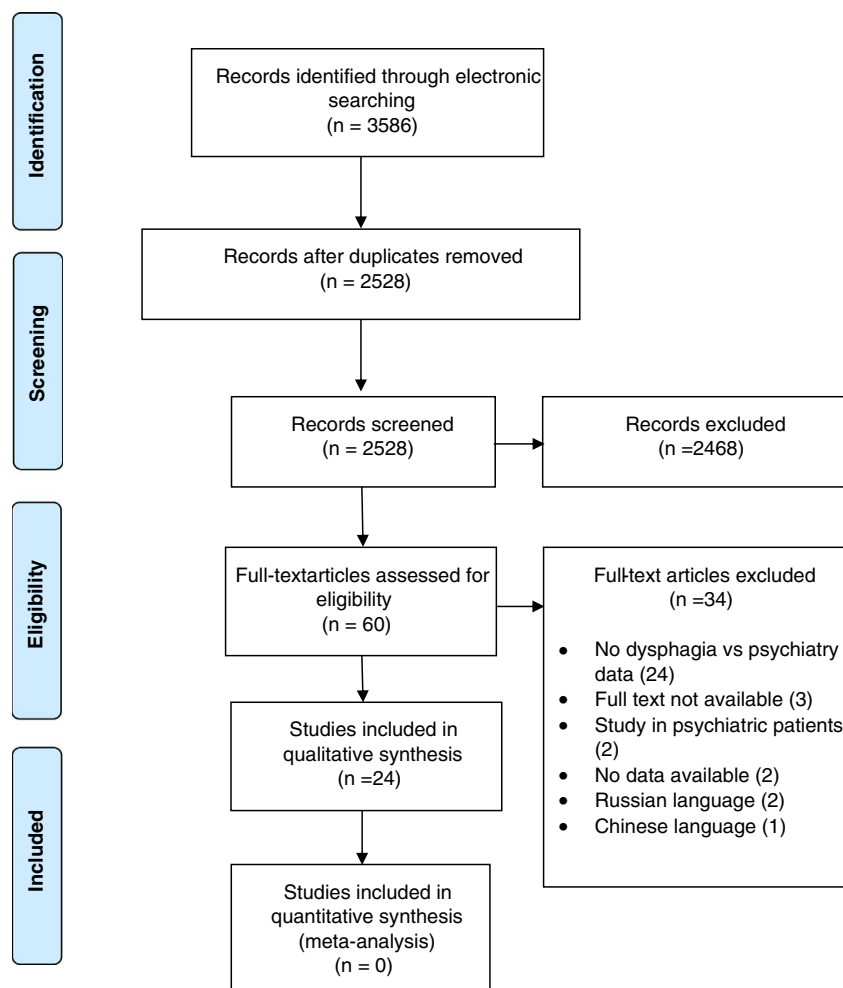


Fig. 1. Flowchart of the literature review process.

91.3% (263 of the 288 QUADAS items). After discussion full consensus was achieved. Thirteen of the included studies met all criteria for external validity [20,22,24,29–31,33,34,36,37,39–41], whereas none met all criteria for internal validity. Eight studies fulfilled 6 out of 8 criteria for internal validity [9,11,23,26,30,31,35,36]. Twenty-three studies were rated ‘unclear’ on items 9 and 10, as the article did not reveal whether results of the swallowing test were interpreted without knowledge of the psychiatric assessment and vice versa [9,10,20,22–41].

3.2. Assessment tools

Various assessment tools for swallowing function and affective symptoms were used. In order to assess swallowing function, most studies used self-reporting questionnaires or rating scales [9,20,22–27,29,32,33,35]. With regard to the assessment of affective symptoms, most studies [11,20,24,26,33,34,37,38,41] used the Hospital Anxiety and Depression Scale (HADS). In 19 studies the swallowing assessment and the assessment of depression and/or anxiety symptoms were performed on the same day [9–11,20,22–24,26,28–31,34–37,39–41]. In 5 studies time points of the assessments were unclear. See Table 3 for a complete overview of the assessment tools used for swallowing function and affective symptoms.

3.3. Videofluoroscopic swallowing study and fiber-optic endoscopic evaluation of swallowing

Nguyen et al. [11] performed a study to evaluate OD in patients

treated for head and neck cancer. One hundred and four patients treated for head and neck cancer (e.g. surgery, radiotherapy, chemoradiotherapy, or postoperative radiotherapy), with different disease sites and stages, were retrospectively analyzed. Patients with complaints of dysphagia ($n = 73$) underwent a VFSS to assess its severity (mild, moderate, severe). The control group ($n = 31$) had no complaints. The HADS scores were significantly elevated in the dysphagic group. Scores on anxiety and depression symptoms were significantly higher in moderate and severe OD categories compared to mild OD. In addition, Nguyen et al. [38] compared head and neck cancer patients retrospectively who had received chemoradiation ($N = 101$) with patients who had received postoperative radiation. They did not find any difference in symptoms of anxiety or depression between these 2 treatment groups. However, post-radiation patients who developed complications, of which OD was the most common, reported symptoms of anxiety and depression significantly more often. Kang et al. [40] conducted a non-randomized controlled trial in 50 stroke patients with OD as confirmed by VFSS. A control group of 25 patients received a conventional swallowing therapy (tactile-thermal stimulation, 5 days per week for 2 months). The experimental group of 25 patients received the same conventional therapy but also bedside training, which consisted of oral, pharyngeal, laryngeal, and respiratory exercises (1 h per day for 2 months). Before and after therapy, all 50 patients underwent a VFSS and filled out the BDI. The experimental group showed a significantly better swallowing function and lower levels of depressive symptoms than the control group. In the study of Manor et al. [10], 69 patients with Parkinson's disease underwent a clinical

Table 3
Overview of the included articles.

Author	N/pop/etiology	Measurement tool for dysphagia	Measurement tool for affective symptoms	Design	Results
Nguyen et al. [11]	N = 104 Patient treated for head and neck cancer	Videofluoroscopy of Swallowing	Hospital Anxiety and Depression Scale [46]	Retrospective cohort study	Hospital Anxiety (OR 0.23; 95% CI 0.07–0.69; $p = 0.005$) and Depression (OR 0.15; 95% CI 0.04–0.45; $p = 0.0001$) scores were greater in moderate-to-severe dysphagia compared to absent or mild dysphagia.
Nguyen et al. [38]	N = 101 Head and neck cancer patients	Videofluoroscopy of Swallowing	Hospital Anxiety and Depression Scale [46]	Retrospective cohort study	Hospital Anxiety ($p = 0.001$) and Depression ($p = 0.0001$) scores were greater in patients with post-treatment dysphagia.
Kang et al. [40]	N = 50 Stroke patients	1. Videofluoroscopy of Swallowing 2. Physical examination	Beck Depression Inventory [47–50]	Non-randomized controlled trial	Significant improvement in swallowing function and depression symptom scores ($p < 0.05$) in experimental group compared to control group.
Manor et al. [10]	N = 69 Patients with Parkinson's disease	1. The Swallowing Disturbance Questionnaire [43] Clinical swallowing evaluation 2. Fiber-optic Endoscopic Evaluation of Swallowing	Trait Anxiety Inventory [51] Beck Depression Inventory [47–50]	Cross-sectional study	Correlation between Swallowing Disturbance Questionnaire and scores of anxiety ($r = 0.472$, $p < 0.000$) and depression ($r = 0.357$, $p < 0.003$).
Verdonschot et al. [41]	N = 107 Patients with complaints of oropharyngeal dysphagia	Fiber-optic Endoscopic Evaluation of Swallowing	Hospital Anxiety and Depression Scale [46]	Cross-sectional study	High prevalence (43%) of anxiety and depression symptoms. Significant association between anxiety symptoms and piecemeal deglutition ($p = 0.026$) and postswallow vallecular pooling ($p = 0.015$).
Lin et al. [30]	N = 513 Elderly	1. Self-reported 2. A 16-item swallowing questionnaire 3. Neurological examination designed to detect symptoms and signs of impaired swallowing 4. A timed swallowing test (90 ml cold water) 150 ml water swallowing test	Geriatric Depression Scale [52]	Cross-sectional study	Elderly with depression symptoms had significantly greater impaired swallowing compared to elderly without symptoms ($\chi^2 = 15.34$, $p < 0.001$).
Miller et al. [31]	N = 137 Patients with Parkinson's disease	150 ml water swallowing test	Geriatric Depression Scale [52]	Cross-sectional study	Patients unable to complete 150 ml swallowing test had significantly greater depression symptoms ($p = 0.01$) compared to patients able to complete 150 ml swallowing test.
Thomas et al. [34]	N = 79 Patients with Multiple Sclerosis	Water swallowing test	Hospital Anxiety and Depression Scale [46]	Case-control study	Abnormal swallowing was associated with higher depression symptom scores ($p < 0.001$).
Zhang et al. [39]	N = 59 Tongue cancer patients	Standardized swallowing assessment	Zung Depression Scale [53]	Prospective cohort study	Lower levels of the water swallowing test were associated with lower depression symptom scores.
Yang et al. [28]	N = 415 Elderly (age > 65), living in a single typical South Korean city	Standardized swallowing assessment	Diagnosed according to the DSM-IV criteria [54]	Population-based cross-sectional study (part of a longitudinal study)	Major depressive disorder was significantly associated with dysphagia. (OR 3.0; $p = 0.022$).
Verdonschot et al. [20]	N = 96 Patients with complaints of oropharyngeal dysphagia	1. MD Anderson Dysphagia Inventory [55] 2. Visual Analogue Scale (Dysphagia Severity Scale) [7]	Hospital Anxiety and Depression Scale [46]	Cross-sectional study	High prevalence of affective symptoms (43.7%). MD Anderson Dysphagia Inventory scores were significantly associated with symptoms of depression ($p = 0.05$).
Crossen et al. [37]	N = 67 Head and neck cancer patients	EORTC QLQ-H & N35 swallowing subscale [56]	Hospital Anxiety and Depression Scale [46]	Prospective cohort study	Swallowing problems were associated with anxiety and depression symptom scores at time of diagnosis ($r = 0.52$; $p = 0.00$) and at time of follow up ($r = 0.46$; $p = 0.00$). Regression analysis revealed that depression symptoms significantly affect dysphagia scores ($F = 9.5$; $p = 0.00$).
Holland et al. [27]	N = 634 Healthy elderly in residences in the North of England	Sydney Swallow Questionnaire [57]	Geriatric Depression Scale [52]	Population-based cross-sectional study	Depression symptom scores were significantly related to the total swallowing scores ($r = 0.133$; $p < 0.00$).
Mentz et al. [32]	N = 634 Healthy elderly	Sydney Swallow Questionnaire [57]	Geriatric Depression Scale [52]	Cross-sectional study	Depression symptom scores had significant effect on the Dysphagia Self-Test scores ($p = 0.05$).
Nogueira et al. [36]	N = 266 Nursing home residents	1. Dysphagia Self-Test [58] 2. 3 oz water swallowing test	Beck Depression Inventory [52]	Cross-sectional study	Odds Ratio's (95% CI) of dysphagia on different depression symptom levels were: 3.28 (0.93–11.55) for mild; 13.44 (3.10–58.16) for moderate; 30.35 (5.65–162.97) for severe, suggesting a strong relationship between depression symptoms and dysphagia.
Han et al. [23]	N = 127 Patients with Parkinson's disease	Swallowing Disturbances Questionnaire [43]	Beck Depression Inventory II [47–50]	Cross-sectional study	Logistic regression analysis revealed associations between symptoms of depression and MD Anderson Dysphagia Inventory (continued on next page)
Lin et al. [29]	N = 46 Post-treatment head and neck	1. MD Anderson Dysphagia Inventory [55] 2. 'Question 5' from the University of Washington	Beck Depression Inventory-Fast Screen [47–50]	Prospective cohort	

Table 3 (continued)

Author	N/pop/etiology	Measurement tool for dysphagia	Measurement tool for affective symptoms	Design	Results
Chan et al. [35]	cancer patients N = 77 Head and neck cancer patients	Quality of Life scale MD Anderson Dysphagia Inventory [55]	Beck Depression Inventory Fast Screen [47–50]	Case-control study	scores ($\beta = -21.8, p = 0.038$) and symptoms of depression and a swallowing related question ($\beta = -23.9, p = 0.035$). Depression symptom scores were significantly associated with the functional ($\beta = 17.31; p = 0.009$), physical ($\beta = 14.99; p = 0.032$) and emotional ($\beta = 11.60; p = 0.049$) domains of the MD Anderson Dysphagia Inventory.
MacLean et al. [9]	N = 110 Patients after total laryngectomy	Self-designed Demographic Questionnaire including items on swallowing: - Any difficulty in swallowing? (yes/no) - Changes to their diet texture? (yes/no) - Patients had to list any foods avoided and state why. Those respondents with reported dysphagia were then asked to provide further specific information about their swallowing difficulties	Depression Anxiety Stress Score [59]	Cross-sectional study	Patients with dysphagia had significantly higher levels of symptoms of depression ($z = -2.58; p = 0.010$) and anxiety ($z = -2.94; p = 0.003$).
Perez-Lloret et al. [24]	N = 419 Patients with Parkinson's disease	'Item 7' from the Unified Parkinson's Disease Rating Scale [60]	Hospital Anxiety and Depression Scale [46]	Cross-sectional study	Dysphagia was related to higher depression symptom scores ($p = 0.001$).
Walker et al. [26]	N = 75 Patients with Parkinson's disease	1. 'Item 7' from the Unified Parkinson's Disease Rating Scale [60] 2. Two questions: Do you have difficulty swallowing food or liquid or tablets? Do you cough after eating/drinking	Hospital Anxiety and Depression Scale [46]	Cross-sectional study	Swallowing problems were significantly correlated with anxiety ($r = 0.249; p = 0.033$) and depression symptom scores ($r = 0.281, p = 0.016$).
Althaus et al. [25]	N = 220 Patients with Parkinson's disease	'Item 7' from the Unified Parkinson's Disease Rating Scale [60]	Montgomery Asberg Depression Rating Scale [61]	Cross-sectional study	Dysphagia was a significant predictor for depression symptoms ($R^2 = 0.289$).
Kang et al. [22]	N = 72 Patients with degenerative disc disease of the cervical spine	Bazaz-Yoo dysphagia scale. Four grades (none, mild, moderate, severe) based on subjective symptoms	Zung Depression Scale [53] Zung Anxiety Scale [62]	Prospective cohort study	The presence of psychiatric symptoms ($p = 0.005$) was the only significant predictor of the presence of chronic dysphagia.
Airoldi et al. [33]	N = 36 Patients treated for carcinoma of the oral cavity	1. Dische morbidity recording scheme evaluation [63] 2. Visual Analogue Scale: from 0 (no impairment) to 10 (maximum impairment)	Hospital Anxiety and Depression Scale [46]	Cross-sectional study	Patients with severe dysphagia showed higher symptom levels of anxiety and depression ($p < 0.001$) compared with patients with no/slight dysphagia.

Table 4
Quality assessment.

	1. Was the spectrum of patients representative of the patients who will receive the test in practice?	2. Were selection criteria clearly described?	3. Was the diagnostic swallowing tool (e.g. questionnaire, FEES) likely to correctly classify the swallowing condition?	4. Was the psychiatric screening tool a validated screening tool?	5. Is the time period between the diagnostic swallowing test and the psychiatric screening test short enough to be reasonably sure that the target conditions did not change between the two tests?	6. Did all patients receive the same diagnostic tests?	7. Was the execution of the swallowing test described in sufficient detail to permit replication of the test?	8. Was the execution of the psychiatric test described in sufficient detail to permit replication of the test?	9. Were the psychiatric test results interpreted without knowledge of the results of the swallowing test?	10. Were the swallowing test results interpreted without knowledge of the results of the psychiatric test?	11. Were withdrawals from the study explained?	12. Method of data analyses. Were appropriate statistical methods applied?
Nguyen et al. [11]	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes
Nguyen et al. [38]	Yes	No	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	No	No	Unclear
Kang et al. [40]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	Yes
Manor et al. [10]	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	No	Yes
Verdonschot et al. [41]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	No	Yes
Lin et al. [30]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Miller et al. [31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Thomas et al. [34]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	No	Yes
Zhang et al. [39]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	No	No
Yang et al. [28]	Yes	No	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Verdonschot et al. [20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	Yes
Cnossen et al. [37]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	No	Yes
Holland et al. [27]	Yes	No	Yes	Yes	Unclear	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Mentz et al. [32]	No	No	Yes	Yes	Unclear	Yes	Yes	Unclear	Unclear	No	No	Yes
Nogueira et al. [36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Han et al. [23]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Lin et al. [29]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	No	No	Yes
Chan et al. [35]	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
MacLean et al. [9]	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Perez-Lloret et al. [24]	Yes	Yes	No	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Walker et al. [26]	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Althaus et al. [25]	Yes	No	No	Yes	Unclear	Yes	Yes	Unclear	Unclear	No	No	Yes
Kang et al.	Yes	Yes	No	Yes	Yes	Yes	Yes	Unclear	Unclear	No	No	Yes

(continued on next page)

Table 4 (continued)

1. Was the spectrum of patients representative of the patients who will receive the test in practice?	2. Were selection criteria clearly described?	3. Was the diagnostic swallowing tool (e.g. questionnaire, FEES) likely to correctly classify the swallowing condition?	4. Was the psychiatric screening tool a validated screening tool?	5. Is the time period between the diagnostic swallowing test and the psychiatric screening test short enough to be reasonably sure that the target conditions did not change between the two tests?	6. Did all patients receive the same diagnostic tests?	7. Was the execution of the swallowing test described in sufficient detail to permit replication of the test?	8. Was the execution of the psychiatric test described in sufficient detail to permit replication of the test?	9. Were the psychiatric test results interpreted without knowledge of the results of the swallowing test?	10. Were the swallowing test results interpreted without knowledge of the results of the psychiatric test?	11. Were withdrawals from the study explained?	12. Method of data analyses. Were appropriate statistical methods applied?
Airoldi et al. [22]	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes
Airoldi et al. [33]	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes

observation of swallowing by a speech and language pathologist who reported how the patient manipulated food in the mouth, the oral transit time, the presence of a swallowing reflex, and signs of aspiration (e.g., coughing, choking, change in vocal quality). If there were signs of reduced swallowing function, patients were referred for a FEES examination. Patients with swallowing disturbances showed significantly higher scores of anxiety and depressive symptoms than patients without swallowing disturbances. Verdonschot et al. [41] performed a study in 107 patients with OD of various etiologies. Patients' performances on four FEES-variables were assessed by two independent observers and then compared with the results of the HADS questionnaire. Although clinically relevant symptoms of anxiety and depression were present in 46 (43%) patients, the data revealed only few significant associations between anxiety symptoms and the FEES-variables. The more severe the dysphagia, the less important the affective complaints were.

3.4. Clinical evaluation of swallowing

Several studies used a water-swallowing test as a measurement tool for OD. Lin et al. [30] investigated swallowing function in institutionalized elderly. Elderly with symptoms of depression showed a higher frequency of impaired swallowing compared to elderly without symptoms of depression. Miller et al. [31] found an increased frequency of depressive symptoms related to a poorer outcome of the swallowing tests in Parkinson's patients. Thomas et al. [34] and Zhang et al. [39] found a significant positive association between impaired swallowing and depressive symptoms in patients with multiple sclerosis and tongue cancer, respectively. Yang et al. [28] performed a population-based study among 415 elderly. A clinical observation of swallowing was performed using water-swallowing tests and, if no dysfunction was noted, a meal observation was subsequently performed. Patients diagnosed with a major depressive disorder had dysphagia more often and major depression was an independent risk factor for dysphagia.

3.5. Swallowing-related questionnaires

Various questionnaires were used to assess swallowing and to record affective symptoms. Verdonschot et al. [20] performed swallowing assessment in 96 patients with OD of various etiologies. A high prevalence of symptoms of anxiety and depression in the total population was found. Cnossen et al. [37] found that OD was significantly and positively associated with symptoms of anxiety and depression in head and neck cancer patients. Holland et al. [27] and Mentz et al. [32] studied dysphagia in otherwise healthy elderly. Both study populations consisted of individuals who represented the surviving members of the University of Manchester Longitudinal Study of Cognition in Normal Healthy Old Age [42]. They found significant associations between impaired swallowing scores and symptoms of depression. Han et al. [23] used the Swallowing Disturbances Questionnaire [43] and found a positive association between lower swallowing scores and symptoms of depression in Parkinson patients. For a complete overview of all included articles, see Table 3.

3.6. Single swallowing questions

The following studies used a single item or question to determine swallowing function. Perez-Lloret et al. [24], Walker et al. [26], and Althaus et al. [25] studied Parkinson and showed a significant positive association between OD and depressive symptoms. The study of Walker et al. [26] also showed an association of OD with symptoms of anxiety. Kang et al. [22] concluded that the presence of symptoms of anxiety and/or depression was a predictor for the presence of chronic dysphagia in patients who underwent surgery for degenerative disc disease of the cervical spine. Airoldi et al. [33] described a high prevalence of symptoms of anxiety and depression in oral cancer patients with severe OD after surgical flap reconstruction and postoperative radiotherapy.

4. Discussion

This systematic review is the first to summarize and evaluate the evidence of an association between affective symptoms and oropharyngeal dysphagia. It consists of 24 articles that reported on swallowing function and affective complaints in different populations. Data pooling was prevented by heterogeneity of assessment tools, diversity of study populations, and poor methodological quality. Although no meta-analytic conclusions can be drawn from the included articles, symptoms of anxiety and depression appear to be common in dysphagic patients. All studies concluded that symptoms of depression were significantly and positively associated with impaired swallowing function. Twelve studies investigated symptoms of anxiety as well, and 9 studies found a significant association with dysphagia too. Quality of the included studies varied. Thirteen of the included studies met all criteria for external validity [20,22,24,29–31,33,34,36,37,39–41], whereas none met all criteria for internal validity. Little is known about the relationship between the severity of OD and affective symptoms. Nguyen et al. [11] concluded that anxiety and depressive symptoms scored higher in patients with moderate and severe OD compared to patients with mild OD, while the study of Verdonschot et al. [41] concluded that affective symptoms were common in OD patients, but patients with severe OD did not have a higher probability of affective complaints. Moreover, having affective symptoms might be a predictor of subjectively experienced dysphagia severity [41]. It remains unclear what the exact mechanism behind the association of OD with affective states is. However, in patients with medically unexplained otorhinolaryngological symptoms (MUORLS), including dysphagia, affective conditions are common [12]. This could be a reflection of a state of dysphagia amplification [41] which is comparable to the sensitization and alarm falsification process known from other functional somatic conditions [44]. Anxiety and depressive disorders might influence the perception of swallowing by influencing an ‘alarm’ set point to a dysfunctional state experienced as OD. From a neurobiological perspective, cerebral motor cortex areas may be related to the neural stress connectome in anxiety and depression [45]. Further research on this topic is needed.

The results of the current review should be seen in the light of several limitations. The search strategy used MeSH terms and a limited number of free-text terms. Nonetheless, all of the included studies investigated symptoms of anxiety and/or depression. A broader search strategy could have generated different search results. Due to an assessable stratum, we decided to focus on specific symptomatology rather than on a wide range of sub-threshold psychological complaints. The search was conducted with an experienced university library information specialist, and together it was decided to not include “gray literature” in the search strategy. Moreover, a 12-item critical appraisal tool, as derived from the QUADAS, was used for quality assessment. It is possible that a different tool would have led to a different assessment of the included studies. Overall, it was difficult to compare the results of the 24 studies for several reasons. First of all, despite the focus on affective complaints, the studies were considerably heterogeneous regarding patient populations and outcome parameters. The study populations consisted of stroke patients, head and neck oncology patients, the elderly, and others. Furthermore, the studies applied a wide range of assessment tools for affective symptoms or conditions and swallowing function. Second, most articles had methodological limitations (e.g., no clear description of the selection criteria; little or incomplete information about diagnostic tools and procedures; no information about test result interpretation; and no explanation of withdrawals) (Table 4), which made it impossible to carry out data pooling and meta-analysis. Moreover, most studies used only 1 tool to assess swallowing, while a multidimensional approach is recommended for the diagnosis of OD and assessment of OD severity. A broader protocol should include a structured interview, a clinical observation of oral intake by a speech and language pathologist, and a FEES and/or VFSS [13]. In addition, almost all studies used questionnaires that can only be applied as screening tools for symptoms of anxiety and depression. These tests are not suitable to come

to a diagnosis of affective disorders. Although self-assessment questionnaires give an indication of patients' depressive or anxiety state, a consultation by an experienced psychiatrist or psychologist should be included in order to get a valid diagnosis [12]. Given that the use of psychotropic drugs may have led to an underestimation of affective states, reporting about psycho-pharmacy is essential in cohort studies as well. However, several articles did not mention the use of any psychotropic medication. In 19 articles it remained unclear whether drugs were used or not [9–11,22,26–29,31–40]. Further, affective symptoms could be related to the underlying disease state instead of OD. It is unclear how well the studies controlled or adjusted for the underlying diseases.

Overall, the question remains unsolved whether there is a causal relationship between affective symptoms and swallowing problems in OD patients. Therefore, future studies investigating this topic should use instrumental measurement tools for OD (e.g. FEES, VFSS) and psychiatric assessment should be done by a psychiatrist as a gold standard instead of self-reporting questionnaires. It is important that the execution of the swallowing test is standardized in every included patient. Moreover, the time period between swallowing assessment and psychiatric assessment should be short in order to assure that the conditions of OD and the affective state do not change between the two tests. Nevertheless, it is clear that affective symptoms are common in patients with OD. Screening for affective symptoms could be helpful for caregivers who are not familiar with psychiatric symptomatology in order to estimate influences on possible treatment refractoriness. To date, few treatment-effect studies have been conducted in OD patients with psychiatric comorbidity. Moreover, psychiatric symptoms or diagnoses other than anxiety disorders and depression might be prevalent in OD patients too. However, very few studies have been published on this topic. At least in complex patients with affective comorbidity, the management of OD requires a multidimensional approach to enable patients to adhere to swallowing rehabilitation. For that reason, psychological or psychiatric expertise should be integrated in future multidimensional OD approaches, which might contribute to the treatment satisfaction in OD.

5. Conclusion

The current literature revealed that affective symptoms in patients with OD are common. Screening for affective symptoms in patients with OD is clinically relevant and may help caregivers who are not aware of psychiatric comorbidity to detect cases. Although the likelihood of psychiatric comorbidity in OD patients seems obvious, therapy-effect studies to document effect of integrated care are scarce. As the present review of the literature demonstrates, there is a need for well-designed prospective research to investigate the possible benefit of integrated medical psychiatric care in patients with OD and affective comorbidity.

Conflicts of interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no conflicts of interest to disclose.

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