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REVIEW ARTICLE

Deglutition disorders as a consequence of head and neck cancer therapies: a systematic review and meta-analysis

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Abstract

Purpose In this study, we aimed to estimate the frequency of deglutition disorders in patients pre- and post-treatment for head and neck cancer (HNC).

Methods Search strategies were developed for the following databases: LILACS, PubMed, SpeechBITE, LIVIVO, Web of Science, and Scopus. Additionally, the gray literature was searched using Google Scholar, OpenGrey, and ProQuest. Only studies that conducted an evaluation of deglutition before and after cancer treatment and had sufficient quantitative data were included. We conducted a proportion of random effects meta-analysis using R statistical software.

Results Seventeen studies were included. Aspiration showed a high frequency in the period less than 3 months post-treatment, with 28.6% (total sample = 229). Penetration of fluids above the vocal folds and reduced laryngeal elevation were more frequent in the period less than 6 months post-treatment.

Conclusion The frequency of deglutition disorders and its complications, such as aspiration, appears to be higher in the immediate to 6-month post-treatment period in patients with HNC. The parameter pharyngeal residue continued to increase through the period analyzed.

Keywords Deglutition disorders · Head and neck cancer · Chemotherapy · Radiation therapy

Introduction

Swallowing assessment and treatment have become common practice in patients with head and neck cancer (HNC). However, there is no consensus as to when assessment of deglutition disorders should begin, which methods to use in the evaluation, when and how to start treatment options, and for how long patients should be followed up [1].

The frequency of deglutition disorders varies with the cancer etiology and/or type of cancer treatment. HNC is the sixth most common cancer worldwide, accounting for 2.8% of all malignancies. Treatments available for HNC can include surgery, radiotherapy, chemotherapy, or a combination of treatments [2]. The choice of treatment modality is dependent of patient variables, primary site, clinical stage, and resectability of the tumor. The adverse effects or toxicities of these treatments may include dysphagia and many other disorders that can have an impact on the swallowing function, such as pain, dry mouth, mucositis, dysgeusia, nausea, and loss of appetite [3–7]. Dysphagia and aspiration are recognized as potentially devastating complications of treatment of HNC.

The frequency of dysphagia in HNC differs when considering different variables such as radiotherapy field size and radicality of surgery. Dysphagia has a higher prevalence (63.6%) early following surgery (< 1 year) than delayed (> 5 years) [8]. Similarly, dysphagia has a prevalence of 45.9% after cancer treatment (surgery and/or radiotherapy) [9].

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Two previous systematic reviews [10, 11] investigated the changes in swallowing mechanisms after radiation or drug therapy in HNC. Quantitative analysis was not performed in either review. Further research on this topic is needed, as new and more detailed studies have surfaced over the last 5 years [12–17]. There is also a need for quantitative analysis of the results found in the literature. The aim of this systematic review was therefore to answer the research question: What is the frequency of deglutition disorders pre- and post-treatment among patients who undergo therapy for HNC?

Methods

This systematic review (SR) was reported following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [18].

Protocol and registration

The SR protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) under the number CRD42017067837 [19].

Eligibility criteria

Inclusion criteria

We included studies that measured the frequency of deglutition disorders pre- and post-treatment in patients with head and neck neoplasms that received any type of therapy for cancer (surgery, chemotherapy, radiotherapy, or a combination of therapies). We included only those studies with participants over 18 years old and those who had undergone imaging exams (i.e., videofluoroscopic swallowing study (VFSS)) as diagnostic criteria for the assessment of deglutition disorders and complications. No language or period restriction was applied.

Exclusion criteria

Studies were excluded for the following reasons: (1) patients without cancer or non-malignant tumors; (2) studies that did not use imaging exams such as VFSS or fiber-optic endoscopic evaluation of swallowing (FEES) as diagnostic criteria for deglutition disorders before and after cancer treatment; (3) patients who did not undergo any type of cancer treatment or therapy; (4) patients already receiving treatment for deglutition disorders; (5) studies reporting insufficient quantitative data to perform analysis of deglutition disorders; (6) reviews, letters, conference abstracts, opinions, case reports, and cross-sectional studies; (7) full text unavailable; and (8) duplicate data from another study.

Information sources

For the literature search, an individual strategy was developed for each of the following databases: LILACS, PubMed, SpeechBITE, LIVIVO, Web of Science, and Scopus. An additional search of the gray literature was performed using Google Scholar, OpenGrey, and ProQuest. The search date was 23 March 2017 for all databases and gray literature. An updated search was performed on 19 June 2018. The search strategies used are described in Appendix 1. The references cited in the included articles were checked for any additional studies that could be included in the analysis, as recommended by Greenhalgh and Peacock [20]. Studies were collected using reference manager software (EndNote™ Online, Thomson Reuters, Philadelphia, PA, USA). Duplicate studies were identified with the software and posteriorly, any additional duplicates not identified by EndNote were found with the help of Rayyan QCRI, a free web, and mobile app for systematic reviews (Qatar Computing Research Institute, Doha, Qatar) [21].

Study selection

The process of reference selection was divided into two phases. Phase 1 was performed by two reviewers (I.P.T. and L.Q.P.), who independently screened the title and abstract of the collected studies. This blind process was ensured and registered as it was carried out using the Rayyan QCRI platform. Studies that did not fit the inclusion criteria were excluded. In phase 2, the same reviewers (I.P.T. and L.Q.P.) applied the eligibility criteria to the full text of the studies selected in phase 1. When necessary, a third reviewer (K.F.L.) was consulted to reach a consensus in cases of disagreement between the first two reviewers.

Data collection process

The first reviewer (I.P.T.) collected the required information from the selected studies. The second reviewer (L.Q.P.) cross-checked all the collected information for accuracy. The data collected consisted of: study characteristics (authors, year of publication, country, journal of publication, type of study); population characteristics (sample size, age, type of cancer, cancer stage); exposure characteristics (type of cancer treatment, deglutition assessment); and outcome characteristics (occurrence of deglutition disorders pre-treatment and post-treatment).

Risk of bias in individual studies

The risk of bias in individual studies was assessed using the JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data [22]. The first and second reviewers (I.P.T.

and L.Q.P.) performed this assessment independently. Any disagreements were resolved in discussions among the three first reviewers (I.P.T., L.Q.P., and K.F.L.).

Subgroup analysis

The analysis was planned in subgroups, dividing the deglutition parameters according to the period of assessment with imaging exams (VFSS or FEES) as follows: pre-treatment, less than 6 months post-treatment (from less than 3, 4, and 6 months), at 6 months post-treatment, and post-treatment more than 6 months (from 6 to 12 months).

Summary measures

The data collected for deglutition disorders or complications (aspiration and liquid penetration, among others) in adult patients with HNC who underwent cancer treatment were expressed using mean percentage and 95% confidence interval (CI).

Synthesis of results

A meta-analysis was planned, including those studies that presented sufficient data to determine the frequency of deglutition disorders or complications pre- and post-treatment. These data were analyzed using random effects meta-analysis [23]. Calculations were performed using R Statistical Software version 3.4.2 (The R Foundation, Vienne, Austria). The packages utilized were "metaphor" and "meta," including arcsine transformation to calculate the overall proportion; in addition, the Clopper–Pearson interval was used to calculate 95% CIs. Heterogeneity was calculated using an inconsistency index (I^2), and a value greater than 50% was considered an indicator of substantial heterogeneity within studies [24]. The significance level was set at 5%.

Results

Study selection

In phase 1 of this systematic review, 1368 records were screened from the six main databases, after removing duplicates. An additional 302 records from the gray literature were included. After screening all titles and abstracts, 171 studies were selected for phase 2, which consisted of full-text screening. In this phase, a total of 155 studies were excluded (Appendix 2). No additional articles were selected from the reference list review. In the updated search, 99 studies were screened but only 1 met the inclusion criteria. Finally, 17 studies were included in the qualitative and quantitative analysis. The study selection process is depicted in Fig. 1.

Study characteristics

The 17 included articles [12–17, 25–35] were published in 10 journals, with a quarter of these [13, 29, 32, 33] published in the journal *Head & Neck*, four [14, 25, 26, 35] published in *Dysphagia*, and two [28, 30] studies published in *The Laryngoscope*. The remaining seven studies were published in different oncology, medical, or speech-language pathology journals. The total sample varied from 11 [28] to 133 [16] patients. Sixteen [12, 14–17, 25–35] of the included studies used a VFSS as a diagnostic tool for deglutition disorders, and one [13] study used a FEES. Nearly half [14, 27–29, 31–33] of the studies were from the USA, two [12, 15] were from Turkey, and there was one each from Australia [26], Canada [34], China [30], India [25], Korea [16], The Netherlands [17], the UK [13], and Greece [35]. Because of the nature of the research question of this systematic review, all of the included studies used a convenience sample. A summary of the characteristics of the 17 included studies can be found in Table 1, and a summary of the quantitative data is given in Table 2.

Risk of bias within studies

Ten [13, 15–17, 25, 29, 32–35] of the included studies were classified as having a low risk of bias. Six [14, 26–28, 30, 31] other studies were considered to have a moderate risk of bias, with answers of "yes" to five or six of the ten questions in the assessment tool. Only one [12] study was assessed as having a high risk of bias. All studies produced negative responses to the question "Were study participants recruited in an appropriate way?" because all samples were convenience samples. Nearly half [12, 25–27, 30, 32] of the assessed studies yielded "no" responses to the question "Are all important confounding factors/subgroups/differences identified and accounted for?," which points out a lack of information in the description of the sample and/or selection criteria. Details of study classification can be found in Appendix 3.

Results of included studies

Overall data distribution

All samples in the included studies had a higher proportion (at least two thirds) of male participants than female ones. The most frequent types of cancer reported in the included studies were cancer of the oropharynx, tongue, larynx, hypopharynx, nasopharynx, tonsil, unknown sites, and others. Most studies that presented data concerning cancer stages grouped participants according to stages III–IV. Eleven [12, 13, 25–27, 29–33, 35] of the included studies reported concurrent chemoradiotherapy as the main treatment modality for cancer; the remaining five [14–16, 28, 34] studies reported the modalities surgery and conventional radiotherapy and/or chemotherapy.

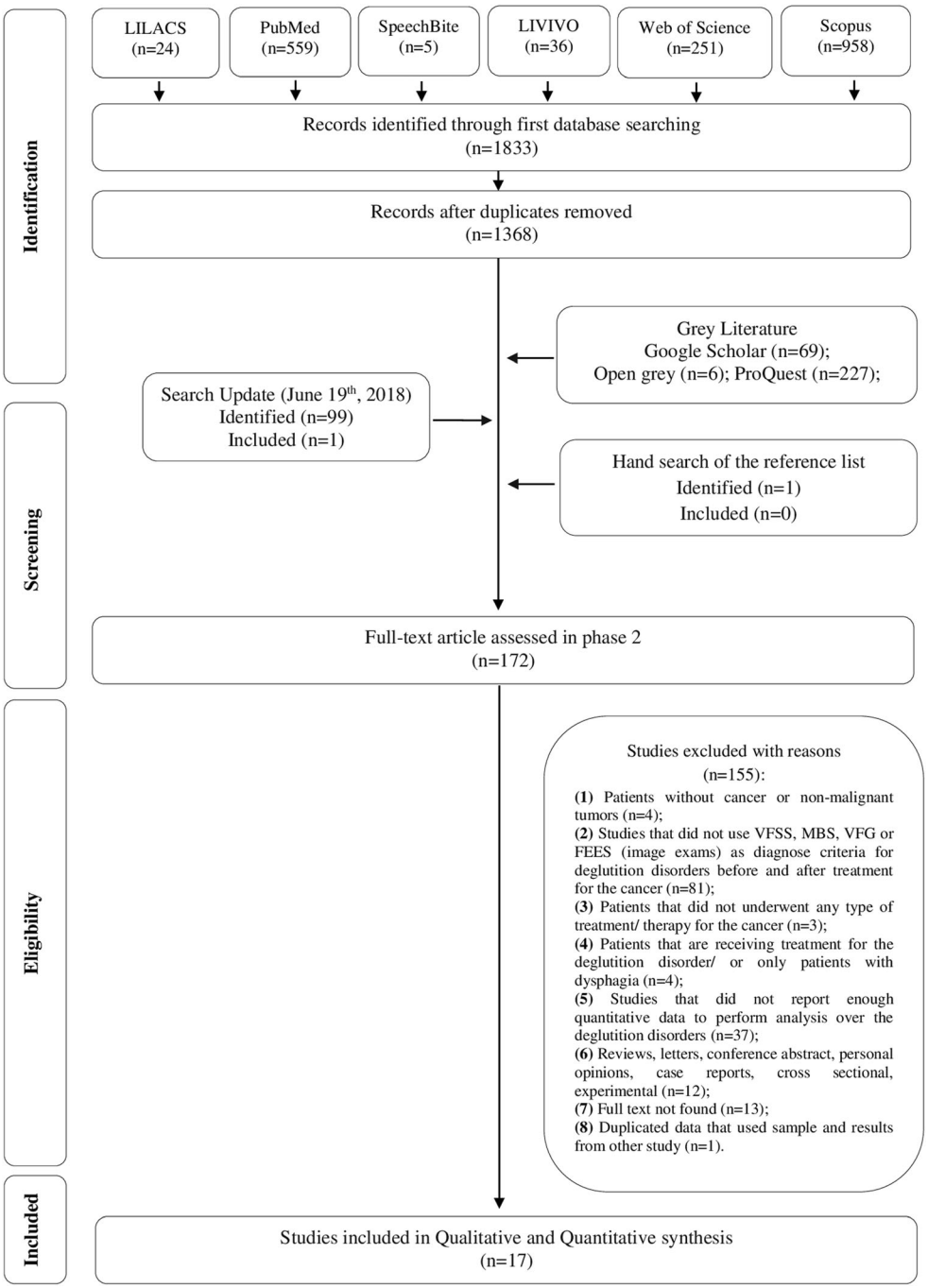

Fig. 1 Flow diagram of literature search and selection criteria adapted from PRISMA

Only one [17] of the included studies presented data for intensity-modulated radiation therapy (IMRT) combined with chemotherapy.

Subgroup analysis

The analysis of deglutition parameters was divided into subgroups. These main groups were selected according to the period in which swallowing assessment with imaging exams (VFSS or FEES) was performed. In all the included studies, one of these exams was performed at baseline and at least once after treatment for HNC. The meta-analysis was then classified according to swallowing parameters, as assessed in imaging exams during the different time periods: pre-treatment, less than 6 months post-treatment (from less than 3, 4, and 6 months), at 6 months post-treatment, and more than 6 months post-treatment (from 6 to 12 months).

Table 1 Summary of study descriptive characteristics of included studies ($n = 17$ cohorts)

Author, year, country	Sample size (M/F)	Mean age or age range (years)	Type of cancer (*n*)	Tumor stages (*n*)	Type of cancer treatment (*n*)	Deglutition assessment (period)	Main conclusions
Agarwal et al., 2011, India	47 (40:7)	40–65	Oropharynx (25[a]) Hypopharynx (16[a])	I/II (11) III/IV (36)	Conventional RT 66–70 Gy/33–35 fractions (40) Conformal RT (7) Concurrent CT cisplatin (40)	MBS (before and up to 12 months post-treatment)	Pre-treatment, swallow function was mainly preserved in the sample. Post-treatment there was a significant impairment in swallowing, with pharyngeal residue and aspiration being the most affected.
Cartmill et al., 2012, Australia	14 (12:2)	53–82	Tonsil (9) Supraglottis (3)	I (2[a]) II (4[a]) III (5[a]) IV (3[a])	AFRT-CB 66 Gy/35 fractions (14)	VFSS (before and up to 6 months post-treatment)	The majority of the pre-treatment sample presented functional swallowing. At 4 to 6 weeks post-treatment, deterioration across all swallowing parameters. At 6 months post-treatment it was observed persistent deterioration of swallowing, nutrition and patient-related functional impact.
Eisbruch et al., 2002, USA	26 (NA)	NA	Oropharynx (14) Nasopharynx (4) Oral cavity (2) Larynx (2) Hypopharyngeal (1) Thyroid (1) Paranasal sinus (1) External ear (1)	III/IV (26)	Conventional RT 70 Gy/35 fractions for primary tumor; 50–54 Gy or 58–64 Gy for metastasis or previous to surgery (26) Concurrent CT gemcitabine (26)	VFSS (before and up to 12 months post-treatment)	Aspiration rates were higher in the post-treatment group, reaching 68% of the sample, with five of these patients developing pneumonia.
Erkal et al., 2014, Turkey	20 (17:3)	30–76	Nasopharynx (10) Supraglottic larynx (10)	NA	3 DCRT 70 Gy for the primary tumor; 66–70 Gy involved cervical lymph nodes; 50–60 Gy uninvolved cervical lymph nodes; 46-50Gy supraclavicular lymph nodes/daily fractions 2 Gy (8) 3DCRT with Concomitant CT (12)	VFSS (before and up to 6 months post-treatment)	Aspiration and penetration above the vocal cords had a higher frequency at 6 months post-treatment, when compared to 3 months post-treatment and the baseline.
Graner et al., 2003, USA	11 (7:4)	37–78	Oropharynx (5)Larynx (3) Hypopharynx (3)	III–IV (11)	CT 150 mg/m^2 of cisplatin for 4 weeks (11) Concomitant RT 72 Gy, 6 weeks for primary tumor (11) Surgery (select, modified or radical neck dissection = 7)	VFSS (before and up to 5 months post-treatment)	All the swallowing parameters analyzed increased from the baseline to the 5 months post-treatment, with aspiration in over half of the sample.
Kotz et al., 2004, USA	12 (9:3)	31–72	Oropharynx (7) Larynx (3) Oral cavity (1) Unknown primary (1)	III–IV (12)	Induction CT 2–3 cycles CT docetaxel during 4 weeks of RT and 3 weeks of hyperfractionated RT (5) CT carboplatin 6–7 weeks and once-a-day RT (7)	VFSS (before and 1–4 weeks post-treatment)	Aspiration and pharyngeal residue were present in a third of the sample at 1 to 14 weeks post-treatment. These parameters were not present at baseline.
Ku et al., 2007, China	20 (14:6)	33–62	Nasopharyngeal carcinoma (20)	I–II (9) III–IV (11)	RT 66 Gy (20) RT boost of 20 Gy for pharyngeal extension (17) Concurrent CT cisplatin (11)	VFSS (before and up to 12 months post-treatment)	Penetration of fluids above the vocal cords increased from the baseline in the period 6 to 12 months post-treatment. Aspiration reduced to half when compared to pre-treatment.

Table 1 (continued)

Author, year, country	Sample size (M/F)	Mean age or age range (years)	Type of cancer (*n*)	Tumor stages (*n*)	Type of cancer treatment (*n*)	Deglutition assessment (period)	Main conclusions
Lazarus et al., 2000, USA	13 (10:3)	38–72	Tongue base (6) Floor of the mouth (3) Tonsil(4)	I (1) IV (12)	RT high dose ≥ 7000 cGy (13) Concomitant CT cisplatin (12)	VFG (before and up to 2 months post-treatment)	The parameter aspiration increased in over half of the sample at the assessment at 2 months post-treatment when compared to the baseline.
Logemann et al., 2006, USA	53 (41:12)	NA	Oropharynx (22) Larynx (14) Hypopharynx (4) Nasopharynx (3) Unknown primary (10)	T1 (2) T2 (11) T3 (16) T4 (19) IV (42–53[a])	TFHX, Taxol infusion (13) TFHX, Taxol bolus (16) TFHX, bolus, induction (15) RADPLAT (9) RT dose range 6700–7275 cGy (53)	VFSS (before and up to 3 months post-treatment)	The presence of gastrostomy and jejunostomy more than double in the sample at 3 months post-treatment, when compared to the baseline. Aspiration was also 3 times the amount of the pre-treatment.
Logemann et al., 2008, USA	48 (38:10)	38–76	Oropharynx (21) Laryngeal (21) Nasopharynx (3) Hypopharynx (3)	I (1) II (7) III–IV (40)	CT (36) Concurrent RT dose range from 6500 to 7920 cGy (36) Induction CT (6) RT dose range from 6500 to 7920 cGy (12)	VFSS (before and up to 12 months post-treatment)	The 38 patients of the total sample were considered as having a normal diet at baseline. This decreased to 22 patients at 3 months, with a slight increase to 29 at 12 months post-treatment. Functional swallowing was attributed to 40 patients at the 12 months mark.
O'Connell et al., 2008, Canada	20 (14:6)	44–70	Base of tongue (20)	II (2) III (8) IV (10)	Primary Surgery and reconstruction with beavertail modification of the radial forearm free flap (20) Postoperative RT (20) Primary CT and RT (5)	VFSS (before and at 12 months post-treatment)	Severe pharyngeal residue was found in eight patients of the total sample at 12 months post-treatment. Aspiration was present in only one patient at the 12 months mark.
Patterson et al., 2014, UK	112 (90:22)	42–77	Oropharynx (59) Hypopharynx (22) Larynx (16) Nasopharynx (5) Unknown primary (10)	NA	RT 3D conformal, dose 63Gy in 30 fractions over 6 weeks (112) Combined CT cisplatin 40 mg/m^2 in 6 cycles or mitomycin C 15 mg/m^2 in 2 cycles (112)	FEES (before and at 3 months post-treatment)	Silent aspiration was observed in 8 of 97 analyzed patients at 3 months post-treatment. This parameter was not observed at baseline. Aspiration was more than double at the 3 months mark when compared to pre-treatment.
Rogus-Pulia et al., 2014, USA	21 (17:4)	36–80	Base of tongue (8) Tonsil (6) Nasopharynx (3) Hypopharynx (1) Tongue (1) Vocal Fold (1) Unknown primary (1)	T0 (2) T1 (6) T2 (9) T4 (4) I–IV (21)	RT dose of 66 to 70 Gy over a mean of 7 weeks (21) Concurrent CT (21) Induction CT (6) Tonsillectomy (4) Neck dissection (3) Partial Glossectomy (1) Tumor debulking (1)	MBS (before and mean of 5 months post-treatment)	Penetration during swallowing was 3 times the amount at 5 months post-treatment, when compared to the baseline.
Serel et al., 2013, Turkey	40 (33:7)	20–65	Larynx (20) Nasopharynx (5) Tongue (5) Tonsil (3) Retromolar trigone (2)	I (5) II (1) IIA (2) IIB (1) III (20)	RT dose from 5400 to 7000 cGy (40) Concomitant CT (33) Surgery for the primary tumor (2) Surgery for the primary tumor and neck dissection (24)	VFSS (before and up to 3 months post-treatment)	Aspiration with liquids were higher than with pudding or biscuit in all the periods assessed. And aspiration with all three consistencies was higher at 1 month and

Table 1 (continued)

Author, year, country	Sample size (M/F)	Mean age or age range (years)	Type of cancer (*n*)	Tumor stages (*n*)	Type of cancer treatment (*n*)	Deglutition assessment (period)	Main conclusions
			Parotid (2) Lips (1) Tongue base (1) Hypopharynx (1)	IVA (11)			3 months post-treatment when compared to the baseline.
Son et al., 2015, Korea	133 (85:48)	53.5 ± 15	Tongue (133)	T1 (38) T2 (40) T3 (3) T4 (52)	Hemiglossectomy (16) Wide resection (82) Partial glossectomy (23) Total glossectomy (5) Supraomohyoid neck dissection (61) Modified radical neck dissection (59) Reconstruction surgery (81) RT (70) CT (57)	VFSS (was administered to 87 patients after surgery and to 74 patients prior to surgery before and mean of 4 months post-treatment)	The ASHA-NOMS mean score was lower in the sample analyzed at a mean of 4 months post-treatment, when compared to the baseline. Aspiration or penetration were over 3 times the amount at the 4 months mark.
Van der Molen et al., 2013, The Netherlands	55 (44:11)	32–79	Oral cavity/oropharynx (29) Laryngo/hypopharynx (19) Nasopharynx (7)	III (17) IV (38)	CT-IMRT Cisplatin 100 mg/m^2 (40 min for 3 non-consecutive days); 70 Gy in 35 daily fractions of 2 Gy—total of 7000 cGy over 7 weeks plus sequential boost of IMRT (55)	VFSS (before—55 patients/at 10 weeks-48 patients/at 12 months-36 patients)	Aspiration/penetration at baseline was observed in 9 out of 55 patients. At 10 weeks post-treatment, 8 patients aspirated/penetration.
Xinou et al., 2018, Greece	69 (56:13)	37–75	Larynx (29) Nasopharynx (9) Oropharynx (13) Hypopharynx (8) Oral cavity (4) Maxillary sinus (1) Parotid (3) Unknown (2)	II (2) III (31) IVa (31) IVb (5)	Concurrent CRT once daily radiation therapy and weekly carboplatin or cisplatin 40–50 mg/m^2. RT total dose of 65 Gy in 35 fractions over 5 weeks	VFSS (before and up to 12 months post-treatment)	It was observed severe swallowing deficits and aspiration rates pre-CRT in the sample. Worsening of swallowing and aspiration in the post-CRT, which peaked at 3 months.

M male; *F* female; *RT* radiotherapy; *CT* chemotherapy; *CRT* chemoradiation; *AFRT-CB* altered fractionation radiotherapy with concomitant boost; *Gy* Gray (absorbed dose); *cGy* centigray; *IMRT* intensity-modulated radiotherapy; *DCRT* three-dimensional conformal radiotherapy; *MBS* modified barium swallow; *VFSS* videofluroscopy; *VFG* videofluorographic; *FEES* fiber-optic endoscopic evaluation of swallowing; *RADPLAT* intraarterial cisplatin radiation; *TFHX*, Taxol infusion hydroxyurea, 5-fluorouracil, and paclitaxel infusion for 1 week; *TFHX*, Taxol bolus hydroxyurea, 5-fluorouracil, and paclitaxel 1-h bolus; *TFHX, bolus, induction* induction chemotherapy with carboplatin and paclitaxel followed by concurrent chemoradiation with hydroxyurea, 5-fluorouracil, and paclitaxel 1-h bolus; *ASHA-NOMS scale* American Association of Speech-Language Pathology-National System of Measurement Results, scores from 1 (not able to swallow) up to 7 (Safe swallow); *NA* not available

[a] Values calculated by the authors

Table 2 Quantitative summary of the included studies ($n = 17$)

Author, year, country	Total sample (n)	Deglutition disorder Pre-treatment	Deglutition disorder < 6 months of treatment	Deglutition disorder > 6 months of treatment
Agarwal et al., 2011, India	47	Total of 47: Aspiration = 9 Residual barium = 11 Posture change = 10 Regurgitation = 5 PAS score, total of 47: Grade 1–2 = 34 Grade 3–6 = 10 Grade 7–8 = 3	Total of 46, 2 months post: Aspiration = 11 Residual barium = 16 Posture change = 6 Regurgitation = 3 PAS score, total of 46, 2 months post: Grade 1–2 = 24 Grade 3–6 = 19 Grade 7–8 = 3	Total of 38, 6 months post: Aspiration = 11 Residual barium = 7 Posture change = 6 Regurgitation = 8 PAS score, total of 38, 6 months post: Grade 1–2 = 24 Grade 3–6 = 11 Grade 7–8 = 3 PAS score, total of 17, 12 months post: Grade 1–2 = 5 Grade 3–6 = 10 Grade 7–8 = 2 Total of 17, 12 months post: Aspiration = 5 Residual barium = 10 Posture change = 4 Regurgitation = 1
Cartmill et al., 2012, Australia	14	Total of 14: Aspiration events on fluids/solids = 0/1 Penetration events on fluids/solids = 1/3 Labial closure = 0 Lingual control = 2[a] Palatal closure = 4[a] Mastication = 10[a] Position of bolus = 10[a] Swallow timing = 6[a] Velopharyngeal closure = 0 Pharyngeal contraction = 8[a] Laryngeal excursion = 6[a] Bolus propulsion UES = 3[a] Clearance of pyriform sinus residual = 4[a] Upper esophageal parameters = 0 PAS score, total of 14 for fluids: Grade 1–2 = 12 Grade 3–6 = 1 Grade 7–8 = 0 Total of 14 for solids: Grade 1–2 = 9 Grade 3–6 = 3 Grade 7–8 = 1	Total of 14, 4–6 weeks post: Aspiration events on fluids/solids = 1/1 Penetration events on fluids/solids = 3/3 Labial closure = 0 Lingual control = 2[a] Palatal closure = 7[a] Mastication = 10[a] Position of bolus = 6[a] Swallow timing = 5[a] Velopharyngeal closure = 3[a] Pharyngeal contraction = 10[a] Laryngeal excursion = 7[a] Bolus propulsion UES = 5[a] Clearance of pyriform sinus residual = 4[a] Upper esophageal parameters = 0 PAS score, total of 14, 4–6 weeks post for fluids: Grade 1–2 = 10 Grade 3–6 = 3 Grade 7–8 = 1 Total of 14, 4–6 weeks post for solids: Grade 1–2 = 9 Grade 3–6 = 3 Grade 7–8 = 1	Total of 14, 6 months post: Aspiration events on fluids/solids = 1/2 Penetration events on fluids/solids = 1/4 Labial closure = 0 Lingual control = 1[a] Palatal closure = 7[a] Mastication = 14[a] Position of bolus = 6[a] Swallow timing = 6[a] Velopharyngeal closure = 0 Pharyngeal contraction = 12[a] Laryngeal excursion = 7[a] Bolus propulsion UES = 7[a] Clearance of pyriform sinus residual = 7[a] Upper esophageal parameters = 0 PAS score, total of 14, 6 months post for fluids: Grade 1–2 = 12 Grade 3–6 = 1 Grade 7–8 = 1 Total of 14, 6 months post for solids: Grade 1–2 = 8 Grade 3–6 = 4 Grade 7–8 = 2
Eisbruch et al., 2002, USA	26	Total of 26: Base of tongue weakness = 9	Total of 26, 1–3 months post: Base of tongue weakness = 11	Total of 26, 6–12 months post: Base of tongue weakness = 11

Table 2 (continued)

Author, year, country	Total sample (*n*)	Deglutition disorder Pre-treatment	Deglutition disorder < 6 months of treatment	Deglutition disorder > 6 months of treatment
		Pharyngeal residue = 5 Reduced larynx/hyoid elevation = 4 Reduced epiglottic inversion = 3 Swallow reflex delay = 8 Velopharyngeal incompetence = 1 Cricopharyngeal m. dysfunction = 0 Upper esophageal stricture = 2 Penetration = 4 Aspiration = 1 Silent aspiration = 2	Pharyngeal residue = 15 Reduced larynx/hyoid elevation = 7 Reduced epiglottic inversion = 10 Swallow reflex delay = 6 Velopharyngeal incompetence = 5 Cricopharyngeal m. dysfunction = 1 Upper esophageal stricture = 7 Penetration = 5 Aspiration = 10 Silent aspiration = 3	Pharyngeal residue = 10 Reduced larynx/hyoid elevation = 6 Reduced epiglottic inversion = 7 Swallow reflex delay = 8 Velopharyngeal incompetence = 2 Cricopharyngeal m. dysfunction = 1 Upper esophageal stricture = 6 Penetration = 3 Aspiration = 5 Silent aspiration = 3
Erkal et al., 2014, Turkey	20	Total of 20: Impaired lingual movement = 1 Base of tongue weakness = 10 Pharyngeal residue = 7 Reduced laryngeal elevation = 2 Reduced epiglottic inversion = 0 Swallow reflex delay = 0 Cricopharyngeal muscle dysfunction = 0 Proximal esophageal stricture = 3 Penetration = 5 Aspiration = 0	Total of 20, 3 months post: Impaired lingual movement = 4 Base of tongue weakness = 15 Pharyngeal residue = 11 Reduced laryngeal elevation = 2 Reduced epiglottic inversion = 6 Swallow reflex delay = 1 Cricopharyngeal muscle dysfunction = 2 Proximal esophageal stricture = 5 Penetration = 10 Aspiration = 1	Total of 20, 6 months post: Impaired lingual movement = 2 Base of tongue weakness = 12 Pharyngeal residue = 10 Reduced laryngeal elevation = 3 Reduced epiglottic inversion = 5 Swallow reflex delay = 1 Cricopharyngeal muscle dysfunction = 2 Proximal esophageal stricture = 6 Penetration = 14 Aspiration = 4
Graner et al., 2003, USA	11	Total of 11: Oral residue = 0 Nasal regurgitation = 0 Diffuse falling over tongue base = 1 Delayed pharyngeal response = 3 Reduced tongue base retraction = 5 Reduced laryngeal elevation = 5 Laryngeal vestibule, thin liquid = 6 Laryngeal vestibule, thick liquid = 6 Laryngeal vestibule, pureed = 1 Aspiration = 3 Valleculae residue, thin liquid = 3 Valleculae residue, thick liquid = 6 Valleculae residue, pureed = 3 Pyriform sinus residue, thin liquid = 1 Pyriform sinus residue, thick liquid = 3 Pyriform sinus residue, pureed = 3 Tight cricopharyngeal segment = 2 Backflow to pharynx = 1	Total of 11, 5 months post: Oral residue = 1 Nasal regurgitation = 1 Diffuse falling over tongue base = 0 Delayed pharyngeal response = 4 Reduced tongue base retraction = 9 Reduced laryngeal elevation = 9 Laryngeal vestibule, thin liquid = 9 Laryngeal vestibule, thick liquid = 9 Laryngeal vestibule, pureed = 5 Aspiration = 7 Valleculae residue, thin liquid = 7 Valleculae residue, thick liquid = 10 Valleculae residue, pureed = 7 Pyriform sinus residue, thin liquid = 8 Pyriform sinus residue, thick liquid = 8 Pyriform sinus residue, pureed = 4 Tight cricopharyngeal segment = 4 Backflow to pharynx = 1	NA
Kotz et al., 2004, USA	12	Total of 12: Reduced tongue base to posterior pharyngeal wall = 1[a] Reduced laryngeal elevation = 1[a]	Total of 12, 1 to 14 weeks post: Reduced tongue base to posterior pharyngeal wall = 12[a] Reduced laryngeal elevation = 10[a] 3 ml/11[a] 5 ml	NA

Table 2 (continued)

Author, year, country	Total sample (*n*)	Deglutition disorder Pre-treatment	Deglutition disorder < 6 months of treatment	Deglutition disorder > 6 months of treatment
		Reduced laryngeal vestibule closure = 1[a] Reduced upper esophageal sphincter opening = 0	Reduced laryngeal vestibule closure = 9[a] 3 ml/8[a] 5 ml Reduced upper esophageal sphincter opening = 2[a] Laryngeal aspiration = 4 Penetration = 9 Pharyngeal residue = 4	
Ku et al., 2007, China	20	Total of 20: Impaired lingual control = 0 Impaired oral transfer food = 0 Stasis in vallecula = 0 Stasis in pyriform fossa = 0 Impaired pharyngeal peristalsis = 3[a] Impaired tongue propulsion = 1[a] Penetration = 2[a] Aspiration = 2[a]	NA	Total of 20, 6 months post: Impaired lingual control = 8[a] Impaired oral transfer food = 9[a] Stasis in vallecula = 17[a] Stasis in pyriform fossa = 12[a] Impaired pharyngeal peristalsis = 12[a] Impaired tongue propulsion = 3[a] Penetration = 7[a] Aspiration = 0 Total of 20, 12 months post: Impaired lingual control = 8[a] Impaired oral transfer food = 8[a] Stasis in vallecula = 20[a] Stasis in pyriform fossa = 12[a] Impaired pharyngeal peristalsis = 12[a] Impaired tongue propulsion = 6[a] Penetration = 5[a] Aspiration = 1[a]
Lazarus et al., 2000, USA	13	Total of 13: Aspiration = 1	Total of 13, 2 months post: Aspiration = 7	NA
Logemann et al., 2006, USA	53	Total of 53: Reduced Tongue base retraction = 26[a] Reduced tongue strength = 20[a] Delayed laryngeal vestibule closure = 10[a] Reduced tongue control = 9[a] Delayed pharyngeal swallow = 8[a] Reduced laryngeal elevation = 7[a] Reduced propulsion of bolus = 6[a] Reduced tongue stabilization = 3[a] Bilateral pharyngeal weakness = 3[a] Reduced vertical tongue movement = 2[a] Reduced cricopharyngeal opening = 1[a] Visible cricopharyngeal bar = 1[a] Unilateral pharyngeal weakness = 1[a] Gastrostomy or jejunostomy = 8	Total of 53, 3 months post: Reduced Tongue base retraction = 47[a] Reduced tongue strength = 27[a] Delayed laryngeal vestibule closure = 16[a] Reduced lateral/anterior tongue Stabilization = 2[a] Incomplete laryngeal vestibule Closure = 2[a] Reduced velopharyngeal closure = 2[a] Reduced vertical tongue movement = 1[a] Reduced glottic closure = 0[a] Gastrostomy or jejunostomy = 21 Aspiration = 12	NA

Table 2 (continued)

Author, year, country	Total sample (*n*)	Deglutition disorder Pre-treatment	Deglutition disorder < 6 months of treatment	Deglutition disorder > 6 months of treatment
		Aspiration = 4		
Logemann et al., 2008, USA	48	Total of 48: Reduced tongue base retraction = 32[a] Reduced tongue strength = 24[a] Delay in triggering the pharyngeal swallow = 19[a] Slowed/delayed vestibule closure = 13[a] Reduced tongue control = 16[a] Reduced anterior-Posterior tongue movement = 12[a] Reduced laryngeal elevation = 8[a] Reduced tongue stabilization = 7[a] Bilateral pharyngeal weakness = 4[a] Reduced cricopharyngeal opening = 4[a] Visible cricopharyngeal bar = 5[a] Incomplete laryngeal vestibule closure = 3 Functional swallowing = 47[a] Oral intake < 50% = 1[a] Normal diet = 38[a]	Total of 48, 3 months post: Reduced tongue base retraction = 43[a] Reduced tongue strength = 29[a] Delay in triggering the pharyngeal swallow = 27[a] Slowed/delayed vestibule closure = 29[a] Reduced tongue control = 22[a] Reduced anterior-posterior tongue movement = 22[a] Reduced laryngeal elevation = 15[a] Reduced tongue stabilization = 6[a] Bilateral pharyngeal weakness = 11[a] Reduced cricopharyngeal opening = 11[a] Visible cricopharyngeal bar = 6[a] Incomplete laryngeal vestibule closure = 6[a] Functional swallowing = 38[a] Oral intake < 50% = 12[a] Normal diet = 22[a]	Total of 48, 12 months post: Reduced tongue base retraction = 41[a] Reduced tongue strength = 27[a] Delay in triggering the pharyngeal swallow = 20[a] Slowed/delayed vestibule closure = 26[a] Reduced tongue control = 18[a] Reduced anterior-posterior tongue movement = 27[a] Reduced laryngeal elevation = 17[a] Reduced tongue stabilization = 7[a] Bilateral pharyngeal weakness = 10[a] Reduced cricopharyngeal opening = 10[a] Visible cricopharyngeal bar = 7[a] Incomplete laryngeal vestibule closure = 6[a] Functional swallowing = 40[a] Oral intake < 50% = 10[a] Normal diet = 29[a] Gastrostomy = 5
O'Connell et al., 2008, Canada	20	Total of 20: Mild pharyngeal residue During = 17 Moderate pharyngeal residue = 3 Aspiration = 0	NA	Total of 20, 12 months post: Mild pharyngeal residue During = 6 Moderate pharyngeal residue = 6 Severe pharyngeal residue = 8 Aspiration = 1
Patterson et al., 2014, UK	112	Total of 112: Aspiration = 10	Total of 97, 3 months post: Aspiration = 27[a] Silent aspiration = 8[a]	NA
Rogus-Pulia et al., 2014, USA	21	Total of 21: Penetration during swallow = 2	Total of 21, mean of 5 months post: Penetration during swallow = 6	NA
Serel et al., 2013, Turkey	40	Total of 40: Aspiration with liquid = 2 Aspiration with pudding = 0 Aspiration with biscuit = 0	Total of 40, 1 month post: Aspiration with liquid = 8 Aspiration with pudding = 7 Aspiration with biscuit = 7 Total of 40, 3 months post: Aspiration with liquid = 9 Aspiration with pudding = 7 Aspiration with biscuit = 7	NA
Son et al., 2015, Korea	133	Total of 74: Inadequate lip movement = 0 Inadequate tongue control = 18 Inadequate chewing = 5 Delayed oral transit time = 3	Total of 87, mean of 4 months post: Inadequate lip movement = 3 Inadequate tongue control = 64 Inadequate chewing = 25 Delayed oral transit time = 28	NA

Table 2 (continued)

Author, year, country	Total sample (*n*)	Deglutition disorder Pre-treatment	Deglutition disorder < 6 months of treatment	Deglutition disorder > 6 months of treatment
		Aspiration or penetration = 8 Nasal regurgitation = 0 Vallecular pouch residue = 6 Pyriform sinus residue = 3 Inadequate laryngeal elevation = 1 ASHA-NOMS score = 4.95 ± 2.95	Aspiration or penetration = 26 Nasal regurgitation = 4 Vallecular pouch residue = 39 Pyriform sinus residue = 16 Inadequate laryngeal elevation = 12 ASHA-NOMS score = 2.82 ± 2.78	
Van der Molen et al., 2013, The Netherlands	55	Total of 55: Aspiration and/or penetration = 9	Total of 39, 10 weeks post: Aspiration and/or penetration = 8	Total of 36, 12 months post: Aspiration and/or penetration = 5
Xinou et al., 2018, Greece	69	Total of 69: Lip closure = 0 Tongue control during bolus hold = 45[a] Bolus preparation/mastication = 17[a] Bolus transport/lingual motion = 5[a] Oral residue = 61[a] Initiation of pharyngeal swallow = 43[a] Soft palate elevation = 1[a] Laryngeal elevation = 14[a] Anterior hyoid excursion = 21[a] Epiglottic movement = 28[a] Laryngeal vestibule closure = 24[a] Pharyngeal stripping wave = 8[a] Pharyngeal contraction = 10[a] PES opening = 11[a] Tongue base retraction = 41[a] Pharyngeal residue = 57[a] Esophageal clearance in the upright position = 11[a] Aspiration = 20[a] Silent aspiration = 9[a]	Total of 53, 1 month post: Lip closure = 1[a] Tongue control during bolus hold = 34[a] Bolus preparation/mastication = 21[a] Bolus transport/lingual motion = 10[a] Oral residue = 42[a] Initiation of pharyngeal swallow = 40[a] Soft palate elevation = 0 Laryngeal elevation = 10[a] Anterior hyoid excursion = 16[a] Epiglottic movement = 18[a] Laryngeal vestibule closure = 32[a] Pharyngeal stripping wave = 8[a] Pharyngeal contraction = 6[a] PES opening = 11[a] Tongue base retraction = 37[a] Pharyngeal residue = 42[a] Esophageal clearance in the upright position = 10[a] Aspiration = 17[a] Silent aspiration = 10[a] Total of 53, 3 months post: Lip closure = 2[a] Tongue control during bolus hold = 32[a] Bolus preparation/mastication = 17[a] Bolus transport/lingual motion = 4[a] Oral residue = 44[a] Initiation of pharyngeal swallow = 43[a] Soft palate elevation = 0 Laryngeal elevation = 11[a] Anterior hyoid excursion = 16[a] Epiglottic movement = 15[a] Laryngeal vestibule closure = 28[a] Pharyngeal stripping wave = 6[a] Pharyngeal contraction = 4[a]	Total of 47, 6 months post: Lip closure = 1[a] Tongue control during bolus hold = 30[a] Bolus preparation/mastication = 18[a] Bolus transport/lingual motion = 5[a] Oral residue = 36[a] Initiation of pharyngeal swallow = 37[a] Soft palate elevation = 3[a] Laryngeal elevation = 14[a] Anterior hyoid excursion = 16[a] Epiglottic movement = 13[a] Laryngeal vestibule closure = 25[a] Pharyngeal stripping wave = 6[a] Pharyngeal contraction = 4[a] PES opening = 11[a] Tongue base retraction = 33[a] Pharyngeal residue = 42[a] Esophageal clearance in the upright position = 5[a] Aspiration = 18[a] Silent aspiration = 8[a] Total of 39, 12 months post: Lip closure = 0 Tongue control during bolus hold = 25[a] Bolus preparation/mastication = 12[a] Bolus transport/lingual motion = 2[a] Oral residue = 30[a] Initiation of pharyngeal swallow = 33[a] Soft palate elevation = 0 Laryngeal elevation = 5[a] Anterior hyoid excursion = 6[a] Epiglottic movement = 7[a] Laryngeal vestibule closure = 19[a] Pharyngeal stripping wave = 1[a] Pharyngeal contraction = 1[a]

Table 2 (continued)

Author, year, country	Total sample (*n*)	Deglutition disorder Pre-treatment	Deglutition disorder < 6 months of treatment	Deglutition disorder > 6 months of treatment
			PES opening = 11[a]	PES opening = 5[a]
			Tongue base retraction = 38[a]	Tongue base retraction = 27[a]
			Pharyngeal residue = 45[a]	Pharyngeal residue = 33[a]
			Esophageal clearance in the upright position = 11[a]	Esophageal clearance in the upright position = 5[a]
			Aspiration = 23[a]	Aspiration = 12[a]
			Silent aspiration = 18[a]	Silent aspiration = 6[a]

PAS penetration aspiration scale (1–2 normal, 3–6 penetration, 7–8 aspiration); *ASHA-NOMS scale* American Association of Speech-Language Pathology-National System of Measurement Results, scores from 1 (not able to swallow) up to 7 (safe swallow)

[a] Values calculated by the authors

Pre-treatment

All 17 included studies performed swallowing assessment using imaging exams at baseline. The types of parameters concerning deglutition were reported in different ways across studies. The most frequently reported parameter in 14 of the included studies [12, 13, 15–17, 25, 27–32, 34, 35] was aspiration, a complication of deglutition disorders. The results of meta-analysis at pre-treatment showed a frequency of aspiration of 8.4% (95% CI 4.3–13.7; $p < 0.01$; $n = 572$; $I^2 = 74\%$) (Fig. 2a).

In five [12, 14, 27, 29, 30] of the included studies, it was possible to analyze the total occurrence of penetration of food, liquids, or saliva above the vocal folds in the pre-treatment period. According to results of the analysis, the frequency of penetration was of 10.5% (95% CI 3.3–21.0; $p = 0.07$; $n = 99$; $I^2 = 54\%$) (Fig. 2f).

Two other important parameters related to deglutition disorders are the reduction in elevation of the larynx and pharyngeal residue. Meta-analysis was performed for reduced laryngeal elevation in eight studies [12, 16, 20, 26, 28, 29, 33, 35] at baseline, with a frequency for this parameter of 16.0% (95% CI 7.4–27.0; $p < 0.01$; $n = 301$; $I^2 = 80\%$) (Fig. 2i). For pharyngeal residue, a total of seven studies [12, 16, 25, 27, 29, 30, 35] were included in the analysis, with pre-treatment frequency of 12.7% (95% CI 0.9–34.9; $p < 0.01$; $n = 362$; $I^2 = 96\%$) (Fig. 2n).

Up to 6 months post-treatment

All parameters analyzed in the pre-treatment period were also assessed for less than and at 6 months post-treatment. In the meta-analysis for aspiration at less than 3 months post-treatment, the frequency was 28.6% (95% CI 21.7–36.1; $p = 0.20$; $n = 229$; $I^2 = 30\%$) (Fig. 2b). Similarly, frequency in the period more than 3 months post-treatment reached 28.2% (95% CI 19.3–38.0; $p < 0.01$; $n = 361$; $I^2 = 72\%$) (Fig. 2c). At 6 months post-treatment, this frequency declined to 17.6% (95% CI 19.3–38.0; $p < 0.01$; $n = 125$; $I^2 = 88\%$) (Fig. 2d). The frequency of penetration for the period less than 6 months post-treatment was 41.3% (95% CI 19.7–64.9; $p < 0.01$; $n = 79$; $I^2 = 78\%$) (Fig. 2g). The parameter reduced laryngeal elevation at less than 4 months post-treatment had a frequency of 46.2% (95% CI 17.0–76.9; $p < 0.01$; $n = 105$; $I^2 = 90\%$) (Fig. 2j). This proportion dropped to 27.3% (95% CI 12.8–44.8; $p < 0.01$; $n = 219$; $I^2 = 85\%$) at less than 6 months post-treatment (Fig. 2k) and increased slightly to 29.7% (95% CI 14.5–47.6; $p = 0.08$; $n = 81$; $I^2 = 60\%$) at 6 months (Fig. 2l) post-treatment. The pharyngeal residue parameter showed increasing frequencies over time; at less than 6 months this was 47.1% (95% CI 27.9–66.8; $p < 0.01$; $n = 331$; $I^2 = 92\%$) (Fig. 2o) and at 6 months the frequency was increased to 61.8% (95% CI 30.2–88.7; $p < 0.01$; $n = 145$; $I^2 = 93\%$) (Fig. 2p).

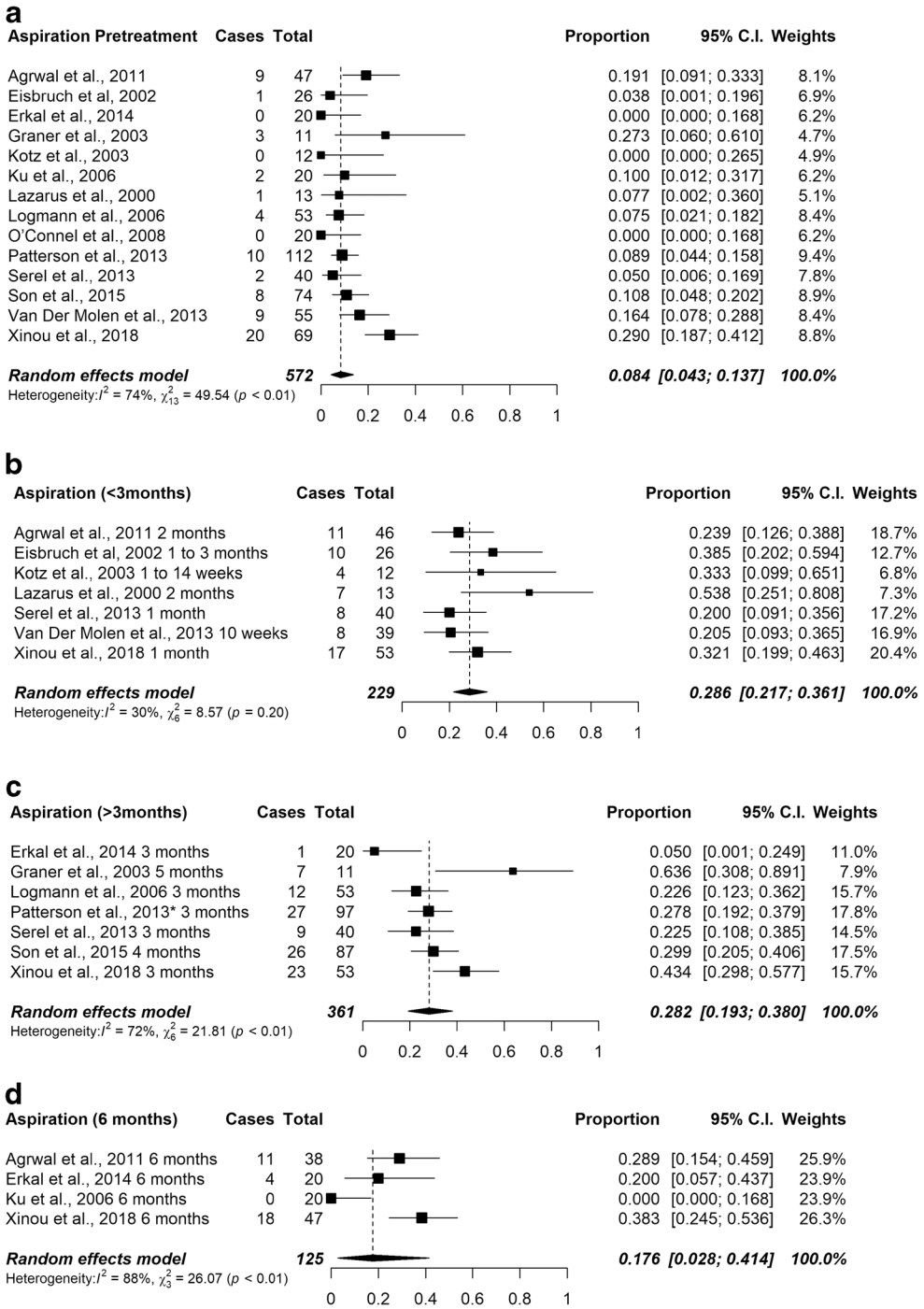

Fig. 2 **a**–**e** Meta-analysis graphs and data for aspiration in different time periods. **f**–**h** Meta-analysis graphs and data for penetration in different time periods. **i**–**m** Meta-analysis graphs and data for reduced laryngeal elevation in different time periods. **n**–**q** Meta-analysis graphs and data for pharyngeal residue in different time periods

More than 6 months post-treatment

There were few studies included in meta-analysis of the four parameters for the period more than 6 months post-treatment. Many included studies did not follow the patient for more than 6 months after receiving treatment for cancer. In the analysis for aspiration, a total of six [17, 25, 27, 30, 34, 35] studies had data collected, only half as many as in the baseline analysis. The frequency of aspiration from 6 to 12 months post-treatment was 16.2% (95% CI 8.1–26.3; $p = 0.03$; $n = 158$; $I^2 = 60\%$) (Fig. 2e). Similarly, for the parameter penetration, only three [12, 27, 30] studies were included in the meta-

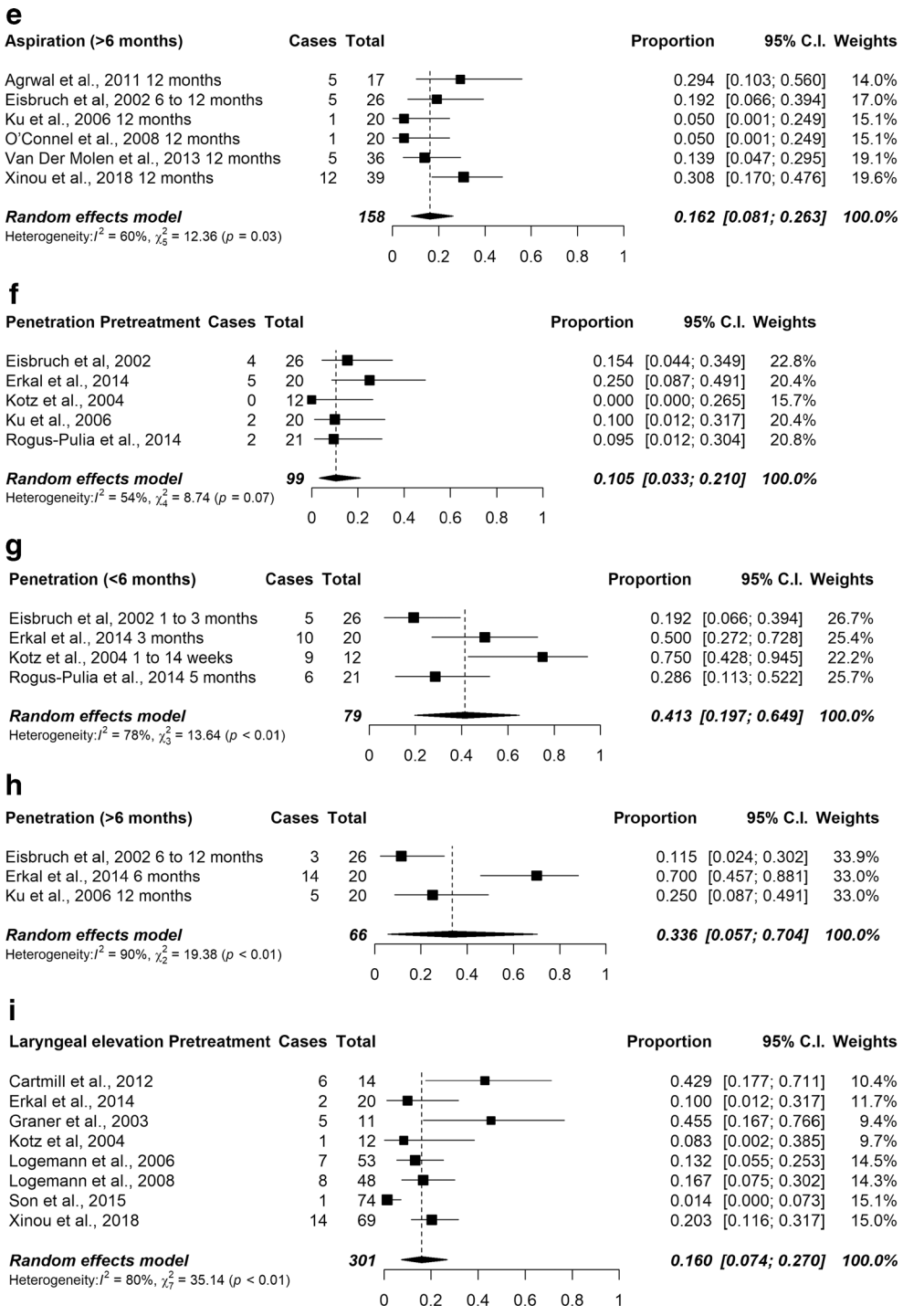

Fig. 2 (continued)

analysis and showed a frequency of 33.6% (95% CI 5.7–70.4; $p < 0.01$; $n = 66$; $I^2 = 90\%$) (Fig. 2h). For the reduction of laryngeal elevation, the frequency was calculated for three studies [27, 33, 35], reaching 23.4% (95% CI 11.0–38.7; $p = 0.04$; $n = 113$; $I^2 = 68\%$) (Fig. 2m). The last parameter calculated was pharyngeal residue, with four included studies [25, 27, 30, 35] in the analysis and a frequency of 73.8% (95% CI 45.2–94.3; $p < 0.01$; $n = 122$; $I^2 = 91\%$), the highest frequency found across periods and parameters (Fig. 2q).

Synthesis of results

A proportion meta-analysis was conducted among the 17 included studies. Data of the analysis performed are shown in

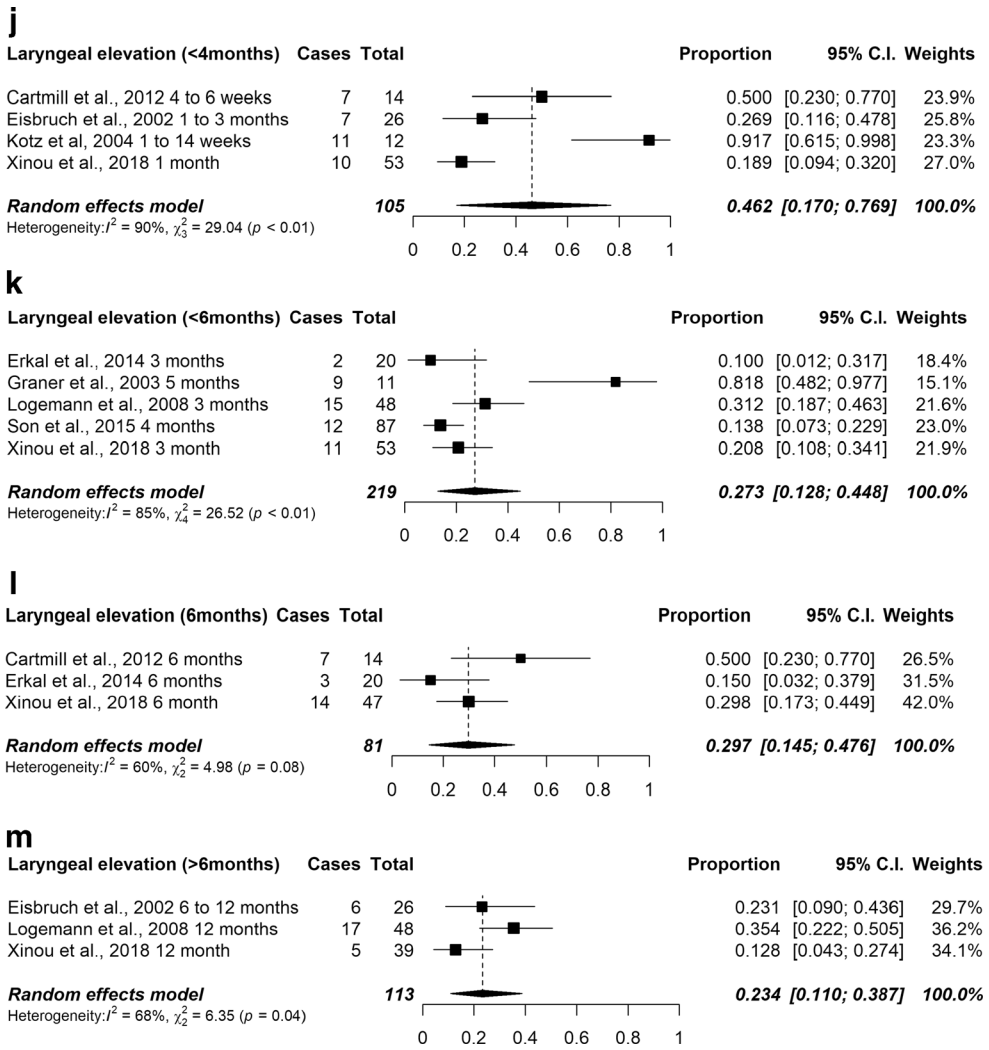

Fig. 2 (continued)

Fig. 2a–q. The heterogeneity between studies varied from 30 to 96%; therefore, a random effects model was chosen [23]. Most higher frequencies of deglutition complications were found in the two periods less than and at 6 months post-treatment. The only exception to this was pharyngeal residue, which presented the highest frequency in the period more than 6 months post-treatment. A higher frequency of deglutition disorders was observed across studies among patients who underwent combination therapy (surgery, radiotherapy, chemotherapy), as compared with patients who only underwent concurrent chemoradiation.

Level of evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for evaluating the quality of evidence was adapted for the analysis of observational studies and applied to subgroups, according to the meta-analysis performed for deglutition parameters before and after cancer treatment. All the outcomes across subgroups were graded as low quality, reflecting the heterogeneity of the meta-analysis, evidenced by the different types of HNC topographies and cancer treatments. A GRADE table of findings is shown in Appendix 4.

Discussion

With the increasing use of aggressive combined modality therapy and radiation techniques for the treatment of locally advanced head and neck cancer, the acute and late effects of treatment have become an area of interest and investigation. Thus, the objective of this SR was to assess the frequency of deglutition disorders in the population of patients with HNC. We investigated parameters of deglutition disorders and complications that were diagnosed using imaging exams for swallowing function. The results indicated a higher frequency of deglutition complications in the period immediately

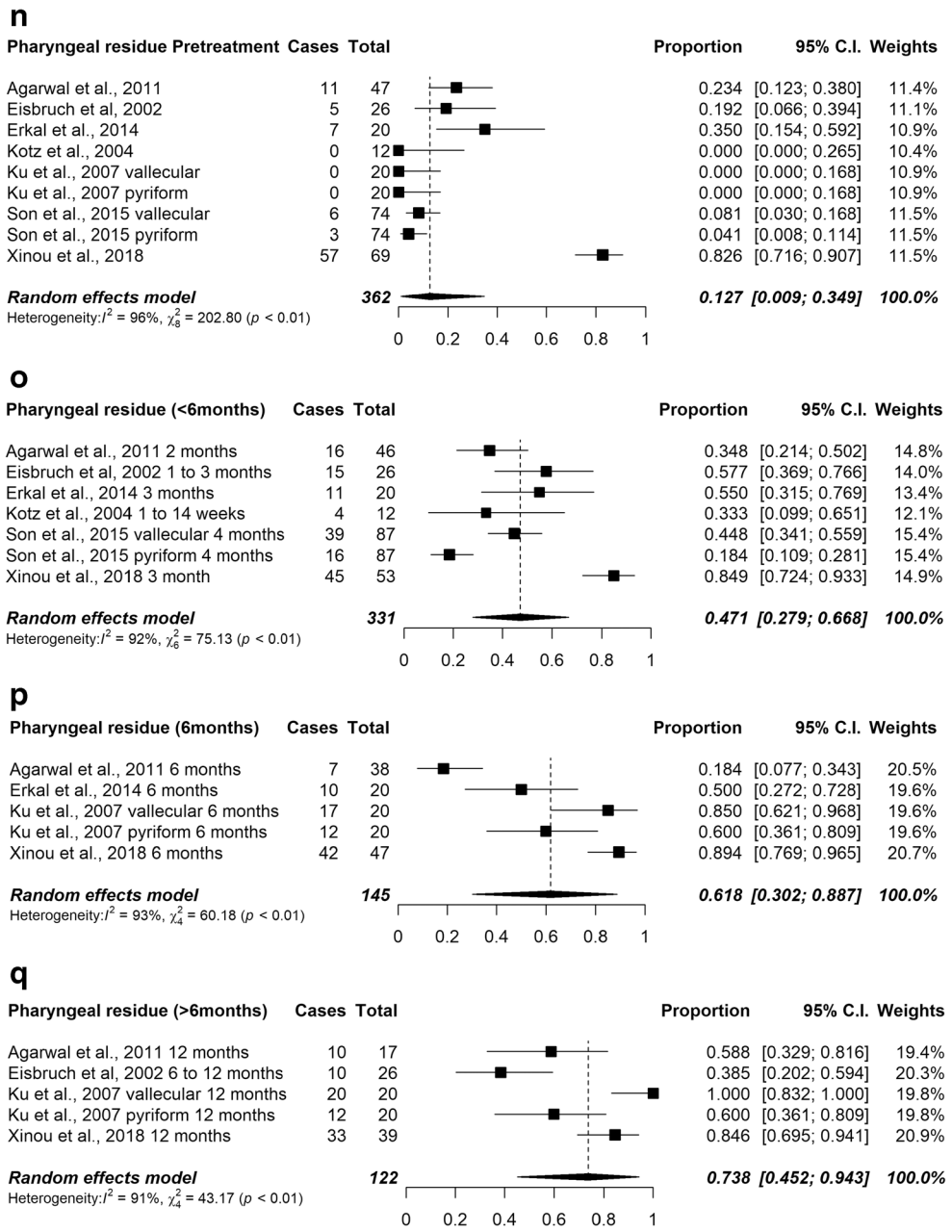

Fig. 2 (continued)

following cancer treatment, from its completion up to 6 months. This only differed for the parameter pharyngeal residue, which increased over time (from 6 to 12 months). Complications of deglutition alterations could include a higher need of long-term feeding tube and higher risk of aspiration pneumonia with its impact on patient's quality of life [36].

Currently, in the hierarchy of evidence, meta-analysis is located at the top of the pyramid. This pooled analysis from various individual studies is able to perform a more precise estimate of the outcome researched [37]. The goal of this review was to minimize bias through the selection criteria and performed a meta-analysis. This was achieved; however, there is still considerable bias in the individual studies, especially in the characterization of the samples, as in the separation of deglutition disorders by the cancer site, stage, and treatment.

Toxicity from cancer treatment is classified as acute or late, based on its temporal relationship to treatment. Acute toxicity develops during or shortly after the completion of treatment and is usually temporary. Late toxicity presents months to years after the completion of treatment and is often permanent [38]. The most common long-term complication of RT and chemoradiotherapy for HNC is xerostomia [39]. Late complications may include lymphedema, carotid artery injury, trismus, thyroid disease, and dysphagia, among others [39].

Some studies have reported the prevalence of swallowing disorders, such as dysphagia, to be 50.6% [8] in patients with HNC. Rinkel et al. [40] assessed a sample of 50 patients and found that 30 had oropharyngeal cancer and 79.0% presented swallowing problems after receiving chemoradiation. In the USA, a population-based study found that over 9 million Americans reported swallowing problems in 2012 and that the third most common cause was HNC (4.9%) [41].

Our data were mostly in line with the findings of previous SRs, the first one was developed in 2006 [10] and the later in 2013 [11]. Heterogeneity of the methods to quantify deglutition disorders in the included studies was a common factor found in all three SRs. However, we tried to integrate criteria that helped to minimize this assessment's heterogeneity and perform a meta-analysis. One of the differences when comparing this review to the previous ones is in the criteria that all the studies included had to present baseline and post-treatment data assessed by an image exam, such as VFSS or FEES.

A total of 81 studies were excluded in the selection process of this review because of the lack of VFSS or FEES assessment before and after cancer treatment (Appendix 2). This data evidences the discrepancies that exist when performing research over swallowing complications. The use of image exams can contribute to better diagnose dysphagia, its severity, and which consistencies are safer for oral ingestion [42].

There was also a deficiency in the use of a common tool to quantify the alterations perceived during the image exams. Only two [25, 26] of the included studies used Penetration Aspiration Scale (PAS) as a mean to quantify levels of penetration/aspiration through an 8-point score (1–2 normal; 3–6 penetration; 7–8 aspiration).

The findings of this SR point out that there is a higher frequency of swallowing complications in patients who undergo surgery, radiation, and/or chemotherapy combined. Furthermore, parameters such as pharyngeal residue are more in evidence in our pooled analysis. Residue in the vallecula and/or the pyriform sinus are linked to the occurrence of penetration/aspiration [43]. A 2016 systematic review [44] that assessed the various pharyngeal residue scales available in the literature highlighted that the severity of pharyngeal residue may indicate the risk for aspiration, in mild residue as low risk and severe residue as high risk. The results found in our study indicates pharyngeal residue as one of the parameters quantified in the meta-analysis that increased over the 12 months period. This result may indicate that pharyngeal mobility, strength, and/or sensitivity could still be more impaired after 12 months post-treatment for the cancer. Hiss and Postma [42] indicate that post-swallow aspiration can occur due to the residue accumulated in the pharynx, due to its incoordination and/or decreased contraction.

Long-term follow-up data is necessary to better understand and assess swallow in head and neck cancer patients, especially in the years after treatment. Fortunately, even with the increase in the pharyngeal residue showed in the pooled data in our review, the aspiration parameter decreased after 6 months post treatment. In a study [45] that performed a long-term follow-up of patients with HNC after cancer treatment, reported late dysphagia for a median 9 years, with a feeding tube present in 21.0% of patients. Another example of long-term follow-up, for over 5 years monitoring survivors of HNC, 53.5% of patients treated with a non-IMRT modality and 22.0% treated with IMRT had dysphagia [46].

Swallowing disorders arising as a result of HNC impairs the quality of life of the patient. Radiotherapy and chemoradiotherapy may affect the oral and pharyngeal phase of swallowing. Strategies such as exercises, maneuvers, IMRT, and cryoprotectors may improve the swallowing function and overall quality of life of the patient. The results of this review indicate that the multidisciplinary team treating HNC must be familiar with the basics of normal swallowing and how swallowing is affected by cancer treatment, due to the moderate to high prevalence of deglutition disorders in these population. Given the high complication rate and adverse impact on quality of life, it is critical to minimize dysphagia and its sequelae.

Study limitations

This SR had some limitations. The data collected for the parameters analyzed were not from the same number of studies or the same periods after cancer treatment. This is even more evidenced by the lack of data for swallowing parameters according to the topography, treatment type, and/or stage of HNC. There was also high heterogeneity among all quantitative analyses. These factors together limit the quality of evidence collected and analyzed in this review.

Conclusions

The frequency of parameters or complications associated with deglutition disorders was highest in the period immediately following cancer treatment (less than 6 months post-treatment), except for pharyngeal residue, which increased from 6 to 12 months post-treatment. The latter swallowing complication had a high frequency in all post-treatment periods analyzed. One of the most serious complications of deglutition disorders, aspiration, had a frequency of 28.6% for the period less than 3 months post-treatment and 28.2% for the period more than 3 months post-treatment. The evidence presented in the literature highlights the need for additional longitudinal studies with follow-up periods longer than 12 months. In addition, assessment of deglutition parameters using imaging exams with global scales or uniformity in the parameters collected is needed, as well as classification according to type of HNC, different cancer stages, and treatment modality.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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