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Dysphagia After Pediatric Laryngotracheal Reconstruction—A Scoping Review

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ABSTRACT

Objective: To review swallowing outcomes after pediatric laryngotracheal reconstruction.

Methods: A scoping review was conducted through PubMed and Google Scholar databases for dysphagia outcomes after common pediatric airway surgery. Original full-text articles written in English between 1987 and 2024 were included. Articles were excluded if data was unavailable to review or were not in English. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) Guidelines were followed.

Results: There were 31 articles included, which assessed swallowing after laryngotracheal reconstruction. Laryngotracheal reconstruction can result in transient post-operative dysphagia, with the degree of severity related to preoperative swallowing status.

Conclusion: Most airway reconstructive surgery in children can be associated with postoperative dysphagia. However, the swallow dysfunction is typically transient and can be predicted by comorbidities or preoperative swallow function. Timely assessments and appropriate multidisciplinary interventions are essential to improve swallowing outcomes after pediatric laryngotracheal reconstruction.

Level of Evidence: 4.

1 | Introduction

Maintenance of appropriate nutrition is critical for supporting growth and global development [1]. Sufficient calories, typically through adequate oral intake, are needed to provide energy for these tasks in children. Though often multifactorial, swallow dysfunction, or dysphagia, is important to recognize and treat. This minimizes malnutrition concerns and can have a positive impact on growth, development, and quality of life.

Swallowing requires complex coordination of the aerodigestive tract. The normal swallow is classically divided into four phases. The preparatory phase involves bringing food into the oral cavity, chewing the bolus, and moistening it with saliva. The oral phase moves the bolus from the oral cavity to the oropharynx, triggering the swallow reflex. Next, the pharyngeal phase begins when the bolus moves through the oropharynx to the hypopharynx and eventually the esophagus via coordinated muscular contractions. In this process, the larynx elevates and the vocal cords adduct to help prevent aspiration [2]. The final phase is the esophageal phase where the bolus moves via peristalsis down the esophagus into the stomach. The process of swallowing involves 30 different muscles and nerves, with maturation in the sequence as a child ages [3]. Each phase of swallowing can be

separately impacted, leading to dysphagia, defined as difficulty swallowing [1, 2].

Pediatric airway reconstructive surgeries have the potential to negatively impact postoperative swallow function. Recognizing patterns and risk factors associated with dysphagia after pediatric laryngotracheal reconstruction (LTR) is important for conditions that require manipulation or alteration of the airway structure. This assists in preoperative counseling and postoperative management strategies. However, the reported outcomes from these surgeries on swallowing are mixed, and studies often have varying quality or reporting consistency. A review of the literature can help summarize the current evidence for surgeons to appraise. The primary objective of this scoping review is to evaluate the literature describing swallowing function after LTR in children.

2 | Methods

A scoping review of the literature was performed using PubMed and Google Scholar following the preferred reporting items for systematic reviews and meta analyses (PRISMA) guidelines [4]. Key words during the search were as follows: "pediatric dysphagia aerodigestive," "pediatric airway surgery aerodigestive," "laryngotracheal surgery dysphagia," "pediatric laryngotracheal reconstruction," "laryngotracheal reconstruction dysphagia," "pediatric laryngotracheal reconstruction dysphagia," "pediatric laryngotracheal reconstruction swallow," "pediatric laryngotracheal reconstruction feeding," "pediatric laryngotracheal reconstruction aspiration," "pediatric laryngotracheoplasty," "pediatric laryngotracheoplasty dysphagia," "pediatric laryngotracheoplasty swallow," "pediatric laryngotracheoplasty feeding," "pediatric cricotracheal resection," "pediatric cricotracheal resection dysphagia," "pediatric cricotracheal resection swallow," "pediatric cricotracheal resection feeding," "pediatric airway reconstruction dysphagia," "pediatric airway reconstruction swallow," "pediatric airway reconstruction aspiration," "pediatric slide tracheoplasty dysphagia," "pediatric slide tracheoplasty swallow," "pediatric slide tracheoplasty feeding."

All identified articles were compiled based on title and abstract. The article screening, selection and reading process was carried out by the authors. The full text was obtained for complete evaluation and final inclusion in the review. Included articles were published or in press, and specifically discussed dysphagia as an outcome after the described airway procedure. Articles meeting inclusion criteria were randomized clinical trials, prospective and retrospective cohort studies, case–control studies, case series, and case reports published from 1987 through 2024. Articles were excluded if it was not written in English or not available for full review. All articles were accessed between July 2023 and January 2025. The risk of bias in nonrandomized studies was measured using the methodological index for nonrandomized studies quality assessment [5].

3 | Results

The database search revealed 1101 studies. After the removal of 346 duplicates and 724 irrelevant records were excluded based on the review of article titles and abstracts. A total of 31 articles were included (Figure 1). Studies included in this report are included in Table 1. The risk of bias in the nonrandomized studies is shown in Table 2. All composite methodological index for non-randomized studies [5] fell at or below 12 of the 16 possible points, suggesting lower quality studies. There were no randomized trials available for this review.

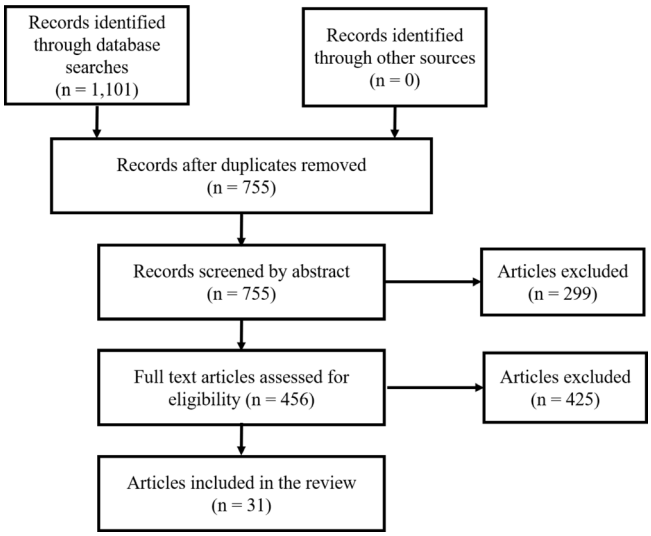

FIGURE 1 | Flowchart of the process for study selection.

3.1 | LTR

LTR is used to manage acquired or congenital laryngeal and/or tracheal stenosis [14]. The goal of the surgery is to create an adequate airway caliber for safe respiration [30], thereby avoiding a tracheostomy or facilitating decannulation. Congenital conditions amenable to reconstruction include incomplete canalization of the larynx in utero leading to subglottic stenosis or laryngeal atresia, bilateral vocal cord paralysis, laryngeal webs, and subglottic lesions [14, 37]. Acquired etiologies include laryngeal or tracheal trauma from intubation leading to stenosis or ingestion and inhalational injury causing scarring.

Several reconstructive options have been developed, including expansion procedures, resection operations, slide tracheoplasty, and glottic or supraglottic surgery [28]. Surgeries can be considered single or double staged, depending on the presence of a tracheostomy at the conclusion of the reconstruction. As these procedures have become more mainstream, long-term outcomes, including voice and swallowing, are important considerations [28]. These surgeries alter the anatomy of the laryngotracheal complex, which can affect swallow function as resulting structures compensate to maintain airway protection [14, 25, 38]. Surgical etiologies for this dysfunction may be related to resection of cartilage, muscle, neurovascular damage sustained during the surgery [14, 18], or related to scarring, vocal cord height mismatch, or cricoarytenoid joint damage once healed [25, 39].

Aspiration and dysphagia may be expected, and in one study were noted to persist for at least 7 to 10 days after these reconstructions [6]. The degree of dysphagia after these procedures

TABLE 1 | Impact of laryngotracheal reconstruction on swallowing, included studies.

Author	Number included	Presence of dysphagia post treatment	Dysphagia assessment	Procedure	Primary or revision procedures
Gray et al. [6]	42	Yes	Not stated, expectedly managed	Laryngotracheal reconstruction—anterior/posterior graft, stenting	100% primary
Smith et al. [7]	63	Yes, only those with long-term stents	Not stated	Laryngotracheal reconstruction—anterior/posterior graft, stenting	58.7% primary, 41.3% revision
Stern et al. [8]	26	Yes	Not stated	Laryngotracheal reconstruction or cricotracheal resection with T tube stent	36 procedures in 26 patients (21 LTR, 15 CTR)
Thomé and Thomé [9]	13	Yes, perioperative	Not stated	Laryngotracheal reconstruction, sometimes with grafting, sometimes with stents	Not stated
Lang et al. [10]	2	Yes, transient	Not stated	Slide tracheoplasty	100% primary
Younis et al. [11]	46	Yes, but no aspiration	Not stated, preoperative evaluation by SLP noted	Posterior cartilage graft, single stage laryngotracheal reconstruction	76% primary, 24% revision
Jaquet et al. [12]	57	No/improved	Questionnaire	Partial cricotracheal resection	68% primary, 32% revision
Phillips et al. [13]	10	Yes, though rare	Not stated	Laryngotracheal reconstruction with T tube	100% revision
Miller et al. [14]	30	Yes, duration ranging from 1 day to 4 weeks	Clinical exam by SLP using CHEOPS (Children's Hospital of Eastern Ontario behavioral pain scale)	Laryngotracheal reconstructions—single stage with anterior or anterior/posterior grafts, staged with anterior or anterior and posterior grafts with or without stents or t tubes, staged cricotracheal resection with t tube	86.7% primary, 13.3% revision

(Continues)

TABLE 1 | (Continued)

Author	Number included	Presence of dysphagia post treatment	Dysphagia assessment	Procedure	Primary or revision procedures
Smith et al. [15]	51	Yes, perioperative	VFSS and/or FEES	Open airway surgeries—single or double stage reconstructions with stents versus t tubes	78.4% primary, 21.6% revision
George et al. [16]	41	2 patients with mild aspiration (coughing with meals)	Not stated	Partial cricotracheal resection	85.4% primary, 14.6% revision
Ikonomidis et al. [17]	36	No	Questionnaires	Partial cricotracheal resection	81% primary, 19% revision
Andreoli et al. [18]	30	No	FEES and MBSS	Laryngotracheal reconstruction—single or double stage with T tubes	96.7% primary, 3.3% revision
Polubothu et al. [19]	30	No	Questionnaire	Laryngotracheal reconstruction or cricotracheal resection	Not stated
Fandiño et al. [20]	1	No	Not stated	Modified slide tracheoplasty with grafting	100% Primary
Yamamoto et al. [21]	45	No in majority	Not stated	Laryngotracheal reconstruction or partial cricotracheal resection	77.8% primary, 22.2% revision
Provenzano et al. [22]	9	No	Not stated	Slide tracheoplasty for TE fistula repair	100% primary
Yamamoto et al. [23]	129	No in majority	Not stated	Partial cricotracheal resection	86% primary, 14% revision
Hewitt et al. [24]	127	No in majority, when present is transient	Not stated	Slide tracheoplasty	Not stated
Ha et al. [25]	Not stated	Yes	VFSS and FEES	Laryngotracheal reconstruction	Not stated

(Continues)

TABLE 1 | (Continued)

Author	Number included	Presence of dysphagia post treatment	Dysphagia assessment	Procedure	Primary or revision procedures
Thottam et al. [26]	45	Yes if preoperative dysphagia	Clinical swallowing assessments and VFSS	Single stage laryngotracheal reconstruction	100% primary
Stewart et al. [27]	43	Yes	VFSS	Slide tracheoplasty	Not stated
Balakrishnan et al. [28]	Not applicable	Yes	Survey of physicians	Laryngotracheal reconstruction	100% revision
Kou et al. [29]	31	Yes, transient	VFSS and/or FEES	Laryngotracheal reconstruction with posterior grafting	71% primary, 29% revision
Hansen et al. [30]	84	Yes	Not stated	Laryngotracheal reconstruction, single or double stage	100% primary
Kaneko et al. [31]	28	Yes	VFSS	Slide tracheoplasty	100% primary
Chen et al. [32]	120	Yes	Not stated	Slide tracheoplasty	Not stated
Todo et al. [33]	1	Yes	Not stated	Slide tracheoplasty	100% primary
Bhawana et al. [34]	4	No	Not stated	Partial cricotracheal resection	100% primary
Gluvajic et al. [35]	46	Yes, 9%	Not stated	Partial cricotracheal resection, extended LTR	100% revision
Dai et al. [36]	13	No	Not stated	Slide tracheoplasty	100% primary

Abbreviations: FEES, functional endoscopic evaluation of swallowing; SLP, speech language pathologist; VFSS, videofluoroscopic swallow study.

TABLE 2 | Methodological index for nonrandomized studies quality assessment [5]. Criteria are scored 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). For noncomparative studies, an ideal score is 16.

	Criterion								
Study	**Clearly stated aim**	**Inclusion of consecutive patients**	**Prospective data collection**	**Endpoint appropriate to study aim**	**Unbiased endpoint evaluation**	**Appropriate follow-up period for major endpoint**	**Loss to follow-up not > 5%**	**Prospective calculation of study size**	**Total**
Gray et al. [6]	1	2	0	1	0	2	2	0	8
Smith et al. [7]	2	2	0	2	1	1	2	0	10
Stern et al. [8]	1	2	0	0	0	1	2	0	6
Thomé and Thomé [9]	0	2	0	0	0	1	2	0	5
Lang et al. [10]	1	1	0	1	0	2	2	0	7
Younis et al. [11]	2	2	0	1	1	2	2	0	9
Jaquet et al. [12]	2	2	0	2	2	2	2	0	12
Phillips et al. [13]	2	2	0	1	1	2	2	0	10
Miller et al. [14]	2	2	0	1	1	2	2	0	10
Smith et al. [15]	2	2	0	2	2	2	2	0	12
George et al. [16]	2	2	2	2	1	1	2	0	12
Ikonomidis et al. [17]	2	2	0	2	2	2	2	0	12
Andreoli et al. [18]	2	2	0	1	1	2	2	0	10
Polubothu et al. [19]	1	1	1	1	0	1	1	0	6
Fandiño et al. [20]	1	0	0	0	0	1	2	0	4
Yamamoto et al. [21]	1	2	0	1	1	2	2	0	9
Provenzano et al. [22]	1	2	0	1	1	1	2	0	8
Yamamoto et al. [23]	1	2	0	1	1	2	2	0	9
Hewitt et al. [24]	0	0	0	0	0	0	0	0	0
Ha et al. [25]	1	0	0	1	2	0	0	0	4
Thottam et al. [26]	2	2	0	1	1	2	2	0	10
Stewart et al. [27]	2	2	0	2	2	2	2	0	12
Balakrishnan et al. [28]	2	2	0	2	2	2	2	0	12
Kou et al. [29]	2	2	0	1	2	2	2	0	11

(Continues)

TABLE 2 | (Continued)

Study	Criterion								
	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoint appropriate to study aim	Unbiased endpoint evaluation	Appropriate follow-up period for major endpoint	Loss to follow-up not >5%	Prospective calculation of study size	Total
Hansen et al. [30]	1	2	0	1	1	2	2	0	9
Kaneko et al. [31]	2	2	0	1	2	2	2	0	11
Chen et al. [32]	0	2	0	0	0	0	1	0	3
Todo et al. [33]	1	1	0	0	0	0	1	0	3
Bhawana et al. [34]	2	2	0	2	2	2	2	0	12
Gluvajic et al. [35]	1	2	0	1	2	2	2	0	10
Dai et al. [36]	1	2	0	1	2	2	2	0	10

may be related to the preoperative feeding skills. In a key study to determine the benefit of formal preoperative swallow testing, younger age was found to be significantly associated with poorer swallow dysfunction, as was preoperative tracheostomy and having a neurological diagnosis. Preoperative swallow function predicted the post-operative dysphagia outcomes in 80% of children [38], supporting the critical role for this metric in preoperative work up [26, 38]. Preoperative swallow testing and function also allow care teams to plan for post-operative swallow rehabilitation [26].

Other studies suggest that the type of reconstruction impacts the pattern of dysphagia, particularly in cases requiring stenting. Stent placement is known to impact post-operative swallowing, which may improve after removal [7]. Berkowitz reported cricoarytenoid joint fixation after stenting leading to aspiration pneumonia, though on subsequent evaluations vocal cord mobility improved [40]. Miller et al. noted the longest duration of post-operative dysphagia was seen in children requiring staged cricotracheal resection (CTR) with a T tube as well as both anterior and posterior grafting with subsequent T tube placement [14]. Other studies have corroborated the presence of dysphagia and aspiration with T tubes [8, 13]. The type of stent chosen is typically related to the location and severity of the stenosis. However, it is hypothesized that dysphagia is particularly evident when the stent extends into the hypopharynx, as this can limit pharyngeal peristalsis while also limiting airway closure via glottic and supraglottic mechanisms [37].

Another risk for protracted dysphagia is LTR combined with supraglottic procedures. Aspiration improved over a course of days, as patients developed airway protective compensation. Vocal fold lateralization in combination with any other reconstructive procedure was associated with persistent clinically impactful aspiration. The authors concluded that all children undergoing LTR will have dysphagia in the recovery period. The severity is increased in the setting of posterior grafting, when the procedure is staged, and if there are multi-level stenoses being managed concurrently [14].

In addition, the use of a posterior graft has been associated with dysphagia. Younis et al. found posterior grafting can lead to post-operative aspiration via dysfunction of the cricoarytenoid joints [11]. Thomé and Thomé found transient dysphagia with posterior cricoidotomy, grafting, and stent placement for subglottic stenosis, though this quickly resolved [9]. Kou et al. also noted transient dysphagia with posterior grafting, though all children resumed an oral diet on follow-up [29]. The implications of posterior cricoid split with grafting on aspiration were corroborated by Jang et al. [41], who noted improvement, though not resolution, of dysphagia on long-term follow-up.

However, data regarding dysphagia in LTR is mixed. Andreoli et al. noted that 97% of children undergoing LTR maintained or advanced their diet after reconstruction. All patients in the cohort who were feeding orally preoperatively maintained this diet. Of the three patients who required a temporary nasogastric or orogastric tube after the surgery, one failed to progress, requiring gastrostomy tube placement [18]. Richard et al. reported 10% of pediatric patients developed aspiration after endoscopic

posterior costal cartilage graft reconstruction [42]. Similarly, Yamamoto et al. noted post-operative swallow function was normal in only 84% of children [21]. These findings are in contradiction to the aforementioned studies.

It is also important to consider the comorbidities of children requiring LTR. Oftentimes, these children have complex medical histories including prematurity, bronchopulmonary dysplasia, cardiovascular diagnoses, and oral aversions [14]. In these cases, the dysphagia postoperatively may be multifactorial. This further emphasizes the importance of preoperative swallow assessment to establish a baseline, as well as to encourage successful rehabilitation. Similarly, the risk of dysphagia after revision procedures may be higher than in primary reconstructions, as one study noted only 91.1% of children were able to feed orally postoperatively [35].

3.2 | Cricotracheal Resection

CTR is an alternative procedure to manage subglottic stenosis. It is typically reserved for severe stenosis, whereby the anterior cricoid is resected and the trachea is secured to the inferior aspect of the thyroid cartilage to remove the stenotic segment of the airway. As this procedure has gained popularity, long-term outcomes for swallowing are being monitored. Jaquet et al. retrospectively evaluated their cohort of 57 children who underwent this procedure. Nine children had preoperative dysphagia, six of whom required nasogastric feeding. Postoperatively, eight of these children had improvement in swallow function [12]. George et al. evaluated a group of 41 children who underwent CTR. Long-term follow-up was available for 38 children, of whom 36 had normal swallowing. The remaining two patients had occasional coughing with meals due to mild aspiration [16].d Yamamoto et al. provided an update of their database of 129 children who underwent CTR. They report that on follow-up data available for 112 children, swallow function was normal or minimally impaired in 98% of patients [23]. Ikonomidis et al. did not report any long-term aspiration or dietary modification after partial CTR [17]. A recent review of four children requiring CTR noted one child had postoperative aspiration which prevented decannulation. Of the three with normal swallowing at final follow-up, one had transient dysphagia which resolved by the six-week evaluation [34]. Overall, dysphagia is not a prominent feature in CTR, which is also supported by parental and caregiver perception of their children [19].

3.3 | Slide Tracheoplasty

Another reconstructive procedure for airway obstruction in children is slide tracheoplasty. This procedure is typically performed for congenital tracheal stenosis, often in the form of complete tracheal rings. The goal is to expand the diameter of the airway in the narrowed segment by dividing and reconnecting the airway in an orientation that makes the lumen wider but tracheal length shorter. Newer indications for this surgery include high cervical or laryngotracheal anomalies, including a-frame deformities, acquired stenosis, and tracheoesophageal fistulas [43]. The literature regarding post-operative dysphagia after slide tracheoplasty has been mixed.

Lang et al. described two cases of slide tracheoplasty for congenital tracheal stenosis. The authors reported that there was transient dysphagia, but both children were taking an oral diet by the fifth post-operative day. On follow-up at 3 years, both had normal swallow function [10]. Hewitt et al. presented a review of a cohort of 127 children with tracheal stenosis requiring slide repair. The authors report “several children” had transient dysphagia after the surgery, which resolved with time [24]. When used for repair of tracheoesophageal fistula, children who previously were unable to feed orally may tolerate a diet once recovered [22].

One known risk with slide tracheoplasty is injury to the recurrent laryngeal nerves, which control vocal cord movement. When injured, vocal cord immobility or paralysis may result. Kaneko et al. evaluated the incidence of vocal cord paralysis in the setting of slide tracheoplasty. The authors noted that the risk of this adverse outcome was 28.6% and was highest when the child also underwent repair of a concomitant pulmonary artery sling. In these patients, nasogastric feeding was required for longer periods compared to children without cord paralysis [31]. However, Fandiño et al. published a case report of a newborn with stenosis involving the distal trachea, carina, and mainstem bronchi requiring a slide tracheoplasty. Postoperatively, the child did have a vocal cord weakness but did not experience dysphagia [20]. Dai et al. report results of 13 children requiring simultaneous repair of long segment tracheal stenosis with congenital cardiovascular defects. In this series, no child suffered from dysphagia during recovery [36].

Several authors do report clinically significant dysphagia after this procedure. Chen et al. reported 21.7% of their 120-infant cohort developed dysphagia after slide tracheoplasty, supporting systematic and detailed swallow assessments for improved outcomes [32]. In a review of slide tracheoplasty, Richardson et al. reported dysphagia is common and can occur independent of vocal cord immobility [43]. In a case report of a neonate undergoing repair of cardiac defects with a slide tracheoplasty, nasogastric tube feedings were required and continued upon discharge [33]. Stewart et al. found that 70% of children had post-operative dysphagia, with 55% having concern for aspiration. The authors noted the presence of an airway stent was the greatest risk factor for dysphagia. In this study, vocal cord immobility was only seen in two children, indicating the dysphagia was separate from this outcome. At 1-year follow-up, two children had persistent dysphagia requiring a gastrostomy tube and two others maintained a nasogastric tube [27]. Therefore, though the dysphagia was common, it did improve in most children.

Despite the known risk of dysphagia in the perioperative period with any of these reconstructions, data suggest it is safe and beneficial to begin early oral feeding trials, with supervision of speech and language pathologists [15]. Rovo et al. support oral alimentation 2–3 days after extubation from slide laryngotracheoplasty [44]. A review by Ha et al. further supports the role of multidisciplinary evaluation and management of children undergoing LTR for optimal recovery. The authors note that dysphagia can be both physiologic and behavioral, adding to the complexity and nuances in the care of these children [11]. Overall, dysphagia is an important post-operative consideration in the management of children undergoing open LTR. The

literature regarding the incidence of dysphagia in these children is mixed. However, swallow evaluation by a specialist is critical and should be considered as part of the preoperative planning as well as in the early recovery period.

4 | Conclusion

Surgical intervention on the pediatric laryngotracheal complex may contribute to postoperative dysphagia. The data around dysphagia in some procedures are mixed, though in others, they are more consistent. Reconstructive procedures involving posterior grafting and/or stenting are more consistently associated with swallow dysfunction. Though postoperative dysphagia is common, it is typically transient and often predicted by preoperative swallow status. Therefore, formal swallow evaluations before LTR should be strongly considered, both to predict difficulty in the recovery period as well as for rehabilitation planning. Management in a multidisciplinary fashion with speech pathology is preferable, affording the best functional outcomes.

There are several limitations to this review worthy of discussion. Most articles included in this review are retrospective in nature, with inherent limitations to the data from these reports as well as inherent bias. Use of prospective or randomized trials would afford stronger data, though the procedures in question are not amenable to these types of studies. In addition, many of the papers had low patient numbers. Some of these surgeries are more commonly required than others, with different availability for data about long-term outcomes, including dysphagia. Future studies to formally address these questions are needed. Overall, preoperative swallow evaluation and assessment by a speech pathologist are important considerations prior to proceeding with any surgery on the airway. Similarly, repeat testing afterwards should be performed to ensure the best outcomes and early swallow rehabilitation when indicated.

Finally, the lack of high-quality studies on this topic results in several knowledge gaps in the literature. The incidence, risk factors, and long-term outcomes of dysphagia post-reconstruction are not well characterized, with variability in reported rates and a lack of standardized assessment tools. The impact of surgical techniques, graft materials, and staged procedures on swallowing function is poorly understood, limiting the ability to predict and mitigate dysphagia. Additionally, the role of early intervention, multidisciplinary management, and long-term rehabilitation strategies remains underexplored, highlighting the need for prospective studies to optimize functional outcomes in this vulnerable population.

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The authors have nothing to report.

Conflicts of Interest

Romaine F. Johnson is editor-in-chief of *Laryngoscope Investigative Otolaryngology*. He was not involved in the editorial evaluation of or decision to accept this article for publication. Stephen R. Chorney is an educational consultant for Smith & Nephew. The other authors declare no conflicts of interest.

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