

Systematic Review

Esophageal Dilation in Head and Neck Cancer Patients: A Systematic Review and Meta-Analysis

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Objective: To characterize the safety profile and effectiveness of esophageal dilation in head and neck cancer patients.

Methods: A systematic review was undertaken for articles reporting outcomes of esophageal dilation in head and neck cancer patients. The Medline, Scopus, Web of Science, and Cochrane databases were searched in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Complications related to esophageal dilation in head and neck cancer patients was the primary outcome of interest. Success rates, demographic data, cancer staging, and treatment data were assessed secondarily. Statistical analyses included both qualitative and quantitative assessments. A limited meta-analysis and pooling of the data was performed using a random effects model.

Results: Of the collective 8,243 initial candidate articles, 15 retrospective studies containing data for a collective 449 patients were ultimately included in the analysis. There was significant heterogeneity in the outcomes data. With an overall complication rate of 10.6% (95% confidence interval [CI]: 4.1%,17%) and a pooled success rate of 72.9% (95% CI: 65.7%,80.1%) per patient, the articles generally supported the use of dilation.

Conclusion: Head and neck cancer patients experience a higher rate of complications following dilation compared to patients with other causes of benign stricture. Esophageal dilation is effective in improving dysphagia, but these benefits are often transient and thus necessitate repeat interventions.

Key Words: Esophageal, pharyngeal, stenosis, stricture, dilation, head and neck cancer, radiation.

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INTRODUCTION

Esophageal stenosis is one of the more common posttreatment morbidities in head and neck cancer patients. Esophageal stricture is most closely associated with radiation therapy, with which there is a dose-dependent relationship.^{1,2} The incidence of esophageal stricture following head and neck cancer treatment has been reported between 5% and 15%, with varying degrees of functional impairment.^{3,4} As shown by the radiation therapy oncology group (RTOG) 91-11 trial, the addition of chemotherapy to a radiation regimen can accentuate esophageal toxicities.⁵

Dilation is a routinely utilized intervention for patients with symptomatic esophageal stricture who fail

conservative therapies. It can be performed with a variety of instruments, including flexible bougies, balloon dilators, rigid and flexible esophagoscopes, and olive-tip dilators. Although there are several large retrospective series and reviews reporting outcomes of esophageal dilation, there is a paucity of data specifically for the head and neck cancer population.⁶⁻⁹ As such, the safety and efficacy of this intervention in head and neck cancer patients remains poorly characterized.

The purpose of the current study was to perform a systematic review of published articles evaluating outcomes of esophageal dilation in head and neck cancer patients. Our primary goal was to investigate and characterize the complication profile of this intervention.

MATERIALS AND METHODS

Literature Search

This systematic review was performed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (www.prisma-statement.org), which are a standardized and widely utilized criterion for performing effective systematic reviews. Using the search terms, “esophageal OR pharyngeal dilation, head and neck esophageal OR pharyngeal stenosis OR stricture” a query of the Medline, Scopus, Web of Science, and Cochrane databases was performed for articles describing complication rates of esophageal dilation in head and neck cancer patients. The date of the final search was February 1, 2016.

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Figure I: Systematic review flowchart

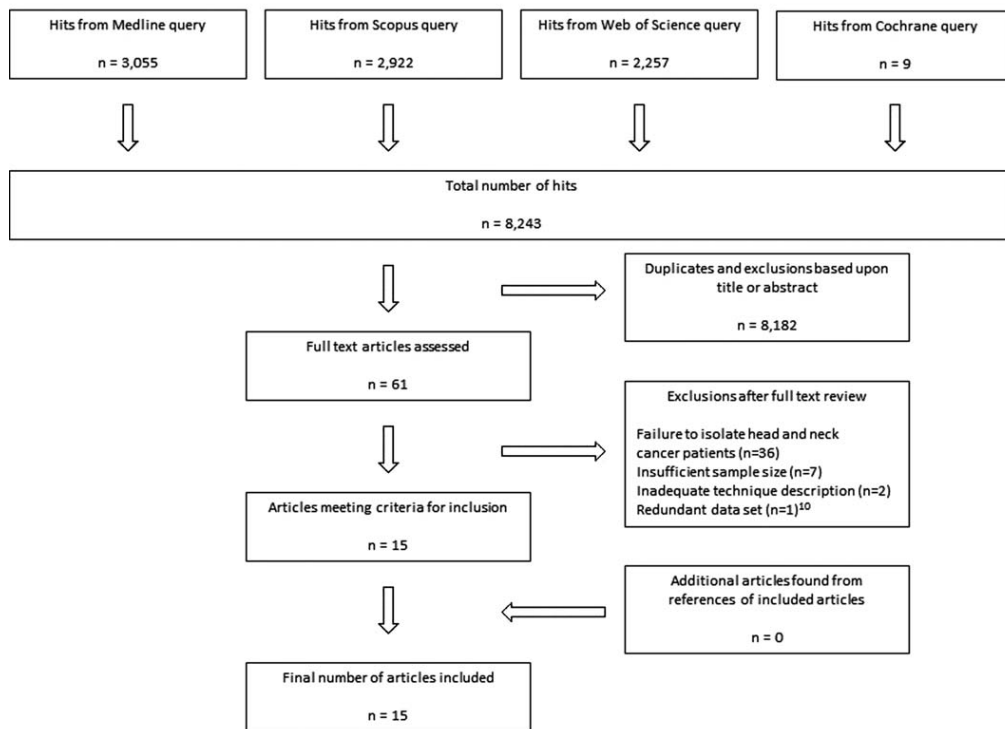


Fig. 1. Systematic review flowchart.

Primary Outcome of Interest

Complications related to esophageal dilation in head and neck cancer patients.

Secondary Outcomes of Interest

Success rates of esophageal dilation in head and neck cancer patients. Demographic, cancer staging, treatment, and other relevant data were also assessed.

Inclusion and Exclusion Criteria

Studies evaluating esophageal dilation in heterogeneous patient populations were assessed if the data particular to a head and neck cancer subgroup could be isolated. Prospective and retrospective studies were considered. Studies that failed to describe the dilation technique were excluded. Pediatric series, foreign language articles, and series with fewer than 10 patients were excluded. Anticipated complications included perforation, bleeding, and infection. Minor complications such as pain, dental trauma, and lip lacerations were not included in the analysis. Success rates of esophageal dilation were analyzed if they were assessed using validated questionnaires.

Data Analysis

The quality of each article was assessed by assigning a score using the methodological index for nonrandomized studies (MINORS).¹⁰ The MINORS criteria represent a validated instrument for assessing nonrandomized studies. Noncomparative studies are assessed in eight domains and comparative studies have an additional four domains. Each domain is scored from zero to 2; therefore, the optimal score is 16 for noncomparative studies and 24 for comparative studies. For the purposes

of this review, a value below 11 was considered to represent a high risk of bias and a value of 11 or greater to represent a low risk of bias.

Statistical analyses included both qualitative and quantitative assessments. A limited meta-analysis and pooling of the data was performed using a random effects model given the variation in the source data. Standard error was estimated as the inverse of sample size. All analyses were performed using STATA IC version 11 (StataCorp LP, College Station, TX).

RESULTS

Study Selection and Overview

The systematic review schema used to identify eligible articles is shown in Figure 1. Two of the authors (W.M, J.P.) independently screened the data and derived the same final list of articles for analysis. Of the 8,243 initial hits, 8,182 were excluded based on title, abstract, or redundancy. Of the 61 unique full-length articles that were reviewed, 36 were excluded due to an inability to isolate outcomes in a head and neck cancer patient subset. An additional seven were excluded due to an insufficient sample size, and two were excluded due to an inadequate description of dilation technique. Following communication with the corresponding authors, one article was excluded because it contained preliminary data that was redundant with a subsequent, larger series.¹¹ Fifteen studies met criteria for analysis following these exclusions. The references sections of these articles were screened, and no additional studies eligible for inclusion

TABLE I.
Summary of Included Studies.

Study and Year	Patients	Dilations	Primary Technique	Other Techniques	Follow-up	Outcome Measure	Success Rate	Complications	MINORS
Dhir ¹² 1996	21	28	Bougie over guidewire 21/21 (100%)	None	2 month min	Dysphagia score 0–5, success defined as score of 0–1	15/21 (71%)	0/21 (0%)	10
Laurell ¹³ 2003	21	NR	Bougie with or without guidewire 14/21 (67%)	Rigid dilation 4/21 (19%)	NR	NG or G-tube removal	14/21 (67%)	1/21 (5%) 1 perforation and death	8
Ahlawat ¹⁴ 2008	24	NR	Bougie over guidewire 23/24 (96%)	Balloon dilators 11/24 (46%)	22 month avg	Dysphagia score 0–5, success defined as score of 0–1	18/24 (75%)	1/24 (4%) 1 hypoxia	11
Harris ¹⁵ 2009	20	45	Balloon over guidewire 20/20 (100%)	None	4 month min	NR	NR	0/20 (0%)	9
Williams ¹⁶ 2009	20	46	Balloon over guidewire 20/20 (100%)	None	6 month min	Dysphagia score 0–4, success defined as score decrease of 1 or more	15/20 (75%)	5/20 (25%) 3 bleeding 1 perforation 1 fistula	9
Ahlberg ¹⁷ 2010	66	NR	Bougie with or without guidewire 63/66 (95%)	Dalloon dilators 5/66 (8%)	NR	NR	NR	1/66 (2%) 1 perforation	9
Dellon ¹⁸ 2010	12	12	CARD with bougie over guidewire 12/12 (100%)	None	NR	Resumption of oral diet	9/12 (75%)	1/12 (8%) 1 perforation	9
Goguen ¹⁹ 2010	45	63	CARD with bougie over guidewire 45/45 (100%)	None	25 month avg	Resumption of oral diet	36/45 (80%)	17/45 (38%) 10 perforations (8 described as “pneumo thorax/mediastinum”) 7 G-tube related	9
Hu ²⁰ 2010	17	41	Balloon over guidewire 17/17 (100%)	None	23 month avg	Dysphagia score 0–4, success defined as score decrease of 1 or more	11/17 (65%)	1 infection 2/17 (12%) 3 perforation	9

TABLE I.
(Continued)

Study and Year	Patients	Dilations	Primary Technique	Other Techniques	Follow-up	Outcome Measure	Success Rate	Complications	MINORS
Fowlkes ²¹ 2012	15	16	CARD with bougie over guidewire 15/15 (100%)	None	13 month avg	Resumption of oral diet	11/15 (73%)	3/15 (20%) 1 air embolization and death 2 G-tube related	9
Tuna ²² 2012	31	NR	Bougie over guidewire 31/31 (100%)	None	26 month avg	Dysphagia score 0-5, success defined as score decrease of 1 or more	26/31 (84%)	1/31 (3%) 1 perforation	9
Chapuy ²³ 2013	89	229	Bougie with or w/o guidewire 89/89 (100%)	None	12 month min	Dysphagia score 0-5 combined with G-tube removal, success defined as score increase of 1 or more	NR	9/89 (10%) 4 perforation (2 with fistula, 1 with epidural abscess) 5 infection	10
Maejima ²⁴ 2014	19	125	Balloon over guidewire 19/19 (100%)	None	15 month avg	Dysphagia score 0-7, success defined as score decrease of 1 or more	15/19 (79%)	2/19 (11%) 1 bleeding requiring transfusion and surgery 1 laryngeal edema requiring tracheostomy	10
Francis ²⁵ 2015	24	276	Balloon over guidewire (NR)	CARD with bougie over guidewire (NR)	21 month avg	Return to unrestricted oral diet	10/24 (42%)	5/24 (21%) 4 perforation 1 bilateral vocal cord paralysis requiring tracheostomy	9
Peng ²⁶ 2015	25	50	Bougie or balloon over guidewire (NR)	CARD with bougie over guidewire (NR)	NR	FOSS score 0-5, success defined as score decrease of 1 or more	22/25 (88%)	0/25 (0%)	10

avg = average; CARD = combined antegrade and retrograde dilation; FOSS = Functional Outcome Swallowing Scale; min = minimum; MINORS = methodological index for nonrandomized studies; NR = not reported.

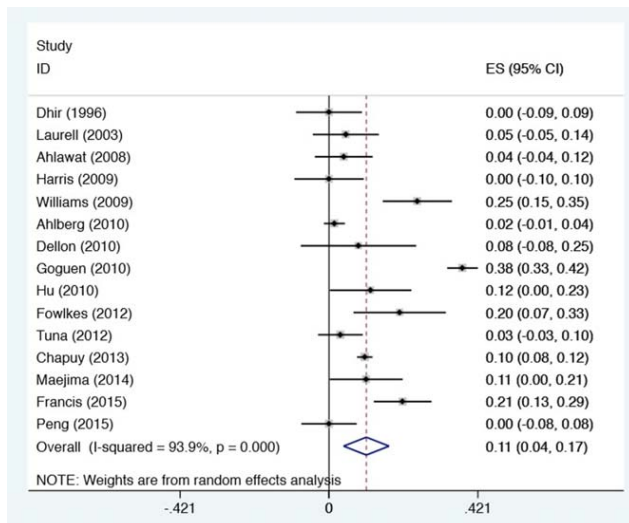


Fig. 2. Forest plot of complications per patient. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

were found, thus giving a final total of 15 publications for review. Data for 449 head and neck cancer patients treated for esophageal stricture were reported collectively.

The included studies are summarized in Table I.^{12–26}

All studies were retrospective, and most reported outcomes of standard anterograde dilations using bougie or balloon dilators with or without guidewires. Some studies reported outcomes of combined anterograde and retrograde dilation (CARD), a technique used in patients with total obstruction.^{18,19,21,25,26} The largest series reported outcomes in 111 patients (89 underwent anterograde dilation, 22 underwent CARD).²³ In another study, the same authors reported outcomes in 45 CARD patients, some which were redundant.¹⁹ As such, the smaller subset of CARD data was excluded from the larger study. The included studies had a MINORS score ranging from 8 to 11, suggesting a moderate risk of bias overall.

Complications

As shown in Figure 2, the overall complication rate per patient was estimated to be 10.6% (95% confidence interval [CI]: 4.1%, 17.0%). The perforation rate per patient was estimated to be 5.4% (95% CI: 1.4%, 9.4%). Per dilation, a complication rate of 7.4% (95% CI: 0.0%, 14.7%) was estimated. A pooled complication rate of 4.4% (95% CI: 0.0%, 10.6%) for patients undergoing a standard anterograde dilation was estimated. For patients undergoing CARD, the complication rate was found to be much higher at 23.3% (95% CI: 4.9%, 41.7%). A comparison between subgroups was precluded by a high degree of heterogeneity and wide CIs. Perforations accounted for roughly half of the complications reported.

Success Rate

As shown in Figure 3, the overall success rate per patient was estimated to be 72.9% (95% CI: 65.7%,

80.1%). All but three studies reported objective assessments of functional outcomes. The data suffered from significant heterogeneity, as noted by the wide CI and high I^2 value (88.4%). Most studies employed a numerical scale corresponding to the consistency of food tolerated. Some studies defined success as any improvement in a dysphagia score, whereas others were more stringent and defined success as a return to a normal or near normal diet. Other authors assessed rates of nasogastric and gastric tube removal.

Demographic, Cancer Staging, Treatment, and Other Data

The average patient age was 60 (range 21–89) years, and there was a near 3:1 male predominance (232:87, 73%:27%).^{12–26} Cancer staging and treatment data were reported variably (Fig. 4). Eleven studies reported primary tumor sites for a collective 318 patients: 46% oropharyngeal/hypopharyngeal, 27% laryngeal, 6% oral cavity, and 6% unknown primary.^{12,14,15,18,20–26} The remaining 15% comprised a collection of less common sites including the nasopharynx, thyroid, trachea, and cervical esophagus. Three studies reported tumor (T) stages and overall stages for a collective 139 patients: T4 11%, T3 27%, T2 28%, T1 23%, and T0 11%.^{15,21,23} Overall stages were dominated by advanced disease: IV 62%, III 28%, II 9%, and I 1%. Eleven studies reported cancer treatment data for a collective 315 patients: 53% received chemoradiation; 22% received surgery and chemoradiation; 14% received surgery and radiation; 6% received radiation alone; and 5% received surgery alone.^{12,14,15,18,20–26} Almost all patients received radiation as part of their treatment (300 of 315, 95%).

Although not always reported, patients routinely required repeat intervention (194 of 306, 63%), adding to the heterogeneity of the data.^{12,14,15,17,20,22–24} Collectively, each patient underwent a mean of three dilations (931 dilations of 306 patients = 3.04).^{12,15,16,18–21,23–26} Of note, this rate varied significantly between studies, with

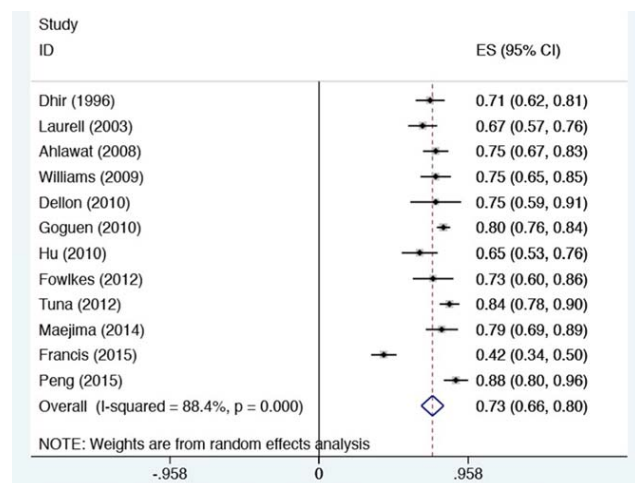


Fig. 3. Forest plot of success rate per patient. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

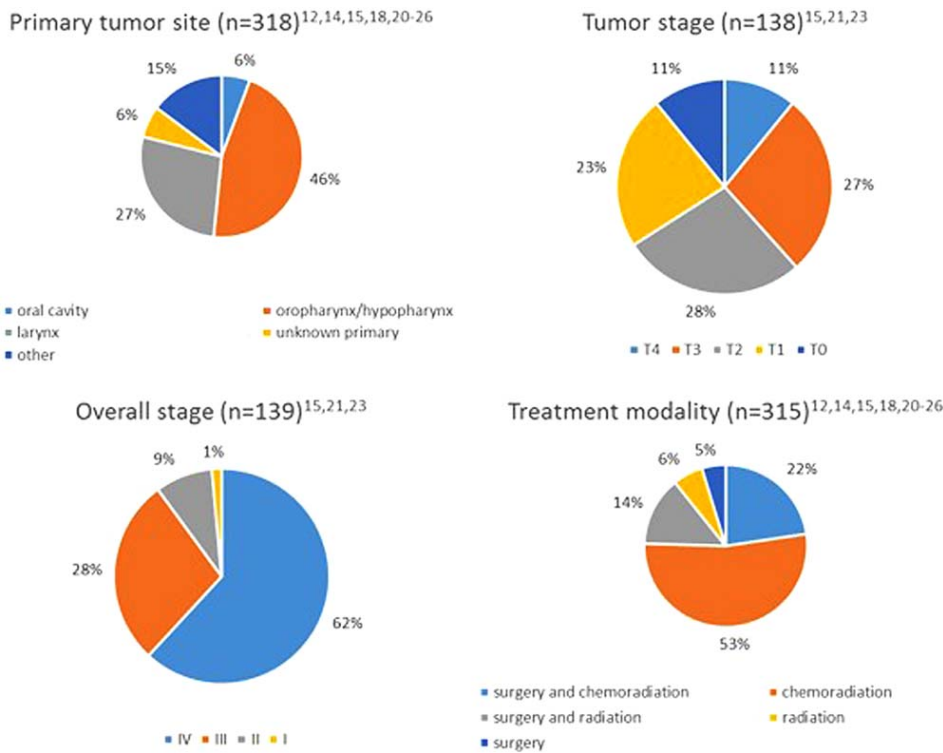


Fig. 4. Cancer staging and treatment data. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

*Reference numbers denote studies from which the corresponding data set was derived

Dellon reporting one dilation per patient and Francis reporting over 10 per patient on average.^{18,25}

DISCUSSION

A number of prior studies have reported lower rates of complications in patient undergoing esophageal dilation who do not have a head and neck cancer history. In 1992, Tucker reported esophageal dilation outcomes in 300 patients, with predominantly benign disease such as peptic strictures and Shatzki's rings.⁶ These patients underwent a total of 1,177 dilations with bougie, balloon, and olive-tip dilators. Tucker reported only two complications—one perforation and one episode of bleeding—thus yielding complication rates of 0.6% per patient and 0.2% per dilation. In 2008, Piotet et al. reported the results of 1,862 esophageal dilations using a bougie-over-guidewire technique.⁷ Of the 1,071 patients with benign strictures, peptic and iatrogenic strictures were the most common types, with postradiation strictures representing just 12% of the benign subgroup (data for this subgroup could not be isolated). The authors reported complications in two of 1,071 of these patients (one episode of bleeding, one perforation and death), a complication rate of 0.18%. Other studies have reported much higher complication rates for esophageal dilation of benign stricture. In 2011, Fan et al. reported on perforation rates following balloon dilation in 589 patients with benign stenosis.⁸ Of the 1,421 dilations performed, 209 resulted in perforation, for a perforation rate per

procedure of 14.7%. Notably, of all stricture types, radiation-induced strictures had the highest perforation rate per procedure (21 per 86 (24%)). This was markedly higher than the perforation rate for nonradiation-induced strictures (188 per 1335 (14%)).

In contrast to patients with a more focal stricture, such as an esophageal web or iatrogenic stricture, head and neck cancer patients treated with radiation often develop posttreatment changes of long segments of the aerodigestive tract. This fibrotic, devascularized, and inelastic tissue is likely more prone to microscopic tearing and full-thickness perforation relative to an otherwise healthy esophagus. Head and neck cancer patients often have multiple medical comorbidities, which may further predispose them to adverse events. The association of esophageal stenosis with radiation therapy merits consideration in the current setting of renewed interest in primary surgery for early stage oropharyngeal and laryngeal cancers. Transoral laser and robotic techniques have been shown to have comparable success rates and often obviate the need for radiation therapy and its associated toxicities.²⁷ Even when postoperative radiation is used, it often is given at a lower dose than primary radiation, which may result in a lower rate of esophageal stricture.

Importantly, the majority of complications reported in this review were not catastrophic and resolved with conservative measures. With an overall success rate of 72.9%, esophageal dilation in head and neck cancer patients can be considered an effective treatment. Improvement often is

transient, however, because many patients require repeat dilation to maintain patency and swallowing.

This review is limited in a variety of ways. Firstly, all of the included studies are retrospective reviews and thus carry the risk of data inaccuracies and selection bias. Between institutions, there likely are different thresholds for when to classify milder adverse events as true complications. Although the degree of stricture always was reported for CARD patients (total obstruction), the severity of stenosis for patients undergoing anterograde dilations was not always classified, which may confound comparisons of safety and effectiveness likely contributing to the marked heterogeneity. The comparison of functional success between the studies also is limited by the variability in how this was reported. Although the source data was quite heterogeneous with high I^2 values, the estimates provide a quantitative assessment for patient counseling. Further prospective investigation comparing the safety, effectiveness, timing, and cost of different dilation techniques would be of benefit to physicians treating esophageal stricture in head and neck cancer patients.

CONCLUSION

Head and neck cancer patients experience an increased rate of complications following dilation of esophageal strictures compared to patients with other causes of benign stricture. Overall, the safety profile is acceptable, and most patients will experience benefit from the dilation procedure. This benefit is often transient, requiring repeat interventions.

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