



## Dilation after laryngectomy: Incidence, risk factors and complications<sup>☆</sup>

Japke F. Petersen<sup>a,1</sup>, Thomas F. Pézier<sup>b,1</sup>, Jolanda M. van Dieren<sup>c</sup>, Vincent van der Noort<sup>d</sup>, Tom van Putten<sup>b</sup>, Sandra I. Bril<sup>b</sup>, Luuk Janssen<sup>b</sup>, Richard Dirven<sup>a</sup>, Michiel W.M. van den Brekel<sup>1a,e,f,\*</sup>, Remco de Bree<sup>b</sup>

<sup>a</sup> Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, the Netherlands

<sup>b</sup> Department of Head and Neck Surgical Oncology, University Medical Center Utrecht, Utrecht, the Netherlands

<sup>c</sup> Department of Gastrointestinal Oncology, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, the Netherlands

<sup>d</sup> Biometrics Department, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, the Netherlands

<sup>e</sup> Institute of Phonetic Sciences, University of Amsterdam, Spuistraat 134, 1012 VB Amsterdam, the Netherlands

<sup>f</sup> Department of Oral and Maxillofacial Surgery, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands



### ARTICLE INFO

#### Keywords:

Larynx cancer  
Total laryngectomy  
Dilation  
Radiotherapy  
Chemoradiation  
Pharyngeal stenosis

### ABSTRACT

**Background:** Neopharyngeal stenosis is a recognized sequela of total laryngectomy (TL). We aim to investigate the incidence of stenosis requiring dilation, risk factors for stenosis and complications of dilation.

**Methods:** Retrospective cohort study of patients undergoing TL in two dedicated head and neck centers in the Netherlands.

**Results:** A total of 477 patients, (81% men, median age of 64 at TL) were included. Indication for TL was previously untreated primary tumor in 41%, salvage following (chemo)radiotherapy (CRT) in 44%, dysfunctional larynx in 9% and a second primary tumor in 6%. The cumulative incidence of dilatation at 5 years was 22.8%, and in total 968 dilatations were performed. Median number of dilatations per patient was 3 (range 1–113). Female gender, a hypopharynx tumor, and (C)RT before or after the TL were significantly associated with stenosis requiring dilation. We observed 8 major complications (0.8%) predominantly during the first dilation procedures. Use of general anesthesia is a risk factor for complications. The most frequent major complication was severe esophageal perforation (n = 6 in 5 patients).

**Conclusion:** The cumulative incidence of pharyngeal stenosis needing dilation was 22.8% at 5 years. Roughly half of these patients could be treated with a limited number of dilatations, the rest however needed ongoing dilatations. Major complications are rare (0.8%) but can be life threatening. General anesthetics is a risk factor for complications, and complications occurred predominantly during the first few dilatations procedures. This should alert the physician to be extra careful in new patients.

### Introduction

Total laryngectomy (TL) with or without (partial) pharyngectomy and adjuvant radiotherapy (RT) is often recommended for bulky advanced stage cancer of the larynx or hypopharynx whilst less bulky disease is often treated with (chemo)radiotherapy (CRT) for organ preservation [1–5]. However, despite initial organ preservation, TL is subsequently still performed in roughly a third of advanced stage patients, either as salvage procedure for a recurrence, treatment of a second primary or for functional reasons [6–8].

Rehabilitation following TL largely focuses on speech rehabilitation. Most Western countries use indwelling voice prostheses (VP) and with this, up to 90% of patients achieve satisfactory speech [9,10]. Less attention however is paid to swallowing function after TL. The majority of patients are expected to return to a normal diet, but some find that swallowing becomes difficult [11,12]. This can be due to anatomical reasons such as narrowing of the neopharyngeal lumen (a lumen < 12 mm invariably leads to dysphagia [13]), pseudo-diverticulum formation [14], or due to functional problems changes in the quality/quantity of saliva, poor pressure built up at the base of tongue or loss of

<sup>☆</sup> This manuscript has been presented at the 6th World congress of the International Federation of Head and Neck Oncologic Societies in Buenos Aires, Argentina, September 2018 and at the Dutch ENT association meeting, November 2018.

\* Corresponding author at: Plesmanlaan 121, 1066 CX Amsterdam, the Netherlands.

E-mail address: [m.vd.brekel@nki.nl](mailto:m.vd.brekel@nki.nl) (M.W.M. van den Brekel).

<sup>1</sup> Japke F. Petersen and Thomas F. Pézier contributed equally to this manuscript.

<https://doi.org/10.1016/j.oraloncology.2019.02.025>

Received 5 November 2018; Received in revised form 12 February 2019; Accepted 23 February 2019

Available online 06 March 2019

1368-8375/ © 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

coordinated muscular contraction in the neopharynx. Rates of anatomical pharyngeal stenosis have been reported as high as 33% in surgically treated patients [15] and over 50% in patients treated with CRT [16]. Severe dysphagia negatively affects patients' quality of life and can lead to nutritional deficiencies and increased healthcare costs [17].

The diagnosis of dysphagia is almost entirely from the patient's self-reported symptoms and the threshold for intervention depends on whether a patient's nutritional status is affected and/or their perceived quality of life. Stepwise interventions can involve dietary advice/modification, the use of supplementary nutritional drinks, dental rehabilitation, proton pump inhibitors, tube feeding, dilation or surgical reconstruction of the neo-pharynx.

Not all patients with dysphagia are suitable for dilation. Some patients have no clear radiographic or endoscopic evidence of a stricture. In these patients it is thought that the dysphagia is more "functional/physiological" than "anatomical" [18,19]. Other patients have clear radiographic evidence of a diverticulum or pseudo-epiglottis [20] which is also not amenable to dilation.

Dilation for benign esophageal strictures caused by inflammation of the esophagus or post-operative stenosis of the anastomosis after esophagectomy is reported to be highly successful [13,21–23]. However, among TL patients who are often treated with chemo-radiotherapy before or after the TL and thereby represent a distinct patient group, only small case series have described the effect of dilation procedures in this group of patients [24].

In this paper we aim to investigate in a cohort of patients having undergone TL:

1. The cumulative incidence of pharyngeal stenosis requiring dilation
2. Risk factors for stenosis requiring dilation
3. The incidence and risk factors for complications following dilation

## Materials and methods

We performed a retrospective cohort study of all patients undergoing total laryngectomy in two dedicated Head and Neck Centres in The Netherlands: the University Medical Center Utrecht, Utrecht (Jan 2008–Dec 2016) and The Netherlands Cancer Institute, Amsterdam (Jan 2000–Dec 2012). Patients' demographic, staging, treatment and outcome data were collected using (scanned) electronic patient records. We recorded TNM classification according to the then applicable AJCC manual, (5th, 6th and 7th editions). All patients underwent total laryngectomy with or without (partial) pharyngectomy either as a primary treatment, salvage treatment, treatment for a second primary or as a functional treatment for a dysfunctional larynx. TLs were performed by a variety of surgeons during the study period and details on the surgical techniques could not be found in all patients. Specifically, myotomy of the cricopharyngeal muscle and neurectomy of the pharyngeal plexus, as well as the method of closure (vertical, T, horizontal, suture type, stitch type) were not well documented and differed between surgeons.

For each dilation procedure we recorded the maximum size of dilation (in mm), type of dilator, type of anesthetic, which physician group performed the dilation (head & neck surgeons or gastroenterologist) and whether any complications occurred. We excluded dilation procedures where the stenosis was due to tumor recurrence. Complications following dilation were grouped into minor or major. Major complications were defined as complications for which the patient had to be admitted to the ward for > 24 h and received medical treatment other than analgesics, antiemetics, and antipyretics. Minor complications were defined as complications which resolved within < 24 h after dilation, for which no medical treatment was necessary (other than replacement of a dislocated voice prosthesis).

### Dilation technique

In our institutes, dilation is performed either by a gastroenterologist

or a head and neck surgeon. The gastroenterologist generally uses procedural sedation (using a combination of fentanyl and midazolam or propofol) whereas the head and neck surgeon dilates under general anesthesia. The gastroenterologists routinely use a flexible endoscope to inspect the esophagus and stomach and place a guidewire for Savary bougies (Savary Gilliard technique [13]). The head and neck surgeons use the same bougies but without placing a guidewire and generally visualize only the upper esophagus with a rigid oesophagoscope. For both physician groups, the stenosis is dilated by passing bougies of increasing diameter through the stenosis until either the maximum diameter is reached (18 mm) or until too much resistance is felt by the operator. Whilst achieving small mucosal tears is necessary to treat the stenosis, an esophageal perforation is a well-known major complication of this procedure that has to be avoided.

### Statistical analysis

Statistical analyses were performed using SPSS® Statistics 20.0 (IBM, Armonk, NY) and R studio. Descriptive analysis was used to summarize patient and treatment characteristics. We used a cumulative incidence technique to assess the effect (expressed as a hazard ratio) of patient and treatment characteristics on dilatation, which is a time dependent outcome, using the R-package 'cmprsk' [25]. Death was treated as a competing risk and patients were censored when lost-to-follow-up. The same technique was used to assess the cumulative incidence of dilatation with death as a competing risk. To calculate the cumulative incidence, we used time in days since TL to date of first dilatation procedure.

Using this technique we performed univariate and multivariate regression analyses to identify patient and treatment characteristics that correlate with the patient having a dilation. Odds ratios on a complication following a dilatation procedure, which was not considered time dependent, were calculated using univariate and multivariate logistic analyses.

### Ethical considerations

This study does not fall under the scope of the Medical Research Involving Human Subjects Act and the institutional review boards of both centers approved this study.

## Results

### Patients

A total of 477 patients (81% men) with a median age at TL of 64 (range 38–91) were included in this study. Median follow-up time in months since TL was 81 months (95% CI 69–96). Indication for TL was salvage surgery in 211 (44%), primary surgery in 193 (41%), a dysfunctional larynx in 45 (9%) and second primary tumor in 28 (6%), see Table 1 for patient characteristics.

### Dilations

In our cohort 111/477 (23%) patients underwent a total of 968 dilations for symptomatic pharyngeal stenosis. The cumulative incidence of dilatation (with death as a competing risk) increased over time. At 5, 10 and 15 years this was respectively 22.8%, 26.5% and 29.0%, see Fig. 1 for a plot of the cumulative incidence. The median number of dilations performed per patient was 3 (range 1–113). Median time to first dilation was 9 months after TL (95% CI 7–11). Twenty-seven (27/111 = 24%) patients underwent one dilation, 23 (21%) required two dilations, 13 (12%) three dilations and the remaining 48 patients (43%) had more than 3 dilations.

The gastroenterologists performed 91% of all dilations, 9% was performed by the head and neck surgeons, though there was

**Table 1**  
characteristics of dilation vs. non-dilation groups and univariable analysis presented in adjusted hazard ratios\* with corresponding p-values.\*\*

	Total N (%)	Non-dilation group N (%)	Dilation group N (%)	Univariate analysis, OR (95% CI)	P value
Mean age at TL (SD)	64 (10.0)	64 (10.2)	64 (9.4)	1.00 (0.98–1.02)	0.890
Gender					
Male	385 (81)	306 (84)	79 (71)	1.00	
Female	92 (19)	60 (16)	32 (29)	1.87 (1.24–2.81)	<b>0.003</b>
Tumor site					
Larynx	344 (72)	277 (76)	67 (60)	1.00	
Hypopharynx	98 (21)	66 (18)	32 (29)	2.06 (1.34–3.15)	< <b>0.001</b>
Other	35 (7)	23 (6)	12 (11)	1.86 (0.98–3.55)	0.057
Initial T-stage					
T1s/T1	71 (15)	52 (14)	19 (17)		
T2 (vsT1)***	106 (22)	79 (22)	27 (24)	1.106 (0.60–1.87)	0.84
T3 (vsT2)	102 (21)	81 (22)	21 (19)	0.74 (0.42–1.32)	0.31
T4 (vsT3)	189 (40)	149 (41)	40 (36)	1.01 (0.59–1.72)	0.99
Unknown	9 (2)	5 (1)	4 (4)	–	–
Initial N-stage					
N0	294 (62)	234 (64)	60 (54)	1.00	
N positive	178 (37)	129 (35)	49 (44)	1.46 (1.00–2.13)	0.050
Unknown	5 (1)	3 (0.8)	2 (1.8)	–	–
Indication TL					
Primary	193 (41)	158 (43)	35 (32)	1.00	
Salvage	211 (44)	167 (46)	44 (40)	1.24 (0.80–1.94)	0.34
2 <sup>nd</sup> primary	28 (6)	14 (4)	14 (13)	2.90 (1.62–5.19)	< <b>0.001</b>
Dysfunctional	45 (9)	27 (7)	18 (16)	2.70 (1.54–4.72)	< <b>0.001</b>
Neck dissection during TL					
None	183 (38)	137 (37)	46 (41)		
Unilateral (vs None)***	142 (30)	111 (30)	31 (28)	0.92 (0.59–1.45)	0.73
Bilateral (vs Unilateral)	152 (32)	118 (32)	34 (31)	0.94 (0.58–1.53)	0.81
Primary puncture					
No	65 (14)	48 (13)	17 (15)	1.00	
Yes	412 (86)	318 (87)	94 (85)	0.78 (0.47–1.32)	0.36
(Chemo)radio-therapy					
Never	56 (12)	53 (15)	3 (3)	1.00	
Before TL	310 (65)	227 (62)	83 (74)	5.42 (1.71–17.2)	<b>0.004</b>
After TL	104 (22)	82 (23)	22 (20)	3.69 (1.10–12.4)	<b>0.035</b>
Before and after TL	7 (1.5)	2 (0.5)	5 (4)	19.29 (5.04–73.8)	< <b>0.001</b>
Flap type					
None	295 (62)	240 (66)	55 (49)	1.00	
PM to reconstruct	105 (22)	71 (20)	34 (30)	1.99 (1.30–3.04)	<b>0.002</b>
PM to overlay	24 (5)	18 (5)	6 (5)	1.48 (0.65–3.38)	0.350
FRFF	14 (3)	8 (2)	6 (5)	2.80 (1.17–6.72)	<b>0.021</b>
ALT	13 (3)	8 (2)	5 (4)	2.39 (0.97–5.87)	0.057
Gastric pull up	10 (2)	7 (2)	3 (3)	1.60 (0.50–5.18)	0.43
Other	8 (2)	7 (2)	1 (0.9)	0.81 (0.10–6.45)	0.84
Unknown	8 (2)	5 (1)	3 (3)	–	–
Post-operative clinical fistula < 30 days after TL					
None	347 (73)	275 (75)	72 (65)	1.00	
Yes	126 (26)	87 (24)	39 (35)	1.68 (1.14–2.48)	<b>0.009</b>
Unknown	4 (0.8)	4 (1)	–	–	–

\* Hazard ratios are calculated using a cumulative incidence technique using (time to) dilatation or death as competing events. Hazard ratios shown here are hazard ratios on first dilatation procedure.

\*\* Bold faced p-values are significant.

\*\*\* In the univariate analysis the ordinal variables T-classification and type of neck dissection were compared with the nearest lower category to assess the effect of 1 higher stage (T3 versus T2, etc.)

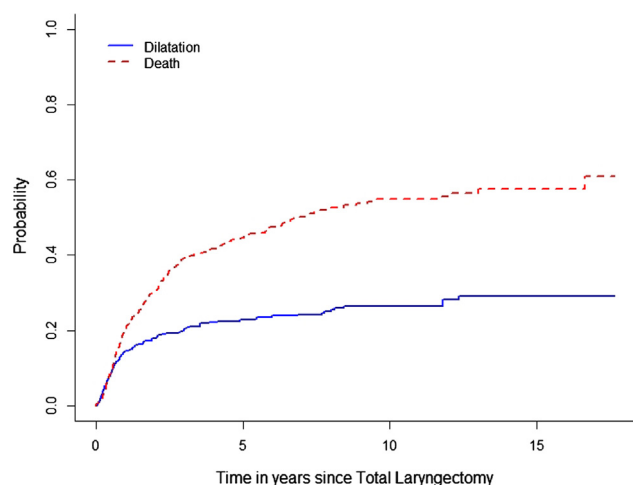
considerable cross-over with patients being dilated by both types of specialists. On a patient level, 43 patients (39%) underwent their first dilatation procedure by the head and neck surgeon. Of these 43 patients, 13 patients were also dilated by the gastroenterologists at a later time point. Of the 68 patients who were initially dilated by gastroenterologists, 8 patients were also dilated by the head and neck surgeon at a later time point.

The stenosis was dilated to a mean maximal diameter of 13 mm (range 6–18 mm) which was similar among dilatation procedures by the head and neck surgeons and gastroenterologists. All patients were dilated using silicon bougie dilators. In 67% of procedures a combination of fentanyl and midazolam for sedation was used, in 18% propofol, 8% was performed under general anesthetics and in 7% the type of sedation was not reported. One patient performed self-dilatations at home. Because the frequency and complication rate of these dilatations were unknown, we did not include these dilatations in our analysis.

#### Risk for stenosis requiring dilatation

We performed a univariate analysis to assess risk factors for dysphagia requiring dilatation using the cumulative incidence technique described in the methods section (see Table 1). Statistically significant variables on univariate analysis included female gender, a hypopharynx tumor (ref = larynx), TL for a dysfunctional larynx or for a second primary (ref = primary TL), (C)RT before, after or before and after TL (ref = no (C)RT), a pectoralis major (PM) flap to reconstruct a mucosal defect (i.e. not as overlay reinforcement), a free radial forearm flap (FRFF (ref = no flap)), and the development of a pharyngo-cutaneous fistula < 30 days after TL.

We subsequently performed a multivariate analysis including the parameters that showed significant interaction with stricture formation on univariate analysis. Using a binary logistic backwards regression model the following parameters remained statistically significantly



**Fig. 1.** Cumulative incidence of dilatation. The X-axis depicts the time in years since total laryngectomy, the Y-axis depicts the cumulative probability on a dilatation procedure (blue straight line) or death (red, dashed line). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

**Table 2**

Multivariate analysis demonstrating adjusted hazard ratio for development of stricture formation necessitating dilatation after total laryngectomy.\*

	HR (95% CI)	P-value
Gender		
Male	1.00	
Female	1.87 (1.20–2.91)	<b>0.006</b>
Tumor site		
Larynx	1.00	
Hypopharynx	2.12 (1.34–3.35)	<b>0.001</b>
Other	1.37 (0.61–3.08)	0.38
Indication TL		
Primary TL	1.00	
Salvage TL	0.80 (0.69–2.61)	0.43
2nd primary	1.42 (0.67–3.01)	0.36
Afunctional	1.42 (0.71–2.84)	0.32
(Neo-)adjuvant (Chemo)radiotherapy		
Never	1.00	
Before TL	6.13 (1.86–20.22)	<b>0.003</b>
After TL	3.65 (1.06–12.60)	<b>0.04</b>
Before and after TL	25.09 (5.76–109.35)	<b>&lt; 0.0001</b>

\* Hazard ratios are calculated using a cumulative incidence technique using (time to) dilatation or death as competing events. Hazard ratios shown here are hazard ratios on first dilatation procedure.

associated with stricture formation necessitating dilatation: female gender (HR 1.87,  $p = 0.006$ ), a hypopharynx tumor (ref = larynx) (HR 2.12,  $p = 0.001$ ), (C)RT before TL (HR 6.13,  $p = 0.003$ ), (C)RT after TL (HR 3.65,  $p = 0.04$ ), and (C)RT before as well as after the TL (HR 25.09,  $p < 0.0001$ ) (ref = no (C)RT) (see Table 2).

**Complications following dilatation**

On a procedure level we observed 27 complications during the 968 dilations (2.8%), of which 19 minor (2.0%) and 8 major (0.8%). On a patient level, 7 patients (6%) suffered 8 major complications.

The major complications were: anaphylactic shock caused by NSAIDs taken before the dilatation procedure ( $n = 1$ ), a voice prosthesis dislodged into the bronchus causing severe cardiac stress, intensive care stay and a Tsako-Tsubo cardiomyopathy ( $n = 1$ ) and transmural esophageal perforations ( $n = 6$  in 5 patients).

Two proximal perforations caused leakage laterally to the carotid artery ( $n = 1$ ) and leakage posteriorly to the pre-vertebral space ( $n = 1$ ). The former developed a pharyngo-cutaneous fistula which was

managed conservatively with wound dressings. The latter underwent multiple surgeries including stabilization of the vertebral column by the spinal surgeons. One distal perforation required intensive care admission ( $n = 1$ ) and another distal perforation necessitated laparotomy ( $n = 1$ ) and direct repair. One patient suffered two major complications at dilatation number 1 and 2, both involving proximal perforations which could be managed conservatively.

Five of the 8 major complications occurred in the first or second dilatation procedure of this patient. The other three occurred during respectively the 8th, 12th and 31st dilatation procedure. Of note, two of these “late” complications were unusual in that one was a distal esophageal perforation in a patient with a hiatus hernia and one was the dislodged voice prosthesis. We observed only one ‘late’ proximal esophageal perforation in a patient during his 31st dilatation.

Minor complications were: loss of voice prosthesis during dilatation or < 24 h due to edema ( $n = 6$ ), suspected mucosal tear/hematemesis for which the patient was observed but that resolved spontaneously < 24 h after dilatation ( $n = 7$ ), edema temporarily worsening dysphagia ( $n = 3$ ), fever with unknown cause which resolved < 24 h after dilatation ( $n = 1$ ), exacerbation COPD ( $n = 1$ ) and transient but significant desaturation during the procedure without any further consequences ( $n = 1$ ).

**Risk factors for complications**

We performed a univariate analysis to assess risk factors for major complications. The following variables were entered into univariate analysis: age, gender, T-stage, N-stage, tumor localization, indication for TL, (C)RT pre- or post TL, clinical fistula after TL, flap reconstruction, maximum size of bougie used (6–12 mm, 12.5–14 mm or 14.5–18 mm), dilatation performed by head and neck surgeon or gastroenterologists, type of anesthetic used, and first dilatation versus subsequent dilatation. The following variables were significantly related to a higher risk on a major complication: first dilatation procedure (OR 4.7, 95% CI 1.12–20.1,  $p = 0.04$ ), general anesthetic (OR 9.15, 95% CI 1.81–46.10,  $p = 0.007$ , ref = other anesthetics (fentanyl, midazolam) and dilatation performed by the head and neck surgeon (OR 5.95, 95% CI 1.40–25.30,  $p = 0.016$ , ref = gastroenterologist).

We subsequently entered the variables into a multivariate analysis, except for type of physician. Since only head and neck surgeons perform dilations under general anesthesia, these two variables are overlapping, thus the variable type of physician was barred from entering the multivariate model. Using a binary logistic backward regression model, only a dilatation procedure under general anesthetics remained significantly associated with a higher risk on a major complication (OR 9.15 95% CI 1.81–46.10,  $p = 0.007$ ).

**Gastric pull-up**

During follow-up, two patients with symptomatic stenosis underwent a gastric pull up reconstruction of the stenotic segment following failed dilations. One of the patients suffered a heart attack intra-operatively and died, the other made an unremarkable recovery although his swallowing function remained impaired, as the jejunostomy tube could not be removed.

**Discussion**

In this consecutive cohort of 477 patients who underwent a laryngectomy, almost a quarter of all patients underwent one or more dilations for dysphagia, with a median of 3 procedures per patient. The cumulative incidence of dilatation increased over time from 22.8% at 5 years to 29% 15 years after TL. Risk factors for dysphagia requiring dilatation were female gender, a hypopharynx tumor, and (chemo) radiotherapy before or after TL. On a procedure level, we observed a major complication rate of 0.8%, which was significantly higher among



patients dilated under general anesthesia.

#### *The incidence of pharyngeal stenosis requiring dilation*

The cumulative incidence of 22.8% requiring dilation at 5 years means that dysphagia is one of the most common sequela of a TL [26]. Indeed, other studies found (dilation and non-dilation necessitating) rates of dysphagia as high as 50–72% after TL [18] and stricture formation rates of 13–50% [27–32]. Due to the retrospective nature of the cohort, we were unable to reliably evaluate the incidence of dysphagia not necessitating dilation. Therefore, the actual incidence of dysphagia in our cohort is probably higher.

#### *Risk factors for stenosis requiring dilation*

Not surprisingly, (C)RT before or after the TL was the most important risk factor for dysphagia requiring dilation besides female gender and a hypopharynx tumor. Dysphagia as a complication after CRT for head and neck cancer has been described by Kraaijenga et al. in a long term follow-up study. In their cohort, at a median follow-up time of 11 years, 54% had moderate to serious swallowing problems, and 14% was still tube feeding dependent [16]. In another retrospective study of 199 patients receiving CRT mainly for T3/T4 larynx, hypopharynx and oropharynx cancer, 21% of patients developed symptomatic strictures. Similarly to our data set, risk factors for stricture formation in their cohort were female gender and a hypopharynx tumor, but also patients receiving twice daily radiotherapy showed an increased risk for stenosis [33].

In our cohort, patients were laryngectomized in the time period 2000–2016 and received RT before (66%) or after (22%) the TL. Only 12% was not treated with RT. Given the time frame in which patients were included and the fact that patients might have had radiotherapy several years before their TL, patients in this cohort were treated with several different radiotherapy techniques. Details regarding type of radiotherapy and dosage were missing not at random, rendering an analysis based on radiotherapy details impossible. The incidence of dysphagia and the necessity for dilations in future patients treated with IMRT or VMAT might be lower as this technique aims to spare organs at risk [34]. Christianen et al. recently demonstrated how swallowing sparing IMRT (SW-IMRT) with dose constraints for both parotid glands and the swallowing organs at risk, can indeed lead to reduced swallowing dysfunction 6 months after completion of treatment [35]. It is however important to note that also preventive swallowing therapy and a dedicated rehabilitation program following (C)RT might further decrease the incidence of dysphagia and necessity for dilatation in future patients [36].

Due to the retrospective nature of our study we were unable to reliably analyse closure technique and its relation to dysphagia. The specific stich technique used (eg. Conley, interrupted, stapler), the suture material (monofilament, polyfilament, barbed), the closure form (vertical, T, horizontal) are all of particular interest and have their proponents in the surgical community. Furthermore, whether the pharynx could be primarily closed or whether partial reconstruction with for example a pectoralis major skin island flap or full 360 degree reconstruction should intuitively impact on dysphagia post-operatively. Indeed in univariate analysis the PM to reconstruct was statistically significant, as was the free forearm flap but these did not remain significant on multivariate analysis.

#### *The incidence and risk factors for complications following dilation*

In the literature, the most important risk factor for a complication of dilation, is the presence of a malignant or complex stricture, or a caustic induced stricture [13,37,38]. Complex strictures are described as narrower or more angulated strictures. Piotet et al. described their experience in 1826 endoscopic dilations in which they observed a

complication rate of 0.8% for benign strictures and 4.6% for malignant strictures [13]. These figures have been indeed reported by other studies [39,40], and the 0.8% is similar to our major complications rate.

In our cohort, 7 patients (6%) suffered 8 major complications, of which 6 perforations. Five of the 6 perforations occurred during the first or second dilations. This should alert the operator to be particularly careful with new patients. On multivariate analysis dilation under general anesthesia was associated with the highest OR for a complication. It is possible that the muscle relaxant used during anesthesia mitigates feedback from the patient, leading to overly ambitious dilation and a higher risk on an esophageal perforation. Furthermore, the indication for the first dilation is invariably given by the head and neck surgeon, who then chooses whether this will be done by a head and neck surgeon under general anesthesia or as an endoscopic procedure by the gastro-enterologist. Reasons to perform the dilatation under general anesthesia by the head and neck surgeon may be to exclude recurrent tumor in the neopharynx or to evaluate severe stenosis for other treatment options like surgical reconstruction of the neo-pharynx. It can be anticipated that these cases are more difficult and harbors a higher risk of complications.

#### *Success rate of dilation*

In our data set, 57% of patients who were dilated required 1–3 dilations. The remaining 43% underwent repeated dilations due to ongoing dysphagia (one patient had > 100 dilations). In these patients, surgical reconstruction of the stenotic segment (for example with a flap or gastric pull up) can be offered. It must however be noted that our experience with gastric pull-up as a functional procedure to treat dysphagia was limited to two patients, making the numbers too small for any meaningful conclusions.

#### **Conclusion**

With an cumulative incidence rate of 22.8% at 5 years, dysphagia necessitating dilation is a common sequela following laryngectomy, and is more common in female patients, patients with hypopharynx tumors and in association with (chemo)radiotherapy before or after the TL. Roughly half the patients requiring dilation could be treated with a limited number of dilations, the others however needed serial dilations. Major complications such as perforations are rare, and occur almost exclusively in the first and second dilations. This should alert the physician to be extra careful in new patients.

#### **Conflict of interest**

The authors declared that there is no conflict of interest.

#### **Funding sources**

The Netherlands Cancer Institute receives a research grant from ATOS Medical Sweden which contributes to the existing infrastructure for health-related quality of life research of the department of Head and Neck Oncology and Surgery.

#### **References**

- [1] The Department of Veterans Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *N Engl J Med* 1991;324:1685–90.
- [2] Kuo P, Chen MM, Decker RH, Yarbrough WG, Judson BL. Hypopharyngeal cancer incidence, treatment, and survival: temporal trends in the United States. *The Laryngoscope* 2014;124:2064–9.
- [3] Hoffman HT, Porter K, Karnell LH, Cooper JS, Weber RS, Langer CJ, et al. Laryngeal cancer in the United States: changes in demographics, patterns of care, and survival. *The Laryngoscope* 2006;116:1–13.
- [4] Timmermans AJ, van Dijk BA, Overbeek LI, van Velthuysen ML, van Tinteren H, Hilgers FJ, et al. Trends in treatment and survival for advanced laryngeal cancer: a

- 20-year population-based study in The Netherlands. *Head Neck* 2016;38(Suppl 1):E1247–55.
- [5] Petersen JF, Timmermans AJ, van Dijk BAC, Overbeek LIH, Smit LA, Hilgers FJM, et al. Trends in treatment, incidence and survival of hypopharynx cancer: a 20-year population-based study in the Netherlands. *Eur Archiv Oto-Rhino-Laryngol: Off J Eur Fed Oto-Rhino-Laryngol Societ (EUROS): Affiliat German Soc Oto-Rhino-Laryngol – Head Neck Surg* 2018;275:181–9.
- [6] Zenga J, Goldsmith T, Bunting G, Deschler DG. State of the art: rehabilitation of speech and swallowing after total laryngectomy. *Oral Oncol* 2018;86:38–47.
- [7] Takes RP, Strojan P, Silver CE, Bradley PJ, Haigentz Jr. M, Wolf GT, et al. Current trends in initial management of hypopharyngeal cancer: the declining use of open surgery. *Head Neck* 2012;34:270–81.
- [8] Timmermans AJ, van Dijk BA, Overbeek LI, van Velthuysen MF, van Tinteren H, Hilgers FJ, et al. Trends in treatment and survival for advanced laryngeal cancer: a 20-year population-based study in The Netherlands. *Head Neck* 2015.
- [9] Op de Coul BM, Hilgers FJ, Balm AJ, Tan IB, van den Hoogen FJ. A decade of postlaryngectomy vocal rehabilitation in 318 patients: a single Institution's experience with consistent application of provox indwelling voice prostheses. *Archiv Otolaryngol – Head Neck Surg* 2000;126:1320–8.
- [10] Petersen JF, Lansaat L, Timmermans AJ, Van der V, Noort, Hilgers FJM, van den Brekel MWM. Postlaryngectomy prosthetic voice rehabilitation outcomes in a consecutive cohort of 232 patients over a 13-year period. *Head Neck* 2018.
- [11] McConnel FM, Cerenko D, Mendelsohn MS. Dysphagia after total laryngectomy. *Otolaryngol Clin North Am* 1988;21:721–6.
- [12] Ward EC, Bishop B, Frisby J, Stevens M. Swallowing outcomes following laryngectomy and pharyngolaryngectomy. *Arch Otolaryngol Head Neck Surg* 2002;128:181–6.
- [13] Pietet E, Escher A, Monnier P. Esophageal and pharyngeal strictures: report on 1,862 endoscopic dilations using the Savary-Gilliard technique. *Eur Archiv Oto-Rhino-Laryngol: Off J Eur Fed Oto-Rhino-Laryngol Societ (EUROS): Affiliat German Soc Oto-Rhino-Laryngol – Head Neck Surg* 2008;265:357–64.
- [14] Oursin C, Pitzer G, Fournier P, Bongartz G, Steinbrich W. Anterior neopharyngeal pseudodiverticulum. A possible cause of dysphagia in laryngectomized patients. *Clin Imag* 1999;23:15–8.
- [15] Vu KN, Day TA, Gillespie MB, Martin-Harris B, Sinha D, Stuart RK, et al. Proximal esophageal stenosis in head and neck cancer patients after total laryngectomy and radiation. *ORL; J Oto-Rhino-Laryngol Relat Specialt* 2008;70:229–35.
- [16] Kraaijenga SA, Oskam IM, van der Molen L, Hamming-Vrieze O, Hilgers FJ, van den Brekel MW. Evaluation of long term (10-years + ) dysphagia and trismus in patients treated with concurrent chemo-radiotherapy for advanced head and neck cancer. *Oral Oncol* 2015.
- [17] Francis DO, Weymuller Jr. EA, Parvathaneni U, Merati AL, Yueh B. Dysphagia, stricture, and pneumonia in head and neck cancer patients: does treatment modality matter? *Ann Otol Rhinol Laryngol* 2010;119:391–7.
- [18] Maclean J, Szczesniak M, Cotton S, Cook I, Perry A. Impact of a laryngectomy and surgical closure technique on swallow biomechanics and dysphagia severity. *Otolaryngol Head Neck Surg* 2011;144:21–8.
- [19] Korsten MA, Rosman AS, Fishbein S, Shlein RD, Goldberg HE, Biener A. Chronic xerostomia increases esophageal acid exposure and is associated with esophageal injury. *Am J Med* 1991;90:701–6.
- [20] Balfé DM. Dysphagia after laryngeal surgery: radiologic assessment. *Dysphagia* 1990;5:20–34.
- [21] Yoda Y, Yano T, Kaneko K, Tsuruta S, Oono Y, Kojima T, et al. Endoscopic balloon dilatation for benign fibrotic strictures after curative nonsurgical treatment for esophageal cancer. *Surg Endosc* 2012;26:2877–83.
- [22] Pereira-Lima JC, Ramires RP, Zamin Jr. I, Cassal AP, Marroni CA, Mattos AA. Endoscopic dilation of benign esophageal strictures: report on 1043 procedures. *Am J Gastroenterol* 1999;94:1497–501.
- [23] Van Halsema EMO, Noordzij IC. Endoscopic dilation of benign esophageal anastomotic strictures over 16 mm has a longer lasting effect. *Surg Endosc* 2017;31:1871–81.
- [24] Harris RL, Grundy A, Odutoye T. Radiologically guided balloon dilatation of neopharyngeal strictures following total laryngectomy and pharyngolaryngectomy: 21 years' experience. *J Laryngol Otol* 2010;124:175–9.
- [25] Bob G. cmprsk: subdistribution analysis of competing risks. R package version 22-7; 2014. <https://CRANR-project.org/package=cmprsk>.
- [26] Sweeny L, Golden JB, White HN, Magnuson JS, Carroll WR, Rosenthal EL. Incidence and outcomes of stricture formation postlaryngectomy. *Otolaryngol – Head Neck Surg: Off J Am Acad Otolaryngol – Head Neck Surg* 2012;146:395–402.
- [27] Scharpf J, Esclamado RM. Reconstruction with radial forearm flaps after ablative surgery for hypopharyngeal cancer. *Head Neck* 2003;25:261–6.
- [28] Tsou YA, Lin MH, Hua CH, Tseng HC, Bau DT, Tsai MH. Comparison of pharyngeal stenosis between hypopharyngeal patients undergoing primary versus salvage laryngopharyngectomy. *Otolaryngol Head Neck Surg* 2010;143:538–43.
- [29] Robertson SM, Yeo JC, Dunnet C, Young D, Mackenzie K. Voice, swallowing, and quality of life after total laryngectomy: results of the west of Scotland laryngectomy audit. *Head Neck* 2012;34:59–65.
- [30] Clark JR, Gilbert R, Irish J, Brown D, Neligan P, Gullane PJ. Morbidity after flap reconstruction of hypopharyngeal defects. *Laryngoscope* 2006;116:173–81.
- [31] Murray DJ, Novak CB, Neligan PC. Fasciocutaneous free flaps in pharyngolaryngo-oesophageal reconstruction: a critical review of the literature. *J Plast Reconstr Aesthet Surg* 2008;61:1148–56.
- [32] Casparie M, Tiebosch AT, Burger G, Blauweers H, van de Pol A, van Krieken JH, et al. Pathology databanking and biobanking in The Netherlands, a central role for PALGA, the nationwide histopathology and cytopathology data network and archive. *Cell Oncol: Off J Int Soc Cell Oncol* 2007;29:19–24.
- [33] Lee WT, Akst LM, Adelstein DJ, Saxton JP, Wood BG, Strome M, et al. Risk factors for hypopharyngeal/upper esophageal stricture formation after concurrent chemoradiation. *Head Neck* 2006;28:808–12.
- [34] Al-Mamgani A, van Rooij P, Verduijn GM, Mehilal R, Kerrebijn JD, Levendag PC. The impact of treatment modality and radiation technique on outcomes and toxicity of patients with locally advanced oropharyngeal cancer. *The Laryngoscope* 2013;123:386–93.
- [35] Christianen ME, van der Schaaf A, van der Laan HP, Verdonck-de Leeuw IM, Doornaert P, Chouvalova O, et al. Swallowing sparing intensity modulated radiotherapy (SW-IMRT) in head and neck cancer: clinical validation according to the model-based approach. *Radiotherap Oncol: J Eur Soc Therapeut Radiol Oncol* 2016;118:298–303.
- [36] Kraaijenga SA, van der Molen L, Jacobi I, Hamming-Vrieze O, Hilgers FJ, van den Brekel MW. Prospective clinical study on long-term swallowing function and voice quality in advanced head and neck cancer patients treated with concurrent chemoradiotherapy and preventive swallowing exercises. *Eur Archiv Oto-Rhino-Laryngol: Off J Eur Fed Oto-Rhino-Laryngol Societ (EUROS): Affiliat German Soc Oto-Rhino-Laryngol – Head Neck Surg* 2014.
- [37] Hernandez LV, Jacobson JW, Harris MS. Comparison among the perforation rates of Maloney, balloon, and savary dilation of esophageal strictures. *Gastrointest Endosc* 2000;51:460–2.
- [38] Lew RJ, Kochman ML. A review of endoscopic methods of esophageal dilation. *J Clin Gastroenterol* 2002;35:117–26.
- [39] D'Souza JN, Luginbuhl AJ, Goldman RA, Heller JE, Curry JM, Cognetti DM. Cervical spine spondylodiscitis after esophageal dilation in patients with a history of laryngectomy or pharyngectomy and pharyngeal irradiation. *JAMA Otolaryngol Head Neck Surg* 2016;142:467–71.
- [40] Hagel AF, Naegel A, Dauth W, Matzel K, Kessler HP, Farnbacher MJ, et al. Perforation during esophageal dilatation: a 10-year experience. *J Gastrointest Liver Dis: JGLD* 2013;22:385–9.