

# Management of the thyroid gland during laryngectomy

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## Abstract

**Objectives:** This study aimed to: describe the incidence of thyroid gland involvement in advanced laryngeal cancer, analyse patterns of spread to the thyroid and elucidate predictors of thyroid involvement.

**Methods:** A retrospective review was performed on patients who underwent laryngectomy from 1991 to 2015 as a primary or salvage treatment for squamous cell carcinoma of the larynx, hypopharynx or base of tongue. The incidence of thyroidectomy during total laryngectomy, type of thyroidectomy, incidence of gland involvement, route of spread, and positive predictors of spread were analysed and reported.

**Results:** A total of 188 patients fit the inclusion criteria. Of these, 125 (66 per cent) underwent thyroidectomy. The thyroid was involved in 10 of the 125 patients (8 per cent), 9 by direct extension and 1 by metastasis. Cartilage invasion was a predictor of thyroid gland involvement, with a positive predictive value of 26 per cent.

**Conclusion:** There is a low incidence of thyroid gland involvement in laryngeal carcinoma. Most cases of gland involvement occurred by direct extension. Thyroidectomy during laryngectomy should be considered for advanced stage tumours with cartilage invasion.

**Key words:** Laryngectomy; Thyroidectomy; Thyroid Cartilage; Squamous Cell Carcinoma

## Introduction

Total laryngectomy is the ‘gold standard’ for the management of advanced stage laryngeal and hypopharyngeal cancers, and for salvage treatment in cases of recurrence following organ preservation therapy. Total laryngectomy was originally described by Bilroth in 1873, in which the infrahyoid muscles were left intact.<sup>1</sup> Jackson and Babcock advocated wide-field laryngectomy, in which the strap muscles and ipsilateral lobe of the thyroid gland were also removed, particularly in cases of tumour spread through the anterior commissure, cricothyroid membrane and thyroid cartilage.<sup>2</sup> Removal of the ipsilateral thyroid lobe continues to be routinely advocated as part of total laryngectomy; however, there is controversy surrounding this practice.

The incidence of thyroid gland involvement in laryngeal cancer ranges from about 1 to 30 per cent.<sup>3,4</sup> Routes of spread of laryngeal cancer to the thyroid include direct extension, and haematogenous or lymphatic spread. Proposed clinical and pathological factors predisposing to thyroid gland involvement include

cricothyroid membrane invasion, subglottic extension, advanced stage and vocal fold fixation.<sup>5,6</sup>

Hypothyroidism following laryngectomy with hemithyroidectomy was reported in up to 25 per cent of patients who had not undergone radiation therapy and in up to 75 per cent who received post-operative radiation therapy.<sup>7</sup> Hypothyroidism in these patients can be insidious, and may lead to impaired wound healing, decreased cardiac function and depression.<sup>8</sup>

In this study, we present our institutional experience of thyroid gland management in patients undergoing total laryngectomy. This study aimed to present the incidence of both thyroidectomy and thyroid gland involvement, and routes of spread, and to provide clinical predictors of thyroid gland involvement, in order to guide surgeons in the decision to remove the thyroid gland during laryngectomy.

## Materials and methods

A retrospective review was performed of patients who underwent total laryngectomy at Dartmouth-Hitchcock

Medical Center between 1991 and 2015. Exclusion criteria included patients who received total laryngectomy for reasons other than primary squamous cell carcinoma of the tongue base, hypopharynx, supraglottic, glottis or subglottis.

Out-patient and in-patient charts, operative reports, and pathological reports were reviewed. Data extracted included: patient demographics, prior treatments, out-patient laryngoscopy findings, tumour characteristics and extent of tumour, as well as type of surgery including whether thyroidectomy was performed.

Prior to surgery, all patients underwent pre-operative staging imaging (either computed tomography or positron emission tomography/computed tomography), and were discussed at the head and neck tumour board. Analysis of pathology was performed by dedicated head and neck pathologists, and reported using standardised templates.

Amongst patients who received thyroidectomy, different patterns of tumour spread were compared between patients with thyroid involvement and patients without using a *t*-test of proportions. Positive and negative predictive values of thyroid involvement were calculated for different patterns of tumour spread.

**Results**

This study investigated 196 patients who fit the inclusion criteria outlined in Figure 1. Of 196 patients who underwent total laryngectomy between 1991 and 2015, 188 underwent the procedure for treatment of primary squamous cell carcinoma. Of these 188 patients, 125 underwent either hemi-thyroidectomy or total thyroidectomy.

Table I compares the characteristics of those patients who underwent thyroidectomy versus those who did not undergo thyroidectomy. The majority of the patients in both groups underwent primary laryngectomy (67 per cent of thyroidectomy patients and 51 per cent of non-thyroidectomy patients). Amongst patients who underwent thyroidectomy, the most common tumour stage was T<sub>4</sub> (60 per cent), the most common primary site was supraglottic (36 per cent), and the most common treatment was laryngectomy with bilateral neck dissection (63 per cent). Amongst

**TABLE I**  
STUDY POPULATION DATA

Parameter	Thyroidectomy*	No thyroidectomy†
Age (mean (range); years)	62 (37–85)	63 (40–85)
Gender (% female)	26	19
Prior treatment (n (%))		
– None	84 (67)	32 (51)
– Radiation	29 (23)	21 (33)
– Chemoradiation	12 (10)	10 (16)
Tumour (T) stage (n (%))		
– T <sub>1</sub>	2 (1)	4 (6)
– T <sub>2</sub>	11 (9)	13 (21)
– T <sub>3</sub>	39 (31)	27 (43)
– T <sub>4</sub>	73 (60)	19 (30)
Primary site (n (%))		
– Supraglottic	45 (36)	31 (49)
– Glottic	31 (25)	17 (27)
– Subglottic	2 (2)	0 (0)
– Transglottic	37 (30)	7 (11)
– Tongue base	0 (0)	1 (2)
– Hypopharynx	11 (9)	7 (11)
Treatment (n (%))		
– Laryngectomy	6 (5)	15 (24)
– Laryngectomy with unilateral neck dissection	29 (22)	14 (22)
– Laryngectomy with bilateral neck dissection	79 (63)	27 (43)
– Laryngectomy with partial pharyngectomy	2 (2)	1 (1)
– Laryngopharyngectomy	8 (7)	3 (5)
– Laryngectomy with glossectomy	1 (1)	3 (5)

\*Total n = 125; †total n = 63

patients who did not undergo thyroidectomy, the most common tumour stage was T<sub>3</sub> (43 per cent), the most common primary site was supraglottic (49 per cent), and the most common treatment was laryngectomy with bilateral neck dissection (43 per cent).

Thyroid extension was seen in 10 patients; in 9 patients this reflected direct extension and in 1 patient it was secondary to metastasis (Figure 2). Patients who underwent thyroidectomy had significantly more cartilage invasion (50 per cent vs 33 per cent; risk difference of 17 per cent; 95 per cent confidence interval (CI) = 1–32 per cent) and subglottic extension (38 per cent vs 17 per cent; risk difference of 21 per cent; 95 per cent CI = 7–33 per cent), but less extralaryngeal

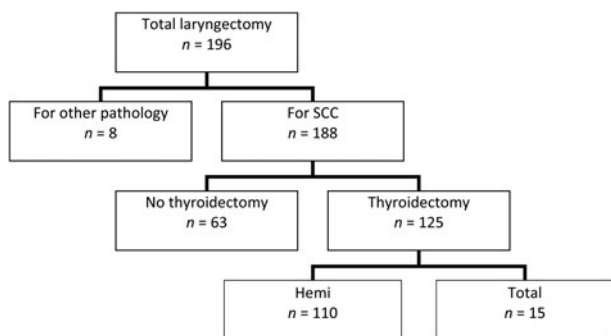


FIG. 1

Inclusion criteria flowchart. SCC = squamous cell carcinoma

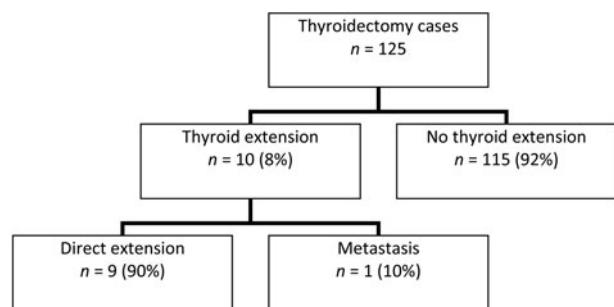


FIG. 2

Routes of thyroid gland extension.

TABLE II  
COMPARISON BETWEEN THYROIDECTOMY AND NON-THYROIDECTOMY PATIENTS

Extent of tumour & local recurrence	Thyroidectomy (n (%))	No thyroidectomy (n (%))	<i>p</i>
Cartilage invasion	62 (50)	21 (33)	0.027
Vocal fold paralysis	68 (54)	33 (52)	0.795
Extralaryngeal spread	40 (32)	36 (57)	0.001
Anterior commissure involvement	38 (30)	22 (35)	0.488
Subglottic extension	48 (38)	11 (17)	0.001
Local recurrence	10 (8)	9 (13)	0.262

TABLE III  
COMPARISON BETWEEN PATIENTS WITH THYROID INVOLVEMENT VERSUS THOSE WITHOUT

Extent of tumour & prior chemoradiation	No thyroid involvement (n (%))*	Thyroid involvement (n (%))†	<i>p</i>	PPV (%)	NPV (%)
Cartilage invasion	53 (46)	9 (90)	0.004	26	95
Vocal fold paralysis	60 (52)	8 (80)	0.090	15	94
Extralaryngeal spread	34 (30)	6 (60)	0.052	18	94
Anterior commissure involvement	35 (30)	3 (30)	1.000	13	91
Subglottic extension	42 (37)	6 (60)	0.153	15	94
Prior chemoradiation	37 (32)	4 (40)	0.603	10	69

\*Total *n* = 115; †total *n* = 10. PPV = positive predictive value; NPV = negative predictive value

spread (32 per cent vs 57 per cent; risk difference of 25 per cent; 95 per cent CI = 9–40 per cent) (Table II). Amongst patients who underwent thyroidectomy, those with thyroid involvement had more cartilage invasion (90 per cent vs 46 per cent; risk difference of 44 per cent; 95 per cent CI = 8–58 per cent). In addition, cartilage invasion had a significant positive predictive value of 26 per cent and negative predictive value of 95 per cent for thyroid extension (Table III). The characteristics of the 10 patients with positive thyroid extension are shown in Table IV.

## Discussion

This study examined the incidence of thyroidectomy, thyroid gland involvement, routes of spread and clinical predictors of gland involvement in a series of 196 patients who underwent laryngectomy. In our series, 125 patients (67 per cent) underwent thyroidectomy,

110 (88 per cent) of whom underwent hemi-thyroidectomy. The overall incidence of gland involvement was 8 per cent (10 patients); of these, 9 patients (90 per cent) had gland involvement by direct extension. All patients with gland involvement in this series had T<sub>4</sub> tumours, and had undergone either total laryngectomy and partial pharyngectomy or total laryngopharyngectomy. The incidence of tumour extension into the thyroid is consistent with previous studies (Table V).<sup>3–5,9–16</sup>

Removal of the ipsilateral lobe of the thyroid gland has been routinely advocated as part of laryngectomy since the time of Jackson and Babcock's study.<sup>2</sup> The rationale for thyroidectomy is that laryngeal tumours may spread to the gland either in a direct fashion through planes of least resistance, or by haematogenous or lymphatic spread. Extralaryngeal cancer spread can occur in a number of ways: through the anterior angle of thyroid cartilage where Broyles' ligament attaches

TABLE IV  
CHARACTERISTICS OF PATIENTS WITH THYROID INVOLVEMENT

Pt no.	TNM stage*	Primary site	Prior treatment	Thyroidectomy type	Route of involvement	Laryngeal surgery
1	T <sub>4</sub> N <sub>0</sub> M <sub>0</sub>	Transglottic	Chemoradiation	Hemi	Direct	Total laryngopharyngectomy
2	T <sub>4</sub> N <sub>0</sub> M <sub>0</sub>	Hypopharynx	None	Total	Direct	Total laryngectomy, partial pharyngectomy
3	T <sub>4</sub> N <sub>2b</sub> M <sub>0</sub>	Hypopharynx	None	Hemi	Direct	Total laryngopharyngectomy
4	T <sub>4</sub> N <sub>0</sub> M <sub>0</sub>	Glottic	Chemoradiation	Total	Direct	Total laryngopharyngectomy
5	T <sub>4</sub> N <sub>0</sub> M <sub>0</sub>	Glottic	Radiation	Total	Direct	Total laryngectomy
6	T <sub>4</sub> N <sub>0</sub> M <sub>0</sub>	Glottic	None	Hemi	Direct	Total laryngopharyngectomy
7	T <sub>4</sub> N <sub>2b</sub> M <sub>0</sub>	Supraglottic	None	Total	Direct	Total laryngectomy
8	T <sub>4</sub> N <sub>1</sub> M <sub>0</sub>	Glottic	None	Hemi	Direct	Total laryngectomy
9	T <sub>4</sub> N <sub>0</sub> M <sub>0</sub>	Glottic	Radiation	Hemi	Direct	Total laryngectomy
10	T <sub>4</sub> N <sub>2b</sub> M <sub>0</sub>	Hypopharynx	None	Hemi	Metastasis	Total laryngectomy, partial pharyngectomy

\*Pathologically confirmed classification. Pt no. = patient number; TNM = tumour–node–metastasis

TABLE V  
PREVIOUSLY REPORTED DATA ON SCC INVOLVEMENT OF THYROID GLAND IN TOTAL LARYNGECTOMY PATIENTS

Study (year)	Laryngectomy (n)	Thyroidectomy (n (%))*	Tumour (T) stage (n (%))†				Thyroid extension (n (%))
			T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	T <sub>4</sub>	
Current study (2017)	196	125 (64)	2 (2)	11 (9)	39 (32)	71 (58)	10 (8)
Iype <i>et al.</i> <sup>10</sup> (2016)	133	89 (67)	25 (19)		108 (81)		28 (21)
Mangussi-Gomes <i>et al.</i> <sup>11</sup> (2016)	83	83 (100)	0 (0)	0 (0)	26 (31)	57 (69)	15 (18)
Arslanoglu <i>et al.</i> <sup>12</sup> (2016)	75	75 (100)	13 (17)		62 (83)		4 (5)
Mourad <i>et al.</i> <sup>9</sup> (2015)	343	262 (100)	NI	NI	NI	NI	7 (3)
Hilly <i>et al.</i> <sup>13</sup> (2012)	59	52 (88)	NI	NI	NI	NI	11 (21)
Elliott <i>et al.</i> <sup>3</sup> (2010)	35	35 (100)	NI	NI	NI	NI	3 (8.5)
Al-Khatib <i>et al.</i> <sup>14</sup> (2009)	61	61 (100)	12 (20)	8 (13)	12 (20)	29 (47)	1 (1.6)
Kim <i>et al.</i> <sup>16</sup> (2008)	28	28 (100)	0 (0)	5 (18)	4 (14)	19 (68)	4 (15)
Sparano <i>et al.</i> <sup>5</sup> (2005)	30	30 (100)	0 (0)	12 (40)	6 (20)	12 (40)	7 (23)
Dadas <i>et al.</i> <sup>4</sup> (2001)	182	182 (100)	NI	NI	NI	NI	2 (1)
Fagan & Kaye <sup>15</sup> (1997)	102	102 (100)	0 (0)	0 (0)	102 (100)		2 (2.7)

\*‘Thyroidectomy’ includes both hemi-thyroidectomy and total thyroidectomy data. †Staging is based on American Joint Committee on Cancer staging classification at the time of publication. NI = not included

directly to cartilage with no perichondrium; through the cricothyroid membrane, from a subglottic primary, from the paraglottic space inferiorly or laterally along the conus elasticus; through the ossified portions of the laryngeal cartilages; through the pyriform sinus; or through the post-cricoid region.

Thyroidectomy patients had higher proportions of cartilage invasion and subglottic extension, and less extralaryngeal spread when compared to patients who did not undergo thyroidectomy. Importantly, there were no statistically significant differences between the two groups regarding local recurrence of disease. This result suggests that amongst patients who did not undergo thyroidectomy, there is unlikely to be residual disease in the thyroid leading to clinically significant local recurrence. Thus, it is conceivable that in lower risk patients, sparing the thyroid gland is safe.

- **Thyroidectomy is routinely performed during laryngectomy for primary squamous cell carcinoma of the larynx, hypopharynx or tongue base**
- **Thyroidectomy is performed because of concern for tumour invasion into the thyroid gland**
- **The incidence of thyroid extension was low (8 per cent) for patients who underwent laryngectomy and concurrent thyroidectomy**
- **Patients with thyroid extension had a higher rate of cartilage invasion (90 vs 46 per cent)**
- **Cartilage invasion has a low positive predictive value (26 per cent) for thyroid extension**
- **This is because of the low incidence of thyroid involvement in primary squamous cell carcinoma of the larynx, hypopharynx or tongue base**

Previous studies have demonstrated that thyroid cartilage involvement and subglottic extension are associated with tumour extension into the thyroid.<sup>17,18</sup> A systematic review and meta-analysis from Newcastle upon Tyne Hospitals highlighted that the relative risk of thyroid gland invasion for patients with subglottic extension was 4.3 (95 per cent CI = 2.5–7.2).<sup>19</sup> While our study confirms the significance of cartilage invasion, the positive predictive value remained low (less than 30 per cent), even for statistically significant associations. The low positive predictive value and high negative predictive value are attributed to the low natural prevalence of thyroid involvement in primary laryngeal squamous cell carcinoma. Thus, increasingly sensitive and specific markers for thyroid invasion would marginally raise the positive predictive value. These findings, or lack thereof, can guide the surgeon in their decision to remove the thyroid gland.

Limitations of this study relate to the retrospective nature of the data. The decision to perform thyroidectomy is based on clinician judgement rather than randomisation. The data on thyroid gland involvement were obtained from a review of the pathological reports. As whole organ serial sectioning of the larynx and thyroid gland is not performed routinely, it is possible that some smaller occult cases of thyroid gland involvement may have been missed. Prospective randomised control trials are needed to expand the study population and to increase the external applicability of findings.

### Conclusion

The likelihood of thyroidectomy during laryngectomy remains high, while the incidence of thyroid invasion is relatively low. Factors such as cartilage invasion are associated with thyroid invasion, but the positive predictive value is low. Thyroidectomy should be considered for patients with advanced stage tumours with cartilage invasion.

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