

Thyroid gland involvement in carcinoma of the hypopharynx

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Abstract

Objective: The thyroid gland is removed en bloc during laryngectomy. There are no objective criteria for deciding the extent of thyroid gland resection in primary hypopharyngeal cancer cases. The present study aimed to determine the incidence of thyroid gland involvement in hypopharyngeal cancer and identify the various predictors of this involvement.

Method: This paper reports a retrospective analysis of 358 patients with hypopharyngeal cancer, who underwent total laryngectomy with partial or total pharyngectomy at Tata Memorial Hospital, Mumbai between 2004 and 2010.

Results: The mean age of this population was 61 years. The pyriform sinus was the most common hypopharyngeal subsite involved (in 89 per cent of cases). Most patients underwent hemi-thyroidectomy as part of their surgery. The thyroid gland was involved in only 13 per cent of cases.

Conclusion: Thyroid gland involvement is not common in hypopharyngeal cancer. Cases that involved the post-cricoid area, subglottic extension, extralaryngeal spread or prior tracheostomy were associated with a higher risk of thyroid gland involvement. Ipsilateral thyroidectomy is sufficient in most patients undergoing surgery (laryngectomy with partial or total pharyngectomy) for hypopharyngeal cancers.

Key words: Carcinoma; Hypopharynx; Thyroid Gland; Pathology

Introduction

Hypopharyngeal cancer is relatively uncommon, with a higher prevalence in South Asia.¹ For organ preservation, primary radiotherapy or chemoradiotherapy is the preferred choice of treatment in the early stages. However, surgery followed by adjuvant radiotherapy or chemoradiotherapy is required for more advanced tumours, and for salvage after radiotherapy.

Most hypopharyngeal cancers are squamous cell carcinomas, and the pyriform sinus is the most common hypopharynx subsite involved.^{2,3} Surgery for hypopharyngeal cancer often requires laryngopharyngectomy, or laryngectomy with partial pharyngectomy. Tumour from the hypopharynx can spread to adjacent structures, including the thyroid or cricoid cartilages, the thyroid gland, and the oesophagus. The thyroid gland is therefore routinely removed during laryngectomy to achieve adequate tumour-free margins. The thyroid gland adjacent to the involved side is routinely removed; however, some surgeons prefer to perform a total thyroidectomy.

The incidence of thyroid gland involvement varies from 1 to 50 per cent.^{4–8} Most of the relevant literature concerns laryngeal cancer; few studies have reported

the incidence of thyroid gland involvement in hypopharyngeal cancer specifically. Hypopharyngeal cancer has a different pattern of spread to laryngeal cancer due to the slight difference in anatomical location. Hence, the incidence and the factors predicting thyroid gland involvement may vary for laryngeal and hypopharyngeal cancer.

Resection of the thyroid gland can lead to hypothyroidism and hypoparathyroidism. When both resection and radiotherapy are carried out, the risk of hypothyroidism increases to 70 per cent.^{9–11} Hypothyroidism in itself can result in fatigue, weight gain, irritability and depression. Hence, thyroid resection should only be carried out if it is absolutely necessary.^{12,13}

This retrospective study aimed to determine the incidence of thyroid gland involvement in carcinoma of the hypopharynx and to evaluate the various factors predicting thyroid gland involvement.

Materials and methods

A retrospective analysis was conducted of all patients with hypopharyngeal cancer who underwent total laryngectomy with partial or total pharyngectomy at Tata Memorial Hospital, Mumbai between 2004 and 2010. Cases were selected based on the following

eligibility criteria: biopsy-confirmed squamous cell carcinoma of the hypopharynx; surgery carried out with curative intent at Tata Memorial Hospital as a primary or salvage treatment; and total laryngectomy with partial or total pharyngectomy performed.

Between 2004 and 2010, 1012 patients underwent laryngectomy for carcinoma of the larynx or hypopharynx. After the eligibility criteria were applied, there were 358 cases of hypopharyngeal cancer for evaluation. Relevant data were retrieved from the hospital's electronic medical records. Those patients treated exclusively for laryngeal cancer or those who underwent partial laryngectomy were not included in this study.

All patients underwent a complete pre-operative evaluation, which included a direct laryngoscopy, contrast-enhanced computed tomography and barium study. The lesions of these patients predominantly involved the hypopharynx. Treatment therefore required partial or complete excision of the pharyngeal walls, achieved via partial or total laryngopharyngectomy.

Eighty-five per cent of patients (304 out of 358) underwent surgery as the first modality of treatment, and the remaining 15 per cent of patients (54 of 358) received radiotherapy or chemoradiotherapy prior to surgery. Cartilage erosion was the most common indication for surgery (in 55 per cent of cases), followed by exolaryngeal spread, or bulky and extensive soft tissue disease.

Statistical analysis was carried out using the Statistical Package for the Social Sciences software version 20.0 (SPSS; IBM, Armonk, New York, USA). *P* values were calculated using chi-square or *t*-tests. A *p* value of less than 0.05 was considered significant. Univariate and multivariate analyses were conducted using the chi-square test and the binary logistic regression test respectively.

Results

The mean age of the patient population was 61 years, with a male to female ratio of 12:1. The pyriform sinus was the most common site of disease (Table I). The adjacent laryngeal framework was involved in the majority of cases (70 per cent, 250 of 358). Seventy-one per cent of patients (253 of 358) had neck nodal metastases; 81 per cent of these patients (205 of 253) had extracapsular spread.

The common indications for thyroidectomy as a part of total laryngectomy included: cartilage erosion, in 53 per cent of cases (191 out of 358); extralaryngeal disease, in 30 per cent of cases (107 of 358); and disease extending to the subglottis, in 25 per cent of cases (90 of 358). Only 4 per cent of patients (13 of 358) underwent total thyroidectomy; hemi-thyroidectomy was carried out in the majority of patients (96 per cent, 345 of 358). Of those who underwent total thyroidectomy, four had bilateral and three had unilateral thyroid lobe involvement. Two patients had gross extralaryngeal disease without thyroid gland involvement. One patient had micropapillary thyroid carcinoma, and one had nodal metastasis of papillary

TABLE I
DEMOGRAPHIC FACTORS

Factor	Patients* (n (%))
Sex	
– Male	331 (92)
– Female	27 (8)
Disease site	
– Pyriform sinus	320 (89)
– Post-cricoid	19 (5)
– Posterior pharyngeal wall	14 (4)
Treatment status	
– Treatment naïve	304 (85)
– Salvage	54 (15)
Thyroidectomy type	
– Hemi	345 (96)
– Total	13 (4)
Differentiation	
– Well	3 (1)
– Moderate	141 (39)
– Poor	207 (58)
– No tumour	5 (1)
– Others	2 (1)
Tumour stage† (T)	
– T3	138 (45)
– T4	166 (55)
Nodal stage† (N)	
– N0	69 (23)
– N1	57 (19)
– N2a	6 (2)
– N2b	100 (33)
– N2c	63 (21)
– N3	9 (3)
Lymphovascular emboli	44 (12)
Perineural invasion	66 (18)

Patients were aged 24–88 years (mean 61 years, median 62 years). *Total *n* = 358. †Refers to treatment naïve patients (*n* = 304)

carcinoma with a normal thyroid gland. Two patients had benign nodules in the ipsilateral thyroid lobe.

The incidence of pathological thyroid gland involvement in this series was 13 per cent (47 out of 358 patients). Associations between thyroid gland involvement and other various factors were evaluated, including disease site, cartilage erosion, extralaryngeal spread, subglottic extension, level VI lymph node metastasis, tumour stage, lateral neck nodes, extracapsular spread, prior tracheostomy, perineural invasion and lymphovascular emboli, and transglottic involvement.

Univariate analysis revealed statistically significant associations (*p* < 0.05) between thyroid gland involvement and the following factors: anatomical location of the tumour in the hypopharynx, perineural invasion, subglottic involvement, extralaryngeal spread, prior tracheostomy and cartilage erosion. Multivariate analysis revealed significant associations (*p* < 0.05) between thyroid gland involvement and prior tracheostomy, subglottic extension of the tumour, thyroid cartilage erosion, extralaryngeal spread and post-cricoid involvement (Table II).

Discussion

Most of the previously published clinical studies analysed hypopharyngeal and laryngeal cancer cases

TABLE II
FACTORS ASSOCIATED WITH THYROID GLAND INVOLVEMENT*

Factor	Pts (n (total n))	Pts (%)
Subsite in hypopharynx		
– Post-cricoid	9 (19)	47
– Posterior pharyngeal wall	3 (14)	21
– Pyriform sinus	35 (320)	11
Subglottic extension	25 (88)	28
Extralaryngeal spread	24 (105)	23
Prior tracheostomy	21 (74)	28

*Statistically significant factors on multivariate analysis. Pts = patients

together. This is partly because hypopharyngeal cancer is uncommon, and because hypopharyngeal and laryngeal tumours are located at anatomically nearby sites. Because of this anatomical proximity, hypopharyngeal cancer surgery often entails laryngectomy also. To our knowledge, the incidence of thyroid gland involvement in hypopharyngeal cancer has not been previously studied. In this study, as in many other studies, hemi or total thyroidectomy was carried out on all patients who underwent total laryngectomy.^{14,15} However, in our series, the disease involved the thyroid gland in only 13 per cent of cases (Table III).

In 1955, Ogura recommended total laryngectomy with ipsilateral thyroidectomy for all cases of laryngeal cancer.⁴ In 1973, Harrison proposed total thyroidectomy for post-cricoid and subglottic tumours, as they are associated with a high incidence of contralateral thyroid gland involvement.⁵ A study by Kim *et al.* reported an incidence rate of 14 per cent for thyroid gland involvement in hypopharyngeal cancer; this incidence was associated with subglottic tumours.¹⁷ A meta-analysis of laryngeal cancer cases showed that the incidence of thyroid gland involvement was 8 per cent.¹⁸

In the meta-analysis by Mendelson *et al.* subglottic extension of the tumour (>10 mm), a transglottic tumour and a subglottic subsite significantly increased the risk of thyroid gland invasion by laryngeal carcinoma.¹⁸ In the current study, subglottic extension was also an important factor for thyroid gland involvement.

However, transglottic involvement was not a significant factor ($p = 0.093$).

Many previous studies indicate that prior tracheostomy is a risk factor for thyroid gland involvement. This could be attributed to subglottic extension of the disease, which requires tracheostomy. In fact, in our series, 49 per cent of patients with subglottic disease had had a prior tracheostomy.

- **Thyroid glands are routinely removed en bloc during laryngectomy**
- **There are no objective criteria for deciding the extent of thyroid gland resection**
- **In this study, the thyroid gland was involved in 13 per cent of hypopharyngeal cancer cases**
- **The thyroid gland was removed unnecessarily in most patients**
- **Hemi-thyroidectomy should be performed when the post-cricoid area or subglottis are involved, or if tumour extends to neck soft tissues**

In a study by Hilly *et al.* the incidence of thyroid gland involvement in laryngeal cancer was 21 per cent; thyroid gland involvement was associated with salvage procedures and paratracheal metastases.¹⁹ In the present study, neither of these factors were associated with thyroid gland involvement.

In a study by Brennen *et al.* the incidence of thyroid gland involvement was 8 per cent. All lesions were found to have transglottic growth and laryngeal cartilage invasion.¹⁶ In the present study too, cartilage invasion was significantly associated with thyroid gland involvement (unlike transglottic involvement, which was not a significant factor).

The location of the tumour within the hypopharynx, involving the post-cricoid area for instance, is often associated with a higher incidence of thyroid gland involvement.^{5,15} Likewise, in our series, we observed thyroid gland involvement in 47 per cent of the cases in which the post-cricoid region was implicated ($p < 0.05$).

TABLE III
INCIDENCE OF THYROID GLAND INVOLVEMENT

Study year	Author(s)	Pts (n)	Disease site	Thyroid gland involvement (% of pts)
1955	Ogura ⁴	59	Larynx	10
1976	Sessions ⁶	791	Larynx	1
1989	Brennan ¹⁶	247	Larynx	8
1997	Fagan & Kaye ⁷	102	Larynx	3
2004	Ceylan <i>et al.</i> ⁸	143	Larynx or hypopharynx	0 in larynx, 57 in hypopharynx
2008	Kim <i>et al.</i> ¹⁷	28	Larynx or hypopharynx	14
2009	Mendelson <i>et al.</i> ¹⁸	399	Larynx (meta-analysis)	8
2012	Hilly <i>et al.</i> ¹⁹	53	Larynx	21
2013	Joshi <i>et al.</i> (present study)	358	Hypopharynx	13

Pts = patients

In the study by Hilly *et al.* there was cartilage invasion in 10 of 11 cases with thyroid gland involvement, and all tumours were in proximity to (or in contact with) areas of calcification and ossification.¹⁹ Similarly, in the current study, multivariate analysis revealed a significant association between cartilage erosion and thyroid gland involvement. However, it must be noted that cartilaginous invasion is often associated with subglottic extension or extralaryngeal disease in hypopharyngeal cancer.

Conclusion

The thyroid gland was involved in 13 per cent of hypopharyngeal cancer cases (47 out of 358) and was thus removed unnecessarily in the majority of patients. Cases that involved the post-cricoid area, subglottic extension, extralaryngeal spread or prior tracheostomy were associated with a higher risk of thyroid gland involvement. It is suggested that hemi-thyroidectomy is sufficient in most such cases to achieve adequate tumour-free margins.

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Dr Sudhir Nair takes responsibility for the integrity of the content of the paper

Competing interests: None declared