

## Thyroid gland invasion in advanced laryngeal and hypopharyngeal carcinoma

### İleri evre larenks ve hipofarenks karsinomlarında tiroid bez tutulumu

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**Objectives:** To assess the rate of thyroid gland invasion and the need for thyroidectomy in advanced laryngeal and hypopharyngeal carcinomas which require total laryngectomy.

**Patients and Methods:** 129 total laryngectomy with ipsilateral hemithyroidectomy and 14 total laryngopharyngectomy with total thyroidectomy were performed for primary squamous cell carcinoma of larynx and hypopharynx between 1994-2001 in the ENT Department of Gazi University Hospital. In the surgical specimens of these 143 patients, the presence of tumor invasion of thyroid cartilage and thyroid gland was evaluated retrospectively according to light microscopic examination.

**Results:** None of the laryngeal carcinoma patients had thyroid gland invasion whereas eight (57%) hypopharyngeal carcinoma patients had thyroid gland invasion. Twenty patients (16%) had evidence of thyroid cartilage invasion in laryngeal carcinoma group. There were only 3 (21%) cases with thyroid cartilage invasion in hypopharyngeal carcinoma patients.

**Conclusion:** There may be no need for performing thyroidectomy in all total laryngectomy cases. We recommend thyroidectomy during total laryngectomy in laryngeal carcinoma cases with subglottic extension and advanced hypopharyngeal tumors. Except for these two conditions, the assessment of extralaryngeal extension and thyroid gland invasion will guide whether thyroidectomy should be performed or not.

**Key Words:** Laryngectomy; laryngeal neoplasms/surgery; pharyngeal neoplasms/surgery; thyroid gland/pathology/surgery; thyroid neoplasms/secondary/ surgery; thyroidectomy; neoplasm invasiveness; prognosis; thyroid cartilage/pathology.

**Amaç:** Total larenjektomi gerektiren ileri evre larenks ve hipofarenks karsinomlarında tiroid bezi tutulumu oranını ve tiroidektomi gerekliliğini değerlendirmek.

**Hastalar ve Yöntemler:** Gazi Üniversitesi Kulak Burun Boğaz Bölümü'nde 1994-2001 yılları arasında, 129 olguda ileri evre primer larenks karsinomu nedeniyle total larenjektomi ile beraber ipsilateral hemitiroidektomi, 14 olguda primer ileri evre hipofarenks karsinomu nedeniyle total larengefarenjektomi ile beraber total tiroidektomi uygulandı. Bu 143 olgunun cerrahi spesimenlerinde, tiroit bezi ve tiroid kıkırdak invazyonunun varlığı, ışık mikroskopik inceleme sonuçları göz önünde bulundurularak, retrospektif olarak değerlendirildi.

**Bulgular:** Larengeal karsinom olgularının hiçbirinde tiroid bez invazyonu saptanmazken, 14 hipofarenks karsinomlu olgunun sekizinde (%57) tiroid bez tutulumu mevcuttu. Larenks karsinomlu grupta 20 olguda (%16), hipofarenks karsinomlu grupta ise üç olguda (%21) tiroid kıkırdak invazyonu olduğu saptandı.

**Sonuç:** Total larenjektomi uygulanan tüm olgularda tiroidektomi yapmanın gerekli olmadığını, ancak subglottik uzanım gösteren larenks karsinomlarında ve ileri evre hipofarenks tümörlerinde total larenjektomi ile birlikte tiroidektominin gerekli olduğunu düşünmekteyiz. Bu iki durum dışında, cerrahi sırasında tümörün larenks dışı dokulara uzanım gösterdiğinin saptanmasının ve makroskopik olarak tiroid bezi tutulumu izlenmesinin tiroidektomi kararını almamızda yol gösterici olacağı kanısındayız.

**Anahtar Sözcükler:** Larenjektomi; larengeal neoplaziler/cerrahi; larengeal neoplaziler/cerrahi; tiroid bezi/patoloji/cerrahi; tiroid neoplazileri/tutulum/cerrahi; tiroidektomi; neoplazi tutulum; prognoz; tiroid kıkırdak/patoloji.

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♦ Received - May 5, 2003 (Dergiye geliş tarihi - 5 Mayıs 2003). Accepted for publication - January 19, 2004 (Yayın için kabul tarihi - 19 Ocak 2004).  
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The close relationship of the thyroid gland with the larynx and laryngopharynx renders the gland at risk in their carcinomas. The percentage of thyroid gland invasion in laryngeal carcinoma has been reported to be between 0 to 14%, and the incidence increases in subglottic tumors and transglottic tumors extending to the subglottic space.<sup>[1-8]</sup> The spread of the tumor to the thyroid gland is mostly by direct extension.<sup>[5-9]</sup> The thyroid isthmus overlies the 2nd, 3rd and 4th tracheal rings, thyroid lobes are in close relation with the thyroid laminae, the inferior constrictor muscles, the cricothyroid muscles, the cricothyroid membrane, the cricoid cartilage, the cricotracheal membrane, the upper tracheal cartilages and the esophagus. The thyroid lobes are at risk of direct invasion by endolaryngeal and subglottic tumors through the thyroid laminae, the cricothyroid membrane, the cricothyroid muscle, the cricoid cartilage, or the cricotracheal membrane.<sup>[10]</sup> The second route of thyroid gland invasion is through lymphatics. Lymphatic spread to the gland is most common in subglottic tumors.<sup>[5-7,9]</sup> The lymphatics of the subglottic region drain anteriorly through the cricothyroid membrane, to the prelaryngeal and pretracheal lymphatics, and posterolaterally through the cricotracheal membrane to the paratracheal nodes.<sup>[11]</sup> All of these lymph nodes are in close proximity to the thyroid gland. Therefore, subglottic tumors can invade the thyroid gland directly or via lymphatic channels.<sup>[11]</sup>

The thyroid gland, along with the adrenal gland, has the richest vascular supply for its size of any organ in the human body,<sup>[12]</sup> but hematogenous spread to the gland remains to be proved.

During laryngectomy for advanced squamous cell carcinoma of the larynx and hypopharynx, the lobe of the thyroid gland on the side of the primary lesion is usually removed.<sup>[5,13-15]</sup> There is 25% risk of development of hypothyroidism in hemithyroidectomy patients<sup>[14]</sup> and when radiotherapy is added to the treatment, the risk of hypothyroidism increases.<sup>[4,6,7,16-21]</sup> Cardiac, psychiatric, and wound healing problems due to hypothyroidism can be devastating in the postoperative period.<sup>[6,7,22-24]</sup> In order to reduce the incidence of postoperative hypothyroidism, thyroidectomy should ideally be performed in selected patients in which the carcinoma has involved the thyroid gland.

Despite the frequent inclusion of thyroid lobectomy in the treatment of advanced laryngeal and

hypopharyngeal carcinomas, there is no consensus especially in the management of advanced laryngeal carcinoma. This retrospective study was undertaken to assess the frequency of thyroid gland invasion and the necessity of thyroidectomy for advanced laryngeal and hypopharyngeal carcinomas that require total laryngectomy.

## MATERIALS AND METHODS

One hundred-forty-three patients who underwent total laryngectomy and thyroidectomy for squamous cell carcinoma of the larynx and hypopharynx at Gazi University Hospital, Ankara, between 1994-2001 were included in this study. The study group composed of 129 laryngeal, 14 hypopharyngeal carcinoma. The patient records were reviewed retrospectively, and data were collected for each patient with regard to sex, age, stage, and pathologic characteristics of the surgical specimen and thyroid gland invasion. Tumors were staged according to the AJCC (1987) tumor, node, metastasis (TNM) classification. The age range was 42 to 71, with a mean age of 51 years. There were 128 males and 15 females. Total laryngectomy and ipsilateral hemithyroidectomy were performed for advanced laryngeal carcinomas; total laryngectomy and total thyroidectomy were performed for hypopharyngeal carcinomas. The specimens were stained with hematoxylin and eosin, and examined under light microscope with regard to tumor invasion of thyroid cartilage and thyroid gland.

## RESULTS

One hundred-twenty-nine patients underwent total laryngectomy for carcinoma of the larynx. Forty-nine of them (38%) were supraglottic, 68 (53%) were glottic, 11 (8%) were transglottic and 1 (1%) was subglottic tumors. Seventy-seven patients (60%) had stage III, 52 patients (40%) had stage IV disease (Table I).

Fourteen patients underwent total laryngectomy for carcinoma of the hypopharynx. Eight (57%) were pyriform fossa tumors, 4 (28.5%) were postcricoid tumors, 2 (14%) were posterior pharyngeal wall tumors. Six (42%) patients were classified as stage III and 8 as stage IV (58%) (Table II).

There was no thyroid gland invasion in laryngeal carcinoma patients. Eight patients (57%) (5 pyriform sinus and 3 postcricoid tumor) in hypopharyngeal

TABLE I  
STAGE, LOCATION, THYROID CARTILAGE AND THYROID GLAND INVASION IN  
ADVANCED LARYNGEAL CARCINOMA

Tumor location	Number	Clinical stage		Thyroid cartilage invasion (%)	Thyroid gland invasion (%)
		Stage III	Stage IV		
Supraglottic	49	27	22	3 (6)	0 (0)
Glottic	68	44	24	8 (6)	0 (0)
Subglottic	1	1	0	1 (100)	0 (0)
Transglottic	11	5	6	8 (73)	0 (0)
<i>Total</i>	129	77	52	20 (16)	0 (0)

carcinoma group had thyroid gland invasion (2 of these patients were stage III and 6 of them were stage IV).

Twenty patients (16%) had evidence of thyroid cartilage invasion in laryngeal carcinoma group. Eight patients (40%) were transglottic, 8 (40%) were glottic, 1 (5%) was subglottic and 3 (15%) were supraglottic carcinoma. There were 3 (21%) cases with thyroid cartilage invasion in hypopharyngeal carcinoma patients.

## DISCUSSION

Ipsilateral hemithyroidectomy has been advocated for tumors that require total laryngectomy.<sup>[5,13-15]</sup> The purpose of hemithyroidectomy is to remove clinically occult laryngeal carcinoma metastasis to the gland and facilitate surgical clearance of the paratracheal nodes.<sup>[6,11,25]</sup>

The risk of hypothyroidism in these patients is attributed to the vascular damage during dissection of the preserved hemithyroid and consequently impairment of its ability to compensate the loss of the opposite lobe.<sup>[15,26]</sup> When laryngectomy and hemithyroidectomy are combined with radiothera-

py to the neck, permanent hypothyroidism ensues in 50-70% of patients.<sup>[4,6,16,17]</sup> Hypothyroidism, especially in elderly, is frequently overlooked. Among the sequels of hypothyroidism, the most prominent are poor wound healing, cardiac morbidity, and mental depression.<sup>[6,7,15,16,22]</sup>

Thyroid gland invasion in advanced laryngeal carcinoma has been reported between 0-14% (Table III).<sup>[1-8,27]</sup> Bahadur et al.<sup>[1]</sup> found that the incidence of thyroid gland involvement was highest in the post-cricoid and subglottic lesions. Biel and Maisel<sup>[6]</sup> reported that all specimens with tumor invasion of the gland were by direct extension through the cartilage and 70% of these patients had subglottic extension. Brennan et al.<sup>[7]</sup> reported that the most common mechanism of spread to the thyroid gland was by direct extension (87.5%). Dadas et al.<sup>[27]</sup> found that 2 of 182 total laryngectomy cases had thyroid gland invasion and both of these cases were transglottic tumors with subglottic extension. Harrison<sup>[11]</sup> mentioned a 25% incidence of thyroid gland invasion in 25 transglottic and subglottic cancer patients. Yuen et al.<sup>[28]</sup> reported 4% incidence of thyroid gland invasion in 226 total laryngectomies; the incidence

TABLE II  
STAGE, LOCATION, THYROID CARTILAGE AND THYROID GLAND INVASION IN ADVANCED  
HYPOPHARYNGEAL CARCINOMA

Tumor location	Number	Clinical stage		Thyroid cartilage invasion (%)	Thyroid gland invasion (%)
		Stage III	Stage IV		
Pyriiform sinus	8	4	4	2 (25)	5 (62)
Postcricoid	4	0	4	1 (25)	3 (75)
Posterior pharyngeal wall	2	2	0	0 (0)	0 (0)
<i>Total</i>	14	6	8	3 (21)	8 (57)

TABLE III  
LITERATURE REVIEW OF THE THYROID GLAND INVASION OF THE SQUAMOUS  
CARCINOMA OF THE LARYNX

Author	Total laryngectomy	Hemithyroidectomy		Thyroid cartilage invasion		Thyroid gland invasion	
	n	%	n	%	n	%	n
Bahadur et al. <sup>[1]</sup>	57	100	57	–	–	1	6
Gammert et al. <sup>[2]</sup>	59	100	59	–	–	0	0
Palmer et al. <sup>[3]</sup>	37	100	37	–	–	0	0
Shafer et al. <sup>[4]</sup>	22	100	22	–	–	0	0
Gilbert et al. <sup>[5]</sup>	266	65	173	14	23	14	23
Biel and Maisel <sup>[6]</sup>	261	72	187	24	63	6	11
Brennan et al. <sup>[7]</sup>	204	52	107	21	42	8	8
Pittam and Carter <sup>[8]</sup>	50	100	50	54	27	2	1
Dadas et al. <sup>[29]</sup>	215	84	182	–	–	1	2

was 16% in these patients with subglottic extension. Fagan et al.<sup>[10]</sup> observed a 2% incidence of thyroid gland invasion in their series of 102 cases of T<sub>3</sub> laryngeal carcinoma. In our study, no thyroid gland invasion was encountered in 129 advanced laryngeal carcinoma patients. However 8 (57%) of 14 hypopharyngeal carcinoma patients had thyroid gland invasion. The thyroid lobes are at risk of direct invasion by endolaryngeal tumors that involve the paraglottic space or the subglottis, and have either extended through the thyroid laminae, the cricothyroid membrane, the cricothyroid muscle, the cricoid cartilage, or the cricotracheal membrane.<sup>[10,29]</sup> Only 12 (9.3%) (11 patients had transglottic tumor with subglottic extension, 1 patient had a pure subglottic tumor) of 129 laryngeal carcinoma patients had subglottic tumor in our study group. This limited number of cases with subglottic involvement might be the cause of absence of thyroid gland invasion in laryngeal carcinoma patients. Twenty patients had thyroid cartilage invasion and 11 of them had extension to subglottic region.

In hypopharyngeal carcinoma patients thyroid gland invasion is also not frequently seen (Table IV).<sup>[1,6]</sup> Bahadur et al.<sup>[1]</sup> found thyroid gland invasion in only 13% of 23 patients (one pyriform sinus carcinoma, 2 post-cricoid carcinoma), Biel and Maisel<sup>[6]</sup> found 2% incidence in 55 patients (one pyriform sinus carcinoma). Sessions<sup>[9]</sup> found thyroid gland invasion in only 1% of 791 patients with hypopharyngeal and laryngeal cancers. In our study, spread of carcinoma to the thyroid gland in hypopharyn-

geal carcinoma was not by direct route. It can be explained by rich lymphatic network of the hypopharyngeal region.

The criteria, indications, and extent of thyroidectomy for treatment of advanced laryngeal and hypopharyngeal carcinoma are vague in the literature. According to Harrison<sup>[11]</sup> in primary subglottic tumors and transglottic tumors with subglottic extension, ipsilateral thyroidectomy should be routinely done; depending on the result of frozen section if there is metastasis to the thyroid gland, total thyroidectomy with paratracheal and paraesophageal lymph node dissection should be performed while preserving the parathyroid glands. Biel and Maisel<sup>[6]</sup> advocate ipsilateral or total thyroidectomy for suspicious thyroid glands, subglottic tumors, T<sub>4</sub> laryngeal tumors with transcartilaginous invasion, and T<sub>4</sub> pyriform sinus tumors. Brennan et al.<sup>[7]</sup> stated that the decision of removing thyroid gland and the extent of the thyroid resection should be made by the surgeon at the time of surgery. Total thyroidectomy is indicated when frozen-section

TABLE IV  
LITERATURE REVIEW OF THYROID GLAND  
INVASION IN HYPOPHARYNGEAL SQUAMOUS  
CELL CARCINOMAS

Author	Case number	Thyroid gland invasion (%)
Bahadur et al. <sup>[1]</sup>	23	3 (13)
Biel and Maisel <sup>[6]</sup>	55	1 (2)

diagnosis confirms tumor invasion to the gland and prophylactic ipsilateral thyroid lobectomy is warranted for transglottic lesions, huge anterior commissure lesions, and subglottic lesions. Fagan and Kaye<sup>[10]</sup> proposed that intraoperative assessment of the thyroid gland should determine the need for thyroidectomy in glottic and transglottic carcinomas. The invasion of the gland should be confirmed by frozen section before proceeding to thyroidectomy and total thyroidectomy should be performed in case of gland invasion and subglottic carcinomas.

There may be no need to perform thyroidectomy in all total laryngectomy cases. Based on the results of the present study, thyroidectomy should be performed only in selected cases with laryngeal squamous carcinoma. With glottic and transglottic carcinomas, the requirement for thyroidectomy should be based on intraoperative assessment of the thyroid gland capsule, outer surface of the larynx and trachea when the thyroid lobes have been reflected from the larynx and trachea on their vascular pedicles. Subglottic tumors have a propensity for rapid invasion of the peritracheal tissues. Our subglottic tumor number is limited to reach a conclusion, but based on the literature,<sup>[6,7,10,11,27]</sup> oncologically, hemithyroidectomy should be performed routinely. In advanced hypopharyngeal carcinoma thyroidectomy should be included in the surgical procedure.

Based on the results of the current study, there may be no need to perform thyroidectomy in all total laryngectomy cases. Requirement for thyroidectomy should be based on intraoperative findings suggesting the thyroid gland invasion and need for surgical clearance of the paratracheal nodes.

We recommend routine thyroidectomy during total laryngectomy in cases with subglottic extension and advanced hypopharyngeal tumors. In other cases, the assessment of extralaryngeal and thyroid gland invasion will guide whether thyroidectomy should be performed or not.

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