

Well-differentiated thyroid carcinoma invading the larynx and trachea

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Abstract: Larynx and trachea invasion by thyroid cancer is an uncommon but difficult problem. There is no consensus on indication for the extent of surgery, particularly when there is a requirement for airway reconstruction. In general, the surgeon must decide between a complete ablation of the tumor at the cost of large-mutilation and a less radical dissection that leaves residual tumor to be treated with radiation therapy and additional radio-iodine.

Keywords: Papillary Carcinoma, Larynx, Trachea, Total Laryngectomy

1. Introduction

Thyroid cancer is one of the most common endocrine malignancies, second only to ovarian cancer [1, 2]. Carcinomas of the thyroid can be classified histologically into four types: papillary, follicular, medullary and anaplastic. These cancers may further be divided into two

main groups: those of low grade and those of high grade malignancy.

Low grade malignant tumours include papillary, follicular and mixed papillary-follicular tumours while medullary and anaplastic tumours are high grade malignancies [2- 5] (Table I).

Table I: Histological classification of thyroid tumors.

Thyroid Carcinomas	Low Grade Malignant	High Grade Malignancies
	<ul style="list-style-type: none">• Papillary• Follicular• Mixed Papillary-Follicular Tumours	<ul style="list-style-type: none">• Medullary• Anaplastic

It is known that 80-90% of all thyroid tumors are of low grade malignancy with only 10-20% being highly malignant. In patients with low grade malignancies life expectancy is quite long, depending on the extent of spread of the tumour; long survival in the presence of lung or bone metastases is not uncommon. In contrast the high grade malignancies show rapid growth and spread, with death being almost inevitable within 2 years [5, 6]. Adverse prognostic factors have been well-established and include age, extra-thyroidal extension, tumor histology, primary tumor size, and distant metastasis [7, 8]. Extra-thyroidal extension has the greatest negative impact on prognosis. Invasion of the larynx and trachea by malignant tumours of the thyroid gland, either low grade or high grade, is a very difficult problem for the surgeon [3].

2. Discussion

Differentiated thyroid carcinoma originates from thyroid follicular cells is the most prominent malignancy of endocrine organs. There are two histological types of differentiated carcinoma, namely, papillary and follicular carcinoma. There are many studies that consider the papillary carcinoma as latent in autopsy specimens [9-16]. The prevalence of latent thyroid carcinoma is 3500 per 100,000 females, which is about 1000 times higher than that of papillary carcinoma treated clinically, 1.9-11.7 per 100,000 female (and 1.0-4.8 per 100,000 males) [16]. Furthermore, the papillary carcinoma is most frequently detected when patients are in their forties [17]. In contrast,

there are several autopsy and clinical studies that have indicated that papillary carcinoma showed a high incidence of lymphnode metastasis and multicentricity even for papillary microcarcinoma, that is, papillary carcinoma measuring 1 cm or less [16, 18-27].

There are some classification systems for papillary carcinoma that were proposed in order to identify high-risk cases. The prominent one is the American Joint Cancer Committee/Union Internationale Contre le Cancer (UICC/AJCC) TNM staging system [28]. This system basically evaluates time-oriented carcinoma progression by upstaging based on tumor size, extrathyroid extension, lymph node metastasis, distant metastases, and patient age. In the 1980s and early 1990s, diagnosis and evaluation of papillary carcinoma was completely reformed. Ultrasound is standard at most institutions for the initial evaluation of thyroid disease and can be combined with fine-needle aspiration biopsy for diagnostic purposes [8, 29-31]. When extrathyroidal extension of thyroid cancer is suspected, based on the patient's history or physical examination, cross-sectional imaging with CT or MRI is essential. CT with contrast represents an ideal study for advanced surgical planning. MRI with gadolinium may be a good alternative

[8]. The extrathyroidal extension of thyroid malignancies is associated with a higher rate of distant metastases and the FDG-PET/CT scanning has been shown to be particularly useful for imaging the more aggressive ones [8, 32-33]. Additional investigations may be performed at the time of surgery, including laryngoscopy/tracheoscopy/bronchoscopy and esophagoscopy [8]. The optimal management of thyroid cancer is dependent on the assessment of the malignant potential of the individual tumor at presentation. The prognostic factors in thyroid cancer are very well defined. Patient age, tumor grade, tumor size and distant metastasis. The most important prognostic factor from a surgical standpoint, however, is extrathyroidal extension. Patients with extrathyroidal extension have an increased incidence of local recurrence, regional spread and distant metastases [34]. Generally, a well-differentiated thyroid cancer as the papillary carcinoma shows an indolent behaviour. Rarely, this cancer show a very rapid growth with an adverse prognosis. A contemporary review from *Honings et al* reported a revision of 20 studies to a total of 10,251 patients with thyroid cancer, of which 595 (5.8%) with invasion of the airways [35-56] (Table modified II).

Table II: Occurrence of laryngotracheal invasion by thyroid carcinoma (Studies >50 cases).

First Author	Year	Period, Yr	No. Of Thyroid Carcinomas	Airway Involvement No.	%	Well Differentated, %
All Thyroid Carcinomas						
Schindel J	1971	15	225	10	4.4	Ns
Bresux Gp	1980	10	210	44	21.0	72.2
Segal K	1984	25	500	29	5.8	65.5
Tsumori T	1985	24	180	28	15.6	Ns
Mccarty Tm	1997	44	597	40	6.7	85
Koike E	2001	0.5	171	16	9.4	93.8
Sywak M	2003	2	97	7	7.2	100
Tsai Yf	2005	15	532	43	8.1	93.0
Randolph Gw	2006	-	135	21	15.6	Ns
Well-Differentiated Thyroid Carcinomas						
Fridman M	1982	30	190	13	6.8	100
Mcconahey Wm	1986	25	859	85	9.9	100
Nishida T	1997	25	301	69	22.9	100
Hu A	2007	38	576	13	2.3	100

*The cases reported by Lawson are not included in the totals.
NS=not stated.

This study may be the best general estimate of laryngotracheal tumor adherence or invasion among all patients presenting for surgical resection. We can therefore say that surgical resection is the primary treatment for patients with locally aggressive thyroid cancer; extrathyroidal extension and local invasion are important for a proper surgical excision of all gross disease and the need for adjuvant therapy, such as external beam radiation therapy and radioactive iodine [34]. The principles of surgical management of locally advanced thyroid cancer are these:

removal of all gross tumor, preservation of functioning structures, preservation of vital structures and use of adjuvant therapies. There are many controversies in the management of differentiated thyroid cancer. Total thyroidectomy is recommended in all prominent guidelines used in Western countries. The benefits of total thyroidectomy are: 1) the serum thyroglobulin level can be used as a marker of carcinoma recurrence; 2) radioiodine ablation therapy or whole body scan can be performed immediately when carcinoma recurrence is suspected; 3)

there is no risk of recurrence to the remnant thyroid. Its demerits are: 1) chronic administration of thyroid hormone becomes absolutely necessary after surgery; 2) persistent hypoparathyroidism may occur; 3) the incidence of recurrent nerve paralysis may increase. Thyroidectomy is more frequently performed for patients with papillary carcinoma having clinicopathological parameters predicting a worse prognosis, such as clinically apparent lateral node metastasis (N1b) and massive extrathyroid extension (pT4), regardless of tumor size or whether the tumor is solitary or multiple [16]. Laryngeal involvement is relatively rare, occurring in 12% of patients with locally invasive thyroid cancer [57] and specific recommendations must be tailored for each individual case. The surgical options are essentially: partial laryngectomy, and total laryngectomy. Thyroid cancer invading the laryngeal cartilage without intraluminal involvement can be treated by shaving the tumor from the underlying cartilage. If the tumor extends intraluminally, however, an open procedure will be necessary. If only one side has been invaded, the tumor may be amenable to a partial laryngectomy. Early cricoid cartilage invasion can be treated by shave excision. Subglottic invasion via direct cricoid cartilage invasion or through the cricothyroid membrane may require a total laryngectomy [34, 58]. Friedman noted higher recurrence rates and worse survival in patients with incomplete resection when compared with those undergoing radical resection [59]. Others have noted success with partial laryngeal surgery for locally invasive thyroid cancer [60]. Indications for total laryngectomy include airway obstruction, luminal hemorrhage, intraluminal invasion, or lack of larynx function [61–64]. This approach has demonstrated good local control for extensive larynx invasion [65] and is less morbid than organ-preserving or palliative therapies [64]. Tracheal invasion has been more extensively studied and characterized due to its greater frequency relative to laryngeal involvement [66]. In fact, tracheal invasion occurs in one third of cases of locally invasive thyroid cancer. In patients with superficial tumor adherence to the trachea, one should consider preservation procedures. In patients with more aggressive variants, complete surgical resection is considered optimal therapy. There are three compartments of regional lymphnodes in thyroid carcinoma: central, lateral and mediastinal compartments. Lymphnode dissection has not been actively recommended and only a guideline from American Thyroid Association has recommended routine dissection of the central compartment. One study recommended prophylactic mediastinal node dissection, but in most departments, the mediastinal compartment is not dissected unless metastasis is highly suspected on imaging studies. Endocrine surgeons in Japan tend to routinely dissect the central compartment during surgery for papillary carcinoma [67–69]. Re-operation for recurrence to the central node may include severe complications such as recurrent laryngeal nerve injury and persistent hypoparathyroidism [70–72]. There are no guidelines recommending lateral node dissection unless clinically

apparent node metastasis has been detected in the compartment. None of the Western guidelines recommended prophylactic dissection of the lateral compartment (modified radical neck dissection) and previous studies showed negative results [73–75], although some departments recommended it [76–78]. The increased surgical duration and blood loss, wound extension, the possibility of injury to other organs such as the thoracic duct, and increased patient complaints such as neck discomfort can be listed as the demerits of prophylactic dissection of the lateral compartment. The range to which patients can tolerate reoperation is actually an important point to consider in the application of prophylactic dissection of the lateral compartment. The application of prophylactic dissection of the lateral compartment remains an open question. A controversial element of remaining thyroid tissue treatment is radioactive iodine ablation. After a partial or subtotal thyroidectomy, radioactive iodine can be used for diagnosis and treatment of remaining thyroid tissue or metastatic tissue. Radioactive iodine ablation has been shown to reduce recurrences [79] and some believe it may even improve survival in selected patients [80–81]. While gross disease is best treated surgically, radioactive iodine is the treatment of choice in patients who are suspected of having persistent and/or occult disease. Radioactive iodine is a vital adjuvant treatment used not only to ablate the thyroid remnant, but also to treat patients deemed to be at high risk of recurrence after pathologic review (local invasion, positive margins or aggressive histological subtype).

3. Conclusion

There is no consensus regarding the management of patients with thyroid malignancies invading larynx and trachea. The surgeon must decide between a complete ablation of tumour at the cost of extensive mutilation and a less radical dissection which leaves residual tumour to be treated by complementary radiotherapy and radio-iodine.

Competing Interests

The authors declare that they have no competing interests.

Author's Contributions

All authors critically revised the manuscript and have approved the final manuscript.

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