



*An understanding of the patterns of invasion and the methods of treatment of invasive thyroid carcinoma promotes optimal treatment of invasive thyroid carcinoma.*

**S. Josué.** *Morning Light, Photo-Realist Landscape.* From the collection of Bruce Siegal, MD, and Maura Cooper, MD.

# Evaluation and Treatment of Aerodigestive Tract Invasion by Well-Differentiated Thyroid Carcinoma

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**Background:** Although rare, invasion of the upper aerodigestive tract by well-differentiated thyroid carcinoma can be a source of significant morbidity as well as mortality for the patient. Effective management of patients with invasive thyroid carcinoma requires an understanding of the patterns of invasion and methods of treatment, including surgical resection and adjuvant therapy.

**Methods:** The author reports on experience with invasive well-differentiated thyroid carcinoma, discussing diagnosis (based on physical examination, imaging studies, and endoscopy) as well as treatment options (based on degree of aerodigestive tract invasion).

**Results:** Direct intraluminal invasion of thyroid carcinoma requires definitive resection of aerodigestive tract lumen to remove all gross disease. However, when the lumen is not involved, "shaving" tumor from airway or esophagus is an acceptable treatment with a similar locoregional control rate and minimal morbidity when compared to definitive aerodigestive tract resection.

**Conclusions:** Successful treatment of invasive thyroid carcinoma should improve survival and reduce not only the morbidity of the disease, but also the morbidity of the surgical procedure.

## Introduction

Well-differentiated thyroid carcinoma infrequently invades the upper aerodigestive tract. However when invasion occurs, it can be a source of significant morbidity as well as mortality for the patient. Several studies have reported that the incidence of extrathyroidal extension of well-differentiated thyroid carcinoma is between 3% and 16%, excludes anaplastic carcinoma, and is considered a poor prognostic indicator of survival, together with patient age, distant metastases, size

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of the primary tumor, and completeness of the resection.<sup>1,2</sup> The most common site of extrathyroidal extension of well-differentiated carcinoma is into the overlying strap muscles. If cases of invasion into the strap muscles alone are eliminated, the incidence of laryngo-tracheal or esophageal invasion by all histologic subtypes is approximately 5% to 7%.<sup>3</sup> Furthermore, when cases of anaplastic carcinoma are excluded, the incidence of invasion of the upper aerodigestive tract by well-differentiated thyroid carcinoma (papillary and follicular subtypes) is less than 4%.

Despite the low incidence of aerodigestive tract invasion of well-differentiated thyroid cancer, significant life-threatening morbidities and mortality can occur. In several studies of thyroid carcinoma, local invasion is the cause of death in many patients. The uncontrollable symptoms related to invasion, namely airway hemorrhage and suffocation, were the cause of death in 47% of patients in one study by Tollefson et al.<sup>4</sup> In another study by McConahey et al,<sup>1</sup> as many patients died of uncontrolled local disease as distant metastases, suggesting that adequate control of local tumor is critical to avoid the mortality as well as the morbidity of the disease. Effective management of patients with invasive thyroid carcinoma requires an understanding of the patterns of invasion and methods of surgical treatment of the disease. This paper discusses the diagnosis and management of aerodigestive tract invasion by well-differentiated thyroid carcinoma and provides an algorithm of surgical options that should effectively control locoregional disease with minimal morbidity. Successful treatment of these tumors should improve survival and reduce not only the morbidity of the disease, but also the morbidity of the surgical procedure.

## Anatomic Relationships and Patterns of Invasion

Because of the intimate relationship of the aerodigestive tract and the thyroid, neoplasms arising in the gland that extend beyond the capsule freely invade locoregional structures. The most common sites of extrathyroidal invasion in 292 patients from a Mayo Clinic series were trachea, larynx, recurrent laryngeal nerve, and esophagus after strap muscle involvement was excluded.<sup>5</sup> Multiple sites of invasion are common, as demonstrated by the same study wherein 642 sites were involved in 292 tumors.<sup>5</sup> It is not surprising that multiple sites are commonly involved as the proximity of the gland to all the structures in the lower neck makes this pattern of invasion almost inevitable.

The patterns of invasion of the tumor are generally by direct extension of the primary or by extension of

metastatic paratracheal lymph nodes in the tracheo-esophageal groove. The degree of airway invasion progresses with advancing disease, with both primary and metastatic disease demonstrating similar patterns of invasion. In early invasion, tumor is seen at the time of resection penetrating perichondrium and invading superficially into laryngeal or tracheal cartilage. As the disease progresses, the tumor continues to invade medially, eventually involving the submucosa of the laryngo-tracheal lumen. At this point, there is no demonstrable mucosal ulceration, but a submucosal mass may be present in cases of gross disease. Tumor that continues to invade will eventually ulcerate the airway mucosa and gross tumor becomes visible (Fig 1).

The perichondrium of the laryngeal cartilage is an ineffective barrier against invasion of thyroid carcinoma. Direct extension of tumor into the larynx occurs readily, either laterally through the thyroid cartilage or anteriorly through the cricoid cartilage. The cricothyroid membrane is also a poor protective barrier and can be invaded by tumor that readily gains entry into the subglottis. Posterolateral invasion of the endolarynx can also occur when tumors in the region of the superior pole grow superolaterally and wrap around the thyroid cartilage lamina, entering the pyriform sinus through gross invasion of the constrictor muscles.

Tracheal invasion occurs most commonly by direct extension of the primary tumor through either the anterior or lateral tracheal wall. The relationship between the perithyroidal fascia of the thyroid gland and the peritracheal fascia has recently been studied in intraluminal invasive thyroid carcinoma.<sup>6</sup> On histopathology, perithyroidal fascia is contiguous with

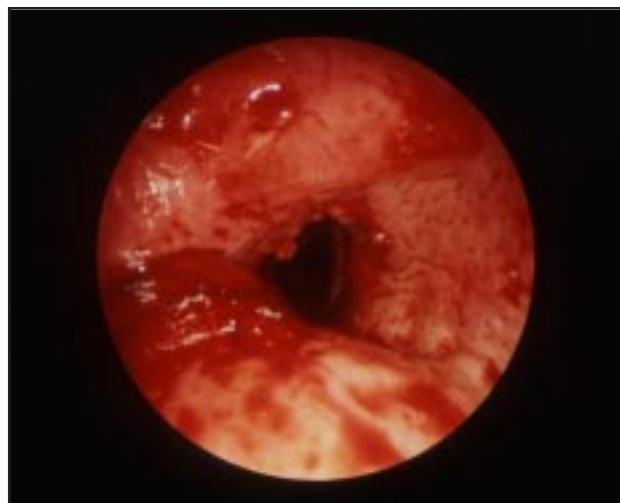


Fig 1. — Intraoperative bronchoscopy in a patient with longstanding hemoptysis and a thyroid malignancy. Tumor has invaded directly through the trachea and tracheal mucosa. Note the cobblestone appearance to the tracheal wall mucosa. The patient underwent tracheal resection with primary anastomosis and total thyroidectomy.

the peritracheal fascia at the intercartilaginous tracheal spaces. The interface between these two fascial layers at the tracheal rings are "points of weakness" where tumor freely penetrates into the airway lumen in advanced cases. Once into and through the submucosa of the trachea, tumor can spread superiorly, inferiorly, and circumferentially, both grossly and microscopically, to involve large portions of the airway.

Involvement of paratracheal lymph nodes in the tracheoesophageal groove with tumor can lead to invasion of recurrent laryngeal nerves as well as esophagus and portions of the trachea. The pattern of tracheal invasion by involved lymph nodes is similar to the pattern described above for direct tumor spread. Recurrent laryngeal nerve invasion occurs solely or often in combination with invasion into other sites. Involved nodes encase a nerve early, resulting in dysphonia or, in advanced cases, stridor or airway obstruction, particularly when a single nerve is invaded in a patient with a preexisting contralateral cord paralysis.

Esophageal invasion is relatively more innocuous than airway involvement. Because of the relative resistance of the esophageal mucosa to invasion, gross intraluminal involvement of the esophagus rarely occurs. However, tumors readily penetrate through esophageal musculature and cause dysphagia secondary to the compressive effects of the tumor mass on the underlying mucosa.

## Signs and Symptoms

De novo invasive thyroid carcinoma is rare; in the majority of cases, patients have received prior treatment for thyroid cancer, including surgical resection and postoperative iodine-131 (<sup>131</sup>I) or external beam radiotherapy. Despite appropriate previous treatments, aggressive recurrences occur that cause a variety of signs and symptoms. In one study by the author, the most common symptoms were hoarseness and stridor secondary to either primary intraluminal invasion of the larynx or trachea, or nodal invasion of the recurrent laryngeal nerve.<sup>5</sup> Other symptoms that have been reported include dysphagia and hemoptysis. The latter is always associated with intraluminal invasion and ulceration of the laryngeal or tracheal mucosa. Most dysphagia is related to the compressive effects of the tumor mass as it surrounds the aerodigestive tract. A lump in the base of the neck in a patient previously operated for thyroid cancer should raise the clinician's suspicion not only for tumor recurrence, but also for invasion into the surrounding midline neck structures. Careful assessment of hardness and mobility of the mass is necessary. Lesions fixed to the underlying air-

way are more suspicious for invasion than those that are mobile with or without swallowing. Complete examination of the head and neck including fiberoptic nasopharyngoscopy should be performed, with photodocumentation if possible. Inspection of the larynx and hypopharynx with flexible endoscopy may reveal true vocal cord paralysis, blood, pooling of secretions, aspiration, submucosal fullness, or direct tumor extension in the subglottic, tracheal, or laryngeal lumen. Palpation of the lateral neck is necessary to determine the presence of cervical metastases. All patients with findings on office endoscopy should undergo direct laryngoscopy and tracheobronchoscopy at the time of resection to adequately evaluate the extent of tumor to determine the surgical procedure required. Consent to proceed as indicated with an intraluminal procedure is required in the management of these cases.

Early invasion through the airway perichondrium or superficially into cartilage cannot be definitively diagnosed prior to surgery in most cases. Many of the patients with early invasion have no symptoms, and the diagnosis is made at the time of surgery. Patients with advanced invasion and direct intraluminal extension will demonstrate signs or symptoms that are recognizable and allow the surgeon to prepare the patient for operative intervention. Between the early and advanced cases is a "gray zone" wherein no symptoms of advanced disease may be present, yet at the time of surgery, the extent of disease requires a larger operation. Therefore, to successfully manage invasive thyroid carcinoma, the operating surgeon should have a working knowledge of surgical techniques that preserve the function of the upper aerodigestive tract while successfully removing the invasive tumor.

## Diagnostic Studies

Although ultrasound is the gold standard for imaging thyroid masses, it is of limited use in the evaluation of upper aerodigestive tract invasion by well-differentiated thyroid carcinoma. Ultrasound may not detect the subtle signs of invasion that both computed tomography (CT) and magnetic resonance imaging (MRI) can detect, and the latter two are the tests of choice in the evaluation of the aerodigestive tract in invasive thyroid carcinoma. Either CT scan or MRI may demonstrate tumor destruction of the laryngotracheal framework, which may not be clinically apparent on physical examination. They also can clearly show extension of tumor beyond the perithyroidal fascia against the airway, a pathognomic feature of invasive thyroid carcinoma that is not apparent on examination. Patients with obvious intraluminal involvement at the time of physical exam-

ination or with symptoms suggesting intraluminal invasion (eg, hemoptysis or stridor) can undergo a contrast-enhanced CT scan or MRI to assist with surgical planning (Figs 2-3). Patients in whom there is a high index of suspicion for invasion can also undergo a CT scan or MRI, particularly those patients with a previous history of thyroidectomy for carcinoma with obvious thyroid bed recurrence. There does not appear to be any obvious advantage or disadvantage to either imaging technique, although some radiologists or surgeons may prefer MRI as a diagnostic tool for demonstration of carcinoma invasion into adjacent tissues. Some patients with early invasion do not undergo preoperative imaging as there is little indication for scan, especially in de novo cases. As stated previously, the surgeon must be aware of the possibility of laryngotracheal cartilage invasion and should be prepared to tailor the operative procedure for adequate removal of the disease.

## Management of Upper Aerodigestive Tract Invasion

### *Surgical Techniques*

Various surgical management options are recommended in the literature for treatment of invasive thyroid carcinoma. In many studies, aggressive wide resection of all structures invaded by tumor is advocated to decrease locoregional recurrence, decrease subsequent morbidity, and improve long term survival regardless of intraluminal invasion.<sup>7-10</sup> However, not every invasive thyroid carcinoma extends into the lumen of the upper aerodigestive tract, as discussed previously. It appears that many cases of "early disease" in some reported studies may be overtreated by aggressive resection. The converse is also true; some advanced cases may be undertreated, leaving behind gross residual. Consequently, there is controversy addressed in these studies

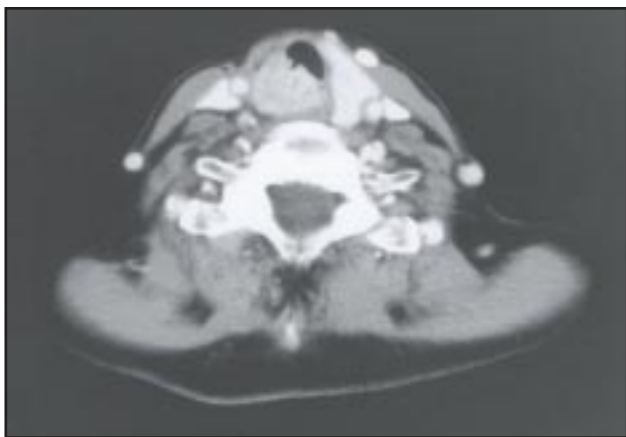


Fig 2. — Computed tomography scan of a patient who previously underwent right hemithyroidectomy for carcinoma. Recurrence has eroded through the tracheal sidewall with evidence of ulceration.

surrounding the "shave excision" vs complete resection of tumor from the aerodigestive tract.

The controversy lies in the definition of "shave excision" and is an opinion that continues to be open to final assessment based on long follow-up of many patients with this condition. In the author's opinion, "shave excision" is defined as the removal of all gross tumor by resection of a partial thickness of the aerodigestive tract wall; however, an assumption is made that microscopic foci of tumor remain. "Shaving" is effectively used in those early cases of aerodigestive tract involvement where there is obvious cartilage invasion but no direct intraluminal involvement. This approach has been shown in many studies to be as effective in locoregional control and survival as complete resection without the morbidity of extensive procedures that affect swallow, speech, and voice.<sup>5,11,12</sup> A study of 292 patients with invasive, well-differentiated thyroid carcinoma retrospectively evaluated over a 40-year period compared types of surgical resection in the management of this disease. Comparison among complete, "shave," and incomplete excision showed a statistically significant difference in survival for all patients. Similarly, when types of surgical excision were compared in patients with laryngotracheal invasion alone, there was a statistically significant difference in survival. However, comparison between complete excision and "shave" excision demonstrated no difference (Figs 4A-B). From the study, it may be concluded that survival rates of patients undergoing "shave" excision were no different from those of patients undergoing radical tumor resection (complete excision) if gross tumor did not remain.<sup>5</sup> "Shave excision" is generally not appropriate in cases of direct intraluminal invasion. Removal of the disease adherent to the airway that leaves residual gross intraluminal tumor is ineffective treatment that leads to death by local disease in many cases.<sup>4</sup> Complete resection of

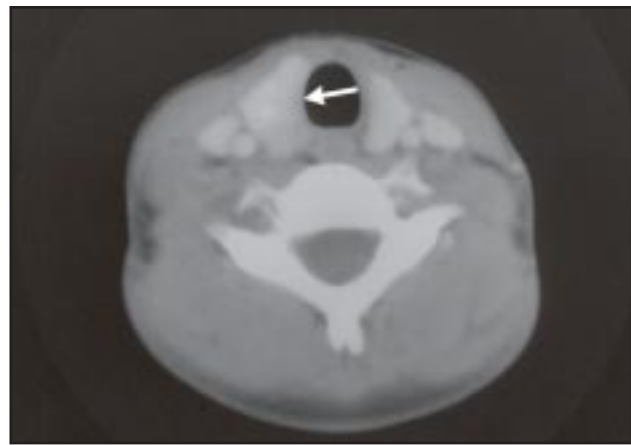
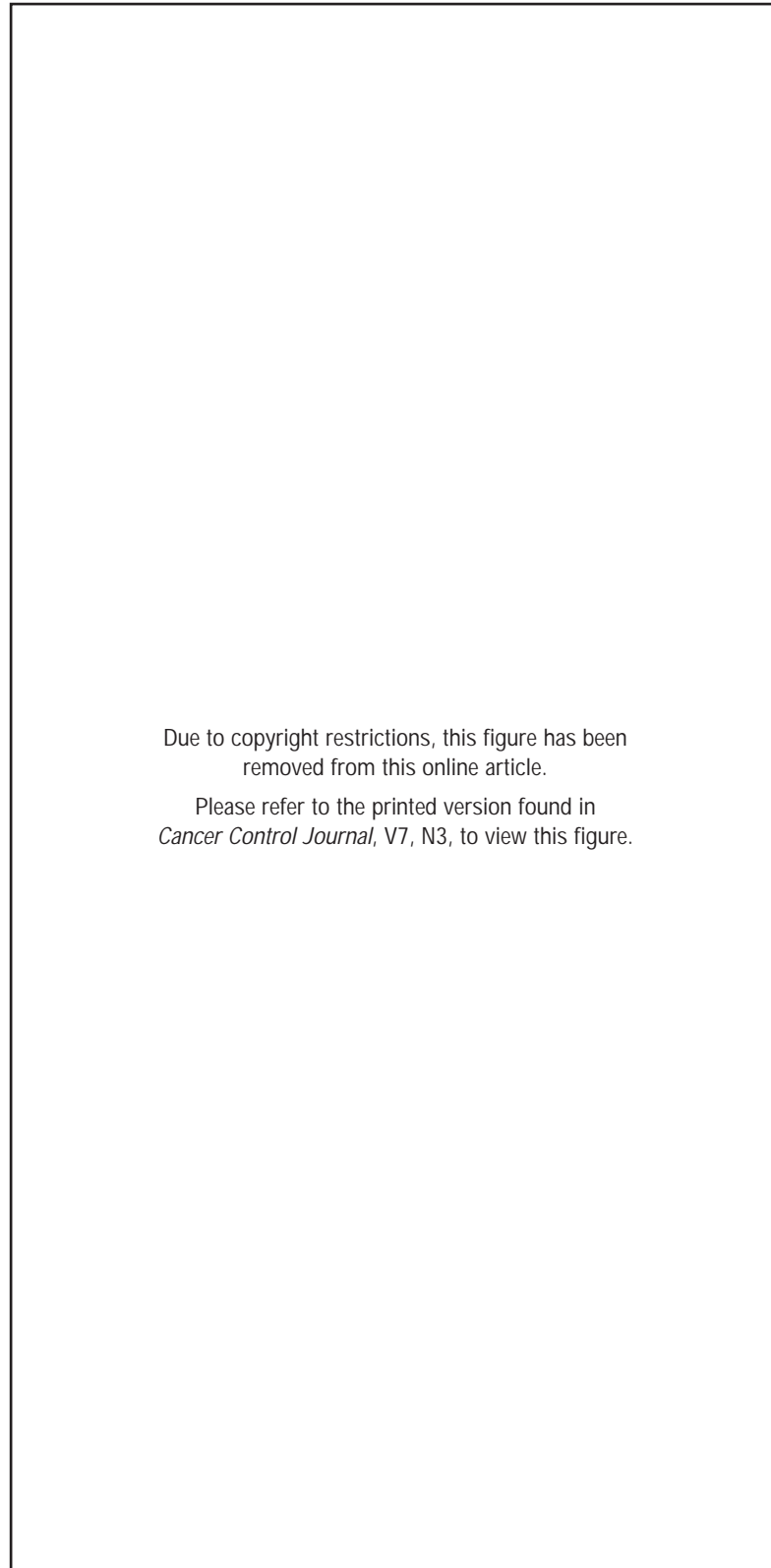


Fig 3. — Computed tomography scan of thyroid carcinoma that has invaded the tracheal cartilage but not the airway lumen. Note the absence of the perithyroidal fascial plane between the gland and the trachea on the right (arrow). Shave excision was performed.

gross intraluminal tumor by procedures violating the aerodigestive tract is necessary in cases of direct intraluminal invasion to improve locoregional control and survival. It is in these cases that more aggressive wide resection is required. However once the decision to

open the aerodigestive tract is made, strong consideration should be given to partial procedures that can preserve function and remove only those portions of the aerodigestive tract that are invaded.



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That it is acceptable to leave presumed positive microscopic margins with the "shave excision" for early cases of invasive thyroid carcinoma is in direct contradiction to the management of upper aerodigestive tract squamous cell carcinoma. However, adjuvant treatment with <sup>131</sup>I or external beam radiotherapy can be used to effectively control microscopic disease and is far more acceptable in most cases than the morbidity associated with a larger procedure that offers little survival advantage.<sup>13</sup>

### Larynx

Tumor invading into the laryngeal cartilage but without direct intraluminal involvement can be shaved from the underlying cartilage. The airway is not entered, and function is preserved. Tumors extending intraluminally (as seen by office fiberoptic examination and intraoperative laryngotracheobronchoscopy) require open procedures. Often, tumor has invaded into one side of the larynx and is amenable to a partial vertical or hemilaryngectomy. The tumor is resected and function is preserved with these procedures. A temporary tracheotomy is required; however, the patient is decannulated quickly and voice is preserved. More extensive involvement may require more complex procedures as dictated by tumor location and its effects on true vocal fold mobility. The algorithm for airway invasion is shown in Fig 5.

Early cricoid cartilage invasion is readily shaved. However, when intraluminal spread has occurred, partial procedures, though possible, are somewhat limited. When approximately one third or more of the cricoid ring is removed, formal laryngotracheal reconstruction should be performed to prevent airway stenosis. Extensive subglottic invasion, either by direct destruction of the cricoid cartilage or through the cricothyroid membrane, requires total laryngectomy for technical reasons.

## Trachea

Anterior or lateral tracheal invasion is the most common route of thyroid carcinoma invasion. Tumor grows into the tracheal ring cartilage and through intercartilaginous spaces into the tracheal lumen. Tumor invasion through perichondrium and superficially into the tracheal cartilage can be shaved without creating a full-thickness defect. Once tumor invades into the tracheal lumen, full-thickness resection is necessary to remove gross disease. Gross tumor confined to the anterior or lateral wall in a small area is amenable to window resection with primary closure or sternocleidomastoid muscle patch closure. It is often possible to remove a wedge of trachea, leaving the posterior wall intact and closing the defect primarily; however, it may be technically more sound to perform tracheal resection and primary anastomosis to avoid any long-term complication related to wedge resection, such as stenosis at the site. More extensive intraluminal tracheal involvement requires a tracheal resection with primary anastomosis. The extent of tracheal surgery in these cases is related to experience of the surgeon and the intraoperative findings.

## Recurrent Laryngeal Nerve

The recurrent laryngeal nerve can be invaded by tumor involving either the gland or the paratracheal lymph nodes. Preoperative assessment of true vocal

fold mobility with fiberoptic endoscopy or mirror examination is necessary to determine nerve function. A patient can have near normal voice with vocal compensation by one functioning fold, and a unilateral cord paralysis may not be diagnosed preoperatively by listening to vocal quality alone. Preexisting recurrent laryngeal nerve paralysis requires resection of the nerve with the tumor in nearly all cases. A preoperatively paralyzed nerve rarely returns to normal function after tumor resection. The more common clinical situation is preoperative normal vocal fold mobility with tumor encasing the nerve at surgery. Carefully “shaving” tumor from nerve can lead to either temporary or permanent vocal fold paralysis. Vocal rehabilitation with true vocal fold medialization is available for patients who remain symptomatic with unilateral vocal fold paralysis after tumor resection. The complication of bilateral cord paralysis does occur, and the threshold for tracheotomy in recurrent invasive thyroid carcinoma cases with preexisting unilateral fold paralysis should be low. However, these clinical situations are unique and require individualized treatments that are beyond discussion in this paper.

## Pharynx and Esophagus

Intraluminal invasion into the pharynx and esophagus is rare, and dysphagia after resection is minimal if not improved, based on the pattern of invasion. The mucosa of the esophagus and pharynx is resistant to

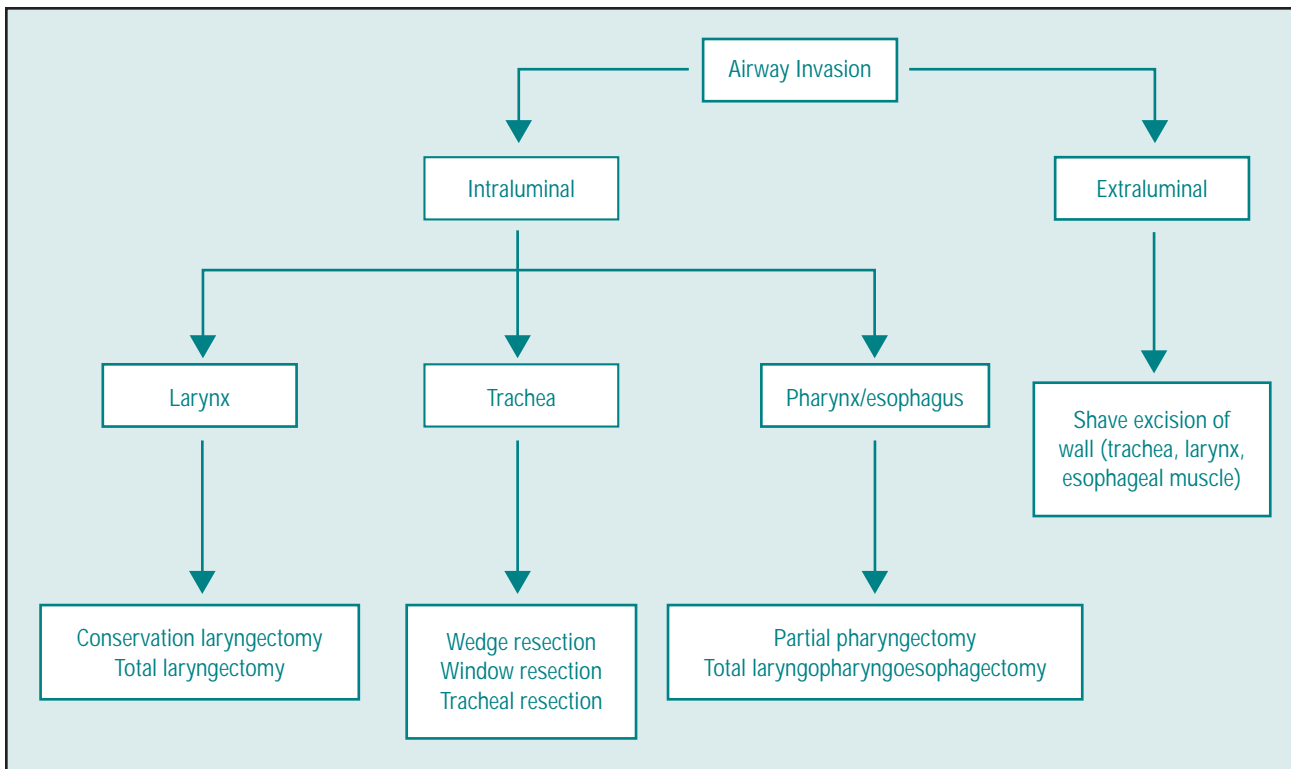


Fig 5. — Algorithm for management of invasive thyroid carcinoma.

direct invasion, but the muscular coat may be readily invaded leading to significant compressive dysphagia. At resection, the tumor is dissected from the underlying mucosa by developing a submucosal plane without difficulty. Tears in the underlying mucosa are repaired primarily. More extensive involvement, including intraluminal invasion, does occur. Partial resection of the pharynx is possible through a lateral pharyngotomy and is often required with a partial laryngeal procedure. Partial esophageal resections of the cervical esophagus are difficult to manage and may require total circumferential cervical esophagectomy with reconstruction by free tissue transfer or tubed myocutaneous pedicled flap. The latter scenarios are rare.

## Adjuvant Therapy for Invasive Thyroid Carcinoma

All patients with invasive thyroid carcinoma are in a poor prognostic category for survival and, as such, require adjuvant postoperative therapy with either  $^{131}\text{I}$  or external beam radiotherapy for adequate locoregional control. In general, most invasive tumors will take up some radioactive iodine, particularly early in the course of disease. However, there are recalcitrant cases that no longer uptake  $^{131}\text{I}$ . In cases of gross residual disease where the morbidity of the procedure required to remove all disease is not acceptable to the patient or the patient is not a surgical candidate, external beam radiotherapy can be effective in controlling locoregional disease. External beam radiotherapy should be considered as an option when surgical and radioactive iodine interventions are exhausted. Suppression with levothyroxine should also be done routinely because prolonged elevation of thyroid-stimulating hormone (TSH) in cases of thyroid carcinoma is associated with a high incidence of tumor recurrence in many cases. Thyroglobulin levels and  $^{131}\text{I}$  scanning may be used to determine tumor recurrence and spread and should be included in the physician's algorithm for the long-term follow-up of patients with thyroid carcinoma.

## Conclusions

Though rare, invasive, well-differentiated thyroid carcinoma is associated with a high incidence of morbidity and mortality. Structures commonly invaded by thyroid carcinoma include the strap muscles, larynx, trachea, esophagus, and recurrent laryngeal nerve. Symptoms that are often life-threatening include stridor, hoarseness, hemoptysis, and dysphagia and occur in most cases in patients with a previous history of treated thyroid malignancy. The goal in treating this dis-

ease is to provide adequate locoregional control while minimizing not only the morbidity of the tumor, but also the morbidity of the surgical treatment. Therefore, procedures that attempt to preserve the functions of the upper aerodigestive tract are preferred to radical extirpative procedures that offer little survival advantage in many studies. Adjuvant therapy is often required in most cases and should be utilized with surgery to improve locoregional control.

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