

TITLE: Management of Invasive Thyroid Carcinoma

SOURCE: Grand Rounds Presentation, UTMB, Dept. of Otolaryngology

DATE: May 2, 2007

RESIDENT PHYSICIAN: Camysha Wright, MD

FACULTY PHYSICIAN: Vicente Resto, MD, PhD

SERIES EDITORS: Francis B. Quinn, Jr., MD and Matthew W. Ryan, MD

"This material was prepared by resident physicians in partial fulfillment of educational requirements established for the Postgraduate Training Program of the UTMB Department of Otolaryngology/Head and Neck Surgery and was not intended for clinical use in its present form. It was prepared for the purpose of stimulating group discussion in a conference setting. No warranties, either express or implied, are made with respect to its accuracy, completeness, or timeliness. The material does not necessarily reflect the current or past opinions of members of the UTMB faculty and should not be used for purposes of diagnosis or treatment without consulting appropriate literature sources and informed professional opinion."

Introduction

Invasive thyroid carcinoma encompasses any malignant tissue that protrudes beyond the capsule of the gland. Although rare, extrathyroidal invasion is associated with a worse prognosis and increased risk of morbidity. Management remains controversial, with some authors advocating conservative treatment with preservation of midline structures and others, aggressive extensive en bloc resection. There are a number of prognostic factors to consider when evaluating thyroid nodules and thyroid cancer risk.

Prognostic Factors

In addition to the standard TNM system (table below), a number of systems have been developed to gauge risk-group classification. The factors that determine prognosis in patients with well-differentiated carcinomas of the thyroid have been well delineated and are based on age, sex, and findings at the time of surgery. Several prognostic schemes, represented by acronyms, have been established by different groups and are as follows: AMES (Lahey Clinic, Burlington, MA), GAMES (Memorial Sloan-Kettering Cancer Center, New York, NY), and AGES (Mayo Clinic, Rochester, MN). The letters stand for A - age, S - sex, E - extent of primary tumor, M - metastasis to distant sites, and G - histologic grade of the tumor.

Depending on variables present, patients can be categorized into one of three groups: high, intermediate, or low risk. The classifications focus on parameters that are well established in the literature as risk factors for a poorer prognosis. A parameter common to all scoring systems is age given that patients over 45 years of age have a worse outcome than their younger counterparts. Larger primary tumor size and extension and the presence of metastases increase a patient's stage and affect 5-year survival. For papillary carcinoma the 5-year relative survival rates by stage are 100% for stages I and II, 95.8% for stage III, and 45.3% for stage IV.

For follicular carcinoma the 5-year relative survival rates are 100% for stages I and II, 79.4% for stage III, and 47.1% for stage IV(17).

Specific prognostic factors are extremely important and include:

- **Histology*: the cell type is one of the most predominant prognostic factors and influences other risk factors.
- **Age*: at the time of diagnosis is a significant effected risk factor, e.g. well-differentiated thyroid carcinoma has a greater tendency to invade the surrounding structures in patients older than 40. Mortality rate increases significantly in patients older than 60.
- **Sex*: females are at a higher risk of developing thyroid nodules; however, males have a higher risk of thyroid cancer. Tumors are more aggressive and the prognoses are poorer in males than those in females.
- **Size of primary lesions*: the larger the size of the tumor the greater the risk of vascular invasion or metastatic spread. Tumors greater than 1.5 cm carry a higher risk of recurrence and mortality.
- *Extracapsular* or vascular invasion and *metastatic* disease are poor prognosis factors. Regional metastasis in papillary carcinoma correlates positively with the incidence of local recurrence. Well-differentiated thyroid cancer, which invades and paralyzes the recurrent laryngeal nerve, requires a wider resection. Distant metastases are rare in papillary cancers, but more often seen in follicular tumors, and are associated with poorer prognosis.
- **History of radiation* is associated with higher risk of papillary carcinomas requiring more extensive resection to eradicate disease.

TNM staging for papillary and follicular carcinoma(17)

Primary tumor (T)

TX Primary tumor cannot be assessed

T0 No evidence of primary tumor

T1 Tumor 2 cm or less in greatest diameter, limited to the thyroid

T2 Tumor > 2 cm and < 4 cm in greatest diameter, limited to the thyroid

T3 Tumor > 4 cm in greatest diameter and limited to the thyroid or any tumor with minimal extrathyroidal extension (eg, extension to sternothyroid muscle or perithyroidal soft tissues)

T4a Tumor of any size extending outside the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve

T4b Tumor invading prevertebral fascia or encases carotid artery or mediastinal vessels

Regional lymph nodes (N)

NX Regional nodes cannot be assessed

N0 No regional lymph node metastases

N1 Regional lymph node metastases

N1a Metastasis to level VI (pretracheal, paratracheal, and prelaryngeal nodes)

N1b Metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes

Distant metastasis (M)

MX Distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastasis

Stage grouping (for papillary and follicular carcinoma)

Under 45 years of age

Stage I Any T Any N Any M

Stage II Any T Any N M1

45 years of age and older

Stage I T1 N0 M0

Stage II T2 N0 M0

Stage III T3 N0 M0

T1 N1a M0

T2 N1a M0

T3 N1a M0

Stage IVa T4a N0 M0

T4a N1a M0

T1 N1b M0

T2 N1b M0

T3 N1b M0

T4a N1b M0

Stage IVb T4b Any N M0

Stage IVc Any T Any N M1

Diagnosis

The most common diagnostic measures include needle biopsy or aspiration, thyroid blood studies, and radiology imaging. Needle biopsy, a superior diagnostic technique, which provides

accurate cytologic finding with little to no morbidity, has become an incremental step in thyroid nodule workup.

History and physical examination: a thorough history should be obtained. Symptoms such as pain, hoarseness, dysphagia, dyspnea, stridor, hemoptysis, and rapid enlargement of the mass may occur with thyroid carcinomas, but are not necessarily to be the signs of malignancy. A history of irradiation, especially in childhood, is an important risk for papillary carcinoma. External low dose irradiation is the treatment for some diseases, e.g. acne, tonsillar hypertrophy, enlarged thymus, cervical adenitis, sinusitis and malignant disease. Previous thyroid diseases such as goiter, Hashimoto's disease and Grave's disease can be risk factors for thyroid cancer.

Physical exam includes the full head and neck examination. A benign thyroid nodule is usually well-circumscribed, soft, non-tender, and movable free to surrounding tissue. A malignant tumor is harder, can be greater than 4 cm in diameter and may be fixed to the surrounding and underlying tissues. Neck examination can reveal palpable metastatic cervical lymph nodes, especially in the anterior compartment (level III, IV, VI) and less common in level V. Pre-operative laryngoscopy evaluates for vocal cord paralysis and should be documented in all patients to determine the function of the recurrent laryngeal nerve and use for preoperative planning. If one cord is noted to be paralyzed, it is likely secondary to an invasive process until proven otherwise, and removal of the nerve can be planned in the future operative intervention.

Fine needle aspiration (*FNA*) is performed on a palpable nodule or under guidance using ultrasonography. Fine needle biopsy is an accurate diagnostic procedure in papillary, medullary, metastatic, anaplastic cancers, and malignant lymphomas. Differentiation between follicular and Hurthle cell neoplasms is based on capsular or vascular invasion. A malignant specimen on fine needle aspiration is a strong indication for surgery; however, a negative result cannot rule out cancer. There are some *limitations of fine needle aspiration* to differentiate (1) adenomatoid nodule vs. follicular neoplasm, (2) papillary carcinoma with cystic change and benign cystic nodules, (3) large multinodular goiters and present malignancy, (4) Hashimoto's thyroiditis vs. oxyphilic cell (Hurthle) neoplasm, (5) multinodular goiter vs. Hurthle cell neoplasm, (6) Hashimoto's vs. malignant lymphoma, (7) malignant melanoma.

Blood test: thyroid function tests include (1) *thyroxin* or T4, (2) *triiodothyronine* or T3, and (3) *thyroid stimulating hormone* or TSH. *Serum calcium and phosphorous* levels may indicate hyperfunction of parathyroid gland adenoma, which may be associated with thyroid gland malignancy. *Thyroglobulin* (Tg) is usually measured as a baseline before and following up after surgery of well-differentiated thyroid carcinomas because it correlates with histologic types of tumors. Recurrent tumors are usually associated with high Tg level. *Calcitonin* is a useful test for diagnosis and screening in patients with medullary thyroid carcinoma and their family members; however, it is not a work up test. *Antimicrosomal and anti-Tg antibody titer* are unrealistic tests for screening or following up a thyroid cancer because of high cost and low-specificity

Imaging studies:

- Ultrasonography: is one of the most sensitive and effective tests for differentiation a thyroid and a non-thyroid nodule in more than 80% of cases. It provides an accurate tri-dimensional location, follows up the nodular size, and indicates nodular location for the

fine needle aspiration. US can detect the nodules as small as 2 to 3 mm and differentiate between solitary and multinodular diseases. It is however not useful in detecting invasive disease. If one suspects invasion based on physical examination findings, such as fixed nodal disease or true vocal cord paralysis, then further imaging, such as CT or MRI is necessary. CT is useful in detecting tracheal invasion and evaluating for cervical metastasis. One drawback to this test for thyroid cancer is that it may delay postoperative radioactive iodine treatment.

- Magnetic resonance imaging (MRI): is very useful to detect residual, recurrent and metastatic cancers. T2 imaging is useful in differentiation between tumors and fibroses in an operated neck tissue, and detection of muscle invasion. MRI also shows tracheal displacement and vascular relationship involved with large masses. Fat-saturation MRI can be used in suspected recurrent tumors, which are not identified by radioiodine scan.
- Chest x-ray is helpful in detecting tracheal deviation, airway narrowing, and existent lung and bone metastasis. Patterns of calcification on chest x-ray are useful in identifying the types of cancer: (1) rim or eggshell calcification suggests a benign lesion, (2) bilateral calcification in superolateral aspect of the thyroid gland indicates MTC and (3) extensive irregular calcification suggests a multinodular goiter.

Classification, Pathology, and Biology

Well-differentiated thyroid carcinomas (WDTC) - Papillary, Follicular, and Hurthle cell

Papillary, follicular, and Hurthle carcinomas are classified as well-differentiated malignancies. Papillary and follicular carcinomas are the two most common malignancies found in the thyroid gland and occur 60-70% and 10% of the time, respectively Hurthle cell makes up about 3% of thyroid malignancies. All three of these cancers arise from the thyroid hormone producing follicular cells, however, their pathogenesis is largely unknown (15). Unlike medullary carcinoma, they do not have a definite genetic inheritance pattern. Only a small number are thought to occur in rare familial syndromes (15). Recent research has led to the identification of a few cancer-causing genes that may be responsible for the benign or malignant transformation of follicular cells. Specifically, RET proto-oncogene mutations have been implicated in papillary and medullary carcinoma but a definitive link has yet to be proven (14). Despite the uncertainty of these molecular events, certain clinical factors, such as exposure to radiation, increases the likelihood for developing thyroid cancer, especially papillary carcinoma. In areas with endemic goiter, in populations that are iodine deficient and therefore have high level of TSH stimulation, the incidence of follicular carcinoma is high. Although this relationship has been confirmed in the laboratory where follicular carcinoma can be induced by exposure to TSH after exposure to a mutagen, the exact mechanism for this is not known (16). This relationship has not been consistent with papillary or Hurthle cell carcinoma (16).

Papillary and follicular carcinomas are more frequently found in women. The mean age of incidence of papillary carcinoma is 35, while follicular tends to occur at an older age than papillary, with a mean age of 50 years (6). Lymph node involvement is relatively common in papillary carcinoma, with lymphatic spread being the major route of metastasis. In contrast to papillary carcinoma, follicular carcinoma tends to metastasize via angioinvasion and hematogenous spread and has a higher frequency of distant metastasis. When nodes are involved in follicular cancer, however, outcome is usually poor. This probably relates to the fact that

patients with lymph node involvement at the time of diagnosis are also likely to have significant local disease and visceral invasion (43). Bone is the most common site of distant metastasis, with lung coming in second.

One of the most controversial and confusing neoplasms of the thyroid gland is the Hurthle cell carcinoma (HCC). This WDTC comprises approximately 3% of thyroid malignancies (6). These cells are believed to be derived from follicular cells and together form a variant of a follicular neoplasm (6). A Hurthle cell neoplasm is defined as an encapsulated group of follicular cells with at least a 75% Hurthle cell component. Like follicular carcinoma, HCC requires histologic proof of vascular and capsular invasion to distinguish it from an adenoma. This makes diagnosis with either FNA or frozen section almost impossible, requiring permanent sections. Although classified as a WDTC carcinoma, HCC is more aggressive than follicular carcinoma. It also has a greater propensity for malignant transformation to anaplastic carcinoma than any other WDTC.

Medullary Thyroid Carcinoma (MTC)

Medullary thyroid carcinoma accounts for approximately 10% of all thyroid cancers and has an incidence of approximately 1000 new cases, in the United States, each year (1). It arises from the parafollicular cells or C-cells of the thyroid gland that differentiate from neural crest cells during embryologic development. Medullary thyroid cancer develops as either sporadic or familial. Overall, MTC tends to be a more aggressive cancer than the WDTCs. It usually spreads early by lymphatic dissemination to peritracheal and mediastinal lymph nodes has an overall incidence of lymph node metastases >50% (29).

Sporadic MTC accounts for approximately 70% of all MTCs (5,29). The mean age at presentation is 50 years (41). This form of MTC tends to occur unilaterally and unifocally and usually presents as an enlarging thyroid nodule. It is slightly more aggressive than familial MTC, which composes the remaining 30% of medullary thyroid carcinomas. The most common clinical presentation of sporadic and inherited MTC is a mass in the neck (36).

Anaplastic carcinoma (ATC)

Anaplastic carcinoma of the thyroid is a rare but highly lethal form of cancer with a median survival in most series of less than 8 months (22,23,25,27). It comprises 1%-10% of all thyroid tumors and up to 30% of thyroid malignancies in patients older than 70 years (26,28,45). ATC usually occurs in the elderly with a mean age of presentation of 60 years and has a slight female predominance (23). The most common clinical symptom is a rapidly enlarging mass and because of its aggressiveness, symptoms of invasion such as hoarseness, dysphagia, dyspnea, and superior vena cava syndrome are not uncommon.

Treatment Considerations

Wein and Weber (50) discussed a number of treatment considerations when evaluating thyroid cancer. These included:

When a follicular neoplasm's obtained on FNA, 80% benign, 20% carcinoma. Of this 20%, up to 50% have the diagnosis of follicular variant of papillary carcinoma.

- For patients with follicular carcinoma the most important prognostic parameter is age, not sex. Patients 45 years of age or older at the time of diagnosis have a worse prognosis than their younger counterparts.
- Individuals with carcinomas greater than 5 cm fare worse, probably because of extracapsular spread.
- Patients with vascular invasion do worse than individuals with capsule invasion.
- Insular carcinoma is also considered to be a variant of follicular carcinoma that presents with more advanced-stage disease at diagnosis, a higher frequency of metastasis, and a decreased survival when compared with pure follicular carcinoma.
- Papillary carcinoma has a number of variants requiring special consideration.
 - The diffuse sclerosing variant is a rare subtype that tends to present in women younger than 25 years of age. Tumor size is large at presentation (mean, 6.9 cm) with 100% of patients developing regional lymph node metastases. Despite these factors, prognosis seems to be favorable when aggressive care is rendered
 - The tall cell variant, representing approximately 5% of papillary carcinomas, is also considered an aggressive subtype with a worse prognosis. Typical presentation is in the older patient with a large tumor, extrathyroidal extension, and nodal metastases.
 - The follicular variant of papillary carcinoma, representing approximately 24% of cases, is more frequently multicentric but has clinical behavior similar to pure papillary carcinoma.
- Hürthle cell carcinomas, considered by some to be a variant of follicular carcinomas, represent only 3% of all thyroid tumors.
 - Ipsilateral lymph node metastases are present in 25% of patients.
 - In patients with metastases, only 38% of lesions demonstrated uptake of radioactive iodine (RAI)

Management

Invasive Carcinoma

The locally invasive presentation of well-differentiated thyroid carcinoma occurs in less than 5% of all cases. The most common pathology involved is papillary carcinoma. There is a male predominance with patients presenting at a higher mean age than those with noninvasive disease (31). Invasive thyroid carcinoma spreads by direct extension from the primary tumor or from extracapsular spread of paratracheal nodal metastasis. Tumor at the primary site has the capacity for invasion through the cricothyroid membrane or the thyroid cartilage anteriorly or may extend posteriorly to wrap around the thyroid cartilage and present in the region of the piriform sinus. Extracapsular spread from paratracheal nodes tends to invade laterally in the region of the tracheoesophageal groove (32).

The goals of treatment for invasive thyroid carcinoma include prevention of hemorrhage and airway obstruction, preservation of a functional upper aerodigestive tract, prevention of locoregional recurrence, and long-term survival. Frequently the mandate for removing all gross disease is at odds with function-sparing surgery. Several authors have advocated a conservative approach of shaving the tumor (24,31,32,33) off the tracheal wall, but other authors advocate more aggressive approaches to accomplish a complete removal of tumor (11,21). Few disagree

that the goal in treating invasive thyroid carcinoma is to remove all macroscopic disease noted at the time of surgery. The controversy lies in the degree of resection required to accomplish this result. For individuals with limited tracheal deficits but gross intraluminal spread of tumor, window and sleeve resections are necessary. For larger defects, up to one third the circumference of the trachea, use of sternocleidomastoid and pectoralis major myoperiosteal flaps over T-tubes has been described (12). For larger defects, tracheal resection with re-anastomosis with release procedures while preserving at least one recurrent laryngeal nerve has been described with favorable results (19). McCaffrey et al (31) retrospectively compared three groups of patients undergoing surgery for thyroid carcinoma with limited tracheal invasion. These groups included individuals undergoing complete surgical excision (group I), shave resection with the potential for microscopic residual disease (group II), and incomplete resection with macroscopic residual disease remaining (group III). The overall 5-year survival was 79%. No significant difference was noted in survival between groups I and II, whereas survival in group III was the lowest. The authors concluded that for selected patients shave resection is a viable option that allows preservation of upper aerodigestive tract anatomy without compromising survival. The importance of postoperative RAI therapy and possible external beam radiation were also stressed.

Esophageal invasion, when present, tends to invade only the outer muscular layers of the esophagus. Because achieving wide tumor-free margins is less of an issue with thyroid carcinoma than with squamous cell carcinoma, limited resection without intraluminal entry is possible. When limited intraluminal invasion is encountered, primary closure of the defect after resection is an option when closure does not predispose to stricture formation. When extensive resections of the esophagus are required, options for reconstruction with pedicled and free tissue transfer parallel those described in the literature for the treatment of squamous cell carcinoma (13).

When a patient presents for thyroidectomy and the preoperative examination indicates paralysis of the recurrent laryngeal nerve, attempts to save the nerve at the time of surgery should not be pursued. Primary thyroplasty may be considered in this scenario. When the recurrent laryngeal nerve is noted to be functional preoperatively, attempts should be made to preserve the nerve if possible. Falk and McCaffrey (10) retrospectively compared patients who had a functional recurrent laryngeal nerve sacrificed at the time of thyroidectomy with those with nerve preservation and noted that complete resection of tumor and nerve sacrifice offered no survival benefit over potentially incomplete resection of tumor and nerve preservation.

Laryngeal invasion requires the surgeon to be aware of the various options in conservation laryngeal surgery if the goal of avoiding total laryngectomy is possible. Vertical partial laryngectomy may be appropriate for patients with unilateral disease, whereas a supracricoid partial laryngectomy may be considered for extensive anterior invasion (13). The indications for total laryngectomy include extensive laryngeal spread beyond the scope of organ-preservation surgery and involvement of more than one third of the cricoid ring (32).

In a recent article by Segal et al (43) they performed a retrospective review of 1200 pts with diagnosis of well-differentiated thyroid carcinoma. 49 pts (5%) showed involvement of an adjacent structure (larynx, trachea, esophagus) - 30 female, 19 male. The type of surgery, radiation treatment radioiodine treatment, and patient demographics were evaluated. Most

common pathologic finding was papillary carcinoma (43 pts, 88%). Follicular carcinoma, including Hurthle cell carcinoma was noted in 6 pts (12%). Anaplastic tumors were excluded. All patients underwent total thyroidectomy and central neck dissection. Eighteen also had functional neck dissection (37%). For extrathyroidal involvement, two main approaches were used - radical surgery to excise all microscopic disease, with or without adjuvant therapy (n=16) and surgery for macroscopic disease only, followed by iodine and radiation treatment for microscopic residual disease (n=33). Overall 5 year survival for invasive carcinoma was 78%, compared to 93% of noninvasive disease. The only statistically significant factor was large tumor size. They concluded that conservative procedures followed by radioiodide treatment were associated with similar survival rates as aggressive techniques, with less perioperative mortality and lower overall mortality.

There is little consensus regarding surgical management of invasive, well-differentiated thyroid carcinoma. The conservative school recommends preservation of the midline structures by shaving carcinoma from the larynx, trachea, and esophagus, which potentially leaves behind microscopic disease requiring radioiodine and radiation treatment. (7) The aggressive school recommends extensive en bloc resection of the tumor, including partial or total laryngectomy, pharyngectomy, or tracheal resection, as necessary, to obtain clear margins. (19)

Undifferentiated Anaplastic Carcinoma

These tumors are usually unresectable. Tracheotomy is considered when airway is compressed. Diagnosis is made by FNA and usually by open biopsy for completed cell study. A combination treatment of surgery, radiation or chemotherapy may help to control the tumors.

Medullary Thyroid Cancer

Cervical metastasis at the time of diagnosis is observed in 50% of cases. Surgical resection includes the anterior compartment node dissection, which removes the lymphatics and adipose tissue from the hyoid bone to the sternal notch and laterally to the internal jugular vein. The lymph node groups removed are pre-tracheal, paratracheal, pre-cricoid, Delphian and perithyroidal nodes. With N(+) cervical lymph nodes, a selective lateral neck dissection of zones II, III, IV can be included.

Adjuvant therapy:

Post-op radioiodine (RAI): with appropriate dose, radiation therapy is safe in both children and adults. When patients have significant hypothyroidism (TSH>50 mU/L), 4 to 5 mCi of ¹³¹I is given and the total body is scanned to look for residual thyroid tissue or metastasis. The scan and treatment are repeated until the scan is negative. Patient will receive follow up annually for several years. For the rest of life, patient's TSH should be held in low normal range by maintaining T4 level in high normal range. According to Attie et al (2), RAI uptake scanning is an essential indication after a thyroidectomy to determine the completeness of the surgical procedure and to detect residual or metastatic disease.

Another controversial complementary treatment is external beam radiation. Some earlier reports recommend the use of external beam radiotherapy in all cases of aggressive disease because it improves local disease control, (20) even though there is no proof that it changes the survival rate. By contrast, others found no improvement in either local control or disease-free survival.(3,42) External beam radiation is thought to be useful in advanced locoregional WDTC whether superficial excision is complete or incomplete, if the tumor no longer picks up radioiodine, and in post-op adjuvant therapy for palliation of unresectable bone metastasis.

Surgical complications

Surgical complications can include injuries to the superior laryngeal nerve or recurrent laryngeal nerve, hemorrhage, airway obstruction, pneumothorax, chyle leak, hypothyroidism and hypocalcemia.

1. Nonmetabolic complications:

- **Nerve injury:** superior (SLN) and recurrent laryngeal nerves (RLN) are most commonly injured. The morbidity caused by nerve injury depends on the extent and nature of the damage. SLN normally courses medially to the superior thyroid artery. Teitelbaum et al.(48) reported unilateral SLN injury in about 5% of thyroidectomies. SLN injury can be avoided by leaving superior pole vessels alone until the isthmus has been divided and the lobe has been substantially mobilized. Patients usually complain of unstable voice, difficulty with high pitch, dysphagia and aspiration due to decreased laryngeal sensation. Classic signs of bowing of the vocal cords, ipsilateral rotation of the posterior glottis and inferior displacement of the affected cord may be missed on indirect laryngoscopy. RLN injury can coexist with SLN paralysis one or both sides. The reasons for nerve injury are: (1) anatomic variations, (2) failure to recognize alteration in the normal course of the nerve because of pathologic conditions, (3) lack of meticulous hemostasis and fastidious anatomic dissection, and (4) suturing, stretching, and crushing injuries of the main trunk or branches. Unilateral RLN paralysis is not life threatening and is usually compensated by the shortening and movement of the opposite vocal cord across the midline and the fibrosis of the arytenoid muscle. Bilateral RLN injury can cause airway obstruction immediately or years later. The early symptoms are stridor and cyanosis shortly after extubation. These patients should be re-intubated, then trached.
- **Hemorrhage:** major post-op bleeding becomes apparent by excessive bloody discharge in the drain, swelling of the neck and cervical venous distension.
- **Airway obstruction:** is the major cause of morbidity and mortality in post-op thyroid surgery. Airway obstruction is caused by postoperative hematoma, laryngeal edema or bilateral vocal cord paralysis. Preceding symptoms are neck pain, swelling and stridor. Fiberoptic endoscopy can identify the extent of airway obstruction. Management includes IV steroids over 24-48 hours, if there is no bilateral VC injury.
- **Chyle leak** is a rare complication of neck dissection and usually occurs in patients with previous neck irradiation or surgery.
- **Pneumothorax** is a rare complication, caused by injury to the apical pleura. It requires immediate recognition and applies of positive pressure respiration to

keep the lungs expanded, as well as prompt closure of the wound to prevent recurrence.

2. *Metabolic complications:*

- Hypothyroidism: usually occur after a total or near total thyroidectomy, more common in Grave's disease.
- Hypocalcemia is caused by an inadvertent parathyroidectomy, in about 5% of thyroidectomies. It can be avoided by meticulous dissection and autotransplantation of the parathyroid glands.

•

Postoperative treatment and follow up

Studies have demonstrated the usefulness of postoperative RAI in decreasing the local recurrence and mortality rates in patients with stage II and stage III well-differentiated thyroid carcinoma. For this reason, the routine use of postoperative RAI and thyroid hormone suppression has been advocated for patients with primary tumors larger than 1.5 cm (30,42). Radiation is also a postoperative consideration for tumors that do not respond to RAI and for management of distant metastasis.

Conclusion

The goal of management for invasive thyroid cancer is to remove all gross disease, especially in medullary carcinomas and Hurthle cell, which are less responsive to postoperative radioactive iodine administration. There is still a debate regarding optimal techniques and extent of surgical resection to perform when dealing with invasive disease. There are a number of techniques which can be performed to complete dissection, however minimally a total thyroidectomy and central neck dissection should be performed for invasive disease. It is also important to remember that the type of cancer and risk grouping can affect both prognosis and influence treatment decisions.

References

- 1) Alexander HR, Norton JA: Biology and management of medullary thyroid carcinoma of the parafollicular cells, in Robbins J (moderator): Thyroid Cancer: a lethal endocrine neoplasm. *Ann Intern Med* 115:133-147, 1991
- 2) 6. Attie et al. Postoperative Radioactive Iodine Evaluation of Total Thyroidectomy for Thyroid Carcinoma: Reappraisal and Therapeutic Implications. *Head & Neck* 1992; 14: 297-302.
- 3) G. Benker, T. Olbricht and D. Reinwein *et al.*, Survival rates in patients with differentiated thyroid carcinoma. Influence of postoperative external radiotherapy, *Cancer* **65** (1990), pp. 1517–1520.
- 4) Campbell JP, Pillsbury HC III: Management of the thyroid nodule. *Head & Neck*. 1989;11:414-425
- 5) 10) Colson YL, Carty SE. Medullary thyroid carcinoma. *Am J Oto*. Vol 14, No2 (March-April), 1993:73-81
- 6) Cummings: Otolaryngology: Head and Neck Surgery, 4th ed. Chapter 119. Mosby, Inc. 2005.
- 7) J.M. Czaja and T.V. McCaffrey, The surgical management of laryngotracheal invasion by well-differentiated papillary thyroid carcinoma, *Arch Otolaryngol Head Neck Surg* **123**
- 8) Dackiw APB, Zeiger M. Extent of surgery for differentiated thyroid cancer. *Surg Clin N Am* 84 (2004) 817-32.
- 9) Degroot LJ, Reilly M, et al. Retrospective and prospective study of radiation-induced thyroid disease. *Am J Med* 1983;74:852-62.
- 10) Falk S.A., McCaffrey T.V., Management of the recurrent laryngeal nerve in suspected and proven thyroid cancer. *Otolaryngol Head Neck Surg* (1995) **113** : pp 42-48.
- 11) Friedman M., Danielzadeh J.A., Calderelli D.D., Treatment of patients with carcinoma of the thyroid invading the airway. *Arch Otolaryngol Head Neck Surg* (1994) **120** : pp 1377-1381
- 12) Friedman M., Surgical management of thyroid carcinoma with laryngotracheal invasion. *Otolaryngol Clin North Am* (1990) **23** : pp 495-507.
- 13) Gillenwater A.M., Goepfert H., Surgical management of laryngotracheal and esophageal involvement by locally advanced thyroid cancer. *Semin Surg Oncol* (1999) **16** : pp 19-29.
- 14) Goepfert. Current therapy in Otolaryngology. 1998
- 15) Goepfert H, Callender DL. Differentiated thyroid cancer - Papillary and follicular carcinomas. *Am J Oto*. Vol 15, No 3 (may-June). 1994: pp 167-179
- 16) Goldman ND, Coniglio JU, Falk SA. Thyroid Cancers I: Papillary, Follicular, and Hurthle Cell. *Otolaryngologic clinics of North America*. 29.4:593-609. August, 1996
- 17) Greene F.L. Page D.L. Fleming I.D. American Joint Committee on Cancer cancer staging manual 6th edition.. 2002New York: Springer Verlag.
- 18) Greenspan FS. Irradiation exposure and thyroid cancer. *JAMA* 1977; 237:2089-91.
- 19) H.C. Grillo and P. Zannini, Resectional management of airway invasion by thyroid carcinoma, *Ann Thorac Surg* **42** (1986), pp. 287–298.
- 20) E. Tubiana Haddad, M. Schlumberger and C. Hill *et al.*, External radiotherapy in thyroid cancers, *Cancer* **55** (1985), pp. 2062–2071.
- 21) Hammoud Z.T., Mathisen D.J., Surgical management of thyroid carcinoma invading the trachea. *Chest Surg Clin N Am* (2003) **13** : pp 359-367.
- 22) Jereb B, Stjernsward J, Lowhagen T. Anaplastic giant-cell carcinoma of the thyroid: A study of treatment and prognosis. *Cancer*. 1975;35:1293-1295
- 23) Junor EJ, Paul J, Reed NS. Anaplastic thyroid carcinoma: 91 patients treated by surgery and radiotherapy. *Eur J Surg Oncol* 1992; 18:83-8
- 24) Kowalski L.P., Filho J.G., Results of the treatment of locally invasive thyroid carcinoma. *Head Neck* (2002) **24** : pp 340-344.
- 25) Lampertico P. Anaplastic (sarcomatoid) carcinoma of the thyroid gland. *Semin Diagn Pathol*. 1993;10:159-68
- 26) Leeper RD: Thyroid cancer. *Med Clin North Am*. 69:1079, 1985
- 27) Levendag PC, De Porre PMZR, van Putten WIJ. Anaplastic carcinoma of the thyroid gland treated by radiation therapy. *Int J Radiat Oncol Biol Phys*. 1993;26:15-8

- 28) LiVolsi V, Marino M: Pathology of thyroid tumors. In Thawley S, Panje W, Batsakis J, *et. al.* (eds): Comprehensive Management of head and neck Tumors. Philadelphia, WB Saunders 1987, p 1599
- 29) Marzano LA, Porcelli A, *et. al.* Surgical Management and follow-up of medullary thyroid carcinoma. *J Surg Onc.* 59:162-168 (1995)
- 30) Mazzaferri E.L., Jhiang S.M., Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med* (1994) **97** : pp 418-428.
- 31) McCaffrey T.V., Bergstralh E.J., Hay I.D., Locally invasive papillary thyroid carcinoma: 1940–1990. *Head Neck* (1994) **16** : pp 165-172.
- 32) McCaffrey T.V., Lipton R.J., Thyroid carcinoma invading the upper aerodigestive system. *Laryngoscope* (1990) **100** : pp 824-830.
- 33) McCaffrey J.C., Evaluation and treatment of aerodigestive tract invasion by well-differentiated thyroid carcinoma. *Cancer Control* (2000) **7** : pp 246-252.
- 34) McHenry C.R., Rosen I.B., Walfish P.G., Prospective management of nodal metastases in differentiated thyroid cancer. *Am J Surg* (1991) **162** : pp 353-356.
- 35) Mizuno S., Funahashi H., Kondo A., Regional lymph node metastasis in the early stage of thyroid cancer with special reference to the dissection method. *Nagoya J Med Sci* (1983) **45** : pp 71-77.
- 36) Moley MF. Medullary thyroid cancer. *Surg Clin North Am.* 75.3:405-420, June 1995
- 37) Molitch M, Beck J, Dreisman M, et al: The cold thyroid nodule: An analysis of diagnostic and therapeutic options. *Endocr Rev*
- 38) N.A. Samaan, P.N. Schultz and R.C. Hickey *et al.*, The results of various modalities of treatment of well differentiated thyroid carcinomas a retrospective review of 1599 patients, *J Clin Endocrinol Metab* **75** (1992), pp. 714–720.
- 39) National Comprehensive Cancer Network. Thyroid carcinoma. Clinical Practice Guidelines in Oncology, Version 2, 2007 Available at www.nccn.org/. Accessed April 2007.
- 40) National Cancer Institute. SEER Cancer Statistics Review, 1975-2004. National Cancer Institute. Bethesda, MD: National Cancer Institute, 2006. Available at http://seer.cancer.gov/csr/1975_2001/. Accessed April 2007.
- 41) Russell CF, van Heerden JA, Sizemore GW, *et. al.* The surgical management of medullary thyroid carcinoma. *Ann Surg.* 197:42-48, 1983(2):185. 1984
- 42) Samaan N.A., Schultz P.N., Hickey R.C., The results of various modalities of treatment of well-differentiated thyroid carcinoma: a retrospective review of 1599 patients. *J Clin Endocrinol Metab* (1992) **75** : pp 714-720.
- 43) Segal K, Shpitzer, et al. Invasive well-differentiated thyroid carcinoma: effect of treatment modalities on outcome. *Otolaryngol Head Neck Surg* (2006) 134. 819-22.
- 44) Sessions RB, Davidson BJ. Thyroid Cancer. *Medical clinics of North America.* 77.3:517-539. May, 1993
- 45) Soh EY, Clark OH. Surgical considerations and approach to thyroid cancer. *Endocrin Metab Clin North Am.* 25.1:115-138, March 1996
- 46) Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Limited-Use, Nov 2006 Sub (1973-2004), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2007, based on the November 2006 submission.
- 47) Sweeney PJ, Haraf DJ, *et. al.* Anaplastic carcinoma of the thyroid: a case report. *Ann Onc.* 7:739-744, 1996
- 48) Teitelbaum et al. Superior Laryngeal Nerve Injury from Thyroid Surgery. *Head & Neck* 1995; 17: 36-40
- 49) Thyroid Carcinoma Task Force. AACE/AAES medical/surgical guidelines for clinical practice: management of thyroid carcinoma. American Association of Clinical Endocrinologists. American College of Endocrinology. *Endocr Pract* 2001;7:202- 220.
- 50) Wein RO, Weber RS. Contemporary Management of Differentiated Thyroid Carcinoma. *Otolaryngol Clin N Am* 38 (2005) 161 -178.