Therapeutic options in locally advanced thyroid carcinoma

Our experience


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INTRODUCTIONS: Thyroid cancer is the most common endocrine malignancy with an incidence equal to 1% of all malignant tumors. Prognostic factors affecting survival are manifold, including in several classifications (AMES, AGES, CORN and TNM). In this sense, the invasion of adjacent structures is one of the most important variables. The authors describe the experience of a single center in surgical treatment of advanced thyroid cancer.

MATERIALS AND METHODS: Between 1986 and 2010, 1565 patients were undergoing surgery with thyroid cancer. In particular, 1403 interventions were made for differentiated cancer, 97 for medullary carcinoma, 25 for insular carcinoma, 29 for anaplastic carcinoma, 2 for plasmacytoma, and 7 for lymphoma and 2 for angiosarcoma. Among these 896 showed invasion of adjacent structures and/or distant metastases.

RESULTS: There were no perioperative deaths or major complications. Surgical procedures consisted of: 13 lobectomy, 519 total thyroidectomy (TT), 325 TT with lymphadenectomy of the central compartment, 7 TT with radical lymphectomy, 621 TT with functional lymphectomy, 6 TT with breast lumpectomy, 5 TT with with video-assisted lung metastasectomy, 16 TT with resection and tracheal anastomosis, 6 TT with laryngotracheal resection, 3 TT with laryngectomy, 4 TT with tracheotomy, 28 TT with respiratory stent placement, 12 tracheotomy. At present, 1328 patients were free of disease, while 104 showed recurrence. Total of 133 deaths were recorded, all linked to disease relapse.

DISCUSSION: The role of surgery in the treatment of advanced thyroid cancer is still undeniable. In the presence of extracapsular trespassing, in fact, the adoption of interventions demolition permits long-term survival, given the lack of aggressiveness of the tumor differentiated representing the majority of cases. The aim of surgical radicalization addition, even in the presence of distant metastases, it is justified by the possibilities offered by the therapeutic radioiodine treatment, which is not feasible in the presence of significant amounts of thyroid tissue which picks. In the presence of undifferentiated tumors, finally, endoscopic or surgical treatment may be indicated by simple purpose of palliation of respiratory symptoms.

KEY WORDS: Advanced thyroid carcinoma, Combined treatment, Local invasion.

Introduction

Thyroid cancer is the most frequent endocrine neoplasm, accounting for 0.7-1% of all malignancies. In Italy incidence reaches 4.3 x 100,000 in males and 12.5 x 100,000 in females. Ninety-four percent of all thyroid malignancies are differentiated carcinomas (DTC), 5% are medullary carcinomas (MC) while 1% are anaplastic carcinoma (AC). Long term survival is 94% at 5 years (DTC), against only 5.6-11.4% for AC. Prognostic factors affecting survival are patient-related (age, gender), tumor-related (size, multicentricity, histologic type, grading, extension to adjacent structures, lymph node spread, blood-borne metastasis), and procedure-related (complete/incomplete
resection). The above mentioned variables are included in the most widely used classification systems: AMES (Age, Metastasis, Extension, Size), AGES (Age, Grade, Extension, Size), MACIS (Metastasis, Age, Completeness, Invasion, Size), and TNM. Recurrence rate (RR) and overall survival (OS) are high-risk indicators influenced by age >45 years, M+ stage, T3-4, histology (tall cell, columnar cell, diffuse sclerosing, widely invasive follicular carcinoma, poorly differentiated “insular” follicular carcinoma). Invasion of adjacent structures is one of the principal prognostic factors in DTC. In such clinical setting surgery plays a central role regarding extent of thyroid resection, of lymphectomy, and resection of adjacent structures involved by the neoplasm.

In the present paper the Authors report the own experience in the management of both locally invasive thyroid tumors and local tumor recurrence.

Materials and methods

A series of 1565 patients (age range 18-89 years), underwent at surgical resection for thyroid carcinoma between 1986 and 2010, are analyzed retrospectively. Specifically, 1403 procedures were performed for DTC, 97 for MC, 25 for insular carcinoma (ITC), 29 for AC, 2 for plasmocitoma, 7 for lymphoma, and 2 for angiosarcoma.

Preoperative workup included:
- FT3, FT4, TSH;
- CEA, Calcitonin;
- anti-TPO, Anti-TGB;
- neck ultrasound;
- FNAB of the lesion;
- chest films;
- I131 Scinti scan;
- laryngo-tracheoscopy.

If local invasion was suspected the following procedures were added:
- FT4, FT4, TSH;
- chest films;
- I131 Scinti scan;
- laryngo-tracheoscopy.

Results

In 896 patients local and/or distant extension was detected (57.25% of operations performed for thyroid cancer). Direct neoplasm extension involved cricothyroid muscles in 43 cases (4.7%), strap muscles in 92 (10.2%), sternocleidomastoid muscle in 7 (0.7%), unilateral recurrent laringeal nerve (RLN)(3.3%), bilateral RLN in 6 (0.6%), laryngo-tracheal axis in 69 (7.7%), cervical esophagus in 7 (0.7%), vessels in 11 (1.2%), skin in 11 (1.2%), cervical sympathetic chain in 4 (0.4%), lymph nodes in 621 (69.3%). Lung secondaries were present in 31 cases (3.4%), bone in 12 (1.3%), breast involvement in 6 (0.6%). The surgical procedures are summarized in Table I.

In 12 cases the occurrence of laterocervical lymphadenopathy led to the diagnosis of thyroid cancer. Of the 13 patients submitted to LI, in 11 cases microcarcinomas were occasionally detected in surgical specimen; in the remaining two the patients refused TT (dimension tumor < 1 cm.). The patients with resectable lung secondaries were managed as follows: TT first and, five days later, VATS lung metastasectomy. In the other 26 cases the lesions were too numerous to permit resection. In case of breast secondary, TT and breast quadrantectomy were performed simultaneously.
For DTC, lymphectomy was always performed in the central compartment, and when necessary in the II, III, IV level.

In the 69 cases of laryngotracheal axis involvement, 40 procedures were performed with palliative intent, due to histology (AC), multi-organs metastatic disease or poor general conditions. Such cases were managed by endoscopic airway stenting (Dumon/Ultraflex) or tracheotomy. Patients free of disease are 1328 (1264 DTC – 64 MTC) The results are summarized in Table II. Recurrence occurred in 104 patients (73 DTC, 31 MTC - Table III). Four ITC patients have bone secondaries. In the DTC group, 71 patients died (TT 3, TT+MAS 10, TT+FND 12, TT+TRR 3, stent 28, TCT 10, TT+TST 4, TT+MTS 1). Six MTC patients (TT+MAS 3, TT+FND 3), all patients with anaplastic carcinoma, insular carcinoma and angiosarcoma died.

Discussion

Aero-digestive tract involvement, by the thyroid neoplasm growth, can occur in different manners: compression, dislocation or infiltration (incidence ranging between 5 and 34%) 10. Symptoms include dyspnea (33%), dysphagia (25%), hemoptysis (25%), hoarseness (18%) 11.

Extrathyroid extension involves neck muscles in 8.1% of cases, trachea in 7.7%, esophagus in 3%, larynx in 2.2%, sternum in 3% 12.

Two studies 13,14 report the following incidences: RLN 47-61%, trachea 55-60%, larynx 34%, neck muscles 43-78%, jugular vein 13-45%, carotid artery 6%, vagus nerve 4-13%, skin 4%, esophageal wall 17-29%, full-thickness esophageal invasion 6%.

At present, extension of surgical resection is matter of debate. The main surgical goal is complete ablation of the tumor, resection of the infiltrated structures and regional lymph-nodes if positive, with minimal morbidity, enabling disease staging. With such basis, adjuvant therapy and follow-up can be established.

In case of locally invasive tumors, the breathing and alimentary functions need to be preserved, minimizing symptoms through local control of the disease.

Patient performance status, extension of disease and histology are the parameters upon which therapeutic decision is made, with a staged interventional philosophy 15.

According to AJCC, a locally advanced tumor is a T4a-T4b lesion extending beyond the thyroid capsule, to infiltrate subcutaneous tissue, laryngo-tracheal axis, esophagus, RLN, prevertebral fascia, carotid artery or mediastinal vessels. It is well-known that extrathyroid extension is a risk factor for recurrence, increasing mortality of DTC, both in papillary and follicular patterns 16, 17. For such reason the surgical resection must be as complete as possible, considering that recurrence rate is about 1% for R0 resections vs about 25% for R1-2 procedures 18. Similarly, metastatic spread and 5-year mortality, in the above mentioned settings, reach 46 and 27% vs 77 and 94%, respectively 19.

Muscle and Vessel Invasion. Infiltration of adjacent muscular structures is very frequent (43-78%); in our experience 63%. If the trachea is involved, incidence of muscular invasion is about 70%. Two aspects deserve consideration: 1) if only muscle infiltration is present, the outlook does not change, so a radical excision is warranted; 2) if muscles are involved by recurrence or metastatic spread, outlook worsens 20. The internal jugular vein is invaded more frequently than the carotid artery: its resection en-bloc with the gland does not influence morbidity or mortality provided monolateral. Carotid artery invasion is surely more worrisome: in such case shave resection is generally performed. If intraluminal growth is present, both en-bloc resection and simple interruption of the vessel have been successfully applied, after evaluation of cerebral vascular reserve.

Esophageal Invasion. Dysphagia is present roughly in 25% of patients affected by locally advanced tumor, but only in few the esophageal wall is totally invaded. Mucosa intact acts as a barrier against disease infiltration.

Laryngotracheal Axis Invasion. The main symptoms of laryngotracheal axis involvement are hemoptysis (11%), dyspnea (5%), stridor (22%), due to the fact that dyspnea ensues for a lumen cross-sectional reduction of at least 50%. Five- and 10-year survival are in the range of 60-79% and 50-63%, respectively 21, 22. Larynx and trachea can be infiltrated both by direct tumor invasion or by lymph node metastatic growth. Perichondrium acts as an efficient barrier against invasion; intact larynx infiltration occurs either laterally through the thyroid cartilage or anteriorly across the cricoid cartilage and cricothyroid membrane. Rarely the pyriform sinus is reached by upper pole neoplasms. Shin et al described 5 stages of neoplastic extension:

- stage 0: tumor limited to the gland;
- stage I: extension to the perichondrium, but no cartilage or soft tissue erosion or invasion;
- stage II: cartilage erosion, but no transmural extension;
- stage III: extension through the cartilage, but not beyond the mucosa;
- stage IV: disease extension beyond the mucosa, reaching the tracheal lumen.

Dralle et al classified 6 types of laryngo-trachael resections, to be performed on the basis of site and extent of visceral invasion:

- type 1: limited area of invasion, often associated with homolateral RLN infiltration, with a longitudinal extension less than 2 cm and not greater than 1/3 of circumference. Possible reconstruction by sternomastoid muscle flap;
- type 2: similar to type 1, but more distal in the trachea. No laryngeal involvement;

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Conclusions

DTC shows very good long term survival. Such result significantly worsens in locally advanced cases (60-70% at 10 years). Local recurrence and distant spread require sound diagnostic workup and surgical planning aimed at gaining the best results with minimal morbidity and mortality. We agree with literature data indicating surgery as the treatment of choice for locally advanced DTC. Surgical results can be consolidated, when necessary, by application of adjuvant therapy, endoluminal laser therapy and stent placement, in order to improve quality of life.

Riassunto

INTRODUZIONE: Il cancro della tiroide è la più frequente neoplasia endocrina con una incidenza pari all’1% di tutti i tumori maligni. I fattori prognostici che influenzano la sopravvivenza sono molteplici, inclusi in numerosissime classificazioni (AMES, AGES, MAIS e TNM). In tal senso l’invasione di strutture adiacenti è tra le variabili di maggior importanza. Gli Autori descrivono l’esperienza di un singolo centro nel trattamento chirurgico dei tumori avanzati della tiroide.

MATERIALI E METODI: Tra il 1986 ed il 2010 sono stati sottoposti a chirurgia 1565 pazienti affetti da neoplasia tiroidea. Tra questi 896 presentavano invasione delle strutture contigue e/o metastasi a distanza. Le procedure chirurgiche sono consistite in: 13 loboistecomi del comparto centrale, 7 TT con linfectomia radicale, 621 TT con linfectomia funzionale, 6 TT con quadranteectomia mammaria, 5 TT con metastasectomia polmonare video assistita, 16 TT con resezione-anastomosi tracheale, 6 TT con resezione anastomosi laringotraceale, 3 TT con laringectomia, 4 TT con trachetomia, 28 TT con posizionamento di stent respiratorio, 12 trachetomia.

RISULTATI: Non sono stati osservati decessi perioperatori, né complicanze maggiori. Al momento attuale 1328 pazienti sono liberi da malattia, mentre 104 mostrano recidiva. Sono stati complessivamente registrati 133 decessi, tutti legati a ripresa di malattia.

DISCUSSIONE: Il ruolo della chirurgia nel trattamento del¬le neoplasie tiroidee avanzate appare tuttora indiscutibile. In presenza di sconfinamenti extracapsulari, infatti, l’adozione di interventi demolitivi consente lunghe sopravvivenze, in considerazione della scarsa agressività delle neoplasie differenziate che rappresentano la mag¬gioranza dei casi. L’intento della radicalizzazione chirur¬gica inoltre, anche in presenza di metastasi a distanza, appare giustificato dalle possibilità terapeutiche offerte dal trattamento radiometabolico, non attuabile in presenza di significativa quantità di tessuto tiroideo captante. In presenza di neoplasie indifferenziate, infine, un tratta-
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References


