Original Article / Çalışma - Araştırma

Management of advanced thyroid carcinoma with laryngotracheal invasion

Larengotrakeal invazyonlu ileri tiroid karsinomunun tedavisi

Ayşegül Batıoğlu Karaaltın, MD.,[1] Murat Haydar Yener, MD.,[1] Mehmet Yılmaz, MD.,[1] Nesrettin Fatih Turgut, MD.,[1] Muhammed Pamukçu, MD.,[2] Harun Cansız, MD.[1]

[1]*Department of Otolaryngology, Istanbul University Cerrahpasa School of Medicine, Istanbul, Turkey*
[2]*Department of Otolaryngology, Kemerburgaz University School of Medicine, Bahcelievler Medicalpark Hospital, Istanbul, Turkey*

ABSTRACT

Objectives: This study aims to evaluate the management of advanced thyroid carcinoma with extra-thyroidal extension.

Patients and Methods: The study included 58 patients (26 males, 32 females; mean age 45.1±8.3 years; range 24 to 72 years) who were referred from general surgery or other otolaryngology departments and had undergone surgery for T_{4a} well-differentiated thyroid carcinoma or T_{4b} anaplastic carcinoma between January 2007 and January 2011 with a minimum of five years of follow-up. The patients with laryngotracheal invasion were divided into two groups according to type of surgery. Patterns of invasion and techniques of surgical resection were evaluated.

Results: Of the patients in group 1 (n=24), total thyroidectomy was performed in all (100%), partial laryngectomy in six (10.4%), tracheal resection in eight (13%), and tracheal window resection in 16 (27%), and the free margins were verified by frozen section. Patients in group 2 (n=34) were performed total thyroidectomy (100%) by shaving the tumor off the underlying cartilage or skeletonizing laryngotracheal segments. During the follow-up period, one patient died because of carotid involvement and four patients died because of local recurrence.

Conclusion: The results of this study suggest that the depth of the invasion and postoperative morbidity should be considered when choosing a surgical approach for patients with advanced thyroid carcinoma with extra-thyroidal extension. Also, patients who undergo tumor shaving should be followed-up closely.

Keywords: Extra-thyroidal extension; segmental laryngotracheal resection; thyroid carcinoma.

ÖZ

Amaç: Bu çalışmada ekstra tiroidal uzantılı ileri tiroid karsinomunun tedavisi değerlendirildi.

Hastalar ve Yöntemler: Çalışmaya genel cerrahi veya diğer kulak-burun-boğaz bölümlerinden sevk edilen ve Ocak 2007 - Ocak 2011 tarihleri arasında T_{4a} iyi diferansiye tiroid karsinomu veya T_{4b} anaplastik karsinomu nedeniyle cerrahi geçiren, en az beş yıl takip edilen 58 hasta (26 erkek, 32 kadın; ort. yaş 45.1±8.3 yıl; dağılım 24-72 yıl) dahil edildi. Larengotrakeal invazyonu olan hastalar cerrahi türüne göre iki gruba ayrıldı. İnvazyon paternleri ve cerrahi rezeksiyon teknikleri değerlendirildi.

Bulgular: Grup 1'deki hastaların (n=24) tamamına (%100) total tiroidektomi, altısına (%10.4) parsiyel larenjektomi, sekizine (%13) trakeal rezeksiyon ve 16'sına (%27) trakeal pencere rezeksiyonu uygulandı; serbest marjinler dondurulmuş kesit ile doğrulandı. Grup 2'deki hastalara (n=34) tümörü alttaki kıkırdaktan kazıyarak veya larengotrakeal segmentleri iskeletleştirerek total tiroidektomi (%100) uygulandı. Takip dönemi sırasında, bir hasta karotis tutulumu ve dört hasta lokal rekürens nedeniyle kaybedildi.

Sonuç: Bu çalışmanın bulguları ekstra tiroidal uzantılı ileri tiroid karsinomlu hastalar için cerrahi bir yaklaşım seçilirken invazyon derinliğinin ve ameliyat sonrası morbiditenin dikkate alınması gerektiğini ortaya koymaktadır. Ayrıca, tümör kazıması geçiren hastalar yakından takip edilmelidir.

Anahtar Sözcükler: Ekstra tiroidal uzantı; segmental larengotrakeal rezeksiyon; tiroid karsinomu.

Available online at
www.kbbihtisas.org
doi: 10.5606/kbbihtisas.2017.24572
QR (Quick Response) Code

Received / *Geliş tarihi:* January 26, 2016 Accepted / *Kabul tarihi:* May 19, 2017

Correspondence / İletişim adresi: Ayşegül Batıoğlu Karaaltın, MD. İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Kulak Burun Boğaz Anabilim Dalı, 34098 Cerrahpaşa, Fatih, İstanbul, Turkey.

Tel: +90 532 - 776 03 85 e-mail *(e-posta):* batioglu@yahoo.com

Extrathyroidal extension (ETE) is defined as extension of the primary tumor outside the thyroid capsule and invasion into surrounding structures such as strap muscles, trachea, larynx, vasculature, esophagus, and recurrent laryngeal nerve (RLN).[1,2] This is also called moderately advanced disease. A tumor of any size that has grown back toward the spine or into nearby large blood vessels is classified T_{4b} by TNM classification. This is also called very advanced disease. T categories for anaplastic thyroid cancer (ATC) are different from others, and tumor still within the thyroid is T_{4a} and T_{4b} similar to tumor that has grown outside the thyroid according to TNM classification of the American Joint Committee on Cancer.[3] The incidence of ETE in well-differentiated thyroid cancer (WDTC) diverges in different series but ranges from 5 to 34%.[1,4] Extrathyroidal extension, which is used in several staging systems such as EORTC (European Organization Research Treatment Cancer), TNM classification, and AGES (age, grade, ETE, and size), is an important adverse prognostic factor.[1,3] Patients with ETE are 12 times more likely to manifest lymph nodes with extranodal extension (ENE) than patients with intra-thyroidal tumors.[5] Extensive ETE is a poor prognostic indicator and indicates a more aggressive tumor.[6,7] Tollefson et al.,[8] showed that 86% of patients who died of thyroid carcinoma had ETE.

In this study, we reviewed our management strategy for advanced thyroid carcinoma with ETE and invasion of surrounding structures such as strap muscles, trachea, larynx, vasculature, esophagus, recurrent laryngeal nerve and extension to the mediastinum and compared the types of surgical resection.

PATIENTS AND METHODS

A medical record review of the Cerrahpasa Medical Faculty Hospital, Istanbul, Turkey, otolaryngology database was performed. Patients with thyroid carcinoma that had ETE or extension to the mediastinum were considered for inclusion in the study. These patients had been referred to the Cerrahpasa Medical Faculty Otolaryngology Department from general surgery or other otolaryngology departments. The study protocol was approved by the Cerrahpasa Medical Faculty Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Records of 58 patients (26 male, 32 female; mean age 45.1±8.3 years; range 24 to 72 years) who had undergone surgery for T_{4a} WDTC and T_{4b} anaplastic thyroid cancer according to the TNM classification between January 2007 and January 2011 with a minimum of five years of follow-up were considered for inclusion. The duration of follow-up was defined as the time from the first surgery to the last contact. Records of patients with evidence of distant metastasis at the time of diagnosis were excluded from the study.

The patients with laryngotracheal invasion underwent two types of surgery, and according to surgery type, they were divided into two groups. The patients in group 1 (n=24) had partial laryngectomy, tracheal resection, or tracheal window resection, and the free margins were verified by frozen section. The patients in group 2 (n=34) had visible tumor resection by shaving the cartilage or skeletonizing laryngotracheal segments or RLN's, assuming that microscopic residual tumor remained after resection. Radioactive iodine therapy was used postoperatively in the majority of cases in each group.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Descriptive analysis was done for demographic and clinical features. The results were presented as mean ± SD/percentages for continuous variables, and number/percentage for categorical variables.

RESULTS

All 58 patients included study had a palpable mass associated with thyroid gland. Most of the cases were unilateral (n=45), whereas 13 patients had bilateral involvement. The symptom breakdown upon first admission to the hospital was as follows: Six patients (10.3%) had hemoptysis; five patients (8.6%) had dyspnea; 10 patients (17.2%) had hoarseness; and 38 patients (65.5%) had neck swelling. Cervical lymphadenopathy was present in 28 patients (48.2%). Recurrent nerve function was normal in 42 patients (72.4%), with unilateral palsy present in 13 patients (22.4%) (Table 1).

Table 1. Clinical symptoms and findings on admission (n=58)

Clinical symptoms	n	%	Clinical findings	n	%
Swelling in neck	38	65.5	Thyroid mass	58	100
Hoarseness	10	17.2	Cervical lymphadenopathy	28	48.2
Hemoptysis	6	10.3	Recurrent nerve paralysis	13	22.4
Dyspnea	5	8.6			

All patients (n=6) with intramural tumor extension had symptomatic hemorrhage, and five had dyspnea. Radiologic evaluation included computed tomography (CT) or magnetic resonance imaging (MRI) for all patients after ultrasonography (USG) was performed. Ultrasonography showed tracheal deviation for 10 patients, and CT and MRI showed tracheal deviation (n=15), suspected laryngotracheal invasion (n=10), laryngotracheal airway invasion (n=5) (Figure 1). Surgical interventions for group 1 included total thyroidectomy for 24 patients (100%) and partial laryngectomy for six patients (10.3%) (Figure 2), tracheal resection (partial anterolateral resection of trachea) for eight patients (13.7%), tracheal window resection 16 (27.5%) (Figure 3), and the free margins were verified by frozen section. It was observed that six patients in group 1 had laryngotracheal airway invasion and 18 patients had expansion into the tracheal mucosa. For group 2, total thyroidectomy and shaving the tumor off the underlying cartilage, skeletonizing laryngotracheal segments was performed for 34 patients (100%). Among these patients, laryngotracheal invasion was first identified intraoperatively in 28 patients (82.4%), whereas the remaining cases were suspected on the basis of preoperative clinical or radiologic appearance. In group 2, 21 patients' tumors extended through the capsule of the thyroid gland and abutted the external perichondrium, exited tangentially; 13 patients had invasion to the cartilage and thyroid scrubbed from the trachea by sharp dissection. The other structures that were invaded were strap muscles (n=20), recurrent nerve with necessity of resection (n=10), esophagus with necessity of wedge resection (n=2), and carotid treated with shaving (n=2) (Table 2).

Of all the studied patients, eight (13%) had extension to the mediastinum, and four required sternotomy for excision. These operations were

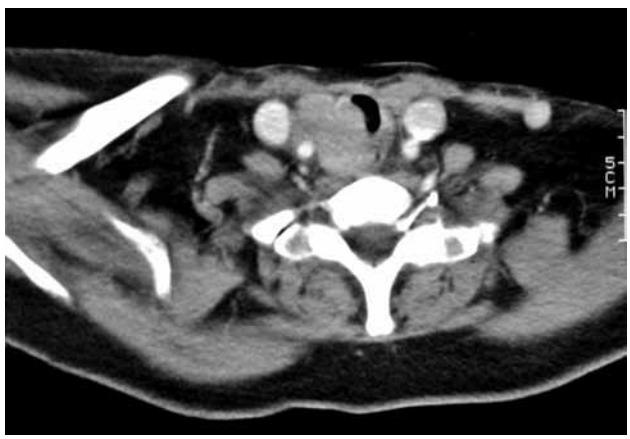

Figure 1. *Contrast enhanced computed tomography section at the level of first thoracic vertebrae, showing right laryngotracheal airway invasion by papillary thyroid carcinoma.*

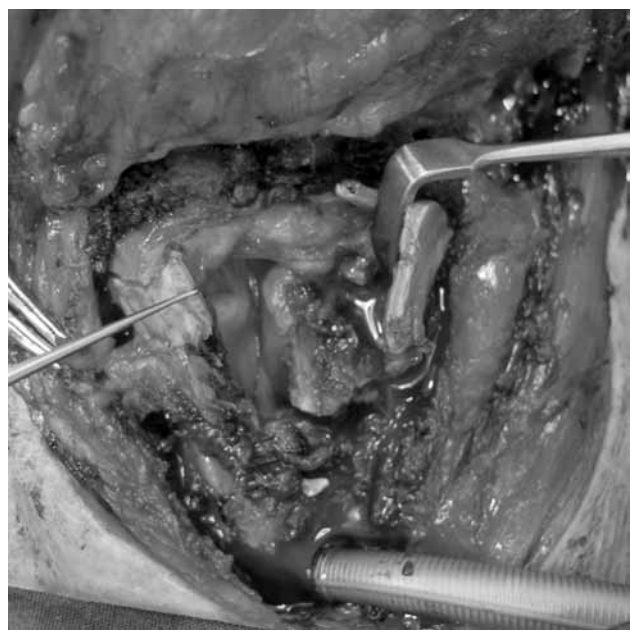

Figure 2. *Intraoperative photo showing excision of tumor that invaded the airway by total thyroidectomy and partial laryngotracheal resection; thyroid retractor is retracting left thyroid cartilage lamina; skin hook is retracting the remaining right thyroid cartilage lamina after resection ; armored tracheostomy tube inferiorly.*

Figure 3. *Intraoperative photo showing excision of tumor that invaded the airway by total thyroidectomy and tracheal window resection; note blue-line endotracheal tube in tracheal window.*

performed by multidisciplinary approaches. Twenty-eight patients (48.3%) underwent nodal dissection, and 10 (17.2%) of the patients who had undergone laryngotracheal and tracheal window resection underwent surgical reconstruction. Other patients with tracheal resection were reconstructed by auricular cartilage during secondary surgery. Histologic subtypes included papillary (n=55) and anaplastic (n=3) (Table 3). Postoperative follow-up revealed that three patients (5%) had newly developed permanent recurrent laryngeal nerve palsy, two patients (3.4%) had permanent hypocalcemia, and 14 patients (24.1%) had transient hypocalcemia.

Table 2. Involvement of surrounding structures

Involved structures	n	%
Trachea	58	100
Strap muscles	20	34.4
Recurrent laryngeal nerve	10	17
Larynx	8	13.8
Esophagus	2	3.4
Carotid	2	3.4

All 34 patients who had undergone cartilage shave procedures had microscopic residual disease involving the trachea. Ablative Iodine 131 (200 mCi) was administered to all patients with differentiated carcinoma. Three patients with anaplastic carcinoma were subjected to radiotherapy at a dose of 5400-6000 cGy after surgery.

One of the patients died because of carotid involvement, and four died because of local recurrence. The histopathology of the dead patients included papillary carcinoma (n=2) (group 2) and anaplastic carcinoma (n=3) (group 2). Recurrence was seen in the patients who had been treated with laryngotracheal shaving (n=5) from group 2 with cartilage invasion only (one of them had undergone total laryngectomy, and the others had undergone tracheal resection) and in patients who were treated with tracheal window resection (n=3) with anaplastic carcinoma histopatology from group 1 (these patients died).

Table 3. Histology, therapy received and outcomes

Parameters	All patients (n=58)		Group 1 (n=24)		Group 2 (n=34)	
Histology						
Differentiated	55	94.8	21	87.5	34	100
Anaplastic	3	5.1	3	12.5	0	0
Iodine 131 therapy						
Yes	55	94.8	21	87.5	34	100
No	3	5.1	3	12.5	0	0
Radiotherapy						
Yes	3	5.1	3	12.5	0	0
No	55	94.8	21	87.5	34	100
Outcomes						
Death	5	9	3	12.5	2	5.88
Recurrence	8	13.7	3	12.5	5	14.7

DISCUSSION

McCarty et al.[9] reported the incidence of airway invasion in thyroid carcinoma patients as 6.7%. The extent of tracheal wall invasion is thought to predict outcome, with intraluminal extension predictive of the poorest survival.[10,11] Less than 1% of all thyroid cancers show mucosal invasion, and laryngotracheal resection may prolong survival. The patients show symptoms according to the grade of their clinical invasion, although patients with intra-luminary invasions generally show dyspnea and hemoptysis.[12] Most of the cases with tracheal invasion represent superficial tracheal involvement and are first diagnosed during thyroidectomy.[13] Surgeons have to decide whether to perform a radical resection, including the trachea and/or larynx, or to perform limited resection with I131 or radiotherapy to ablate the residual disease.

Treatment of advanced thyroid carcinomas with laryngotracheal invasion is still a controversial issue. Some studies suggest a total tumor excision provided that the air route integrity is protected, which is an extensive excision.[11] Nevertheless, several studies report no significant difference between radical surgical procedure and conservative treatment in the case of invasion.[14,15] Cody and Shah[16] suggested the shaving method as the optimal procedure for minimally invasive tumors. Similarly, Breaux and Guilamondegui[17] suggested conservative surgery. Although the shaving method provides less morbidity, long-term follow-up of patients resulted in a lower rate of survival and a higher morbidity. Grilo and Zannini[13] suggested airway resection for all invasive tumor cases.[15]

Different staging schemes for thyroid carcinoma may account for local invasion but not the depth of airway disease. The AMES (age, distant metastases, extent, and size), MACIS (metastases, age, completeness of resection, invasion, size),[18] and AGES (age, grade, extent, size)[19] scores also add a weight factor, whereas the TNM (tumor, node, metastases) system does not account for local invasion.[3] Shin found a relationship between the depth of invasion and intermediate-term (5-year) survival in 22 patients with papillary carcinoma and airway invasion.[20] The staging system is as follows:

- Stage I - extension through the capsule of the thyroid gland and abuts the external perichondrium
- Stage II - invasion between the rings of cartilage or destroying the cartilage
- Stage III - extension through the cartilage or between the cartilaginous plates into the lamina propria of the tracheal mucosa
- Stage IV - extension through the entire thickness of and expansion into the tracheal mucosa.

The Shin staging requires a full-thickness specimen of tracheal or laryngeal wall to determine the depth of invasion. Therefore, this system is not indicated for patients who have undergone shave resection.

Shin showed there is no continuous plane underneath the "external perichondrium" perithyroidal adventitia, and the lymphatics of the tracheal mucosa communicate in the intercartilaginous spaces, allowing the tumor to spread into the trachea. The suggestion made in this report was that shave resection is incomplete, and a high rate of local failure must be expected.[12] Nishida et al.[21] saw no indication for tracheal resection in those carcinomas that abutted the external perichondrium and performed a shave resection. Similarly, in this study, patients who had early stage (stage I according to Shin classification) laryngotracheal invasion did not show recurrence after shaving. Recurrence was seen in the patients who were treated by laryngotracheal shaving (n=5) from group 2 with cartilage invasion only and in patients who were treated with tracheal window resection (n=3) from group 1. Therefore, this may indicate that patients with carcinomas that abut the external perichondrium might benefit from shaving, and patients with cartilage, mucosal, and airway invasion tracheal resection gives superior loco-regional control.

The rate of major complications (including laryngostenosis) of airway resection can be up to 33%.[15,17] McCarty et al.[9] published a study in which air route reconstruction was performed for all the patients who had tracheal ring resection. In our study, tracheal or laryngotracheal resection was performed for 10 patients, and reconstruction was performed during this surgery. The other patients who

underwent airway resection required repetitive surgeries for reconstruction of laryngotracheal stoma.

Tumor recurrence risk is directly correlated to tumor histology. Anaplastic and medullary carcinomas are especially thought to cause local recurrences as well as systematic metastases.[8] For three patients in our study who had anaplastic carcinoma histopathology, airway resection was performed. Postoperative follow-ups of these patients revealed complications such as defects in airway integrity and esophageal fistula. A month later, patients who developed relapse died. Anaplastic thyroid carcinoma is a highly aggressive tumor with median survival time not longer than six to eight months.[22-24] Surgery, chemotherapy, and radiotherapy are conventional therapeutic strategies performed in the attempt to improve survival. Disease was restricted to the thyroid gland (stage IVA) at diagnosis in only 9% of cases. Almost 32% had extrathyroidal infiltration (stage IVB), while 55% had cervical lymph node metastases, and 54% had distant metastases (stage IVC).[25] Surgical treatment of local disease offers the best opportunity for prolonged survival if the tumor is intrathyroidal ATC (T_{4a}). When the tumor is extrathyroidal (T_{4b}), the surgical approach is controversial. Some promising results have recently been reported with chemotherapy and radiation therapy.[22] Complete resection of ATC combined with postoperative adjuvant chemotherapy and irradiation resulted in long-term survival. An aggressive attempt at maximal tumor debulking followed by adjuvant therapy was found to be warranted in patients with localized ATC.[26] In a study done by Wendler,[25] 81% of ATC patients received external beam radiation therapy (EBRT; 32% as adjuvant, 49% as palliative treatment). The median overall dose was 57.6 Gy (range 13.5-80 Gy).

In conclusion, the depth of the invasion and postoperative morbidity should be considered when choosing a surgical approach for these patients, and patients who have undergone tumor shaving as a treatment should be followed closely to monitor for recurrence. Additionally, the importance of reconstructive surgery after a large resection for recovery of functions and a life without tracheostoma must be kept in mind.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Ortiz S, Rodríguez JM, Soria T, Pérez-Flores D, Piñero A, Moreno J, et al. Extrathyroid spread in papillary carcinoma of the thyroid: clinicopathological and prognostic study. Otolaryngol Head Neck Surg 2001;124:261-5.
2. Andersen PE, Kinsella J, Loree TR, Shaha AR, Shah JP. Differentiated carcinoma of the thyroid with extrathyroidal extension. Am J Surg 1995;170:467-70.
3. Compton CC, Byrd DR, Garcia-Aguilar J, Kurtzman SH, Olawaiye A, Washington MK. AJCC cancer staging atlas: a companion to the seventh editions of the AJCC cancer staging manual and handbook. Berlin: Springer Science & Business Media; 2012.
4. Hu A, Clark J, Payne RJ, Eski S, Walfish PG, Freeman JL. Extrathyroidal extension in well-differentiated thyroid cancer: macroscopic vs microscopic as a predictor of outcome. Arch Otolaryngol Head Neck Surg 2007;133:644-9.
5. Clain JB, Scherl S, Dos Reis L, Turk A, Wenig BM, Mehra S, et al. Extrathyroidal extension predicts extranodal extension in patients with positive lymph nodes: an important association that may affect clinical management. Thyroid 2014;24:951-7.
6. Ito Y, Tomoda C, Uruno T, Takamura Y, Miya A, Kobayashi K, et al. Minimal extrathyroid extension does not affect the relapse-free survival of patients with papillary thyroid carcinoma measuring 4 cm or less over the age of 45 years. Surg Today 2006;36:12-8.
7. Leboulleux S, Rubino C, Baudin E, Caillou B, Hartl DM, Bidart JM, et al. Prognostic factors for persistent or recurrent disease of papillary thyroid carcinoma with neck lymph node metastases and/or tumor extension beyond the thyroid capsule at initial diagnosis. J Clin Endocrinol Metab 2005;90:5723-9.
8. Tollefsen HR, Decosse JJ, Hutter RV. Papillary carcinoma of the thyroid. A clinical and pathological study of 70 fatal cases. Cancer 1964;17:1035-44.
9. McCarty TM, Kuhn JA, Williams WL Jr, Ellenhorn JD, O'Brien JC, Preskitt JT, et al. Surgical management of thyroid cancer invading the airway. Ann Surg Oncol 1997;4:403-8.
10. Djalilian M, Beahrs OH, Devine KD, Weiland LH, DeSanto LW. Intraluminal involvement of the larynx and trachea by thyroid cancer. Am J Surg 1974;128:500-4.
11. Tovi F, Goldstein J. Locally aggressive differentiated thyroid carcinoma. J Surg Oncol 1985;29:99-104.
12. Honings J, Stephen AE, Marres HA, Gaissert HA. The management of thyroid carcinoma invading the larynx or trachea. Laryngoscope 2010;120:682-9.
13. Grillo HC, Zannini P. Resectional management of airway invasion by thyroid carcinoma. Ann Thorac Surg 1986;42:287-98.

14. Ishihara T, Kobayashi K, Kikuchi K, Kato R, Kawamura M, Ito K. Surgical treatment of advanced thyroid carcinoma invading the trachea. J Thorac Cardiovasc Surg 1991;102:717-20.
15. Segal K, Abraham A, Levy R, Schindel J. Carcinomas of the thyroid gland invading larynx and trachea. Clin Otolaryngol Allied Sci 1984;9:21-5.
16. Cody HS, Shah JP. Locally invasive, well-differentiated thyroid cancer. 22 years' experience at Memorial Sloan-Kettering Cancer Center. Am J Surg 1981;142:480-3.
17. Breaux GP Jr, Guillamondegui OM. Treatment of locally invasive carcinoma of the thyroid: how radical? Am J Surg 1980;140:514-7.
18. Hay ID, Bergstralh EJ, Goellner JR, Ebersold JR, Grant CS. Predicting outcome in papillary thyroid carcinoma: development of a reliable prognostic scoring system in a cohort of 1779 patients surgically treated at one institution during 1940 through 1989. Surgery 1993;114:1050-7.
19. Hay ID, Grant CS, Taylor WF, McConahey WM. Ipsilateral lobectomy versus bilateral lobar resection in papillary thyroid carcinoma: a retrospective analysis of surgical outcome using a novel prognostic scoring system. Surgery 1987;102:1088-95.
20. Shin DH, Mark EJ, Suen HC, Grillo HC. Pathologic staging of papillary carcinoma of the thyroid with airway invasion based on the anatomic manner of extension to the trachea: a clinicopathologic study based on 22 patients who underwent thyroidectomy and airway resection. Hum Pathol 1993;24:866-70.
21. Nishida T, Nakao K, Hamaji M. Differentiated thyroid carcinoma with airway invasion: indication for tracheal resection based on the extent of cancer invasion. J Thorac Cardiovasc Surg 1997;114:84-92.
22. Chiacchio S, Lorenzoni A, Boni G, Rubello D, Elisei R, Mariani G. Anaplastic thyroid cancer: prevalence, diagnosis and treatment. Minerva Endocrinol 2008;33:341-57.
23. Smallridge RC, Copland JA. Anaplastic thyroid carcinoma: pathogenesis and emerging therapies. Clin Oncol (R Coll Radiol) 2010;22:486-97.
24. Kebebew E. Anaplastic thyroid cancer: rare, fatal, and neglected. Surgery 2012;152:1088-9.
25. Wendler J, Kroiss M, Gast K, Kreissl MC, Allelein S, Lichtenauer U, et al. Clinical presentation, treatment and outcome of anaplastic thyroid carcinoma: results of a multicenter study in Germany. Eur J Endocrinol 2016;175:521-9.
26. Haigh PI, Ituarte PH, Wu HS, Treseler PA, Posner MD, Quivey JM, et al. Completely resected anaplastic thyroid carcinoma combined with adjuvant chemotherapy and irradiation is associated with prolonged survival. Cancer 2001;91:2335-42.