

Prognostic Factors of Anaplastic Thyroid Carcinoma: An Egyptian Single Institution Experience

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Abstract

Background: Anaplastic thyroid carcinoma is an extremely aggressive cancer that has a very poor outcome. We have analyzed predictive factors for overall survival and different therapeutic modalities that could help to determine the optimal therapy for this carcinoma.

Methods: We performed a retrospective analysis of data from 54 cases of anaplastic thyroid carcinoma to evaluate demographic, pathological, and clinical characteristics, along with therapeutic modalities that affected survival. The Kaplan-Meier curve was used to visualize the cumulative probability of survival and comparison among/between groups was performed with the log-rank test. A multivariate Cox proportional hazards model was used to examine overall survival.

Results: We observed overall survival percentages of 50% (one-year), 25% (2-year), and 5.6% (5-year). The 2-year overall survival was 41.7% for stage IVA, 31.5% for stage IVB, and 7.4% for stage IVC ($P=0.04$). The 2-year overall survival rates were 59.3% for patients with negative margins, 30.1% for those with positive margins, and 0.0% in the group without thyroidectomy ($P=0.005$). Surgery plus postoperative radiotherapy indicated better 2-year overall survival (56%) compared to surgery alone (34.7%, $P<0.005$). Multivariate analysis showed that factors predictive of improved overall survival included tumor size (≤ 5 cm), duration of complaint $>$ one month, no reported metastasis at presentation, negative surgical margins, surgery, radiotherapy, and/or chemotherapy.

Conclusion: Anaplastic thyroid carcinoma is an aggressive cancer with a very poor prognosis. Multimodality treatment may improve overall survival in these patients. Duration of symptoms, primary tumor size, distant metastases, surgical treatment, surgical margin status, radiotherapy, and chemotherapy are independent factors that affect prognosis.

Keywords: Prognostic factors, Outcome, Anaplastic thyroid cancer

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Introduction

Although anaplastic thyroid carcinoma (ATC) is rare, it is one of the most aggressive malignancies. This carcinoma accounts for 1.7% of all thyroid malignancies and one-half of all thyroid cancer deaths.¹ The median survival for ATC is 5 months with a one-year survival rate of 20%.² At presentation, ATC is classified as stage IV (A, B, or C) by the American Joint Committee on Cancer (AJCC) TNM system. Anaplastic thyroid carcinoma most commonly presents in the seventh decade of life and is more common in women.³

Optimal ATC treatment is debatable; most sources agree that surgery is of benefit. Although improved survival has been reported with postoperative radiotherapy, other reports questioned the benefit of radiotherapy.^{4,5} Combined chemoradiotherapy was favored over radiation alone.^{6,7} However, several series reported no benefit for chemotherapy.⁸⁻¹⁰ A number of authors noted that factors such as age, gender, presence of acute symptoms, tumor size, extent of disease, extent of surgery, and radiotherapy and chemotherapy doses influenced local control and survival of ATC patients.^{5,11-14}

Here, we reviewed data from ATC patients in an attempt to identify the prognostic factors of this disease that could help ascertain appropriate therapeutic strategies in these patients.

Patients and Methods

We reviewed the recorded data of 54 ATC cases treated at Mansoura University Hospital Clinical Oncology and Nuclear Medicine, and Surgery Departments in Mansoura, Egypt.

Patient selection

All histopathologic specimens were reevaluated to confirm the diagnosis of ATC, including spindle and giant cell variants, and exclude lymphoma medullary carcinoma and differentiated thyroid carcinoma.

Definition of variables

Patient demographic variables were age and

gender. Pathological and clinical characteristics included in our analyses were clinical presentation, duration of symptoms, tumor size (≤ 5 cm/ > 5 cm), extrathyroidal extension (yes/no), distant metastasis (yes/no), type of surgery (total or extensive thyroidectomy with neck dissection or other), surgical margins [negative (R0), positive (R1), or biopsy, palliative tracheotomy, or non-surgical treatment], radiotherapy (yes/no), and chemotherapy (yes/no).

Statistical analysis

Patient characteristics were reported as frequencies and proportions. Kaplan-Meier curve was used to visualize the cumulative probability of survival. Comparison among/between groups was performed using the log-rank test. A multivariate Cox proportional hazards model was used to examine overall survival (OS) after adjustments for clinical and demographic factors. Significance was determined to be $P < 0.05$ for all statistical tests.

Results

A total of 54 ATC cases were treated in our departments from January 2005 until January 2016. These cases comprised 2% (54/2700) of the thyroid cancer cases during this period. Table 1 lists the demographic and clinical characteristics of the 54 patients. They ranged in age from 41-82 years, with 14 patients ≤ 60 years of age and 40 patients > 60 years of age. The median age was 63 years. There were 21 male and 33 female patients.

The most frequent complaint was the presence of a neck mass ($n=35$). Of these 35 cases, 15 had rapidly enlarging masses with or without goiters. Hoarseness of voice was the second most common symptom. Duration of symptoms varied from 2 weeks to ≥ 6 months.

We noted that 41 patients had extra-thyroidal invasion of the surrounding organs. At the time of initial examination, 16 had distant metastases. According to TNM staging (AJCC, 2010), there were 16 patients with stage IVA, 22 with stage IVB, and 14 patients with stage IVC. A total thyroidectomy and extensive thyroidectomy with

neck dissection were performed for 40 patients. There were 2 cases that underwent palliative resection and 8 only underwent tracheotomy. We noted that 18 cases had negative (R0) surgical margins and 22 cases had positive margins (R1) after radical surgery.

There were 36 patients who received radiotherapy as follows: 30 underwent postoperative radiotherapy, 4 received definitive radiotherapy, and 2 patients received palliative radiotherapy. Radiotherapy doses ranged from 40 to 66 Gy and included >50 Gy in 30 cases. Concomitant chemoradiotherapy was administered to 18 patients. Chemotherapeutic regimens consisted of adriamycin or paclitaxel.

As of December 2016, 4 out of the 54 total patients were alive. There were 40 patients whose deaths were attributed to the primary cancer and 10 whose deaths were from distant metastases. We observed that the one-year OS rate was 50%, with 2-year OS of 25%, and 5.6% for 5-year OS in all patients (Figure 1). The 2-year OS rates according to stage were: 40.7% (stage IVA), 31.5% (stage IVB), and 7.4% (stage IVC; $P=0.04$).

Patients in the R0 group had 2-year OS of 59.3%. Those in the R1 group had an OS rate of 30.1%, and the group without radical surgery had a 2-year OS of 0%. This difference was statistically significant ($P=0.005$). The 2-year OS rates were 56% for patients with surgery followed by postoperative radiotherapy and 34.7% for those with only surgery, which was statistically significant ($P=0.022$). However there was no difference in OS between the chemotherapy group and those who received no chemotherapy ($P=0.739$).

Univariate analysis results showed that factors associated with significantly improved OS included small tumor (≤ 5 cm), duration of complaint >1 month, no reported metastasis at presentation, negative margins, surgery, radiotherapy, and chemotherapy.

According to multivariate analysis results, factors predictive of improved OS consisted of tumor size (≤ 5 cm), duration of complaint >1

Table 1. Clinical characteristics of the anaplastic thyroid carcinoma (ATC) patients (n=54).

Characteristics	Number	%
Age (years)		
≤ 60	14	25.9
>60	40	74.1
Gender		
Female	21	38.9
Male	33	61.1
Symptoms		
Neck mass	35	64.8
Hoarseness	20	3.7
Neck pain	7	13
Dyspnea	6	11.1
Dysphagia	4	7.4
Duration of symptoms		
≤ 2 weeks	14	25.9
≤ 1 month	18	33.3
≤ 3 months	10	18.5
≤ 6 months	5	9.3
>6 months	7	13
Tumor size		
≤ 5 cm	14	25.9
>5 cm	40	74.1
Extrathyroidal invasion		
Yes	41	75.9
No	13	24.1
Distant metastasis		
Yes	16	29.6
No	38	70.4
Stage		
IVA	16	29.6
IVB	22	40.8
IVC	16	29.6
Surgery		
R0	18	33.3
R1	22	40.7
Other	14	26
Radiotherapy		
Yes	36	66.7
No	18	33.3
Chemotherapy		
Yes	18	33.3
No	36	66.7

month, no reported metastasis at presentation, negative surgical margins, surgery, radiotherapy, and/or chemotherapy (Table 2).

Discussion

Anaplastic thyroid carcinoma is a rare (1% ~ 2%), extremely aggressive malignancy that has a very poor prognosis with median survival of 5

months and a 20% one-year survival rate.¹ Radical surgical treatment is still a cornerstone treatment that affects the prognosis of ATC. This study has reported an association between radical surgery with significant survival compared to the non-surgical treatment group ($P=0.005$). This finding agreed with a number of studies.¹⁵⁻²⁰ In the current study, we observed 2-year OS rates of 59.3% (R0 group), 30.3% (R1 group), and 0% (group without radical surgery). Liu et al. reported similar results¹⁵ with 2-year OS rates of 58.3% (R0), 31.3% (R1), and 0% (group without radical surgery). This data supported the importance of surgical treatment of ATC.

In the current study, we observed better OS in the surgery group that had postoperative radiotherapy compared to the surgery alone group ($P=0.022$). These findings were similar to results of other studies.²⁰⁻²² The addition of radiotherapy treatment to surgery might be an effective therapeutic modality for improving survival of ATC patients.

Our study reported low one-year (50.0%) and 2-year (25.0%) OS rates. The 2-year OS survival rates according to stage were 40.7% (IVA), 31.5% (IVB), and 7.4% (IVC; $P<0.05$). These findings agreed with results reported by Liu et al.¹⁵

We observed that duration of symptoms,

Table 2. Multivariable Cox proportional hazard models for overall survival (OS).

	HR (95% CI)	P-value
Duration of symptoms		
≤1 month	1.36 (0.94-1.92)	<0.031
>1 month		
Tumor size		
≤5 cm	0.73 (0.65-0.82)	<0.025
>5cm		
Distant metastasis		
Yes	0.62 (0.49-0.78)	<0.012
No		
Surgical margins		
Negative	1.45 (1.05-2.12)	<0.033
Positive/unknown		
Surgery		
Total thyroidectomy	0.83 (0.75-0.92)	<0.042
Other surgery/none		
Radiotherapy		
Yes	0.94 (0.58-1.66)	<0.041
No		
Chemotherapy		
Yes	0.98 (0.68-1.56)	<0.011
No		

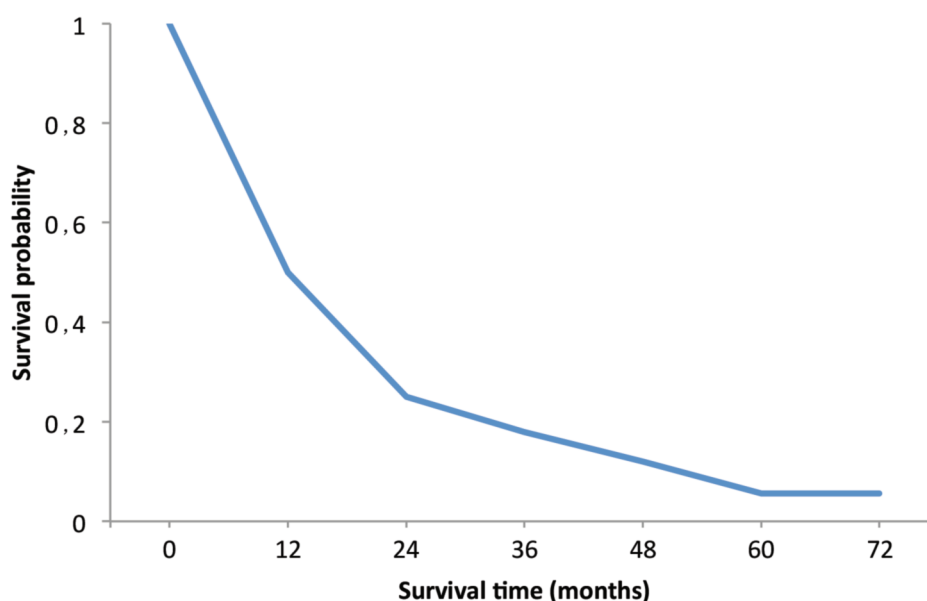


Figure 1. Overall survival (OS) of anaplastic thyroid cancer (ATC) patients (n=54).

primary tumor size (diameter), distant metastases, surgical margin status, surgical treatment, radiotherapy, and chemotherapy might be independent factors which affected prognosis according to multivariate analysis. Sun et al. found that white blood cell counts and surgery with postoperative radiotherapy were independent factors that affected ATC prognosis.²³ Age and tumor size were reported prognostic factors for ATC in a different study.²⁰ Results from another study showed that tumor size, distant metastases, surgical treatment, radiotherapy, and tumor residue were independent prognostic factors.¹⁵

A large, prospective randomized controlled trial is warranted. However, due to the rarity of ATC, it has been difficult to conduct this type of study in the past.

Conclusion

Multimodality treatment might improve OS in ATC patients. Anaplastic thyroid carcinoma is an aggressive cancer with a very poor prognosis. Duration of symptoms, primary tumor size (>5 cm), distant metastases, surgical treatment, surgical margin status, radiotherapy, and chemotherapy are independent factors that affect prognosis.

Conflict of Interest

None declared.

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