

Anaplastic Transformation of Differentiated Thyroid Carcinoma: A Single Institution Case Series

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Introduction

- Anaplastic thyroid carcinomas (ATC) constitute 1-2% of thyroid cancers. They are responsible for 40-50% of thyroid carcinoma-related deaths in the United States.
- Though ATCs are by definition undifferentiated, some ATCs have foci of differentiated carcinoma, most commonly the tall cell variant of papillary thyroid carcinoma.
- Previous studies have reported rates of DTC and ATC concurrence to vary from 10-50%. Due to the high rate of co-occurrence of DTC and ATC, some have posited that some ATC may evolve from previously differentiated thyroid carcinoma.
- The primary objective of this paper was to determine whether the co-occurrence of differentiated thyroid carcinoma with anaplastic thyroid carcinoma was associated with improved outcomes in our cohort of anaplastic thyroid carcinoma patients.

Methods

- All patients who received a biopsy-confirmed diagnosis of ATC at a tertiary academic medical center (UCLA Medical Center) between January 1, 2002, and March 31, 2020, were included in this study.
- Pathology reports were reviewed in detail to identify cases of anaplastic transformation in the thyroid, lateral and central neck, and distant sites.
- Patient characteristics and clinical outcomes were reviewed.
- The Kaplan-Meier method was used to estimate survival by treatment.
- The significance of these variates on measured outcomes was determined using log-rank tests. Cox proportional hazard ratios were used to measure the effects of multiple covariates on overall survival. Analysis was performed using IBM SPSS Version 27.0.0.

Results

- Forty-five patients with ATC were included in this study. 53.3% of cases (n = 24) showed ATDTC on histopathologic exam. The mean age of patients in this study was 69.0 (range, 50-88).
- 51.1% (n = 23) were males. 60% of patients (n = 27) presented with stage T4b disease.
- Over half the patients had locoregional involvement at the time of surgery, with 24.4% (n = 11) N1a and 26.7% (n = 12) N1b. Distant metastasis at presentation was observed in 37.8% of patients (n = 17).

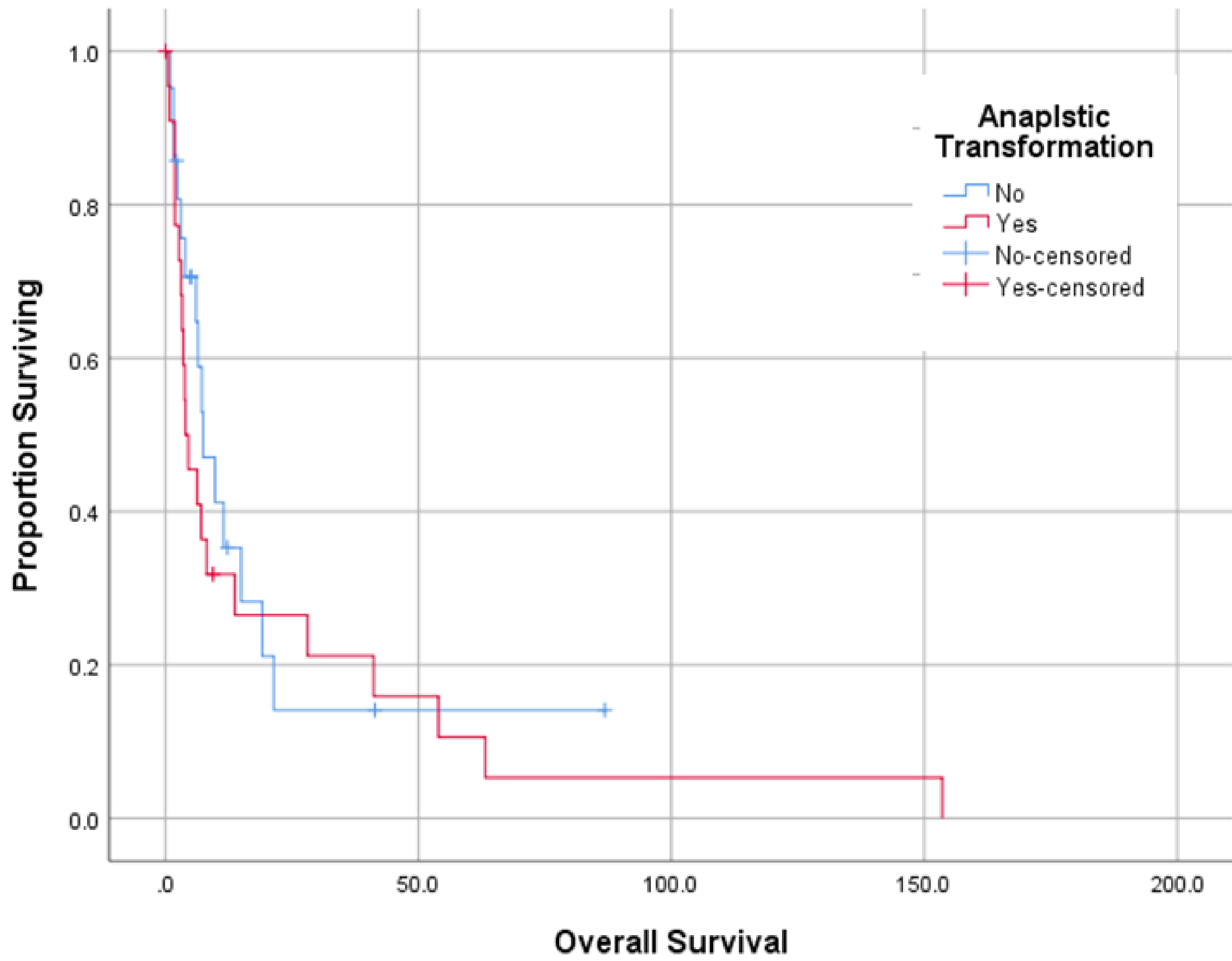


Figure 1. The overall survival of patients with ATDTC compared to those with ATC. As indicated above, the difference in survival was not significant (p = 0.509).

- The mean tumor size was 6.3 cm (range, 1.9 - 24.0).
- Overall survival rates were 34% at one year, 21% at two years, and 11% at five years.
- Mutation analysis demonstrated that BRAF V600E was present in 45.8% of the cases (n = 11).
- The presence of BRAF V600E was also not significantly different between the ATC and ATDTC groups (p = 0.414, Fisher’s exact test). 84% of patients received some form of chemotherapy (conventional, BRAF inhibitor, MEK inhibitor or Her2/Neu inhibitors).
- The administration of chemotherapy was associated with a higher survival (3.8 vs 33.9 months, p = 0.01).
- More than 90% of patients received radiation treatment as part of their management but this was not associated with a greater survival (p = 0.377).

Conclusions

- ATC portends a poor prognosis, even when it arises in association with differentiated thyroid cancers.
- Histological presence of differentiated thyroid carcinoma to suggest anaplastic transformation does not confer additional survival benefit.
- Chemotherapy and targeted therapy were associated with increased survival.
- Additional genetic studies are warranted to provide useful biomarkers for patient stratification as well as assembling the key steps in the anaplastic transformation.

Table 1. Multivariate analysis of the predictors of survival for patients with ATC.

Characteristic	Overall survival (log-rank P)
Age	0.960
Sex	0.706
Differentiated	0.075
Chemo	0.011
Size	0.030
T	0.530
N	0.044
M	0.014