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Original research article

Multivariate analysis of histopathological features as prognostic factors in thyroid neoplasm: A retrospective study

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Abstract

Background: Thyroid neoplasms represent a diverse group of malignancies with varying degrees of aggressiveness. Accurate prognostication is essential for effective management, but identifying reliable prognostic factors remains a challenge. This study aims to evaluate histopathological features and their prognostic significance in thyroid neoplasms through a detailed multivariate analysis.

Methods: This retrospective study analyzed patient data from a tertiary Care Center over a period of 5 years, from January 2010 to December 2014. Data on histopathological characteristics such as tumor size, histological subtype, lymph node involvement, and extrathyroidal extension were collected. Multivariate logistic regression was employed to determine the independent prognostic factors for overall survival (OS), disease-free survival (DFS), and recurrence-free survival (RFS). The analysis followed the STROBE guidelines to ensure methodological rigor.

Results: Among 250 patients, multivariate analysis identified tumor size, extrathyroidal extension, lymph node involvement, and histological subtype as significant prognostic factors. Larger tumor size (odds ratio [OR] 2.3, 95% confidence interval [CI] 1.5-3.5), extrathyroidal extension (OR 3.8, 95% CI 2.1-6.9), and aggressive histological subtypes (OR 4.5, 95% CI 2.8-7.2) were all associated with poorer outcomes. These findings highlight the critical role of these factors in predicting patient prognosis.

Conclusion: The study underscores the importance of tumor size, extrathyroidal extension, and histological subtype in assessing the prognosis of thyroid neoplasms. These results can enhance risk stratification and inform clinical decision-making, ultimately improving patient management and outcomes.

Keywords: Thyroid neoplasm, histopathology, multivariate analysis, prognostic factors, retrospective study

Introduction

Thyroid neoplasms encompass a spectrum of tumors with varying clinical and biological behaviours. Accurate prognostication is pivotal for guiding treatment decisions and improving patient outcomes. The diversity in histopathological features, such as tumor size, histological subtype, and the presence of extrathyroidal extension, presents challenges in predicting patient prognosis. As the management of thyroid cancer evolves, understanding which histopathological features are most indicative of adverse outcomes becomes increasingly important [1-3].

Historically, various studies have identified key prognostic factors for thyroid neoplasms, but the relative importance of these factors often varies across studies. This discrepancy highlights the need for comprehensive analyses that can integrate multiple prognostic variables to provide a more nuanced understanding of disease outcomes. Multivariate analysis offers a robust approach to elucidate the interplay between different prognostic factors and their collective impact on patient survival and recurrence [4, 5].

This study aims to perform a thorough multivariate analysis of histopathological features to identify and quantify their prognostic significance in thyroid neoplasms. By analyzing a large cohort of patients and adhering to rigorous methodological standards, we seek to provide valuable insights into the factors that most reliably predict patient outcomes, thereby informing clinical practice and guiding future research.

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Methodology

Study Design and Participants

This retrospective cohort study was conducted in a tertiary care center, covering the period from January 2010 to December 2014. The study was approved by the institutional review board, ensuring compliance with ethical standards. Inclusion criteria comprised adult patients (≥18 years) diagnosed with thyroid neoplasms who underwent surgical resection. Patients with incomplete data, prior malignancies, or non-thyroidal neoplasms were excluded to ensure the study's focus on primary thyroid cancer.

Data Collection

Patient demographics, clinical characteristics, and detailed histopathological data were extracted from medical records. Key histopathological features assessed included tumor size, histological subtype, lymph node involvement, vascular invasion, extrathyroidal extension, and the presence of distant metastases. Tumor size was measured in centimeters, and histological subtypes were classified as papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma, and anaplastic thyroid carcinoma.

Clinical data such as age at diagnosis, gender, and treatment modalities (surgical approach, adjuvant therapy) were also recorded. Follow-up information on survival outcomes was obtained from patient records and subsequent clinical visits.

Outcome Measures

The primary outcome measure was overall survival (OS), defined as the time from initial diagnosis to death from any cause. Secondary outcomes included disease-free survival (DFS), which represents the time from diagnosis to disease recurrence, and recurrence-free survival (RFS), which measures the period from treatment to the first recurrence of the disease.

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical characteristics. Univariate analyses were performed using chi-square tests for categorical variables and t-tests or Mann-Whitney U tests for continuous variables. To identify independent prognostic factors, multivariate logistic regression analysis was conducted. Hazard ratios (HRs) with 95% confidence intervals (CIs) were computed to assess the association between prognostic factors and survival outcomes. All analyses were conducted using SSPS version 23, with a significance threshold set at $p<0.05$.

The multivariate models were adjusted for potential confounders, including age, gender, and treatment type, to isolate the effects of histopathological features. Model diagnostics were performed to ensure the adequacy and robustness of the regression models.

Results

Table 1: Patient demographics and clinical characteristics

Variable	N = 250	Percentage (%)
Age (mean ± SD)	54.3±12.5	-
Gender		
- Male	80	32.0
- Female	170	68.0
Tumor Size (mean ± SD)	3.2±1.1 cm	-
Histological Subtype		
Papillary Thyroid Carcinoma	180	72.0
Follicular Thyroid Carcinoma	40	16.0
Medullary Thyroid Carcinoma	20	8.0
Anaplastic Thyroid Carcinoma	10	4.0
Lymph Node Involvement	110	44.0
Extrathyroidal Extension	75	30.0

Table 1 provides a comprehensive overview of patient demographics and clinical characteristics. The cohort comprised 250 patients, with a mean age of 54.3 years. There was a predominance of female patients (68.0%), and the average tumor size was 3.2 cm. Histological analysis revealed a majority of papillary thyroid carcinomas (72.0%), with a smaller proportion of follicular, medullary, and anaplastic types. Lymph node involvement was observed in 44.0% of patients, and extrathyroidal extension was noted in 30.0% of cases.

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Table 2: Univariate Analysis of Prognostic Factors for Overall Survival

Variable	HR (95% CI)	p-value
Tumor Size	2.5 (1.8-3.4)	<0.001
Lymph Node Involvement	2.1 (1.5-2.9)	<0.001
Extrathyroidal Extension	3.0 (2.0-4.6)	<0.001
Histological Subtype		
Papillary Thyroid Carcinoma	1.0 (Reference)	-
Follicular Thyroid Carcinoma	1.7 (1.1-2.5)	0.014
Medullary Thyroid Carcinoma	2.5 (1.5-4.0)	0.002
Anaplastic Thyroid Carcinoma	4.0 (2.5-6.3)	<0.001

Table 2 presents the results of the univariate analysis for overall survival. Larger tumor size, lymph node involvement, and extrathyroidal extension were significantly associated with worse survival outcomes. Histological subtypes also showed varying impacts, with anaplastic thyroid carcinoma associated with the highest risk of mortality.

Table 3: Multivariate Analysis of Prognostic Factors for Overall Survival

Variable	OR (95% CI)	p-value
Tumor Size	2.3 (1.5-3.5)	<0.001
Lymph Node Involvement	1.8 (1.1-2.8)	0.022
Extrathyroidal Extension	3.8 (2.1-6.9)	<0.001
Histological Subtype		
Papillary Thyroid Carcinoma	1.0 (Reference)	-
Follicular Thyroid Carcinoma	1.5 (0.9-2.4)	0.129
Medullary Thyroid Carcinoma	2.1 (1.2-3.5)	0.010
Anaplastic Thyroid Carcinoma	4.5 (2.8-7.2)	<0.001

Table 3 details the results of the multivariate analysis for overall survival. This analysis confirmed that tumor size, extrathyroidal extension, and aggressive histological subtypes independently predicted poorer outcomes. Tumor size and extrathyroidal extension were particularly significant, with high odds ratios indicating a strong association with reduced survival.

Table 4: Disease-free survival by histological subtype

Histological Subtype	DFS (months)	p-value
Papillary Thyroid Carcinoma	72.5±5.2	-
Follicular Thyroid Carcinoma	60.0±7.5	0.045
Medullary Thyroid Carcinoma	50.0±10.2	0.030
Anaplastic Thyroid Carcinoma	30.0±8.0	0.005

Table 4 presents disease-free survival rates stratified by histological subtype. Papillary thyroid carcinoma patients had the longest DFS, while anaplastic thyroid carcinoma was associated with the shortest DFS. These differences underscore the variability in disease progression and recurrence risk across different histological subtypes.

Table 5: Recurrence-Free Survival by Tumor Size

Tumor Size (cm)	RFS (months)	p-value
<2.0	85.0±4.5	-
2.0-4.0	65.0±6.0	<0.001
>4.0	40.0±7.5	<0.001

Table 5 shows recurrence-free survival based on tumor size. Patients with tumors smaller than 2 cm had the longest RFS, while those with larger tumors experienced significantly shorter RFS. This highlights the impact of tumor size on the likelihood of disease recurrence.

Table 6: Impact of Lymph Node Involvement on Disease-Free Survival

Lymph Node Involvement	DFS (months)	p-value
Absent	75.0±5.0	-
Present	55.0±6.5	<0.001

Table 6 evaluates the impact of lymph node involvement on disease-free survival. The presence of lymph node involvement was associated with a significant reduction in DFS, reinforcing its role as a negative prognostic factor.

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Table 7: Prognostic Factors Associated with Extrathyroidal Extension

Factor	OR (95% CI)	p-value
Tumor Size	3.0 (2.0-4.5)	<0.001
Lymph Node Involvement	2.5 (1.6-3.8)	0.004
Histological Subtype		
Papillary Thyroid Carcinoma	1.0 (Reference)	-
Follicular Thyroid Carcinoma	1.6 (0.9-2.7)	0.090
Medullary Thyroid Carcinoma	2.0 (1.2-3.5)	0.015
Anaplastic Thyroid Carcinoma	3.5 (2.0-6.1)	<0.001

Table 7 explores prognostic factors associated with extrathyroidal extension. Larger tumor size and lymph node involvement were strongly associated with extrathyroidal extension. Aggressive histological subtypes, particularly anaplastic thyroid carcinoma, were also significantly linked to this feature.

Discussion

The analysis of the results reveals several critical insights into the prognostic significance of histopathological features in thyroid neoplasms. The study confirms that larger tumor size, extrathyroidal extension, and aggressive histological subtypes are pivotal in predicting patient outcomes [6, 7].

Tumor size was found to be a robust predictor of survival, with larger tumors correlating with worse overall survival, disease-free survival, and recurrence-free survival. This finding is consistent with existing literature, which highlights the importance of tumor burden in determining prognosis [8].

Extrathyroidal extension emerged as a particularly strong prognostic factor. Its association with adverse outcomes underscores the aggressive nature of tumors that invade surrounding tissues. This aligns with previous studies that have established extrathyroidal extension as a marker of poor prognosis [9].

Histological subtype also plays a crucial role in prognosis. The study found that aggressive subtypes, such as anaplastic and medullary thyroid carcinomas, were associated with poorer outcomes. These findings are consistent with established knowledge that these subtypes exhibit more aggressive behavior and are associated with worse survival rates [10].

The presence of lymph node involvement was another significant factor impacting disease-free survival. Patients with lymph node metastases had a significantly reduced DFS, highlighting the importance of nodal status in prognostication.

The study's limitations include its retrospective design, which may introduce biases related to data collection and interpretation. Variability in diagnostic and treatment protocols over the study period could also affect the results. Future prospective studies are needed to validate these findings and explore additional biomarkers and clinical variables that may further refine prognostic models [1, 11].

Conclusion

In conclusion, this study provides valuable insights into the prognostic factors associated with thyroid neoplasms. By highlighting the significance of tumor size, extrathyroidal extension, and histological subtype, the study contributes to a better understanding of thyroid cancer prognosis and offers practical implications for patient management and treatment strategies. Further research is essential to build on these findings and enhance the accuracy of prognostic assessments in thyroid neoplasms.

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