International Journal of Otorhinolaryngology
2024, Vol. 10, No. 2, pp. 58-64
https://doi.org/10.11648/j.ijo.20241002.13

Research Article

Thyroid Cancer Recurrence: Risk Factors and Preventive Strategies

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Abstract

Introduction: Several risk factors influence the recurrence of thyroid cancer, including age, tumor size, lymph node involvement, and other prognostic indicators. The purpose of this study is to evaluate the impact of these risk factors on the recurrence rates of thyroid cancer, with the aim of improving diagnostic and treatment strategies for better patient outcomes. *Aim of the study*: The aim of the study was to evaluate risk factors for thyroid cancer recurrence and preventive strategies. *Methods*: This retrospective cohort study conducted at the Department of Otolaryngology-Head & Neck Surgery at Bangabandhu Sheikh Mujib Medical University (BSMMU) included 108 thyroid cancer patients treated between April 2023 and March 2024. Patients were categorized into low-risk and high-risk groups based on prognostic factors. Follow-up for three years assessed recurrence and survival through outpatient visits and telephone interviews. Statistical analyses using SPSS version 22.0 included descriptive statistics, chi-square tests for recurrence rates, and Kaplan-Meier survival analysis. Result: The study identified Differentiated Thyroid Carcinoma (DTC) as the most common type, with Papillary Thyroid Carcinoma being the predominant subtype. Recurrence rates were notably higher in patients aged ≥45 and in males. Significant predictors of recurrence included age, gender, tumor diameter, and lymph node metastasis. High-risk patients mostly received Total Thyroidectomy, Radioiodine ablation, and Thyroxin. Follow-up showed recurrence rates of 8.33% in low-risk and 7.55% in high-risk patients over three years. *Conclusion*: The study highlights the critical role of age, gender, tumor diameter, and lymph node metastasis in predicting thyroid cancer recurrence, emphasizing the need for personalized treatment and monitoring based on risk levels.

Keywords

Thyroid Cancer Recurrence, Differentiated Thyroid Carcinoma, Risk Factors, Surgical Treatment, Follow-Up Outcomes

1. Introduction

Thyroid cancer accounts for 3% of all cancer cases worldwide, with an estimated 586,000 new diagnoses in 2020. [1, 2] Over the past three decades, its incidence has notably increased in several high-income and middle-income countries. [3] Among the different histological forms of thyroid cancer, roughly 90% are papillary thyroid carcinomas (PTC), 4% are follicular thyroid carcinomas (FTC), 2% are Hürthle cell carcinomas, 2% are medullary thyroid carcino-

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Received: 19 August 2024; **Accepted:** 7 September 2024; **Published:** 23 September 2024

mas (MTC), and 1% are anaplastic thyroid carcinomas (ATC). [4] The clinical behavior of the disease varies widely, from the common and largely asymptomatic papillary tumors [5] to the rare but highly aggressive anaplastic malignancies. [6]

Several risk factors influence the recurrence of thyroid cancer, including age, tumor size, lymph node involvement, and other prognostic indicators. Key factors that increase the likelihood of recurrence are age, male sex, larger tumor size, extra-thyroidal extension, nodal metastases at diagnosis, and aggressive histological types. [7] Lymph node metastasis is notably a critical pathological feature of papillary thyroid carcinoma (PTC), associated with higher disease stages and an elevated risk of recurrence. [8] The lymph node positivity ratio (LNPR), which represents the ratio of positive lymph nodes to the total number of nodes removed, is an important metric for evaluating the extent of lymph node metastasis and its effect on recurrence risk. [9] Additionally, improvements in diagnostic and treatment techniques have facilitated earlier detection of recurrences. Recent estimates suggest that approximately 30% of well-differentiated thyroid cancer (WDTC) cases will recur, mainly within the first decade after initial treatment. [10]

Surgical resection remains the primary treatment for differentiated thyroid cancer, especially for papillary and follicular types, which generally have a favorable prognosis. [11] However, total thyroidectomy, though effective, can result in complications such as laryngeal nerve palsy and hypoparathyroidism. [11] Despite comprehensive surgical efforts, the intricate anatomy of the thyroid gland often contributes to postoperative recurrence rates ranging from 23% to 30%, highlighting the need for early identification of risk factors to enhance patient outcomes. [12]

With the increasing incidence of small, slow-growing papillary thyroid cancers, follow-up protocols need to be carefully designed to prevent overtreatment while ensuring that patients at higher risk receive appropriate care and monitoring. [13, 14]

As the management of thyroid cancer continues to evolve, it is essential to balance the benefits of aggressive treatment with the potential risks of complications and overtreatment. The increasing incidence of small, indolent papillary thyroid cancers emphasizes the need for individualized treatment plans and careful follow-up strategies tailored to the patient's risk profile. Given the significant risk of recurrence even after comprehensive surgical intervention, ongoing research is crucial to identify and mitigate these risks effectively.

The purpose of this study is to evaluate the outcomes of surgical resection in thyroid cancer patients, with a particular focus on recurrence rates, risk factors associated with recurrence, and the effectiveness of current follow-up protocols in improving long-term patient outcomes.

2. Objectives

The aim of the study was to evaluate risk factors for thyroid cancer recurrence and preventive strategies.

3. Methodology & Materials

This retrospective cohort study was conducted at the Department of Otolaryngology-Head & Neck Surgery, Bangabandhu Sheikh Mujib Medical University, over a 12-months period from April 2023 to March 2024. The study included 108 patients diagnosed with thyroid cancer who received treatment at the Department of Otolaryngology-Head & Neck Surgery, Bangabandhu Sheikh Mujib Medical University.

Inclusion Criteria

1. Patients diagnosed with thyroid cancer confirmed by histopathology.
2. Patients who underwent surgical treatment for thyroid cancer at the Department of Otolaryngology-Head & Neck Surgery, Bangabandhu Sheikh Mujib Medical University.
3. Patients with complete clinical records and follow-up data.

Exclusion Criteria

1. Patients who declined to provide informed consent.
2. Patients with severe comorbid conditions that could compromise treatment outcomes (e.g., advanced heart failure or severe liver disease).
3. Patients who were lost to follow-up or who had incomplete follow-up data.

Ethical clearance was taken from the hospital authority, and ethical considerations were addressed according to the Helsinki Declaration. Informed written consent was obtained from all participants. Data were retrospectively collected from medical records, including demographic details, tumor characteristics, and treatment information. Patients were classified into low-risk and high-risk groups based on prognostic factors such as age, tumor size, and presence of metastasis. Follow-up was conducted for three years through outpatient visits and telephone interviews to assess recurrence (local, nodal, or distant) and survival outcomes. Statistical analyses were performed using SPSS version 22.0. Descriptive statistics summarized patient demographics and tumor characteristics, chi-square tests compared recurrence rates between risk groups, and Kaplan-Meier analysis assessed survival. A p-value of <0.05 was considered statistically significant.

4. Result

Table 1. Distribution of Thyroid Malignancy by Histological Type (n = 108).

Histological Type	Number of Patients	Percentage (%)
Differentiated Thyroid Carcinoma (DTC)		
Papillary Thyroid Carcinoma	69	63.89
Follicular Thyroid Carcinoma	22	20.37
Total	91	84.26
Hurthle Cell Carcinoma	11	10.19
Medullary Thyroid Carcinoma	5	4.63
Undifferentiated Thyroid Carcinoma	1	0.93

Differentiated Thyroid Carcinoma (DTC), which includes Papillary Thyroid Carcinoma and Follicular Thyroid Carcinoma, was the most prevalent, accounting for 91 (84.26%) patients. Papillary Thyroid Carcinoma was the most common subtype, with 69 (63.89%) patients, followed by Follicular Thyroid Carcinoma with 22 (20.37%) patients. Other subtypes included Hurthle Cell Carcinoma with 11 (10.19%) patients, Medullary Thyroid Carcinoma with 5 (4.63%) patients, and Undifferentiated Thyroid Carcinoma with 1 (0.93%) patient.

Table 2. Predictive Variables for Recurrence in Thyroid Cancer Among Study Patients (n=108).

Variable		n	Presence of recurrence n=13	(%)	Absence of recurrence n=95	(%)	Odds ratio	P-value
Age (years)	<45	47	2	4.26	45	95.74	0.214	0.015
	≥45	64	11	17.19	53	82.81		
Gender	Male	20	6	30.00	14	70.00	4.97	0.003
	Female	88	7	7.95	81	92.05		
BMI (kg×m-2)	≤25	39	5	12.82	34	87.18	0.53	0.87
	25-28	55	7	12.73	48	87.27		
	≤28	14	1	7.14	13	92.86		

Recurrence rates of thyroid cancer were significantly higher in patients aged ≥45 and in male. No significant difference in recurrence was found across different BMI categories.

Table 3. Comparisons of Tumor Characteristics between The Two Groups of The Study Patients (n=108).

Variable		n	Presence of recurrence n=13	(%)	Absence of recurrence n=95	(%)	Odds ratio	P-value
Tumor diameter	≤1	12	1	8.33	11	91.67	0.154	0.020

Variable		n	Presence of recurrence		Absence of recurrence		Odds ratio	P-value
			n=13	(%)	n=95	(%)		
(cm)	1-4	86	8	9.30	78	90.70		
	≥4	10	4	40.00	6	60.00		
Lymph node metastasis	Yes	21	10	47.62	11	52.38	25.45	<0.001
	No	87	3	3.45	84	96.55		
Distant metastasis	Yes	17	2	11.76	15	88.24	0.97	0.670
	No	91	11	12.09	80	87.91		

This table compares tumor characteristics between patients with and without thyroid cancer recurrence. Significant differences are observed in tumor diameter (cm) and lymph node metastasis. Tumor diameter ≥4 cm and the presence of lymph node metastasis are associated with a higher likelihood of recurrence. No significant difference is found for distant metastasis ($p > 0.05$ for all comparisons).

Table 4. *Significant Risk Factors for Recurrence Among Study Patients with Thyroid Cancer.*

Risk Factor	P-Value
Age	0.015
Gender	0.003
Tumor Diameter (cm)	0.02
Lymph Node Metastasis	<0.001

This table presents the significant risk factors associated with thyroid cancer recurrence. The analysis indicates that age, gender, tumor diameter, and lymph node metastasis are significant predictors of recurrence.

Table 5. *Treatment of Thyroid Carcinoma (DTC) (n=91).*

Risk group	Treatment type	No of Patients	Percentage (%)
Low risk	Hemithyroidectomy + Thyroxin	31	28.70
	Total thyroidectomy + Radioiodine ablation + Thyroxin	44	40.74
High risk	Total thyroidectomy +/- Neck dissection +/- Removal of metastatic lesion + Radioiodine + Thyroxin	32	29.63
	Inoperable +/- Radiotherapy	1	0.93

For low-risk patients, 31 (28.70%) received Hemithyroidectomy, and Thyroxin. High-risk patients were treated with Total Thyroidectomy, Radioiodine ablation, and Thyroxin in 44 (40.74%) cases, and with Total Thyroidectomy plus additional procedures in 32 (29.63%) cases. 1 (0.93%) patient with inoperable cancer underwent Radiotherapy.

Table 6. Follow up of the Study Patients with Thyroid Cancer.

	Low risk Group		High risk Group	
	(n=24)	%	(n=53)	%
Recurrence	2	8.33	4	7.55
Local	1	4.17	2	3.77
Nodal	1	4.17	4	7.55
Distant	nil	nil	2	3.77
Death	nil	nil	1	1.89

This table shows the follow-up outcomes of patients at the end of three years, divided into low-risk and high-risk groups. In the low-risk group (n=24), 2 (8.33%) patients experienced recurrence, with 1 (4.17%) patient having a local recurrence and 1 (4.17%) patient having a nodal recurrence. In the high-risk group (n=53), 4 (7.55%) patients had recurrences, including 2 (3.77%) patients with local recurrences, 4 (7.55%) patients with nodal recurrences, and 2 (3.77%) patients with distant recurrences. Additionally, 1 (1.89%) patient in the high-risk group died.

5. Discussion

This retrospective cohort study was at the Department of Otolaryngology-Head & Neck Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU) from April 2023 to March 2024. A total of 108 patients with diagnosed thyroid cancer who received treatment at BSMMU were included.

In this study, Differentiated Thyroid Carcinoma (DTC), including Papillary Thyroid Carcinoma and Follicular Thyroid Carcinoma, was the most prevalent, accounting for 91 (84.26%) patients. Papillary Thyroid Carcinoma was the most common subtype, with 69 (63.89%) patients, followed by Follicular Thyroid Carcinoma with 22 (20.37%) patients. Other subtypes included Hurthle Cell Carcinoma with 11 (10.19%) patients, Medullary Thyroid Carcinoma with 5 (4.63%) patients, and Undifferentiated Thyroid Carcinoma with 1 (0.93%) patient. This finding is consistent with Alauddin et al. [15], who also reported 84.41% Differentiated Thyroid Carcinoma in their study, aligning with other research showing that most thyroid cancers in the USA are papillary (80%), with follicular cancers comprising about 11% of new cases. [16]

In this study, recurrence rates of thyroid cancer were significantly higher in patients aged ≥45, consistent with findings by Luo et al. [17] and other studies that highlight a higher risk of recurrence in individuals aged 45 and older, particularly in Papillary Thyroid Cancer. [18] Additionally, recurrence rates were significantly higher in male patients, aligning with the results of Cunningham et al. [19], Kruijff et al. [20], who noted that male patients are more vulnerable to postoperative recurrence, possibly due to the effects of estrogen on thyroid cell proliferation. However, no significant difference in recurrence was found across different BMI categories, a finding that contrasts with Luo et al. [17], who reported significance in BMI.

In this study, significant differences were identified in tumor diameter and lymph node metastasis between patients who experienced thyroid cancer recurrence and those who did not. A tumor diameter of 4 cm or more was associated with a higher likelihood of recurrence, a finding that is consistent with another study. [17] As tumors increase in size, the risk of central lesion formation and capsule infiltration rises, making complete surgical removal more challenging and leading to a higher rate of postoperative recurrence. [21]

Similarly, lymph node metastasis was found to be a significant predictor of recurrence, aligning with research that indicates patients with lymph node involvement have a higher postoperative recurrence rate than those without. [17, 18]

In this study, age, gender, tumor diameter, and lymph node metastasis were identified as significant risk factors for thyroid cancer recurrence. These findings are in line with Luo et al. [17], who also found gender, tumor diameter, and lymph node metastasis as key predictors of recurrence. Additionally, Lo et al. [18] highlighted age and lymph node metastasis as significant risk factors specifically in Papillary thyroid cancer, along with distant metastasis. The consistency of these risk factors across multiple studies underscores their critical role in predicting thyroid cancer recurrence, particularly in Papillary thyroid cancer, and the importance of targeted interventions for patients presenting with these characteristics.

In this study, treatment strategies for thyroid cancer varied based on patient risk levels, with low-risk patients primarily receiving Hemithyroidectomy, and Thyroxin, and high-risk patients undergoing Total Thyroidectomy, Radioiodine ablation, and Thyroxin, similar to the findings reported by Alauddin et al. [15], where 37 low-risk DTC cases were managed with similar interventions.

In the follow-up at the end of three years, recurrence rates were observed in both low-risk (8.33%) and high-risk (7.55%) groups, with a mortality rate of 1.89% in the high-

risk group. These outcomes are consistent with previous studies, such as those by Hay et al. [22] and Cady et al. [23], who reported varying recurrence and mortality rates based on risk stratification and treatment approaches. The consistency of these findings highlights the importance of tailored treatment and long-term monitoring, especially in high-risk patients, to manage and mitigate the risk of recurrence and mortality.

This study highlights the critical role of personalized treatment in managing thyroid cancer, with specific factors like tumor diameter and lymph node metastasis being key predictors of recurrence. These findings underscore the necessity for ongoing research to refine therapeutic strategies and improve patient outcomes.

6. Limitations of the Study

This study had several limitations:

1. It was conducted in a single tertiary-level hospital, which may limit the diversity of the sample.
2. The sample was not randomly selected, potentially introducing selection bias.
3. The sample size was relatively small, affecting the statistical power of the findings.

7. Conclusion

This study identified key risk factors for thyroid cancer recurrence, including age, gender, tumor diameter, and lymph node metastasis. Differentiated Thyroid Carcinoma was the most prevalent, and treatment varied by risk group, with higher-risk patients receiving more aggressive therapies. Follow-up at three years revealed differences in recurrence and outcomes between risk groups, underscoring the importance of personalized treatment and monitoring strategies.

Abbreviations

DTC	Differentiated Thyroid Carcinoma
PTC	Papillary Thyroid Carcinoma
FTC	Follicular Thyroid Carcinoma
MTC	Medullary Thyroid Carcinoma
ATC	Anaplastic Thyroid Carcinoma
LNPR	Lymph Node Positivity Ratio
WDTC	Well-Differentiated Thyroid Cancer

Author Contributions

Masroor Rahman: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Mohammad Anwar Hossain: Data curation, Formal Analysis, Project administration, Software

Tawfiqur Rahman: Data curation, Funding acquisition, Investigation, Resources, Validation, Writing – original draft

Arif Mahmud Jewel: Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Writing – original draft, Writing – review & editing

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Ferlay J, Ervik M, Lam F, et al. Global Cancer Observatory: cancer today. Lyon: International Agency for Research on Cancer; 2020.

[2] Miranda-Filho A, Lortet-Tieulent J, Bray F, Cao B, Franceschi S, Vaccarella S, et al. Thyroid cancer incidence trends by histology in 25 countries: a population-based study. Lancet Diabetes Endocrinol. 2021; 9(4): 225–34.

[3] Li M, Dal Maso L, Vaccarella S. Global trends in thyroid cancer incidence and the impact of overdiagnosis. Lancet Diabetes Endocrinol. 2020; 8(6): 468–70.

[4] Surveillance, Epidemiology, and End Results Program (SEER). Cancer statistics review, 1975–2018. Bethesda, MD: National Cancer Institute; 2021 Apr 15.

[5] Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends in thyroid cancer incidence and mortality in the United States, 1974-2013. JAMA. 2017; 317(13): 1338.

[6] Asa SL. The current histologic classification of thyroid cancer. Endocrinol Metab Clin North Am. 2019; 48(1): 1–22.

[7] Baek S-K, Jung K-Y, Kang S-M, Kwon S-Y, Woo J-S, Cho S-H, et al. Clinical risk factors associated with cervical lymph node recurrence in papillary thyroid carcinoma. Thyroid. 2010; 20(2): 147–52.

[8] Feng J-W, Qin A-C, Ye J, Pan H, Jiang Y, Qu Z. Predictive factors for lateral lymph node metastasis and skip metastasis in papillary thyroid carcinoma. Endocr Pathol. 2020; 31(1): 67–76.

[9] Ryu IS, Song CI, Choi S-H, Roh J-L, Nam SY, Kim SY. Lymph node ratio of the central compartment is a significant predictor for locoregional recurrence after prophylactic central neck dissection in patients with thyroid papillary carcinoma. Ann Surg Oncol. 2014; 21(1): 277–83.

[10] Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. Am J Med. 1994; 97(5): 418–28.

[11] Minimally invasive video-assisted thyroidectomy for papillary carcinoma. Surgery. 2002; 132: 107–11.

[12] Yang X, Liang J, Li T-J, Yang K, Liang D-Q, Yu Z, et al. Postoperative stimulated thyroglobulin level and recurrence risk stratification in differentiated thyroid cancer. Chin Med J (Engl). 2015; 128(8): 1058–64.

[13] Takami H, Ito Y, Okamoto T, Onoda N, Noguchi H, Yoshida A. Revisiting the guidelines issued by the Japanese Society of Thyroid Surgeons and Japan Association of Endocrine Surgeons: a gradual move towards consensus between Japanese and western practice in the management of thyroid carcinoma. World J Surg. 2014; 38(8): 2002–10.

[14] Dralle H, Musholt TJ, Schabram J, Steinmüller T, Frilling A, Simon D, et al. German Association of Endocrine Surgeons practice guideline for the surgical management of malignant thyroid tumors. Langenbecks Arch Surg. 2013; 398(3): 347–75.

[15] Alauddin M, Joarder AH. Management of thyroid carcinoma-an experience in Bangladesh. Indian J Otolaryngol Head Neck Surg. 2004; 56(3): 201–5.

[16] Mazzaferri EL, Massoll N. Management of papillary and follicular (differentiated) thyroid cancer: new paradigms using recombinant human thyrotropin. Endocr Relat Cancer. 2002; 9(4): 227-247.

[17] Luo X, Wu ACYZYJBZJ. Analysis of risk factors for postoperative recurrence of thyroid cancer. J BUON. 2019; 24(2): 813–8.

[18] Lo TEN, Canto AU, Maningat PDD. Risk factors for recurrence in Filipinos with well-differentiated thyroid cancer. Endocrinol Metab (Seoul). 2015; 30(4): 543–50.

[19] Kruijff S, Petersen JF, Chen P, Aniss AM, Clifton-Bligh RJ, Sidhu SB, et al. Patterns of structural recurrence in papillary thyroid cancer. World J Surg. 2014; 38(3): 653–9.

[20] Yi JW, Kim SJ, Kim JK. Upregulation of the ESR1 Gene and ESR Ratio (ESR1/ESR2) is Associated with a Worse Prognosis in Papillary Thyroid Carcinoma: The Impact of the Estrogen Receptor alpha/beta Expression on Clinical Outcomes in Papillary Thyroid Carcinoma Patients. Ann Surg Oncol. 2017; 24: 3754–62.

[21] Cho SY, Lee TH, Ku YH, Kim HI, Lee GH, Kim MJ. Central lymph node metastasis in papillary thyroid microcarcinoma can be stratified according to the number, the size of metastatic foci, and the presence of desmoplasia. Surgery. 2015; 157(1): 111–8.

[22] Hay ID, Thompson GB, Grant CS, Bergstralh EJ, Dvorak CE, Gorman CA, Maurer MS, McIver B, Mullan BP, Oberg AL, Powell CC, van Heerden JA, Goellner JR. Papillary thyroid carcinoma managed at the Mayo Clinic during six decades (1940-1999): temporal trends in initial therapy and long-term outcome in 2444 consecutively treated patients. World J Surg. 2002; 26(8): 879-885.

[23] Cady B, Rossi R. An expanded view of risk group definition in differentiated thyroid carcinoma. Surgery. 1988; 104(6): 947-953.

Research Field

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