Original Article

Multifocal cancer is associated with better survival than solitary cancer in non-Hispanic White patients with thyroid carcinoma

Yu Li[1#], Da Huang[2#], Jian Ding[3], Wei Mao[3], Dan Luo[3], Yuan Zhou[3], Baoxin Wang[3], Haiting Liang[4], Zhiqiang Wang[1], Pin Dong[3]

[1]Department of Otolaryngology-Head and Neck Surgery, The Eighth Affiliated Hospital, Sun Yat-sen University, Shenzhen, China; [2]Department of Urology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [3]Department of Otolaryngology-Head and Neck Surgery, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [4]Nursing Department, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Contributions: (I) Conception and design: Y Li, D Huang, Z Wang; (II) Administrative support: P Dong, H Liang, Z Wang; (III) Provision of study materials or patients: D Luo, Y Zhou, B Wang; (IV) Collection and assembly of data: D Huang, J Ding, W Mao; (V) Data analysis and interpretation: Y Li, D Huang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Zhiqiang Wang, MD. Department of Otolaryngology-Head and Neck Surgery, The Eighth Affiliated Hospital, Sun Yat-sen University, 3025 Shennan Zhong Road, Shenzhen 518033, China. Email: wangzqx@163.com; Haiting Liang, BSc. Nursing Department, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, 100 Haining Road, Shanghai 200080, China. Email: 18918282863@163.com; Pin Dong, MD. Department of Otolaryngology-Head and Neck Surgery, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, 100 Haining Road, Shanghai 200080, China. Email: dongpin64@aliyun.com.

Background: Multifocal carcinoma is commonly reported in thyroid cancer. However, its impact on cancer survival is unclear. This study aims to evaluate whether multifocal disease is associated with better thyroid cancer outcomes in different ethnicities.

Methods: Cancer registration data in the US from 2000 to 2016 were obtained via the Surveillance, Epidemiology, and End Results (SEER) 18 Registries database. Patients diagnosed with thyroid carcinoma and without other malignancies were enrolled. Univariable and multivariable Cox regressions were applied to evaluate the association of multifocal disease with cancer-specific survival (CSS) and overall survival (OS). Multivariable analyses were performed after adjusting for age, gender, stage, and treatment.

Results: A total of 82,217, 8,551, 13,445, and 19,558 non-Hispanic White (NHW), non-Hispanic African American (AA), non-Hispanic Asian or Pacific Islander (AP), and Hispanic White (HW) patients were enrolled in this study, respectively. Univariable analysis suggested that multifocal carcinoma would have significant better CSS [hazard ratio (HR) =0.89, 95% confidence interval (CI): 0.77–1.02, P=0.09; adjusted HR =0.67, 95% CI: 0.53–0.85, P<0.001] and OS (HR =0.83, 95% CI: 0.77–0.90, P<0.001; adjusted HR =0.76, 95% CI: 0.65–0.87, P<0.001) than solitary disease in NHW.

Conclusions: Multifocal thyroid carcinoma is associated with better CSS and OS than solitary cancer in NHW patients.

Keywords: Multifocal; solitary; thyroid cancer; Caucasian; Surveillance, Epidemiology, and End Results (SEER)

Submitted Dec 02, 2024. Accepted for publication Mar 04, 2025. Published online Mar 26, 2025.
doi: 10.21037/gs-2024-523
View this article at: https://dx.doi.org/10.21037/gs-2024-523

Introduction

Thyroid cancer is one of the most common malignancies in both male and female worldwide, with an estimated 586,202 new cases and 43,646 deaths every year (1). In the United States, the incidence ranks in the seventh place among women population (2). Although the incidence in

female is approximately three times higher than in male, the mortality is similar in both genders (2).

The most common type of thyroid cancer is adenocarcinoma, and its incidence has been increasing rapidly for the past decades (3,4). It is relatively indolent compared with other types of thyroid cancer; however, up to 90% of the cases may have regional lymph node invasion, and ~3% of the patients may have distant metastasis, which are lethal phenotypes indicating a poorer prognosis (3,5,6). One of the risk factors for regional lymph node invasion is multifocal diseases, which have been reported to be commonly found in post-operational specimens (3,7,8). However, direct evidence between multifocal thyroid carcinoma and cancer survival is rarely reported. The impact of multifocality on cancer-specific survival (CSS) and overall survival (OS) remains unclear. Furthermore, there is limited evidence on whether this relationship varies across ethnic groups, which has motivated us to explore this question.

Therefore, we conducted the present study using the nationwide cancer registration data via the Surveillance, Epidemiology, and End Results (SEER) database. Our objective is to evaluate whether multifocal disease is associated with cancer outcomes in different ethnicities. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-2024-523/rc).

Highlight box

Key findings

- First, multifocal disease was significantly associated with better cancer-specific survival (CSS) and overall survival (OS) in non-Hispanic White patients with thyroid carcinoma, but not in other ethnicities.
- Second, multifocal disease was an independent protective factor of thyroid carcinoma regardless of tumor stage and treatment.

What is known and what is new?

- Ninety percent of the thyroid cancer cases may have regional lymph node invasion where multifocal disease is the most common risk factor. However, direct evidence between multifocal thyroid carcinoma and cancer survival was rarely reported.
- This study is to demonstrate an ethnicity-specificity regarding multifocal disease in relation to better CSS and OS in patients with thyroid carcinoma.

What is the implication, and what should change now?

- The findings of this study would inform a personalized management for ethnicity-specific patients with thyroid multifocal cancer in clinical practice.

Methods

Study population

The study population was obtained from the SEER 18 Registries Custom database between 2000 and 2016, which covered nearly 30% of the total population of the United States (9). The inclusion criteria were: (I) cases with pathological confirmation [International Classification of Disease for Oncology, Third Edition (ICD-O-3) code 8140–8389]; (II) behavior code of ICD-O-3 is marked as "malignant" to exclude the benign adenoma; and (III) cases under active follow-up. We excluded the cases with multiple primary cancers. Finally, we identified 123,771 individuals diagnosed with primary "thyroid adenocarcinoma" (the thyroid cancer was the first malignant and only primary tumor that the patients had). Here, "thyroid adenocarcinoma" in the SEER database indicates differentiated thyroid carcinoma including papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC). The study was approved by the Institutional Review Board of Shanghai General Hospital, Shanghai, China. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Outcomes assessment

The primary outcome in the present study was time to cancer-specific death. The secondary outcome was time to all causes of death. CSS was defined as time to death, and the primary cause of death was thyroid papillary adenocarcinoma. OS was defined as time to any cause of death.

Statistical analysis

Mean and standard deviation (SD) were used to describe normally distributed variables. Number of count and percentage were used to describe categorical variables. Univariable and multivariable Cox regressions were performed to evaluate the association between variables and outcomes with time effect. A two-tailed $P<0.05$ is considered as statistically significant. All statistics were performed using R software (ver 4.1.3) (10).

Results

A total of 82,217, 8,551, 13,445, and 19,558 non-Hispanic White (NHW), non-Hispanic African American

Table 1 Characteristics of study population with diagnosis of thyroid adenocarcinoma as the only primary cancer based on the SEER 18 Registries database between 2000 and 2016

Characteristics	NHW	Non-Hispanic AA	Non-Hispanic AP	HW
Number of patients	82,217	8,551	13,445	19,558
Age at diagnosis (years)	48.86±15.22	49.27±14.37	47.73±15.00	44.54±15.06
Gender				
Male	19,934 (24.25)	1,420 (16.61)	2,745 (20.42)	3,412 (17.45)
Female	62,283 (75.75)	7,131 (83.39)	10,700 (79.58)	16,146 (82.55)
Stage				
I	31,819 (38.70)	3,497 (40.90)	5,234 (38.93)	8,318 (42.53)
II	3,388 (4.12)	429 (5.02)	423 (3.15)	615 (3.14)
III	5,493 (6.68)	548 (6.41)	1,148 (8.54)	1,465 (7.49)
IV	2,503 (3.04)	221 (2.58)	633 (4.71)	873 (4.46)
Unknown	39,014 (47.45)	3,856 (45.09)	6,007 (44.68)	8,287 (42.37)
Solitary or multifocal				
Solitary	41,711 (50.73)	5,013 (58.62)	6,685 (49.72)	9,869 (50.46)
Multifocal	27,939 (33.98)	2,187 (25.58)	4,907 (36.50)	7,159 (36.60)
Ectopic or unknown	12,567 (15.29)	1,351 (15.80)	1,853 (13.78)	2,530 (12.94)
Treatment				
No treatment	2,010 (2.44)	291 (3.40)	500 (3.72)	620 (3.17)
Surgical treatment	41,356 (50.30)	4,745 (55.49)	5,990 (44.55)	8,985 (45.94)
Both surgical and radiational treatment	38,851 (47.25)	3,515 (41.11)	6,955 (51.73)	9,953 (50.89)
Outcomes				
All death	4,514 (5.49)	641 (7.50)	616 (4.58)	870 (4.45)
Disease-specific death	1,556 (1.89)	168 (1.96)	307 (2.28)	389 (1.99)
Alive	77,703 (94.51)	7,910 (92.50)	12,829 (95.42)	18,688 (95.55)

Data are presented as number, mean ± SD, or number (%). AA, African American; AP, Asian or Pacific Islander; HW, Hispanic White; NHW, non-Hispanic White; SD, standard deviation; SEER, Surveillance, Epidemiology, and End Results.

(AA), Non-Hispanic Asian or Pacific Islander (AP), and Hispanic White (HW) patients were enrolled in this study, respectively. Characteristics of the study population are described in *Table 1*. The highest male-to-female ratio was observed in NHW with 24.25% of male and 75.75% of female patients (~1:3), while the lowest male-to-female ratio was found in AA with 16.61% of male and 83.39% (~1:5) of female patients (*Table 1*). About 45–55% of patients received only surgical treatment, 41–52% of patients received both surgical and radiation treatment, while about 2–3% of patients did not receive any treatment.

By the end of the latest follow-up, 1,556 (1.89%), 168 (1.96%), 307 (2.28%), and 389 (1.99%) patients died from thyroid carcinoma in NHW, AA, AP, and HW, respectively. In terms of all causes of death, 4,514 (5.49%), 641 (7.50%), 616 (4.58%), and 870 (4.45%) records were observed respectively (*Table 1*). In univariable analysis, an 11% reduction of cancer-specific death was observed in NHW who had multifocal cancer compared with those who had solitary cancer [hazard ratio (HR) =0.89, 95% confidence interval (CI): 0.77–1.02, P=0.09, *Table 2*]. Combined analysis with all the ethnicities suggested an 18% reduction of cancer-specific death among who had multifocal cancer compared with those who had solitary cancer (HR =0.72,

Table 2 Univariable analysis for the association between multifocal cancer and outcomes among different races

Race	CSS				OS			
	Solitary	Multifocal	HR (95% CI)	P value	Solitary	Multifocal	HR (95% CI)	P value
NHW (n=82,217)	550/41,617 (1.32)	326/27,921 (1.17)	0.89 (0.77–1.02)	0.09	1,698/41,617 (4.08)	939/27,921 (3.36)	0.83 (0.77–0.90)	<0.001
Non-Hispanic AA (n=8,551)	54/4,978 (1.08)	26/2,185 (1.19)	1.08 (0.68–1.73)	0.74	238/4,978 (4.78)	109/2,185 (4.99)	1.03 (0.82–1.29)	0.80
Non-Hispanic AP (n=13,445)	113/6,672 (1.69)	71/4,903 (1.45)	0.88 (0.66–1.19)	0.41	214/6,672 (3.21)	146/4,903 (2.98)	0.96 (0.78–1.19)	0.72
HW (n=19,558)	139/9,842 (1.41)	92/7,158 (1.29)	0.93 (0.72–1.21)	0.60	313/9,842 (3.18)	206/7,158 (2.88)	0.93 (0.78–1.11)	0.43
Combined analysis	–	–	0.72 (0.66–0.78)	<0.001	–	–	0.79 (0.76–0.83)	<0.001

Data are presented as event/total number (%), unless otherwise stated. AA, African American; AP, Asian or Pacific Islander; CI, confidence interval; CSS, cancer-specific survival; HR, hazard ratio; HW, Hispanic White; NHW, non-Hispanic White; OS, overall survival.

95% CI: 0.66–0.78, P<0.001, *Table 2*). Such reduction of cancer-specific death became more significant in multivariable analysis after adjusting for age, gender, stage, and treatment (in NHW: HR =0.63, 95% CI: 0.50–0.79, P<0.001, *Table 3*; in all ethnicities: HR =0.64, 95% CI: 0.56–0.73, P<0.001).

A significant better OS was also observed in NHW who had multifocal cancer compared with those who had solitary cancer (HR =0.83, 95% CI: 0.77–0.90, P<0.001, *Table 2*). The results were stronger in the combined analysis with all the ethnicities cancer (HR =0.79, 95% CI: 0.76–0.83, P<0.001, *Table 2*). This remains significant after multivariable adjustment (in NHW: HR =0.73, 95% CI: 0.63–0.84, P<0.001, *Table 4*; in all ethnicities: HR =0.81, 95% CI: 0.75–0.87, P<0.001). Similar trends of reduction (although not statistically significant) of cancer-specific death or all-cause death were also found in AP or HW who had multifocal disease compared with those who had solitary disease (*Tables 2-4*). Such a trend was not found in AA.

In addition to tumor foci, multivariable analyses also showed several risk factors for CSS and OS. Tumor stage was a strong predictor for CS and OS as expected in different ethnicities (all P values below 0.05, *Tables 3*,*4*). Surgical treatment only, as well as the combination treatment of surgical and radiational treatment were both effective treatment methods to promote CSS and OS; however, the combination treatment would provide a slightly better survival (*Tables 3*,*4*).

Discussion

Unlike other well-investigated risk factors for thyroid carcinoma such as lymph node invasion, tumor size, unilateral or bilateral disease, etc., the association between multifocal diseases and cancer outcomes was poorly studied. Possible reasons include the relatively low report rate in the pathological reports in terms of multifocal or solitary disease compared with other risk factors, as well as duplication information among tumor size, tumor burden, and multifocal diseases. The present study provided direct evidence on this topic. Firstly, multifocal disease was significantly associated with better CSS and OS in NHW patients with thyroid carcinoma, but not in other ethnicities. Secondly, multifocal disease was an independent protective factor of thyroid carcinoma regardless of tumor stage, and treatment. These interesting results are straight forward and critical for clinical practice. Consistent trends are observed in other ethnicities, although the results did not reach statistical significance.

The association between multifocal thyroid carcinoma and disease outcomes are long controversial. A retrospective study with more than 600 patients from Greece suggested that multifocal disease was associated with lymph node spreading and T3/T4 cancers (11). Another study based on a Chinese population with similar sample size indicated similar results, which suggested a significant association with disease recurrence (12). A systematic review reported

Table 3 Multivariable analysis for the association between multifocal cancer and cancer-specific death among different races

Characteristics	NHW		Non-Hispanic AA		Non-Hispanic AP		HW	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age at diagnosis	1.05 (1.04–1.06)	<0.001	1.02 (0.99–1.05)	0.29	1.06 (1.04–1.09)	<0.001	1.05 (1.04–1.07)	<0.001
Gender								
Male	Ref.		Ref.		Ref.		Ref.	
Female	0.93 (0.74–1.16)	0.50	0.86 (0.36–2.06)	0.73	0.70 (0.41–1.20)	0.19	0.70 (0.47–1.05)	0.088
Stage								
I	Ref.		Ref.		Ref.		Ref.	
II	2.71 (1.28–5.79)	0.009	2.58 (0.26–25.23)	0.42	8.91 (1.95–40.73)	0.005	1.32 (0.28–6.08)	0.72
III	6.18 (3.53–10.82)	<0.001	9.98 (2.23–44.59)	0.003	8.90 (2.37–33.36)	0.001	2.18 (0.81–5.88)	0.13
IV	100.12 (62.34–160.82)	<0.001	104.78 (27.11–404.91)	<0.001	46.47 (13.40–161.19)	<0.001	35.39 (17.13–73.13)	<0.001
Treatment								
No treatment	Ref.		Ref.		Ref.			
Surgical treatment	0.18 (0.12–0.25)	<0.001	0.19 (0.06–0.58)	0.003	0.20 (0.09–0.43)	<0.001	0.19 (0.10–0.35)	<0.001
Both surgical and radiational treatment	0.13 (0.09–0.17)	<0.001	0.10 (0.04–0.30)	<0.001	0.13 (0.06–0.28)	<0.001	0.14 (0.08–0.24)	<0.001
Solitary or multifocal								
Solitary	Ref.		Ref.		Ref.		Ref.	
Multifocal	0.63 (0.50–0.79)	<0.001	0.86 (0.39–1.89)	0.70	0.83 (0.48–1.43)	0.50	0.75 (0.49–1.13)	0.20

AA, African American; AP, Asian or Pacific Islander; CI, confidence interval; HR, hazard ratio; HW, Hispanic White; NHW, non-Hispanic White; ref., reference.

that multifocality was associated with increased recurrence risks in patients with thyroid carcinoma, whereas no significant difference was shown in CSS. However, several recently well-designed prospective studies demonstrated non-significant difference of cancer outcomes between multifocal and solitary diseases (13,14). Aside from the contradictory results from different studies, limitations in these studies were obvious. For example, the number of observed outcomes were small, which made the statistical power questionable. On the other hand, the effects of different treatment methods were unable to evaluate. For instance, surgeons tend to dissect more lymph nodes in patients with multifocal cancer than solitary cancers. In our study, with the largest sample size so far, could provide stronger evidence that patients with multifocality would have better survival than those with unifocality. Such associations remained significant after adjusting for treatment methods.

Biological mechanism underneath the results from the present study is unclear. In an early study, researchers believed that multifocal diseases were associated with heredity thyroid cancer and heredity syndromes such as multiple endocrine neoplasm (MEN) diseases (15). Multiple mutations in *BRAF*, *RAS*, *RET/PTC* were found in multifocal thyroid carcinoma (16,17). However, another study using whole-exome sequencing in 8 multifocal cancers did not report any significant findings (18). In addition to genetic factors, a recent study indicated that chronic lymphocytic thyroiditis (CLT) was highly coexistent with multifocal thyroid carcinoma (19). While the concurrent CLT was repeatedly shown related to lower recurrence and better prognosis (20-23). The protective effect of multifocality on survival is likely attributable to the protective effect of CLT against tumors spread via immunological and genetic mechanisms, such as the FAS/FAS ligand pathway, interleukin-1, interleukin-8, chemokine

Table 4 Multivariable analysis for the association between multifocal cancer and all cause death among different races

Characteristics	NHW		Non-Hispanic AA		Non-Hispanic AP		HW	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age at diagnosis	1.07 (1.06–1.07)	<0.001	1.06 (1.04–1.07)	<0.001	1.07 (1.06–1.09)	<0.001	1.06 (1.05–1.07)	<0.001
Gender								
Male	Ref.		Ref.		Ref.		Ref.	
Female	0.66 (0.58–0.76)	<0.001	0.69 (0.45–1.05)	0.09	0.60 (0.41–0.89)	0.01	0.66 (0.49–0.90)	0.008
Stage								
I	Ref.		Ref.		Ref.		Ref.	
II	1.26 (0.97–1.63)	0.08	0.78 (0.35–1.72)	0.54	2.94 (1.37–6.31)	0.006	0.81 (0.39–1.72)	0.59
III	1.59 (1.28–1.97)	<0.001	1.90 (1.15–3.12)	0.01	2.77 (1.52–5.06)	0.001	1.35 (0.84–2.16)	0.21
IV	7.87 (6.52–9.49)	<0.001	4.50 (2.58–7.84)	<0.001	7.69 (4.37–13.52)	<0.001	6.76 (4.63–9.87)	<0.001
Treatment								
No treatment	Ref.		Ref.		Ref.			
Surgical treatment	0.22 (0.17–0.28)	<0.001	0.17 (0.09–0.33)	<0.001	0.27 (0.15–0.48)	<0.001	0.20 (0.13–0.31)	<0.001
Both surgical and radiational treatment	0.14 (0.11–0.18)	<0.001	0.09 (0.05–0.18)	<0.001	0.14 (0.08–0.26)	<0.001	0.12 (0.08–0.18)	<0.001
Solitary or multifocal								
Solitary	Ref.		Ref.		Ref.		Ref.	
Multifocal	0.73 (0.63–0.84)	<0.001	1.08 (0.73–1.59)	0.71	0.87 (0.59–1.29)	0.49	0.85 (0.64–1.15)	0.29

AA, African American; AP, Asian or Pacific Islander; CI, confidence interval; HR, hazard ratio; HW, Hispanic White; NHW, non-Hispanic White; ref., reference.

ligand 20, and recruitment of lymphocyte subtypes (24,25). Therefore, further research using bioinformatic and experimental approaches is warranted to interpret the causal relationship between multifocality and cancer outcomes.

Several limitations should be noted. First, we were only able to observe a significant association between multifocal disease and cancer survival in NHW patients. Similar trends were observed in other ethnicities; however, the results did not reach statistical significance. The relatively small sample size and the limited number of observed outcomes in these ethnicities could not provide enough statistical power in the present analysis. These trends need to be further tested in the future. Second, the missing rates of some clinical information were high, such as tumor stage. Although imputation is an optional way to provide simulation results for the missing data, it is not necessary for the current research. For example, treatment information was completed, and it was highly correlated with the tumor stages (patients with higher tumor stage would be more likely to receive combination treatment). A retrospective study is currently being conducted by our team to further investigate this topic. Finally, given the nature of the SEER database, we were unable to incorporate other important factors such as lymphovascular invasion, macroscopic extracapsular extension, and lymph node positivity in the analysis. These should be comprehensively evaluated in our future study.

Conclusions

Multifocal thyroid carcinoma is associated with better CSS and OS than solitary cancer in NHW races. The findings of this study may inform personalized management for ethnicity-specific patients with thyroid multifocal cancer in clinical practice.

Acknowledgments

We thanked the SEER program for approving our protocol and providing the custom datasets.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-2024-523/rc

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-2024-523/prf

Funding: This work was supported by grants from the National Natural Science Foundation of China (No. 81800893) and the Shanghai Sailing Program (No. 22YF1440500).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-2024-523/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
2. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. CA Cancer J Clin 2022;72:7-33.
3. Pellegriti G, Frasca F, Regalbuto C, et al. Worldwide increasing incidence of thyroid cancer: update on epidemiology and risk factors. J Cancer Epidemiol 2013;2013:965212.
4. Miranda-Filho A, Lortet-Tieulent J, Bray F, et al. Thyroid cancer incidence trends by histology in 25 countries: a population-based study. Lancet Diabetes Endocrinol 2021;9:225-34.
5. Heng Y, Yang Z, Lin J, et al. Risks of central lymph node metastasis in papillary thyroid carcinoma with or without multifocality in at least one lobe: A multi-center analysis. Oral Oncol 2022;134:106185.
6. Maciel J, Cavaco D, Silvestre C, et al. Clinical outcomes of a cohort of 271 patients with lung metastases from differentiated thyroid carcinoma. Clin Endocrinol (Oxf) 2022;97:814-21.
7. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2016;26:1-133.
8. Min Y, Xiang K, Feng Y, et al. Development and validation of a population-based model for predicting the regional lymph node metastasis in adolescent differentiated thyroid carcinoma. Oral Oncol 2021;121:105507.
9. Cronin KA, Ries LA, Edwards BK. The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute. Cancer 2014;120 Suppl 23:3755-7.
10. R Core Team. R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2020. Available online: https://www.R-project.org/
11. Kiriakopoulos A, Petralias A, Linos D. Multifocal Versus Solitary Papillary Thyroid Carcinoma. World J Surg 2016;40:2139-43.
12. Feng JW, Qu Z, Qin AC, et al. Significance of multifocality in papillary thyroid carcinoma. Eur J Surg Oncol 2020;46:1820-8.
13. Harries V, Wang LY, McGill M, et al. Should multifocality be an indication for completion thyroidectomy in papillary thyroid carcinoma? Surgery 2020;167:10-7.
14. Nagaoka R, Ebina A, Toda K, et al. Multifocality and Progression of Papillary Thyroid Microcarcinoma During Active Surveillance. World J Surg 2021;45:2769-76.
15. Dralle H, Machens A, Lorenz K. Hereditary thyroid cancer. Chirurg 2008;79:1017-28.
16. Bansal M, Gandhi M, Ferris RL, et al. Molecular and histopathologic characteristics of multifocal papillary thyroid carcinoma. Am J Surg Pathol 2013;37:1586-91.
17. Lin X, Finkelstein SD, Zhu B, et al. Molecular analysis of multifocal papillary thyroid carcinoma. J Mol Endocrinol

2008;41:195-203.
18. Lu Z, Sheng J, Zhang Y, et al. Clonality analysis of multifocal papillary thyroid carcinoma by using genetic profiles. J Pathol 2016;239:72-83.
19. Aydemirli MD, Morreau H. Multi-UniFocality (MUF), in contrast to multifocality, in thyroid lesions: Relation to lymphocytic thyroiditis. Pathol Int 2024;74:274-84.
20. Battistella E, Pomba L, Costantini A, et al. Hashimoto's Thyroiditis and Papillary Cancer Thyroid Coexistence Exerts a Protective Effect: a Single Centre Experience. Indian J Surg Oncol 2022;13:164-8.
21. Lee I, Kim HK, Soh EY, et al. The Association Between Chronic Lymphocytic Thyroiditis and the Progress of Papillary Thyroid Cancer. World J Surg 2020;44:1506-13.
22. Liang J, Zeng W, Fang F, et al. Clinical analysis of Hashimoto thyroiditis coexistent with papillary thyroid cancer in 1392 patients. Acta Otorhinolaryngol Ital 2017;37:393-400.
23. Marotta V, Sciammarella C, Chiofalo MG, et al. Hashimoto's thyroiditis predicts outcome in intrathyroidal papillary thyroid cancer. Endocr Relat Cancer 2017;24:485-93.
24. Ehlers M, Schott M. Hashimoto's thyroiditis and papillary thyroid cancer: are they immunologically linked? Trends Endocrinol Metab 2014;25:656-64.
25. Babli S, Payne RJ, Mitmaker E, et al. Effects of Chronic Lymphocytic Thyroiditis on the Clinicopathological Features of Papillary Thyroid Cancer. Eur Thyroid J 2018;7:95-101.

Cite this article as: Li Y, Huang D, Ding J, Mao W, Luo D, Zhou Y, Wang B, Liang H, Wang Z, Dong P. Multifocal cancer is associated with better survival than solitary cancer in non-Hispanic White patients with thyroid carcinoma. Gland Surg 2025;14(3):327-334. doi: 10.21037/gs-2024-523