Scientific Reports

https://doi.org/10.1038/s41598-026-40070-z

Article in Press

Comparison of cancer-specific survival between total thyroidectomy and lobectomy in tall cell variant of papillary thyroid carcinoma

Received: 3 December 2025

Accepted: 10 February 2026

Published online: 09 March 2026

Cite this article as: Sun Y., Jia Y. & Zhang H. Comparison of cancer-specific survival between total thyroidectomy and lobectomy in tall cell variant of papillary thyroid carcinoma. *Sci Rep* (2026). https://doi.org/10.1038/s41598-026-40070-z

Yubo Sun, Yuxin Jia & Hao Zhang

Comparison of Cancer-Specific Survival Between Total Thyroidectomy and Lobectomy in Tall Cell Variant of Papillary Thyroid Carcinoma

Running title: Total vs Lobectomy for TCV-PTC.

Authors: Yubo Sun[1*]; Yuxin Jia[2*]; Hao Zhang[1#]

1. Department of Thyroid Surgery, The First Hospital of China Medical University, Shenyang 110001, China

2. Department of Ultrasound, Shengjing Hospital of China Medical University, Shenyang 110004, China

***Equal contribution**

#Corresponding author: Hao Zhang, E-mail haozhang@cmu.edu.cn

ABSTRACT

Background: The tall cell variant of papillary thyroid carcinoma (TCV-PTC) is an aggressive subtype with a poorer prognosis. Controversy persists regarding the surgical strategy for TCV-PTC.

Methods: Using the SEER database (2005-2017), we analyzed 1,463 patients with pathologically confirmed TCV-PTC who underwent either total thyroidectomy (TT) (n=1,369) or lobectomy (n=94). Propensity score matching (PSM) was used to address confounding biases. The primary endpoint was cancer-specific survival (CSS), assessed using Kaplan-Meier analysis and Cox regression.

Results: After PSM (n=376), TT demonstrated superior CSS compared to lobectomy (p=0.019). The 5-year and 10-year CSS for TT were 97.8% and 95.0% versus 90.7% and 89.1% for lobectomy in the matched cohort. This survival benefit of TT persisted regardless of radioiodine therapy (RAI) (p<0.05). Multivariable analysis identified lobectomy, tumor size >40 mm, extrathyroidal extension, and lymph node metastasis as independent risk factors for reduced CSS.

Conclusion: Total thyroidectomy is associated with improved CSS compared to lobectomy in TCV-PTC, independent of RAI. Greater caution should be considered in selecting lobectomy for TCV patients, especially for patients

with tumors >40 mm, lymph node metastasis, or extrathyroidal extension. Completion thyroidectomy may be beneficial for patients diagnosed with TCV-PTC after lobectomy.

Keywords: Papillary thyroid carcinoma; tall cell variant; surgery; SEER database; cancer-specific survival.

Introduction

Papillary thyroid carcinoma (PTC) is the most common malignant tumor in the endocrine system, with its global incidence continuing to rise(1, 2). Most patients with PTC exhibit a long-term prognosis, the tall cell variant (TCV). It is classified as a highly aggressive subtype in the 2022 WHO classification. It also demonstrates stronger invasiveness and poorer outcomes(3). TCV-PTC is a subtype of PTC characterized by tall cells (with a height at least twice their width) comprising at least 30% of the tumor tissue(3, 4). First described in 1976, it is characterized by a high frequency of BRAF V600E mutations and resistance to radioiodine therapy (RAI), factors that may contribute to treatment resistance and increased risk of disease recurrence(5, 6).

Controversy persists regarding optimal surgical strategies for TCV. According to the 2015 American Thyroid Association (ATA) guidelines, aggressive PTC subtypes, including TCV, are categorized as intermediate risk for recurrence(7). The new 2025 ATA guidelines further classify TCV as intermediate to high risk which may be considered for RAI(8). However, regarding the initial surgical approach for TCV, the guidelines do not provide specific recommendations.

Recent studies revealed that RAI does not improve the prognosis of TCV(9). Total thyroidectomy (TT) also carries risks of complications such as hypoparathyroidism and recurrent laryngeal nerve injury(10, 11). A recent study suggested that lobectomy may be an appropriate treatment option for patients with T1-T2, node-negative TCV-PTC(12). Therefore, completion TT solely based on RAI considerations may lack sufficient evidence, and there

remains an ongoing controversy regarding whether patients with TCV following initial lobectomy should undergo completion TT. In this study, we analyzed survival outcomes of TT versus lobectomy in TCV using the Surveillance, Epidemiology, and End Results (SEER) database, aiming to provide evidence-based insights for surgical decision-making.

Results

Clinicopathological Characteristics

A total of 1,577 patients with TCV-PTC were initially identified from the SEER database. After excluding 114 patients who did not meet the inclusion criteria, 1,463 patients were included in the final analysis. Specifically, 1,369 (93.6%) patients underwent TT and 94 (6.4%) received lobectomy (Figure 1). Compared to the lobectomy group, patients in the TT group exhibited a higher proportion of age ≥ 55 years (62.1% versus 48.9%, $p = 0.011$), larger tumor size (> 40 mm: 24.3% versus 12.8%, $p < 0.001$), and increased rates of lymph node metastasis (42.1% versus 28.7%, $p = 0.007$). RAI therapy was administered to 69.3% of patients treated with TT. Detailed baseline characteristics before and after PSM are summarized in Table 1.

Impact of Surgical Extent on Cancer-Specific Survival

With a median follow-up of 83 months (range: 1–203 months; IQR: 54–125 months), the overall 5- and 10-year cancer-specific survival (CSS) rates were 95.1% and 91.9%, respectively. Before PSM, no significant survival difference was observed between the TT and lobectomy groups ($p = 0.230$; Figure 2). After PSM (1:3 matched cohort, n = 376), TT demonstrated superior CSS outcomes ($p = 0.019$; Figure 2).

Effect of RAI Therapy on Survival

To evaluate the independent role of surgical extent, patients with TT were stratified by RAI administration. In the RAI-treated subgroup, the TT group achieved better CSS compared to the lobectomy group ($p = 0.043$; Figure 3). Without RAI, TT still demonstrated a similar survival advantage ($p = 0.040$; Figure 3). These findings suggest that the survival benefit

associated with TT persists regardless of adjuvant RAI administration.

Prognostic Factors for CSS

Multivariable Cox regression identified tumor size > 40 mm (hazard ratio [HR] = 53.164, 95% confidence interval [CI]: 5.704–495.493), extrathyroidal extension (HR = 4.072, 95% CI: 1.150–14.412), lymph node metastasis (HR = 4.834, 95% CI: 1.278–18.160), and lobectomy (HR = 2.437, 95% CI: 1.138–7.547) as independent risk factors for reduced CSS in the PSM cohort (all $p < 0.05$; Table 2). Similar trends were observed in the pre-PSM analysis.

Discussion

TCV-PTC, a histological subtype with inherently aggressive biological behavior, exhibits poorer disease-specific survival than the classical subtype(3, 13). Our analysis of a large population-based cohort from the SEER database revealed that TT was associated with improved CSS compared to lobectomy after PSM. The survival advantage of TT persisted across both 5-year (97.8% versus 90.7%) and 10-year (95.0% versus 89.1%) intervals in the matched cohort, suggesting a strong protective effect. These findings hold significant implications for surgical strategies in TCV management.

Regarding RAI therapy, the 2015 ATA guidelines suggest that RAI may improve the prognosis of TCV-PTC; hence, recommending total thyroidectomy followed by RAI(7). However, recent research has presented opposing results. For instance, Dai et al. reported that RAI did not improve outcomes in patients with TCV after total thyroidectomy(9). Our study revealed that the survival benefit persisted even after stratifying by RAI administration (Figure 3). This finding suggests that the extent of surgery independently contributes to oncologic outcomes beyond its role in enabling adjuvant therapy.

Identifying which patients with TCV will benefit most from TT remains a critical clinical question. Our multivariate analysis in the PSM cohort identified lobectomy as an independent risk factor for CSS, alongside

established predictors like lymph node metastasis, extrathyroidal extension, and tumor size > 40 mm. Wu et al. reached similar conclusions, such as identifying positive surgical margins, node-positive disease (regional lymph node metastasis), and a tumor size of ≥ 3 cm as risk factors for recurrence(14). Additionally, BRAF and TERT mutations are associated with poor prognosis(15, 16). For patients harboring these risk factors, TT may be the preferred treatment option.

Several pathophysiological mechanisms could explain TT's superiority. First, TCV is an aggressive subtype with biological behavior distinct from classic PTC, and a more extensive surgical approach is safer. Studies have revealed that patients with TCV are more prone to extrathyroidal extension (ETE)(17, 18). In our study, the rate of extrathyroidal extension was 36.7%, which was significantly higher than that in classic PTC. Moreover, even after adjusting for ETE and other prognostic factors, only the TCV remained an independent predictor of prognosis(19). Second, TT enables the removal of occult contralateral carcinoma in the contralateral lobe. Studies have demonstrated that the incidence of occult contralateral carcinoma in patients with PTC reaches 16.7%–44.6%(20-22). As a more aggressive subtype, TCV-PTC may carry a higher risk of occult contralateral carcinoma. Third, TT facilitates serial thyroglobulin monitoring without interference from residual thyroid tissue. This enables accurate tracking of serum Tg and TgAb levels, allowing for early detection and management of potential recurrence or metastasis, thereby improving long-term patient outcomes.

These results partially contrast with recent trends advocating de-escalation in low-risk PTC. The new 2025 ATA guidelines classify TCV as an intermediate to high risk for recurrence, our findings also suggest that its biological behavior may warrant a more aggressive initial surgical approach than conventional PTC(8). This supports emerging consensus in the 2022 WHO classification that TCV requires distinct management paradigms(3). Therefore, in clinical practice, it has been observed that the selection of

lobectomy for TCV-PTC should be approached with greater caution, even though total thyroidectomy may lead to an increase in postoperative complications.

Several limitations remain in this study. First, the retrospective design inherently introduces selection biases, although PSM mitigates measurable confounders. Second, critical clinicopathological variables such as BRAF V600E mutation status, surgical margin status, and completion thyroidectomy were unavailable in the SEER database, potentially influencing outcome interpretation. Third, the relatively small sample size of the lobectomy (n = 94), despite a 13-year inclusion period, limited the subgroup analyses. Furthermore, recurrence data and quality-of-life outcomes were unavailable, preventing cost-benefit assessments of complication risks versus survival benefits.

In conclusion, for patients with TCV-PTC, total thyroidectomy demonstrated superior cancer-specific survival compared to lobectomy. These findings strengthen the evidence supporting greater caution in selecting lobectomy for TCV patients, particularly those with tumors > 40 mm, lymph node involvement, or extrathyroidal extension. Patients diagnosed with TCV subtype after lobectomy may benefit from the option of completing TT.

Methods

Study Population

The data were obtained from the SEER database, maintained by the National Cancer Institute. This database provides comprehensive clinical and pathological information on cancer patients, offering robust support for our analysis. The study cohort comprised patients diagnosed with TCV-PTC (ICD-O-3 code: 8344/3) between 2005 and 2017.

The inclusion criteria were as follows: Pathologically confirmed TCV-PTC; and surgical treatment with either lobectomy (SEER surgery code: 30) or TT (SEER surgery code: 40). The exclusion criteria were as follows: Age < 18 or >

80 years; follow-up duration < 1 month; or incomplete clinicopathological records.

Demographic and clinicopathological variables were extracted, including age (categorized as ≥ 55 or < 55 years), sex, race, tumor size (stratified into ≤ 20 mm, > 20–40 mm, > 40 mm), extrathyroidal extension, multifocality, lymph node metastasis, distant metastasis, surgical method, and RAI therapy. The primary endpoint was cancer-specific survival (CSS), defined as the time from diagnosis to death attributable to thyroid cancer.

Statistical Analysis

All analyses were performed using the Statistical Product and Service Solutions (SPSS; version 27.0; URL: https://www.ibm.com/products/spss-statistics) and the R Project for Statistical Computing (version 4.4.1; URL: https://www.r-project.org). To address potential confounding biases, propensity score matching (PSM) was implemented through a 1:n nearest neighbor algorithm with a caliper width of 0.3. Covariates included age, sex, tumor size, extrathyroidal extension, and nodal status. Descriptive statistics are reported as frequencies (%) for categorical variables and compared using chi-square or Fisher's exact test before and after PSM. Survival curves were generated using the Kaplan–Meier method, and differences between groups were assessed using log-rank tests. Multivariable Cox proportional hazards models identified independent prognostic factors. A two-sided $p < 0.05$ was considered statistically significant.

References

1. Pizzato M, Li M, Vignat J, Laversanne M, Singh D, La Vecchia C, et al. The epidemiological landscape of thyroid cancer worldwide: GLOBOCAN estimates for incidence and mortality rates in 2020. Lancet Diabetes Endocrinol. 2022;10(4):264-72.

2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, 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(3):209-49.

3. Baloch ZW, Asa SL, Barletta JA, Ghossein RA, Juhlin CC, Jung CK, et al. Overview of the 2022 WHO Classification of Thyroid Neoplasms. Endocr Pathol. 2022;33(1):27-63.
4. Turchini J, Fuchs TL, Chou A, Sioson L, Clarkson A, Sheen A, et al. A Critical Assessment of Diagnostic Criteria for the Tall Cell Subtype of Papillary Thyroid Carcinoma-How Much? How Tall? And When Is It Relevant? Endocr Pathol. 2023;34(4):461-70.
5. Dettmer MS, Schmitt A, Steinert H, Capper D, Moch H, Komminoth P, et al. Tall cell papillary thyroid carcinoma: new diagnostic criteria and mutations in BRAF and TERT. Endocr Relat Cancer. 2015;22(3):419-29.
6. Hawk WA, Hazard JB. The many appearances of papillary carcinoma of the thyroid. Cleve Clin Q. 1976;43(4):207-15.
7. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, 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):1-133.
8. Ringel MD, Sosa JA, Baloch Z, Bischoff L, Bloom G, Brent GA, et al. 2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer. Thyroid. 2025;35(8):841-985.
9. Dai P, Zhao W, Zheng X, Luo H, Wang X. Effect of Radioactive Iodine Therapy on Cancer-Specific Survival of Papillary Thyroid Cancer Tall Cell Variant. J Clin Endocrinol Metab. 2024;109(3):e1260-e6.
10. Hsiao V, Light TJ, Adil AA, Tao M, Chiu AS, Hitchcock M, et al. Complication Rates of Total Thyroidectomy vs Hemithyroidectomy for Treatment of Papillary Thyroid Microcarcinoma: A Systematic Review and Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2022;148(6):531-9.
11. Kwon H, Jeon MJ, Kim WG, Park S, Kim M, Song DE, et al. A comparison of lobectomy and total thyroidectomy in patients with papillary thyroid microcarcinoma: a retrospective individual risk factor-matched cohort study. Eur J Endocrinol. 2017;176(4):371-8.
12. Woods RSR, Fitzgerald CWR, Valero C, Lopez J, Morris LGT, Cohen MA, et al. Surgical management of T1/T2 node-negative papillary thyroid cancer with tall cell histology: Is lobectomy enough? Surgery. 2023;173(1):246-51.
13. Axelsson TA, Hrafnkelsson J, Olafsdottir EJ, Jonasson JG. Tall cell variant of papillary thyroid carcinoma: a population-based study in Iceland. Thyroid. 2015;25(2):216-20.
14. Wu SS, Joshi N, Sharrett J, Rao S, Shah A, Scharpf J, et al. Risk Factors Associated With Recurrence and Death in Patients With Tall Cell Papillary Thyroid Cancer: A Single-Institution Cohort Study With Predictive Nomogram. JAMA Otolaryngol Head Neck Surg. 2023;149(1):79-86.
15. Moon S, Song YS, Kim YA, Lim JA, Cho SW, Moon JH, et al. Effects of Coexistent BRAF(V600E) and TERT Promoter Mutations on Poor Clinical Outcomes in Papillary Thyroid Cancer: A Meta-Analysis. Thyroid.

2017;27(5):651-60.
16. Xing M, Liu R, Liu X, Murugan AK, Zhu G, Zeiger MA, et al. BRAF V600E and TERT promoter mutations cooperatively identify the most aggressive papillary thyroid cancer with highest recurrence. J Clin Oncol. 2014;32(25):2718-26.
17. Kim K, Jung CK, Lim DJ, Bae JS, Kim JS. Comparison of the clinicopathological features and oncologic outcomes of the classic papillary thyroid carcinoma with tall cell features and tall cell variant. Gland Surg. 2022;11(1):56-66.
18. Liu Z, Zeng W, Chen T, Guo Y, Zhang C, Liu C, et al. A comparison of the clinicopathological features and prognoses of the classical and the tall cell variant of papillary thyroid cancer: a meta-analysis. Oncotarget. 2017;8(4):6222-32.
19. Morris LG, Shaha AR, Tuttle RM, Sikora AG, Ganly I. Tall-cell variant of papillary thyroid carcinoma: a matched-pair analysis of survival. Thyroid. 2010;20(2):153-8.
20. Chen ML, Xu D, Yan XQ, Xie BJ. Delphian lymph node metastasis predicts occult contralateral carcinoma for unilateral papillary thyroid carcinoma patients with contralateral benign nodules. Asian J Surg. 2023;46(1):156-9.
21. Chen X, Zhong Z, Song M, Yuan J, Huang Z, Du J, et al. Predictive factors of contralateral occult carcinoma in patients with papillary thyroid carcinoma: a retrospective study. Gland Surg. 2020;9(4):872-8.
22. Zhang F, Zheng B, Yu X, Wang X, Wang S, Teng W. Risk Factors for Contralateral Occult Carcinoma in Patients With Unilateral Papillary Thyroid Carcinoma: A Retrospective Study and Meta-Analysis. Front Endocrinol (Lausanne). 2021;12:675643.

Funding declaration

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author contributions

Hao Zhang was responsible for the conceptualization and proofreading of the manuscript. Yubo Sun and Yuxin Jia contributed to the data analysis and the drafting of the initial manuscript. All authors have read and approved the final manuscript.

Data availability statement

The data that support the findings of this study are openly available in software package SEER*Stat 8.3.6 (https://seer.cancer.gov/seerstat/).

Competing interests

The author(s) declare no competing interests.

Figure Legends

Figure 1. Patient screening flowchart. TT: total thyroidectomy; LT: lobectomy.

Figure 2. Kaplan–Meier curves of cancer-specific survival between the tall cell variant of papillary thyroid carcinoma (TCV-PTC) patients with total thyroidectomy (TT) and those with lobectomy (LT) in the entire and propensity score matching (PSM) cohorts. (A) Entire cohort. (B) PSM cohort.

Figure 3. Kaplan-Meier cancer-specific survival curves in TCV-PTC patients: total thyroidectomy (TT) with or without radioiodine therapy (RAI) compared to lobectomy (LT). (A)TT with RAI. (B) TT without RAI.

Table 1. Demographic and clinicopathologic characteristics at baseline for TCV-PTC patients in entire and PSM cohorts.

Characteristic	**Entire cohort**			**PSM cohort**		
	Lobectomy NO.(%)	Total thyroidectomy NO.(%)	*P* value	Lobectomy NO.(%)	Total thyroidectomy NO.(%)	*P* value
Total	94(6.4)	1369(93.6)		94(50.0)	282(75.0)	
Age(years)			0.028			0.719
<55	40(42.6)	743(54.3)		40(42.6)	128(45.5)	
≥55	54(57.4)	626(45.7)		54(57.4)	154(54.6)	
Gender			0.782			0.894
Female	68(72.3)	972(71.0)		68(72.3)	206(73.1)	
Male	26(27.7)	397(29.0)		26(27.7)	76(26.9)	
Race			0.761			0.815
White	79(84.	1152(84.1)		79(84.	244(86.5)	

	0)			0)		
Black	6(6.4)	67(4.9)		6(6.4)	14(5.0)	
Others	9(9.6)	150(11.0)		9(9.6)	24(8.5)	
Tumor size(mm)			0.268			0.380
≤20	57(60.6)	713(52.1)		57(60.6)	183(64.9)	
21-40	24(25.5)	438(32.0)		24(25.5)	74(26.2)	
>40	13(13.8)	218(15.9)		13(13.8)	25(11.7)	
ETE			0.061			0.682
No	68(72.3)	858(62.7)		68(72.3)	212(75.2)	
Yes	26(27.7)	511(37.3)		26(27.7)	70(24.8)	
Mutifocality			0.001			0.950
No	62(66.0)	663(48.4)		62(66.0)	187(66.3)	
Yes	32(34.0)	706(51.6)		32(34.0)	95(33.7)	
Lymph node metastases			<0.001			0.928
No	82(87.2)	850(62.1)		82(87.2)	247(87.6)	
Yes	12(12.8)	519(37.9)		12(12.8)	35(12.4)	
Distant metastases			0.672			0.680
No	91(96.8)	1335(97.5)		91(96.8)	277(98.2)	
Yes	3(3.2)	34(2.5)		3(3.2)	5(1.8)	
RAI						
No	NA	420(30.6)	NA	NA	120(42.6)	NA
Yes	NA	949(69.3)		NA	162(57.4)	

Table 2. Cox proportional hazards model for cancer-specific survival in entire and PSM cohorts

Characteristic	**Entire cohort**			**PSM cohort**		
	HR (95%CI)	*P*		HR (95%CI)	*P*	

		value		value
Age(years)				
<55	Ref		Ref	
≥55	3.981 (2.322,6.826)	<0.001	7.437 (2.322,6.826)	0.066
Gender				
Female	Ref		Ref	
Male	1.072 (0.704,1.631)	0.747	1.939 (0.647,5.807)	0.237
Race				
White	Ref		Ref	
Black	1.129 (0.347,3.678)	0.840	0.948 (0.116,7.771)	0.960
Others	1.263 (0.676,2.361)	0.464	2.225 (0.385,12.859)	0.371
Tumor size(mm)				
≤20	Ref		Ref	
21-40	6.931 (3.082,15.586)	<0.001	8.856 (0.919,85.334)	0.059
>40	15.896 (7.041,35.889)	<0.001	53.164 (5.704,495.493)	<0.001
ETE				
No	Ref		Ref	
Yes	2.146 (1.360,3.386)	0.001	4.072 (1.150,14.412)	0.029
Mutifocality				
No	Ref		Ref	
Yes	0.854 (0.557,1.309)	0.469	0.878 (0.161,4.758)	0.878
Lymph node metastases				
No	Ref		Ref	
Yes	1.932 (1.236,3.021)	0.004	4.834 (1.278,18.160)	0.020
Distant metastases				
No	Ref		Ref	
Yes	6.382 (3.806,10.702)	<0.001	3.637 (0.770,17.173)	0.103
Surgery				
Total thyroidectomy	Ref		Ref	

Lobectomy	2.090 (1.002,4.360)	0.049	□	2.437 (1.138,7.547)	0.043

Figure 1

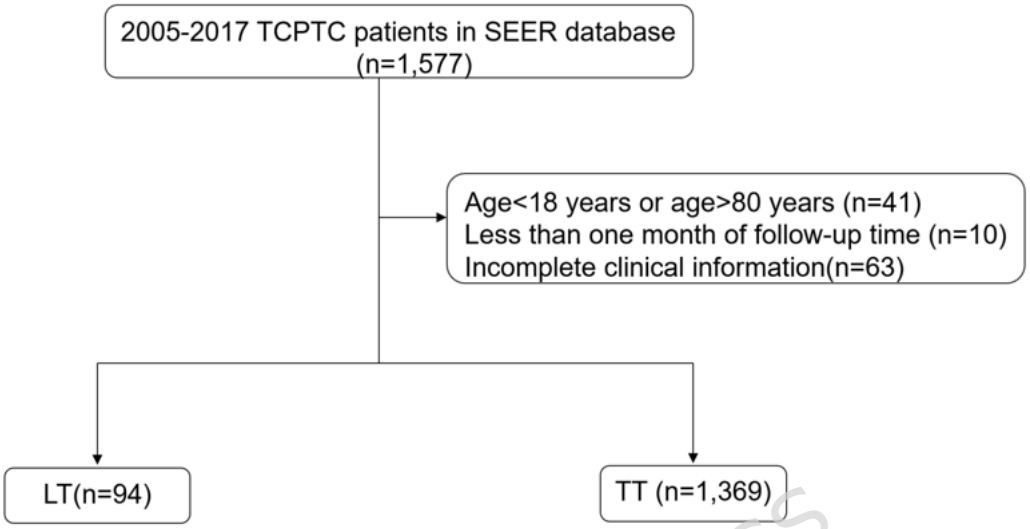

Figure 2

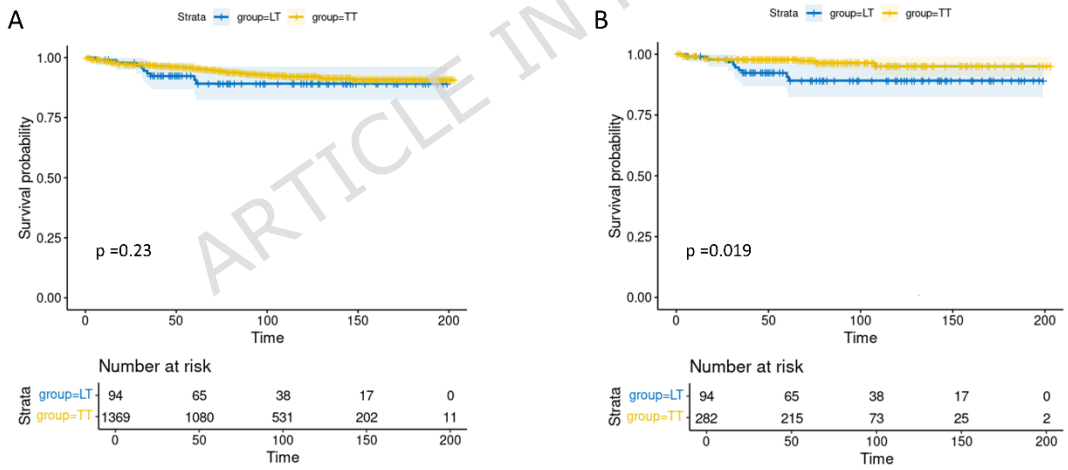

Figure 3