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Research article

Microscopic extrathyroidal extension does not affect the prognosis of patients with papillary thyroid carcinoma: A propensity score matching analysis

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A R T I C L E I N F O

Keywords:
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Prognosis

A B S T R A C T

Background: Extrathyroidal extension (ETE) in papillary thyroid carcinoma (PTC) can be divided into two categories based on different degrees of invasion: microscopic ETE (micro-ETE) and macroscopic ETE (macro-ETE). At present, there is a consensus that macro-ETE significantly affects PTC prognosis, while the prognostic significance of micro-ETE remains controversial.
Methods: The clinicopathological and follow-up data for PTC patients who underwent surgical treatment at the Hangzhou First People's Hospital between 2015 and 2018 were retrospectively analyzed. According to the degree of ETE, patients were divided into three groups: non-ETE, micro-ETE and macro-ETE. Cox regression analysis was performed to evaluate the effect of ETE on recurrence-free survival (RFS). The propensity score matching (PSM) method was used to reduce the interference of confounding factors, and Kaplan-Meier curves were utilized to compare the RFS.
Results: Both micro- and macro-ETE were associated with some aggressive tumor features, including tumor size, multifocality, and lymph node metastasis. Univariate and multivariate Cox regression analyses showed that macro-ETE was an independent risk factor for recurrence, while micro-ETE was not associated with recurrence. The K-M curves showed that RFS for micro-ETE and non-ETE were not statistically different before and after PSM, while RFS for macro-ETE was significantly shorter than that for non-ETE.
Conclusion: The presence of micro-ETE in PTC did not affect prognosis of patients, suggesting that its treatment should be consistent with the treatment for intrathyroidal tumors. The surgical method and the necessity for radioiodine therapy should be carefully evaluated to reduce overtreatment.

1. Introduction

Extrathyroidal extension (ETE) is an important factor affecting tumor invasiveness, and is directly related to the choice of surgical methods and postoperative treatment [1]. ETE can be divided into two categories: microscopic ETE (micro-ETE) and macroscopic ETE (macro-ETE). At present, there is no dispute that macro-ETE affects the prognosis and requires total thyroidectomy and radioiodine

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(RAI) therapy [2]. Micro-ETE is generally considered to be related to some tumor characteristics, such as size, multifocality, and lymph node metastasis, but its prognostic significance remains controversial.

In the eighth edition of the American Joint Commission on Cancer (AJCC) staging system, micro-ETE was removed from T3 staging, suggesting that it does not have an impact on prognosis [3]. In contrast, the American Thyroid Association (ATA) recurrence risk stratification classifies patients with micro-ETE to be at intermediate risk, recommending that they should receive more aggressive treatment and to consider the RAI therapy [4]. Similarly, some previous retrospective studies have also demonstrated contradictory results, where the prognostic significance was still uncertain [5–7].

However, prior studies were all carried out under natural conditions and were affected by different degrees of confounding factors, such as age, sex, and lymph node metastasis. The present study utilized the propensity score matching (PSM) method to eliminate the influence of confounding factors and further evaluate the prognostic significance of micro-ETE in PTC. This may provide more updated and comprehensive evidence for the understanding and clinical treatment of micro-ETE.

2. Materials and methods

2.1. Data collection

The electronic medical records of all pathologically confirmed PTC patients between January 2015 and December 2018 in the Department of Surgical Oncology of Hangzhou First People's Hospital were reviewed. The exclusion criteria were as follows: 1. lack of complete pathological data; 2. combination with other malignant tumors; 3. second operation; 4. mixed PTC (one or more different types of thyroid carcinoma in the gland in addition to PTC [8]); and 5. prior non-curative surgery. A total of 2138 patients were analyzed in the study. The collected data included ETE status, age, sex, tumor size, multifocality characteristics, central lymph node metastasis (CLNM), and lateral lymph node metastasis (LLNM). All of the above pathological data were independently reviewed by two experienced pathologists. The study flowchart was shown in Fig. 1.

2.2. Definition

The micro-ETE is defined as the tumor that breaks through the capsule and extends to the perithyroid soft tissue and sternothyroid muscles, which is evident under the pathological microscope. The macro-ETE is defined as the tumor invasion of subcutaneous soft tissue, larynx, trachea, esophagus, recurrent laryngeal nerve, or prevertebral fascia that is visible to the naked eye during the operation.

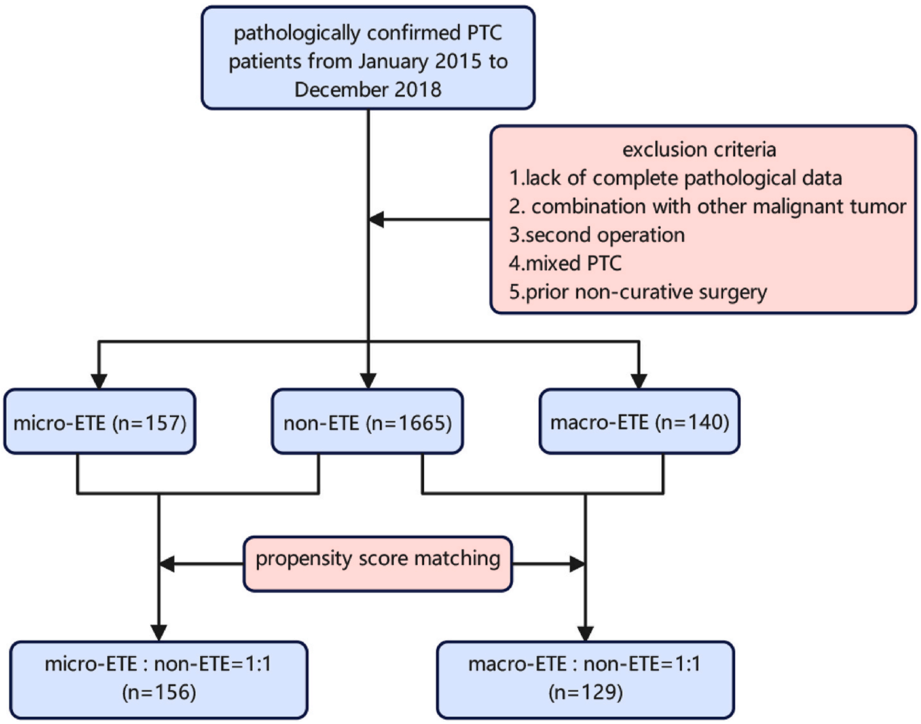

Fig. 1. The flowchart of this study. ETE, extrathyroidal extension; PTC, papillary thyroid carcinoma.

2.3. Surgical strategy

All patients enrolled in the study underwent radical surgery. Thyroidectomy and cervical lymph node dissection were performed simultaneously. For unilateral lesions, unilateral lobectomy and isthmus resection as well as ipsilateral central lymph node dissection were performed. For bilateral lesions and lesions with macro-ETE, total thyroidectomy and bilateral central lymph node dissection were carried out. Lateral lymph node dissection was carried out in patients with cervical lymph node metastasis diagnosed via fine-needle aspiration biopsy or preoperative imaging and confirmed by the intraoperative frozen sections.

2.4. Follow-up strategy

All patients were managed postoperatively according to the ATA guidelines. Patients underwent clinical evaluation, thyroid function tests, serum thyroglobulin level measurement, and ultrasound examinations every 3 months during the first year after surgery and every 6 months to 1 year thereafter. In the present study, the end point was recurrence-free survival (RFS), which was the time from the first surgery to the latest follow-up or the first recurrence. If the patient was lost to follow-up, the follow-up time was censored. Recurrence was defined as structural recurrence confirmed by pathology, including local recurrence and distant metastases.

2.5. Statistical analysis

R software (R Core Team, Version 4.1.2, Vienna, Austria) was used for all data analysis in the present study. PSM analysis was performed using the "Matchit" package. The matching method used the nearest neighbor algorithm with a ratio of 1:1 and a hole diameter of 0.02. The nearest neighbor algorithm was used as the matching method with the ratio set to 1:1 and the caliper value set to 0.02. Categorical variables were described by frequencies and percentages and compared by the chi-square test or Fisher's exact test. Continuous variables were expressed as mean ± standard deviation (mean ± SD) and compared using the *t*-test. Univariate and multivariate Cox regression analyses were utilized to evaluate the relationship between clinicopathological features and RFS. The cumulative recurrence curves were generated by the Kaplan-Meier (K-M) method and analyzed using the log-rank test. Bilateral $P < 0.05$ served as the significance threshold.

3. Results

3.1. Comparison of baseline characteristics and RFS before PSM

A total of 176 patients were lost to follow-up during the study, resulting in 1962 patients included in the final evaluation. This cohort included 1665 patients without ETE, 157 patients with micro-ETE, and 140 patients with macro-ETE. The median follow-up time was 63.42 ± 14.80 months. Overall, 32 patients experienced recurrence, including 31 regional recurrence cases and one distant metastasis case. The baseline patient characteristics are shown in Table 1. There were differences in clinicopathological features among the three groups, except for sex. In general, patients with ETE demonstrated a higher age, tumor size, multifocality

Table 1
| Comparison of baseline patient characteristics before propensity score matching.

	non-ETE	micro-ETE	macro-ETE	*P*-value (non-ETE vs micro-ETE)	*P*-value (non-ETE vs macro-ETE)
Age	45.76 ± 11.95	47.59 ± 13.17	49.93 ± 13.30		
<55	1248(74.95 %)	107(68.15 %)	86(61.43 %)	0.062	<0.001
≥55	417(25.05 %)	50(31.85 %)	54(38.57 %)		
Gender					
Female	1295(77.78 %)	118(75.16 %)	109(77.86 %)	0.452	0.983
Male	370(22.22 %)	39(24.84 %)	31(22.14 %)		
Size (cm)	0.69 ± 0.50	1.12 ± 0.79	1.71 ± 1.27		
≤1 cm	1724(85.53 %)	102(64.97 %)	50(35.71 %)	<0.001	<0.001
>1 cm	241(14.47 %)	55(35.03 %)	90(64.29 %)		
Multifocality					
Unifocal	1292(77.60 %)	102(64.97 %)	95(32.14 %)	<0.001	0.009
Multifocal	373(22.40 %)	55(35.03 %)	45(64.29 %)		
CLNM					
Negative	1111(66.73 %)	93(59.24 %)	48(34.29 %)	0.058	<0.001
Positive	554(33.23 %)	64(40.76 %)	92(65.71 %)		
LLNM					
Negative	1517(91.11 %)	130(82.80 %)	74(82.86 %)	0.001	<0.001
Positive	148(8.89 %)	27(17.20 %)	66(47.14 %)		
RAI therapy					
No	1569(94.23 %)	105(66.88 %)	37(26.43 %)	<0.001	<0.001
Yes	96(5.77 %)	52(33.12 %)	103(73.57 %)		
Recurrence					
No	1646(98.86 %)	153(97.45 %)	131(93.57 %)	0.131	<0.001
Yes	19(1.14 %)	4(2.55 %)	9(6.43 %)		

proportion, and lymph node metastasis than those without ETE. In addition, compared to patients without ETE, the proportion of patients with ETE receiving RAI treatment was higher. The three groups' recurrence rates were 1.14 %, 2.55 %, and 6.43 %, respectively. There was no significant difference in recurrence rate between micro-ETE and non-ETE groups, while the recurrence rate of macro-ETE increased significantly.

The RFS of the three patient groups was also compared (Fig. 2). The RFS of patients with micro-ETE was not statistically different compared to patients without ETE (P = 0.008), while the RFS of patients with macro-ETE was significantly lower (P < 0.001).

3.2. Univariate and multivariate cox regression analyses of recurrence risk factors

Univariate Cox regression analysis showed that tumor size, multifocality, CLNM, LLNM, and macro-ETE were identified as significant risk factors for recurrence, while age, sex, and micro-ETE were not associated with RFS (Table 2). Factors with univariate p < 0.05 were included in the multivariate Cox regression analysis. The results showed that multifocality, CLNM, and macro-ETE were significantly correlated with RFS, but size and LLNM were not risk factors for recurrence.

3.3. Comparison of baseline characteristics and RFS after PSM

To reduce the influence of confounding factors on the results, PSM analysis was performed on the patients based on the following factors: age, sex, tumor size, multifocality, CLNM, and LLNM. For non-ETE and micro-ETE, a total of 312 patients were included after 1:1 PSM. The baseline data showed that all clinicopathological features were consistent (Table 3). The cumulative hazard curves demonstrated that there was no significant difference in prognosis between the two groups, as before the PSM (Fig. 3). The macro-ETE and non-ETE groups were also compared. After the PSM, the baseline of 258 patients was completely consistent (Table 4). According to the K-M curve analysis, the difference between the two groups was statistically significant (P = 0.016), and the RFS for macro-ETE was significantly lower than that for non-ETE (Fig. 4). The results of Univariate and multivariate Cox regression analyses after PSM were shown in Table 5.

4. Discussion

It is necessary to improve the layered diagnosis and treatment of ETE and distinguish between them in clinical practice to achieve accurate treatment [9]. The present results demonstrated that micro-ETE of PTC may not be a prognostic factor for thyroid cancer patients at our center. The PSM method was used to evaluate the difference between micro-ETE and macro-ETE in PTC, with the purpose of reducing selection bias and eliminating outliers [10]. The results demonstrated that there is no significant difference between the prognosis for micro-ETE and non-ETE. This suggests that reducing overdiagnosis and treatment of micro-ETE might be necessary to appropriately reduce the scope of cleaning and avoid unnecessary RAI therapy. Furthermore, the present study also showed that the RFS for macro-ETE was significantly lower than that for non-ETE. This indicated that macro-ETE was more aggressive,

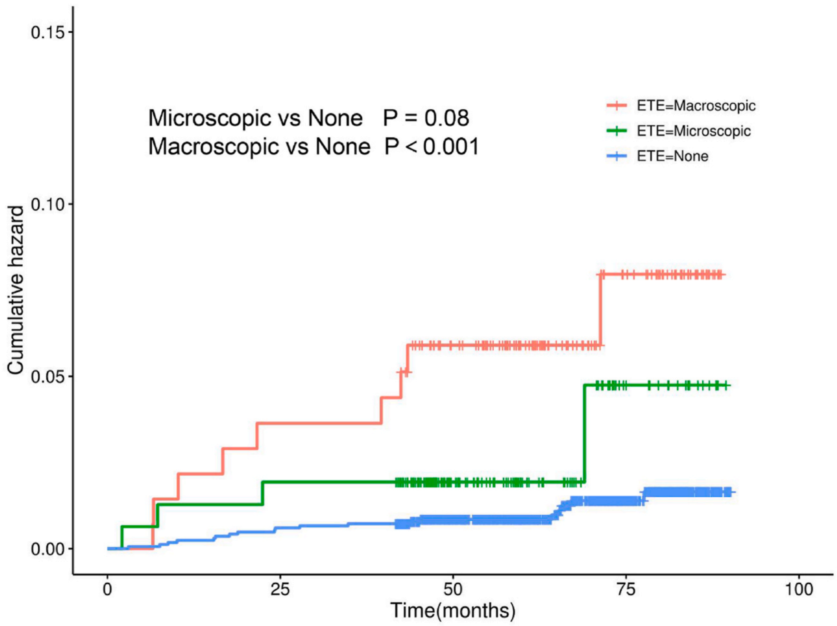

Fig. 2. Comparison of recurrence-free survival in PTC patients with different ETE classifications before propensity score matching. ETE, extrathyroidal extension.

Table 2
| Univariate and multivariate Cox analyses of risk factors for recurrence before propensity score matching.

	Univariate analysis			Multivariate analysis		
	HR	95 %CI	*P*-value	HR	95 %CI	*P*-value
Age (vs < 55)	1.482	0.302–1.066	0.291			
Sex (vs male)	0.858	0.385–1.910	0.707			
Size (vs ≤ 1 cm)	2.743	1.355–5.555	0.005	1.084	0.474–2.482	0.848
Multifocality (vs unifocal)	3.257	1.629–6.514	0.001	2.485	1.2245.044	0.012
CLNM (vs negative)	9.393	3.617–24.395	<0.001	7.089	2.599–19.333	<0.001
LLNM (vs negative)	4.252	2.078–8.699	<0.001	1.278	0.541–3.019	0.575
ETE (vs None)						
Microscopic	2.481	0.842–7.305	0.099	2.02	0.676–6.036	0.208
Macroscopic	5.621	2.543–12.426	<0.001	3.093	1.277–7.493	0.012

Table 3
| Comparison of baseline patient characteristics between non-ETE and micro-ETE groups after propensity score matching.

	non-ETE	micro-ETE	*P*-value
Age	45.78 ± 12.90	47.54 ± 13.20	
<55	107(68.59 %)	107(68.59 %)	1
≥55	49(31.41 %)	49(31.41 %)	
Gender			
Female	118(75.64 %)	118(75.64 %)	1
Male	38(24.36 %)	38(24.36 %)	
Size (cm)	0.89 ± 0.54	1.12 ± 0.79	
≤1 cm	102(65.38 %)	102(65.38 %)	1
>1 cm	54(34.62 %)	54(34.62 %)	
Multifocality			
Unifocal	102(65.38 %)	102(65.38 %)	1
Multifocal	54(34.62 %)	54(34.62 %)	
CLNM			
Negative	92(58.97 %)	92(58.97 %)	1
Positive	64(41.03 %)	64(41.03 %)	
LLNM			
Negative	129(82.69 %)	129(82.69 %)	1
Positive	27(17.31 %)	27(17.31 %)	

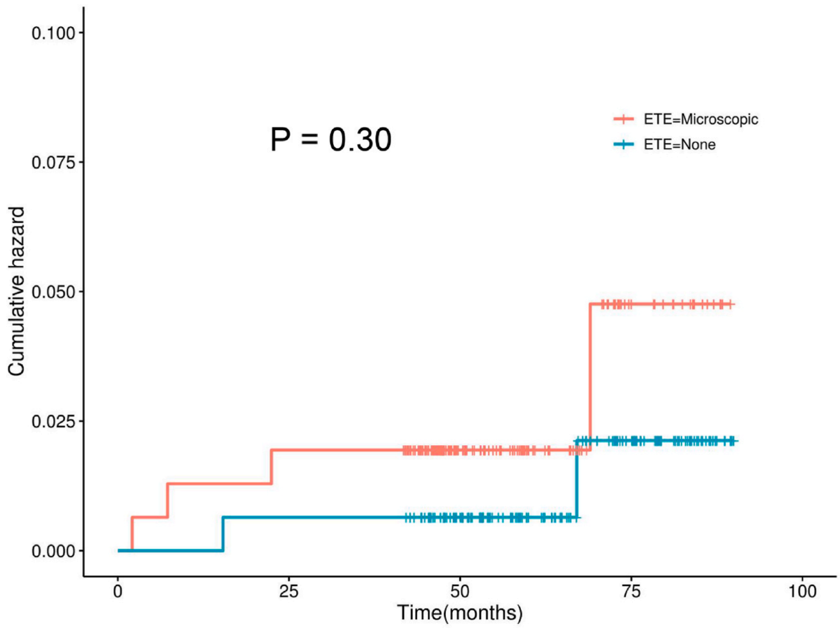

Fig. 3. Comparison of recurrence-free survival in patients with micro-ETE and no ETE after propensity score matching. ETE, extra-thyroidal extension.

Table 4
| Comparison of baseline patient characteristics between non-ETE and macro-ETE groups after propensity score matching.

	None	Macroscopic	*P*-value
Age	45.17 ± 13.28	48.74 ± 12.98	
<55	86(66.67 %)	86(66.67 %)	1
≥55	43(33.33 %)	43(33.33 %)	
Gender			
Female	101(78.29 %)	101(78.29 %)	1
Male	28(21.71 %)	28(21.71 %)	
Size (cm)	1.32 ± 0.77	1.67 ± 1.26	
≤1 cm	80(62.02 %)	80(62.02 %)	1
>1 cm	49(32.56 %)	49(37.98 %)	
Multifocality			
Unifocal	87(67.44 %)	87(67.44 %)	1
Multifocal	42(34.62 %)	42(34.62 %)	
CLNM			
Negative	48(37.21 %)	48(37.21 %)	1
Positive	81(62.79 %)	81(62.79 %)	
LLNM			
Negative	71(55.04 %)	71(55.04 %)	1
Positive	58(44.96 %)	58(44.96 %)	

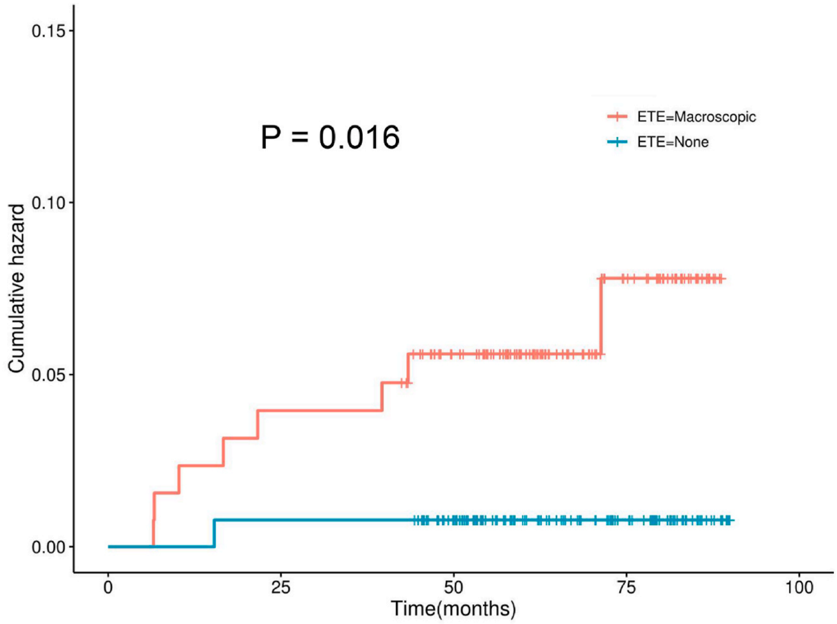

Fig. 4. Comparison of recurrence-free survival in patients with macro-ETE and no ETE after propensity score matching. ETE, extra-thyroidal extension.

Table 5
| Univariate and multivariate Cox analyses of risk factors for recurrence after propensity score matching.

	Univariate analysis			Multivariate analysis		
	HR	95 %CI	*P*-value	HR	95 %CI	*P*-value
Age (vs < 55)	1.388	0.494–3.899	0.543			
Sex (vs male)	0.607	0.207–1.766	0.362			
Size (vs ≤ 1 cm)	1.287	0.467–3.551	0.626			
Multifocality (vs unifocal)	5.590	1.780–17.557	0.003	4.719	1.489–14.955	0.008
CLNM (vs negative)	14.160	1.862–107.682	0.010	10.060	1.208–87.795	0.033
LLNM (vs negative)	3.590	1.278–10.089	0.015	1.386	0.457–4.206	0.565
ETE (vs None)						
Microscopic	1.999	0.445–8.970	0.366	2.672	0.587–12.156	0.204
Macroscopic	4.417	1.172–16.651	0.028	3.887	1.020–14.817	0.047

suggesting that comprehensive evaluation of macro-ETE should be performed before surgery and that radical surgery and RAI therapy should be carried out.

The significance of micro-ETE, also known as minimal ETE in some literature, in PTC remains controversial. In the eighth edition of the AJCC staging system, only grossly evident (macroscopic) ETE involving strap muscles (not microscopic ETE involving perithyroidal soft tissue) affects tumor staging [11]. This system considers that micro-ETE detected only in the histological examination has no effect on mortality and proposes that only the macro-ETE is clinically relevant and affects the tumor stage. In the 2015 ATA initial risk stratification, the presence of micro-ETE advanced low risk patients to moderate risk and the recurrence risk associated with micro-ETE ranged from 3 % to 9 % [4]. Therefore, a more aggressive initial treatment was strongly recommended, even if micro-ETE had no other adverse features. However, the stage and risk, as well as other factors, such as recurrence and complications, should be taken into account when choosing the surgical procedure in clinical practice. Therefore, understanding the influence of different degrees of ETE on survival and prognosis can help clinicians to realize individualized operation mode selection and avoid overtreatment.

Some previous retrospective studies have suggested that micro-ETE may lead to poor cancer-specific and overall survival outcomes. A retrospective study of 77 patients with micro-ETE by Seifert et al. [12] found that micro-ETE is a statistically significant and independent risk factor for relapse through LNMs and distant metastases. Some reports [13] suggest that all levels of extrathyroidal extension, including microscopic, are associated with an increased risk of lymph node and distant metastases, as well as decreased overall survival. Other scholars hold the opposite view, stating that not all levels of ETE have a poor prognosis. Marques et al. [14] found there was no significant association between micro-ETE and recurrence rate, persistence of disease or disease-specific mortality. Li et al. [11] research results also showed that there was no difference in tumor size, multifocality, lymph node metastasis, and recurrence between micro-ETE and non-ETE patients. However, once the tumor invaded beyond the strap muscles, patients' overall survival decreased. In addition, Patti et al. [15] also found that distinguishing micro-ETE and macro-ETE provides a better predictive probability of recurrence. The present study findings are similar, indicating that micro-ETE is not an appropriate indication for aggressive surgery or RAI treatment for PTC.

The use of radioactive iodine therapy after total thyroidectomy has been practiced for a long time. In the 2009 ATA guidelines, minimal ETE or vascular invasion was considered an 'intermediate' risk feature with a recommendation for RAI therapy. In contrast, the 2015 ATA guidelines altered the RAI recommendations [16,17]. Damage to the salivary glands, impaired gonadal function, and secondary neoplasm are common adverse effects in patients undergoing high dose RAI. In the present study, patients with microscopic ETE were not candidates for high dose RAI and had good prognoses. Because micro-ETE is not a risk factor for PTC recurrence, tumors with micro-ETE are biologically less aggressive and there is no need to strengthen the treatment. In particular, patients with macro-ETE in thyroidectomy samples may benefit from the initial RAI. Before further study to clarify the benefits of RAI in patients with micro-ETE, clinicians must carefully review the pathological reports after thyroidectomy and consider the choice of auxiliary RAI in the presence of micro-ETE.

There were some limitations in the present study. First, this was a retrospective study. Even though PSM was performed to reduce selection bias, it did not completely eliminate its impact on the results. Second, given the low incidence of micro-ETE and the small study sample size, a multicenter analysis should be performed to confirm the present preliminary findings. Another limitation came from the difference in the definition of micro-ETE at different centers, which may lead to the lack of universality and objectivity in the histological evaluation of micro-ETE.

5. Conclusion

There was no statistically significant difference in prognosis between the micro-ETE and non-ETE groups in the present study. This suggested that the diagnosis and treatment of micro-ETE should be synchronized with the diagnosis and treatment of thyroid tumors to reduce overtreatment. In addition, the significance of micro-ETE in recurrence risk stratification should be reassessed.

Ethics statement

The study was approved by the Ethics Committee of the Hangzhou First People's Hospital (No. 2018 (146)-1, 1 October 2018). Written informed consent was obtained from the individual(s) for the publication of any potential data included in this article.

Data availability statement

The data that has been used is confidential.

CRediT authorship contribution statement

Ke-cheng Jiang: Writing - review & editing, Writing – original draft, Validation, Software, Formal analysis, Data curation, Conceptualization. **Dong-hui Zhou:** Writing – review & editing, Conceptualization. **Ding-cun Luo:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] A.R. Shaha, Extrathyroidal extension—what does it mean, Oral Oncol. 68 (2017) 50–52.
[2] F. Nabhan, P.H. Dedhia, M.D. Ringel, Thyroid cancer, recent advances in diagnosis and therapy, Int. J. Cancer 149 (5) (2021) 984–992.
[3] A.T. Turk, S.L. Asa, Z.W. Baloch, et al., Interobserver Variability in the Histopathologic assessment of extrathyroidal extension of well differentiated thyroid carcinoma supports the new American Joint committee on cancer eighth edition criteria for tumor staging, Thyroid 29 (5) (2019) 619–624.
[4] B.R. Haugen, E.K. Alexander, K.C. Bible, 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 26 (1) (2016) 1–133.
[5] V. Harries, M. McGill, A. Yuan, et al., Does macroscopic extrathyroidal extension to the strap muscles alone affect survival in papillary thyroid carcinoma? Surgery 171 (5) (2022) 1341–1347.
[6] J. Ruiz Pardo, A. Ríos Zambudio, J.M. Rodríguez González, et al., Papillary thyroid microcarcinoma with minimal extrathyroidal extension. Is its course so indolent that it requires a less aggressive treatment? Rev. Clínica Española 221 (3) (2021) 131–138.
[7] S.K. Parvathareddy, A.K. Siraj, Z. Qadri, et al., Microscopic extrathyroidal extension results in increased rate of tumor recurrence and is an independent predictor of patient's outcome in middle eastern papillary thyroid carcinoma, Front. Oncol. (2021) 11.
[8] C. Liu, Q. Zhao, Z. Li, et al., Mixed subtype thyroid cancer: a surveillance, epidemiology, and end results database analysis, Oncotarget 8 (49) (2017) 86556–86565.
[9] D.W. Chen, B.H.H. Lang, D.S.A. McLeod, K. Newbold, M.R. Haymart, Thyroid cancer, Lancet 401 (10387) (2023) 1531–1544.
[10] L.T. Kane, T. Fang, M.S. Galetta, et al., Propensity score matching: a statistical method, Clin. Spine Surg. 33 (3) (2020) 120–122.
[11] G. Li, R. Li, L. Song, et al., Implications of extrathyroidal extension invading only the strap muscles in papillary thyroid carcinomas, Thyroid 30 (1) (2020) 57–64.
[12] R. Seifert, M. Schäfers, B. Heitplatz, L. Kerschke, B. Riemann, B. Noto, Minimal extrathyroidal extension in papillary thyroid microcarcinoma is an independent risk factor for relapse through lymph node and distant metastases, J. Nucl. Med. 62 (12) (2021) 1702–1709.
[13] M.D. Bortz, K. Kuchta, D.J. Winchester, R.A. Prinz, T.A. Moo-Young, Extrathyroidal extension predicts negative clinical outcomes in papillary thyroid cancer, Surgery 169 (1) (2021) 2–6.
[14] B. Marques, R.G. Martins, J. Couto, J. Santos, T. Martins, F. Rodrigues, Microscopic extrathyroid extension in papillary thyroid carcinoma: impact on response to therapy, Arch. Endocrinol. Metabol. 64 (2) (2020) 144–149.
[15] L. Patti, S. Gay, L. Musso, et al., Impact of microscopic extrathyroidal extension on differentiated thyroid cancer post-surgical risk of recurrence: a retrospective analysis, J. Endocrinol. Invest. 46 (10) (2023) 2157–2164.
[16] D.S. Cooper, G.M. Doherty, B.R. Haugen, et al., Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer, Thyroid 19 (11) (2009) 1167–1214.
[17] J.S. Radowsky, R.S. Howard, H.B. Burch, A. Stojadinovic, Impact of degree of extrathyroidal extension of disease on papillary thyroid cancer outcome, Thyroid 24 (2) (2014) 241–244.