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Research Article

Ultrasound and gene-guided microwave ablation vs. surgery for low-risk papillary thyroid carcinoma: a prospective observational cohort study

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Abstract

Objective: This prospective observational cohort real-world study evaluates and compares the efficacy and prognosis of ultrasound (US) and gene-based microwave ablation (MWA) and surgical treatment in patients with low-risk papillary thyroid carcinoma (PTC), emphasizing the influence of genetic mutations on low-risk patient selection.

Background: MWA, a minimally invasive technique, is increasingly recognized in the management of PTC. While traditional criteria for ablation focus on tumor size, number, and location, the impact of genetic mutations on treatment efficacy remains underexplored.

Methods: A total of 201 patients with low-risk PTC without metastasis were prospectively enrolled. All patients underwent US and next-generation sequencing to confirm low-risk status. Patients chose either ablation or surgery and were monitored until November 2024. Efficacy and complications were assessed using thyroid US and contrast-enhanced US.

Results: The median follow-up of this study is 12 months. There is no significant difference between the ablation group (3.0%) and the surgery group (1.0%) in disease free survival ($P = 0.360$). However, the surgery group exhibited a significantly higher complication rate, particularly for temporary hypoparathyroidism ($P < 0.001$). Ablation offers notable advantages, including shorter treatment duration, faster recovery, less intraoperative blood loss, and reduced costs ($P < 0.001$), while maintaining favorable safety and comparable efficiency.

Conclusions: For patients with low-risk genetic mutations, ablation provides comparable efficacy and disease free survival to surgery, with significant benefits in safety, recovery, and overall cost. Guided by US and next-generation sequencing, precise patient selection enhances the potential of ablation as a promising, minimally invasive alternative to surgery in the management of low-risk PTC .

Keywords: papillary thyroid carcinoma; next-generation sequencing; microwave ablation; surgical treatment

Introduction

Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer, accounting for 80%–90% of all thyroid malignancies [1, 2]. In recent years, the detection rate of PTC has significantly increased, primarily due to the widespread use of high-resolution ultrasound (US). Despite this increase, the mortality rate of PTC has not risen accordingly [3, 4]. Currently, surgery is the standard treatment for PTC; however, it is associated with potential complications such as hypothyroidism, hypoparathyroidism, recurrent laryngeal nerve injury, and scar formation, which can significantly impact patients' quality of life [5]. For asymptomatic, non-metastatic PTC patients, active surveillance has emerged as an alternative to surgery, potentially avoiding unnecessary surgical side effects [6, 7]. Nonetheless, the long-term, dynamic nature of active surveillance may be challenging for some patients, particularly due to the anxiety and psychological stress often associated with a cancer diagnosis [8, 9]. Additionally, certain PTC cases present more aggressive features, including early metastasis and lymph node involvement, necessitating prompt intervention [10, 11]. Against this backdrop, ablation therapy has garnered increasing interest as an emerging treatment modality.

Recent advances in interventional US have expanded the application of US-guided thermal ablation techniques—such as radiofrequency ablation, laser ablation, and microwave ablation (MWA)—in the treatment of malignant thyroid nodules, demonstrating promising outcomes. Under US guidance, thermal ablation can precisely target the tumor and locally heat the tumor

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tissue, reducing the trauma and risk of complications associated with traditional surgery. Studies have shown that US-guided thermal ablation has favorable results in PTC patients, including fewer complications, shorter hospital stays, and reduced disruption to daily life compared to surgery, suggesting that ablation may serve as an alternative to both surgery and active surveillance [12, 13]. Current guidelines for PTC ablation recommend its use under the following conditions: tumor diameter ≤ 5 mm (or up to ≤ 1 cm if not closely adjacent to the capsule), distance of the nodule from the inner posterior capsule > 2 mm, confirmed low-risk pathological subtype, absence of thyroid capsule or surrounding tissue invasion, no evidence of multifocal thyroid cancer or metastasis, and no family history of thyroid cancer or history of neck radiation exposure during childhood/adolescence. Ablation therapy may be considered after fully informing patients that surgery remains the primary treatment option, especially for those refusing surgery and close follow-up [14]. However, these guidelines do not adequately consider the role of genetic mutations, which are critical for assessing prognosis and determining individualized treatment.

Advances in genetic testing have made it an essential tool for clinical diagnosis and prognosis assessment, particularly in tumor risk stratification and personalized treatment. The development, progression, and prognosis of thyroid cancer are known to be influenced by various genetic mutations, including point mutations such as B-Raf proto-oncogene, serine/threonine kinase V600E (BRAF V600E), rat sarcoma virus (RAS), rearranged during transfection (RET), telomerase reverse transcriptase (TERT), tumor protein 53 (TP53), and phosphoinositide-3-kinase catalytic subunit alpha (PIK3CA), as well as gene fusions like coiled-coil domain containing 6-rearranged during transfection (CCDC6-RET) and E26 transformation-specific (ETS) variant transcription factor 6-neurotrophic tyrosine receptor kinase 3 (ETV6-NTRK3) [15–19]. Overlooking these genetic alterations may negatively impact treatment efficacy and long-term prognosis. Mutations such as BRAF V600E (without concurrent TERT promoter mutation), RAS, including Harvey rat sarcoma virus oncogene (HRAS), neuroblastoma RAS viral oncogene homolog (NRAS), Kirsten rat sarcoma viral oncogene homolog (KRAS), and RET proto-oncogene/papillary thyroid carcinoma (RET/PTC) rearrangements are generally associated with less aggressive tumor behavior and slower progression, indicating a favorable prognosis. Patients with these mutations, presenting with tumors ≤ 1 cm in diameter, solitary lesions, no metastasis, no extrathyroidal extension, and non-invasive pathological subtypes, as well as no history of radiation exposure or family history, may be considered as having low-risk PTC and potentially suitable for minimally invasive ablation therapy [14]. Conversely, patients with tumors > 1 cm, multifocal disease, local or distant metastasis, extrathyroidal extension, vascular invasion, aggressive pathological subtypes, history of radiation exposure, or family history, and those carrying high-risk mutations (e.g. BRAF V600E with TERT promoter mutation, RAS mutation with eukaryotic translation initiation factor 1A, X-linked (EIF1AX) mutation, TP53 mutation, PIK3CA mutation, or protein kinase B (AKT) serine/threonine kinase (AKT1) mutation are classified as having Intermediate-high risk PTC. These patients typically have more aggressive disease, a poorer prognosis, and an increased risk of recurrence, warranting more aggressive treatments such as total thyroidectomy [20–23]. The 2021 European guidelines, based on clinical and molecular evidence linking TERT promoter and TP53 mutations to tumor aggressiveness and poor prognosis, recommend against ablation therapy in patients with these mutations [24]. However, this recommendation lacks robust evidence from high-level clinical trials, and the relationship between other common mutations (such as BRAF and RAS) and the efficacy of ablation therapy remains inadequately addressed. While BRAF V600E and RAS mutations have been linked to increased tumor aggressiveness and recurrence risk, their impact on long-term outcomes following ablation therapy is still unclear. Current guidelines do not fully address the role of genetic mutations in determining the appropriateness of ablation therapy for low-risk PTC patients, particularly regarding how different mutations may affect treatment outcomes. Therefore, further research is warranted to elucidate the influence of genetic mutations on ablation therapy in low-risk PTC, to establish consensus, and to optimize treatment strategies.

The critical importance of genetic testing in assessing the biological behavior and prognosis of PTC underscores its value in the decision-making process for ablation therapy in low-risk PTC, especially in real-world clinical settings. Investigating the impact of genetic mutations on the efficacy and prognosis of ablation therapy in low-risk PTC could provide a stronger foundation for personalized treatment. Additionally, US guidance plays a key role in accurately locating the tumor and ensuring the effectiveness and safety of ablation therapy in real-world practice. This study aims to evaluate the effectiveness of US and gene-guided ablation therapy in low-risk PTC patients and explore the role of genetic testing in risk assessment, with the goal of providing new insights and evidence to support clinical decision-making in real-world scenarios.

Methods

Study design and participants

From January 2022 to November 2024, a total of 400 participants were initially screened for this prospective observational cohort study, and 201 eligible participants were ultimately enrolled. All patients underwent next-generation sequencing (NGS) and US before standard surgery or MWA at Sun Yat-sen Memorial Hospital (SYSMH) (Fig. 1). All patients provided written informed consent before treatment; it was emphasized that surgery was the standard treatment recommended by guidelines, while MWA could not prevent recurrent PTC or undetectable lymph node metastasis.

The inclusion criteria of this study were as follows: (i) PTC confirmed by fine-needle aspiration (FNA); (ii) confirmed low-risk mutation types by NGS before surgery; (iii) no severe functional diseases, such as heart failure, severe respiratory diseases, or renal failure; and (iv) availability of complete follow-up data. The exclusion criteria were as follows: (i) no local or distant metastasis assessed by imaging evaluations, including US or computed tomography (CT); (ii) lack of preoperative genetic testing or inability to assess genetic test results; and (iii) inability to complete follow-up or lost to follow-up during the study. Low-risk PTC is defined as: (i) maximum tumor diameter ≤ 1 cm; (ii) solitary lesion; (iii) no local or distant metastasis; (iv) no tumor invasion into extrathyroidal tissues; (v) no vascular invasion; (vi) non-invasive pathological subtype for the primary lesion (invasive subtypes include tall cell, columnar cell, diffuse sclerosing, solid/trabecular, and oncocytic variants); (vii) no history of head and neck radiotherapy during adolescence; (viii) no family history of thyroid cancer; and (ix) genetic testing showing BRAF V600E mutation (without concurrent TERT mutation), RAS family gene mutations, (HRAS, NRAS, KRAS), or other low-risk mutations, such as isolated RET/PTC) rearrangements [14, 20, 24]. Intermediate-high risk PTC is defined

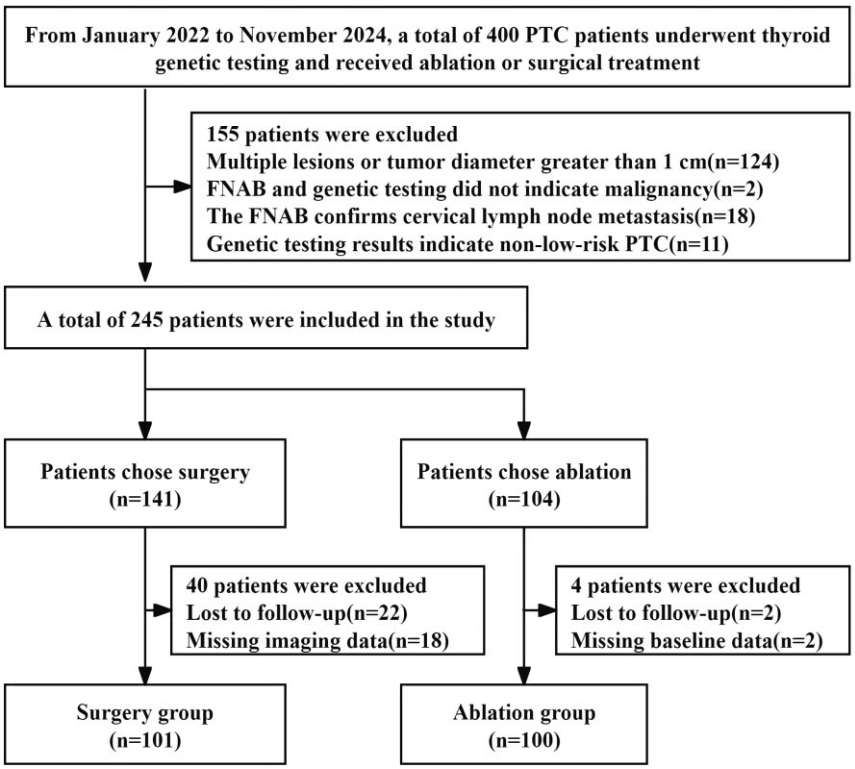

Figure 1. Study flow diagram. Study flowchart of patient inclusion for the study on low-risk PTC treatments at SYSMH. A total of 400 patients who underwent ablation or surgical treatment from January 2022 to November 2024 were initially screened for the prospective obversational cohort study. Exclusions included patients with multiple lesions or tumor diameters > 1 cm ($n = 124$), those without malignancy indications in fine-needle aspiration biopsy (FNAB) and genetic testing (n = 2), and patients with genetic testing indicating intermediate-high risk PTC ($n = 11$). Additionally, patients with cervical lymph node metastasis ($n = 18$) were excluded. Ultimately, 245 patients with low-risk PTC were included, with 141 opting for surgery and 104 choosing ablation. After further exclusions for incomplete data, the final groups included 101 patients in the surgery group and 100 patients in the ablation group.

as: (i) maximum tumor diameter > 1 cm; (ii) multifocal thyroid cancer; (iii) local or distant metastasis; (iv) primary lesion with extrathyroidal extension; (v) vascular invasion; (vi) primary lesion with an invasive pathological subtype; (vii) history of head and neck radiotherapy during adolescence; (viii) family history of thyroid cancer; and (ix) genetic testing revealing high-risk mutation combinations, such as BRAF V600E or RAS mutations with concurrent TERT or TP53 mutations, or RAS mutations combined with EIF1AX mutations.

This study was approved by the institutional review boards of SYSMH (approval No. SYSKY-2024–169-02) and adhered to the principles outlined in the Declaration of Helsinki.

Assessment

All participants underwent a pre-treatment evaluation, including laboratory tests, chest X-ray or CT scan, electrocardiogram (ECG), US, and contrasted-enhanced US (CEUS). Laboratory tests included complete blood count, thyroid function tests, and coagulation tests. Imaging evaluations, such as US and chest CT, were conducted to exclude extrathyroidal extension or evidence of local/distant metastasis. US-guided FNA was performed to confirm the diagnosis, and for patients with a history of neck surgery, laryngoscopy was conducted to evaluate the status of the recurrent laryngeal nerve. Preoperative genetic testing was conducted to assess tumor aggressiveness. Tumor volume was calculated using the formula $V = \pi \times a \times b \times c/6$, where V represents tumor volume, and a, b, c are the three perpendicular dimensions of the tumor. The volume reduction ratio (VRR) was calculated as VRR = [(initial volume − final volume) × 100]/initial volume.

NGS

During US-guided FNA, part of the tissue sample was allocated for routine pathological diagnosis, while the remainder was preserved in a nucleic acid preservation tube to maintain DNA integrity. DNA extraction was performed, and its concentration was measured using a Qubit fluorometer. The extracted DNA underwent sequencing preparation, including fragmentation, end-repair, and adapter ligation. Libraries were sequenced on the Illumina MiniSeq platform. NGS was performed using a customized thyroid cancer gene panel covering BRAF, RAS, RET, TERT, TP53, PIK3CA, and EIF1AX mutations, among others. The sequencing depth was set at a minimum of 500 × to ensure high sensitivity for mutation detection. Bioinformatics analyses included quality control, alignment to the hg19 reference genome, and variant calling using GATK and Annovar. Post-sequencing data were analyzed against thyroid cancer-related databases to generate genetic testing reports. All genetic testing was conducted at the Molecular and Cellular Diagnostics Center of SYSMH, with rigorous quality control and bioinformatics analysis ensuring data accuracy and reliability.

Ablation procedures

Ablation was performed by an experienced thyroid surgeon using US guidance. A high-frequency (10–15 MHz) linear-array transducer was used for real-time US guidance. The imaging

protocol included grayscale US and color Doppler flow imaging to assess tumor vascularity. CEUS was performed pre- and post-procedure to confirm complete ablation. Patients were positioned supine, and local anesthesia was administered. Hydrodissection was achieved by injecting a mixture of 2% lidocaine and saline to separate the tumor from surrounding structures. Ablation was performed using the ECO-100A1 system with a disposable MWA needle, with output power between 30 and 45 W. The procedure aimed to achieve complete ablation of the tumor and surrounding thyroid tissue to prevent recurrence. Post-ablation US was performed to confirm complete ablation. Operative time was defined as the time from the start of disinfection to US confirmation of complete tumor ablation. Hospitalization costs included preoperative examinations, ablation materials, anesthesia, and postoperative care.

Surgical procedures

Thyroidectomy was performed by an experienced thyroid surgeon using either open or endoscopic methods. The extent of surgery was determined based on American Thyroid Association guidelines and patient preferences, typically involving unilateral lobectomy and isthmus resection with central compartment lymph node dissection. Operative time was defined from the initial incision to wound closure. Hospitalization costs included preoperative examinations, surgical materials, anesthesia, and postoperative care.

Outcome

The primary endpoint was disease progression, defined as: (i) local recurrence or cervical lymph node metastasis confirmed by FNA; (ii) distant organ metastasis; and (iii) death due to tumor progression.

Secondary endpoints included the following. (i) Complications, such as permanent or transient hypoparathyroidism, recurrent laryngeal nerve injury, postoperative hypertension, infection, fever, pain, and nausea or vomiting. Permanent hypoparathyroidism was defined as the need for calcium or vitamin D supplementation beyond 6 months, while transient hypoparathyroidism indicated recovery within 6 months. Permanent recurrent laryngeal nerve injury was defined as persistent voice changes beyond 6 months, while transient injury indicated recovery within 6 months. (ii) Treatment costs, including preoperative, surgical, and postoperative costs. (iii) Time of hospital stay. (iv) Operative time. (v) Ablation efficacy, defined as complete or incomplete ablation based on CEUS. (vi) Changes in ablation zone volume, measured before and after treatment. (vii) Changes in thyroid function during the follow-up period.

Statistical analysis

All data analyses were performed using R software (version 3.6.1), with all statistical tests conducted as two-sided tests, and a P-value < 0.05 was considered statistically significant. Continuous variables were described as mean ± standard deviation (SD) and compared between groups using the independent samples t-test. For non-normally distributed data, the median (interquartile range) was used for description, and group comparisons were performed using the Mann–Whitney U test. Categorical variables were presented as frequency (percentage) and analyzed using Pearson's χ^2 test or Fisher's exact test to assess differences in distribution between groups. Disease-free survival (DFS) was visualized using Kaplan–Meier survival curves, and group comparisons were performed using the log-rank test to evaluate the long-term effects of ablation therapy vs. surgery. The Cox proportional hazards model was used to assess the impact of various factors on DFS, calculating the hazard ratio (HR) and its 95% confidence interval (95% CI). Selection of variables for the Cox regression included a univariate Cox regression analysis to screen factors influencing DFS, such as patient age, sex, tumor size, gene mutation type, and treatment modality. Variables with a P-value < 0.10 in univariate analysis were included in the multivariate Cox regression to control for potential confounding effects on DFS. Additionally, subgroup analyses were conducted based on gene mutation types (BRAF V600E single mutation vs. BRAF combined with other mutations vs. non-BRAF mutations vs. no detectable mutations) to explore differences in tumor characteristics and the impact of ablation and surgery on treatment outcomes.

To ensure sufficient statistical power for detecting differences in complication rates between the two treatment groups, a sample-size calculation was performed using PASS software (version 15.0). Based on relevant literature and retrospective data from our center, we assumed a complication rate of 0.45% in the ablation group and 7.98% in the surgery group. A one-sided Z-test was applied with a significance level (α) of 0.05 and a statistical power of 80%. After accounting for a 15% dropout rate, the final required sample size was 200 patients, with 100 patients in each group. In this study, we enrolled 100 patients in the ablation group and 101 patients in the surgery group, meeting the sample size requirement and ensuring adequate statistical power.

Results

Patient characteristics

A total of 400 patients were prospectively enrolled at SYSMH, of whom 201 met the eligibility criteria for this study. Among them, 100 patients opted for ablation therapy, while 101 chose surgical treatment. The mean age was 41.89 years in the ablation group and 40.79 years in the surgery group, with no statistically significant difference ($P = 0.481$). No significant differences were observed between the two groups in terms of tumor location, morphology, length-to-width ratio, maximum diameter, tumor volume, US classification, blood flow signal, American College of Radiology Thyroid Imaging Reporting and Data System (TI-RADS) grade, or gene mutation types (all $P > 0.05$). The median follow-up duration was also comparable between the groups, at 11.51 months for the ablation group and 11.50 months for the surgery group ($P = 0.434$). Furthermore, no significant difference in disease progression rates was identified between the ablation and surgery groups ($P = 0.308$) (Table 1).

Gene profiles in low-risk PTC patients

All patients underwent preoperative NGS (Fig. S1, see online supplementary material). A comparison of gene mutations between the ablation and surgery groups revealed that BRAF mutations were prevalent in both groups, with no significant difference in distribution (95.00% vs. 91.09%, $P = 0.186$). However, RET gene mutations occurred significantly more frequently in the surgery group than in the ablation group ($P = 0.031$), indicating a statistically significant difference. Other genes, including NRAS, KRAS, and DNA polymerase epsilon, catalytic subunit (POLE), showed varying mutation frequencies between the groups, but these differences were not statistically significant ($P > 0.05$) (Table S1, see online supplementary material).

Among enrolled patients, there were no significant differences in age ($P = 0.796$) or gender ($P = 0.479$) across subgroups based

Table 1. Patients characteristics.

	Ablation (n = 100)	Surgery (n = 101)	P value
Age (year), mean (SD)	41.89 (11.13)	40.79 (10.89)	0.481
Gender (%)			0.154
Male	25 (25.0)	17 (16.8)	
Female	75 (75.0)	84 (83.2)	
Tumor location (%)			0.295
Left	51 (51.0)	41 (40.6)	
Isthmus	5 (5.0)	8 (7.9)	
Right	44 (44.0)	52 (51.5)	
Tumor morphology (%)			0.912
Sharp margins	51 (51.0)	52 (51.5)	
Fairly clear margins	16 (16.0)	18 (17.8)	
Blurred margins	33 (33.0)	31 (30.7)	
Tumor aspect ratio (%)			0.301
<1	52 (52.0)	49 (48.5)	
=1	4 (4.0)	1 (1.0)	
>1	44 (44.0)	51 (50.5)	
Maximum tumor diameter (mm), mean (SD)	6.14 (2.10)	6.25 (2.11)	0.696
Tumor volume (ml), mean (SD)	0.08 (0.09)	0.08 (0.07)	0.462
UItrasound classification (%)			0.484
TI-RADS 1	0 (0)	0 (0)	
TI-RADS 2	1 (1.0)	0 (0)	
TI-RADS 3	1 (1.0)	2 (2.0)	
TI-RADS 4	28 (28.0)	30 (29.7)	
TI-RADS 5	70 (70.0)	67 (66.3)	
TI-RADS 6	0 (0)	2 (2.0)	
CDFI[a] (%)			0.468
Blood flow signal within the nodule	43(43.0)	51 (50.5)	
Peripheral ring-like blood flow signal	7 (7.0)	4 (4.0)	
Ring-like blood flow signal within and around the nodule	14(14.0)	17 (16.8)	
No ring-like blood flow signal within and around the nodule	36(36.0)	29 (28.7)	
FNAB (%)			0.505
TBS-I	0 (0)	0 (0)	
TBS-II	0 (0)	0 (0)	
TBS-III	5(5.0)	2 (2.0)	
TBS-IV	0 (0)	0 (0)	
TBS-V	4(4.0)	4 (4.0)	
TBS-VI	91(91.0)	95 (94.0)	
Gene mutation type (%)			0.664
Single BRAF gene mutation	58(58.0)	54 (53.4)	
BRAF gene mutation combined with other gene mutations	37(37.0)	38 (37.6)	
Other gene mutations	2(2.0)	5 (5.0)	
No gene mutation detected	3(3.0)	4 (4.0)	
Follow-up time (months), mean (SD)	11.51 (5.45)	11.50 (3.12)	0.434
Disease progression (%)			0.308
Yes	3 (3.0)	1 (1.0)	
No	97(97.0)	100 (99.0)	

[a]CDFI, Color Doppler flow imaging; FNAB, fine needle aspiration biopsy; TBS, the Bethesda system for reporting thyroid cytopathology.

on genetic profiles: BRAF single mutation, BRAF combined with other mutations, non-BRAF mutations, and no detectable mutations. Similarly, no significant differences were observed in tumor characteristics, including location, morphology, size, or aspect ratio (all $P > 0.05$) (Table 2).

In the subgroup analysis of gene mutations in different treatment groups, 58 cases (58.0%) in the ablation group and 54 cases (53.4%) in the surgery group were identified with a single BRAF gene mutation. A 21% decrease was observed in BRAF mutations accompanied by other gene mutations (e.g. RET, NRAS, EIF1AX) compared with BRAF single mutations in the ablation group, with a similar trend noted in the surgery group. Non-BRAF mutations accounted for 2.0% of the ablation group and 5.0% of the surgery group. Additionally, three patients (3.0%) in the ablation group and four patients (4.0%) in the surgery group had no detectable mutations. There is no significant difference in prognosis between ablation group and surgery group in terms of single BRAF gene mutation, BRAF accompanied with other gene mutations, non-BRAF mutations, and no detectable gene mutation (Table S2, see online supplementary material). Figure 2 shows the detailed distribution of gene mutations in patients with PTC who underwent different treatments. The specific distribution of gene

Table 2. Patients baseline between different gene mutations.

	Single BRAF gene mutation ($n = 112$)	BRAF accompanied with other gene mutations ($n = 75$)	Non-BRAF gene mutations ($n = 7$)	No gene mutation ($n = 7$)	*P*-value
Age (years), mean (SD)	40.93 (11.13)	42.16 (11.00)	38.57 (12.43)	41.86 (8.53)	0.796
Gender (%)					0.479
Female	89 (79.5)	57 (76.0)	7 (100.0)	6 (85.7)	
Male	23 (20.5)	18 (24.0)	0 (0.0)	1 (14.3)	
Tumor location (%)					0.631
Left	54 (48.2)	31 (41.3)	4 (57.1)	3 (42.9)	
Right	50 (44.6)	41 (54.7)	2 (28.6)	3 (42.9)	
Isthmus	8(7.2)	3(4.0)	1(14.3)	1(14.2)	
Tumor morphology (%)					0.410
Sharp margins	52 (46.4)	43 (57.3)	4 (57.1)	4 (57.1)	
Fairly clear margins	24 (21.4)	10 (13.3)	0 (0.0)	0 (0.0)	
Blurred margins	36 (32.2)	22 (29.4)	3 (42.9)	3 (42.9)	
Tumor aspect ratio (%)					0.397
<1	57 (50.9)	36 (48.0)	6 (85.7)	2 (28.6)	
=1	2 (1.8)	3 (4.0)	0 (0.0)	0 (0.0)	
>1	53 (47.3)	36 (48.0)	1 (14.3)	5 (71.4)	
Tumor diameter (mm), mean (SD)	6.12 (2.06)	6.28 (2.13)	7.03 (2.61)	5.71 (2.21)	0.636
Tumor volume (ml), mean (SD)	0.07 (0.07)	0.09 (0.09)	0.08 (0.07)	0.07 (0.05)	0.732
TI-RADS (%)					0.213
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
2	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	
3	1 (0.9)	1 (1.3)	1 (14.3)	0 (0.0)	
4	30 (26.8)	25 (33.3)	2 (28.6)	1 (14.3)	
5	81 (72.3)	46 (61.4)	4 (57.1)	6 (85.7)	
6	0 (0.0)	2 (2.7)	0 (0.0)	0 (0.0)	

mutations in the ablation group and surgery group is further detailed in Fig. S2A and S2B, respectively, see online supplementary material.

Comparison of DFS and recurrence in relation to genetic mutations

Notably, there is no significant difference in DFS between ablation group and surgery group (HR 0.378, 95% CI 0.038–3.786, $P = 0.39$) (Fig. 3). As of November 2024, 3 patients in the ablation group and 1 patient in the surgery group experienced disease progression ($P = 0.360$). Additionally, 2 patients in the ablation group experienced local recurrence, while no local recurrences were observed in the surgery group. Neither group exhibited cervical lymph node metastasis and distant metastases were not detected. There were no cancer-related deaths or occurrences of other types of thyroid cancer. All cases of local recurrence or new tumors underwent repeat ablation or surgery (Table 3). Table S3, see online supplementary material, shows the distribution of different gene mutation types in the ablation and surgery groups, indicating that there is no significant difference in gene mutation types between the two groups.

Of the 2 patients in the ablation group who experienced recurrence, both had BRAF mutations. Patient A had a single BRAF mutation, while Patient B had a BRAF mutation along with additional gene mutations. Despite being the same age, Patient A presented with a smaller tumor volume and experienced shorter DFS of 6 months whereas Patient B had a larger tumor volume but a longer DFS of 18 months. This suggests that while the presence of a BRAF mutation may influence DFS in patients undergoing ablation, co-occurring gene mutations alongside BRAF may contribute to prolonged DFS (Table S4. see online supplementary material).

Treatment variables

All patients successfully underwent their respective treatments, either ablation or surgery. The mean ablation duration was 0.29 ± 0.04 h, significantly shorter than the mean surgery time of 1.31 ± 0.58 h. No bleeding or postoperative hematoma was observed in the ablation group, while the mean blood loss in the surgery group was 8.72 ± 3.74 ml. The average treatment cost was notably lower in the ablation group (17 669.73 ± 175.14 CNY) compared to the surgery group (35 757.29 ± 2 781.39 CNY). Hospital stays were also significantly shorter in the ablation group (1.00 ± 0 days) vs. the surgery group (2.88 ± 0.41 days). All these differences were statistically significant ($P < 0.001$; Table 4).

Treatment safety

The overall complication rate was significantly lower in the ablation group (0%) compared to the surgery group (26.73%). In the surgery group, complications included postoperative fever in 1 patient (1.0%), cervical pain in 5 patients (5.0%), and nausea or vomiting in 2 patients (2.0%), all resolving within 24 h. Temporary hypoparathyroidism occurred in 19 patients (18.8%). No cases of permanent hypoparathyroidism, recurrent laryngeal nerve injury, postoperative hypertension, or infection were reported in either group (Table 4).

Patients after surgery routinely required thyroid hormone supplementation, while none of the ablation group needed hormone therapy. At the last follow-up, 69 patients (68.3%) in the surgery group were dependent on levothyroxine to maintain normal thyroid function, but 32 patients (31.7%) exhibited abnormal thyroid hormone levels, requiring dosage adjustments. In contrast, 93 patients (93.0%) in the ablation group maintained normal thyroid function without medication, with only

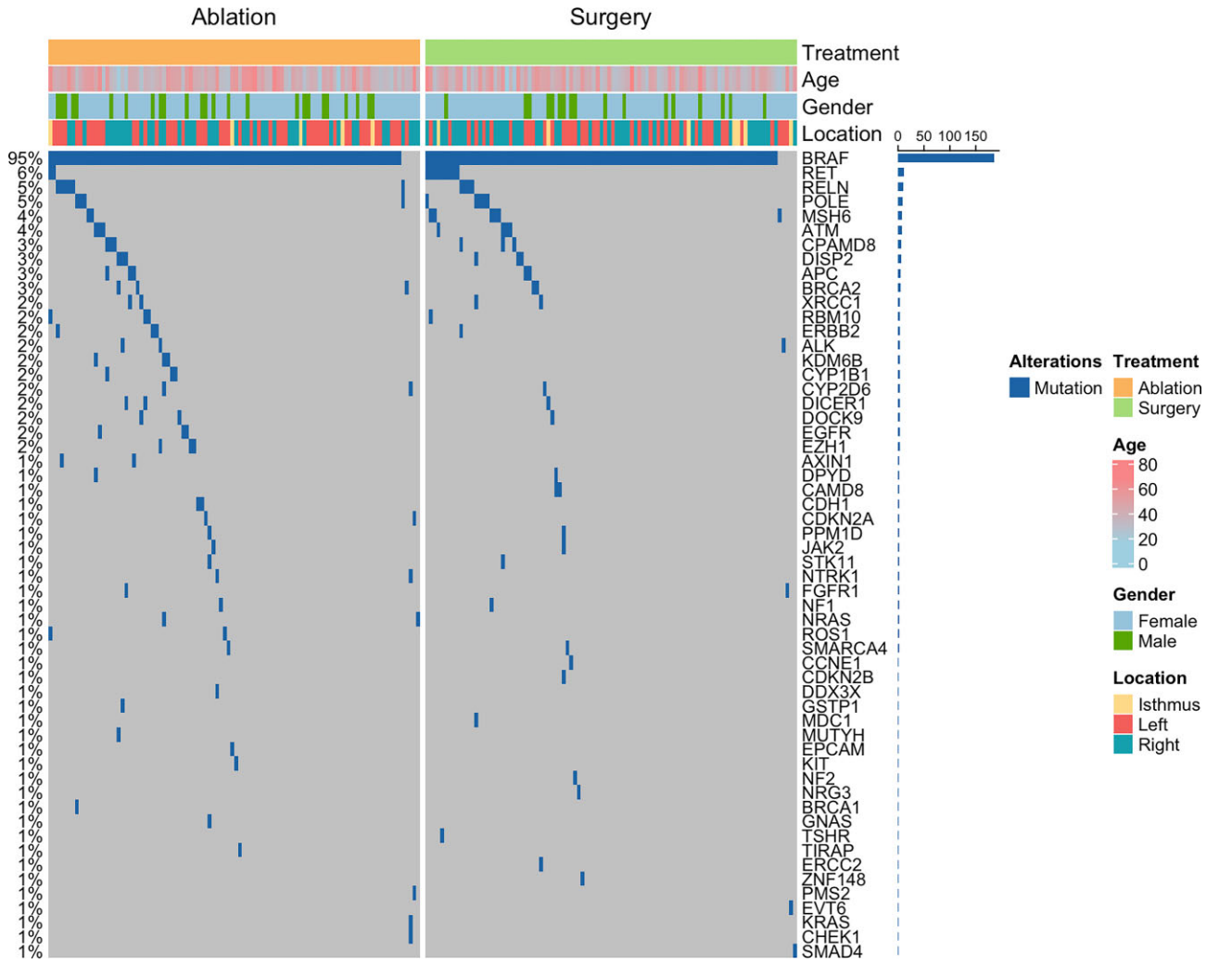

Figure 2. Distribution of genetic mutations, demographic characteristics, and treatment types among patients with low-risk PTC. The figure shows the frequency of genetic mutations in patients undergoing ablation and surgery, with B-Raf proto-oncogene, serine/threonine kinase V600E (BRAF V600E) mutations being the most common.

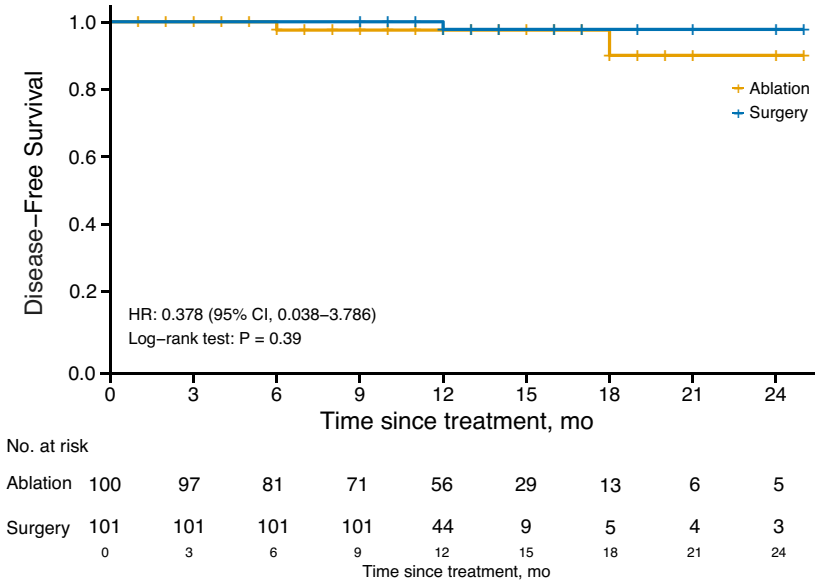

Figure 3. DFS curves of ablation vs. surgery. Kaplan–Meier curve illustrating DFS for patients with low-risk PTC who underwent either ablation or surgery.

Table 3. Disease progression between ablation and surgery groups.

	Ablation (n = 100)	Surgery (n = 101)	P-value
Disease progression (%)			0.360
Cervical lymph node metastasis	0 (0.0)	0 (0.0)	
Local tumor progression[a]	2 (2.00)	0 (0.0)	
Tumor recurrence	1 (1.0)	1 (1.0)	
Distant metastasis	0 (0.0)	0 (0.0)	
Recurrence location (%)			0.368
PTC-RT[b]	1 (1.0)	0 (0.0)	
PTC-LT[c]	0 (0.0)	1 (1.0)	

[a]Local tumor progression, the tumor continues to grow within the ablation zone. [b]PTC-RT, PTC of the right lobe. [c]PTC-LT, PTC of the left lobe.

Table 4. Complications and hospitalizations in ablation and surgery groups.

	Ablation (n = 100)	Surgery (n = 101)	P-value
Complication (%)			<0.001
Postoperative fever	0 (0.0)	1 (1.0)	
Postoperative cervical pain	0 (0.0)	5 (5.0)	
Postoperative nausea	0 (0.0)	2 (2.0)	
Temporary hypoparathyroidism	0 (0.0)	19 (18.8)	
Postoperative hypertension	0 (0.0)	0 (0.0)	
Hemorrhage (ml), mean (SD)	0.00 (0.00)	8.72 (3.74)	<0.001
Hospitalization time (days), mean (SD)	1.00 (0.00)	2.88 (0.41)	<0.001
Treatment time (h), mean (SD)	0.29 (0.04)	1.31 (0.58)	<0.001
Cost (CNY), mean (SD)	17 669.73 (175.14)	35 757.29 (2781.39)	<0.001

7 patients (7.0%) displaying mild hormonal abnormalities (Fig. S3, see online supplementary material). The majority of abnormalities in the surgery group involved reduced thyroid-stimulating hormone (TSH) levels, highlighting the importance of dynamic hormone dose adjustments to prevent drug-induced hyperthyroidism and reduce long-term cardiovascular risks.

Complete absorption of the ablation area takes ~2 years after thyroid ablation. In this study, the mean pre-ablation tumor volume was 0.08 ± 0.08 ml, whereas the ablation zone volume at the final follow-up was 0.60 ± 0.73 ml (Table S5, see online supplementary material). The ablation zone exhibited limited shrinkage during follow-up, often remaining larger than the original tumor size due to post-ablation processes such as inflammation, liquefaction, and fibrosis. By the final follow-up, all patients demonstrated a complete response (Fig. 4).

This study evaluated the efficacy of ablation vs. surgery in treating low-risk PTC based on genetic mutation analysis. The results indicate that ablation offers similar efficacy to surgery, with significantly lower complication rates, shorter hospital stays, and reduced treatment costs. No significant differences in disease progression were observed between the two groups. These results suggest that ablation may be a viable and effective treatment option for low-risk PTC. However, while short-term outcomes are promising, further research is necessary to confirm the long-term efficacy of ablation. Larger, multi-center studies with extended follow-up periods are essential to better understand its impact on recurrence rates and overall prognosis. These findings will be instrumental in guiding future clinical decision-making and optimizing treatment strategies for low-risk PTC.

Discussion

This study prospectively included patients with low-risk PTC who underwent either ablation or surgery at SYSMH between January 2022 and November 2024, aiming to evaluate the efficacy and prognosis of these treatment modalities. The findings revealed no significant difference in DFS between the two groups. However, the ablation group demonstrated several advantages, including fewer complications, faster recovery, shorter hospital stays, and lower treatment costs. Notably, patients treated with ablation did not require long-term thyroid hormone replacement therapy, contributing to improved quality of life.

Importantly, our results suggest that US-guided ablation therapy is effective and safe for patients with low-risk genetic mutations, such as BRAF and RAS. These patients did not exhibit increased recurrence risk after ablation therapy. Subgroup analyses further demonstrated no significant differences in outcomes based on variables such as age, sex, tumor location, diameter, or volume. The comparable safety and efficacy across these subgroups underscore the broad applicability of ablation therapy in low-risk PTC cases. Unlike most studies that rely solely on pathological and imaging-based risk stratification, this study uniquely incorporated genetic testing into the pre-ablation screening process. This approach aligns with real-world research, where clinical decisions increasingly rely on genetic profiling to provide more personalized and precise treatment strategies for thyroid cancer. The approach excluded patients with a high risk of metastasis, thereby optimizing treatment outcomes. By refining patient selection, genetic testing enhanced both the safety and efficacy of ablation therapy. For example, the recurrence rates observed in previous studies—5.8% in Guo *et al.* [12] and 7.7% in Yan *et al.* [25]—were higher than those reported in our study. Additionally, treatment variables such as operation time, hospitalization duration, complication rates, and economic costs favored ablation, consistent with previous findings [26–29]. Notably, patients undergoing ablation therapy avoided the need for levothyroxine or other hormone supplementation, further reinforcing the clinical benefits of this minimally invasive approach.

US-guided ablation therapy offers multiple advantages over traditional surgery. As a minimally invasive procedure, it

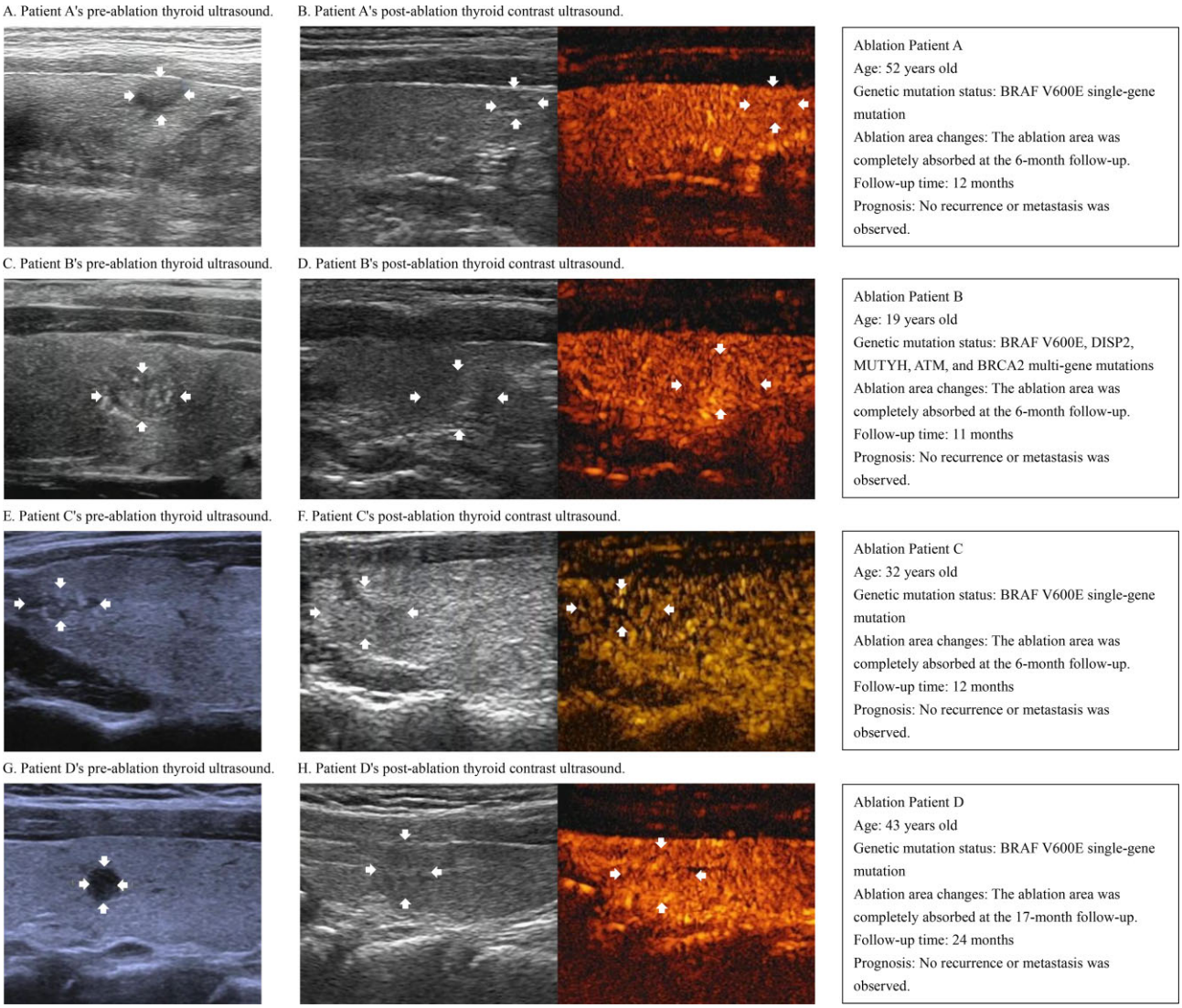

Figure 4. US images for patients with thyroid carcinoma before and after MWA. (**A**) Pre-ablation thyroid US of Patient A. (**B**) Post-ablation thyroid CEUS of Patient A. (**C**) Pre-ablation thyroid US of Patient B. (**D**) Post-ablation thyroid CEUS of Patient B. (**E**) Pre-ablation thyroid US of Patient C. (**F**) Post-ablation thyroid CEUS of Patient C. (**G**) Pre-ablation thyroid US of Patient D. (**H**) Post-ablation thyroid CEUS of Patient D.

minimizes thyroid tissue disruption, reducing recovery time, hospital stays, and healthcare costs. Precision in targeting the treatment area enables the preservation of healthy thyroid tissue, maintaining stable thyroid function and eliminating the need for lifelong hormonal therapy [30–32]. This benefit enhances the quality of life for patients, particularly those concerned about medication dependence or side effects associated with hormone therapy.

Moreover, ablation therapy's high procedural repeatability is a key advantage. Residual or recurrent tumors can be addressed with re-ablation, which is less complex and traumatic than repeat surgery. This makes ablation particularly suitable for elderly or frail patients, or those with comorbidities who are not ideal surgical candidates [33]. As molecular diagnostics advance, incorporating more sophisticated genetic screening methods could further personalize treatment and optimize outcomes [34, 35]. Although this study primarily focuses on low-risk PTC, the application of MWA in intermediate- and high-risk patients has gained increasing attention in recent years. For patients with larger tumors or more aggressive genetic mutations, MWA may serve as a viable alternative treatment option. With advancements in genetic testing and improvements in the precision and safety of ablation techniques, future research should further assess the efficacy and safety of MWA in higher-risk PTC populations to broaden its clinical applicability.

Despite its promising findings, this study has limitations. Being a single-center retrospective study with a relatively small sample size, the results may be subject to selection bias and limited generalizability. Additionally, the short follow-up period precludes comprehensive assessment of long-term recurrence and survival outcomes. Furthermore, this study excluded patients with high-risk genetic mutations, leaving the effects of ablation therapy in this population unexamined. Future studies should conduct larger-scale, multicenter research with extended follow-up periods to improve the external generalizability of findings and validate the applicability of ablation therapy across diverse clinical settings. Additionally, expanding the sample size and incorporating a more diverse patient population, particularly those with high-risk genetic mutations, will further clarify the scope of ablation therapy. With continuous advancements in genetic diagnostics and

ablation technology, this approach may become viable for patients at higher risk of recurrence or metastasis, providing a more comprehensive scientific foundation for the precision treatment of PTC.

The rapid advancement of gene sequencing technology has ushered in a new era of precision diagnosis and treatment for thyroid cancer. NGS has enabled the detection of key driver-gene mutations, such as BRAF V600E, RAS, and RET/PTC rearrangements, providing a robust basis for risk stratification and personalized management of patients. Precision treatment strategies based on genetic profiling allow for the early identification of high-risk patients and the guidance of individualized therapeutic decisions. In the future, multimodal data analysis integrating genetic profiling and imaging features may further optimize personalized treatment strategies for thyroid cancer, enhancing the precision and safety of ablation therapy. With the deepening application of artificial intelligence and machine learning in medicine, intelligent decision-making models that integrate molecular characteristics, imaging data, and clinical indicators are expected to further refine treatment personalization, offering patients more optimized therapeutic options. This precision medicine approach not only reduces unnecessary surgical interventions and alleviates the healthcare burden but also maximizes patient survival benefits and quality of life.

In conclusion, ablation therapy is a safe and effective alternative for treating low-risk PTC, offering significant clinical advantages over surgery. By incorporating genetic testing into patient selection, this approach enhances precision, safety, and efficacy. Although the follow-up period was relatively short, the current data support the use of ablation therapy in this context. Further research is required to validate long-term outcomes, but ablation therapy holds considerable promise for advancing thyroid cancer treatment.

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Author contributions

Yunfang Yu (Conceptualization, Funding acquisition, Writing – review & editing), Yuxin Shen (Data curation, Formal analysis, Writing – original draft, Writing – review & editing), Yujie Tan (Writing – original draft, Writing – review & editing), Yisikandaer Yalikun (Data curation, Formal analysis, Writing – original draft, Writing – review & editing), Tian Tian (Formal analysis, Writing – original draft, Writing – review & editing), Qingqing Tang (Formal analysis, Writing – original draft, Writing – review & editing), Qiyun Ou (Conceptualization, Writing – original draft, Writing – review & editing), Yue Zhu (Conceptualization, Writing – original draft, Writing – review & editing), and Miaoyun Long (Conceptualization, Writing – original draft, Writing – review & editing).

Supplementary data

Supplementary data are available at *PCMEDI Journal* online.

Conflicts of interest

None declared.

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