Ultrasound and Gene-Guided Microwave Ablation versus Surgery for Low-Risk Papillary Thyroid Carcinoma: A Prospective Study

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Mini Abstract

This study examines the efficacy of ultrasound-guided, gene-based microwave ablation compared to surgery in managing low-risk papillary thyroid carcinoma. It highlights the critical role of genetic testing in tailoring treatment strategies, thereby improving patient safety and optimizing clinical outcomes.

Abstract

Objective: This study evaluates and compares the efficacy and prognosis of ultrasound and gene-based microwave ablation (MWA) and surgical treatment in patients with lowrisk papillary thyroid carcinoma (PTC), emphasizing the influence of genetic mutations on low-risk patients' 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 ultrasound 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 ultrasound and contrast-enhanced ultrasound.

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 (DFS) (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.

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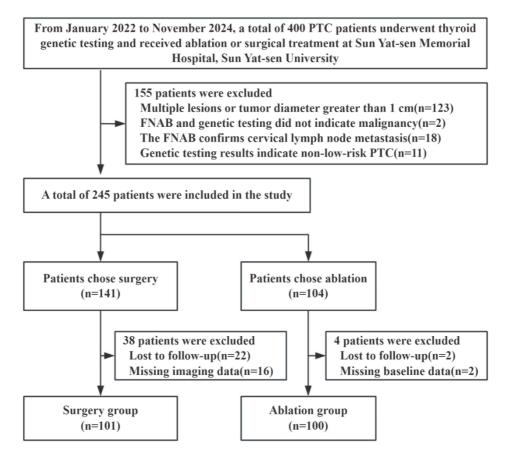
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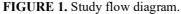
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Conclusion: For patients with low-risk genetic mutations, ablation provides comparable efficacy and DFS to surgery, with with significant benefits in safety, recovery, and overall cost. Guided by ultrasound and next-generation sequencing, precise patient 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*

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Study flowchart of patient inclusion for the study on low-risk PTC treatments at Sun Yat-sen Memorial Hospital. A total of 400 patients who underwent ablation or surgical treatment from January 2022 to November 2024 were initially screened for the prospectively observational cohort study. Exclusions included patients with multiple lesions or tumor diameters greater than 1 cm (n=123), 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.

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 (%) | | | 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 (month), 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) | |

CDFI: Color Doppler Flow Imaging; FNAB: Fine Needle Aspiration Biopsy; SD: Standard Deviation; TBS: The Bethesda System for Reporting Thyroid Cytopathology; TI-RADS: American College of Radiology Thyroid Imaging, Reporting and Data System.

| | Single BRAF | BRAF | Non-BRAF | No gene | <i>P</i> -value |
|------------------------------|---------------|---------------------|---------------|--------------|-----------------|
| | gene mutation | accompanied | gene | mutation | |
| | (N=112) | with other | mutations | (N=7) | |
| | | gene | (N=7) | | |
| | | mutations (N=75) | | | |
| 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(14.3) | |
| 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 (32.1) | 22 (33.4) | 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 | 6.12 (2.06) | 6.28 (2.13) | 7.03 (2.61) | 5.71 (2.21) | 0.636 |
| (SD) | | | | | |
| 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 (61.3) | 4 (57.1) | 6 (85.7) | |
| 6 | 0 (0.0) | 2 (2.7) | 0 (0.0) | 0 (0.0) | |

TABLE 2. Patients baseline between different gene mutations.

SD: Standard Deviation; TBS: The Bethesda System for Reporting Thyroid Cytopathology; TI-RADS: American College of Radiology Thyroid Imaging, Reporting and Data System.

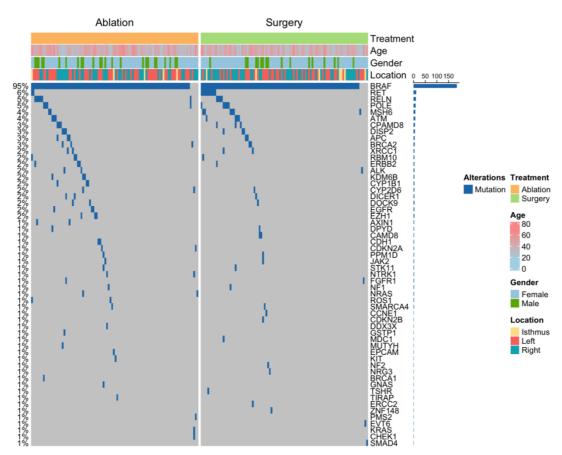


FIGURE 2. Distribution of genetic mutations, demographic characteristics, and treatment types among patients with low-risk papillary thyroid carcinoma.

The figure shows the frequency of genetic mutations in patients undergoing ablation and surgery, with B-Raf protooncogene, serine/threonine kinase V600E (BRAF V600E) mutations being the most common.

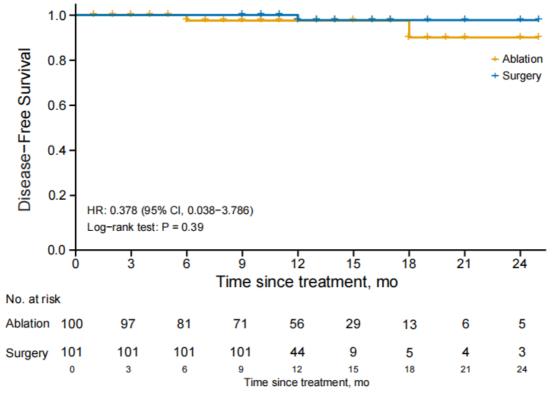


FIGURE 3. Disease-free survival curves of ablation versus surgery.

Kaplan-Meier curve illustrating disease free survival (DFS) for patients with low-risk PTC who underwent either ablation or surgery.

TABLE 3. Disease progression between ablation and surgery groups.

| 0,001 | | |
|------------------|---|---|
| Ablation (N=100) | Surgery (N=101) | <i>P</i> -value |
| | | 0.360 |
| 0 (0.0) | 0 (0.0) | |
| 2 (2.00) | 0 (0.0) | |
| 1 (1.0) | 1 (1.0) | |
| 0 (0.0) | 0 (0.0) | |
| | | 0.368 |
| 1 (1.0) | 0 (0.0) | |
| 0 (0.0) | 1 (1.0) | |
| | Ablation (N=100) 0 (0.0) 2 (2.00) 1 (1.0) 0 (0.0) 1 (1.0) | Ablation (N=100) Surgery (N=101) 0 (0.0) 0 (0.0) 2 (2.00) 0 (0.0) 1 (1.0) 1 (1.0) 0 (0.0) 0 (0.0) 1 (1.0) 0 (0.0) |

Local tumor progression, the tumor continues to grow within the ablation zone.

PCT: Papillary Thyroid Carcinoma; PTC-RT: PTC of the Right Lobe; PTC-LT, PTC of the Left Lobe.

| | Ablation | Surgery | <i>P</i> -value | |
|-------------------------------------|-------------------|--------------------|-----------------|--|
| | (N=100) | (N=101) | | |
| 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 (d), 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) | 17669.73 (175.14) | 35757.29 (2781.39) | < 0.001 | |

| TABLE 4. Com | plications and | l hospitalizations ir | n ablation and | surgery groups. |
|--------------|----------------|-----------------------|----------------|-----------------|
| | | | | |

SD: Standard Deviation.

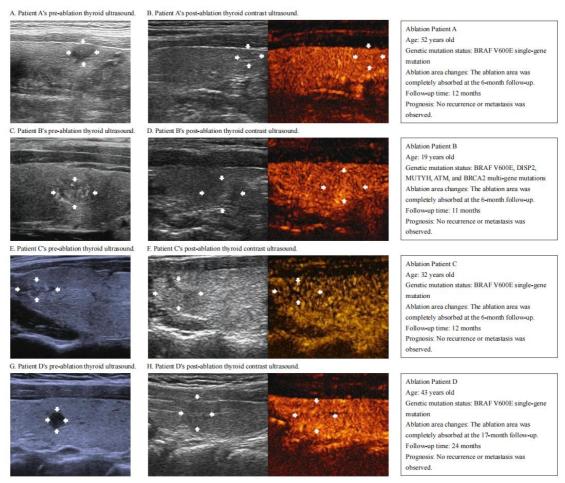


FIGURE 4. Ultrasound images for patients with thyroid carcinoma before and after Microwave ablation.A) Pre-ablation thyroid ultrasound of patient A. B) Post-ablation thyroid contrast-enhanced ultrasound of patient A.C) Pre-ablation thyroid ultrasound of patient B. D) Post-ablation thyroid contrast-enhanced ultrasound of patient B.

E) Pre-ablation thyroid ultrasound of patient C. F) Post-ablation thyroid contrast-enhanced ultrasound of patient C.G) Pre-ablation thyroid ultrasound of patient D. H) Post-ablation thyroid contrast-enhanced ultrasound of Patient D.

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