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Chronological Age and Outcomes after Ultrasound-guided Thermal Ablation for Thyroid Nodules: A Single-center Retrospective Cohort Study

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Abstract

Background

Chronological age is often used to select candidates for minimally invasive treatment, but whether age itself affects outcomes after ultrasound-guided thermal ablation of thyroid nodules is unclear. We examined whether age was associated with postablation ablation-zone volume reduction and treatment-related complications, using both a clinically relevant age threshold and continuous age.

Methods

This single-center retrospective cohort study included patients who underwent thyroid radiofrequency or microwave ablation and completed at least one ultrasound follow-up. Age at first treatment was categorized as older than 55 years or 55 years or younger, based on the thyroid cancer staging threshold, and also analyzed as a continuous variable and using conventional geriatric thresholds (> 60 and > 65 years). The primary effectiveness outcome was patient-level postablation ablation-zone volume reduction ratio (VRR) at 9–15 months, estimated using multivariable linear regression with robust standard errors; IPTW and IPCW sensitivity analyses were also performed. The primary safety outcome was any recorded treatment-related complication, summarized as risk differences with 95% CIs.

Results

Among 799 patients (669 aged ≤ 55 years, 130 aged > 55 years), 272 contributed to the primary 9-15-month effectiveness analysis. Raw median VRR was 93.3% (younger) and 93.8% (older); adjusted VRR was 86.5% and 86.3%, respectively, with an older-minus-younger difference of -0.3 percentage points (95% CI: -8.0, 7.5; *P* = .94). Supportive estimates from last-imaging, IPCW-weighted, and IPTW-weighted analyses ranged from 2.9 to 3.6 percentage points, all in the same direction. Any recorded complication occurred in 67 of 669 (10.0%) younger and 11 of 130 (8.5%) older patients (risk difference, -1.6 percentage points; 95% CI: -6.0, 4.8; *P* = .75); no serious complications occurred. Modeling age continuously or using 60- and 65-year thresholds gave directionally consistent, though imprecise, results.

Conclusions

Chronological age, on its own, did not distinguish short-term effectiveness or recorded safety in this single-center cohort of patients selected for ultrasound-guided thyroid thermal ablation. Across the age definitions and sensitivity analyses used here, older patients had similar adjusted postablation ablation-zone volume reduction and no higher rate of recorded complications than younger patients. Ablation candidacy for older adults should rest on lesion characteristics, technical feasibility, comorbidity, functional status, and patient goals rather than an age cutoff. Frailty and comorbidity were incompletely

captured, so these results should not be extended to unselected or functionally dependent older populations.

Background

The clinical spectrum of thyroid disease in China is shifting as the population ages and high-resolution ultrasonography becomes more widely used. Thyroid nodule prevalence rises with age: ultrasound-based estimates range from approximately 20% in young adults to as high as 70% in older adults, with a female predominance.[19, 20] Hypertension, diabetes, cardiovascular disease, and chronic pulmonary or renal disease are also common in older patients and can interact with thyroid disease in ways that shape diagnostic and treatment choices.[19] With longer life expectancy, more sensitive imaging, and greater multimorbidity all increasing together, managing thyroid nodules now depends as much on a patient's overall health status and tolerance for treatment as on the characteristics of the lesion itself.

Older adults are not a uniform high-risk group but a heterogeneous one. Eligibility for surgery or ablation should not rest on chronologic age alone; reduced physiologic reserve, cardiopulmonary or renal impairment, frailty, anticoagulant or antiplatelet therapy, and multimorbidity are what actually lower anesthesia tolerance and prolong recovery.[19, 21] A fit, independent older patient may tolerate thyroid surgery with acceptable risk, while a patient with multiple comorbidities or poor functional status faces a higher risk of perioperative complications and a greater loss of quality of life.[21] Treatment goals in this group therefore extend beyond disease control alone to preservation of thyroid function, less procedural trauma, maintained quality of life, shorter hospital stays, and a quicker return to daily activities.

RFA, MWA, and laser ablation together make up the ultrasound-guided thermal ablation options for thyroid nodules. Performed under local anesthesia with real-time ultrasound guidance, these techniques can lower treatment burden in appropriately selected patients: they spare more of the uninvolved thyroid, treat the nodule focally, and allow relatively short recovery.[2, 6, 22, 23] In an elderly benign-nodule cohort, RFA took less procedure time and carried fewer treatment-related consequences than thyroidectomy, and a meta-analysis focused on elderly patients likewise reported volume reduction after RFA, MWA, and laser ablation.[14, 15] Ablation is not a universal substitute for surgery; its role is to match local treatment intensity to disease risk, comorbidity burden, life expectancy, functional priorities, and what the patient actually wants.

Current guidelines and expert statements converge on a handful of settings where thyroid ablation may apply: symptomatic or enlarging benign nonfunctioning nodules; autonomously functioning nodules in patients who prefer an alternative to surgery or radioactive iodine; selected low-risk papillary thyroid carcinoma in patients who decline active surveillance and cannot or will not undergo surgery; and limited cervical recurrence or nodal metastasis when repeat surgery is high-risk, declined, or the disease no longer responds to radioactive iodine.[2–6, 22–27] Recent Chinese, international, and North American statements have gone further to specify patient selection, operator training, technical safeguards, complication management, and follow-up, but they still treat ablation as an option for selected patients,

not a basis for expanding treatment indiscriminately.[22–27] Evidence to guide personalized management in older adults, however, remains thin: the limited ablation literature in this population is mostly about benign nodules, uses inconsistent age and outcome definitions, and rarely compares older with younger patients treated with both RFA and MWA.[14, 15, 19, 28] Whether age itself blunts ablation-zone involution or raises the complication rate is therefore still an open question.

Our hypothesis was that, after adjusting for measured patient, lesion, and treatment characteristics, older chronological age would not be associated with lower postablation ablation-zone volume reduction or a higher recorded complication rate, whether analyzed using the 55-year threshold, broader age strata, or as a continuous variable. This study accordingly examined whether chronological age was associated with the effectiveness and safety of ultrasound-guided thyroid thermal ablation, and tested the robustness of the effectiveness findings against alternative age definitions, follow-up windows, IPTW, and IPCW. Because documentary evidence of their clinical justification and prespecification could not be located, the − 10-percentage-point effectiveness and + 5-percentage-point safety margins used for comparison were treated as exploratory rather than confirmatory.

Methods

Study Design and Ethics

This retrospective observational cohort study was conducted at the China-Japan Friendship Hospital, Beijing, China. The study was approved by the Ethics Committee of the China-Japan Friendship Hospital. The informed consent was obtained. The study is reported with reference to the Strengthening the Reporting of Observational Studies in Epidemiology statement.[17, 18]

The study included eligible patients treated between October 13, 2021, and June 9, 2026, as determined from the actual treatment dates in the study cohort. Clinical follow-up information was updated through July 21, 2026, and the study dataset was finalized on July 22, 2026.

Participants

Patients who underwent ultrasound-guided radiofrequency ablation or microwave ablation for thyroid nodules at the study center were retrospectively reviewed. Among 918 treated patients in the source database, 799 patients who completed at least one ultrasound follow-up were included in the final analysis. Patients without ultrasound follow-up were excluded.

For patients who underwent more than one ablation procedure, age group was determined according to age at the first recorded procedure. Patients were classified as older than 55 years or 55 years or younger, based on the 55-year cutoff used in the eighth edition of the American Joint Committee on Cancer TNM staging system for differentiated thyroid cancer. The effectiveness analysis included patients with a valid immediate postablation ablation-zone volume and at least one valid follow-up

volume. For the 12-month effectiveness analysis, examinations performed 9–15 months after treatment were considered eligible, and the examination closest to 12 months was selected for each lesion. Lesion-level results were then summarized at the patient level. This threshold is not a conventional geriatric definition; sensitivity analyses therefore used age as a continuous variable (per 5-year increase) and conventional geriatric thresholds of 60 and 65 years where sample size allowed. Comorbidity data, including hypertension, diabetes mellitus, coronary artery disease, cerebrovascular disease, chronic pulmonary disease, and renal impairment, were recorded for a subset of patients and summarized descriptively; these data were too incomplete to support risk-adjusted or frailty-based analyses.

Disease Classification and Treatment Eligibility

Lesions were classified as malignant or suspicious for malignancy, benign, or not definitively characterized according to the available clinical, cytologic, histologic, and ultrasound findings. For the disease-nature covariate reported in Table 1 and used in the adjusted models, benign and not-definitively-characterized lesions were combined into a single non-malignant/suspicious category, because the study database records disease nature as this binary distinction rather than as three separate categories. Disease nature was included as a covariate because its distribution differed between age groups and might influence treatment selection and follow-up. For malignant or suspicious lesions, diagnosis and risk assessment were based on cytologic or core-needle biopsy findings and high-resolution ultrasound evaluation of the thyroid and cervical lymph nodes. Before ablation, lesion size, location, relationship to the thyroid capsule, isthmus involvement, proximity to the trachea, esophagus, and expected recurrent laryngeal nerve region, suspicious cervical lymph nodes, gross extrathyroidal extension, and the feasibility of hydrodissection or other protective maneuvers were assessed. Lesions were classified as being in a dangerous location if the operator recorded them as adjacent to the tracheal cartilage, adjacent to the thyroid capsule, or located within the isthmus; these were categorical operator judgments rather than measured distances, as the source records do not include a numeric distance field. Ablation was considered after discussion of available management options and confirmation of the patient's preference for thyroid-preserving treatment. These anatomic and procedural selection principles were applied throughout the cohort. For benign lesions, benignity was established by needle biopsy. Eligibility also required coagulation test results within the normal range and no contraindications to thermal ablation.

Table 1
Baseline Characteristics of the Study Cohort

Characteristic	Age ≤ 55 y (n = 669)	Age > 55 y (n = 130)	SMD
Age, y	38.0 (33.0–45.0)	60.0 (57.0–65.0)	3.333
Female	493/669 (73.7%)	102/130 (78.5%)	0.112
Malignant or suspicious lesion	525/669 (78.5%)	69/130 (53.1%)	-0.556
Number of lesions	1.0 (1.0–2.0)	1.0 (1.0–2.0)	-0.070
Multiple lesions	245/669 (36.6%)	45/130 (34.6%)	-0.042
Preablation nodule volume, mL	0.1 (0.0-0.3) [n = 641]	0.3 (0.1–4.7) [n = 122]	0.332
Immediate postablation ablation-zone volume, mL	1.8 (1.3–2.9) [n = 558]	2.1 (1.4–4.7) [n = 107]	0.268
Dangerous location	385/669 (57.5%)	65/130 (50.0%)	-0.152
Microwave ablation	52/669 (7.8%)	23/130 (17.7%)	0.301
Treatment year	2024.0 (2023.0-2025.0)	2025.0 (2023.0-2025.0)	0.086

Data are median (IQR) or n (%). Available n is shown in brackets for variables with missing data. SMDs are calculated as age > 55 y minus age ≤ 55 y. SMD = standardized mean difference.

Ultrasound Examination and Volume Measurement

Ultrasound examinations were performed using a Philips EPIQ Elite ultrasound system (Philips Healthcare). Pretreatment ultrasound planning assessed lesion size, number, location, composition, vascularity, capsule relationship, isthmus involvement, cervical lymph nodes, and proximity to the trachea, esophagus, and expected recurrent laryngeal nerve region. Lesions near critical perithyroidal structures were evaluated for whether hydrodissection could create a safe treatment path and, when clinically indicated, an adequate circumferential treatment margin. Ablation-zone volume was calculated as

$$V = \pi abc/6$$

where a, b, and c were orthogonal diameters. When only two valid diameters were available, volume was estimated as $\pi ab^2/6$, with the larger measurement assigned to a and the smaller to b. Three-diameter measurements were prioritized over two-diameter estimates.

The immediate postablation ablation-zone volume was the confirmed baseline for the effectiveness endpoint. When both contrast-enhanced and gray-scale measurements were available, contrast-enhanced measurements were prioritized; otherwise, valid gray-scale measurements were used. At follow-up, the modality matching the baseline examination was prioritized, followed by the alternative modality when the matching measurement was unavailable.

Thermal Ablation Procedure

All procedures were performed under real-time ultrasound guidance by a single experienced operator with 30 years of experience in diagnostic ultrasonography and 5 years of experience in thyroid thermal ablation. The choice of radiofrequency ablation or microwave ablation was based on preprocedural planning and the operator's assessment of lesion anatomy, feasibility of safe applicator placement, and need for protection of adjacent critical structures. A total of 805 ablation procedures were performed, including 725 radiofrequency ablations, 77 microwave ablations, and 3 procedures with unclear ablation modality.

Local anesthesia with 2% lidocaine was used in 800 of 805 procedures. Hydrodissection with normal saline was performed in 798 of 805 procedures, when necessary, to separate the target lesion from the thyroid capsule, trachea, esophagus, or expected recurrent laryngeal nerve region. Cystic-fluid aspiration was performed in 32 procedures.

Radiofrequency ablation was performed using an S-1500 radiofrequency generator and a 10-141281 electrode with a 10-cm shaft and 1-cm active tip (Shanghai Maide, Shanghai, China), at a nominal power of 35 W. Microwave ablation was performed using an MTC-3C microwave generator and an MTC-3CA-I/1 microwave antenna with a 10-cm shaft and 1-cm active tip (Nanjing Weijing, Nanjing, China), at a nominal power of 35 W. A transisthmic approach and moving-shot technique were used when appropriate. The applicator route and ablation strategy were individualized according to nodule size, location, relationship to adjacent structures, expected ablation extent, and patient tolerance.

During ablation, ultrasound was used continuously to monitor the target lesion and adjacent structures. For malignant nodules, the procedural endpoint was complete coverage of the lesion by the ablation zone, with an intended circumferential margin of more than 5 mm beyond the lesion boundary. For benign nodules, the primary goal was volume reduction, and near-total ablation was attempted when feasible, provided that the safety of adjacent critical structures and patient tolerance could be maintained.

Approximately 1 hour after ablation, contrast-enhanced ultrasound was performed using sulfur hexafluoride microbubbles (SonoVue) to evaluate the treated region. Absence of enhancement was considered the imaging endpoint. For malignant nodules, if residual enhancement was observed, additional ablation was performed immediately until the nonenhancing zone covered the lesion with the intended margin. Patients were observed for approximately 1 hour after treatment. Blood pressure, heart

rate, and peripheral oxygen saturation were monitored, and ultrasound was used to assess postprocedural bleeding. Phonation and hoarseness were evaluated before discharge.

Although immediate contrast-enhanced ultrasound was part of the institutional protocol, structured documentation of this item was available for only 37 of 805 procedures; therefore, it was not analyzed as a cohort-wide technical success endpoint.[1, 16]

Follow-up and Outcomes

Patients were followed according to routine clinical practice, with ultrasound examinations generally scheduled at approximately 1, 3, 6, 12, 18, and 24 months after ablation. For descriptive analyses, follow-up examinations were grouped into the corresponding nominal visit windows. Actual examination dates were used to calculate follow-up duration.

Primary Effectiveness Outcome

The primary effectiveness outcome was patient-level postablation ablation-zone VRR at 9–15 months. Lesion-level VRR was calculated as

$$\text{VRR}\ (\%) = (V_0 - V_t) / V_0 \times 100$$

where V0 was the immediate postablation ablation-zone volume and Vt was the follow-up volume. For each lesion, the examination closest to 12 months within the 9-15-month window was selected. For patients with multiple lesions, lesion-level VRRs were averaged to yield one patient-level outcome.

This endpoint differs from the conventional thyroid nodule VRR calculated from preablation nodule volume; therefore, absolute values were not directly equated with conventional VRRs in prior studies.

Primary Safety Outcome

The primary safety outcome was any recorded treatment-related complication in the 799-patient cohort. Events were grouped as voice- or nerve-related events, hemorrhage or hematoma, circulatory/vagal/systemic reactions, or other recorded events. No serious complications occurred. Hoarseness resolved within 1–6 months; all other recorded complications resolved on the treatment day. Routine laryngoscopy was performed.

Secondary and Supportive Outcomes

Supportive effectiveness outcomes included patient-level VRR at nominal 6, 12, and 24 months; VRR at the last valid imaging examination; and proportions with VRR of at least 50% and at least 75%. Follow-up completion was described at nominal 1, 3, 6, 12, 18, and 24 months among patients with sufficient calendar time to reach each visit.

Statistical Analysis

Continuous variables are presented as medians with interquartile ranges, and categorical variables as numbers and percentages. Baseline differences between patients older than 55 years and those aged 55 years or younger were assessed using standardized mean differences, with an absolute value of 0.10 or greater considered indicative of imbalance. Mann-Whitney U tests and Fisher exact tests were used as descriptive comparisons when appropriate.

The primary effectiveness outcome was analyzed at the patient level using multivariable linear regression with HC3 robust standard errors. The model adjusted for age group, follow-up time (including age-by-follow-up-time interaction terms), sex, log-transformed baseline ablation-zone volume, multiple-lesion status, treatment year, disease nature, and ablation modality. Adjusted volume reduction ratio estimates at 12 months and between-group differences were reported with two-sided 95% confidence intervals and *P* values. For patients with multiple lesions, lesion-level volume reduction ratios were averaged before patient-level analysis. In sensitivity analyses, age was additionally modeled as a continuous variable (per 5-year increase) and using conventional geriatric thresholds (> 60 and > 65 years) within a last-imaging longitudinal adjustment framework refitted directly from patient-level records that had passed internal data-quality review (excluding records flagged for anomalous volume reduction ratios, e.g., <-100%, and requiring a positive baseline ablation-zone volume). Baseline characteristics of patients with versus without imaging in the primary 9-15-month window were compared descriptively to assess selection related to missing follow-up. Interaction terms between age group and disease nature, baseline ablation-zone volume, dangerous location, multiple-lesion status, and ablation modality were tested to assess effect modification.

Additional analyses were performed at the nominal 6-, 12-, and 24-month follow-up time points using similar multivariable regression models. Inverse probability weighting was used in sensitivity analyses to assess the robustness of findings related to follow-up timing and missing 12-month imaging.

Safety outcomes were summarized as event rates and absolute risk differences with two-sided 95% confidence intervals, and groups were compared using Fisher exact tests. Exploratory margin-based and subgroup analyses were considered hypothesis-generating. No adjustment for multiple comparisons was applied.

All analyses were performed using Python 3.14.6, pandas 3.0.3, and NumPy 2.4.6. Two-sided *P* values less than .05 were considered statistically significant.

Results

Participant Flow

The source database contained 918 treated patients and 930 treatment courses. After exclusion of 119 patients without ultrasound follow-up, the manuscript cohort included 799 patients, 805 treatment

courses, and 1206 lesions. A valid immediate postablation ablation-zone baseline was available for 665 patients, 670 treatment courses, and 879 lesions. Valid longitudinal VRR data were available for 662 patients, 667 treatment courses, and 861 lesions. Of these 662 patients, 272 had a valid examination within the 9-15-month window and contributed to the primary effectiveness analysis (230 aged 55 years or younger and 42 older than 55 years). The remaining 390 patients had no valid examination in that window (325 and 65, respectively) but were not removed from the study cohort and remained eligible for other time-point, last-imaging, safety, and sensitivity analyses, as applicable (Fig. 1).

Baseline Characteristics

Among 799 patients, median age was 38.0 years (IQR, 33.0–45.0 years) in the younger group and 60.0 years (IQR, 57.0–65.0 years) in the older group. Female patients accounted for 493 of 669 (73.7%) and 102 of 130 (78.5%), respectively (SMD, 0.112). Malignant or suspicious lesions were more frequent in the younger group (525 of 669 [78.5%] vs 69 of 130 [53.1%]; absolute SMD, 0.556) (Table 1). Comorbidity data were recorded for 213 of 799 patients (26.7%: 168 younger, 45 older); hypertension was documented in 11 of 168 (6.5%) younger and 14 of 45 (31.1%) older patients (SMD, 0.662), and diabetes mellitus in three of 168 (1.8%) younger and five of 45 (11.1%) older patients (SMD, 0.387). No cases of coronary artery disease, cerebrovascular disease, chronic pulmonary disease, or renal impairment were documented in either group, which most likely reflects incomplete rather than absent disease; because of this incompleteness, comorbidity burden could not be used for risk adjustment (Additional file 1: Table S1).

Median preablation nodule volume was 0.1 mL (IQR, 0.0-0.3 mL; n = 641) in the younger group and 0.3 mL (IQR, 0.1–4.7 mL; n = 122) in the older group (SMD, 0.332). Median immediate postablation ablation-zone volume was 1.8 mL (IQR, 1.3–2.9 mL; n = 558) and 2.1 mL (IQR, 1.4–4.7 mL; n = 107), respectively (SMD, 0.268). MWA was used in 52 of 669 (7.8%) younger and 23 of 130 (17.7%) older patients (SMD, 0.301). Multiple lesions were present in 245 of 669 (36.6%) and 45 of 130 (34.6%), respectively (SMD, 0.042) (Table 1).

Primary Effectiveness Outcome

The primary analysis included 272 patients with valid imaging in the 9-15-month window. This was an endpoint-specific analysis subset rather than the sole effectiveness cohort; all 662 patients with valid longitudinal VRR data were included in the last-imaging analysis, and patients contributed to other analyses whenever their measurements met the corresponding endpoint definition. Raw median VRR was 93.3% in the younger group and 93.8% in the older group. Adjusted VRR at 12 months was 86.5% and 86.3%, respectively. The adjusted older-minus-younger difference was − 0.3 percentage points (95% CI: -8.0, 7.5; P = .9437) (Table 2; Fig. 2). The lower confidence limit (-8.0 percentage points) stayed above the exploratory − 10-percentage-point margin; because the margin's clinical basis and prespecification were not established, this result indicated compatibility with the margin rather than confirmation of noninferiority.

Table 2
Adjusted Ablation-zone Volume Reduction According to Age Group

Analysis	n ≤ 55/>55 y	Adjusted VRR, % ≤55 y	Adjusted VRR, % >55 y	Difference, pp	95% CI	*P* value
Primary 9-15-month window	230/42	86.5	86.3	-0.3	-8.0 to 7.5	.9437
Nominal 12-month visit	231/42	86.3	89.0	2.7	-3.3 to 8.7	.3771
Last valid imaging examination	555/107	85.2	88.8	3.6	-2.7 to 9.8	.2610

Differences are calculated as age > 55 y minus age ≤ 55 y. Models were adjusted for prespecified baseline and treatment covariates. VRR = volume reduction ratio; pp = percentage points.

Age as a Continuous Variable and Alternative Age Strata

In a last-imaging longitudinal model refitted directly from patient-level data after excluding records flagged for anomalous volume reduction ratios (635 patients with quality-reviewed last follow-up measurements), each 5-year increase in age was not associated with a meaningful change in adjusted volume reduction across the full age range of 17–82 years (-0.02 percentage points; 95% CI: -1.06, 1.03; P = .97). Using conventional geriatric thresholds within the same model, the adjusted difference was −2.3 percentage points (95% CI: -13.2, 8.6; P = .68; n = 44 aged > 60 years) for patients older than 60 years and − 11.0 percentage points (95% CI: -33.3, 11.3; P = .33; n = 20 aged > 65 years) for patients older than 65 years, both relative to younger patients; the > 65-year estimate was imprecise given the small number of older patients with quality-reviewed last-imaging data and should be interpreted as exploratory rather than definitive. As a validation check, reapplying this refitted model at the 55-year threshold yielded a difference of 4.0 percentage points (95% CI: -2.6, 10.6; n = 635), consistent in direction and magnitude with the primary last-imaging estimate reported above (3.6 percentage points; n = 662). The association between age group and adjusted volume reduction did not differ significantly by disease nature, baseline ablation-zone volume, dangerous location, multiple-lesion status, or ablation modality (all interaction P > .07).

Supportive Effectiveness Analyses

Median VRR increased over follow-up in both groups. At nominal 1, 3, 6, and 12 months, median VRR was 42.1%, 69.7%, 86.6%, and 93.4%, respectively, in the younger group and 34.6%, 64.1%, 79.3%, and 93.8% in the older group. Patient numbers decreased from 516 and 96 at 1 month to 231 and 42 at 12 months. At 24 months, data were available for only 45 younger and nine older patients (Fig. 3).

In node-specific adjusted analyses, the older-minus-younger difference was 0.6 percentage points at 6 months (95% CI: -16.4, 17.6; *P* = .9467; n = 484), 2.7 percentage points at 12 months (95% CI: -3.3, 8.7; *P* = .3771; n = 273), and 11.5 percentage points at 24 months (95% CI: -5.5, 28.4; *P* = .1839; n = 54). The 24-month estimate was imprecise.

At the last valid imaging examination, the adjusted difference was 3.6 percentage points (95% CI: -2.7, 9.8; *P* = .2610; n = 662) (Table 2; Fig. 2). The IPCW-weighted 12-month difference was 3.5 percentage points (95% CI: -2.5, 9.6; n = 240), and the IPTW-weighted last-imaging difference was 2.9 percentage points (95% CI: -3.3, 9.2; n = 662) (Additional file 1: Table S2).

Treatment-related Complications

Any recorded complication occurred in 67 of 669 (10.0%) younger patients and 11 of 130 (8.5%) older patients, corresponding to a risk difference of -1.6 percentage points (95% CI: -6.0, 4.8; *P* = .7465) (Table 3; Fig. 4). Voice- or nerve-related events occurred in 36 of 669 (5.4%) and six of 130 (4.6%) patients, respectively; hoarseness resolved within 1–6 months. Hemorrhage or hematoma occurred in 17 of 669 (2.5%) and one of 130 (0.8%) patients. Circulatory, vagal, or systemic reactions occurred in 18 of 669 (2.7%) and three of 130 (2.3%) patients. Other recorded events occurred in five of 669 (0.7%) and one of 130 (0.8%) patients. Events outside the voice/nerve category resolved on the treatment day. No serious complications were recorded.

Table 3
Treatment-related Complications According to Age Group

Outcome	**Age ≤ 55 y (n = 669)**	**Age > 55 y (n = 130)**	**Risk difference, pp**	**95% CI**	***P* value**
Any documented complication	67 (10.0)	11 (8.5)	-1.6	-6.0 to 4.8	.7465
Voice- or nerve-related event	36 (5.4)	6 (4.6)	-0.8	-3.9 to 4.5	.8327
Hemorrhage or hematoma	17 (2.5)	1 (0.8)	-1.8	-3.4 to 1.8	.3346
Circulatory, vagal, or systemic reaction	18 (2.7)	3 (2.3)	-0.4	-2.5 to 4.0	> .99
Other recorded event	5 (0.7)	1 (0.8)	0.0	-1.2 to 3.5	> .99
Serious complication	0 (0.0)	0 (0.0)	-	-	-

Data are n (%). Risk differences are calculated as age > 55 y minus age ≤ 55 y; CIs are Newcombe hybrid score intervals, and P values are from Fisher exact tests. Complication categories are not mutually exclusive because a patient could have more than one recorded event type. No serious complications occurred. pp = percentage points.

Because ultrasound follow-up was required for inclusion in the manuscript cohort, complications were also checked in the 119 excluded patients to assess whether this criterion biased the safety estimate. These patients had documented complication rates of 11 of 94 (11.7%) in the younger group and three of 25 (12.0%) in the older group, both numerically higher than the rates reported above. Combining all 918 treated patients raised the overall complication rate from 78 of 799 (9.8%) to 92 of 918 (10.0%), with rates of 78 of 763 (10.2%) in the younger group and 14 of 155 (9.0%) in the older group (Fisher exact P = .77); this was similar in direction and magnitude to the 799-patient estimate above, indicating that restricting the safety population to patients with ultrasound follow-up did not materially affect the age comparison, although it modestly understated the overall complication rate.

The upper confidence limit for any complication was 4.8 percentage points, 0.2 percentage points below the exploratory + 5-percentage-point margin. This proximity was considered borderline and did not support definitive safety noninferiority.

Follow-up Completeness and Weighting Diagnostics

Among patients with sufficient calendar time, imaging completion in the younger and older groups was 77.1% (516 of 669) and 73.8% (96 of 130) at 1 month; 66.5% (413 of 621) and 62.3% (71 of 114) at 6 months; and 44.8% (206 of 460) and 47.9% (34 of 71) at 12 months. At 24 months, completion was 16.9% (41 of 243) and 18.8% (nine of 48), respectively (Fig. 5).

A total of 531 patients had sufficient calendar opportunity for 12-month follow-up; 400 had complete IPCW covariates, and 240 had observed 12-month imaging. This calendar-time-eligible group of 531 was defined from the full 799-patient manuscript cohort using elapsed calendar time alone, independent of whether a patient's imaging data passed the validity checks required for the longitudinal VRR pipeline; it is therefore a different denominator from the 272-patient primary effectiveness population, which was drawn from the 662 patients with valid longitudinal VRR data and additionally required an actual examination within the 9-15-month window. IPCW weights among observed patients ranged from 0.7045 to 1.6615, with an effective sample size of 231.69. For IPTW, 662 patients were included; after 1st/99th percentile truncation, weights ranged from 0.4839 to 1.7690 and the effective sample size was 638.17. Maximum absolute SMD decreased from 0.511 before weighting to 0.101 after weighting, indicating substantial improvement with slight residual imbalance.

Comparison of Patients With and Without Primary 9-15-month Imaging

Among 531 patients with sufficient calendar time for 12-month follow-up, 240 had imaging within the primary 9-15-month window and 291 did not. Baseline and treatment characteristics were generally similar between the two groups, except for a higher proportion of female patients among those with primary-window imaging (78.3% vs 69.8%; SMD, -0.197; *P* = .029); no evidence of selection related to disease severity or safety events was observed (all other *P* > .19) (Additional file 1: Table S3).

Discussion

A practical question runs through the management of thyroid nodules in an ageing population: should chronological age itself influence eligibility for ultrasound-guided thyroid thermal ablation? Across the ways age was analyzed in this single-center retrospective cohort, the answer did not favor treating age as a barrier. Using the 55-year threshold relevant to thyroid cancer staging, the adjusted difference in postablation ablation-zone volume reduction was − 0.3 percentage points (95% CI: -8.0, 7.5); modeled continuously across the full age range, each 5-year increase in age shifted the estimate by -0.02 percentage points (95% CI: -1.06, 1.03); and the 60- and 65-year thresholds pointed the same way, though the latter estimate was imprecise given how few patients were older than 65. The complication risk difference was − 1.6 percentage points (95% CI: -6.0, 4.8), and the last-imaging, IPTW, and IPCW estimates all landed in the same direction. None of this establishes causation or equivalence: the design is observational, imaging follow-up was incomplete, the two age groups differed at baseline, and comorbidity data were incomplete.

Prior prospective and long-term thyroid-ablation studies have consistently found progressive volume reduction, alongside recognized risks such as voice change and hematoma.[7–9] RFA and MWA both reduce volume; the two modalities may diverge at later follow-up, and complication comparisons between them remain imprecise in some studies.[10–13] MWA was used more often in our older patients than in the younger group, highlighting the need to adjust for modality and to interpret any residual treatment-selection bias with caution.

Our absolute VRR values are not directly comparable to those in most of this literature. Most thyroid-ablation studies calculate VRR from the initial preablation nodule volume.[7–13] Our endpoint, in contrast, used the immediate postablation ablation-zone volume, describing how the treated zone shrinks rather than how much smaller the nodule became. Any future validation work should preserve this distinction rather than collapse the two definitions together.

Age-specific evidence for thyroid ablation is still sparse. One propensity-matched study of patients aged 60 years or older found substantial RFA-associated volume reduction and favorable treatment characteristics compared with thyroidectomy, and a meta-analysis focused on elderly patients similarly supported volume reduction after RFA, MWA, and laser ablation.[14, 15] Both were largely limited to benign nodules and did not test the > 55-versus-≤55 comparison in a heterogeneous cohort as we did here. Our data add to age-stratified observational evidence on this question, but they do not point to any single age cutoff as universally meaningful.

A common clinical dilemma sits behind these numbers: should chronological age alone gate eligibility for a lower-burden, thyroid-preserving intervention? Among patients already judged suitable for ablation, being older than 55 years was not linked to worse short-term imaging outcomes or more recorded complications in our cohort, and the sensitivity analyses modeling age continuously or at the 60- and 65-year thresholds told the same story. Read at face value, that argues against excluding otherwise suitable patients from thermal ablation on the basis of age alone. But comorbidity data were recorded for only

213 of 799 patients (26.7%), and even within that subset several conditions were never documented in either group, which rules out any meaningful adjustment for comorbidity burden. Frailty, functional status, polypharmacy, anticoagulant or antiplatelet use, and patient-reported outcomes were simply not available. It is these factors, not chronological age itself, that typically drive perioperative risk and treatment tolerance in older adults, so our results should not be extended to frail or functionally dependent patients; they describe a population already selected as fit for ablation, not an unselected older population.

Complication rates did not rise with age: patients older than 55 years had no higher recorded rate, and no serious complications occurred. Hoarseness took 1–6 months to resolve; every other recorded event resolved the same day. That said, this study did not compare ablation against surgery or surveillance, so it cannot claim superior safety, and the upper confidence limit for the risk difference sat close to the exploratory + 5-percentage-point margin. Complication grading and ascertainment were also retrospective and not formally standardized, which is a limitation rather than a settled strength. In short, recorded events did not increase with age in this cohort; that is not the same claim as safety being equivalent between age groups.

This study's strengths include building patient-level outcomes for patients with multiple lesions, defining the primary window as an actual 9-15-month interval, reporting effect estimates with confidence intervals, and running sensitivity analyses for both measured confounding and missing imaging. We also reconstructed the cohort and endpoint flow explicitly and reported weight distributions, effective sample sizes, and residual balance.

Several limitations should be considered. The retrospective, single-center design leaves treatment-selection bias, residual confounding, and center- or operator-specific effects unaddressed, and 55 years is not a universal definition of older age; we chose this cutoff with reference to the eighth edition of the American Joint Committee on Cancer TNM staging system for differentiated thyroid cancer, but other thresholds are used elsewhere. The two age groups also differed in disease nature, baseline volume, and ablation modality, and data on comorbidity, frailty, body mass index, and anesthetic risk were incomplete. The 799-patient safety population also excluded 119 patients without ultrasound follow-up who had a numerically higher complication rate than the included cohort (Results); this did not change the direction of the age comparison but means the reported complication rates are likely conservative. Only 272 patients, including 42 older patients, had valid imaging within the 9-15-month window and contributed to the primary endpoint; the other 390 patients with otherwise valid longitudinal VRR data had no examination that fell inside that window. They remained eligible for other analyses, and IPCW was used to probe the effect of missing 12-month imaging, but selection bias tied to endpoint-specific follow-up and sparse long-term data cannot be ruled out: IPCW cannot correct for follow-up that is unmeasured or missing not at random. Benign, suspicious, and malignant lesions were analyzed together, and we could not assess lesion-attributable local progression, nodal metastasis, or retreatment outcomes. The postablation ablation-zone VRR we report is also not directly comparable to the conventional preablation nodule VRR used elsewhere, and standardized complication grading still needs confirmation, as do the

clinical justification and prespecification of the exploratory margins. Finally, because linear regression is not bounded, it can generate VRR predictions outside the clinically possible range; a bounded or robust sensitivity model would strengthen future analyses of this kind. Comorbidity data were available for only 213 patients (26.7%), and the absence of any documented cardiovascular, cerebrovascular, pulmonary, or renal disease in this subset most likely reflects incomplete ascertainment rather than a genuinely healthy population, so comorbidity burden could not be adjusted for or used to characterize frailty.

Taken as a whole, chronological age did not mark out a subgroup with worse adjusted ablation-zone volume reduction or more treatment-related complications among patients selected as suitable for ultrasound-guided thyroid thermal ablation. That held across the 55-year threshold, continuous age, the conventional older-age thresholds, the last-imaging analyses, and the weighting-based sensitivity analyses; the pattern is consistent enough to suggest that age thresholds alone are the wrong basis for ablation candidacy decisions. Treatment selection for older adults should instead weigh lesion risk, technical feasibility, physiological reserve, comorbidity, functional status, medication burden, life expectancy, and what the patient wants. None of this proves equivalence, and none of it applies to frail or functionally dependent older adults, but it does argue against ruling out otherwise suitable patients from thyroid-preserving ablation on the basis of age alone. Confirming and extending it will take prospective, multicenter studies with standardized age definitions, frailty and comorbidity measures, patient-centred outcomes, and longer clinical and oncologic follow-up.

Abbreviations

CI
confidence interval
HC3
heteroscedasticity-consistent standard error type 3
IPCW
inverse probability of censoring weighting
IPTW
inverse probability of treatment weighting
MWA
microwave ablation
RFA
radiofrequency ablation
SMD
standardized mean difference
VRR
volume reduction ratio.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of the China-Japan Friendship Hospital. The informed consent was obtained.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

Jiaojiao Ma: Conceptualization, clinical oversight. Yang Li: Data curation. Shanshan Wang, Xuehua Xi, Xuejiao Yu, Wanlin Huang, and Mingyu Feng: Case collection. Yong Cheng: Statistical methodology. Bo Zhang: Supervision, project administration. All authors have read and agreed to the published version of the manuscript.

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Data Availability

Deidentified data are available from the corresponding author upon reasonable request.

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Figures

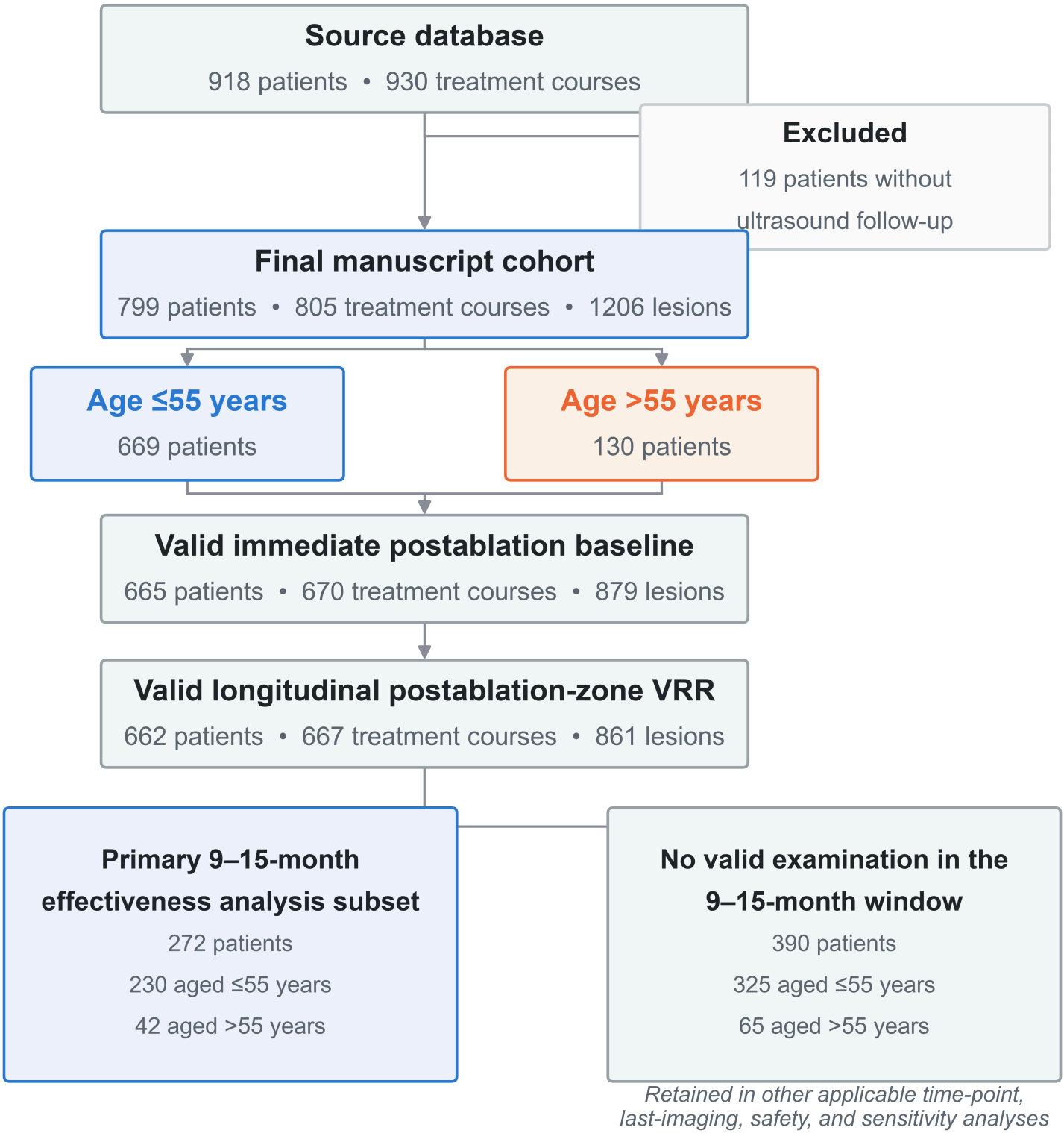


Figure 1

Study Flowchart

The source database contained 918 treated patients. After exclusion of 119 patients without ultrasound follow-up, 799 patients formed the manuscript cohort and primary safety population. Of these, 665 had a valid immediate postablation ablation-zone baseline and 662 had valid longitudinal postablation

ablation-zone VRR data. Among the latter, 272 had valid imaging in the 9-15-month window and contributed to the primary effectiveness analysis; 390 had no valid examination in that window. Absence of a 9-15-month examination was an endpoint-specific exclusion only: these patients were not removed from the study cohort and remained eligible for other time-point, last-imaging, safety, and sensitivity analyses, as applicable. VRR = volume reduction ratio.

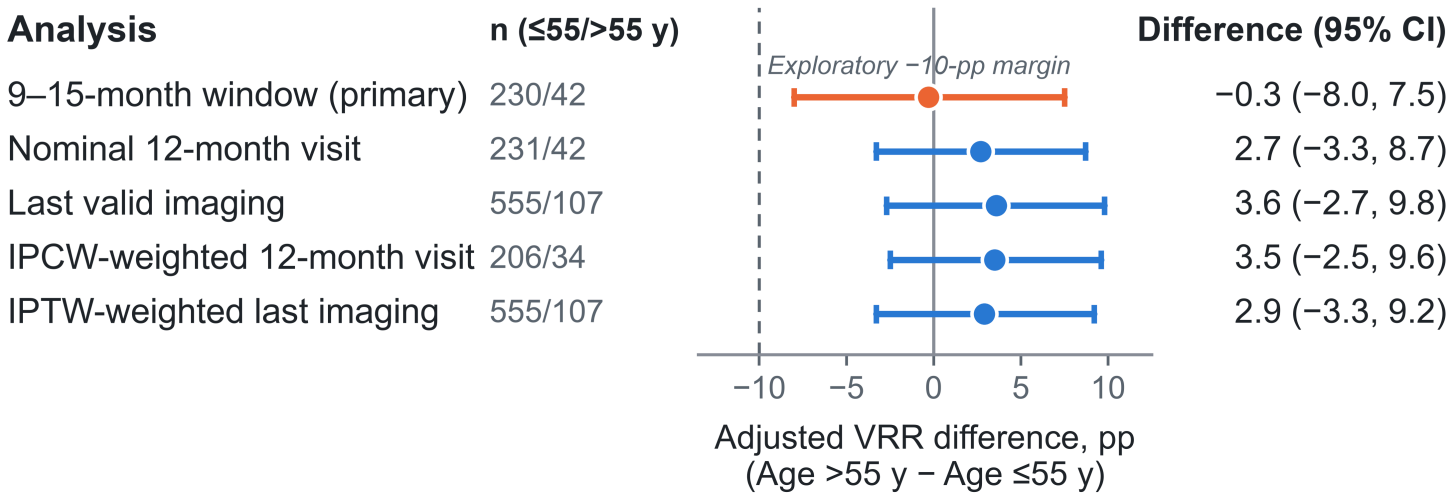


Figure 2

Primary and Supportive Effectiveness Analyses

Forest plot of adjusted postablation ablation-zone VRR differences between patients older than 55 years and those aged 55 years or younger. Positive estimates indicate greater volume reduction in the older group. Horizontal lines indicate two-sided 95% CIs. The solid vertical line indicates no difference; the dashed line at -10 percentage points indicates the exploratory effectiveness margin. IPCW = inverse probability of censoring weighting; IPTW = inverse probability of treatment weighting; VRR = volume reduction ratio.

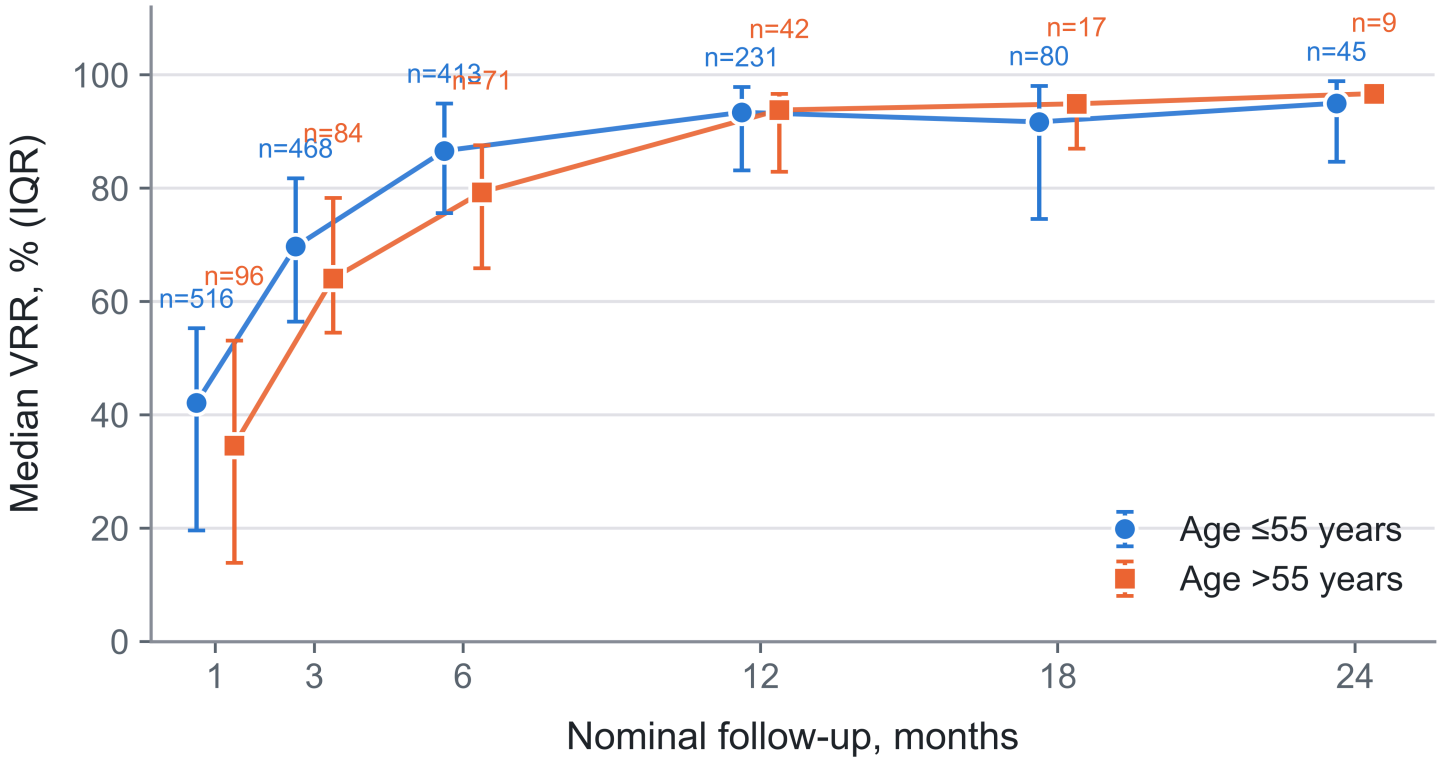


Figure 3

Postablation Ablation-zone Volume Reduction over Follow-up

Median patient-level postablation ablation-zone VRR by age group at nominal 1, 3, 6, 12, 18, and 24 months. Error bars indicate IQRs. The number of contributing patients is shown at each visit. Lines connect visit-specific summaries and do not imply complete follow-up of the same patients across all time points. VRR = volume reduction ratio.

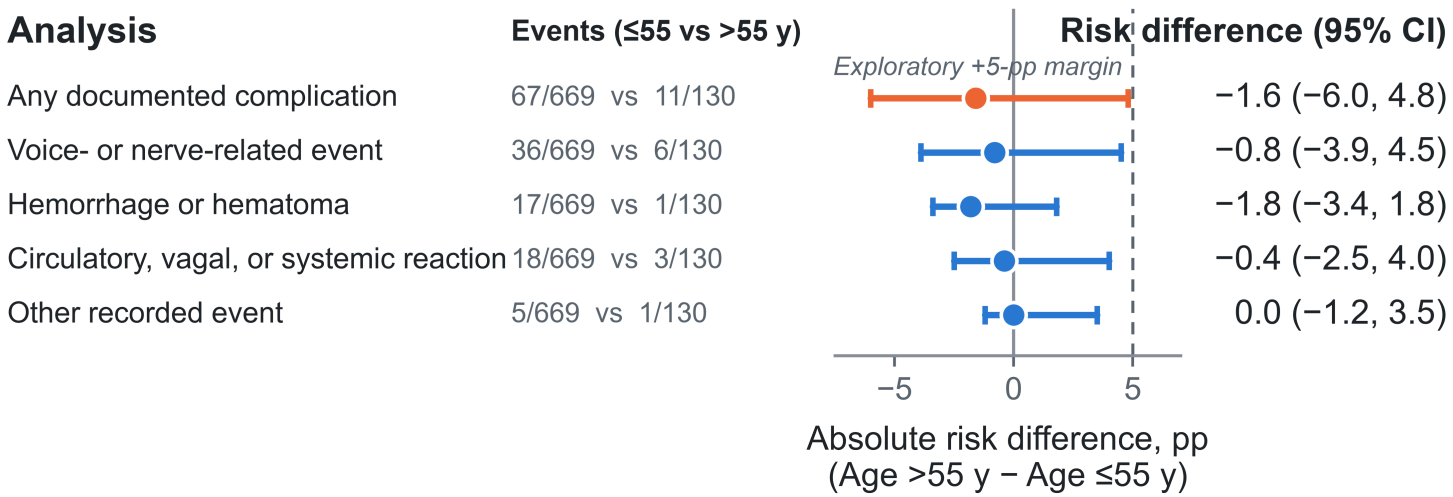


Figure 4

Recorded Treatment-related Complications

Forest plot of absolute risk differences for recorded treatment-related complications between patients older than 55 years and those aged 55 years or younger. Positive estimates indicate higher risk in the older group. Horizontal lines indicate 95% CIs. The solid vertical line indicates no risk difference; the dashed line at +5 percentage points indicates the exploratory safety margin. All 799 patients in the manuscript cohort were included.

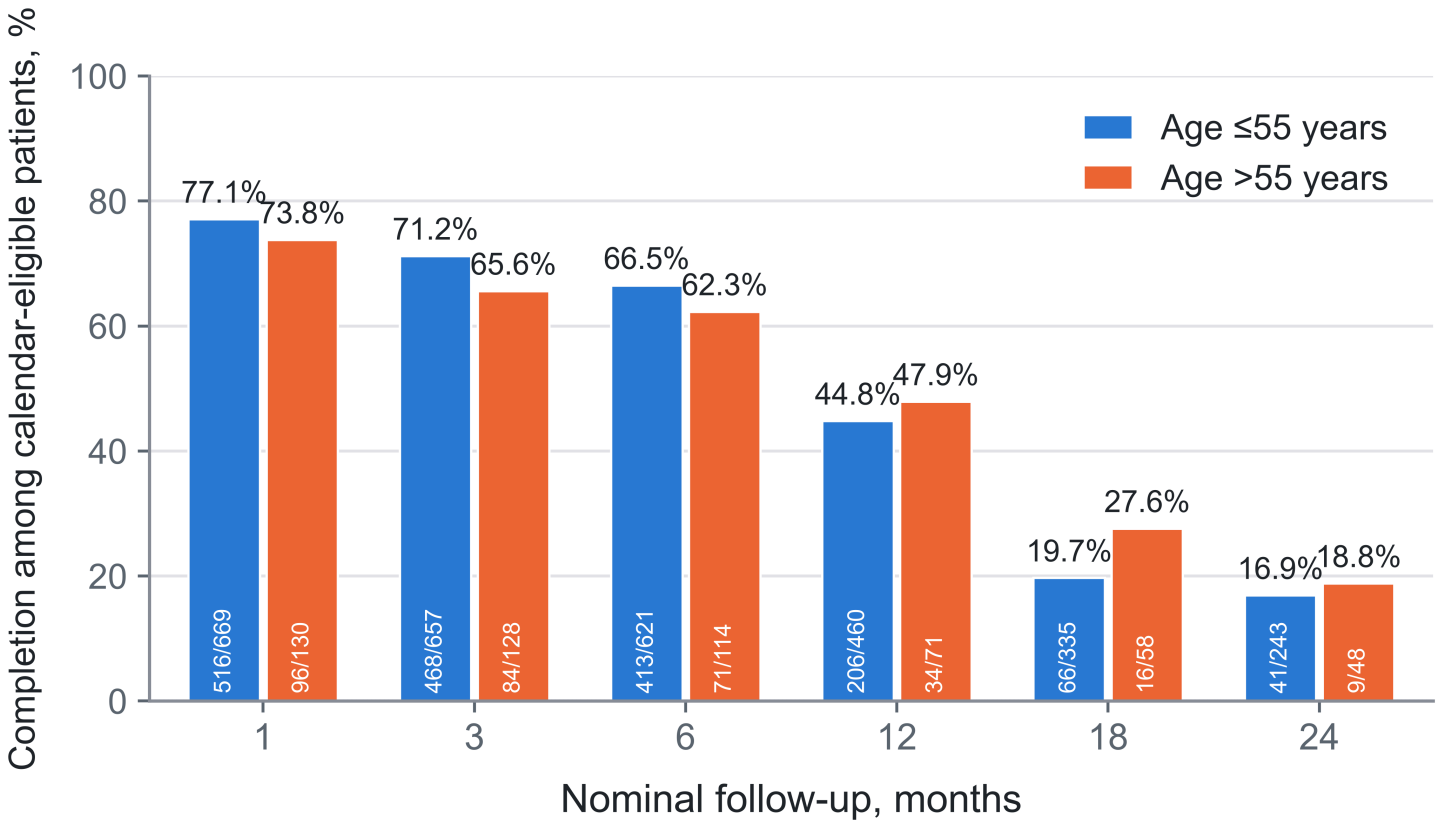


Figure 5

Ultrasound Follow-up Completion

Ultrasound follow-up completion by age group at nominal 1, 3, 6, 12, 18, and 24 months among patients with sufficient calendar time to reach each visit. Denominators vary by visit and age group.

Supplementary Files

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