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A propensity-matched analysis of clinical outcomes between open thyroid lobectomy and high-intensity focused ultrasound (HIFU) ablation of benign thyroid nodules ☆

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ABSTRACT

Background: High-intensity focused ultrasound is a promising, nonoperative treatment for benign thyroid nodules. Our study aimed to compare treatment outcomes of single-session high-intensity focused ultrasound ablation with open lobectomy after propensity score matching.

Methods: After propensity matching, we compared treatment-related morbidity, treatment time, duration of hospitalization, improvement in symptom score, cost, and acoustic parameters of consecutive patients who underwent high-intensity focused ultrasound ablation or lobectomy. All eligible patients completed the computerized, multidimensional voice program and Voice Handicap Index questionnaire before, and 3 and 6 months after treatment.

Results: The matched cohort comprised 154 patients (77 in each group). Although treatment-related morbidity was comparable between the two groups ($P = .368$), treatment time ($P < .001$), duration of hospitalization ($P < .001$), and medical cost ($P < .001$) were less in the high-intensity focused ultrasound group. After high-intensity focused ultrasound ablation, the 6-month nodule shrinkage (mean ± SD) was 64% ± 26% and the 6-month symptom improvement score was comparable with lobectomy ($P = .283$). At 6 months, none of the acoustic parameters were changed from the baseline in both groups ($P > .05$), and the Voice Handicap Index questionnaire did not differ between the two groups ($P > .05$).

Conclusion: Despite having similar treatment-related morbidity and voice outcomes, there were possibly some advantages with high-intensity focused ultrasound during open lobectomy, including the avoidance of a neck scar, shorter treatment time and duration of hospitalization, and lower medical cost.

Introduction

Thyroid nodules are common and, although most are benign and will remain relatively unchanged, some can become large and cause local symptoms.[1–3] Under that circumstance, operative resection is usually indicated.[1,2] Operative resection, however, can lead to complications and requires a general anesthesia. As a result, there has been a growing interest in developing less invasive, nonoperative treatments like percutaneous ethanol injection therapy, laser ablation therapy, and radiofrequency ablation (RFA).[4–6] In general, percutaneous ethanol injection therapy is recommended for recurrent, benign thyroid cysts, and thermal ablation techniques like laser ablation therapy and RFA are recommended for solid and predominantly solid nodules.[4–6] High-intensity focused ultrasound (HIFU) is a new, validated technique of thermal ablation that has been shown prospectively to be effective in not only inducing marked nodule shrinkage but also in relieving nodule-related symptoms when compared with patients who were managed expectantly.[7–9]

It remains unclear whether HIFU ablation can be a safer and more efficacious form of treatment over open surgery in the treatment of symptomatic benign thyroid nodules. Although favorable

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outcomes with HIFU ablation relative to the open surgery have been reported, the study was small and the follow-up period was short.[10] Also, because the choice of treatment (ie, HIFU or resection) was made by patients themselves, confounding differences in patient demographics were seen.[10] To address these issues, our study compared complications, treatment outcomes, and acoustic parameters of the voice of a relatively large patient cohort who underwent HIFU ablation or open thyroid lobectomy with propensity score matching of their demographics.

Methods

This retrospective analysis was approved by our local institutional review board. All relevant clinical and treatment data were recorded prospectively after obtaining informed consent. We reviewed all consecutive patients who underwent a unilateral thyroid resection (ie, lobectomy) or a HIFU ablation for a symptomatic benign thyroid nodule from 2015 to June 2017 and were followed up for a minimum period of 6 months. Outcomes, including treatment-related complications, total treatment time, duration of hospitalization, direct medical costs, and voice quality (by acoustic voice analysis) were compared between those who underwent single-session HIFU ablation and an open lobectomy. Propensity score matching (with age and sex as covariates) was performed to obtain a well-matched cohort.

Patient selection

Only patients who were unwilling to undergo lobectomy were considered for HIFU ablation. To be eligible for ablation, patients had to meet the following criteria:

1. The nodule had to be benign (ie, Bethesda class II on fine-needle aspiration cytology)[2] and to have a low or very-low suspicion pattern on ultrasonography (US).[2]
2. The nodule (which may be a solitary nodule or a dominant nodule in a multinodular gland) had to be causing local pressure with or without cosmetic symptoms. Patients were asked to rate their pressure symptoms by using a visual analogue scale.
3. The index nodule had to have all three orthogonal dimensions $\geq$10mm but $\leq$50mm on US.
4. The index nodule had to be solid or predominantly solid ($<$30% cystic areas) on US.
5. The index nodule had to be within the treatable ablation depth (ie, 5–30 mm between the skin and the nodule center).
6. Patients had to have normal serum free T4 (FT4) and thyroid-stimulating hormone (TSH).

The exclusions were age $\leq$18 years, pregnant or lactating women, a nodule with indeterminate or malignant fine-needle aspiration cytology or with intranodular macrocalcifications (ie, precluding HIFU treatment), history of head and neck irradiation, family history of nonmedullary thyroid carcinoma, pre-existing vocal cord palsy, or any medical conditions precluding intravenous sedation.

HIFU treatment

All treatments were performed by one person (B.H.L), using the same commercially available US-guided HIFU device (EchoPulse; Theraclion, Paris, France). This device comprises an energy generator, a treatment head, a skin cooling device, and a touchscreen interface for planning. The treatment head incorporated an image transducer (7.5 MHz, 128 elements, linear array) and HIFU transducer (3 MHz, single element, 60 mm in diameter). All patients were placed in a supine position, with neck slightly extended. A bolus of intravenous diazepam (Actavis, Barnstaple, UK) (10–15mg) and pethidine (Martindale Pharmaceuticals, Romford, Essex, UK) (50–100mg) were given before treatment. Once the treatment head was positioned correctly over the nodule, the device computer (Beamotion v TUS 3.2.2: Theraclion) automatically divided the nodule into multiple subunits for ablation. Each subunit measured approximately 7.3 mm in thickness and 5 mm in width. Each subunit received a continuous, 8-second pulse of HIFU energy followed by 30 seconds of cooling before the beam moved to another subunit. This cycle continued until all subunits received these pulses. To ensure safety, nearby structures like the carotid artery, trachea, and skin were marked on the screen and left unablated. A laser-based movement detector enabled immediate power interruption when the patient moved or swallowed during ablation. To avoid skin burn, the skin was cooled by a balloon (filled with 10°C liquids) at the tip of the treatment head. All ablations started at 256 Joules (J) per pulse and increased up to 360 J until hyperechoic marks (HEMs; ie, microbubbles as a result of tissue heating from HIFU energy) appeared on the screen (Fig 1).[11] Throughout each treatment, each patient's vital signs were monitored. Oral diet was resumed immediately, and patients were discharged 2 hours after treatment.

Open lobectomy

All patients underwent a standardized lobectomy via the cervical approach by one surgical team. The recurrent laryngeal nerve and external branch of the superior laryngeal nerve on the operated side were carefully sought and mapped out by the intraoperative nerve monitor ([IONM] Medtronic NIM-Response 3.0 system; Medtronic, Dublin, Ireland). An IONM was used to confirm the integrity of the nerves at the end of the lobectomy. The strap muscles were not transected routinely during the procedure. Alternate energy was not be used when the line of dissection was close to Berry's ligament. No drain was placed after the procedure. Oral diet was resumed immediately afterward, and patients were allowed to go home after one overnight hospital stay.

Assessment of complications and treatment outcomes

All patients underwent a transcutaneous US of the vocal cords (VC)[12] before and immediately after HIFU or thyroid lobectomy. Laryngoscopic examination was not done routinely unless VCs were not clearly visible on US. Other complications, like Horner's syndrome, skin burn, bleeding infection, and post-treatment hypothyroidism, were recorded if present. All patients had their thyroid function (serum TSH and FT4) checked at on treatment day (baseline), and at 3 months and 6 months afterward. Hypothyroidism was defined as a biochemical state of low serum FT4 ($<$12 pmol/L) (Normal: 12–23 pmol/L). For the sake of comparison, the total treatment time in the HIFU group was taken as the time when the patient first entered into the treatment room to the time when the patient exited from the room. In the lobectomy group, treatment time was taken as the time when the patient first entered the operating theatre to the time the patient exited the theatre.

In the HIFU group, each nodule was measured by US at baseline, and at 3 months and 6 months after treatment by an independent clinician. Dimensions of the nodule were measured using the LOGIQ e (GE Healthcare, Milwaukee, WI, USA) scanner equipped with a 10–14 MHz, linear matrix transducer. Three orthogonal diameters of the index nodule (its greatest diameter and two other perpendicular diameters) were measured. In general, the greatest diameter was the cranio-caudal dimension (length) of the nodule, and the other two perpendicular diameters were the medio-lateral (width) and antero-posterior (depth) dimensions of

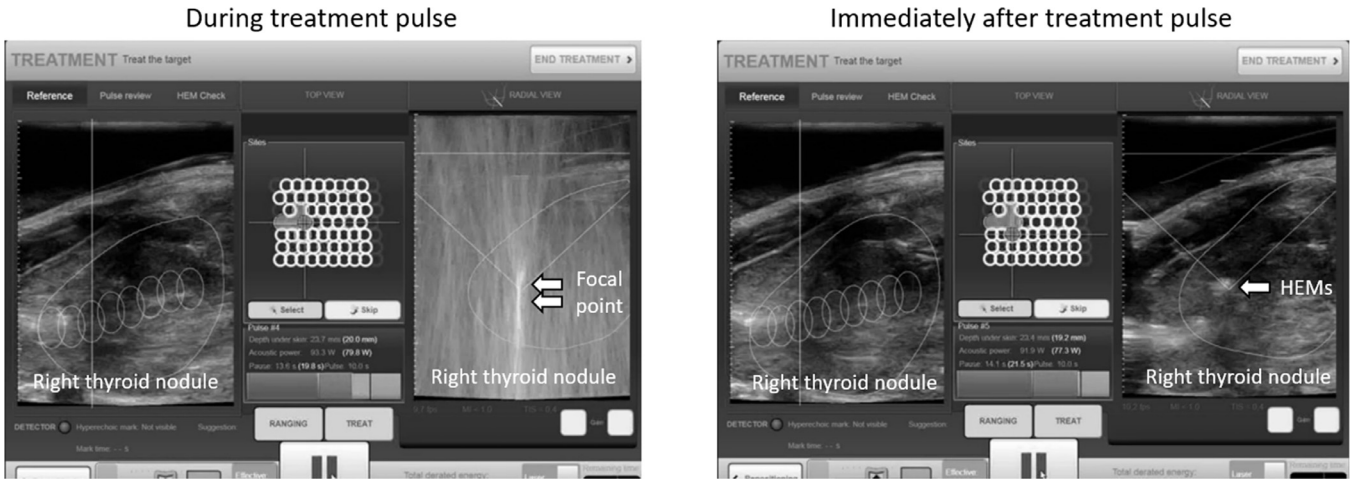

Fig 1. Two treatment images. *Left*: aken during an 8-second pulse. *Right*: Taken immediately after the pulse. HEMs were clearly seen at the focal point of the HIFU beams. HEM, Hyperechoic marks; HIFU, high-intensity focused ultrasound.

the nodule. All measurements were made to the nearest 0.1 mm. To estimate nodule volume, we used the formula of an ellipsoid: volume (mL) = (width (cm) × length (cm) × depth (cm)) × (π/6) where π was taken as 3.1416. The extent of shrinkage was calculated based on the formula: [baseline volume – volume at visit] / [baseline volume] * 100. Treatment success was defined as >50% in nodule shrinkage at 6 months. At 6 months, patients in each group were also asked to rate how their local pressure symptoms had improved after treatment (0 = same; 1 = slight improvement; 2 = moderate improvement; 3 = significant improvement).

For calculation of costs, only direct medical costs were included. Indirect costs, such as loss of productivity and wages, were not analyzed. Treatment cost included the cost of the procedure, annual maintenance cost of the device, medical and supporting staffs, drugs related to the procedure, operating room, consumables, and other expenses. The cost of hospitalization was calculated separately. All monetary values were expressed in USD.

For voice quality, patients were asked to undergo a series of multidimensional voice program (MVDP) testing and to complete a voice-related questionnaire (Voice Handicap Index [VHI]-30) on the day of treatment (baseline), and at 3 months and 6 months afterward. Patients with an apparent vocal cord palsy or history of laryngeal or neurologic disease that may affect the voice function were not subjected to the MVDP and VHI-30. MVDP was performed in a quiet room under a standardized condition by 1 person. Each patient was instructed to read aloud the same 22-word sentence 5 times. Voice was recorded directly into the KayPENTAX MDVP (PENTAX Medical, USA), using a professional grade AKG C420 microphone (AKG Acoustics, USA). The microphone was placed 10 cm from the patient's mouth to avoid air burst. The middle 3 of the 5 trials were used for analysis. The entire sentence was analyzed by MDVP. Measures to be analyzed included fundamental frequency (F_0), jitter, shimmer, noise to harmonic ratio (NHR), and maximum phonation time (MPT). These 5 objective parameters measured different aspects of voice quality. F_0 measured vocal pitch level; jitter and shimmer measured pitch and amplitude variability, respectively.[13,14] NHR measured the amount of noise present, and MPT measured voice capacity (ie, efficiency of voice production).

VHI-30 questionnaire

VHI-30 is a self-administered questionnaire to measure the impact of a voice disorder on a person's vocal functions, vocal physical ability, and emotion. It produces a total single score (0–120) by adding the score of 30 questions, with each having a response option from 0 (never) to 4 (always).[13]

Statistical analysis

To minimize selection bias and potential confounders, propensity score matching was performed to adjust for the differences in patient baseline demographics. The propensity score was defined as the probability of being assigned to the HIFU or surgery group based on patients' baseline observed covariates. Covariates included age-to-sex ratio. The propensity score mapping was made by using the "psmatch2" command by one-to-one matching, with the nearest neighbor and without replacement approach in STATA (StataCorp, LLC, College Station, TX, USA).[14] After propensity score matching, the baseline covariates and outcomes at baseline of the two groups were compared, using the independent *t* test for continuous variables and χ^2 test for categorical variables. All statistical analyses were performed using STATA v 13.0 (StataCorp, LLC). All significance tests were two-tailed. Continuous variables are presented as mean ± standard deviation.

Results

During the study period, 108 consecutive patients completed a single session of HIFU ablation, and 104 patients underwent an open lobectomy for a symptomatic, benign thyroid nodule. All patients had local pressure symptoms arising from their thyroid swelling. After excluding patients with incomplete 6-month follow-up data, 97 (90%) in the HIFU grpi[and 88 (85%) in the lobectomy group were analyzed. Before propensity score matching, significant differences in the age-to-sex ratio were found between the two groups, with the HIFU group being younger at treatment ($P = .009$) and having a greater female ratio ($P = .006$) (Table 1), but size and volume of the dominant nodule were not different between the two groups ($P > .05$). After propensity score matching (HIFU group $n = 77$ versus lobectomy group $n = 77$), the age-to-sex ratio became comparable between the two groups.

A total of 3 (4%) patients in each group suffered a unilateral VC palsy (VCP) immediately afterward (Table 2), none of which were permanent, and all recovered within the first 3 months. In the HIFU group, the times to recovery were 4, 6, and 6 weeks, respectively, whereas in the lobectomy group, the time to recovery were 4, 6, and 10 weeks, respectively. No patient in the HIFU group suffered from skin burn. A patient in the HIFU group suffered Horner's syndrome on the treatment side. In that patient,

Table 1
A comparison of baseline characteristics and voice quality between patients who underwent HIFU or operative resection before and after propensity score matching

Variable	Before propensity matching			After propensity matching		
	HIFU ($n=97$)	Lobectomy ($n=88$)	P value	HIFU ($n=77$)	Lobectomy ($n=77$)	P value
Age at treatment (years)	48 ± 12	54 ± 15.17	**.009**	49 ± 13	51 ± 14	.191
Sex (male: female)	12: 85	25: 63	**.006**	12: 65	17: 60	.303
BMI (kg/m^2)	19.2 ± 12.73	20.6 ± 9.0	.418	19.6 ± 14.2	20.9 ± 12.7	.511
Serum TSH (mIU/L)	0.93 ± 0.46	0.81 ± 0.51	.642	0.90 ± 0.49	0.87 ± 0.48	.729
Size of dominant nodule (cm)	3.5 ± 1.1	3.9 ± 1.5	.253	4.0 ± 1.0	4.0 ± 1.0	.960
Volume of dominant nodule (mL)*	25.2 ± 14.0	26.67± 13.9	.682	24.8 ± 14.5	24.0 ± 17.2	.399

* Estimated by the formula: volume (mL) = (width (cm) × length (cm) × depth (cm)) × (π/6), where π was taken as 3.1416.

Table 2
Treatment outcomes between single-session HIFU and open lobectomy for a benign thyroid nodule after propensity score matching

	HIFU ($n=77$)	Lobectomy ($n=77$)	P value
Treatment-related morbidities			
Vocal cord palsy	3 (3.9)	3 (3.9)	1.000
Horner's syndrome	1 (1.3)	0 (0.0)	.497
Bleeding	0 (0.0)	1 (1.3)	.497
Infection	0 (0.0)	0 (0.0)	—
Hypothyroidism	0 (0.0)	4 (5.2)	.120
Overall morbidity	4 (5.2)	8 (10.4)	.368
Treatment time (min)*	53 ± 6	86 ± 12	**<.001**
Days of hospital stay (% of patients)			**<.001**
0	75 (9)	0	
1	2 (3)	76 (99)	
2	0	1 (1)	
Efficacy by nodule shrinkage (%)†			
3 months	50 ± 22	—	
6 months	64 ± 26	—	
Symptom improvement score at 6 months (% of patients)			.283
0 (no improvement)	4 (5))	10 (13)	
1 (slight improvement)	20 (26)	15 (20)	
2 (moderate improvement)	30 (39)	33 (43)	
3 (significant improvement)	23 (30)	19 (25)	
Direct medical costs (USD)			
Treatment‡	2010 ± 70	5989 ± 333	**<.001**
Hospitalization	329 ± 69	854 ± 70	**<.001**

* In the HIFU group, this was the time taken from the patient first entered to treatment room to the patient exited from the room. In lobectomy group, taken from the patient entered into operating theater to the patient exited from the theater.
† Calculated based on the formula: [baseline volume – volume at visit] / [baseline volume] * 100.
‡ Including the cost of the procedure, anesthesia, staff, consumables, operating room, drugs related to the procedure, and other general expenses.

partial ptosis and miosis were found immediately after treatment. These signs improved gradually over time and became unnoticeable clinically after 5 months. A patient in the lobectomy group suffered bleeding that required re-exploration 3 hours after initial lobectomy. After 6 months, no patients in the HIFU group developed hypothyroidism, 4 (5%) patients in the lobectomy group had hypothyroidism, 3 of whom required thyroxine supplementation because of hypothyroid symptoms. In the lobectomy group, 3 (4%) patients were found to have an occult papillary microcarcinoma in the excised lobe, but none were present inside the dominant nodule. The overall morbidity rate was comparable between the HIFU and lobectomy groups (5% and 10%, respectively, $P=.368$). Mean total treatment time was less in the HIFU group (55 minutes vs 86 minutes, $P<.001$). Also mean duration of hospital stay was less in the HIFU group (0.1 day vs 1 day, $P<.001$).

In the HIFU group, the 3- and 6-month nodule shrinkage was 50 ± 22% and 64 ± 26% (Fig 2). The treatment success was 63/77 or 82%. At 6 months, the symptom improvement scores were comparable between the two treatment groups ($P=.283$). Both treatment and hospitalization costs were less in the HIFU group ($P<.001$).

On acoustic voice analysis by MVDP, baseline mean F_0 was not different between the two groups (200 Hz versus 194 Hz, $P=.472$), but at 6 months, the mean F_0 was less after lobectomy compared with HIFU ablation (192 Hz versus 208 Hz, $P=.031$). Nevertheless, relative to baseline, the mean F_0 level at 3 and 6 months did not deteriorate in both groups. Other acoustic parameters including jitter, shimmer, NHR, then MPT, and the VHI-30 score were not statistically different between the two treatment groups or from baseline (Table 3).

Discussion

Although thermal ablation could become a possible alternative to open thyroidectomy in the treatment of symptomatic benign thyroid nodules, its clinical outcomes have rarely been directly compared with open thyroidectomy. To date, four such comparative studies have been published and, of these, three compared outcomes of RFA with open thyroidectomy,[15–17] and only one (from our group) compared HIFU with open thyroidectomy.[10] Although favorable outcomes were reported with the RFA technique, there were some issues with previous studies.[15–17] First, some of the studies compared the outcomes of RFA with patients who underwent bilateral instead of unilateral thyroid resections.[17] Given that thermal ablation mostly only treats a single nodule within one lobe, unilateral thyroid resection would have been

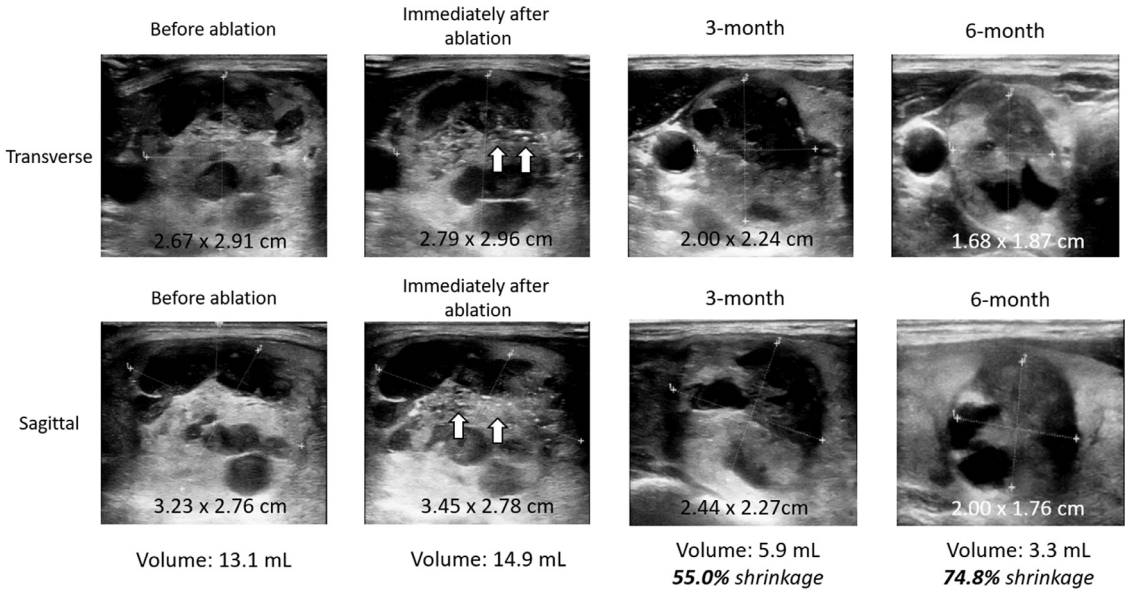

Fig 2. Serial ultrasound images of a right predominantly solid thyroid nodule obtained before, 3 months and 6 months after HIFU) treatment. HIFU, high-intensity focused ultrasound.

Table 3
A comparison of acoustic changes from the baseline between those who underwent single-session HIFU and those who underwent surgery

	HIFU ($n=74$)*	Surgery (n = 74)*	*P* value
Mean F_0 (Hz)			
Baseline	200 ± 51	194 ± 46	.472
3 months	204 ± 57	189 ± 45	.151
6 months	208 ± 45	192 ± 46	**.031**
Jitter or pitch perturbation (%)			
Baseline	0.40 ± 0.31	0.40 ± 0.65	.499
3 month	0.62 ± 0.56	0.48 ± 0.42	.101
6 month	0.60 ± 0.51	0.50 ± 0.67	.442
Shimmer or amplitude perturbation (%)			
Baseline	0.57 ± 0.39	0.57 ± 0.34	.947
3 months	0.92 ± 0.50	0.68 ± 0.48	.078
6 months	0.98 ± 0.50	0.70 ± 0.48	.075
Noise-to-harmonic ratio (NHR)			
Baseline	0.04 ± 0.07	0.05 ± 0.07	.083
3 months	0.08 ± 0.10	0.06 ± 0.07	.952
6 months	0.11 ± 0.17	0.08 ± 0.10	.851
Maximum phonation time (MPT) (sec)			
Baseline	10.70± 4.8	10.0 ± 4.6	.561
3 months	9.9 ± 3.8	9.6 ± 4.3	.463
6 months	10.0 ± 3.7	9.9 ± 3.7	.183
Total VHI-30 score			
Baseline	7.9 ± 7.9	7.9 ± 10.5	.867
3 months	9.1 ± 14.6	10.1± 17.3	.371
6 months	8.6 ± 12.2	9.4 ± 15.6	.739
Mean VHI score per item			
Baseline	0.26 ± 0.30	0.26 ± 0.40	.867
3 month	0.48 ± 0.51	0.56 ± 0.52	.269
6 month	0.36 ± 0.52	0.48 ± 0.58	.634

* After excluding patients who suffered vocal cord palsy shortly after HIFU treatment or lobectomy.
F_0, fundamental frequency; *VHI*, Voice Handicap Index.

a better comparative group. The other issue was the failure to examine the VCs routinely before and after the procedure, and, therefore, the reported incidence of treatment-related VCP might have been inaccurate and underreported. In fact, our data showed that, with routine VC assessment, the incidence of VCP after HIFU ablation was not negligibly low. Our data showed the incidence of VCP in HIFU ablation was not as different from that of open lobectomy (3.9% vs 3.9%, $P > .99$). It is worth noting that the present rates were comparable with our previously reported rates and, thus, they perhaps do reflect our normal moving averages.[12,18] Nevertheless, it should be pointed out that VCP is preventable, provided a reasonable distance can be kept between the HIFU beam and the tracheoesophageal groove.[18]

Although Horner's syndrome occurs rarely after open thyroidectomy, it appears to be more common with HIFU ablation of thyroid gland.[19] This finding is because at times, heat energy may travel and damage the adjacent plexuses of the sympathetic trunk when nodules are located close to the carotid sheath.[20] Fortunately, this is rare and can be resolved spontaneously without treatment.

Other known complications, like skin burn, bleeding, and infection, were not seen in the present series; although they can occur in all forms of thermal ablation.[20] Biochemical hypothyroidism is very rare after HIFU ablation, but in the lobectomy group, around 1 in 20 patients may become biochemically hypothyroid, requiring thyroxine replacement.[21]

As expected, treatment time, duration of hospital stay, and cost were statistically less in the HIFU group when compared with the lobectomy group, related primarily to the fact that all HIFU patients were allowed to be discharged 2 hours after the procedure and all lobectomy patients were only allowed to be discharged after an overnight stay. With many centers now practicing same-day surgery, the reported difference in duration of hospital stay and cost could have been less if the operation was done on a same-day basis. Nevertheless, total treatment time would have remained somewhat less because general anesthesia is not required during HIFU treatment. Although on the subject of treatment time, it should be noted that the treatment time in HIFU ablation still remains generally long when compared with other ablation techniques, because focused energy needs to propagate across the skin, subcutaneous tissue, and muscle into the target.

Of interest, despite the fact that the lobectomy group involved the removal of the thyroid nodule and the associated lobe as opposed to nodule shrinkage only in HIFU ablation, our study did not find a difference in symptom score improvement between the two groups ($P = .283$). One possibility might have been related to the problem of fibrosis after operative lobectomy, because the feeling of "tethering" has been reported frequently after open surgery.[22] Although an average nodule shrinkage rate of 64% in volume (or from a 4-cm to 2.8-cm diameter nodule) might seem underwhelming initially, reapplication of HIFU to the same nodule is technically feasible and effective.[23]

In terms of voice quality, our data showed that the mean F_0 in the lobectomy group was less at 6 months than that in the HIFU group, but because none of the acoustic parameters deteriorated from the baseline and the VHI did not differ between groups, one can safely conclude that both procedures had minimal impact on voice outcomes. This finding is somewhat in discord with our previous study, which showed, in the absence of VCP, pitch deteriorated in the first few months after open thyroidectomy.[22,24]

Despite these findings, there were several shortcomings with our study. First, despite being a propensity matched analysis, our study did not assess cosmetic results, pain, and psychosocial issues, some of which could have favored one treatment over the other. Second, our study did not account for the capital outlay of the HIFU device, which currently costs about USD 450,000, as well as all the indirect costs associated with the treatment. The latter is likely to favor HIFU ablation because most patients can resume work almost immediately after treatment. One important omission was the possibility of future growth of the nodule and recurrence that may occur years after the initial ablation. Therefore, greater follow-up studies are needed to evaluate the long-term efficacy and cost of HIFU.[25] Finally, despite being an alternative to each other, it is evident that there are some fundamental differences between the two treatments, with lobectomy being a definitive treatment and HIFU ablation being a temporizing treatment. Perhaps, in the future, rather than being a substitute for lobectomy, HIFU may have a unique complementary role in the surgical treatment of benign thyroid nodules.

In conclusion, despite the similar rate of treatment-related morbidity and voice outcomes, there were possibly some distinct advantages with HIFU ablation over open lobectomy, including the avoidance of a neck scar, less treatment time and duration of hospital stay, and less direct medical cost.

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Discussion

Dr Alberto Treiguer (Brazil): As the nodule is bigger, the accuracy of fine-needle biopsy decreases. How do you follow these patients that go through an interventional ultrasound ablation?

Dr Brian H. Lang: We only include patients who have Bethesda 2 FNA result and also patients who have a low or very-low suspicion sonographic pattern on the ultrasound. If you use that combination, the risk of malignancy is quite low (less than 1%). We follow our patients at 3 months, 6 months, and every year up to about 3 years. There hasn't been anybody with malignant change after a year.

Dr Cortney Lee (Lexington, KY): You mentioned that you collected symptomatic data on these patients. Unless I missed it, I didn't hear the difference in those groups as far as symptom improvement. You are decreasing the nodule size by only about 63%, so there are still decent size nodules remaining, especially if you started with large nodules. So, what was the symptomatic improvement?

Second, for the group that underwent ablation, and the patients were only followed up to 6 months, do you have any data about

the ones that may have decided that the nodule was still bothering them and they wanted it out?

Dr Brian H. Lang: This is a very select group of patients. I remember only one patient not included in this cohort that actually had surgery after HIFU. So, if they still have symptoms, we would treat them with the same technique. Basically, we ask them whether they have any pressure symptoms.

Dr Cortney Lee (Lexington, KY): What was the difference between the groups, though, in terms of their symptom improvement?

Dr Brian H. Lang: We asked them to rate their symptom improvement at 6 months after treatment.

Dr Cortney Lee (Lexington, KY): Were they equal? Were your surgery group symptom improvement scores the same?

Dr Brian H. Lang: Yes, the same.

Dr Sarah Oltmann (Dallas, TX): I have a follow-up to that. In the one patient that you had to reoperate on, what did you find as far as the scarring?

Dr Brian H. Lang: There wasn't any significant scarring because the ablation occurs within the thyroid, so there's no real scarring outside the thyroid.

Dr Scott Wilhelm (Cleveland, OH): Brian, great work as always.

In terms of the actual mapping technique for the nodule and the coverage zones that you are able to get, do you have any problems with motion artifact? Obviously, even when we are just doing thyroid biopsies in clinic, they occasionally are swallowing, things move, you have to reorient your ultrasound, etc. How does your targeting system work from that standpoint?

Also, what kind of billing codes are you using for this? Are you following radiology-type billing techniques for this? What are you doing to recoup your costs for the technique and your time compared with surgery?

Dr Brian H. Lang: To minimize movement, we actually sedate our patients. It's not general anesthesia but it is deep sedation. Afterward, they actually don't remember having treatment, and they go home the same day.

Regarding the billing, we work in a very different medical system than you. We don't actually bill our patients. The patients need only to pay for the consumables, which include the balloon that cools the skin to avoid a burn. That costs around $500 USD out of pocket.

Dr Sareh Parangi (Boston, MA): Thank you, Brian, for this presentation. What do you think about the temporary nerve injuries you saw? Were those related to dissipation of heat, and was it influenced by the composition of the nodule? If the nodule was more cystic, did it cause less heat or more heat dissipation, and did more of those patients have an injury or not?

Dr Brian H. Lang: For the three, we believe it was an issue of heat dissipation over a shorter distance. We were too close, and that was the reason for the injury. They all improved over a period of 3 months. We believe it was not related to the consistency of the nodule. There could be some relationship, but we didn't see that clearly. We record all our treatments, so we looked back at the videos and we believe it was the distance.

Dr Richard A. Prinz (Evanston, IL): Brian, very nice presentation. I have a question about your patient selection. You said that your patients refused surgery. We have the impression in the West that Asian patients may be more resistant to having a scar on their neck. Can you tell us how many of your patients refused surgery because of that reason? How many were for severe comorbidities that would make surgery more hazardous?

Dr Brian H. Lang: If we offered this to 100 patients, perhaps 30 or 40 patients might have preferred this treatment over surgery. So, just under half of patients didn't accept operation.