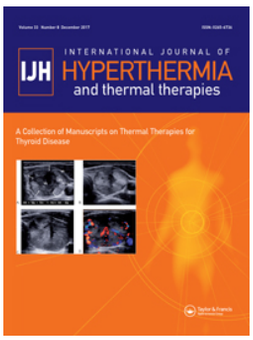

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Single-session high intensity focussed ablation (HIFU) versus open cervical hemithyroidectomy for benign thyroid nodule: analysis on early efficacy, safety and voice quality

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ABSTRACT

Background: High intensity focussed ultrasound (HIFU) is a promising non-surgical treatment for symptomatic benign thyroid nodule. We aimed to compare early efficacy, safety and voice quality between HIFU ablation and open thyroidectomy.

Methods: Consecutive patients who underwent single-session HIFU ablation or a hemithyroidectomy for symptomatic benign thyroid nodule were included. The 6-month extent of nodule shrinkage, symptom improvement score, thyroid function, hospital stay and cost were compared between the two procedures. Safety was defined by absence of major complications like recurrent laryngeal nerve injury and skin burn. Voice quality was assessed by a computerised multi-dimensional voice programme and a Voice Handicap Index (VHI) questionnaire 1-month after treatment.

Results: Altogether, 43 patients had HIFU and 103 patients had a hemithyroidectomy. In the HIFU group, the extent of nodule shrinkage at 6-month was 51.71 ± 16.04%. No patients in the HIFU group suffered skin burn or hypothyroidism. The HIFU group had a significantly shorter length of hospital stay (0.3 vs. 1.0 day, $p < 0.001$), lower incidence of subclinical hypothyroidism (1/43 vs. 21/103, $p = 0.008$), higher symptom improvement score ($p = 0.009$) and was less costly (USD 1923.1 vs. USD 5384.6). Relative to HIFU, pitch quality also worsen after surgery ($p < 0.05$).

Conclusions: Relative to surgery, single HIFU ablation appeared efficacious and safe. Apart from shorter hospital stay, less subclinical hypothyroidism, being scar-less, lower cost and more symptom improvement, HIFU patients were less affected by a pitch problem in the first month. This study provides a strong argument for HIFU ablation as a treatment for symptomatic benign thyroid nodule.

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Introduction

Thyroid nodules are common and although most are benign and remain relatively static in size, some do become large and cause local symptoms [1–3]. Under this circumstance, thyroidectomy is usually indicated [1,2]. However, surgery is associated with complication risks, high cost and need for general anaesthesia. As a result, there has been a growing interest in developing less invasive, non-surgical treatment for benign thyroid nodules [4–6]. For predominantly-solid nodules, thermal ablation techniques are generally highly effective [4,6]. High intensity focussed ultrasound (HIFU) is one of these non-surgical techniques which utilises focussed ultrasound energy to induce thermal ablation. Recent studies have shown that it is effective in not only inducing significant nodule shrinkage by thermal ablation but also relieving symptoms in patients with nodule-related complaints [7–9].

However, relative to other thermal ablation techniques such as radiofrequency ablation (RFA) or laser ablation (LA), the efficacy and safety of HIFU ablation in benign thyroid nodules have been less well-described. It is particularly unclear what the efficacy and safety of HIFU ablation are relative to the conventional treatment (i.e. surgery). Furthermore, given that surgery could impair patient's post-operative voice quality even when both recurrent laryngeal nerves (RLN) remain functionally intact afterwards [10–12], it would also be interesting to compare voice quality between the two procedures using a computerised acoustic voice programme like the multi-dimensional voice programme (MDVP) [13,14]. Previous studies have reported that shortly after surgery, patients typically may have a lower pitch and a narrower voice range on MVDP [13–16]. We hypothesised that voice quality might be less affected following HIFU ablation. Given these controversies, our study aimed to compare early efficacy, safety and early voice quality between HIFU and open cervical thyroidectomy.

Methods

This retrospective analysis was approved by local institutional review board. All consecutive patients who underwent either a single-session HIFU ablation or a unilateral thyroid resection (in the form of lobectomy or hemithyroidectomy) for a

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symptomatic benign thyroid nodule from August 2015 to April 2016 were included. Over this 9-month period, HIFU ablation of a benign thyroid nodule was only indicated when the patient did not wish to have surgery. For the MVDP assessment, patients who had a history of voice, laryngeal disease or neurological disease that may affect voice function, previous head and neck surgery or radiotherapy and thyroid malignancy necessitating neck dissection, known laryngeal abnormality, sustained injury to either a RLN or external branch of the superior laryngeal nerve (ESBLN) intraoperatively or a pre-existing vocal cord paralysis (VCP) were not included.

Treatment efficacy

Each nodule was graded by USG measurement at the day of treatment (baseline), 1-month and 6-month. Nodule dimensions were measured using the LOGIQ e (GE Healthcare, Milwaukee, WI) scanner equipped with a 10–14 MHz linear matrix transducer. Three orthogonal diameters of the index nodule (its longest diameter and two other perpendicular diameters) were measured. In general, the longest diameter was the cranio-caudal dimension (length) of the nodule while the other two perpendicular diameters were the mediolateral (width) and antero-posterior (depth) dimensions of the nodule. All measurements were made to the nearest 0.1 mm. To estimate nodule volume, we used the formula: volume (mL) = (width (in cm) × length (in cm) × depth (in cm)) × (π/6) where π was taken as 3.1416. The volume reduction ratio (VRR) was calculated based on the formula: [Baseline volume − volume at visit]/[Baseline volume] × 100. At 6-month, patients in the HIFU group had their nodule assessed clinically using the *WHO* grading system [17] and were asked to rate how much their obstructive and/or local pressure symptoms had improved from baseline (0 = same; 1 = slight improvement; 2 = moderate improvement; and 3 = significant improvement). Patients' serum TSH (normal: 0.35–4.78 mIU/L) and FT4 (normal: 12–23 pmol/L) were also checked. Subclinical hypothyroidism was defined as a biochemical state of high TSH (>4.78 mIU/L) while hypothyroidism was defined as a biochemical state of low serum FT4 (<12 pmol/L).

Safety

All patients underwent laryngoscopic or transcutaneous USG examination of the VCs [18] before and after HIFU or surgery. Any reduced cord movement was recorded as VCP. Those with VCP were examined every 6–8 weeks by otolaryngologists in the first 6 months. The presence of VCP lasting >6 months was regarded as permanent. Any skin burn, swelling and hoarseness of voice during HIFU were recorded. For skin burn, if present, it was graded into the first, second or third degree burn. Patients were also asked to rate their pain during, immediately after treatment and before hospital discharge on a visual analogue scale (VAS) (0 = no pain and 10 = worse possible pain). During the first week, patients were specifically instructed to record any specific problems/complaints related to the treatment (such as swelling or dysphonia).

MVDP

Patients were encouraged to undergo a MVDP testing and to fill in a voice-related questionnaire (Voice Handicap Index [VHI]-30)) one day before (Baseline) and one month after treatment (1-month). The reason for choosing 1-month was because in the surgical group, the effect of endotracheal intubation itself may adversely affect voice quality for up to 2–3 weeks afterwards (10). All tests were performed in a quiet room under a standardised condition by one personnel. Each patient was asked to read aloud the same 22-word sentence five times. Voice was recorded directly into the KayPENTAX MDVP using a professional grade microphone (AKG C420). The microphone was placed 10 cm from the patient's mouth to avoid air burst. The middle three of the five trials were used for analysis. The entire sentence was analysed by MDVP. Measures to be analysed 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 while Jitter and Shimmer measured pitch and amplitude variability, respectively [19,20]. NHR measured the amount of noise present while MPT measured voice capacity (i.e. efficiency of voice production). The percentage change of each acoustic parameter over time was calculated based on the formula: [(1-month value − baseline value)/(baseline value)] × 100.

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) [21].

HIFU treatment

All treatments were performed by one person (B.H.L.) with >2 years of experience using the USG-guided HIFU device (EchoPulse; Theraclion, Paris, France). This device comprised an energy generator, a treatment head, a skin cooling device and a touch-screen 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). After positioning, patients were sedated with diazepam (10–15 mg) and pethidine (50–100 mg). Under USG guidance, the treatment head was adjusted until the entire index nodule was within the treatable depth. The device computer (Beamotion version no. TUS 3.2.2, Theraclion, Paris, France) automatically divided the nodule into multiple ablation subunits. Each subunit measured approximately 7.3 mm in thickness and 5 mm in width. Each subunit received continuous 8-s pulses of HIFU energy

Figure 1. Treatment screen. The central panel shows the top view reconstruction of the nodule which is made up of multiple white cycles. The empty circles represent the un-ablated subunits while the filled circles represent the ablated subunits.

followed by 40 s of cooling time before the beam moved to the adjacent subunit. This cycle continued until all subunits were ablated. To ensure safety, nearby structures such as the carotid artery, trachea and skin were marked on the treatment screen and left un-ablated (Figure 1). 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 204 J/pulse and increased up to 280 J/pulse until hyperechoic marks appeared at the focal point (Figure 1). Oral diet was resumed immediately afterwards, and patients were allowed to go home 2 h after treatment.

Surgery

All patients underwent a standardised hemithyroidectomy by one surgical team. Both the RLN and EBSLN on the operated side were carefully sought and mapped out by the IONM (Medtronic NIM-Response 3.0 system). An IONM was used to confirm the integrity of the nerves at the end of each procedure. The strap muscles were not be routinely transected during the procedure. Alternate energy was not be used to minimise collateral heat damage. No drain was placed. All patients required at least one overnight stay.

Cost of treatment

Only direct medical costs were calculated. Direct costs included procedure, associated aesthesia and hospitalisation. Indirect costs such as loss of productivity and wages were not included. The unit cost of each service has been listed in the Government Gazette [22].

Statistical analysis

Continuous variables were expressed as mean ± SD, and groups were compared using the Mann–Whitney *U* test. Chi-square tests were used to compare categorical variables. For voice quality comparison, separate linear regression models were performed to estimate the effects of HIFU and surgery on the change in each voice outcome at 1 month after baseline. All statistical analyses were performed using STATA Version 13.0 (StataCorp LP, College Station, TX). All significance tests were two-tailed and those with p values less than 0.05 were considered statistically significant.

Results

During this period, 43 patients completed single session of HIFU ablation and 103 who underwent a hemithyroidectomy

for a symptomatic benign thyroid nodule. All completed their baseline, 1-month and 6-month USG assessments afterwards. However, in the HIFU group, 1 had an apparent unilateral VCP afterwards and 2 failed to complete the 1-month MVDP testing while in the surgical group, 3 patients had an apparent unilateral VCP afterwards. All 4 VCPs recovered within 6 months. Therefore, only 40 patients in HIFU and 100 patients in surgery were included for the voice quality analysis.

Table 1. A comparison of baseline characteristics and voice quality between patients who underwent high intensity focussed ultrasound (HIFU) or hemithyroidectomy (surgery).

Variable	HIFU ($n = 43$)	Surgery ($n = 103$)	p value
Age at treatment (years)	47.9 ± 11.8	51.4 ± 15.7	**0.016**
Sex (Male:female)	2:41	28:75	**0.003**
Largest diameter of dominant nodule (cm)	3.6 ± 1.2	4.5 ± 1.5	**<0.001**
Nodule volume (cm^3)	5.15 ± 4.38	10.23 ± 9.97	**<0.001**
TSH (mIU/L)	1.4 ± 0.6	1.3 ± 1.3	0.701
Free T4 (pmol/L)	17.4 ± 1.5	17.8 ± 2.4	0.310
Mean F_0 (Hz)	205.4 ± 36.8	188.1 ± 42.6	**0.026**
Minimum F_0 (Hz)	154.0 ± 50.7	147.8 ± 48.2	0.501
Maximum F_0 (Hz)	251.1 ± 53.3	228.2 ± 56.4	**0.030**
Jitter or pitch perturbation (%)	0.4 ± 0.3	0.4 ± 0.6	0.739
Shimmer or amplitude perturbation (%)	0.5 ± 0.4	0.5 ± 0.3	0.787
Noise-to-harmonic ratio (NHR)	0.04 ± 0.1	0.04 ± 0.1	0.927
Maximum phonation time (MPT) (s)	11.5 ± 6.6	10.2 ± 4.6	0.185
Total VHI-30 score	6.0 ± 7.9	6.6 ± 11.8	0.782
Mean VHI score per item	0.2 ± 0.3	0.2 ± 0.4	0.800

Abbreviations: F_0: fundamental frequency; VHI: Voice Handicap Index.
*Bold signifies statistical significance ($p < 0.05$).

Table 1 shows a comparison of the baseline characteristics between the HIFU and surgery groups. Age at treatment, sex ratio, size and volume of the dominant nodule were significantly different between the two groups ($p < 0.05$) while the side of treatment (right lobe/left lobe) and thyroid function were comparable between the two groups ($p > 0.05$). Also both the baseline mean F_0 ($p = 0.026$) and max. F_0 ($p = 0.030$) were significantly higher in the HIFU group but this may be related to the fact that there were more female patients in the HIFU group.

Table 2 compares the treatment efficacy and safety between HIFU and surgery. Both had comparable procedure time ($p = 0.286$). For HIFU, pain was most severe during ablation (VAS: 3.5 ± 4.0) but improved immediately after ablation (VAS: 1.0 ± 1.0). During ablation, a few (13.9%) patients had pain radiating to the ipsilateral shoulders. On discharge, the pain score fell to almost zero (VAS: 0.0 ± 1.0). Three (13.6%) patients had mild residual discomfort during the first week. No patients suffered skin burn. Redness and swelling were noted in 13 (30.0%) patients but they all resolved in the first-week. The incidence of subclinical hypothyroidism was significantly higher in the surgical group than the HIFU group (20.4% vs. 2.3%, $p = 0.008$), but hypothyroidism (low serum FT4) was not detected within the first 6 months in both groups. Relative to surgery, the hospital stay was significantly shorter in the HIFU group (0.3 ± 0.2 day vs. 1.0 ± 0.0 day, $p < 0.001$). The cost of single-session HIFU was USD 1923.1 while the cost of a hemithyroidectomy was USD 5384.6. In terms of efficacy, the VRR at 1-month and 6-month in the

Table 2. A comparison of treatment efficacy and safety between the HIFU and surgery groups.

	HIFU ($n = 43$)	Surgery ($n = 103$)	p value
Treatment parameters (range)			
- Total energy delivered (KJ)	14.17 ± 5.44	–	–
- Total duration of treatment (min)	55.20 ± 30.10	57.1 ± 15.3	0.286
Pain scores by visual analogue scale			
- During treatment	3.5 ± 4.0	–	–
- Immediately after treatment	1.0 ± 1.0	–	–
- Before hospital discharge	0.0 ± 1.0	–	–
Skin burn (%)	0 (0.0)	–	–
Recurrent laryngeal nerve injury[a] (%)	1 (2.3)	3 (2.9)	1.000
Subclinical hypothyroidism[b] (%)	1 (2.3)	21 (20.4)	**0.008**
Hypothyroidism (FT4 < 12 pmol/L) (%)	0 (0.0)	0 (0.0)	–
Hospital stay (d)	0.3 ± 0.2	1.0 ± 0.0	**<0.001**
Size/volume of index nodule (mL)			
- Baseline	5.15 ± 4.38	10.23 ± 9.97	**<0.001**
- 1-week	5.31 ± 4.46	–	–
- 1-month	4.23 ± 3.58	–	–
- 6-month	2.54 ± 2.28	–	–
Volume reduction from baseline			
- 1-week (%)	−3.05 ± 4.63	–	
- 1-month (%)	17.84 ± 5.56	–	
- 6-month (%)	51.71 ± 16.04	–	
WHO nodule grade at 6-month			
- Grade 1a (*palpable but not visible when neck is extended*)	29 (67.4)	–	
- Grade 1b (*palpable and visible when neck extended*)	11 (25.6)	–	
- Grade 2 (*visible when neck is in the normal position*)	3 (7.0)	–	
- Grade 3 (*visible from distance*)	0 (0.0)	–	
Symptom improvement score			**0.009**
- 0 (*no improvement*)	3 (7.0)	10 (9.7)	
- 1 (*slight improvement*)	2 (4.7)	22 (21.4)	
- 2 (*moderate improvement*)	8 (18.6)	31 (30.0)	
- 3 (*significant improvement*)	29 (67.4)	40 (38.8)	

[a]Transient (i.e. complete vocal cord recovery within 6 months of treatment). No permanent injury in either group.
[b]Defined as serum thyroid-stimulating hormone (TSH) exceeding 4.78 mIU/L within the first 6 months following treatment.
*Bold signifies statistical significance ($p < 0.05$).

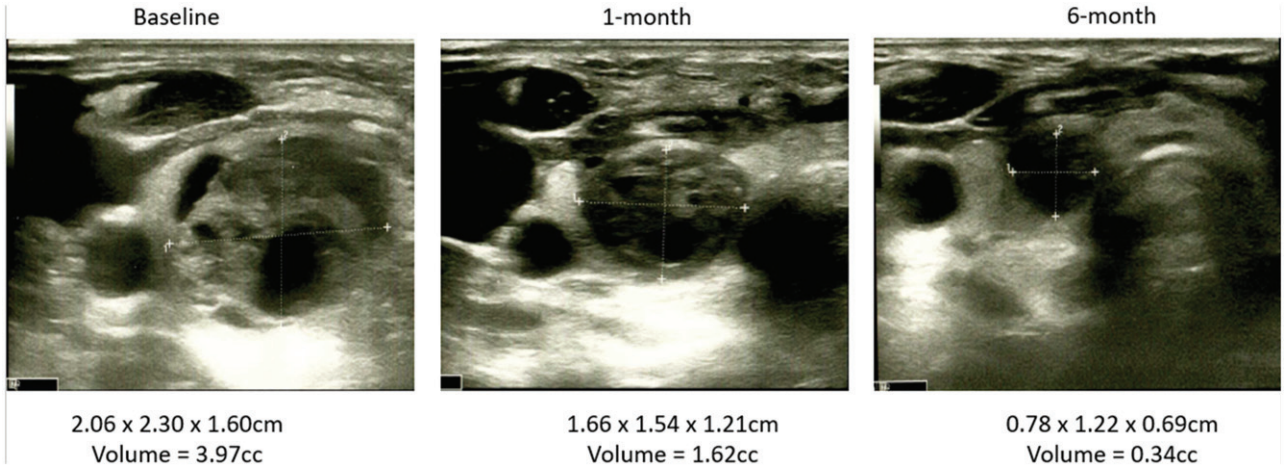

Figure 2. The ultrasound images obtained at baseline, 1-month and 6-month.

Table 3. A comparison of the difference in acoustic parameters and VHI between baseline and post 1-month.

	HIFU ($n = 42$)		Surgery ($n = 100$)		Linear regression (unadjusted)		
Variable	Baseline	1-month	Baseline	1-month	Coeff.	95%CI	p value
Mean F_0 (Hz)	205.4 ± 36.8	212.7 ± 44.5	188.1 ± 42.6	182.2 ± 46.2			
Difference in mean F_0 (Hz)	7.2 ± 32.5		−6.2 ± 26.5		13.47	2.90 – 24.05	**0.013**
Minimum F_0 (Hz)	154.0 ± 50.7	167.3 ± 57.4	147.8 ± 48.2	135.3 ± 48.9			
Difference in min. F_0 (Hz)	13.3 ± 52.3		−13.2 ± 41.5		26.52	9.80 to 43.25	**0.002**
Maximum F_0 (Hz)	251.1 ± 53.3	257.1 ± 57.7	228.2 ± 56.4	238.2 ± 63.2			
Difference in max. F_0 (Hz)	6.1 ± 55.0		13.2 ± 56.7		−7.14	−28.05 to 13.78	0.501
Jitter (%)	0.4 ± 0.3	0.3 ± 0.3	0.4 ± 0.6	0.5 ± 0.5			
Difference in Jitter (%)	−0.07 ± 0.20		0.15 ± 0.65		−0.22	−0.43 to 0.01	**0.038**
Shimmer (%)	0.5 ± 0.4	0.5 ± 0.4	0.5 ± 0.3	0.6 ± 0.4			
Difference in Shimmer (%)	−0.05 ± 0.32		0.08 ± 0.35		−0.13	−0.26 to 0.00	**0.044**
NHR	0.04 ± 0.1	0.03 ± 0.1	0.04 ± 0.1	0.06 ± 0.1			
Difference in NHR	−0.015 ± 0.054		0.015 ± 0.086		−0.03	−0.06 to 0.00	0.044
MPT (s)	11.5 ± 6.6	10.1 ± 5.6	10.2 ± 4.6	9.5 ± 5.7			
Difference in MPT (s)	−1.4 ± 5.0		−0.7 ± 8.1		−0.71	−3.44 to 2.03	0.609
Total VHI-30 score	6.0 ± 7.9	10.8 ± 18.0	6.6 ± 11.9	16.0 ± 20.1			
Difference in total VHI-30	4.8 ± 19.5		9.77 ± 20.2		−4.65	−12.08 to 2.78	0.218
Mean VHI-30 score per item	0.2 ± 0.3	0.4 ± 0.6	0.2 ± 0.4	0.5 ± 0.7			
Difference in mean VHI score per item	0.16 ± 0.65		0.32 ± 0.69		−0.16	−0.41 to 0.10	0.228

Abbreviations: F_0: fundamental frequency; NHR: noise-to-harmonic ratio; VHI: Voice Handicap Index.
*Bold signifies statistical significance ($p < 0.05$).

HIFU group was 17.84 ± 5.56% and 51.71 ±.16.04%, respectively (see Figure 2). Interestingly, the proportion of patients experiencing "significant improvement" was significantly more after single HIFU ablation than surgery (67.4% vs. 38.8%, $p = 0.009$).

The overall difference in mean F_0, minimum F_0 and maximum F_0 in the HIFU group was positive (i.e. 1-month pitch was higher than baseline) while in the surgical group, the overall difference was in negative (see Table 3). This meant the 1-month pitch in the surgical group was generally lower than baseline while in the HIFU group, pitch was not significant affected. Among the vocal parameters, the change in mean F_0, minimum F_0, Jitter and Shimmer was significantly different between the two groups. However, there were no significant differences in VHI-30 score between the two groups.

Discussion

To our knowledge, this is the first study to formally compare efficacy, safety and the early change in voice quality between patients who undergo HIFU and surgery in the treatment for symptomatic benign thyroid nodule. Although previous studies have compared the efficacy and safety between thermal ablation and surgery, only RFA was assessed [23,24]. Our data showed that HIFU was an efficacious and safe ablation method for benign thyroid nodules. For the first 6 months, we observed progressive nodule shrinkage starting from the first month and gradually extending to 6 months. Interestingly, similar to our previous observation, the first-week volume of the treated nodule swelled by 5% from baseline [9]. We believe this might be related to tissue oedema from tissue destruction. However, at 6-month, the mean nodule volume reduction with a single treatment was 51.71 ± 16.04% which seemed comparable to that of previous studies [7–9]. Although the volume reduction is like to increase with a longer follow-up period [25], it appears the volume reduction might be similar to those with LA but slightly less than those with single session of RFA [6,26].

In terms of safety, despite the mild neck swelling observed in about one third of cases, none of them actually resulted in skin burn afterwards. Only 1 patient (2.3%)

suffered immediate hoarseness and was later confirmed to have VCP presumably from a RLN thermal injury. However, this patient's paralysed VC recovered within 6 weeks and her voice normalised within 4 weeks. In our early experience, the incidence of temporary RLN injury from HIFU was not significantly different from that of surgery (2.3% vs. 2.9%, $p = 1.000$). This finding was also reported in previous comparisons between RFA and surgery [23,24]. We believe this injury is preventable and it is best prevented by avoiding the "danger triangle" (i.e. the area around the trachea-esophageal groove) where the RLN is located [6].

In terms of benefits over surgery, HIFU was associated with a significantly shorter length of hospital stay (0.3 day vs. 1.0 day, $p < 0.001$) and cost significantly less. In addition, this is a truly "scar-less" procedure and there was a significantly lower incidence of subclinical hypothyroidism following HIFU (2.3% vs. 20.4%, $p = 0.008$). Also interestingly, those who underwent HIFU had significant better symptom improvement score than those who underwent surgery ($p = 0.009$).

Although hypothyroidism (i.e. low FT4) was not found between the two groups, it should be noted that the incidence of hypothyroidism following surgery depends on a multitude of factors including the primary excised pathology, size of remnant lobe, concomitant thyroiditis and most importantly, the definition of hypothyroidism [27] and therefore, there is a significant difference in the reported incidence of hypothyroidism after surgery in the literature [23,24].

In terms of voice quality, the surgery group had a significantly poorer quality at 1-month than the HIFU group. Using MVDP as an objective measurement tool, our data showed that the surgical group had a significantly lower mean F_0 ($p = 0.013$) and minimum F_0 ($p = 0.002$) but a significantly increase in Jitter ($p < 0.038$) and Shimmer ($p = 0.044$) than the HIFU group (see Table 3). Perceptually, the two former findings meant that patients generally had a lower pitched voice while the latter meant more pitch perturbation (or rough voice). Interestingly, since these three parameters are linked to pitch, this would suggest that our findings were internally consistent and there might be factors specific to surgery which made pitch particularly affected. We postulate the unintentional surgical trauma to the surrounding soft tissues and minor nerves (such as the external branch of the superior laryngeal nerve) might be responsible for the impaired pitch quality in the surgical group. However, since this is the first study of its kind, more studies are required to look more closely at the effect of extra-corporeal HIFU treatment on voice and its production by the larynx.

Another point worth pointing out is the fact that despite the noticeable changes in acoustic parameters at 1-month, there appeared to be no real difference in the subjective voice. With a validated voice-related questionnaire like the VHI-30, we were not able to find any significance differences between the two groups at 1-month after treatment.

The clinical implication of our findings is that it lends support to the use of HIFU ablation as an alternative treatment for symptomatic benign thyroid nodule. Although these findings were expected because of the minimally invasiveness of HIFU ablation relative to open surgery, it does provide important information on the expected voice quality changes in the early post-treatment period between the two procedures.

Our study showed that HIFU treatment was a highly-efficacious and well-tolerated procedure that could be performed in an outpatient setting. The one-year VRR or extent of nodule shrinkage after a single HIFU ablation ranged between 49 and 69% with minimal complications [7–9,28]. In our experience, the hospital stay was significantly shorter in the HIFU group than the surgery group ($p < 0.001$), and the direct cost of single-session HIFU treatment was approximately one-third of that of a hemithyroidectomy. In line with these findings, a recent study compared the health-related quality of life (HRQOL) and cost-effectiveness between RFA and surgery and reported that HRQOL 6 months after RFA was significantly better that after surgery [29]. However, due to the relatively low cost of surgery in China, the study was not able to show RFA to be more cost-effective than surgery unless the cost of the RFA device was lowered by 30% [29].

However, despite these findings, we would like to acknowledge the following shortcomings. First, since this was a non-randomized study, there were significant differences in the baseline characteristics between the two groups that may account for some of the differences in outcomes (i.e. selection biases). Second, our study was a relatively small study and so, our results were prone to type II errors (i.e. non-significant findings might have been due to inadequate power of the study). Third, considering the relatively small size of the treated nodules by HIFU, the ablation time was not significantly shorter than surgery and in fact, it appeared relatively longer than other ablation techniques.

Conclusions

Relative to surgery, single HIFU ablation was highly efficacious and safe. Apart from shorter hospital stay, less subclinical hypothyroidism, being scar-less, lower cost and more symptom improvement, patients who had HIFU were less affected by a pitch problem in the first month than those who had surgery. This study provides a strong argument for HIFU ablation as a treatment for symptomatic benign thyroid nodules.

Disclosure statement

All authors had nothing to disclose. No competing financial interests exist.

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