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Evolving patient preferences from surgery to thermal ablation in solitary thyroid nodule treatment

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A changing landscape of patients' preferences for treatment of solitary and benign thyroid nodules (SBTN) form conventional surgery to other minimally invasive treatments (MITs) has been witnessed. The aim of this study was to evaluate indications, patients' preferences and outcomes of conventional surgery vs. transoral endoscopic thyroid surgery by vestibular approach (TOETVA) vs. laser ablation (LA) treatments for SBTN. This prospective cohort study included patients with SBTN causing compression symptoms treated at our institution throughout 2020–2023. Primary endpoint was patients' preferences for treatment. Secondary endpoints were: success rate, overall morbidity, need for second line treatment, and satisfaction rate. Some 204 patients (F: M = 161:43) with SBTN were offered conventional surgery (thyroid lobectomy) vs. TOETVA vs. LA. Patients' preferences were: 23 (11.3%) for conventional surgery vs. 17 (8.3%) for TOETVA vs. 164 (80.4%) for LA ($p < 0.01$). Overall morbidity was 2/23 (8.7%) for conventional surgery vs. 2/17 (11.8%) for TOETVA vs. 3/164 (1.8%) for LA ($p < 0.01$). Volume reduction ratio (VRR) for LA was 63% (range: 32 – 98%) at 6 months following treatment. Spongiform nodules vs. predominantly solid tumors vs. solid tumors had VRR of 83% vs. 67% vs. 51%, respectively ($p < 0.01$). Second line treatment was needed for 3/101 (3.0%) patients following LA within a 3-year follow-up. Satisfaction rate was higher for LA and TOETVA vs. conventional surgery ($p < 0.01$). Currently most patients prefer MITs for SBTN. TOETVA is chosen by minority of patients with a strong motivation to avoid scar whereas thermal ablation is the preferred MIT nowadays.

Keywords Solitary thyroid nodule, Autonomously functioning thyroid nodule, Thyroid surgery, Thyroid lobectomy, Minimally invasive treatment, Thermal ablation, Laser ablation

Thyroid nodules are common and affect up to 50% of women and 20% of men. Most thyroid nodules remain stable over time on follow-up but some of them may require treatment due growth leading to development of compressive symptoms, cosmetic concerns, suspicion of malignancy or presentation with hyperthyroidism as a result of autonomous functioning thyroid nodule (AFTN)[1]. Pretreatment workup should include sonographic risk-stratification assessment based on well-validated systems e.g. European Thyroid Imaging Reporting and Data Systems (EU-TIRADS) or equivalent which can be used to estimate the risk of malignancy and the need for fine-needle aspiration (FNA) based on nodule features and size[2,3]. As shown by recent European Thyroid Association (ETA) survey, for most thyroid nodules including benign ones, surgery still remains the first choice option for many physicians whereas minimally invasive treatments (MITs) including thermal ablation or scarless / remote access surgical approaches are not well recognized[4]. Hemithyroidecomy can be considered a radical treatment for some patients with asymmetrical nodular goiter and in particular with a solitary benign thyroid nodule (SBTN). Thyroid lobectomy presents a low risk of recurrent disease and hypothyroidism, offering a safer alternative to total thyroidectomy. While lifelong follow-up is necessary, the likelihood of recurrence or the need for levothyroxine supplementation and revision surgery remains uncommon and affects only select cases[5,6]. On the other hand image-guided thermal ablation (TA) procedures are increasingly proposed as therapy options for selected benign nodules that cause symptoms or cosmetic concern. Presently, laser (LA) and radiofrequency ablation (RFA) are the most thoroughly assessed techniques of thyroid function sparing MITs, with similar satisfactory clinical results[7]. Many studies have shown that a single session of TA can significantly reduce the volume of the thyroid nodule leading to disappearance of compression symptoms, or cosmetic defects, in the

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absence of thyroid function changes[7–11]. Treatments are usually well tolerated and risk of major complications remains 3-fold lower than after thyroid surgery[8].

The hypothesis explored in this study is that there is a changing landscape of patients' preferences for treatment of SBTN as a result of a shared decision-making (SDM) with a potential for shift of paradigm form conventional thyroid surgery to other scarless surgical approaches like transoral endoscopic thyroid surgery by vestibular approach (TOETVA) or other MITs. The aim of this study was to evaluate indications, patients' preferences and outcomes of conventional surgery vs. TOETVA vs. LA treatments for SBTN.

Materials and methods

Study design and patient selection

Patients referred to the Thyroid Disease Treatment Center, Na Klinach Hospital, Kraków, Poland for first-time thyroid treatment between January 2020 and December 2023 were registered. Eligible patients with an asymmetric nodular goiter were assessed for this prospective cohort study (Fig. 1). This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board (IRB): Bioethics Committee of the Jagiellonian University (approval no: 1072.6120.63.2019).

The inclusion criteria were: a SBTN with the contralateral thyroid lobe appearing normal on ultrasound, in an euthyroid patient, nodule volume ≥ 5 mL, spongiform, predominantly solid (solid portion > 80%), or solid nodule, compression symptoms or cosmetic concerns, confirmation of a benign thyroid nodule in two FNAs, normal calcitonin serum level with the absence of antithyroglobulin antibodies (TgAb) and antithyroid peroxidase antibodies (TPOAb), or a solitary autonomously functioning thyroid nodule (AFTN) < 10 mL in a patient refusing radioactive iodine (RAI) treatment.

The exclusion criteria were: multinodular/bilateral euthyroid or toxic goiter, nodules showing ultrasonographic features suggestive high risk of malignancy (EU-TIRADS 5), previous thyroid surgery or nodule treatment, pregnancy or lactation, age < 18 years, ASA 4 grade (American Society of Anesthesiology), and inability to comply with the follow-up protocol.

Ultimately, 204 eligible patients were offered to choose the treatment modality between surgery (open lobectomy or TOETVA) and LA based on their preferences as a result of the SDM process. Patients signed the informed consent form, and were scheduled for individually tailored treatment of their choice within 4 weeks form the timepoint of counseling.

The primary endpoint was patients' preferences for treatment. Secondary endpoints were: success rate, overall morbidity, need for second line treatment, and satisfaction rate.

Success rate was defined as proportion of nodules with more than 50% reduction in volume at 12 months (technical success rate), and relief of compression symptoms (clinical success rate).

Pretreatment and posttreatment laryngoscopy were mandatory for all patients undergoing surgery, but it was recommended for patient with a voice change after LA.

Laboratory workup

Serum TSH, free T4 (FT4), thyroglobulin (Tg), TPOAb, TgAb, and calcitonin levels were assessed before treatment and annually thereafter.

Thyroid ultrasound

Thyroid ultrasound evaluation was performed by the same physician (M.B. or J.B.) at baseline using a commercially available ultrasound machine (Voluson P8, GE, San Jose, CA, USA) equipped with a 7.5–13.0 MHz linear transducer and tuned with the ModiLite system (EchoLaser, ELESTA srl, Florence, Italy). Nodule volume was reported in mL using the following ellipsoid volume formula: (length × width × depth) × 0.53. Nodules were classified as spongiform (EU-TIRADS 2) if the nodule composition was characterized by the presence of intervening multiple diffuse microcystic lacunae or solid (EU-TIRADS 3–4) or predominantly solid (solid portion > 80% of the nodule volume). The nodules were classified based on their size as small (≤ 10 mL), medium (10–30mL), and large (> 30 mL).

Surgical technique

Surgical operations were performed under general anesthesia with endotracheal intubation and neuromonitoring (NIM Vital™, Medtronic, Jacksonville, USA) as previously described[12,13].

All total extracapsular unilateral thyroid lobectomies were performed by the same experienced endocrine surgeon involved in the study (M.B.) using either open technique or TOETVA[14–17]. In each patient, the ipsilateral recurrent laryngeal nerve was exposed, and the branches of the superior and inferior thyroid arteries were divided close to the thyroid capsule (peripheral ligation) using Ligasure Exact™ energy-based device for open surgery or LigaSure™ XP Maryland jaw device for TOETVA (Medtronic, Jacksonville, FL, USA). The parathyroid glands were meticulously dissected from the thyroid gland, and effort was made to identify both ipsilateral parathyroid glands and preserve them "in situ". Contralateral thyroid disease was excluded preoperatively by ultrasonography of the neck. An overnight hospital stay was mandatory for all patients undergoing surgery.

Laser ablation

Two operators, an experienced endocrine surgeon (M.B.) and endocrinologist (J.B.), both trained in interventional endocrinology, who have regularly performed LA (~ 50 treatments) for 6 months before onset of this study, performed all the procedures in the Outpatient Setting, including the initial diagnostic evaluation, and use of the same ultrasonography equipment for guidance during LA. Patients were placed supine with their neck fully extended. After an ultrasound examination of the neck and planning of the entry point of the needles, local anesthesia was administered. The ModiLite system (Echolaser, ELESTA srl, Florence, Italy) was used with a

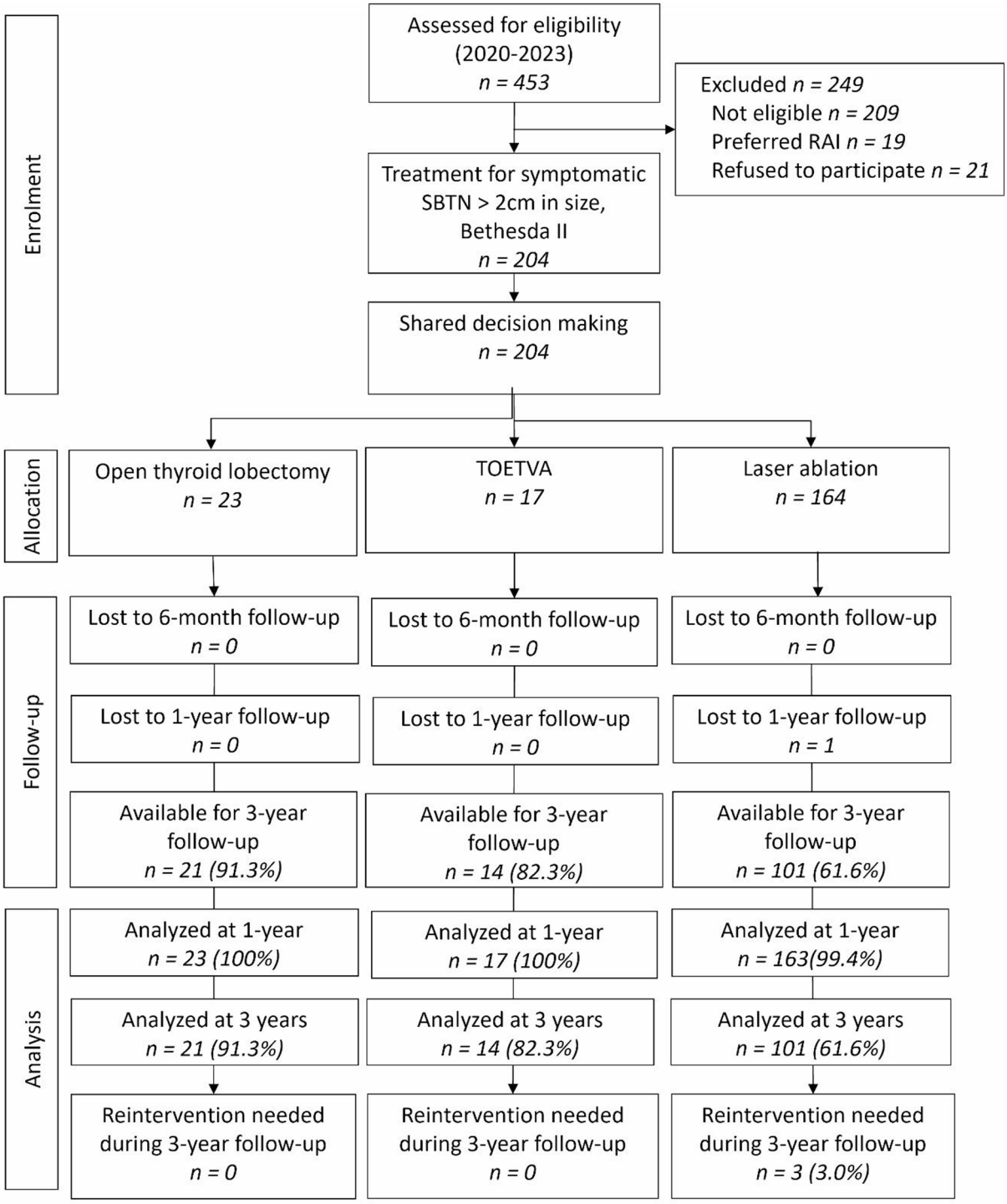

Fig. 1. Flow chart of patients in the study. SBTN – solitary benign thyroid nodule; Bethesda II (fine needle-aspiration cytology result suggestive for benign tumor); TOETVA – transoral thyroid lobectomy by vestibular approach.

dedicated multi-applicator Guiding Systems for ultrasound probes specifically designed for the anatomical area of the thyroid, with the relative Biopsy Software (the Echolaser Smart Interface, version 18.1, ESI, Elesta SpA, Italy, www.elesta-echolaser.com/echolaser-evo) that displays the guidelines on the screen and Planning Software (the Echolaser Smart Interface, version 18.1, ESI, Elesta SpA, Italy, www.elesta-echolaser.com/echolaser-evo) in the ultrasound unit that allows physicians to choose among the various treatment possibilities, the most suitable and safest for each specific case, and verify the correct positioning of the needles inside the nodule (Fig. 2).

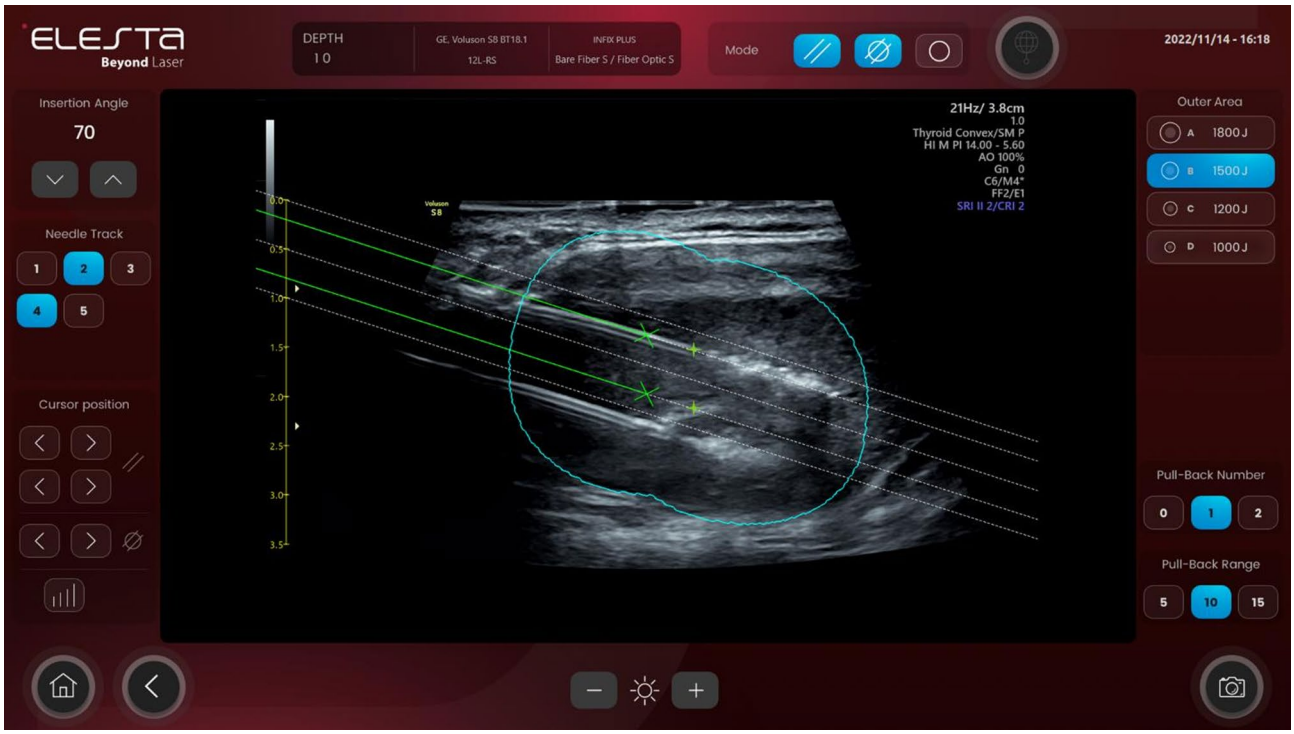

Fig. 2. Laser ablation of a 12 ml in volume right thyroid lobe autonomous functioning thyroid nodule is done with 2 laser beams and under the Echolaser Smart Interface (version 18.1, ESI, Elesta SpA, Italy) ultrasound guided control.

LA was performed by inserting 21-gauge spinal needles into the target thyroid lesion under ultrasound guidance. After ultrasound guided needle introduction and positioning of the needle tips, a 300 µm diameter plane-cut quartz optical fiber was introduced through the sheath of the needle, and the fiber tip was placed in direct contact with the tissue. Optic fibers were connected to the laser source, a continuous-wave Nd-YAG laser operating at 1064 µm with an optical beam splitting device (EchoLaser, Elesta, Florence, Italy) and an output power of 3–4 W. One to two needles were manually placed along the longitudinal, craniocaudal, and major nodule axes at a distance of 10 mm each, fitting the shape of the nodule as best as possible (Fig. 2). The procedure started with deposition energy of 1500–1800 J per fiber in the caudal part of the nodule, 10 mm from the lower margin, trachea, and carotid. By upward needle/fiber pullbacks of 10 mm, additional energy was administered until a distance of 5–10 mm from the upper part of the nodule was reached. During ultrasound monitoring, the treatment area was visualized as a transient hyperechoic zone, which enlarged over time because of the formation of gas microbubbles within the coagulated tissue[7]. The effectiveness of this pullback technique was well-validated in previous publications[7–11,18,19]. Patients were discharged from the Outpatient Department within 2 h of the procedure.

Posttreatment follow-up

High-resolution ultrasound of the neck was performed on follow-up visits by the same physicians as at baseline. All the patients were evaluated at 6 and 12 months during the first year and every 12 months for the following years up to completion of the assumed 36-month follow-up. Changes in nodule volume were expressed as volume reduction rate (VRR) calculated using the following formula: (initial volume − final nodule volume) × 100/initial volume.

The following indication for reintervention among LA patients was used: the nodule regrowth defined as > 20% increase in volume form the lowest posttreatment volume at 6 or 12 months in a patient with recurrent compressive symptoms.

Statistical analysis

Statistical significance of categorical variables was evaluated by the χ^2-test, whereas the Student t test and F-test were used for the evaluation of continuous variables. Comparison of technical success rate for open surgery and TOETVA versus LA was done assuming that surgical treatment lead to 100% VRR. Satisfaction rate was measured on the Visual Analogue Scale (0–10 points) and calculated as continuous variable. All the data were entered onto a dedicated spreadsheet (Microsoft Excel 2020; Microsoft Corporation, Redmond, Washington, USA) by a medical assistant and then analyzed by a statistician (MedCalc® v22.032). $p < 0.05$ was considered to indicate significance.

Results

Flow chart of the study is presented on Fig. 1. Demographic characteristics of the 204 patients in the study is shown in Table 1.

Some 204 patients (F: M = 161:43) with symptomatic SBTN were offered conventional surgery (thyroid lobectomy) vs. TOETVA vs. LA during first-time counseling at our institution using the SDM process. As a result our patients had the following preferences regarding their treatment for a SBTN: 23 (11.3%) decided to undergo conventional surgery (open thyroid lobectomy) vs. 17 (8.3%) opted for TOETVA vs. 164 (80.4%) chose LA ($p < 0.01$).

The technical and clinical success rate at 12 months was achieved in all patients operated on by open thyroid lobectomy or TOETVA, but in 74.2% and 90.2% of patient undergoing LA, respectively ($p < 0.001$). All patients with VRR of 50% or more had disappearance of compression symptoms, whereas some patients with less than 50% VRR experienced remarkable relief.

Median nodule VRR for LA was 63% (range: 32–98%) at 6 months following treatment. Spongiform nodules vs. predominantly solid tumors vs. solid tumors had median VRR of 83% vs. 67% vs. 51%, respectively ($p < 0.01$). Median nodule VRR after LA at 12-month follow-up was durable and equal to 67.0% (range: 31–99%). Spongiform nodules vs. predominantly solid tumors vs. solid tumors had median VRR at 12 months of 84.4% vs. 69.1% vs. 51.9%, respectively ($p < 0.01$). Second line treatment for nodule regrowth (> 20% increase in nodule volume from VRR at 12 month) and reoccurrence of compression symptoms was needed for 3/101 (3.0%) patients following LA available for a 3-year follow-up (Table 2), whereas it was not needed for any of the patients following open thyroid lobectomy or TOETVA at the same time-frame (Tables 3, 4). None of the patients in the LA arm experienced nodule regrowth exceeding baseline nodule volume and none of them underwent thyroid surgery during 3-year follow-up.

Among 15 patients with an AFTN refusing RAI treatment with median nodule volume at baseline of 6.3 mL median VRR at 6 months was 65.0% (range: 49–85%) and 74.0% (range: 55–89%) at 12 months. This effect of treatment was translated into the clinical benefit in the majority of patients as 13/15 (86.7%) of individuals had stable normal TSH serum value after LA with no need for antithyroid medication (Table 3). However, it is important to note that patients with AFTN received higher energy delivered per mL of nodule tissue which was equal to 910.0 J (range: 720–1100 J) whereas patients with nonfunctioning SBTN received lower energy delivered per mL which was equal to 651.0 J (range: 500–850 J), $p < 0.001$.

Overall morbidity was 2/23 (8.7%) for conventional surgery vs. 2/17 (11.8%) for TOETVA vs. 3/164 (1.8%) for LA ($p < 0.01$). Details are presented in Table 4. Inadvertent removal of parathyroid gland was identified in 3 out of 40 patients (7.5%) who underwent thyroid lobectomy. None of them had postoperative hypocalcemia. One patient with abscess in the LA arm had US-guided percutaneous evacuation with antibiotic treatment, whereas 2 patients with hematoma required only conservative treatment. Twelve of 40 thyroid lobectomy patients (30%) had elevated serum TSH and required levothyroxine for hypothyroidism. All had pre-operative anti-TPO elevation, confirming Hashimoto thyroiditis, with chronic lymphocytic thyroiditis in surgical specimens.

Satisfaction rate was higher for LA and TOETVA vs. conventional surgery ($p < 0.01$). However, satisfaction rate was higher after TOETVA vs. LA ($p = 0.006$).

Discussion

In the present study the SDM process for thyroid nodules involving a collaborative approach between the patient and the physician to make informed decisions about treatment options was used[20]. First, the diagnosis and the available treatment options, including their benefits, risks, and potential outcomes were discussed in detail.

	Open thyroid lobectomy ***N*** **= 23**	**TOETVA** ***N*** **= 17**	**Laser ablation** ***N*** **= 164**
Sex (male/female)	3:20	2:15	24:140
Age (years ± SD)	53.2 ± 7.6	41.2 ± 6.7	46.7 ± 9.3
Location (right/left)	10:13	10:7	81:83
Non-functioning (%) / AFTN (%)	18 (78.3%) / 5 (21.7%)	14 (82.4%) / 3 (17.6%)	149 (90.8%) / 15 (9.2%)
Mean nodule volume (ml ± SD)	15.9 ± 3.9	12.4 ± 2.3	11.8 ± 2.7
Mean nodule diameter (mm ± SD)	39.4 ± 6.6	37.3 ± 5.5	36.2 ± 8.6
Mean lobe volume (ml ± SD)	24.3 ± 10.6	20.1 ± 4.3	20.1 ± 4.3
Treatment time (mean ± SD)	30 ± 5.2	90.4 ± 10.9	35.0 ± 5.0
FNA cytology: Bethesda II	23 (100%)	17 (100%)	164 (100%)
Pathology report:			NA
- Colloid nodule	15 (65.2%)	10 (58.8%)	
- Hyperplastic nodule	5 (21.8%)	5 (29.4%)	
- Nodular hyperplasia	3 (13.0)	2 (11.8%)	

Table 1. Baseline characteristics of 204 patients in this study. TOETVA: Transoral thyroid lobectomy by vestibular approach, AFTN: autonomic functioning thyroid nodule, SD: standard deviation; non-significant differences for all parameters / values except treatment time (for open thyroid lobectomy and laser ablation vs. TOETVA, $p < 0.001$); NA: not applicable.

Nodule characteristics: number (%)	
- Spongiform	**72 (43.9%)**
- Partially cystic/solid	**41 (25%)**
- Solid	**51 (31.1%)**
1 laser beam / 2 laser beams, number (%)	123 (75%) / 41 (25%)
Energy delivered (J) (Median; 25.0–75.0%)	7500 (4000–10000)
Energy delivered/mL (Median; 25.0–75.0%)	651.0 (532–770)
Nodule volume at baseline (mL) (Median; 25.0–75.0%)	11.8 (7–17)
Small nodules (≤ 10 mL) number, (%)	99 (60.4%)
Medium nodules (10–30 mL) number, (%)	60 (36.6%)
Large nodules (> 30 mL) number, (%)	5 (3.0%)
VRR at 6-month follow-up (%) (median; 25.0–75.0%)	63.0 (49–73)
- Spongiform	83.2 (65–89)
- Predominantly solid	67.4 (47–77)
- Solid	51.1 (38–61)
VRR at 12-month follow-up (%) (median; 25.0–75.0%)	67.0 (51–75)
- Spongiform	84.4 (67–90)
- Predominantly solid	69.1 (49–79)
- Solid	51.9 (39–62)
Nodule regrowth within 3-year follow-up [> 20% form VRR at 12 month; 101/164 patients available for follow-up], number (%)	3 (3.0%)

Table 2. Outcomes of 164 patients who underwent laser ablation. VRR: volume reduction ratio.

Nodule characteristics: solid, number (%)	15 (100%)
TSH < 0.001 (mIU/L) at diagnosis, number (%)	15 (100%)
Nodule volume at baseline (mL) (Median; 25.0–75.0%)	6.3 (5.0–7.7)
Energy delivered (J) (Median; 25.0–75.0%)	6000 (4000–7200)
Energy delivered/mL (Median; 25.0–75.0%)	910.0 (757–1005)
VRR at 6-month follow-up (%) (median; 25.0–75.0%)	65.0 (55–75)
VRR at 12-month follow-up (%) (median; 25.0–75.0%)	74.0 (64–85)
Antithyroid medication at 6 month follow-up: number (%)	
- Continued with the same dose	1 (0.7%)
- Dose reduced	1 (0.7%)
- Withdrawn	13 (86.7%)

Table 3. Outcomes of 15 patients who underwent laser ablation for AFTN. AFTN: autonomously functioning thyroid nodule.

Patients had an opportunity to share their values, preferences, and concerns regarding the treatment options. This usually included factors like the desire to avoid surgery, maintain unaltered thyroid function, concerns about potential surgical complications, or the importance of cosmetic outcomes. The individual patient's preferences and medical history were considered to arrive at a mutually agreed-upon decision on the best course of action. The patients were provided with a clear plan for treatment and further follow-up including option for adjustment of the treatment plan if necessary[20,21]. As a result of the SDM process our patients' preferences were: 23 (11.3%) for conventional surgery (open thyroid lobectomy) vs. 17 (8.3%) for TOETVA vs. 164 (80.4%) for LA ($p < 0.01$). Patients opting for radical treatment preferred open surgery with neuromonitoring or TOETVA. The latter one was attractive mostly to young female patients wishing to avoid scar. However, majority of patients with SBTN preferred to undergo non-surgical MIT under local anaesthesia offering disappearance/relief of compressing symptoms and/or improved cosmetic outcome with no scar, short stay in the hospital in the outpatient setting, an unaltered thyroid function, and no need for life-long thyroid substitution therapy with levothyroxine. Many published studies have proven these clinical benefits of TA which are in line with our observations[7,9,10]. A single LA treatment leads to a significant and persistent reduction in the volume of the thyroid nodule and improves local symptoms without any changes to the thyroid function[9]. Negro et al. reported recently that VRR of thyroid nodules subjected to similar amounts of laser energy varied widely and depended on the nodule composition; non-spongiform nodules were reduced to a lesser extent and regrow more frequently than spongiform nodules. A 12-month VRR < 50.0% is a predictive risk factor for regrowth and correlates with the time to regrowth[22]. Outcomes reached in our study confirm these findings as spongiform nodules followed by partially solid were most prone to shrinkage after LA whereas solid nodules had lower but still satisfactory VRR at 6 and 12 months with a durable effect during 3-year follow-up. Need for reintervention was 3.0% at our hands during 3-year

	Open thyroid lobectomy $N=23$	TOETVA $N=17$	Laser ablation $N=164$
Technical success rate, number (%)			
- At 12 months	23 (100%) $^{\alpha}$	17 (100%) $^{\alpha}$	121/163 (74.2%) $^{\alpha}$
- At 36 months	20/21 (95.2%) $^{\alpha}$	14/14 (100%) $^{\alpha}$	72/101 (71.3%) $^{\alpha}$
Clinical success rate, number (%)			
- At 12 months	23 (100%)	17 (100%)	147/163 (90.2%)
- At 36 months	20/21 (95.2%)	14/14 (100%)	86/101 (85.1%)
Overall morbidity, number (%)	2 (8.7%) $^{\beta}$	2 (11.8%) $^{\beta}$	3 (1.8%) $^{\beta}$
- Transient RLN paresis	1 (4.3%)	1 (5.9%)	0 (0%)
- Wound infection / abscess	1 (4.3%)	0 (0%)	1 (0.6%)
- Hematoma	0 (0%)	0 (0%)	2 (1.2%)
- Transient mental nerve injury	0 (0%)	1 (5.9%)	0 (0%)
Patient satisfaction, VAS (points) - At 2 months - At 6 months	7.82 ± 1.64 $^{\mu}$ 9.39 ± 1.03 $^{\mu}$	9.52 ± 0.80 $^{\mu}$ 9.88 ± 0.33 $^{\mu}$	8.61 ± 1.68 $^{\mu}$ 9.70 ± 0.62 $^{\mu}$

Table 4. Success rate, morbidity and patient reported satisfaction of 204 patients in this study. TOETVA: Transoral endoscopic lobectomy by vestibular approach; VAS: visual analogue scale (0–10 points); (α) $p<0.001$ for open thyroid lobectomy and TOETVA vs. laser ablation; (β) $p<0.01$; (μ) $p<0.05$.

follow-up, but one can expect that this value may increase with time of surveillance mandating long-term observation after MITs on yearly basis. Nevertheless, some patients with VRR of less than 50% after initial treatment may still be candidates for re-treatment with TA. As shown by Bernardi et al. re-treatment led to VRR of 50% and 52.2% after 6 and 12 months. VRR after re-treatment was greater than after first treatment in small and medium size nodules (< 30 mL), while there were no differences for large nodules (> 30 mL)[23]. Hence, for large nodules in volume other TA techniques like RFA or microwave ablation (MWA) might be useful. Alberti et al. reported recently that ultrasound-guided MWA was most effective and safe MIT also for large benign thyroid nodules and VRR of 73.5% has been reached among this patient population at 6 months[24].

Among patients in this study there were also 23 individuals with AFTN who refused to undergo radioactive iodine treatment. Only 5 (21.7%) and 3 (13.0%) of them decided to undergo open thyroid lobectomy or TOETVA, respectively, whereas 15 (65.2%) patients preferred LA. Median nodule volume at baseline for these AFTN was 6.3 mL and median VRR at 6 months was 65.0% (range: 49–85%), and 74.0% (range: 55–89%) at 12 months. This effect of treatment was paralleled by TSH serum level normalization and anti-thyroid drug therapy discontinuation in 13/15 (86.7%) patients (Table 3). Similar outcomes were presented by Mauri et al. who reported in a study comprised of 361 patients with AFTN that nodule volume was significantly reduced of 60% at 12-month which corresponded to serum TSH values normalization in 41.3% of patients at 12 months, but increase in TSH from baseline was noted in all the remaining patients. A significant difference in the rate of patients who withdrawn antithyroid medication at 12 months was registered in this study between small (< 10 mL) (74%), medium (49%), or large (> 30 mL) nodules (19%)[25]. Similar encouraging results were presented by Duenas et al. in a multicenter study from Latin America comprised of 81 patients with a solitary, benign AFTN. The VRR was 78.4% at 6 months and 90.2% at 12 months. The rate of resolution of hyperthyroidism was 93.8% at 3 months. In bivariate analyses, a VRR ≥ 50% at the 6-month follow-up was associated with the resolution of hyperthyroidism[26]. In general, ETA recommend against TA as first-line treatment for large AFTN; due to the low rate of restoration of normal thyroid function, TA should be considered only for patients who decline or are not candidates for RAI therapy or surgery. However, TA should be considered in young patients with small AFTN and incomplete suppression of perinodular thyroid tissue due to the higher probability of normalization of thyroid function and the advantage of avoiding irradiation and restricting risk of late hypothyroidism[7].

Thyroid lobectomy remains an effective therapeutic strategy for unilateral, benign nodules, resulting in a low rate of clinically relevant nodular relapse in a mildly iodine-deficient area. Patients with uninodular disease and a contralateral lobe of normal size are particularly good candidates for lobectomy[5,6,27]. Hemithyroidectomy can be done nowadays by TOETVA which represents a true scarless approach as surgical access is gained through the mouth meeting ideally the concept of natural orifice transluminal endoscopic surgery (NOTES)[14]. The TOETVA technique has been matured and adopted in many high-volume endocrine surgical units worldwide offering radical treatment for small symptomatic thyroid nodules and low-risk papillary thyroid cancer[14–17,28]. Karimov et al. published recently a multicenter study which comprised of 406 patients who underwent TOETVA showing that complications occurred only in 11 (2.7%) patients[28]. On the other hand, data presented by Arikan et al. and based on the European TOETVA Study Group experience in 391 patients indicated on the risk of transient recurrent laryngeal nerve (RLN) palsy which was present in 18 (4.6%) but improved over time leading to permanent events in 2 (0.5%) patients only. These data have shown that TOETVA performed by experienced endocrine surgeons is a safe alternative to conventional thyroid surgery[15]. In our series of 17 patients who underwent TOETVA 1 transient RLN paresis and 1 transient mental nerve injury occurred, but none of the patients had a permanent sequel.

In general, patients at our institution with symptomatic solitary benign thyroid nodules choose between surgery and thermal ablation. However, the risk of overlooking thyroid malignancy may be a concern. Pre-

treatment requires two fine-needle aspirations confirming benign disease (Bethesda II) and no high-risk ultrasound findings (EU-TIRADS 2–4). Those classified as EU-TIRADS 5 are only eligible for surgery. In this study, none of the 40 surgical patients had EU-TIRADS 5 tumors or thyroid cancer in pathology reports.

TA tends to have a better safety profile with fewer and less severe complications compared to traditional thyroid surgery[29]. As shown by outcomes of our study the overall morbidity of LA (1.8%) was 4-fold lower than open thyroid lobectomy (8.7%) or TOETVA (11.8%). However, nearly all events were transient in our series irrespective of the treatment modality with no long-term sequel. Nevertheless, the choice of treatment should be individualized based on the patient's specific condition, preferences, and the surgeon's expertise[29]. As the clinical application of TA grows and follow-up periods extends, the long-term clinical outcomes of TA have revealed several issues, including nodule regrowth and diagnosis of malignancy in ablated lesions, which may necessitate delayed surgery, and patients should be aware of this low but not negligible risk[29,30].

Our data pointed on higher satisfaction rate for LA and TOETVA vs. conventional surgery ($p < 0.01$). However, satisfaction rate was higher after TOETVA vs. LA ($p = 0.006$), which is consistent with other most recent reports in the field. Yadav et al. noted that TOETVA compared to MWA resulted in significantly superior clinical outcome, thyroid-related quality of life, and swallowing-related quality of life in the long-term[31]. In addition, Deshkmuh et al. confirmed superior swallowing related quality of life in the majority of domains among TOETVA patients compared to open surgery ones[32].

This study has some limitations: (1) a prospective cohort, but non-randomized design, which would be impossible to run incorporating the SDM process, (2) relatively small numbers of patients in the open thyroid lobectomy and TOETVA arms, (3) and a single center design which may limit the reproducibility of the presented approach in other health care environments.

On the other hand this study has clear strengths including: (1) a prospective design with mandatory 12 months follow-up, and available 3-year follow-up data in the majority of patients, (2) a novel insight into the current approach to the management of benign thyroid nodules in a high-volume Thyroid Disease Treatment Center with a comprehensive and diversified options of treatment in a SDM process. Such an approach allows for tailoring treatment modality on individual basis including patient's preferences rather than offering one size that fits all.

In conclusions, currently most patients prefer MITs in lieu of surgery for SBTN or AFTN. TOETVA is chosen by minority of patients with a strong motivation to avoid scar whereas thermal ablation is the preferred MIT nowadays.

Data availability

The data used to support the findings of this study are included within the article.

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Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Marcin Barczyński, and Jacek Belowski. The first draft of the manuscript was written by Marcin Barczyński and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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