

Original Article

Ultrasound-guided percutaneous laser ablation for recurrent nodular goiter: a preliminary study

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Abstract: Objective: To investigate the feasibility of modified ultrasound-guided percutaneous laser ablation (UPLA) for recurrent nodular goiter (RNG). Methods: Twenty-one patients with single RNG were treated with modified ultrasound-guided PLA. After treatment, the size of the RNG in conventional ultrasonography, the ablation extent of lesions in contrast-enhanced ultrasonography, and the related complications were recorded and analyzed. Results: All patients completed the treatment successfully. During the follow-up, the ablation extent was none perfusion after 24 hours. The volume of the nodules was 5.19 ± 1.04 ml, 4.49 ± 0.9 ml, 3.53 ± 0.71 ml at month 1, month 3 and month 6 post-operation respectively, which reduced gradually after treatment (all $P < 0.05$). The reduction rate of the nodules was $28.13 \pm 0.78\%$, $37.76 \pm 0.41\%$ and $51.36 \pm 0.46\%$, which gradually increased compared between groups (all $P < 0.05$). There was no obvious complication during and after the operation. The thyroid function showed no significant changes after the treatment ($P > 0.05$). Conclusion: Ultrasound-guided PLA is a safe and effective minimally invasive treatment of RGN.

Keywords: Laser ablation, recurrent nodular goiter

Introduction

Nodular goiter is one of benign thyroid diseases and surgical treatment is the main means. However, the recurrence rate of nodular goiter after surgery is relatively higher. In China, the recurrence rate of nodular goiter can be as high as 15% to 40%, which in the foreign countries is 10% to 30% [1, 2]. In addition, Qiu et al. reported an approximate 30% recurrence rate after subtotal thyroidectomy [3]. Postoperative normal thyroid hormone replacement therapy is generally believed to reduce the recurrence rate significantly. However, studies have also shown that even adequate amounts of thyroid hormone suppression therapy can't prevent nodular regeneration and the recurrence rate is relatively higher [4]. Compared with the initial surgery, the gland and surrounding tissue adhesion, disordered tissue anatomical level and the position changes of recurrent laryngeal nerve and parathyroid make the reoperation difficult [5, 6]. Meanwhile, initial surgery almost ligates all thyroid blood vessels, forms a large

number of collateral circulation around the gland, therefore bleeding significantly often occurs during operation, which also increases the difficulty of operation and causes injuries easily [7]. Thereby, clinicians and patients has been always plagued by whether reoperation or not.

In recent years, percutaneous laser ablation (PLA) has been developed gradually in the treatment of benign thyroid nodules, autonomic function thyroid adenoma as well as recurrent thyroid malignant tumor, with the characteristic of minimal invasion and satisfied efficacy in clinic [8]. Ultrasound-guided laser ablation refers to radiating laser to biological tissues, heating them and coagulating or cutting target tissues by thermal injury, gasification, melting, pyrolysis and so on, so as to achieve ablation [9]. However, there are few researches focusing on whether the PLA also has a satisfied effect for the recurrent nodular goiter (RNG). Hence, the aim of this study is to investigate the feasibility of PLA for the treatment of RNG, and lay a foundation for future clinical promotion.

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Figure 1. A. The isolation zone separated from thyroid and muscle and carotid artery; B. The insertion of 21G trocar needle under ultrasound; C. Laser ablation under ultrasound; D. Complete ablation of nodule; E. No perfusion in the ablation lesions 24 hours after surgery under contrast-enhanced ultrasonography; F. Neck skin image immediately after surgery.

Materials and methods

Subjects

From August 2013 to January 2014, a total of 21 subjects were enrolled in this study, who were diagnosed with recurrent nodular goiter by high-frequency ultrasound and ultrasound-guided biopsy pathological assessments. Among them, there were 8 nodules in the left lobe and 13 in the right lobe. We explained the process of laser ablation of thyroid nodules in details before surgery and all participants had provided written informed consent according to a protocol approved by the Research Ethics Committee of the Affiliated Jiangyin Hospital of Medical School of Southeast University.

Instruments and equipments

Laser ablation instrument model (Yum Company, Italy) adopted EchoLaser X4, with an emission of yttrium neodymium laser at 1064 nm and a laser carrier of quartz optical fiber. The diameter, length, output power and output laser energy were 300 μ m, 11 cm, 3.5 W and 1200 J, respectively. And 1 to 4 fiber synergy ablation was selected based on clinical needs. Ultrasonic instrument was MyLab Twice that was also made in Yum Company in Italy. The probe was LA523 and LA522E, respectively,

and LA522E probe was dedicated to imaging. Mechanical index was 0.05 for radiography. Contrast agent was SonoVue (Bracco Company, Italy), with a single branch dosage of 59 mg. Dilute 1 ml contrast agent with 5 ml normal saline for intravenous injection, and wash with 1 to 2 ml normal saline.

Ablation methods

Patients were in a supine position, wearing goggles, padding shoulders, fully exposed necks, and slightly turning head and neck when necessary for ultrasound examination or guided puncture. SonoVue contrast-enhanced ultrasound was used to examine and retain thyroid nodules, followed by conventional disinfection on the operation areas of the skin and punctured after lidocaine local anesthesia.

If the target ablation nodule was close to vital organs or tissues with a distance of less than 0.5 cm, 0.2% lidocaine-saline solution was needed to inject between them, to form a 0.5 to 1.0 cm liquid isolation zone (**Figure 1A**). Then the optical fiber was placed into nodules by 21G needle under ultrasound (**Figure 1B**), with a perfect distance of 1.0 cm between the top of the optical fiber and the outer edge that beam pointed to and 0.5 cm between the side edge and trailing edge. The puncture trocar should

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Table 1. The patient's basic information

Serial number	Gender	Age	Nodule location	Maximum diameter (cm)	Degree of swelling	Compression symptoms	Oral thyroid gland hormone	Coagulation function, infectious diseases screening and thyroid function	Complete follow-up
1	Male	35	Left	1.5	I	None	None	Normal	Have
2	Female	38	Right	1.8	II	None	Have	Normal	Have
3	Female	45	Left	2.1	I	None	None	Normal	Have
4	Female	52	Right	1.9	I	None	None	Normal	Have
5	Male	39	Right	3.2	II	None	Have	Normal	Have
6	Female	40	Right	2.8	I	None	None	Normal	Have
7	Female	46	Right	3.1	II	None	None	Normal	Have
8	Male	60	Left	1.8	I	None	Have	Normal	Have
9	Female	38	Right	3.2	II	None	None	Normal	Have
10	Female	37	Left	2.6	I	None	None	Normal	Have
11	Male	44	Right	2.4	II	None	Have	Normal	Have
12	Female	45	Right	1.7	I	None	None	Normal	Have
13	Male	37	Left	2.2	II	None	Have	Normal	Have
14	Female	47	Right	3.4	II	None	Have	Normal	Have
15	Female	39	Right	3.3	I	None	None	Normal	Have
16	Female	45	Left	2.5	I	None	Have	Normal	Have
17	Male	47	Right	2.5	I	None	None	Normal	Have
18	Female	56	Left	2.3	I	None	None	Normal	Have
19	Female	39	Right	2.4	I	None	Have	Normal	Have
20	Female	42	Right	2.3	I	None	None	Normal	Have
21	Female	37	Left	1.9	I	None	None	Normal	Have

be 0.5 cm back before placing optical fiber, and if there were liquids in the nodules, draw the liquids as much as possible, then placed and confirmed the position of the fiber tip. And 1 to 4 optical fibers needed to be placed according to the size and shape of the nodules, then PLA foot controller was started after confirming the output energy and every part was ready. Real-time monitoring of the whole treatment process was conducted by ultrasound, and hyperechoic gasification zone could be seen in and around the fiber tip (**Figure 1C**). Hyperechoic zone gradually expanded over time with part of the micro bubbles escaping along the blood vessels, and ended with hyperechoic zone completely covering and exceeding the end of the ablation lesion (**Figure 1D**). To narrow nodules, optical fiber gradually exiting segmented ablation could be considered. Turn off the laser power after treatment, slowly pull out the fiber optic trocar under ultrasound, and handle the puncture site. Nodule volume less than 15 ml generally required a single needle ablation, and nodule volume greater than 15 ml generally required two or more multi-needle ablation.

Whether there was bleeding or not was observed in and around the nodules, treatment time and total energy released by laser were recorded, and we also asked whether patients discomforted or not. Patients' vital signs and responses were monitored during operation. If patients had obvious discomfort, ablation was suspended and the needle position was adjusted immediately; if serious, the operation was stopped.

Postoperative follow-up

Contrast-enhanced ultrasonography was performed 24 h after ablation. If contrast-enhanced ultrasound echo area was equal to or slightly greater than the ablation nodules, it indicated complete ablation, and if there still had residual focals, added ablation was recommended.

Postoperative return visit was performed to observe the postoperative complications. All the patients underwent routine ultrasound examination 1, 3, and 6 months after surgery to observe nodule volume change and reduction ratio. Nodule volume was calculated as antero-

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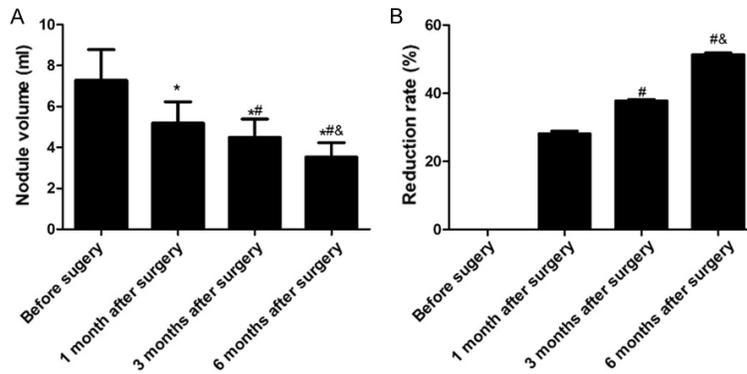


Figure 2. Comparison of the nodule volume and reduction rate before and after laser ablation. A. Nodule volume; B. Reduction rate. * $P < 0.05$ vs. before surgery; # $P < 0.05$ vs. 1 month after operation; & $P < 0.05$ vs. 3 months after operation.

posterior diameter (cm) * transverse diameter (cm) * vertical diameter (cm) * 0.52, and nodule volume reduction ratio was calculated as (preoperative volume - follow-up volume)/preoperative volume * 100%.

Statistical analysis

Statistical analysis was processed by SPSS 13.0. Measurement data were reported as mean \pm standard deviation and the comparison of nodule volume and reduction rate at pre-operation and 1, 3, 6 months post-operation was analyzed by variance analysis. $P < 0.05$ was considered statistically significant.

Results

Basic information

Among the 21 RNG subjects, there were 15 females and 6 males aged 35-60 years. All of them were single recurrence: there were 8 nodules in the left lobe and 13 in the right lobe. The maximum diameter of the nodules ranged from 1.5 to 3.5 cm. Eight patients took oral thyroid gland hormone tablets before surgery for a long term, and took them regularly after surgery. Patients had no obvious compression symptoms, seven of whom reached II degree swelling and necks were obviously protruding. Their preoperative blood coagulation function, infectious diseases screening and thyroid function all suggested normal. All the patients were followed up successfully. See **Table 1**.

Treatment outcome

All patients completed laser ablation successfully. Laser output energy was 1,200-3,600 J

and treatment time was 20-40 min.

Postoperative contrast-enhanced ultrasonography within 24 h showed no perfusion in the ablation lesions (**Figure 1E**). Routine ultrasound examination at 1, 3, and 6 months post-operation revealed a significant reduction of nodule volume compared with pre-operation respectively (5.19 ± 1.04 ml, 4.49 ± 0.90 ml, 3.53 ± 0.71 ml, $P < 0.05$) and a significant increase of nodules reduction rate respective-

ly ($28.13 \pm 0.78\%$, $37.76 \pm 0.41\%$, $51.36 \pm 0.46\%$, $P < 0.05$). See **Figure 2**.

Complications

Ultrasound was used to monitor the whole ablation process, and there was no significant bleeding surrounding the thyroid. Five patients complained of slight neck pain and discomfort during operation, and improved after comfort without special treatment. One patient had severe pain and radiated to the neck, so we turned off the laser immediately, and then adjusted the optical fiber tip position. When the patient felt better, ablation continued. After the surgery, only a small needle could be seen on the neck skin, and skin burns didn't occur (**Figure 1F**).

Postoperative follow-up also indicated that neck pain disappeared in the short term; no nerve, trachea, esophagus and other major vascular injury complications were observed. Additionally, the neck appearance had improved and patients achieved higher satisfaction.

Discussion

Nodular goiter is a common disease in thyroid surgery; however, even operated carefully, the incidence rate of recurrent laryngeal nerve, superior laryngeal nerve and parathyroid injuries is still far higher than initial surgery [10, 11]. In addition, the ways of RNG reoperation are subtotalthyroidectomy and total thyroidectomy, so there exists a high probability of post-operative hypothyroidism, which needs long-term drug substitution therapy [12]. Long-term use of thyroid tablets is easy to cause heart

diseases and osteoporosis. Therefore, there isn't still a safe and effective way to control and treat RNG in clinic.

Ultrasound-guided PLA has been mature by far in clinic [13-15]. For example, Liu et al. evaluated the safety and short-term efficacy of ultrasound-guided PLA in the treatment of benign solid thyroid nodule and found a positive result [16]; Achille et al. reported that ultrasound-guided PLA was a safe and effective method for the treatment of symptomatic benign thyroid nodules, and nodule volume could be reduced after treatment without significant effects on thyroid function to a certain extent [17]. The above studies all have confirmed ultrasound-guided PLA is a safe and effective minimally invasive approach for thyroid nodules. Therefore, this study applied laser ablation to treating RNG, and contrast-enhanced ultrasonography was used to determine whether ablate completely or not after operation to observe if ultrasound-guided PLA is also useful in the treatment of RNG. The result showed that no perfusion in the ablation lesions, indicating a complete ablation; routine ultrasound examination at 1, 3, and 6 months post-operation revealed a significant reduction of nodule volume compared with pre-operation respectively and a significant increase of nodules reduction rate respectively; postoperative follow-up in our study showed that nodules gradually reduce and the average reduction rate has reached to $51.36\pm 0.46\%$ in 6 months after operation. All of these finding suggested that ultrasound-guided PLA also had a good treatment outcome in the RNG treatment.

Except the difficulty of the surgical procedure, reoperation can also induce malignancy and complications, such as papillary microcarcinomas, vocal cord paralysis, hypoparathyroidism, intraoperative [7, 18, 19]. Additionally, there are also recurrent laryngeal nerve and tracheal injuries reported [20, 21]. Our results confirmed the security of ultrasound-guided PLA for RNG, with mild and transient postoperative pains and without serious complications. These may be related to our use of saline buffer zone during operation, avoiding damage to large vessels in the neck, recurrent laryngeal nerve, tracheal tubes and other vital organs.

In summary, ultrasound-guided PLA is a good method for the treatment of RNG with high pre-

cision, small trauma, reliable effects, leaving no scars and avoiding the risks and complications of reoperation, meanwhile without impacts on thyroid function. Therefore, it provides a good choice for the clinical treatment of RNG. However, the research still has some limitations, so large-sample and controlled studies with long-term follow up are needed to confirm the results.

Disclosure of conflict of interest

None.

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