

THYROID

Minimally-invasive conservative techniques in management of thyroid carcinoma: a narrative review

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SUMMARY

Increased diagnostic surveillance and technological innovation have considerably increased the number of thyroidectomies for carcinoma in the last decades. While thyroidectomy remains the first line of treatment, other minimally-invasive and conservative options to be applied in very selected cases have been proposed. The objective of this review is to illustrate the advantages and disadvantages of these techniques.

KEY WORDS: thyroidectomy, thyroid carcinoma, minimally-invasive, percutaneous ethanol injection, radiofrequency ablation, thermal ablation

Introduction

As a result of technological innovation in diagnostics and increased surveillance, the number of thyroidectomies has progressively increased over the years ¹. Conventional thyroidectomy has been for many years the first line treatment for thyroid nodules. This technique offers excellent exposure of the surgical field, but it frequently results in a wide neck scar and possible complications related to vertical opening of the pre-laryngeal muscles, bleeding, recurrent nerve(s) temporary or permanent palsy, and temporary or permanent hypoparathyroidism ^{2,3}.

Since the 1990s, alternative therapeutic options, both minimally-invasive and conservative, have been constantly sought to avoid open surgery, thus improving the quality of life and reduce hospitalisations and costs.

These techniques have also been adopted to highly-selected cases of thyroid carcinoma.

The consolidated experience of thyroid echo-interventional techniques aimed at the cytopathological characterisation of thyroid nodules (by fine needle aspiration biopsy) has formed the technical basis of the interventional evolution of ultrasound-guided techniques.

The echo-interventional techniques most currently used are:

1. ultrasound-guided percutaneous ethanol injection (PEI);
2. ultrasound-guided thermoablative (TA) techniques with different energy sources (Nd-YAG laser, microwave, radiofrequency).

Ultrasound-guided percutaneous ethanol injection

Ultrasound-guided PEI was the first method tested and subsequently used widely. It consists in the infiltration of substances that promote a necrotic-inflammatory reaction of the target structure, such as 90% ethyl alcohol ⁴.

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This substance, by promoting inflammation, coagulative necrosis and haemorrhagic infarction⁵ of the nodular formation, allows a dimensional reduction of the formation itself, with a consequent reduction of the mechanical compressive symptoms on the airway, oesophagus and vessels⁶. Despite the promising initial results, this experience has undergone changes over the years especially regarding the indications, in relation to the verified greater efficacy in some types of nodular structures.

Numerous experiences have in fact shown that nodules with a liquid component greater than 25% of the volume are more vulnerable to this treatment, while nodules with a greater solid component, on the other hand, are more resistant to the infiltration of the coagulating agent⁷. Due to this characteristic, in the treatment of solid nodules, extranodular extravasation of ethyl alcohol occurred more often, with possible complications due to infiltration of the healthy thyroid parenchyma⁸.

For reasons listed above, PEI does not appear to be the correct treatment for solid nodules, in particular for papillary thyroid carcinoma (PTC). However, this method has been proposed in selected cases of PTC recurrence. In 2011 Heilo et al.⁹ in a retrospective study described successful treatment of 84% of lymph nodes (requiring from 1 to 3 treatments), with a mean follow-up of 38 months and minor complications such as brief discomfort at the level of the PEI site. Another study retrospectively reviewed 25 patients who had 37 lymph nodes ablated between the years 1994 and 2012, with a relatively long mean follow-up of 65 months¹⁰. All lymph nodes were successfully ablated in one to five treatment sessions. Most of the lymph nodes decreased in size and 46% completely disappeared. Repeated treatment is probably at the basis of a good response. Guenette et al.¹¹ describes a study with one shot treatment of lymph nodes with a high rate of recurrence (24%).

Despite some promising results, a review in 2015 concluded that given the poor efficacy of PEI it seems to be inferior to reoperation. Further and well-designed studies are needed to evaluate the actual efficacy of PEI. At the moment, this method should be considered only in patients who are poor surgical candidates. Many patients will likely need more than one treatment session¹².

In 2017, Kim et al.¹³ reached the same conclusions suggesting PEI for recurrence of PTC in thyroid bed or cervical node metastasis (larger than 1 cm) in patients ineligible for intervention or refusing further surgery.

A recent study evaluated the long-term efficacy of PEI for metastatic lymph nodes from PTC. The investigators enrolled adult patients with PTC who had received PEI in lymph node metastasis and were included in a study from 2011: 51 of 63 patients were re-examined with a median

follow-up of 11.3 years. Local control was permanently achieved in most patients (80%). Recurrence within an ablated node was registered in 13 metastases in 10 patients. Seven of these patients also had recurrent disease elsewhere in the neck¹⁴.

In conclusion, PEI represents a minimally-invasive technique useful in neck recurrence of PTC in patients which are not candidates for surgery. Multiple treatment sessions are required. Selected patients can obtain good disease control even in the long-term.

Ultrasound-guided thermoablative techniques

Ultrasound-guided TA techniques can be applied with different source of energy: Nd-YAG laser, microwave, or radiofrequency.

This conservative technique has been proposed for recurrent and symptomatic PTC. In 2011, a Korean study¹⁵ described the efficacy of radiofrequency ablation (RFA) for local control and relief of symptoms with a mean tumour volume reduction of 50.9%. Regrowth of the treated tumour was observed in only 2 cases. A similar analysis was conducted in another Korean study in which successful treatment of lung and bones metastases from well differentiated thyroid carcinoma was described¹⁶.

PEI and laser or RFA share the same indications but differ in terms of complications¹⁷: RFA is more effective but is associated with more side effects such as discomfort, pain, skin burning, and recurrent nerve temporary or permanent palsy. In 2012¹⁸, the Task Force Committee of the Korean Society of Thyroid Radiology developed recommendations for the optimal use of RFA in thyroid nodules. In recurrent thyroid cancers (surgical bed and lymph nodes), they conclude that reoperation is the standard treatment for recurrent thyroid cancers, followed by radioactive iodine. RFA, however, can be used in patients at high surgical risk and in those who refuse to undergo repeated surgery.

In 2013, Papini et al.¹⁹ described the rapid cytorreduction and control obtained by laser ablation in recurrent PTC and metastatic lymph nodes. Mean follow-up was only 12 months.

Over the years TA has gained success in the treatment of hepatic and renal carcinoma²⁰. In parallel to overdiagnosis of well differentiated thyroid carcinoma, this technique was adopted both in cases of thyroid papillary microcarcinoma (< 1 cm) and PTC.

In a recent large review²¹, an analysis regarding the efficacy of TA in treatment of thyroid PTC staged as T1N0M0 was conducted. Among the minimally-invasive techniques described, the most effective seems to be laser ablation, but

in the analysis of all criteria (complete disappearance rate, recurrence rate, distant metastasis, lymph node metastasis), RFA presented advantages for most outcomes. Moreover, patients with T1aNOM0 disease may experience fewer side effects than those with a T1bNOM0 tumour.

Conclusions

Minimally-invasive conservative techniques represent a viable option in highly-selected patients with early well-differentiated thyroid carcinoma or poor surgical candidates with loco-regional recurrence in order to guarantee better quality of life.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

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Ethical consideration

No ethic committee approval was required due to the nature of narrative review and no involvement of patients.

References

- 1 Stewart LA, Kuo JH. Advancements in the treatment of differentiated thyroid cancer. *Ther Adv Endocrinol Metab* 2021;12:20420188211000251. <https://doi.org/10.1177/20420188211000251>
- 2 Neri G, Castiello F, Vitullo F, et al. Post-thyroidectomy dysphonia in patients with bilateral resection of the superior laryngeal nerve: a comparative spectrographic study. *Acta Otorhinolaryngol Ital* 2011;31:228-234.
- 3 Rulli F, Ambrogi V, Dionigi G, et al. Meta-analysis of recurrent laryngeal nerve injury in thyroid surgery with or without intraoperative nerve monitoring. *Acta Otorhinolaryngol Ital* 2014;34:223-229.
- 4 Fukunari N. PEI therapy for thyroid lesions. *Biomed Pharmacother* 2002;56(Suppl 1):S79-S82. [https://doi.org/10.1016/s0753-3322\(02\)00214-7](https://doi.org/10.1016/s0753-3322(02)00214-7)

- 5 Crescenzi A, Papini E, Pacella CM, et al. Morphological changes in a hyperfunctioning thyroid adenoma after percutaneous ethanol injection: histological, enzymatic and sub-microscopical alterations. *J Endocrinol Invest* 1996;19:371-376. <https://doi.org/10.1007/BF03344972>
- 6 Guglielmi R, Pacella CM, Bianchini A, et al. Percutaneous ethanol injection treatment in benign thyroid lesions: role and efficacy. *Thyroid* 2004;14:125-131. <https://doi.org/10.1089/105072504322880364>
- 7 Ferreira MC, Piaia C, Cadore AC. Percutaneous ethanol injection versus conservative treatment for benign cystic and mixed thyroid nodules. *Arch Endocrinol Metab* 2016;60:211-216. <https://doi.org/10.1590/2359-3997000000120>
- 8 Hahn SY, Shin JH, Na DG, et al. Korean Society of Thyroid Radiology (KSThR); Korean Society of Radiology. Ethanol ablation of the thyroid nodules: 2018 Consensus Statement by the Korean Society of Thyroid Radiology. *Korean J Radiol* 2019;20:609-620. <https://doi.org/10.3348/kjr.2018.0696>
- 9 Heilo A, Sigstad E, Fagerlid KH, et al. Efficacy of ultrasound-guided percutaneous ethanol injection treatment in patients with a limited number of metastatic cervical lymph nodes from papillary thyroid carcinoma. *J Clin Endocrinol Metab* 2011;96:2750-2755. <https://doi.org/10.1210/jc.2010-2952>
- 10 Hay ID, Lee RA, Davidge-Pitts C, et al. Long-term outcome of ultrasound-guided percutaneous ethanol ablation of selected "recurrent" neck nodal metastases in 25 patients with TNM stages III or IVA papillary thyroid carcinoma previously treated by surgery and ¹³¹I therapy. *Surgery* 2013;154:1448-1454; discussion 1454-1455. <https://doi.org/10.1016/j.surg.2013.07.007>
- 11 Guenette JP, Monchik JM, Dupuy DE. Image-guided ablation of post-surgical locoregional recurrence of biopsy-proven well-differentiated thyroid carcinoma. *J Vasc Interv Radiol* 2013;24:672-679. <https://doi.org/10.1016/j.jvir.2013.02.001>
- 12 Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on thyroid nodules and differentiated thyroid cancer. *Thyroid* 2016;26:1-133. <https://doi.org/10.1089/thy.2015.0020>
- 13 Kim SY, Kim SM, Chang H, et al. Long-term outcomes of ethanol injection therapy for locally recurrent papillary thyroid cancer. *Eur Arch Otorhinolaryngol* 2017;274:3497-3501. <https://doi.org/10.1007/s00405-017-4660-2>
- 14 Hay ID, Lee RA, Charboneau JW. Efficacy of ethanol ablation in long-term local control of neck nodal metastases in adult papillary thyroid carcinoma. *J Clin Endocrinol Metab* 2022;107:E2636-E2637. <https://doi.org/10.1210/clinem/dgac018>
- 15 Park KW, Shin JH, Han BK, et al. Inoperable symptomatic recurrent thyroid cancers: preliminary result of radiofrequency ablation. *Ann Surg Oncol* 2011;18:2564-2568. <https://doi.org/10.1245/s10434-011-1619-1>
- 16 Baek JH, Kim YS, Sung JY, et al. Locoregional control of metastatic well-differentiated thyroid cancer by ultrasound-guided radiofrequency ablation. *AJR Am J Roentgenol* 2011;197:W331-W336. <https://doi.org/10.2214/AJR.10.5345>
- 17 Shin JE, Baek JH, Lee JH. Radiofrequency and ethanol ablation for the treatment of recurrent thyroid cancers: current status and challenges. *Curr Opin Oncol* 2013;25:14-19. <https://doi.org/10.973/CCO.0b013e32835a583d>
- 18 Na DG, Lee JH, Jung SL, et al. Korean Society of Thyroid Radiology (KSThR); Korean Society of Radiology. Radiofrequency ablation of benign thyroid nodules and recurrent thyroid cancers: consensus statement and recommendations. *Korean J Radiol* 2012;13:117-125. <https://doi.org/10.3348/kjr.2012.13.2.117>

- ¹⁹ Papini E, Bizzarri G, Bianchini A, et al. Percutaneous ultrasound-guided laser ablation is effective for treating selected nodal metastases in papillary thyroid cancer. *J Clin Endocrinol Metab* 2013;98:E92-E97. <https://doi.org/10.1210/jc.2012-2991>
- ²⁰ Min Y, Wang X, Chen H, et al. Thermal ablation for papillary thyroid microcarcinoma: how far we have come? *Cancer Manag Res* 2020;12:13369-13379. <https://doi.org/10.2147/CMAR.S287473>
- ²¹ Gao X, Yang Y, Wang Y, et al. Efficacy and safety of ultrasound-guided radiofrequency, microwave and laser ablation for the treatment of T1N0M0 papillary thyroid carcinoma on a large scale: a systematic review and meta-analysis. *Int J Hyperthermia* 2023;40:2244713. <https://doi.org/10.1080/02656736.2023.2244713>