



EDITORIAL

Non-surgical treatment of benign symptomatic thyroid nodules



Tratamiento no quirúrgico de los nódulos tiroideos benignos sintomáticos

Iñaki Argüelles*, Santiago Tofé

Servicio de Endocrinología y Nutrición, Hospital Universitario Son Espases, Palma de Mallorca, Spain

The prevalence of thyroid nodules is very high and can even reach values over 50% in the adult population,¹ particularly now that the use of thyroid ultrasounds has become widespread. Faced with a problem of this magnitude, we should be careful when indicating and performing ultrasounds to avoid overdiagnosis of structural thyroid diseases. This article reviews the treatment of patients with previously diagnosed nodules who come to our clinic and whom we need to manage correctly while avoiding overtreatment.

When taking action, we must always ask why are doing it and what the objective is. In other words, what the intended outcome is. In the case of thyroid nodules, there are two main reasons: the first is that the nodule is malignant or suspicious and the second, which applies here, is that the nodule is symptomatic. Our objectives are different in the two situations. In the case of malignant or suspicious nodules, we generally indicate surgery to confirm the diagnosis, stratify risk and prevent disease progression. In the case of a sympathetic benign nodule, our main objective is to resolve the symptoms or at least alleviate them.

In these cases, as an alternative to surgery, we have the option, one that has been available for more than 25 years² but has enjoyed greater development in the last 10–15 years, of non-surgical or minimally-invasive techniques: mainly percutaneous ethanol injection ablation,

particularly useful in cystic nodules, and thermal ablation in solid or predominantly solid nodules by laser (LA), radiofrequency (RFA), microwaves (MWA) or, to a lesser extent, high-intensity focused ultrasound (HIFU).³

When opting for these treatments, we should seek to strike a balance and not use them either by default or excessively.

Up to 90% of cystic thyroid nodules are known to recur after drainage.⁴ For many years, numerous endocrinologists have sent these patients for surgery. However, if the above premises are observed we start with a benign nodule. Therefore, malignancy is not a reason for surgery, and once functional signs and symptoms have been ruled out, we are only left with those resulting from volume occupation. Therefore, our objective is to alleviate compressive symptoms, which can easily be achieved by reducing the volume of the nodule. The enolisation of cystic or predominantly cystic nodules delivers excellent outcomes with follow-ups of up to 10 years, with volume reductions of 69%–80%, as well as the resolution of compressive clinical symptoms. Furthermore, it is a simple, quick and economical method that can be performed on an outpatient basis without the need for general anaesthetic and without significant complications.² A hemithyroidectomy would also alleviate compressive symptoms, although we would have to accept a risk of surgical complications of around 3% and a long-term risk of hypothyroidism of 20%–30%,⁵ without forgetting the financial cost of a surgical operation with general anaesthetic and inpatient admission.

* Corresponding author.

E-mail address: inaki.arguelles@ssib.es (I. Argüelles).

Therefore, in the case of cysts or predominantly cystic nodules, the treatment of choice could be enolisation, which surgery being relegated to exceptional situations only.

In the case of solid or mixed predominantly solid nodules, the initial premises should be the same: if the nodule is benign, our objective should be to alleviate the symptoms and therefore, as an alternative to surgery, thermal ablation techniques should always be considered. LA, RFA, MWA and HIFU are available.

In general, the most effective volume reduction techniques are RFA and MWA, which have no significant differences, followed by LA. However, the European Thyroid Association's guidelines do not consider MWA to be a first-choice treatment due to the smaller number of published works.³ At the same time, nowadays the volume reductions reported with HIFU are lower than with the other three techniques. Furthermore, the duration of treatment and its cost are higher. Therefore, it is not regarded as a first-line technique.

The long-term post-RFA follow-up data showed mean volume reductions of 67%–93%.^{6,7} In mixed modules, there is also the option of combining enolisation and thermal ablation. The routine technique consists of thermal ablation of the solid remnants after enolisation.⁸

In view of these data, thermal ablation could be the treatment of choice in solid or predominantly solid mixed thyroid nodules, since the volume reductions described would undoubtedly alleviate both compressive and cosmetic symptoms in these patients at a lower cost and risk than surgery. The exception would be an autonomous or toxic nodule, where the alternative to surgery is treatment with I-131, and in which thermal ablation remains the second-line treatment in patients that reject I-131 or surgery, for example women who want to get pregnant in the short term.³

In any case, surgery is a treatment option that should be offered to patients and is the treatment of choice in large or compressive multinodular nodules or goitres, as well as nodules which, despite having benign cytology, grow quickly or have ultrasound characteristics that lead to a suspicion of malignancy.

In summary, and as demonstrated by the high degree of consensus among several scientific entities such as the Italian, Austrian, Korean and European associations, minimally-invasive treatments should be offered as a treat-

ment option to patients with benign symptomatic thyroid nodules, with enolisation being the treatment of choice in cystic nodules and thermal ablation the treatment of choice in solid nodules.⁹

Finally, we should insist upon the appropriate indication of treatment: both overtreatment and overdiagnosis should be avoided. There is no reason to treat asymptomatic nodules and the adequate indication should be chosen for every patient. For this reason, it is vital that the endocrinologist be involved in the entire process: diagnosis, follow-up, and where possible in the treatment as well.

References

- Gharib H, Papini E. Thyroid nodules: clinical importance, assessment, and treatment. *Endocrinol Metab Clin North Am.* 2007;36:707–35.
- Bennedbaek FN, Karstrup S, Hegedüs L. Percutaneous ethanol injection therapy in the treatment of thyroid and parathyroid diseases. *Eur J Endocrinol.* 1997;136(3):240–50.
- Papini E, Monpeyssen H, Frasoldati A, Hegedüs L. 2020 European Thyroid Association Clinical Practice Guideline for the use of image-guided ablation in benign thyroid nodules. *Eur Thyroid J.* 2020;9:172–85.
- Cesareo R, Tabacco G, Naciu AM, Crescenzi A, Bernardi S, Romanelli F, et al. Long-term efficacy and safety of percutaneous ethanol injection (PEI) in cystic thyroid nodules: a systematic review and meta-analysis. *Clin Endocrinol (Oxf).* 2022;96:97–106.
- Li Z, Qiu Y, Fei Y, Xing Z, Zhu J, Su A. Prevalence of and risk factors for hypothyroidism after hemithyroidectomy: a systematic review and meta-analysis. *Endocrine.* 2020;70(2):243–55.
- Bernardi S, Palermo A, Grasso RF, Fabris B, Stacul F, Cesareo R. Current status and challenges of US-guided radiofrequency ablation of thyroid nodules in the long term: a systematic review. *Cancers.* 2021;13:2746.
- Li J, Xue W, Xu P, Deng Z, Duan C, Zhang D, et al. Efficacy on radiofrequency ablation according to the types of benign thyroid nodules. *Sci Rep.* 2021;11:22270.
- Park HS, Baek JH, Choi YJ, Lee JH. Innovative techniques for image-guided ablation of benign thyroid nodules: combined ethanol and radiofrequency ablation. *Korean J Radiol.* 2017;18(3):461–9.
- Muhammad H, Santhanam P, Russell JO, Kuo JH. RFA and benign thyroid nodules: review of the current literature. *Laryngoscope Investig Otolaryngol.* 2021;6:155–65.