

Ultrasound-guided percutaneous radiofrequency ablation for benign thyroid nodules

Interventional procedures guidance
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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

1 Recommendations

- 1.1 Current evidence on the safety and efficacy of ultrasound-guided percutaneous radiofrequency ablation for benign thyroid nodules is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit. Find out what standard arrangements mean on the NICE interventional procedures guidance page.

2 Indications and current treatments

- 2.1 Thyroid nodules may be cystic, colloid, hyperplastic, adenomatous or cancerous. The majority of thyroid nodules are benign and they are often asymptomatic. There may be a single thyroid nodule (solitary nodule) or multiple thyroid nodules (multinodular goitre). Thyroid nodules can cause an overactive thyroid, which affects the normal production of thyroxine or triiodothyronine.
- 2.2 Treatment of benign thyroid nodules may be necessary if they are symptomatic or causing cosmetic problems. Conventional treatment includes suppressive levothyroxine therapy or surgery. More recently, other approaches that are less invasive than conventional surgery have been introduced, such as ethanol ablation and percutaneous laser ablation.

3 The procedure

- 3.1 Radiofrequency ablation is a minimally invasive technique that aims to reduce symptoms and improve cosmetic appearance, while preserving thyroid function, and with fewer complications than surgery.
- 3.2 Before treatment, the thyroid nodule is confirmed as benign, typically by the use of 2 fine-needle aspiration biopsies. Ultrasound-guided percutaneous radiofrequency ablation for benign thyroid nodules is usually done in an outpatient setting using local anaesthesia. The patient lies in the supine position with moderate neck extension. A radiofrequency electrode is inserted into the nodule using ultrasound guidance to visualise the electrode during the procedure. Once in position, the radiofrequency electrode is activated to heat and destroy the tissue.

4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 In a systematic review of 284 patients with benign thyroid nodules treated by radiofrequency ablation (RFA), the mean nodule volume reduced by 9.8 ml after the procedure (95% confidence interval [CI] -13.83 to -5.72; 9 studies, n=284 nodules; $I^2=98%$ [significant heterogeneity]). In a randomised controlled trial (RCT) of 84 patients with benign solid thyroid nodules, the mean nodule volume reduced from 24.5(\pm 19.6) ml at baseline to 8.6(\pm 9.5) ml at 6-month follow-up ($p<0.001$) in patients treated by RFA, compared with no volume reduction in patients randomised to no treatment (27.5 \pm 22.1 ml at baseline and 27.8 \pm 22.1 ml at 6-month follow-up). In an RCT of 80 patients with solid, compressive, non-functioning benign thyroid nodules treated by RFA or no treatment, the median percentage volume changes were 71% reduction and 3% increase respectively ($p=0.0001$). In a non-randomised comparative study of 400 patients with nodular goitre treated by RFA or surgery there was a mean percentage volume reduction of 85(\pm 17.1)%

after RFA at 12-month follow-up ($p=0.002$). In a case series of 111 patients with benign, non-functioning thyroid nodules there was a mean volume reduction of $91(\pm 15.8)\%$ after RFA at 3-year follow-up. In an RCT of 50 patients with a single benign cystic thyroid nodule treated by RFA or ethanol ablation (also included in the systematic review), there were median percentage volume reductions of $93(\pm 5.4)\%$ and $97(\pm 4.1)\%$ respectively at 6-month follow-up (p value not reported). In a second RCT of 50 patients with predominantly cystic thyroid nodules treated by RFA or ethanol ablation, mean volume reductions were $87.5(\pm 11.5)\%$ and $82.4(\pm 28.6)\%$ respectively at 6-month follow-up ($p=0.710$).

- 4.2 In the systematic review of 284 patients there was a reduction in the mean symptom score (measured on a 10-point visual analogue scale, with lower scores indicating less severe symptoms) of 2.89 after RFA (95% CI -2.51 to -3.28 ; 4 studies, $n=85$; $I^2=56\%$). In the RCT of 84 patients the mean pressure symptom score (measured on a 10-point visual analogue scale, with lower scores indicating less severe symptoms) reduced from $2.8(\pm 3.3)$ at baseline to $0.4(\pm 0.8)$ at 6-month follow-up ($p<0.001$) in patients treated by RFA compared with no reduction for patients with no treatment (2.7 ± 3 at baseline and 2.9 ± 3.2 at 6-month follow-up). In the RCT of 80 patients the symptom score (on a scale of 0 to 10, with lower scores indicating less severe symptoms) was $0.4(\pm 0.7)$ for patients treated by RFA compared with $3.3(\pm 1.7)$ for patients with no treatment ($p=0.0001$) at 6-month follow-up. In the case series of 111 patients, the symptom score (assessed on a scale of 0 to 10, with lower scores indicating less severe symptoms) reduced from $4.3(\pm 1.6)$ at baseline to $0.8(\pm 0.9)$ at last follow-up (mean follow-up 49 months, $p<0.001$). In the RCT of 50 patients treated by RFA or ethanol ablation (also included in the systematic review) symptom scores (assessed on a scale of 0 to 10, with lower scores indicating less severe symptoms) were $0.5(\pm 0.8)$ and $0.5(\pm 0.7)$ respectively at 6-month follow-up ($p=0.806$).
- 4.3 In the systematic review of 284 patients the mean reduction in cosmetic score (scored by a physician from 1 to 4, with lower scores indicating better cosmetic appearance) was 2.02 (95% CI -1.69 to -2.35 ; 5 studies, $n=114$; $I^2=78\%$) after RFA. In the RCT of 84 patients the mean cosmetic score (assessed on a scale of 1 to 4, with lower scores indicating better

cosmetic appearance) reduced from 2.6(\pm 0.9) at baseline to 1.7(\pm 0.7) at 6-month follow-up ($p < 0.001$) in patients treated by RFA, compared with no reduction for patients with no treatment (2.6 \pm 1.0 at baseline and at 6-month follow-up). In the RCT of 80 patients cosmetic scores (assessed on a scale of 1 to 4, with lower scores indicating better cosmetic appearance) were 1.7(\pm 0.8) for patients treated by RFA and 3.5(\pm 0.7) for patients with no treatment ($p = 0.0001$) at 6-month follow-up. In the case series of 111 patients the cosmetic score (on a scale of 1 to 4, with lower scores indicating better cosmetic appearance) reduced from 3.2(\pm 0.8) at baseline to 1.3(\pm 0.6) at last follow-up (mean follow-up 49 months, $p < 0.001$). In the RCT of 50 patients treated by RFA or ethanol ablation (also included in the systematic review) cosmetic scores (on a scale of 1 to 4, with lower scores indicating better cosmetic appearance) were 1.1(\pm 0.4) and 1.2(\pm 0.4) respectively at 6-month follow-up ($p = 0.682$).

- 4.4 In the systematic review of 284 patients, 60 patients with 'hot' nodules were given methimazole at doses sufficient to maintain thyroid-stimulating hormone within the normal range before RFA treatment. After RFA treatment, 29 patients continued to need some dose of this medication to maintain euthyroidism based on thyroid-stimulating hormone measurements and symptoms (odds ratio 40.34, 95% CI 7.78 to 209.1; 3 studies, $n = 60$; $I^2 = 2\%$).
- 4.5 In the non-randomised comparative study of 400 patients, no patients treated by RFA needed medication for hypothyroidism compared with 71.5% of patients treated by surgery ($p = 0.002$).
- 4.6 In the case series of 111 patients (126 nodules) the overall recurrence rate (defined as increases in nodule volume of greater than 50% compared with previous ultrasound images at a minimum of 3 years of follow-up) was 6% (7/126). All nodules were benign on repeat fine-needle aspirate biopsy. Four of the recurrent nodules decreased in size after repeat RFA, 2 were treated with repeat RFA without further follow-up and 1 patient chose not to have further treatment and was lost to follow-up.
- 4.7 The specialist advisers listed key efficacy outcomes as reduction in thyroid nodule volume, and improvement in compression symptoms and cosmetic appearance.

5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 Nodule rupture was reported in 1 patient treated by radiofrequency ablation (RFA) in a non-randomised comparative study of 400 patients. Nodule rupture was reported in less than 1% (2/1459) of patients in a case series of 1,459 patients: 1 patient recovered without treatment and 1 patient was admitted to hospital and treated with antibiotics and analgesics. In the same study, 1 patient had nodule rupture with abscess formation: the patient was treated by left thyroidectomy. Nodule rupture was reported in 1 patient in a case series of 40 patients: this occurred 26 days after RFA and was treated with anti-inflammatory medication.
- 5.2 Vocal fold palsy was reported in 1 patient in a systematic review of 284 patients. This was diagnosed at 1-month follow-up, but the patient was subsequently lost to follow-up. Permanent vocal cord palsy with inspiratory stridor without dysphonia was reported in 1 patient treated by RFA in a randomised controlled trial (RCT) of 84 patients.
- 5.3 Voice change immediately after the procedure was reported in 5% (2/42) of patients treated by RFA in the RCT of 84 patients; this resolved completely within 3 hours of the procedure. Transient hoarseness was reported in less than 1% (1/200) of patients treated by RFA and in 1.5% (3/200) of patients treated by surgery in the non-randomised comparative study of 400 patients. Voice change was reported in 1% (15/1459) of patients in the case series of 1,459 patients; all patients recovered completely, except for 2 patients who were lost to follow-up.
- 5.4 Brachial plexus injury was reported in 1 patient in the case series of 1,459 patients. The patient had numbness and decreased sensation in the fourth and fifth fingers of the left hand; this gradually recovered during the next 2 months.
- 5.5 Diffuse glandular haemorrhage was reported in 1 patient in the systematic review of 284 patients. This resulted in interruption of the

procedure. The patient was given oral analgesics for pain relief for 3 days. Intranodular bleeding was reported in 8% (3/40) of patients in the case series of 40 patients: this was stopped by swift needle-electrode insertion and heat administration. In the same study, pericapsular bleeding was reported in 1 patient, who had extensive neck bruising 5 to 10 days after the procedure. Haematoma was reported in 1 patient in the systematic review of 284 patients and in 1% (15/1459) of patients in the case series of 1,459 patients: most completely disappeared within 1 to 2 weeks.

- 5.6 Postoperative oedema was reported in 1% (3/284) of patients in the systematic review of 284 patients. This was treated with betamethasone medication.
- 5.7 A full-thickness skin burn was described in a case report. The burn took more than 1 month to heal but its final appearance looked almost like the normal skin. First-degree skin burns at the puncture sites were reported in less than 1% (4/1459) of patients in the case series of 1,459 patients: all patients recovered from pain and skin colour changes within 7 days without sequelae.
- 5.8 Vasovagal reaction during the procedure was reported in less than 1% of patients in the case series of 1,459 patients. This included sweating, difficulty breathing and hesitation; it was treated by elevation of the patient's legs and stopping the ablation. Vasovagal reaction was reported in 1 patient in the case series of 40 patients. The patient had bradycardia, hypotension, vomiting and defecation; the bed was tilted, ablation was stopped and the patient recovered within a few minutes. The patient had a subsequent RFA session 3 weeks later. Vomiting was reported in less than 1% (9/1459) of patients in the case series of 1,459 patients: this improved within 1 to 2 days after treatment with antiemetics.
- 5.9 Pseudocystic transformation was reported in 1 patient in the case series of 40 patients: the patient had a painful sudden swelling 3 weeks after RFA, which was treated with oral corticosteroids.
- 5.10 Permanent hypothyroidism was reported in 1 patient in the case series of

1,459 patients: the patient had gradual neck bulging and ultrasound showed diffuse enlargement of the thyroid gland without a thyroid nodule.

- 5.11 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following theoretical adverse events: oesophageal or tracheal thermal injury, cardiac arrhythmia, and sympathetic or spinal nerve injury.

6 Committee comments

- 6.1 The committee noted that this procedure has also been used for treating malignant nodules, but the evidence base for this appears limited and is not covered by this guidance.

7 Further information

- 7.1 For related NICE guidance, see the [NICE website](#).

Information for patients

NICE has produced [information on this procedure for patients and carers](#). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

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Endorsing organisation

This guidance has been endorsed by [Healthcare Improvement Scotland](#).