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## Q / What is the best approach to goiter in euthyroid patients?

### EVIDENCE-BASED ANSWER

**A** / **IN THE ABSENCE OF OUTCOME STUDIES**, experts recommend ultrasound evaluation of nontoxic multinodular goiters (MNG) followed by fine-needle aspiration (FNA) of suspicious nodules (strength of recommendation [SOR]: **C**, consensus-based guidelines).

Thyroid hormone suppression therapy reduces the size of MNG (SOR: **A**, systematic review of randomized controlled trials [RCTs]), but it risks inducing hyperthyroidism (SOR: **C**, expert opinion).

Experts recommend thyroidectomy for compressive symptoms, progressive growth, or ultrasound or FNA results indicating thyroid cancer (SOR: **C**, consensus based guidelines).

Expert guidelines recommend repeat ultrasound at 6 to 18 months to follow up benign nodules or nonendemic MNG in patients at low risk of malignancy and subsequent follow-up of stable nodules every 3 to 5 years (SOR: **C**, consensus-based guidelines).

### Evidence summary

This summary updates the 2007 Clinical Inquiry, "What is the best approach to goiter for euthyroid patients?"<sup>1</sup>

#### Initial evaluation of palpable goiter with a normal thyrotropin

In the United States, MNG is generally nonendemic and unrelated to iodine deficiency, as distinguished from endemic goiter caused by iodine deficiency in other parts of the world.

Our structured search of the literature found no randomized trials or prospective cohort studies comparing diagnostic approaches. The American Association of Clinical Endocrinologists' (AACE) 2010 guidelines and American Thyroid Association (ATA) guidelines recommend ultrasound for all MNG.<sup>2,3</sup> The AACE guidelines recommend thyroid scintigraphy when clinicians suspect retrosternal MNG.<sup>2</sup>

#### Ultrasound findings can change management, avoid biopsy

In a retrospective analysis of 223 patients with

nodular thyroid disease, thyroid ultrasound altered clinical management of 63% of patients with abnormal thyroid exams.<sup>4</sup> A single center retrospective cohort study of 650 FNA biopsies identified 4 morphologic patterns on ultrasound that predicted benign cytology with 100% specificity. The authors concluded that using ultrasound pattern to determine which patients require FNA could have obviated more than 60% of thyroid biopsies.<sup>5</sup>

#### Thyroid hormone suppression therapy risks hyperthyroidism

A systematic review of 9 RCTs of 18-month or shorter duration found that thyroid hormone suppression therapy reduced benign thyroid nodule volume (relative risk=1.88 compared with placebo or no treatment; 95% confidence interval [CI], 1.18-3.01;  $P=.008$ ). The number needed to treat was 8 to reduce volume by >50% (risk difference=0.13; 95% CI, 0.06-0.19;  $P=.0003$ ).<sup>6</sup> However, thyroid hormone suppression therapy risks inducing hyperthyroidism and is not routinely recommended by the AACE or the ATA.<sup>2,3</sup>

CONTINUED

**> Experts recommend ultrasound evaluation of nontoxic multinodular goiters followed by fine-needle aspiration of suspicious nodules.**

## Thyroidectomy: The treatment of choice

Thyroidectomy is the definitive therapy for MNG. A narrative review of 15 mostly retrospective cohort studies demonstrated MNG recurrence rates of 0% to 0.3% after total thyroidectomy, with follow-up intervals of 4.8 to 30 years.<sup>7</sup>

AACE consensus opinion recommends thyroidectomy for compressive symptoms, progressive growth, or when ultrasound or FNA results indicate thyroid cancer.<sup>2</sup>

A retrospective cohort study of 462 thyroidectomies for MNG found incidental thyroid carcinomas in 8.9% (41 patients). Risk factors included neck irradiation (odds ratio [OR]=21.64; 95% CI, 3.28-143), parenchymal calcifications on imaging (OR=2.30; 95% CI, 0.85-6.23), and family history of thyroid disease (OR=8.2; 95% CI, 2.15-29.87). Living in a goiter-endemic area was protective (OR=0.24; 95% CI, 0.07-0.83).<sup>8</sup>

## Follow-up of patients with initial benign evaluation

Consensus opinion regarding follow-up of MNG is based on observational studies of the natural history of the condition. Benign MNG rarely progresses to malignancy. A review of 6 cohort studies, including 1265 patients with untreated nontoxic MNG who were fol-

lowed for 60 to 130 months from 1990 to 2007, yielded an annual incidence range of 1.3 to 3.7 new cases of thyroid carcinoma per 1000 patients.<sup>9</sup>

Some goiters are more likely to enlarge. A retrospective cohort study of 488 patients treated surgically for MNG identified risk factors for enlargement: African American (OR=3.3; 95% CI, 2.0-5.4), age >40 years (OR=2.1; 95% CI, 1.2-3.8), and body mass index >30 (OR=2.5; 95% CI, 1.5-4.0).<sup>10</sup>

## Recommendations

The AACE and the ATA recommend that patients with MNG with benign nodules have a repeat examination, TSH, and ultrasound in 6 to 18 months. Follow-up of stable nodules can then be done in 3 to 5 years.

An enlarging nodule requires repeat FNA.<sup>2</sup> If palpation or ultrasound reveal evidence of nodule growth (more than a 50% change in volume or a 20% increase in at least 2 nodule dimensions, with a minimal increase of 2 mm in solid nodules or the solid portion of mixed cystic-solid nodules), the AACE and ATA recommend FNA, preferably with ultrasound guidance.<sup>3</sup> Low TSH suggests autonomous nodules and the ATA recommends radio-nuclide scanning with FNA of hypofunctioning nodules with suspicious US features.<sup>3</sup> **JFP**

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