

Treatment of Multinodular Goiter: A Critical Review of Guidelines and Comparative Evidence

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doi: <https://doi.org/10.37745/ejbmsr.2013/vol14n41835>

Published October 11, 2026

Citation: Prifti J. (2026) Treatment of Multinodular Goiter: A Critical Review of Guidelines and Comparative Evidence, *European Journal of Biology and Medical Science Research*, 14(4),18-35

Abstract: *Multinodular goiter ranges from asymptomatic nodules to compressive enlargement or thyroid autonomy. This narrative review compares guidelines and selected comparative studies for adults with nontoxic and toxic disease. Thyroid function, malignancy risk, and compression determine the initial pathway. Observation is appropriate for selected asymptomatic, low-risk nontoxic disease. Surgery reduces tissue burden and provides a specimen for histology when obstruction or suspicious findings warrant it; symptom relief is assessed after recovery. Radioiodine offers gradual biochemical control and volume reduction in suitable patients. Thermal ablation addresses selected benign dominant nodules but does not treat the entire gland. In toxic disease, antithyroid medication controls hormone excess, while surgery and radioiodine offer definitive options with distinct anatomical and biochemical outcomes. Comparative evidence is limited by mixed populations, differing endpoints, and short follow-up for focal therapies. Decisions should identify the patient's principal goal and account for anatomy, operative risk, replacement needs, and retreatment.*

Keywords: multinodular goiter, toxic multinodular goiter, thyroidectomy, radioiodine, thermal ablation, guidelines.

INTRODUCTION

Multinodular goiter is a structural enlargement of the thyroid containing multiple nodules. It encompasses a heterogeneous group of patients: some have small, asymptomatic lesions and normal thyroid function, whereas others develop progressive enlargement, compressive symptoms, autonomous hormone production, or a nodule that requires evaluation for malignancy. The presence of several nodules is therefore not, by itself, an indication for surgery. Management begins by defining the problem that treatment is expected to solve and assessing each clinically relevant nodule according to its ultrasound features and, where appropriate, cytology (Durante et al., 2023; Patel et al., 2020; Haugen et al., 2016; Russ et al., 2017).

The term "multinodular goiter" describes anatomy rather than a single disease mechanism. A gland may contain benign colloid nodules, one or more autonomously functioning regions, and a separate sonographically suspicious lesion. A management recommendation directed at a solitary benign nodule cannot automatically be applied to every lesion in a bilateral goiter. Likewise, the absence of a suspicious biopsy in one nodule does not characterize unsampled nodules elsewhere in the gland. A useful review must therefore distinguish the patient-level question—whether the gland causes

hyperthyroidism or compression—from the nodule-level question of malignancy risk (Durante et al., 2023; Haugen et al., 2016; Russ et al., 2017).

Thyroid functional status is a central distinction. In nontoxic multinodular goiter, observation may be appropriate when structural risk is low and symptoms are absent; treatment is considered when a goiter causes clinically meaningful pressure or cosmetic concerns, grows, extends below the sternum, or contains a suspicious lesion. In toxic multinodular goiter, autonomous hormone production adds the need to address overt or clinically important subclinical hyperthyroidism. The balance among surgery, radioiodine, medical control, and continued observation then depends on the degree of hormonal excess, goiter size and anatomy, comorbidity, expected treatment effect, and patient preference (Durante et al., 2023; Campennì et al., 2023; Ross et al., 2016; Biondi et al., 2015).

Treatment options have widened beyond conventional thyroidectomy. The 2023 European Thyroid Association guideline places multinodular disease within a risk-adapted nodule pathway; the 2023 European Association of Nuclear Medicine guideline describes radioiodine for toxic nodular disease and selected nontoxic goiters. Guidance on image-guided ablation considers a carefully selected dominant benign nodule but acknowledges its limited role for a multinodular gland as a whole. Meanwhile, surgical and hyperthyroidism guidelines address operative indications, procedure selection, and biochemical preparation. Because these documents have different populations, treatment goals, and outcome measures, their recommendations should be compared within the relevant clinical scenario rather than treated as interchangeable (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Ross et al., 2016; Papini et al., 2020).

This narrative review compares adult multinodular goiter treatments through three linked questions: what clinical problem requires treatment, which interventions are feasible, and which comparative evidence applies to that patient. Its contribution is a scenario-based framework that distinguishes nontoxic from toxic disease and anatomical from biochemical outcomes. The review evaluates observation, surgery, radioiodine, medication, and selected focal interventions without proposing a universal treatment ranking. It contains no new analysis of the historical thesis cohort.

LITERATURE AND CLINICAL BACKGROUND

Thyroid Function and Clinical Features

Serum thyrotropin (TSH) is the initial biochemical test in the evaluation of multinodular goiter. When TSH is below the reference range, free thyroxine (FT4) should be measured; triiodothyronine (T3) assessment is useful when FT4 is normal but TSH remains suppressed, because autonomous nodules may produce a predominantly T3-mediated excess. Elevated thyroid hormone concentrations with suppressed TSH indicate overt hyperthyroidism. Persistently low TSH with FT4 and T3 within their reference intervals defines subclinical hyperthyroidism, provided other causes of TSH suppression have been considered (Durante et al., 2023; Ross et al., 2016; Biondi et al., 2015).

A suppressed TSH changes the diagnostic pathway. The 2023 European Thyroid Association guideline recommends thyroid scintigraphy to identify functioning areas and guide the decision about biopsy and radioiodine treatment (Durante et al., 2023). A concordant hyperfunctioning nodule generally does

not require FNA solely because it is present; nonfunctioning or sonographically suspicious nodules within the same gland still need risk-based ultrasound assessment and possible cytology (Durante et al., 2023; Haugen et al., 2016; Ross et al., 2016). In current or previously iodine-deficient regions, scintigraphy may also be considered in selected patients with nodular goiter despite a normal TSH (Durante et al., 2023). Scintigraphy and ultrasound answer different questions and should be interpreted together.

Clinical assessment records the duration and pace of enlargement, dysphagia, dyspnea, positional breathing difficulty, voice change, and relevant radiation or family history. Cervical lymph nodes and signs of tracheal displacement warrant focused evaluation. A normal TSH does not exclude a structural problem, and a suppressed TSH does not mean that every nodule is autonomously functioning (Durante et al., 2023; Patel et al., 2020; Ross et al., 2016).

Ultrasound and Selective Cytology

High-resolution ultrasound maps both lobes, the isthmus, and suspicious cervical lymph nodes. Each clinically relevant nodule should be described by size, location, composition, echogenicity, margins, shape, and echogenic foci. A risk system such as EU-TIRADS helps prioritize nodules for sampling; the largest nodule is not automatically the most suspicious (Durante et al., 2023; Haugen et al., 2016; Russ et al., 2017).

The 2023 ETA guideline uses sonographic risk and size together to select FNA rather than biopsying the largest nodule by default. Its usual cutoffs are greater than 10 mm for EU-TIRADS 5, greater than 15 mm for EU-TIRADS 4, and greater than 20 mm for EU-TIRADS 3, with clinical exceptions such as suspicious nodes or worrisome location. These thresholds concern nodule assessment and should not be mistaken for treatment thresholds for an entire goiter. A small high-risk lesion may matter more for surgical planning than a much larger low-risk colloid nodule (Durante et al., 2023; Russ et al., 2017).

A reproducible ultrasound report records the size and position of each relevant lesion, the distribution of normal tissue, and any abnormal lymph nodes. It should identify which nodule was aspirated so that cytology cannot later be attributed to a different lesion. When local treatment is contemplated, the report must also establish whether a single dominant nodule plausibly explains pressure or cosmetic symptoms and whether untreated nodules could become the main problem. This distinction is crucial when assessing focal ablation in a gland containing several benign nodules (Durante et al., 2023; Papini et al., 2020; Sinclair et al., 2023).

Cytology must be interpreted with sonographic findings. A nondiagnostic sample may need repetition, while indeterminate cytology can lead to repeat sampling, molecular testing where available, or diagnostic surgery depending on risk and preference. A benign result supports surveillance when the clinical and imaging findings are concordant; a discordant suspicious pattern deserves reassessment rather than an assumption that the entire gland is benign (Durante et al., 2023; Haugen et al., 2016).

Ultrasound may not define substernal extent or airway anatomy in a large goiter. When intrathoracic extension, tracheal narrowing, or major-vessel relationships could change management, cross-sectional neck and upper mediastinal imaging can establish the lower extent and operative anatomy. Imaging should not delay urgent airway assessment. Iodinated contrast needs coordination with a planned radioiodine treatment because recent iodine exposure can affect uptake; CT or MRI is selected

for the clinical question rather than ordered routinely for every multinodular gland (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023).

METHODOLOGY

This focused narrative review addresses adults with nontoxic or toxic multinodular goiter. It compares observation, medication for hormone control, surgery, radioiodine, and focal treatment of selected benign nodules. Graves disease, pregnancy, pediatric disease, and definitive thyroid cancer therapy are outside its scope; suspected cancer is considered as a reason for further workup or referral (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Ross et al., 2016; Papini et al., 2020).

The review does not estimate a pooled effect size. Its unit of interpretation is the clinical scenario: asymptomatic nontoxic disease, symptomatic benign enlargement, a dominant benign target within a multinodular gland, overt toxic disease, or persistent subclinical autonomy. Guideline recommendations are treated as advice within their stated scope, not as direct comparative trials. The included studies are discussed in terms of eligibility, intervention, comparator, outcome, and follow-up before any result is generalized. This is particularly important when a study excludes a large obstructive gland or compares focal treatment only with limited surgery (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Papini et al., 2020; Goichot et al., 2024; Azizi et al., 2022; Guo et al., 2025).

The principal sources are the 2023 European Thyroid Association (ETA) nodule guideline (Durante et al., 2023), 2023 European Association of Nuclear Medicine (EANM) radioiodine guideline (Campennì et al., 2023), 2020 ETA ablation guideline (Papini et al., 2020), 2016 American Thyroid Association (ATA) hyperthyroidism guideline (Ross et al., 2016), and 2020 American Association of Endocrine Surgeons (AAES) surgical guideline (Patel et al., 2020). The 2015 ETA subclinical hyperthyroidism guideline informs the suppressed-TSH subgroup (Biondi et al., 2015). Nodule risk assessment draws on ATA and EU-TIRADS guidance (Haugen et al., 2016; Russ et al., 2017); the 2023 ATA ablation statement addresses procedural selection and safety (Sinclair et al., 2023).

The evidence base is a purposive narrative selection rather than an exhaustive database search. During manuscript revision on 1 October 2026, targeted web searches identified PubMed-indexed records, society guideline listings, and publisher pages. The update query was “site.pubmed.ncbi.nlm.nih.gov multinodular goiter surgery radioiodine ablation comparative 2025 2026”; further checks used exact cited titles or DOIs. Relevant records were selected for adult multinodular disease, clinical treatment decisions, identifiable publications, and interpretable designs and outcomes. Full text was consulted where accessible; some recent records were assessed at abstract level. This was a web-based verification and update, not a search executed within PubMed or an exhaustive search of all databases. Search-engine ranking limits reproducibility; no database-wide hit count, duplicate screening, formal risk-of-bias grading, or meta-analysis was performed. No assertion is made that all eligible studies were identified.

Guidelines were selected for their direct relevance to nodule assessment, surgery, radioiodine, hyperthyroidism, or ablation. Comparative clinical studies were retained when their population and endpoint informed a treatment decision; older evidence supplies historical context. Studies of solitary

nodules or mixed thyroid disorders were used only with an explicit applicability limit. Selected recent records were examined during revision, but the update was not a comprehensive review of all publications through October 2026. A subsequent systematic review would require a protocol, reproducible database strategies, screening records, and formal study-quality assessment.

The synthesis separates focal-nodule from whole-gland evidence and compares thyroid function, symptoms, volume, hypothyroidism, adverse events, and retreatment. Supporting studies include radioiodine versus surveillance in selected subclinical autonomy (Goichot et al., 2024), total versus partial thyroidectomy (Al-Hakami et al., 2024), long-term methimazole versus radioiodine (Azizi et al., 2022), radioiodine follow-up (Roque et al., 2020), older observational surgery-versus-radioiodine data (Kang et al., 2002), multinodular versus solitary ablation cohorts (Lang and Fung, 2022; van der Meeren et al., 2023), and a matched ablation-versus-limited-surgery study (Guo et al., 2025). Their designs and eligibility criteria are considered alongside the claims they can support.

FINDINGS

Observation in Nontoxic Multinodular Goiter

Observation requires a documented baseline and triggers for earlier review. Record thyroid function, ultrasound risk categories, any targeted cytology, symptoms, and suspected inferior extension. Surveillance differs for a high-risk nodule, a symptomatic but benign gland, and autonomous function; no uniform interval fits every lesion. New dysphagia, positional dyspnea, voice change, significant growth or suspicious change, or biochemical autonomy prompts reassessment (Durante et al., 2023; Patel et al., 2020; Haugen et al., 2016; Biondi et al., 2015).

Growth should be interpreted in the context of measurement variability and sonographic appearance rather than as an automatic instruction for surgery. A change in one dimension can reflect technique, while new suspicious features, discordant cytology, or a clinically meaningful rise in symptom burden may be more consequential. Surveillance can also become less attractive when a patient cannot reliably return for reassessment. Conversely, intervention has its own burdens and may not improve an asymptomatic patient's health simply because the gland is enlarged. Shared decision making should acknowledge both courses (Durante et al., 2023; Haugen et al., 2016).

Surgery and Radioiodine

The pathology benefit is especially relevant when suspicious cytology, rapid unexplained growth, or discordant imaging makes a purely functional treatment inadequate. Radioiodine and focal ablation may reduce benign tissue but cannot provide the same examination of an entire resected specimen. That advantage must be balanced against the surgical morbidity of more extensive dissection. If disease appears unilateral, a more limited operation may preserve some function, yet residual nodules can later become symptomatic. An explicit discussion of that future possibility is preferable to suggesting that any thyroid operation is necessarily definitive (Patel et al., 2020; Haugen et al., 2016; Al-Hakami et al., 2024).

A 2024 meta-analysis of seven randomized trials involving 1,909 participants compared total with partial thyroidectomy for nontoxic multinodular goiter. Total thyroidectomy reduced recurrence (risk ratio 0.05, 95% confidence interval 0.02–0.13) but increased transient adverse events (risk ratio 2.18,

95% confidence interval 1.64–2.89). Persistent adverse events did not differ significantly. These findings inform surgical extent; they do not compare surgery with radioiodine or focal ablation (Al-Hakami et al., 2024).

Complication counseling should name the outcome rather than combine all harms into one percentage. Temporary biochemical hypocalcemia, long-lasting hypoparathyroidism, transient voice change, permanent recurrent laryngeal nerve injury, bleeding, and anesthetic complications differ in likelihood and consequences. Published rates are influenced by operative extent, gland size, reoperation, definitions, and surgical experience. A prospective plan should include discussion of pre-existing voice symptoms, whether preoperative laryngeal assessment is appropriate, postoperative calcium monitoring, and long-term levothyroxine after complete gland removal (Patel et al., 2020; Al-Hakami et al., 2024).

For confirmed benign nontoxic goiter, radioiodine can be considered when surgery is declined or less suitable and uptake is adequate. The EANM guideline reports approximate mean volume reductions of 40–50% after one year and up to 60% after two to five years in published series (Campennì et al., 2023). These are group-level anatomical outcomes, not a guarantee of relief for an individual with dysphagia or tracheal narrowing. A very large baseline gland may remain symptomatic despite substantial percentage shrinkage; the patient must be able to accept gradual response.

A need for rapid relief of tracheal compression is a contraindication to radioiodine in the EANM guidance (Campennì et al., 2023). Low uptake, very large volume, or a symptomatic cold lesion may make it less suitable or require further investigation. Transient enlargement matters when the airway is narrow. Radioiodine provides no histology, so malignancy concerns need evaluation before treatment. Follow-up should assess the original symptom as well as thyroid function and, where relevant, residual anatomical compression (Patel et al., 2020; Campennì et al., 2023).

The preparation and follow-up burden of radioiodine deserves equal attention to the treatment itself. Uptake can be reduced by recent iodine-containing contrast or medication, and the nuclear medicine team must determine whether the activity and uptake are appropriate for the intended goal. Patients require radiation-safety advice, information about temporary or delayed effects, and biochemical monitoring for persistent excess hormone or later hypothyroidism. The EANM guidance also identifies pregnancy and lactation as contraindications. These practical constraints may shift a preference even when radioiodine appears anatomically feasible (Campennì et al., 2023).

Focal Interventions

Focal thermal ablation is most defensible for a proven benign, well-defined dominant nodule that explains symptoms or cosmetic concern. ETA guidance does not support routine ablation of an entire diffuse multinodular gland and restricts this role to a dominant target or selected palliative circumstances when surgery or radioiodine is unsuitable (Papini et al., 2020). Identify which nodules remain untreated, the potential need for repeat procedures, and the surveillance plan (Durante et al., 2023; Papini et al., 2020; Sinclair et al., 2023).

Thermal and ethanol ablation should not be grouped indiscriminately. Ethanol is often favored for a recurrent predominantly cystic benign lesion, whereas thermal techniques are used for selected solid or mixed benign symptomatic targets. A multinodular gland may contain both patterns, but one procedure need not address every lesion. The consent discussion should identify the actual target, its size and proximity to sensitive structures, the expected course of shrinkage, and a plan for nodules left untreated. This is more informative than offering “ablation” as if it were a uniform whole-gland alternative (Durante et al., 2023; Papini et al., 2020; Sinclair et al., 2023).

Ablation eligibility begins with a benign diagnosis and agreement between imaging, cytology, and the clinical problem. For most nodules with a prior benign aspirate, repeat cytological confirmation is appropriate before thermal ablation, with exceptions tied to very low-risk appearances in guidance. Technique-related risks include pain, voice change, skin injury, and injury to nearby structures; their probability depends on lesion location and operator experience. A reduction in target volume is a useful technical measure, but relief of the patient's pressure complaint and maintenance of normal thyroid function are separate outcomes (Papini et al., 2020; Sinclair et al., 2023; Lang and Fung, 2022).

A 2025 retrospective propensity-matched study compared 86 pairs with selected benign glands containing 2–5 nodules, more than 50% normal tissue, and 1–3 dominant targets. At 24 months, the study's all-nodule-burden progressive-disease endpoint (9.30% versus 6.98%) and retreatment (1.16% versus 2.33%) did not differ significantly between thermal ablation and lobectomy or subtotal thyroidectomy (Guo et al., 2025). These results concern selected glands and two-year follow-up; they do not establish equivalence, or apply directly to diffuse, obstructive, or toxic goiter or to total thyroidectomy. Ethanol ablation may suit recurrent predominantly cystic nodules (Durante et al., 2023; Papini et al., 2020).

Hormone Control in Toxic Multinodular Goiter

Toxic multinodular goiter changes the treatment goal. A smaller gland is not sufficient if biochemical thyrotoxicosis persists, and a normal TSH after medication does not establish that autonomy has disappeared. Severity ranges from overt hyperthyroidism, with elevated circulating hormone concentrations, to persistent subclinical disease with normal free hormones. Age, atrial arrhythmia, cardiovascular disease, osteoporosis or fracture risk, symptoms, and degree of TSH suppression influence how strongly treatment is favored. These considerations should be recorded before discussing radioactive iodine, an operation, or prolonged medical control (Ross et al., 2016; Biondi et al., 2015).

In persistent subclinical hyperthyroidism, the 2015 ETA guideline favors treatment more strongly for older adults with TSH below 0.1 mIU/L, especially with cardiac or skeletal risk; milder suppression requires individual assessment (Biondi et al., 2015). In a randomized trial of adults at least 50 years old with scintigraphic autonomy, few atrial fibrillation events and difficult recruitment left the primary treatment-versus-surveillance comparison nonsignificant (Goichot et al., 2024). Biochemical normalization should therefore not be stated as proof that treating every risk group prevents atrial fibrillation, fracture, or mortality.

Methimazole can control hormone excess before definitive treatment or provide ongoing control in selected patients. In a randomized trial of 130 patients with toxic multinodular goiter, 53 methimazole

and 54 radioiodine recipients completed long-term follow-up after losses and treatment changes. Median follow-up was 120 and 132 months, respectively. Time spent euthyroid averaged $95.8\% \pm 5.9\%$ with methimazole versus $72.4\% \pm 14.8\%$ with radioiodine ($P < 0.001$). This biochemical endpoint does not establish relief of compression or comparative quality of life; attrition and treatment changes also limit interpretation (Azizi et al., 2022).

The choice of continuing medication requires discussion of adherence, thyroid laboratory surveillance, possible adverse effects, and the fact that autonomy usually persists when the drug is stopped. The medication-versus-radioiodine trial enrolled selected patients aged 60 or younger at entry and reported that its goiters were not representative of very large glands. Its biochemical advantage cannot be generalized without qualification to older, frailer patients, large substernal goiters, or those with urgent symptoms. In a patient with serious compression, anatomical assessment still takes precedence over a favorable biochemical result on tablets (Ross et al., 2016; Azizi et al., 2022).

Radioiodine Versus Surgery

Radioiodine is often reasonable when operative risk is high or surgery is declined, assuming adequate uptake and no cancer concern. Persistent hyperthyroidism or later hypothyroidism requires follow-up and sometimes another treatment; transient hormone worsening warrants care in patients with cardiovascular risk (Campennì et al., 2023; Ross et al., 2016; Roque et al., 2020). A 2002 retrospective comparison of surgery and radioiodine in nodular hyperthyroidism informs historical practice, but mixed nodular phenotypes, treatment selection, and older techniques limit present-day causal inference (Kang et al., 2002).

Radioiodine planning includes confirmation of the cause of thyrotoxicosis, uptake assessment, medication and iodine exposure review, pregnancy and breastfeeding exclusion, radiation precautions, and a follow-up arrangement. A transient hormone rise after treatment is relevant to patients with cardiovascular disease. Longer-term outcomes may include euthyroidism, persistent or recurrent hyperthyroidism needing further intervention, or hypothyroidism requiring replacement. The EANM guideline emphasizes that these probabilities depend on the specific benign disease, uptake and dose approach, extranodular suppression, and duration of observation (Campennì et al., 2023; Ross et al., 2016; Roque et al., 2020).

When toxic disease coexists with a large bilateral or substernal gland, near-total or total thyroidectomy can address hormone excess and compression in one operation. ATA guidance favors near-total or total resection when surgery is selected for toxic multinodular goiter to reduce recurrence. The same guidance recommends an experienced, high-volume thyroid surgeon. Assessment should still account for cardiopulmonary status, laryngeal symptoms, operative anatomy, and lifelong levothyroxine after complete gland removal (Patel et al., 2020; Ross et al., 2016).

Treatment extent and timing



Treatment scope and timing do not compare clinical success rates.

Figure 1. Extent and timing of common treatments

Original conceptual illustration for this review, informed by (Patel et al., 2020; Campennì et al., 2023; Papini et al., 2020). It is not anatomical imaging and is not endorsed by the cited societies. No numerical outcome is depicted.

Preoperative Preparation

Elective thyroidectomy in overt toxic multinodular disease requires a preparation plan distinct from that used for nontoxic goiter. ATA recommendation 46 advises rendering the patient euthyroid with methimazole before surgery when possible, with or without beta-blockade; it specifically advises against preoperative iodine in toxic nodular disease. Thyroid function should be rechecked and cardiovascular symptoms stabilized. Urgent surgery when biochemical control cannot be achieved is a specialist decision requiring a tailored anesthesia and endocrine strategy rather than routine application of an elective pathway (Patel et al., 2020; Ross et al., 2016). A 2026 retrospective study of 100 patients with Graves disease or toxic multinodular goiter compared preoperative Lugol's solution in 57 patients with no Lugol's solution in 43. The abstract reported no significant differences in the principal operative or postoperative outcomes. Its mixed disease population and nonrandom treatment assignment do not establish the safety or benefit of iodine specifically in toxic multinodular goiter and do not replace ATA recommendation 46 (Ciriotta et al., 2026).

Ultrasound assesses nodules and nodes; cross-sectional imaging helps define substernal extent or tracheal displacement when clinically indicated (Durante et al., 2023; Patel et al., 2020; Haugen et al., 2016). Consider vocal-cord assessment according to symptoms and operative risk, and explain postoperative replacement and potential voice or calcium complications (Patel et al., 2020).

DISCUSSION

The apparent variation among society documents is often a difference of question. ETA nodule guidance asks which nodules deserve sampling or observation; the EANM guidance asks how to select and deliver radioiodine; ATA guidance addresses hyperthyroidism and definitive toxic-disease options; and AAES guidance addresses the indications, conduct, and outcomes of surgery. A sentence

from one source can be correct within its population yet misleading when transferred to another. The comparison in Table 1 is therefore organized by population and decision rather than by a purported ranking of societies (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Ross et al., 2016).

Table 1. Scope and contribution of the principal guideline sources

Source	Relevant population and decision	Contribution and applicability limit
ETA 2023 (Durante et al., 2023)	Adults with thyroid nodules, including multinodular glands	Risk-adapted workup and benign nodule management; not a thyroid cancer treatment guideline.
EANM 2023 (Campennì et al., 2023)	Toxic nodular disease and selected benign nontoxic goiters	Radioiodine selection, delivery, and follow-up; not a direct surgery-versus-radioiodine trial.
ETA 2020 (Papini et al., 2020)	Symptomatic benign nodules considered for ablation	Dominant-nodule role; limited evidence for treatment of an entire multinodular gland.
ATA 2016 (Ross et al., 2016)	Hyperthyroidism, including toxic multinodular goiter	Control of hormone excess and definitive choices; does not govern every nontoxic goiter.
AAES 2020 (Patel et al., 2020)	Adults considered for thyroid surgery	Operative indications and perioperative care; surgery-focused scope.

Original comparative table based on the cited guidelines. ETA = European Thyroid Association; EANM = European Association of Nuclear Medicine; ATA = American Thyroid Association; AAES = American Association of Endocrine Surgeons.

Comparative validity requires alignment of denominators and follow-up. A report of target-nodule shrinkage counts treated nodules, while a report of recurrent goiter counts patients after a particular extent of resection. Similarly, “euthyroid” may mean normal function without medication, normal function while taking methimazole, or adequate replacement after ablation, each with a different burden for the patient. Short studies can undercount regrowth or late hypothyroidism. This review reports numerical outcomes only when the source population and endpoint can be identified and deliberately avoids an indirect pooled percentage across modalities (Campennì et al., 2023; Papini et al., 2020; Al-Hakami et al., 2024; Azizi et al., 2022; van der Meeren et al., 2023; Guo et al., 2025).

Multinodular anatomy also changes the meaning of focal success. In a retrospective ablation cohort, medication-free biochemical euthyroidism at one year was reported in 25% of the toxic multinodular group (12 patients) versus 72% of the solitary toxic adenoma group (36 patients) (van der Meeren et al., 2023). This small, selected comparison argues against applying solitary-nodule cure estimates to diffuse autonomy; it is not a direct ablation-versus-radioiodine trial. In nontoxic disease, treating several dominant nodules may work for selected glands (Guo et al., 2025), whereas ETA guidance remains cautious about whole-gland ablation (Papini et al., 2020).

The proposed sequence is an interpretation, not a society-endorsed algorithm. It first identifies urgent airway compromise or suspicious malignancy findings for prompt anatomical or oncological assessment. For patients without these concerns, thyroid function and nodule-specific risk define which treatments are feasible; choices then reflect the principal goal of hormonal control, pressure relief, preservation of function, or avoidance of an operation (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Ross et al., 2016; Biondi et al., 2015; Papini et al., 2020).

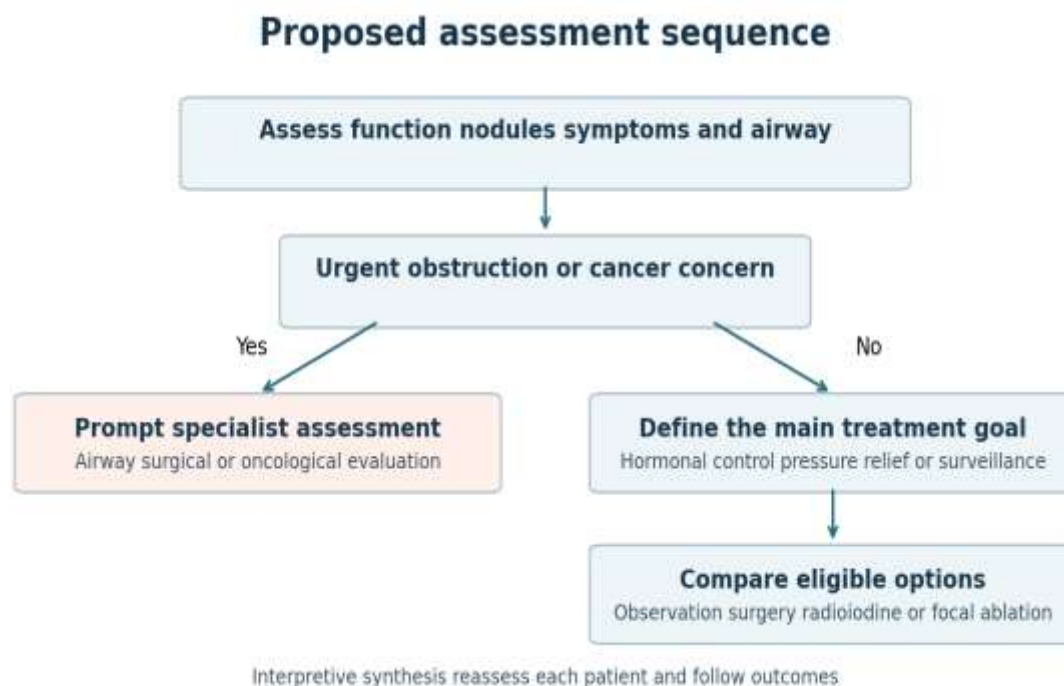


Figure 2. Proposed pathway for adult multinodular goiter

Original decision schematic for this review, informed by (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Ross et al., 2016; Biondi et al., 2015; Papini et al., 2020). This is an interpretive synthesis, not a reproduced or society-endorsed guideline algorithm. Each branch requires individualized assessment.

Strengths and Limitations of the Evidence

Multispecialty guidance and several comparative designs support a more specific discussion than a list of recommendations (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Ross et al., 2016; Papini et al., 2020; Goichot et al., 2024; Al-Hakami et al., 2024; Azizi et al., 2022; Lang and Fung, 2022; van der Meeren et al., 2023; Guo et al., 2025). Yet few studies enroll patients for whom all options are truly feasible or use common measures of swallowing, dyspnea, quality of life, thyroid function, and retreatment.

The historical surgery-versus-radioiodine cohort is observational and mixes nodular phenotypes (Kang et al., 2002). The methimazole trial evaluates biochemical control and excludes some patients with cardiovascular disease or very large glands (Azizi et al., 2022). The 2025 matched ablation study includes only selected benign glands, uses lobectomy or subtotal surgery as comparators, and follows patients for two years (Guo et al., 2025). These designs answer narrower questions than an overall treatment ranking.

Implications for Research and Practice

A practical consultation can proceed in stages. First identify whether the immediate issue is a suspicious lesion, substantial compression, excess hormone production, or an isolated benign dominant nodule. Next establish which treatments are actually feasible for that patient's anatomy, uptake, comorbidity, and preferences. Finally compare only those feasible options using the outcome that matters most to the patient. A desire to avoid lifelong replacement, for example, may favor preserving tissue in a suitable gland but cannot make focal treatment appropriate for an unsampled suspicious lesion or severe diffuse obstruction (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Papini et al., 2020).

Consider three distinct presentations. A stable, euthyroid patient with several low-risk nodules and no symptoms chiefly needs risk-based observation. A patient with benign cytology but progressive tracheal displacement needs an anatomical treatment discussion, including surgical assessment and whether gradual radioiodine response is appropriate. A patient with autonomous hyperthyroidism and a separate suspicious cold nodule needs both functional and malignancy evaluation. These are illustrative decision patterns, not cases from a new cohort and not substitutes for local specialist review (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Ross et al., 2016).

Documentation should also distinguish the expected and the observed course. Before intervention, record thyroid function, the target symptoms, imaging where relevant, and the anticipated timing of improvement. At follow-up, reassess those same measures rather than relying on a different endpoint chosen after treatment. A patient whose nodule shrinks but whose swallowing remains difficult may need a new evaluation for persistent thyroid or nonthyroid causes. A patient whose TSH normalizes but whose gland continues to obstruct the airway has achieved one goal but not the other (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Papini et al., 2020).

Shared decision making should identify the main outcome sought and explain each feasible option's likely timing, need for hormone replacement, adverse effects, and possibility of retreatment. Table 2 summarizes these tradeoffs without claiming a universal ranking (Durante et al., 2023; Patel et al., 2020; Campennì et al., 2023; Ross et al., 2016; Papini et al., 2020).

Table 2. Treatment goals and tradeoffs in benign multinodular goiter

Option	Most relevant context	Important tradeoff
Observation (Durante et al., 2023)	Stable, asymptomatic, low-risk nontoxic goiter	Avoids immediate intervention; requires reassessment if function, nodules, or symptoms change.
Surgery (Patel et al., 2020; Ross et al., 2016)	Major compression, substernal extent, suspicious lesion, or toxic goiter requiring removal	Prompt anatomical effect and tissue diagnosis; operative risks and often lifelong replacement.
Radioiodine (Campennì et al., 2023; Ross et al., 2016)	Toxic goiter without suspected cancer; selected benign nontoxic goiter when surgery is less suitable	Gradual volume reduction; thyroid function follow-up and possible repeat treatment.
Focal ablation (Papini et al., 2020; Sinclair et al., 2023)	Symptomatic, proven benign dominant nodule in a carefully selected gland	Treats the target nodule; untreated nodules and possible regrowth require surveillance.

Original synthesis. Suitability depends on gland anatomy, thyroid function, cytology, comorbidity, local expertise, and patient preference; this table is not a society-endorsed algorithm.

Table 3. Populations, endpoints, and limits of the comparative evidence

Source and design	Population and follow up	Outcome and interpretation
Goichot et al. (2024) Randomized study	Adults 50 years or older with subclinical hyperthyroidism and scintigraphic autonomy; treatment versus surveillance.	New atrial fibrillation was the primary clinical endpoint. Few events and recruitment constraints led to a nonsignificant primary comparison; the study cannot establish prevention for all subgroups.
Al-Hakami et al. (2024) Meta-analysis of randomized trials	7 randomized trials; 1,909 participants; total versus partial thyroidectomy for nontoxic multinodular goiter. Follow-up varied among trials.	Recurrence RR 0.05 (95% CI 0.02–0.13), favoring total surgery; transient adverse events RR 2.18 (95% CI 1.64–2.89), higher with total surgery. Persistent harms did not differ significantly. Compares surgical extent only.

Source and design	Population and follow up	Outcome and interpretation
Azizi et al. (2022) Randomized trial with long follow up	130 randomized; 53 methimazole and 54 radioiodine recipients completed follow-up. Median follow-up 120 versus 132 months.	Time euthyroid 95.8% $\pm$ 5.9% versus 72.4% $\pm$ 14.8% (P < 0.001). A biochemical outcome; attrition, treatment changes, and selected eligibility limit inference. Compression and quality of life were not comparative endpoints.
Roque et al. (2020) Longitudinal radioiodine cohort	Patients treated with radioiodine for toxic multinodular goiter; thyroid function and volume over time.	Describes functional and anatomical course after treatment. Without a concurrent randomized surgical comparator, it cannot quantify comparative superiority.
Kang et al. (2002) Retrospective comparison	Historical nodular hyperthyroidism treated with surgery or radioiodine.	Treatment selection and older practice introduce confounding. Mixed nodular phenotypes limit transfer to contemporary toxic multinodular disease.
Lang and Fung (2022) Retrospective ablation cohort	Selected benign nontoxic multinodular patients receiving multiple-nodule versus single-nodule radiofrequency ablation.	Higher procedural pain with multiple targets and six-month shrinkage were reported. Short follow-up does not establish durable whole-gland control.
van der Meeren et al. (2023) Retrospective subgroup	36 solitary toxic adenoma and 12 toxic multinodular goiter patients after radiofrequency ablation.	Medication-free biochemical euthyroidism at one year was 72% versus 25%. Small, selected groups do not directly compare ablation with surgery or radioiodine.

Source and design	Population and follow up	Outcome and interpretation
Guo et al. (2025) Propensity matched cohort	86 pairs with selected benign glands; thermal ablation versus lobectomy or subtotal thyroidectomy.	At 24 months, progression 9.30% versus 6.98% ($P = 0.577$) and retreatment 1.16% versus 2.33% ($P = 0.560$). No equivalence margin or random assignment; findings do not apply to total thyroidectomy or unselected glands.
Ciriotta et al. (2026) Retrospective comparison	100 patients with Graves disease or toxic multinodular goiter; Lugol's solution 57 versus no Lugol's solution 43. Surgery during 2014–2024.	No significant differences in the principal perioperative outcomes in the abstract. Mixed diagnoses, nonrandom assignment, and lack of a disease-specific result preclude replacing guideline advice for toxic nodular disease.

This evidence matrix summarizes selected comparative studies. Each result is tied to its design, denominator, outcome, and follow-up. Nonsignificant differences do not establish equivalence, and outcomes from unlike populations should not be pooled into a treatment ranking.

Table 4. Follow-up questions after each management strategy

Strategy	Early review	Longer-term question
Observation	Revisit symptoms, TSH when clinically indicated, and ultrasound risk or cytology concerns.	Has a nodule developed suspicious features, has function changed, or has pressure become important? The interval reflects risk rather than a universal timetable (Durante et al., 2023; Haugen et al., 2016).

Strategy	Early review	Longer-term question
Surgery	Assess voice, wound, calcium and parathyroid function where relevant, and thyroid replacement after complete removal.	Are symptoms relieved and replacement levels appropriate? After limited resection, is remaining nodular tissue causing a new problem (Patel et al., 2020; Al-Hakami et al., 2024)?
Radioiodine	Monitor thyroid function and symptoms as the effect develops; assess for transient worsening in vulnerable patients.	Is there persistent or recurrent hyperthyroidism, hypothyroidism, inadequate volume response, or residual compression needing another strategy (Campennì et al., 2023; Ross et al., 2016; Roque et al., 2020)?
Focal ablation	Assess the target nodule, symptoms, and potential procedure effects with clinical and ultrasound review.	Has the target regrown or another nodule become symptomatic? Is repeat ablation or another treatment needed (Papini et al., 2020; Sinclair et al., 2023; Lang and Fung, 2022; van der Meeren et al., 2023; Guo et al., 2025)?

CONCLUSION

Multinodular goiter management begins with thyroid function, nodule-specific cancer risk, and the symptoms and anatomy of the whole gland (Durante et al., 2023; Patel et al., 2020; Ross et al., 2016). Observation, surgery, radioiodine, and focal ablation address different goals and timescales. Suspicious lesions or important airway compression require directed assessment; toxic disease requires a plan for hormone excess. Comparative studies clarify selected endpoints but do not provide an unbiased universal ranking across heterogeneous glands. Counseling should state the intended benefit, likely timing, adverse effects, replacement and follow-up needs, and the possibility of retreatment.

Future Research

Future trials should prospectively define what counts as symptomatic improvement, specify baseline gland volume and substernal extent, and report both biochemical and anatomical results. Ideally, investigators would enroll patients for whom the compared options are genuinely feasible and record

why others were excluded. Outcomes should include validated patient-reported symptoms and quality of life, thyroid function with or without replacement, complications using consistent definitions, repeat interventions, and follow-up long enough to detect regrowth. Separate analyses of nontoxic and toxic disease would prevent a functional benefit from obscuring a structural failure (Campennì et al., 2023; Papini et al., 2020; Al-Hakami et al., 2024; Azizi et al., 2022).

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