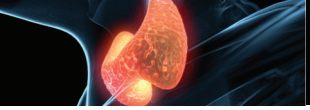


Management of
THYROID DISORDERS

QUICK REFERENCE GUIDE
FOR HEALTHCARE PROFESSIONALS

MEMS Established 1961
Malaysian Endocrine & Metabolic Society

Ministry of Health Malaysia

Academy of Medicine Malaysia

This Quick Reference Guide provides key messages and the recommendations in the Clinical Practice Guidelines (CPG) for the Management of Thyroid Disorders, 1st Edition.

OVERT HYPERTHYROIDISM

1. Patients with overt Graves' hyperthyroidism should be treated with any of the following modalities: ATDs, RAI therapy, or thyroidectomy
2. Patients should be informed about the side effects of ATDs and the necessity of informing the physician promptly if they develop pruritic rash, jaundice, acholic stools or dark urine, arthralgias, abdominal pain, nausea, fatigue, fever, or pharyngitis
3. Patients with overtly TMNG or TA should be treated with RAI therapy or thyroidectomy. On occasion, long-term, low-dose treatment with MMI may be appropriate

SUBCLINICAL HYPERTHYROIDISM

1. ECG, echo and bone mineral density assessments are recommended for patients with subclinical hyperthyroidism
2. Treatment should be considered in patients with subclinical hyperthyroidism who are either elderly (age >65 years old) or with comorbidities (cardiac disease or osteoporosis) or TSH level less than 0.1 mU/L
3. Patients with subclinical hyperthyroidism at a younger age (age <65 years) and those without comorbidities (cardiac disease or osteoporosis) and TSH between 0.1 and 0.5 mIU/L and asymptomatic should be observed
4. Treatment if decided, should be based on aetiology and follow the same outlined principles for overt hyperthyroidism

OVERT HYPOTHYROIDISM

1. Levothyroxine is the mainstay of treatment for hypothyroidism, best taken on empty stomach (1 hour before breakfast or at bedtime, at least 3 hours after the last meal of the day) separated from other potentially interfering medications and supplements
2. Levothyroxine replacement therapy can be started as an initial full replacement or as a partial replacement with gradual dose increments titrated using serum TSH as the goal in primary hypothyroidism, and free thyroxine levels in secondary hypothyroidism
3. In hospitalized patients, if enteral administration is contraindicated (e.g. perforated viscus) then intravenous levothyroxine (at approximately 75% of oral dose, assuming enteral levothyroxine dose achieved euthyroidism)

may be used till enteral absorption improves. The possibility of adrenal insufficiency should be considered, and if there is sufficient clinical or biochemical evidence, empiric treatment should be provided

SUBCLINICAL HYPOTHYROIDISM

1. Subclinical hypothyroidism is defined as a serum TSH concentration above the statistically defined upper limit of the reference range when serum fT4 is within its reference range
2. Investigation of raised TSH requires repeat measurements, to establish a firm diagnosis
3. Determination of anti-TPO antibodies may be helpful in defining the risk of progression

THYROID NODULES/GOITRE

1. All patients with a suspected thyroid nodule/nodular goitre or radiographic abnormality suggesting a thyroid nodule incidentally detected on another imaging study should undergo a dedicated thyroid/neck US that encompasses the thyroid as well as the central and lateral neck compartments

THYROID STORM

1. The diagnosis of thyroid storm is clinical. Both the BWPS and JTA diagnostic tools could be used to aid diagnosis, but we recommend the use of BWPS, as this scoring tool is more sensitive
2. Thyroid storm should be treated with a combination of high-dose PTU or MMI, beta-blockers, glucocorticoids and Lugol's iodine
3. TPE (with FFP as fluid replacement) should be considered in severe/rapidly deteriorating thyroid storm or with contraindications to standard multimodal therapy
4. All patients with thyroid storm should have early definitive therapy with RAI. In patients with large obstructing goitre, early thyroidectomy should be considered instead

MYXOEDEMA COMA

1. Intravenous hydrocortisone 200 mg stat, then 100 mg 6–8 hourly should be administered prior to levothyroxine
2. Initial intravenous levothyroxine of 200–400 µg followed by 1.6 µg/kg/day (75% if administered intravenously) should be given thereafter. Alternatively oral levothyroxine can be given as 500 µg loading followed by maintenance dose

PRE-/PERIOPERATIVE MANAGEMENT

1. All elective surgery should be postponed until euthyroid or near euthyroid state is achieved
2. For urgent surgeries, clinical and biochemical assessment of patient's thyroid state should be ascertained
3. In patients who are hyperthyroid and require urgent surgery, rapid control with high-dose MMI or PTU, beta-blockers, Lugol's iodine and glucocorticoids are recommended
4. Only patients with risk factors for hypothyroidism or those who exhibit symptoms of hypothyroidism should be screened
5. In mild hypothyroidism, i.e. those with subclinical hypothyroidism, surgery should not be postponed
6. In moderate hypothyroidism (overt hypothyroidism), urgent surgeries should be undertaken without delays. In elective surgeries, it is recommended that euthyroid state is restored before surgery

SUBACUTE THYROIDITIS (DE QUERVAIN'S THYROIDITIS)

1. Subacute thyroiditis should be suspected in all patients who present with painful goitre
2. An ESR or CRP should be measured in patients with painful thyroid swelling. Elevated ESR and CRP is suggestive of subacute thyroiditis
3. Non-steroidal anti-inflammatory drugs are the first-line therapy and should be used for patients with mild symptoms

ACUTE/SUPPURATIVE THYROIDITIS

1. In patients who had ultrasound findings suggestive of abscess or acute/suppurative thyroiditis, aspiration should be done; and sample sent for Gram stain, culture and sensitivity
2. Acute/suppurative thyroiditis should be treated with antibiotics and surgical drainage determined by clinical judgement

HYPOTHYROIDISM AND PREGNANCY

1. As there is no published data on the pregnancy-specific reference range representative of the Malaysian pregnant population, we recommend a TSH upper reference limit of 4 mIU/L
2. Pregnant women with OH should be treated with LT4
3. For maternal SCHypo, LT4 treatment is recommended in the following situations to reduce the risk of miscarriage and preterm delivery:
   a) Pregnant women with negative TPOAb:
      - LT4 is recommended if TSH is >10 mIU/L
      - LT4 may be considered if TSH is above the pregnancy-specific reference range or 4.0 mIU/L

b) Pregnant women with positive TPOAb:
   - LT4 is recommended if TSH is above the pregnancy-specific reference range or 4.0 mIU/L
   - LT4 may be considered if TSH is >2.5 mIU/L

4. Pregnant women who are already treated with LT4 before conception are recommended to have their LT4 dosage increased by 30%–50% upon conception with a higher percentage being considered for postablative hypothyroidism and lower percentage for autoimmune hypothyroidism

HYPERTHYROIDISM AND PREGNANCY

1. Each institution should establish its own pregnancy-specific reference intervals for each trimester of pregnancy using local population data
2. When a suppressed TSH and elevated fT4 are detected in the first trimester, clinical history and physical examination should be performed to determine the aetiology. Graves' disease is differentiated from gestational thyrotoxicosis clinically. TRAb supports the diagnosis of Graves' disease
3. Management of gestational transient thyrotoxicosis is mainly supportive therapy: rehydration and hospitalisation if needed in the presence of hyperemesis gravidarum; and beta-blocker if very symptomatic. Antithyroid drugs are not recommended
4. Women with hyperthyroidism should be counselled on the importance of euthyroid state before attempting pregnancy. The risks and benefits of all treatment options to achieve a euthyroid state (radioactive treatment, thyroidectomy and ATD therapy) should also be discussed
5. Women with hyperthyroidism who require high doses of ATD to achieve a euthyroid state should be considered for definitive therapy before becoming pregnant
6. Women who are well-controlled on carbimazole and who desire pregnancy could switch to PTU before trying to conceive

POSTPARTUM THYROIDITIS (PPT)

1. Women in thyrotoxic phase of PPT who are symptomatic should be treated with beta-blockers. Antithyroid drugs are not recommended
2. Women in hypothyroid phase of PPT and who are symptomatic should be treated with LT4. Women with mild symptoms who choose not to be treated need to have their TFT checked every 4- to 8-weekly until a euthyroid state is restored
3. Women who choose to get pregnant again while in hypothyroid phase of PPT or who are breastfeeding should be treated with LT4
4. Women with resolution of PPT and high risk of permanent hypothyroidism should have TFT screened annually to monitor for development of permanent hypothyroidism

ACQUIRED HYPOTHYROIDISM IN CHILDREN AND ADOLESCENTS

1. The clinical features of hypothyroidism in children and adolescents are similar to adults; however, in children, evaluations of height and puberty are essential since growth retardation, abnormal puberty are common
2. It is recommended to examine for goitre, measure antithyroid antibodies, and evaluate TSH pattern, as these are the predictive factors for future development of hypothyroidism
3. Levothyroxine is recommended as the medication of choice for treating Hashimoto's thyroiditis
4. The recommended target range for TSH is in the lower half of the reference range
5. The recommended target range for free T4 is in the upper half of the reference range
6. All children with Turner Syndrome, Trisomy 21, Klinefelter Syndrome and Prader-Willi Syndrome should have a thyroid function screen performed at diagnosis and every 1–2 years thereafter

HYPERTHYROIDISM IN CHILDREN AND ADOLESCENTS

1. The diagnosis is based on the clinical suspicion and confirmed by elevated free T4 and/or T3 levels with suppressed TSH
2. In a patient with a symmetrically enlarged thyroid, recent onset of ophthalmopathy and moderate-to–severe hyperthyroidism, the diagnosis of GD is likely and further evaluation of the aetiology is often unnecessary
3. However, if the aetiology of hyperthyroidism is unclear, TSH receptor antibodies, which are specific to GD, should be measured
4. The first-line initial treatment is ATD, which is carbimazole or its active metabolite MMI
5. Methimazole/carbimazole dose typically used is 0.2–0.5 mg/kg daily, with a range from 0.1 mg/kg to 1.0 mg/kg daily (maximal initial dose: 30 mg daily)
6. Propylthiouracil (PTU) should be avoided in children, except in selected circumstances because of the risk of idiosyncratic liver failure
7. Beta-adrenergic blockade should be considered for children with significant symptoms of hyperthyroidism at diagnosis or relapse, especially if there is tachycardia. In patients with asthma or reactive airway disease, cardioselective beta-blockers, such as atenolol or metoprolol, should be used cautiously
8. In general, PTU should not be used in children. But if it is used, it should be stopped immediately, and liver function assessed in children who develop anorexia, pruritus, rash, jaundice, light-coloured stool or dark urine, joint pain, right upper quadrant pain or abdominal bloating, nausea or malaise
9. Definitive therapy available for GD is RAI or thyroidectomy

10. Indications for definitive therapy in children include relapse after an appropriate duration of ATD, compliance issues, or adverse effects of ATD

THYROID DISORDERS IN THE ELDERLY

1. Patients with overt Graves' hyperthyroidism should be treated with any of the following modalities: RAI therapy, ATDs, or surgery
2. When TSH is persistently <0.1 mU/L, treatment of SCHyper is recommended in all individuals >65 years of age
3. When TSH is persistently below the lower limit of normal but >0.1 mU/L, treatment of SCHyper should be considered in individuals >65 years of age with cardiac disease, osteoporosis, or symptoms of hyperthyroidism
4. In elderly patients with overt hypothyroidism, small dose of levothyroxine should be started, 25 or 50 µg daily. The dose of levothyroxine should be increased by 25 µg/day every 14–21 days until a full replacement dose is reached

DRUG-INDUCED THYROID DISORDERS

AMIODARONE INDUCED THYROID DISEASE

1. Type 1 AIT should be treated with high-dose carbimazole 40 mg per day or its equivalent
2. Type 2 AIT should be treated with corticosteroids: prednisolone 40 mg given once daily for 2–4 weeks, followed by a gradual taper over 2–3 months
3. Combined carbimazole and corticosteroids should be used if the patient fails on monotherapy or if the distinction between Type 1 and Type 2 is not clear

GRAVES' OPHTHALMOPATHY

1. Assessment of GO includes assessment of activity and severity using standardised criteria. It is categorised as active or inactive; mild, moderate, severe, or sight threatening
2. For mild active GO, topical treatment and measures to control the risk factors are the mainstay of treatment. A 6-month selenium supplement at a dose of 100 µg bd can be considered
3. We recommend an intermediate dose of IV methylprednisolone at 0.5 g weekly for 6 weeks followed by 0.25 g weekly for 6 weeks (cumulative dose 4.5 g) in most cases of moderate-to–severe GO
4. We recommend that a cumulative dose of IV methylprednisolone should not exceed 8 g
5. Dysthyroid optic neuropathy should be treated immediately with very high doses of intravenous GCs (500–1000 mg methylprednisolone) for 3 consecutive days or on alternate days during the first week. The doses should be repeated in the second week. If the response is absent or poor, urgent orbital decompression should be done

6. Oral prednisolone prophylaxis of 0.4–0.5 mg/kg per day for a total of 3 months is recommended in patients with mild-to–moderate GO who are undergoing radioiodine therapy

Figure 1: Algorithm for the investigations of suspected hyperthyroidism.[4(Level III)]

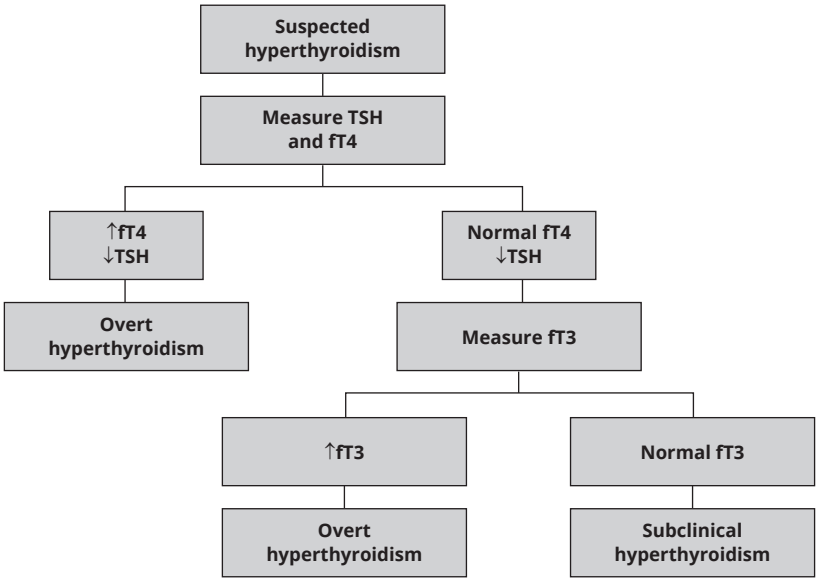


Figure 2: Algorithm for diagnostic testing for aetiology of hyperthyroidism.[36 (Level II);39(Level III); 49 (Level III)]

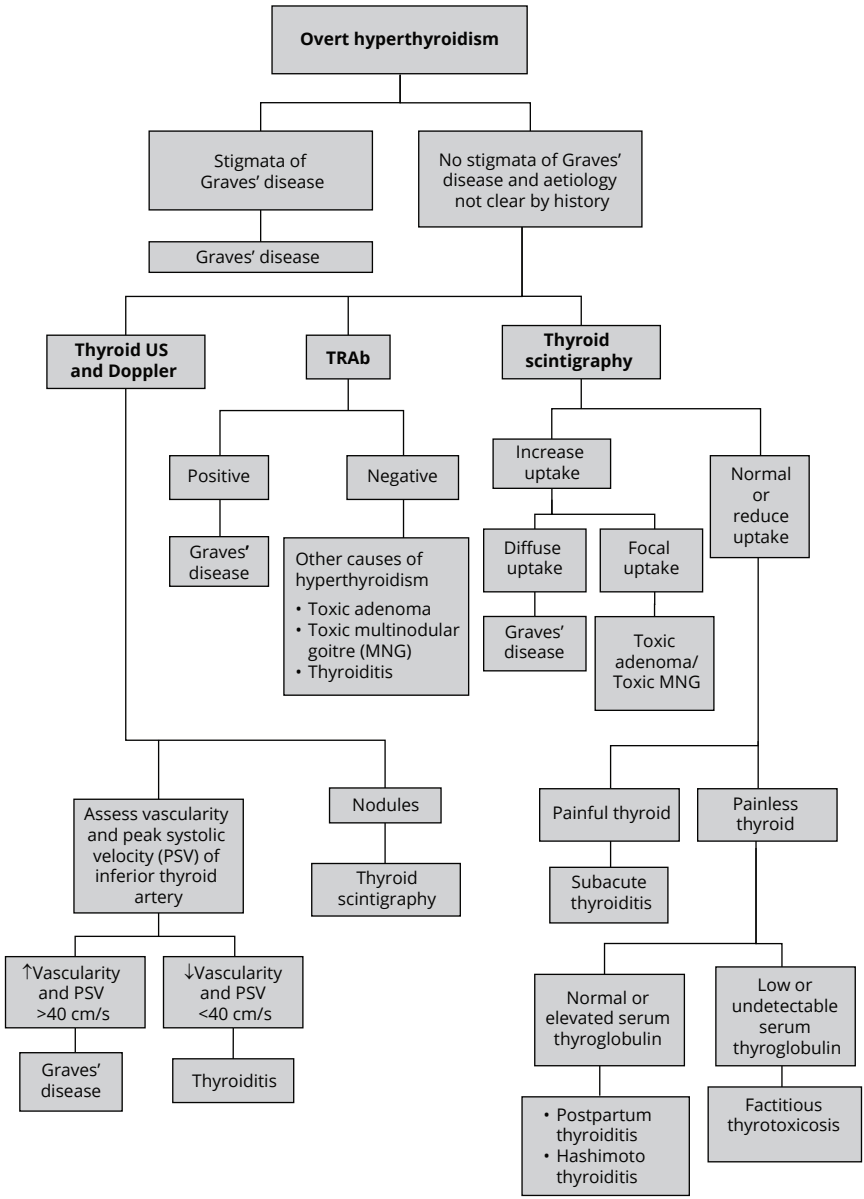


Figure 3: Algorithm for determining aetiology of low TSH level. [Adapted from[4(Level II)]]

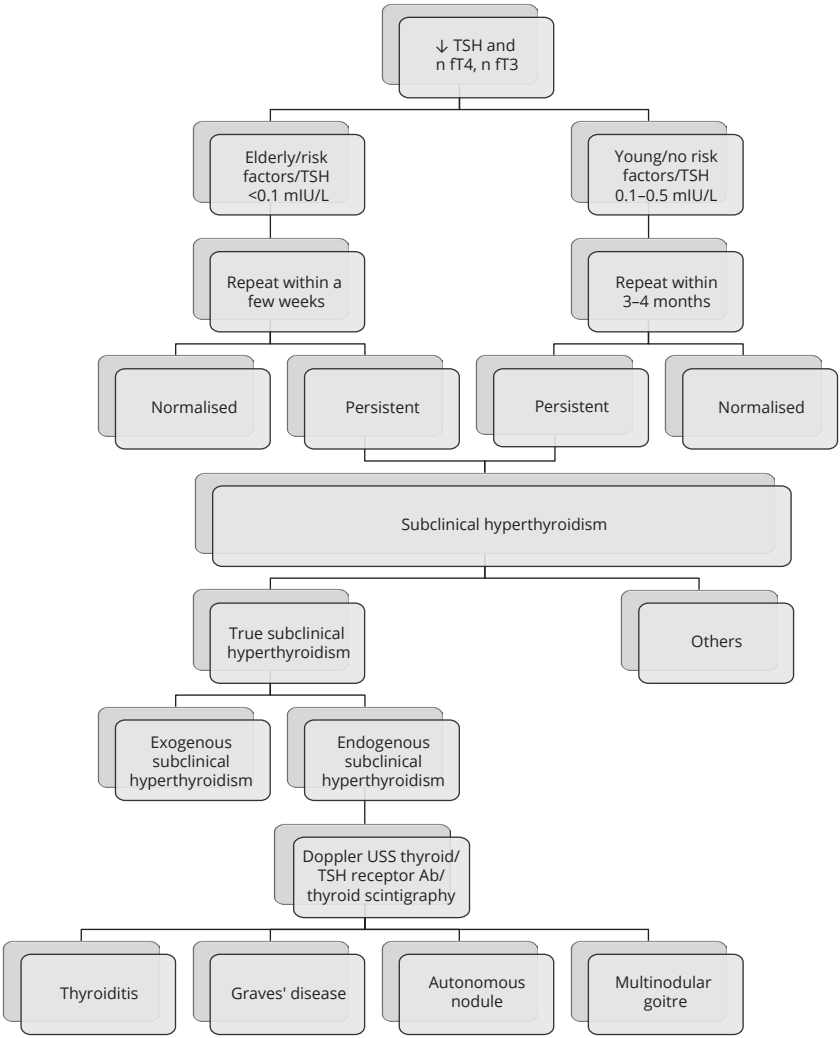
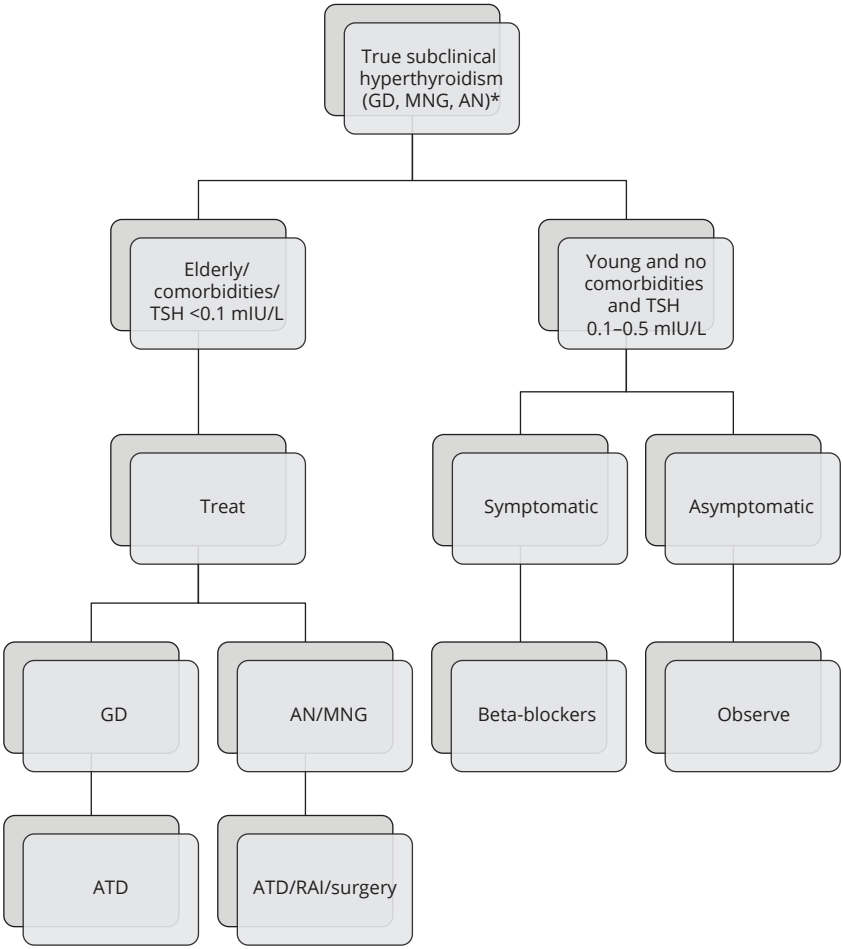
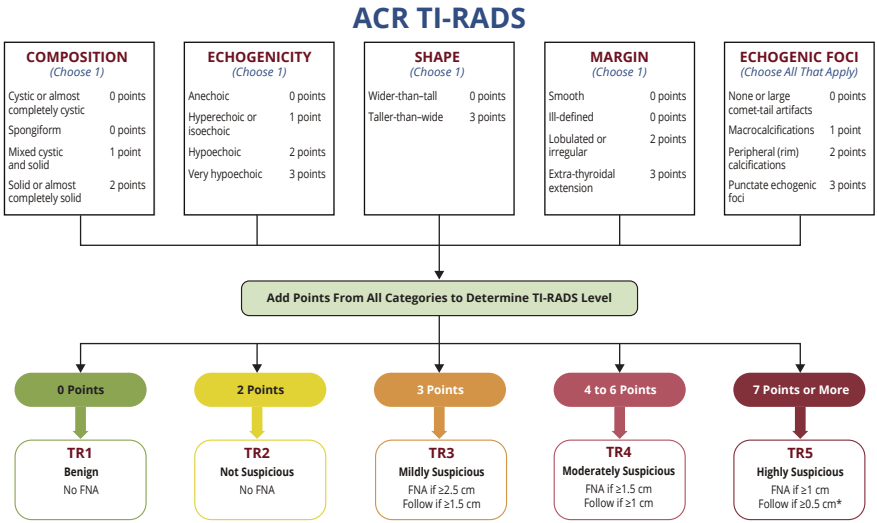


Figure 4: Algorithm for treatment of subclinical hyperthyroidism. [Adapted from [4(Level II)]]



*GD: Graves' Disease; MNG: Multinodular goitre; AN: Autonomous nodule.

Figure 5: ACR TI-RADS 2017 structured reporting system for ultrasound of thyroid nodules.



COMPOSITION	COMPOSITION	SHAPE	MARGIN	ECHOGENIC FOCI
Spongiform: Composed predominantly (>50%) of small cystic spaces. Do not add further points for other categories. *Mixed cystic and solid:* Assign points for predominant solid component. Assign 2 points if composition cannot be determined because of calcification.	*Anechoic:* Applies to cystic or almost completely cystic nodules. *Hyperechoic/isoechoic/hypoechoic:* Compared to adjacent parenchyma. Very hypoechoic: More hypoechoic than strap muscles. Assign 1 point if echogenicity cannot be determined.	*Taller-than-wide:* Should be assessed on a transverse image with measurements parallel to sound beam for height and perpendicular to sound beam for width. This can usually be assessed by visual inspection.	*Lobulated:* Protrusions into adjacent tissue. *Irregular:* Jagged, spiculated, or sharp angles. *Extrathyroidal extension:* Obvious invasion = malignancy. Assign 0 points if margin cannot be determined.	*Large comet-tail artifacts:* V-shaped, >1 mm, in cystic components. *Macrocalcifications:* Cause acoustic shadowing. *Peripheral:* Complete or incomplete along margin. *Punctate echogenic foci:* May have small comet-tail artifacts.

**Refer to discussion of papillary microcarcinomas for 5–9 mm TR5 nodules.*

Figure 6: Algorithm for management of patients with thyroid nodules.
[Adapted from [153 (Level III)]]

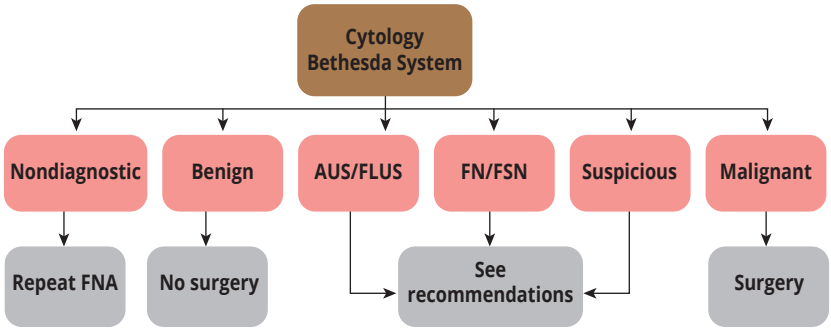
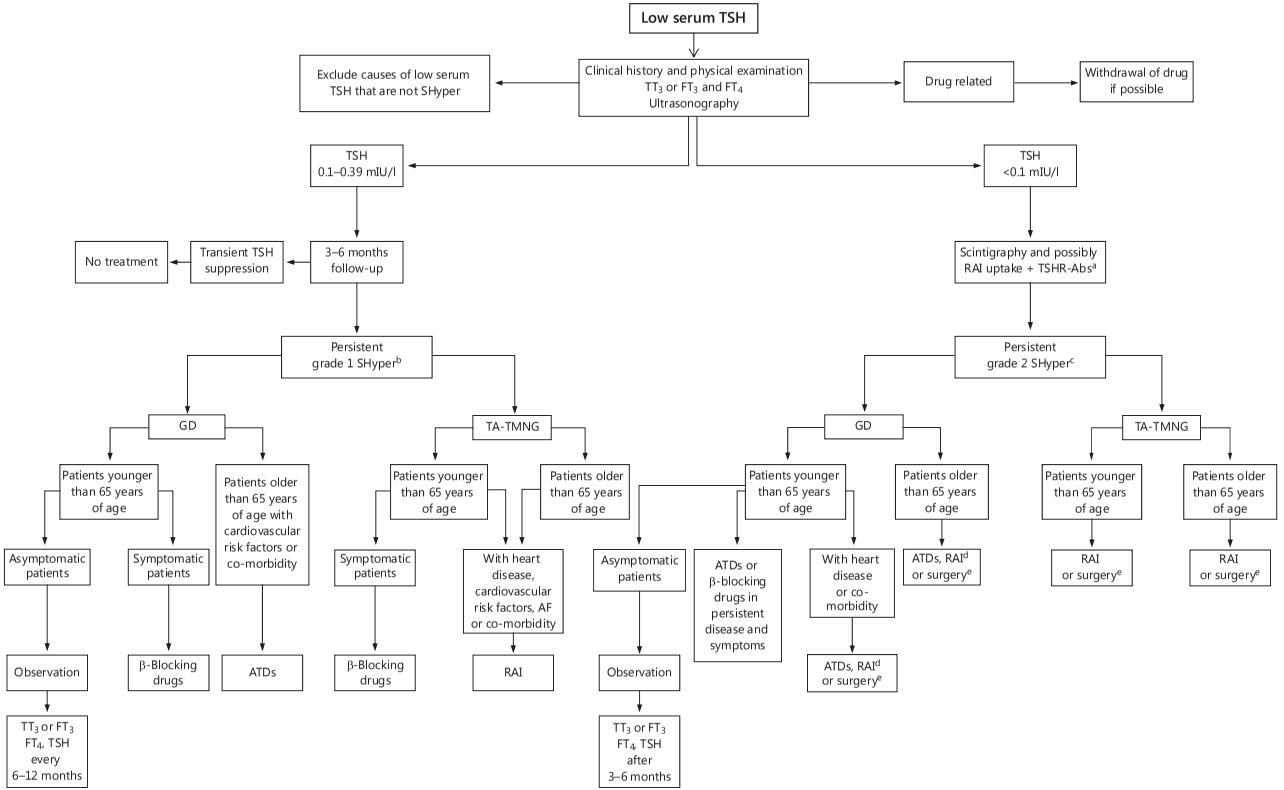


Figure 7: Algorithm for the management of SHyper. [Adapted from [54 (Level II)]]



[a]TSHR-Antibody = TSH-receptor antibodies. [b]Grade 1 SHyper (TSH levels: 0.1–0.39 mIU/L). [c]Grade 2 SHyper (TSH levels <0.1 mIU/L). [d]RAI in patients with recurrences or if ATDs are not tolerated. [e]Surgery in patients with large goitre, symptoms of compression, or thyroid malignancies.

Figure 8: Suggested management algorithm for SHypo. [Adapted from [409(Level II)]]

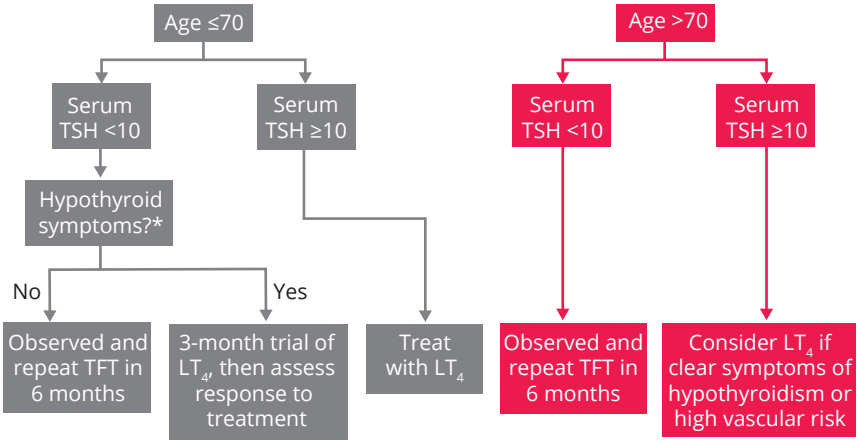


Figure 9: Management of Graves' Ophthalmopathy (GO).[455 (Level II)]