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CLINICAL PRACTICE

Subclinical Hyperthyroidism

CASE

- **A 65-year-old**
- **paroxysmal atrial fibrillation**
- **osteoporosis(bisphosphonate)**
- **no history of thyroid disease**
- **no symptoms of hyperthyroidism.**
- **pr=80**
- **The left thyroid lobe is enlarged**
- **PH.E normal**
- **ECG normal**
- **TSH= 0.2 mU per liter (reference range, 0.5 to 4.5)**
  T4= 1.2 ng per deciliter (reference range, 0.8 to 1.8).
- **How should this patient be evaluated and treated?**

Overt primary hyperthyroidism

Suppressed thyrotropin levels and elevated levels of free thyroxine (T4) and triiodothyronine (T3) or elevated levels of T3 only

Subclinical hyperthyroidism

In mild cases, low but detectable serum thyrotropin levels (0.1 to 0.4 mU per liter) with normal levels of free T4 and T3 in severe cases, undetectable serum thyrotropin level <0.1 mU per liter

- overt hyperthyroidism

  serum levels of free T4 and T3 are elevated

  Serum thyrotropin levels are suppressed.

- Subclinical hyperthyroidism

  levels of free T4 and T 3 are normal

  thyrotropin levels are suppressed,

  thyroid hormone levels are usually in the middle to upper range of normal.

- Mild

  Between 65% and 75% of persons with subclinical hyperthyroidism have serum thyrotropin levels of 0.1 to 0.4 mU per liter (referred to here as mild subclinical hyperthyroidism).

- Sever

  The remainder have thyrotropin levels of less than 0.1 mU per liter (severe subclinical hyperthyroidism).

Causes

the same as the causes of overt hyperthyroidism

Endogenous

Toxic multinodular goiter or toxic adenom

Graves' disease,

Exogenous

excessive intake of levothyroxine, liothyronine overtreatment

purposeful overuse

Exogenous subclinical hyperthyroidism is far more common than endogenous subclinical hyperthyroidism

Key Clinical Points

Subclinical Hyperthyroidism

• Serum thyroid hormone levels are within the reference range but serum thyrotropin levels are subnormal (≤0.4 mU per liter), may be caused by overproduction of endogenous thyroid hormone or excessive ingestion of exogenous thyroid hormone.

• Progression to overt hyperthyroidism may occur, especially when serum thyrotropin levels are less than 0.1 mU per liter.

Key Clinical Points

Subclinical Hyperthyroidism

- Even without progression to overt hyperthyroidism, subclinical hyperthyroidism can be associated with adverse outcomes, including cardiovascular disease (e.g., atrial fibrillation, heart failure, and coronary heart disease), bone loss, fractures, and dementia, particularly in persons older than 65 years of age with severe disease.

Potential Clinical Consequences

- progression to overt hyperthyroidism
- cardiovascular conditions
- bone loss
- fractures
- dementia

Progression to Overt Hyperthyroidism

- The best predictor of progression is the baseline serum thyrotropin level rather than the cause of the disease.

- Serum thyrotropin levels in patients with mild subclinical hyperthyroidism frequently normalize during followup

- patients with thyrotropin levels lower than 0.1 mU per liter usually have persistent disease or progression to overt hyperthyroidism.

- Patients with nodular thyroid disease and subclinical hyperthyroidism are at increase risk for progression to overt hyperthyroidism after exposure to a large iodine load. Pretreatment with methimazole may reduce this risk, but its efficacy is uncertain.

Cardiovascular Conditions

- Sinus tachycardia, premature atrial and ventricular beats, and diastolic dysfunction are associated with severe subclinical hyperthyroidism.

- Population-based studies,prospectiv observational studies and meta-analyses have shown a significantly higher risk of atria fibrillation, heart failure , death from coronary heart disease,death from any cause,and major adverse cardiovascular events among patients who have severe subclinical hyperthyroidism than among those who do not .

- Some studies indicate greater cardiovascular risks
especially the risk of atrial fibrillation, with greater thyrotropin suppression ;
absolute risks, but not relative risks, increase with age.

- Increases in cardiovascular disease and arrhythmia and cardiovascular mortality are also associated with doses of thyroxine that suppress thyrotropin to levels below 0.1 mU perliter.

Bone Loss and Fractures

- The risk of osteoporotic fractures is significantly increased among patients with severe endogenous subclinical hyperthyroidism
- some studies also show an increased risk of fracture among those with mild cases of the disease.
- Exogenous subclinical hyperthyroidism in patients whose serum thyrotropin levels are lower than 0.03 mU per liter has also been associated with an increased risk of fractures and fracture-related deaths.
- Subclinical hyperthyroidism among men older than 65 years of age has been associated with an increased risk of frailty.

Dementia

- Associations have been reported between subclinical hyperthyroidism and cognitive impairment or dementia

- A prospective cohort study involving persons in their 70s showed higher risk of dementia among participants with severe subclinical hyperthyroidism (but not among those with mild subclinical hyperthyroidism) than among those with normal thyroid function.

Other causes of low serum thyrotropin levels

The following causes of low serum thyrotropin levels should be ruled out before a diagnosis of subclinical hyperthyroidism is made:

- Severe nonthyroidal illness
- Administration of drugs that suppress serum thyrotropin levels (e.g.,dopamine, high doses of glucocorticoids, dobutamine, somatostatin analogues, amphetamines, bromocriptine, and bexarotene)
- Pituitary or hypothalamic disease that causes thyroid hormone or thyrotropin deficiency
- Psychiatric illness
- Late first-trimester of pregnancy
- Hyperemesis gravidarum
- Older age (i.e., age-induced changes in the hypothalamic–pituitary thyroid
- axis in areas of the world with iodine deficiency)
- African descent (thyrotropin levels are below the reference range in 3 to 4% of patient.

Evaluation

- Establishment of cause

  anti-thyrotropin-reseptor-Ab

  thyroid-stimulating-Ab

  ultrasonography

  thyroid scintigraphy,24-hr radioactive iodine uptake

  assessment of 24-hr urinary iodine excretion

Evaluation

- Assessment of risks
  - Evaluation of cardiovascular RF
  - Elecrtocardiography
  - Holter monitoring
  - Echocardiography
  - Assessment of RF of stroke
  - Bone density test

Treatment

- Although data are lacking from randomized clinical trials to guide treatment decisions, professional organizations recommend treatment of subclinical hyperthyroidism in persons older than 65 years of age and postmenopausal women, especially when serum thyrotropin levels are less than 0.1 mU per liter

Treatment

- Exogenous

  dose of levothyroxine should be lowered

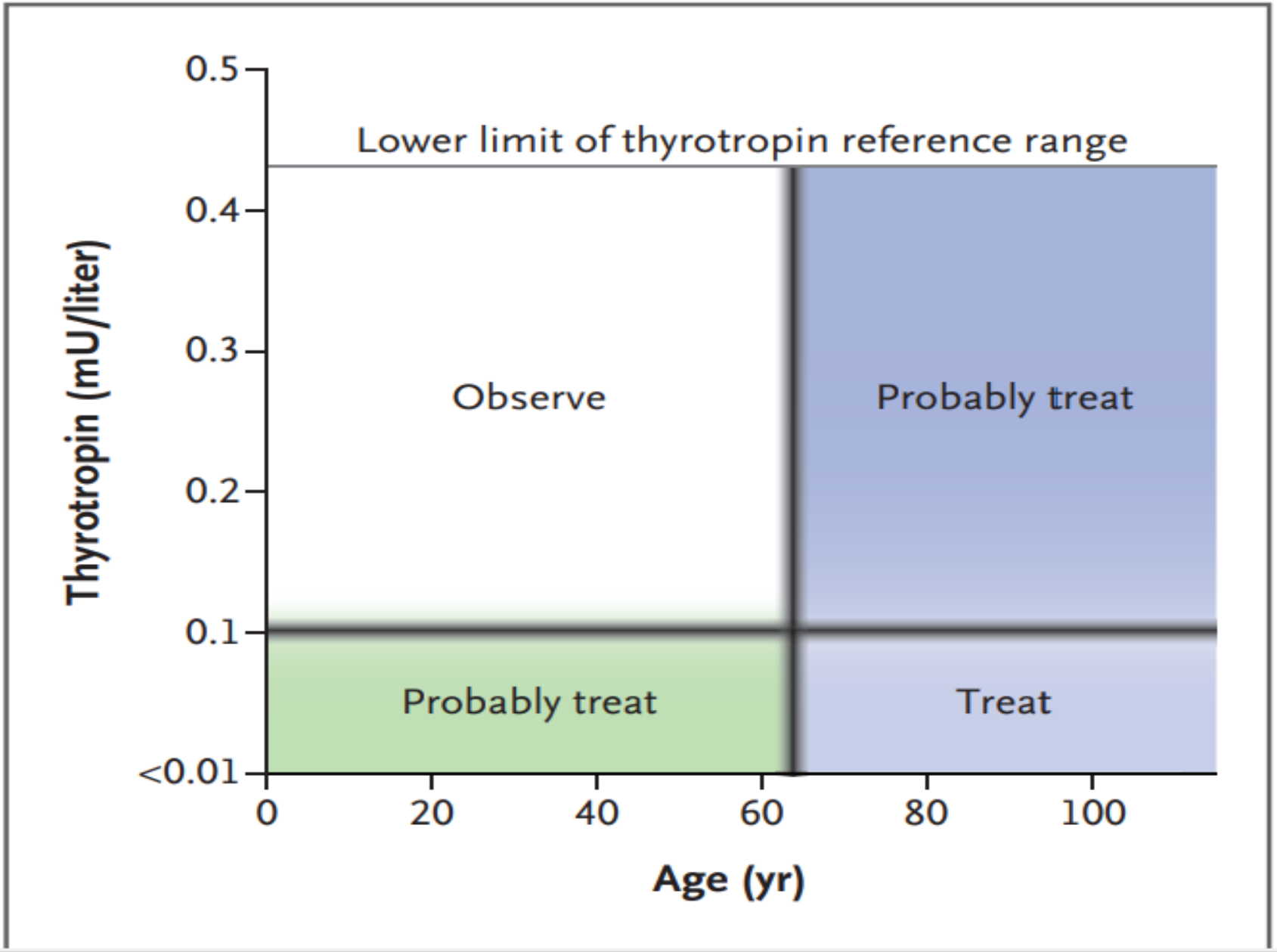
- Endogenous

  methimazole

  radioiodine

  surgery

  beta-blocker


Lower limit of thyrotropin reference range
Observe
Probably treat
Probably treat
Treat
Thyrotropin (mU/liter)
0.5
0.4
0.3
0.2
0.1
<0.01
0
20
40
60
80
100
Age (yr)

Thank you