

Approach to Thyroid Dysfunction in the Elderly

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Objective

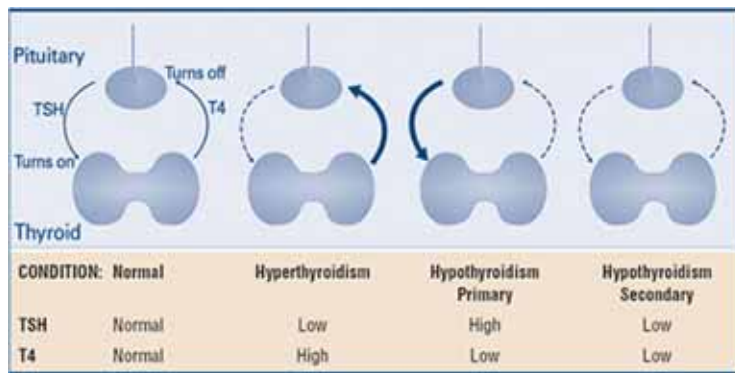
- The objective of this lecture is to review the epidemiology, clinical presentation, risks and complications, and management of thyroid disorders in older adults, including:
 - hyperthyroidism
 - hypothyroidism
 - thyroid nodules
 - thyroid cancer



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Introduction

- Interpretation of thyroid function tests in older adults is difficult due to:
 - age-dependent physiological changes in thyroid function
 - coexistent chronic illness and polypharmacy¹⁻⁴
- However, thyroid dysfunction is common in older adults and may be associated with **significant morbidity if not treated.**
- The **classic symptoms of thyroid dysfunction are usually absent or may be overlooked** in older patients, making the diagnosis and subsequent management challenging.



Thyroid Function in older adults

- Several studies have investigated the role of thyroid function in the aging process.
- Recent reports have shown increased serum TSH levels with increasing age, independent of antithyroid antibody presence¹, while in contrast, others have demonstrated decreased serum TSH in older adults.^{2,3}



Thyroid Function in older adults

- Populations in which the dominant thyroid pathology is thyroid deficiency secondary to *Hashimotos' thyroiditis* display a trend for the TSH upper limit to increase with age.^{6,7}
- On the contrary, an inverse relationship between TSH and age is seen in *iodine-deficient populations* in which the dominant thyroid pathology is nodularity and increasing thyroid autonomy with age.⁸



Thyroid Function in older adults

- In regards to free T₃ levels, most studies have demonstrated an age-dependent decline, while free T₄ levels remain relatively unchanged^{2,3} and rT₃ levels increase with increasing age.
- However, *interpretation of thyroid function tests in older adults is often complicated* by the presence of **chronic illness** (where free T₃ can be low and rT₃ high) and **polypharmacy**.⁴



Thyroid Function in older adults

- There is convincing evidence that **higher levels of TSH** are associated with **longevity**.
- Atzmon G et al, concluded that **serum TSH levels were significantly higher in centenarians** (mean age=98 years) as compared to controls (p<0.001).¹⁰
- Several other studies have also shown **increased TSH levels** (mean age=85 years) and low to low-normal FT₄ levels (mean age=78 years) to be associated with a **better survival** in older adults.^{11,12}



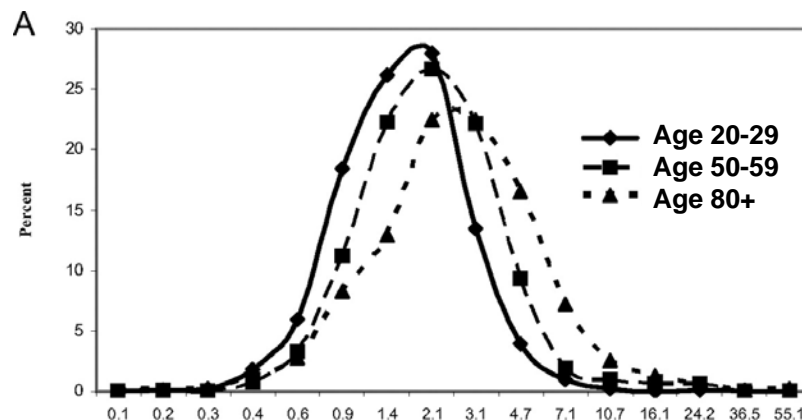
Thyroid Function in older adults

- It is hypothesized that the association of a **higher TSH level with longevity** may be due to a correlated lower bioactivity of thyroid hormone, which in turn leads to a lower basal metabolic rate and thus potentially may serve as an adaptive mechanism to prevent catabolism in older adults.¹²
- Moreover, the offspring of individuals with longevity were also shown to have higher TSH levels than age-matched controls without familial longevity (mean age=70 years), indicating a **genetic predisposition**.



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Disease-Free Thyroid Function Levels: May Narrow in Young But widens in Elderly



Surks MI, Hollowell JG. J Clin Endocrinol Metab. 2007;92:4575-82 – FROM LADENSON



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Hyperthyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - ▣ *Atrial Fibrillation*
 - ▣ *Cardiovascular mortality*
 - ▣ *Osteoporosis*
 - ▣ *Ophthalmopathy*
- Management



Hyperthyroidism

Epidemiology/Clinical Presentation – *common causes*

- ✓ Very low TSH (<0.1 mU/L)
 - ✓ Increased Free T₄

- Graves' Disease
- Toxic MNG (adenomas)
- Solitary toxic nodule
- Subacute thyroiditis
- Iodine-induced
- Iatrogenic



DDx: 24 hour RAIU

High RAIU (>20%)

- Graves' disease
- Toxic MNG
- Solitary toxic nodule

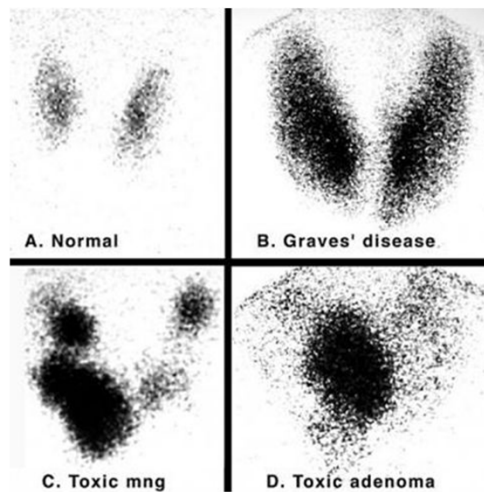
Low RAIU (<5%)

- Subacute thyroiditis
- Iodine-induced
- Iatrogenic

➤ (may only climb to high-normal in elderly)



Radioactive iodine uptake (RAIU) can help diagnose thyroid disease



Hyperthyroidism

Epidemiology/Clinical Presentation

- The prevalence of hyperthyroidism in older adults is estimated to be 0.5–4%.¹⁴
- Even though Graves' disease still remains the most common etiology, the prevalence of multinodular goiter and toxic nodular adenomas tends to increase with age.^{15,16}



Hyperthyroidism

Epidemiology/Clinical Presentation

- Two-thirds of older adults with hyperthyroidism will present similarly to younger patients.
- Symptoms will be consistent with sympathetic overactivity and include tremors, anxiety, palpitations, weight loss and heat intolerance.



Hyperthyroidism

Epidemiology/Clinical Presentation

- However, **one-third** of older adults will present with **apathetic hyperthyroidism**.
- The **rareness of clinical signs** of hyperthyroidism in older adults (age \geq 70) has been confirmed by several studies,^{18,19} with **weight loss, apathy and tachycardia** the most commonly occurring symptoms (p<0.001).



Hyperthyroidism

Epidemiology/Clinical Presentation

- A large cross-sectional study by Boelaert K et al. (n=3049) showed an increased prevalence of **weight loss** in older patients (over the age of 61) and identified **shortness of breath** as a symptom commonly reported in older adults (p<0.001).



Hyperthyroidism

Epidemiology/Clinical Presentation

- This study also demonstrated a higher proportion of **older adults reporting only one or two symptoms**, versus five or more in the younger patients.²⁰
- The absence of classical symptoms and signs in older adults presents a **diagnostic challenge** and may lead to delay in treatment and worse outcome.



Hyperthyroidism

Epidemiology/Clinical Presentation

- More common than overt hyperthyroidism in older adults is **subclinical hyperthyroidism** which is estimated to have a prevalence of 3–8%²¹⁻²³
 - more common in **women** than men, especially in patients over the age of 70.²⁴



Hyperthyroidism

Epidemiology/Clinical Presentation

- **Subclinical hyperthyroidism (SH)** is defined biochemically by a **low (or undetectable) thyroid stimulating hormone (TSH)** level with a **normal serum free T₄** and **normal serum total T₃** levels due to thyroid disease or exogenous excess thyroid hormone administration.



Hyperthyroidism

Epidemiology/Clinical Presentation

- The prevalence of SH is approximately **1%**, although it tends to be more common in areas with relative iodine deficiency.
- By comparison, **overt hyperthyroidism** occurs when the **TSH level is low** (or undetectable) and the **free T₄ level and/or total T₃ level is elevated**.



Hyperthyroidism

Epidemiology/Clinical Presentation

- In a study of the natural history of **subclinical hyperthyroidism** in female patients ≥ 60 years of age (n=102), Rosario showed that progression to overt hyperthyroidism is infrequent at 1% per year.²⁵



Hyperthyroidism

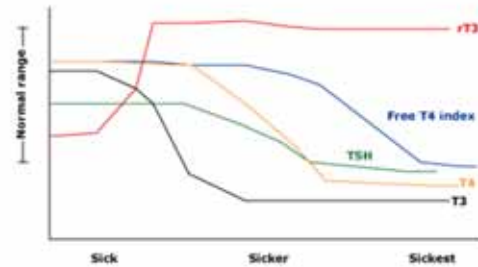
Epidemiology/Clinical Presentation

- As in younger patients, the initial diagnostic test for suspected hyperthyroidism in older adults is a serum **TSH**.
- However, hospitalized elderly who are **acutely ill** may demonstrate a **depressed TSH** without actually being hyperthyroid.
- When the clinical presentation of thyrotoxicosis is not diagnostic of Graves' disease, a radioactive iodine uptake should be performed to help determine etiology.
- A scan should be added if thyroid nodules are also identified.⁵



Euthyroid Sick Syndrome

- Also known as **nonthyroidal illness syndrome**
- can be described as abnormal findings on thyroid function tests that occur in the setting of a nonthyroidal illness (NTI) without preexisting hypothalamic-pituitary gland dysfunction.
- After recovery from an NTI, these thyroid function test results abnormalities should completely reverse.



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Euthyroid Sick Syndrome

Lab findings:

- Low but detectable TSH
- Low FT4, T4
- Low to very low T3
- TSH sometimes high during recovery

Hyperthyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - *Atrial Fibrillation*
 - *Cardiovascular mortality*
 - *Osteoporosis*
 - *Ophthalmopathy*
- Management



Hyperthyroidism

Risks/Complications/Sequelae – *Atrial Fibrillation*

- It has been clearly demonstrated that age is independently associated with an increased risk of developing atrial fibrillation.
- Atrial fibrillation is estimated to be present in up to 20–35% of older patients suffering from hyperthyroidism^{19,26,27} and is especially common in those with hyperthyroidism secondary to *toxic nodule(s)*.¹⁹



Hyperthyroidism

Risks/Complications/Sequelae – *Atrial Fibrillation*

- Long-standing low serum TSH concentration in older patients is associated with a **3-fold** increased risk of developing atrial fibrillation²⁸
- Because of greater incidence of underlying cardiac disease, the risk of developing atrial fibrillation is increased in patients over the age of 60.



Hyperthyroidism

Risks/Complications/Sequelae – *Atrial Fibrillation*

- Atrial fibrillation in older adults *may sometimes be the only clinical sign of hyperthyroidism.*
- However, the degeneration of the sinus node and fibrotic changes in the cardiac conduction system make the **presence of palpitations less likely.**
- In addition, frequent use of **beta-blockers or amiodarone** in these patients **can mask** the arrhythmia.
- In contrast, younger hyperthyroid patients often present with sinus tachycardia.²⁰



Hyperthyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - *Atrial Fibrillation*
 - ***Cardiovascular mortality***
 - *Osteoporosis*
 - *Ophthalmopathy*
- Management



Hyperthyroidism

Risks/Complications/Sequelae – *CV mortality*

- Overt hyperthyroidism, and less often subclinical hyperthyroidism, can be accompanied by several cardiovascular changes including:
 - widened pulse pressure
 - exercise intolerance
 - increased risk for atrial fibrillation
 - increased cardiac mass.²⁹



Hyperthyroidism

Risks/Complications/Sequelae – *CV mortality*

- Several cross-sectional and case-control studies have found that decreased levels of serum TSH are associated with increased cardiovascular mortality in older adults.³⁰
- In addition, subclinical hyperthyroidism has been shown to be associated with left ventricular hypertrophy, which is a predictor of cardiovascular mortality.²⁹



Hyperthyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - *Atrial Fibrillation*
 - *Cardiovascular mortality*
 - *Osteoporosis*
 - *Ophthalmopathy*
- Management



Hyperthyroidism

Risks/Complications/Sequelae – *Osteoporosis*

- Overt hyperthyroidism is a well-recognized risk factor leading to low bone mineral density and osteoporotic fractures, especially in older women.³¹
- Thyroid hormone acts on osteoblasts and osteoclasts to **increase bone turnover**, leading to net bone loss.³²
- Notably, most studies investigating the relationship between thyroid dysfunction and fracture risk have been specific to women.



Hyperthyroidism

Risks/Complications/Sequelae – *Osteoporosis*

- Bauer DC et al, in a large prospective fracture study (n=686), reported that women over the age of 65 with TSH level ≤ 0.1 mIU/L had a **threefold increased risk for hip fracture** and a **fourfold increased risk for vertebral fracture** as compared to euthyroid counterparts.³³
- In a study of *subclinical hyperthyroidism* in older adults (mean age=72.8 years) with sex-specific analysis, **men** were found to have increased incidence of hip fractures compared to women (13.8% vs. 12%; $p < 0.01$).³⁴



Hyperthyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - Atrial Fibrillation
 - Cardiovascular mortality
 - Osteoporosis
 - **Ophthalmopathy**
- Management



Hyperthyroidism

Risks/Complications/Sequelae – *Ophthalmopathy*

- Contradicting studies exist regarding the association of symptoms and signs of ophthalmopathy in Graves' disease with increasing age.
- Most studies published on this subject demonstrated a **positive correlation between prevalence and severity of ophthalmopathy with increasing age**.^{19,35}
- However, one prospective cohort study found ophthalmopathy to be frequent in younger patients with Graves' as compared to older adults (46% vs. 6%; $p < 0.001$).²⁰



Hyperthyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - ▣ *Atrial Fibrillation*
 - ▣ *Cardiovascular mortality*
 - ▣ *Osteoporosis*
 - ▣ *Ophthalmopathy*
- **Management**



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Treatment

High RAIU (>20%)

- Graves' disease
- Toxic MNG
- Solitary toxic nodule

- **Definitive treatment:**
 - RAI ablation
 - Surgery

Low RAIU (<5%)

- Subacute thyroiditis
- Iodine-induced
- Iatrogenic

- **Self-limiting**
- **Symptomatic Tx**



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Hyperthyroidism

Risks/Complications/Sequelae – *Management*

- Symptomatic treatment for hyperthyroidism in older adults consist of **beta-adrenergic blockade**.
- Beta-adrenergic blockade decreases the heart rate and systolic blood pressure.
- It can also improve tremor, irritability, emotional lability, and exercise intolerance.
- Anticoagulation may be indicated in patients who present with atrial fibrillation.



Hyperthyroidism

Risks/Complications/Sequelae – *Management*

- Treatment modalities that may be used for the hyperthyroidism include:
 - ▣ radioactive iodine ablation therapy
 - ▣ antithyroid medications
 - ▣ thyroidectomy



Hyperthyroidism

Risks/Complications/Sequelae – Management

- Radioactive iodine ablation is often used in older adults because of its efficacy, safety and cost-effectiveness.³⁶
- An appropriate dose is calculated from the previous thyroid uptake scan.
- A drawback to this management approach is that hyperthyroidism is reversed gradually over months, and cardiac issues may need to be managed aggressively until the thyrotoxic state is reversed.
- These patients subsequently develop hypothyroidism and require thyroid hormone replacement therapy.³⁶



Hyperthyroidism

Risks/Complications/Sequelae – Management

- In regards to antithyroid medications, methimazole (tapazole) is preferred (vs. propylthiouracil - PTU). However, older adults may be at greater risk of recurrence of hyperthyroidism after drug therapy and for medication side effects.³⁶
- Agranulocytosis is the major adverse event in this population, occurring in 0.5% of those treated.
- Rash, arthralgia and myalgia also occur more frequently (5-10%)³⁶



Hyperthyroidism

Risks/Complications/Sequelae – *Management*

- Depending on co-morbidities, **surgical approaches** are less commonly used in older adults with hyperthyroidism due to increased risk of morbidity.³⁷
- They are reserved for large goiters with obstructive symptoms, or known or suspected malignancy.³⁸



Hyperthyroidism

Risks/Complications/Sequelae – *Management*

- Regarding **subclinical hyperthyroidism** in older adults, guidelines advocate periodic clinical and biochemical assessment.
 - Low TSH (<0.1 mU/L)
 - Normal FT4
 - Normal T3
- Recent ATA/AACE guidelines recommend patients over 65 years be *treated* if their TSH is <0.1 mIU/L and that treatment can be *considered* if their TSH is 0.1–0.5 mIU/L.^{22,39}



Hypothyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - *Cognitive impairment*
 - *Cardiovascular effects*
 - *Myxedema Coma*
- Management



Hypothyroidism

Epidemiology/Clinical Presentation

- Estimates of the prevalence and incidence of hypothyroidism among older adults are variable depending on populations studied and criteria used to define the condition.⁴⁰
- A large screening study (n=25,000) revealed that **10% of men** and **16% of women aged 65–74** had TSH levels above the upper limit of the reference range.⁴¹



Hypothyroidism

Epidemiology/Clinical Presentation

- A recent National Health and Nutrition Examination Survey (NHANES) reported that a significantly greater number of **women** aged 50–69 met criteria for **subclinical** (n. FT4, slightly elevated TSH) and **clinical hypothyroidism** compared to men in the same age range.⁶
- Moreover, a study evaluating geriatric patients under medical care demonstrated that **15% of the women** and **17% of the men** had **previously undiagnosed hypothyroidism**.⁴²



Hypothyroidism

Epidemiology/Clinical Presentation

- The incidence of hypothyroidism steadily increases with advancing age, predominantly due to a rising incidence of autoimmune thyroiditis (Hashimoto's).⁴³⁻⁴⁵
- In a survey by Reinhardt et al., the reported incidence of **Hashimoto's thyroiditis** was **67%** in a patient population with a mean age of 73 years (n=24).⁴⁶



Hypothyroidism

Epidemiology/Clinical Presentation

- A survey of endocrinology clinic patients aged 55 years and older presenting with primary hypothyroidism revealed that:
 - 47% of patients carried a diagnosis of autoimmune thyroiditis
 - 27% had postsurgical hypothyroidism
 - 10% had post-radioiodine hypothyroidism⁴⁷



Hypothyroidism

Epidemiology/Clinical Presentation

- A **high index of suspicion** is required for diagnosis of hypothyroidism in older adults because symptoms and signs such as:
 - fatigue
 - weakness
 - constipation
 - dry skin cold intolerance
- may be attributed to other diseases common in older patients, medication side effects or aging itself.^{3,48}
- Psychiatric symptoms, such as depression, are also common in older adults with hypothyroidism.



Hypothyroidism

Epidemiology/Clinical Presentation

- A prospective study by Doucet J et al⁴⁹, compared 24 clinical symptoms and signs of hypothyroidism between older (n=67; mean age=79.3 years) and younger patients (n=54; mean age=40.8 years).
- It was concluded that the mean number of clinical signs in older adults was 6.6 versus 9.3 in the younger population.
- **Fatigue and weakness** were the most common symptoms in older adults, while cold intolerance, paresthesia, weight gain and abdominal cramps were less common.



Hypothyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - **Cognitive impairment**
 - **Cardiovascular effects**
 - **Myxedema Coma**
- Management



Hypothyroidism

Risks/Complications/Sequelae - *Cognitive Impairment*

- Hypothyroidism in older adults has been associated with impairment of several cognitive domains:
 - memory
 - attention and concentration
 - language
 - executive function
 - perceptual and visuospatial function^{50,51}
- Severe hypothyroidism may mimic depression and dementia.
- Neuropsychiatric symptoms usually improve with treatment and restoration of a euthyroid state.⁵²



Hypothyroidism

Risks/Complications/Sequelae - *Cognitive Impairment*

- The relationship between **subclinical hypothyroidism** and cognition is less clear.
- It is postulated that older adults may be more vulnerable to the effects of subclinical hypothyroidism given age-related changes to the hypothalamic-pituitary-thyroid axis.
- However, several studies in older adults did not show a significant association between mildly elevated TSH and reduced cognitive performance.^{53,54}



Hypothyroidism

Subclinical

- TSH usually < 10
- Normal Free T4
- 5% or more USA

Overt

- TSH usually > 10
- Low Free T4
- Less than 1% USA



Hypothyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - ▣ *Cognitive impairment*
 - ▣ *Cardiovascular effects*
 - ▣ *Myxedema Coma*
- Management



Hypothyroidism

Risks/Complications/Sequelae - *Cardiovascular effects*

- The cardiovascular consequences of hypothyroidism in older adults are thought to be due to a **reduction in both stroke volume and heart rate**.⁵⁵
- Other contributing factors include hyperlipidemia, increased risk of atherosclerosis, increased arterial stiffness, endothelial dysfunction and altered coagulation parameters.⁵⁶
- All of these abnormalities regress with levothyroxine replacement.



Hypothyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - *Cognitive impairment*
 - *Cardiovascular effects*
 - *Myxedema Coma*
- Management



Hypothyroidism

Risks/Complications/Sequelae – *Myxedema Coma*

- Myxedema coma occurs almost exclusively in older adults with longstanding primary hypothyroidism.
- It is usually precipitated by a concomitant medical illness.
- Patients may present with a rapid development of stupor, seizures, or coma along with respiratory depression.



Hypothyroidism

Risks/Complications/Sequelae – *Myxedema Coma*

- Hallmark signs of myxedema coma include⁵⁵:
 - localized neurological signs
 - hypothermia
 - bradycardia
 - hyponatremia
 - hypoglycemia
- Myxedema coma is a **severe and life-threatening clinical state** in older adults with a mortality rate as high as 40%.⁵⁷⁻⁵⁹



Hypothyroidism

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
 - Cognitive impairment
 - Cardiovascular effects
 - Myxedema Coma
- **Management**



Hypothyroidism

Management

- Despite the high prevalence of thyroid hormone use in this population, there are no concrete data on when and at what dose to initiate thyroid hormone replacement in older adults.
- Somwaru LL et al, collected thyroid hormone medication data from community-dwelling individuals aged 65 years and older (mean age=72.8 years) enrolled in the Cardiovascular Health Study (n=5,888) over the span of 16 years.⁶⁰



Hypothyroidism

Management

- It was concluded that thyroid hormone use is common in patients over the age of 65.
- The incidence of thyroid hormone replacement in adults aged 85 years and older was more than twice as frequent as that in adults aged 65–89 years (hazard ratio 2.34; CI 95%).⁶⁰



Hypothyroidism

Management

- Older patients often have lower levothyroxine dose requirements.
- This may be related to several factors including declining metabolic clearance, slow progression of underlying thyroid failure, declining body mass, and interactions with other medications.⁶¹
- On average, older adults with primary hypothyroidism receive initial daily doses that are 20 mcg lower and maintenance daily doses that are 40 mcg lower than those prescribed for younger patients of comparable weight.⁶²⁻⁶⁴



Hypothyroidism

Management

- Thyroid hormone increases myocardial oxygen demand, which **may induce cardiac arrhythmias, angina pectoris, or myocardial infarction** in older patients.
- Once the cardiovascular tolerance of a starting dose has been assessed, a gradual increase by 12.5–25 mcg every four to six weeks is recommended until adequate replacement is confirmed by serum TSH measurement.⁶⁵



Hypothyroidism

Management

- Physicians treating hypothyroidism in older adults should target a normal TSH range.⁶⁵
- In a recent survey of ATA members, while 39% of them recommended targeting a TSH range of 0.5–2.0 mIU/L when treating younger patients, a comparable number reported being **more liberal in their approach to older adults**, targeting **TSH ranges of 1.0–4.0 mIU/L**.⁶⁵
- This avoids **overtreatment** with excessive doses of levothyroxine, which can be associated with increased risks of **atrial fibrillation** and progressive **loss of bone mineral density** in this population.⁶⁶



Hypothyroidism

Management

- Management of **subclinical hypothyroidism** in older adults is controversial and guidelines have been published both for⁶⁷ and against^{68,69} routine treatment in older adults.
- Several placebo-controlled randomized trials fail to find a reduction in the symptoms of subclinical hypothyroidism with treatment^{70,71}, suggesting there is **no benefit to treatment**.^{72,73}
- General recommendation: follow labs to monitor change



Hypothyroidism

Management

- Surks MI, et al recommend **against** routine treatment of patients aged over 58 years with **TSH levels between 4.5–10 mIU/L** due to lack of evidence indicating adverse health outcomes in untreated patients in this group, excluding progression to overt hypothyroidism.⁶⁸



Hypothyroidism

Management

- Chu JW et al. **recommends levothyroxine replacement** therapy in patients with a **TSH>10 mIU/L** on repeated measurements, clear symptoms or signs associated with thyroid failure, family history of thyroid disease or severe hyperlipidemia not previously diagnosed.⁶⁹



Thyroid Nodules

- **Epidemiology/Clinical Presentation**
- Management



Thyroid Nodules

Epidemiology/Clinical Presentation

- It is known that the prevalence of thyroid nodules increases with age.⁷⁴
- By age of 65 years, nearly 50% of individuals in iodine-sufficient areas have thyroid nodules when evaluated with ultrasound.⁷⁵
- A survey by Cavaliere R et al. showed that the prevalence of multinodular goiter in older adults in an iodine-deficient area was 74% in patients aged 55–75 years and 54% in patients aged 76–84 years.⁷⁶
- Thyroid nodules may be benign adenomas, cysts, cancer or inflammation.



Thyroid Nodules

- Epidemiology/Clinical Presentation
- **Management**



Thyroid Nodules

Management

- The approach to the management of a solitary thyroid nodule in an older adult is the same as that in a younger patient.

- With the discovery of a new thyroid nodule, a complete history and physical examination should be performed.



Thyroid Nodules

Management

- Pertinent questions should include:
 - history of head and neck or whole body irradiation
 - exposure to ionizing radiation
 - family history of thyroid cancer
 - syndromes such as multiple endocrine neoplasia



Thyroid Nodules

Management

- Physical findings **raise suspicion for malignancy:**
 - palpable cervical lymphadenopathy
 - voice hoarseness
 - fixation of the nodule to surrounding tissue



Thyroid Nodules

Management

- As per recent American Thyroid Association (ATA) guidelines⁷⁷, initial evaluation constitutes measurement of serum TSH.
- If the TSH is subnormal, the next step consists of a radionuclide thyroid scan using either technetium pertechnetate or ¹²³I.
- A diagnostic thyroid ultrasound should be performed in all patients with known or suspected thyroid nodules when TSH is found to be normal or high.



Thyroid Nodules

Management

- Ultrasonographic features associated with a **higher likelihood of malignancy** include:
 - hypoechogenicity
 - increased intranodular vascularity
 - presence of microcalcifications
 - absence of a halo
 - irregular borders
 - a nodule with a height greater than width
 - presence of suspicious cervical lymphadenopathy



Thyroid Nodules

Management

- Ultrasound-guided fine needle aspiration (FNA) is the subsequent specific diagnostic test, but it is not generally recommended for subcentimeter nodules.



Thyroid Cancer

- **Epidemiology/Clinical Presentation**
- Risks/Complications/Sequelae
- Management



Thyroid Cancer

Epidemiology/Clinical Presentation

- The prevalence of clinically apparent thyroid cancer in adults aged 50–70 years old is estimated to be 0.1%.⁷⁸
- As patients age, there is a greater incidence in poorly-differentiated thyroid cancer types.^{79,80}



Thyroid Cancer

Epidemiology/Clinical Presentation

- However, **well-differentiated papillary thyroid cancer** is still the most common thyroid cancer in older adults and it presents similar to younger patients.
- These are slow-growing tumors and the majority of patients are asymptomatic or may present with a painless neck mass.
- More advanced disease may present with palpable cervical lymphadenopathy, hoarseness, dysphagia and respiratory distress secondary to local invasion and compression.



Thyroid Cancer

Epidemiology/Clinical Presentation

- In a retrospective study of data from the National Cancer Institute's SEER registry, it was demonstrated that the incidence of **papillary thyroid cancer** is increasing disproportionately in patients older than 45 years and the most commonly found tumor in this group is now a papillary thyroid microcarcinoma (<1 cm).⁸¹
- It is speculated that these increased rates are due to growing use of imaging studies and subsequent discovery of incidental thyroid nodules in older patients.



Thyroid Cancer

Epidemiology/Clinical Presentation

- **Follicular thyroid cancer** is more common in areas of iodine deficiency with the peak incidence in the sixth decade of life.^{74,82}
- It commonly presents with an asymptomatic neck mass, which may be incidentally discovered with imaging studies.



Thyroid Cancer

Epidemiology/Clinical Presentation

- In regards to **medullary thyroid cancer**, sporadic forms are more common in older patients as compared to familial forms.⁸³
- Many patients present with a palpable neck mass.
- There may be local or systemic symptoms secondary to metastases.
- Symptoms of hormone hypersecretion include diarrhea, flushing and bronchospasm.



Thyroid Cancer

Epidemiology/Clinical Presentation

- **Anaplastic thyroid cancer** is aggressive and has a peak incidence in the seventh decade of life.⁷⁴
- It often arises within a more differentiated thyroid cancer, and usually presents as a rapidly growing neck mass with metastases at time of diagnosis.
- In a recent retrospective study, 26 anaplastic thyroid cancers were identified out of 1500 thyroid cancers over a span of 16 years.
- The average anaplastic tumor size at diagnosis was 7.35 cm, with lymph node involvement in 61.5% and distant metastases in 34.5% of cases.⁸⁴



Thyroid Cancer

- Epidemiology/Clinical Presentation
- **Risks/Complications/Sequelae**
- Management



Thyroid Cancer

Risks/Complications/Sequela

- Thyroid cancer is the only cancer where age is included in the AJCC TNM staging system.⁸⁵⁻⁸⁷
- The mortality rates of patients with thyroid cancer increase starting at age 45.⁸⁸
- A steady decline in survival rates has been reported with increasing age, regardless of the degree of differentiation of the thyroid cancer.^{89,90}



Thyroid Cancer

Risks/Complications/Sequelae

- A large retrospective study (n=53,856) demonstrated lower 10-year survival rates in patients over the age of 45 with:
 - papillary (47–85% vs. 97%)
 - follicular (57–66% vs. 98%)
 - medullary (63–80% vs. 88%)
 - anaplastic (5-year survival rate: 13% vs. 55%)⁷⁸
- Extension of thyroid cancer outside the gland significantly worsened prognosis in older patients while it did not alter the favorable prognosis in younger patients.^{91,92-94}



Thyroid Cancer

Risks/Complications/Sequelae

- In a study of the SEER database, the presence of lymph node metastases had no effect on survival in patients aged less than 45 years of age.
- However, in patients aged 45 years or older, there was an associated 46% increased risk of death if positive lymph nodes ($p < 0.001$).⁹⁵
- Distant metastases are also a worst prognostic sign in older patients with thyroid cancer.⁹¹
- This may be related to thyroid cancer being less radioactive iodine-avid in older patients compared to younger patients.^{85,96}



Thyroid Cancer

Risks/Complications/Sequelae

- Thyroid cancer recurrence rates have also been shown to be influenced by age.⁸⁶
- Cady B et al demonstrated that women over the age of 50 had a 32% risk of thyroid cancer recurrence as compared to 10% in those younger than 50 years old.⁹¹



Thyroid Cancer

- Epidemiology/Clinical Presentation
- Risks/Complications/Sequelae
- **Management**



Thyroid Cancer

Management

- The modalities used for the management of thyroid cancer in older adults are essentially the same as those used in younger patients.
- Frequently, the surgical approach for thyroid cancer >1cm is near-total or total thyroidectomy.
- Thyroid lobectomy alone may be sufficient for tumors <1cm.



Thyroid Cancer

Management

- Central neck dissection should accompany total thyroidectomy in patients with clinically involved central or lateral neck lymph nodes.⁷⁷

- Even though older patients may exhibit a higher surgical risk due to co-morbidities, age by itself is not a contra-indication to thyroidectomy.



Thyroid Cancer

Management

- Post-operative radioiodine ablation (RAI) of thyroid remnants is indicated for all patients with:
 - known iodine-avid distant metastases
 - gross extrathyroidal extension of the tumor regardless of tumor size
 - or primary tumor size >4 cm even in the absence of other risk factors⁷⁷



Thyroid Cancer

Management

- Dosimetry-guided RAI therapy may be preferable to fixed-dose RAI treatment strategies in older patients with advanced thyroid cancer as evidenced by a study showing that administered doses above 7.4 GBq (200 mCi) will exceed the maximal safe level in a substantial number of patients over the age of 70.⁹⁷
- Older age, renal failure and liver failure are associated with lower clearance of radioactive iodine.⁹⁷



Thyroid Cancer

Management

- Unstimulated thyroglobulin should be periodically assessed.
- Then, one year after radioiodine ablation, measurement of thyroglobulin under TSH stimulation is useful as it is more sensitive.
- If the stimulated level is >2 ng/ml, then diagnostic imaging studies should be performed for localization of persistent versus recurrent disease.



Thyroid Cancer

Management

- Thyroxine suppression therapy is used for treatment of differentiated thyroid cancers.
- Jonklaas et al. showed that aggressive thyroid hormone suppression therapy was independently associated with longer overall survival in high-risk patients, while moderate thyroid hormone suppression predicted improved overall survival in stage II patients.
- Because outcome is good regardless of intervention, survival was not altered in stage I patients.⁹⁸



Thyroid Cancer

Management

- The TSH-suppressive doses of 2–2.2 mcg/kg often required in younger patients with thyroid cancer may be excessive in older adults as thyroxine degradation is reduced with age.⁹⁹



Thyroid Cancer

Management

- In the Framingham Heart Study, individuals greater than 60 years of age with TSH values of 0.1 mIU/L or less had an adjusted relative risk of 3.8 for developing **atrial fibrillation** during a 10-year follow-up,
- and those with TSH values between 0.1 mIU/L and 0.4 mIU/L had an adjusted relative risk of 1.6.²⁸
- The beneficial effect of TSH suppression is a considerable reduction in recurrence rates of differentiated thyroid cancer, but this should be weighed against potential complications.



Thyroid Cancer

Management

- Indications for **external beam radiation** include the presence of aggressive and unresectable cancer, painful bone metastases or risk for spinal cord compression.⁷⁷
- Current clinical trials for novel therapies in thyroid cancer treatment, e.g. tyrosine kinase inhibitors, are promising and older age may not preclude participation.



Summary

- Thyroid gland dysfunction is prevalent in older adults and may be associated with significant morbidity if misdiagnosed and untreated.
- Factors contributing to misinterpretation of thyroid function tests in older adults include age-dependent physiological changes, co-morbidities and polypharmacy.



Summary

- Moreover, clinical signs and symptoms of thyroid dysfunction may be subtle or absent, making diagnosis more difficult.
- As thyroid disorders are often amenable to effective treatments that can improve quality of life, a high index of clinical suspicion is warranted.



Summary

- Hyperthyroidism in older adults is usually treated similarly to younger adults, with antithyroid medications, radioactive iodine ablation or surgery.
- Antithyroid medication side effects occur more commonly in older adults and surgery is less favorable due to increased morbidity and mortality risks.



Summary

- There are no concrete guidelines as to when and at what dose to initiate levothyroxine replacement therapy in older adults with hypothyroidism.
- However, after assessing the cardiovascular tolerance of a starting dose, the dose should be gradually increased by 12.5–25 mcg every four to six weeks until adequate replacement is confirmed by serum TSH measurement.



Summary

- Thyroid nodules are more common in older adults and are managed with an initial measurement of a TSH, followed by an ultrasound if TSH is normal or high.
- Depending on nodule size and ultrasound features, ultrasound-guided fine needle aspiration may be performed.



Summary

- With increasing age, the incidence of thyroid cancer shifts from well-differentiated to poorly-differentiated types. Thyroid cancer is unique because age is included in the staging system.
- The modalities used for the management of thyroid cancer in older adults are in essence the same as those used in younger patients.
- These include surgery, and when appropriate, postoperative radioactive iodine ablation, serial thyroglobulin measurements and thyroxine suppression therapy.



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THANK YOU

