

Diagnosis and Management of Hyperthyroidism in Older Adults

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Older patients with hyperthyroidism present with atypical symptoms such as difficulty concentrating. This is in contrast to younger patients, who present with classic symptoms such as heat intolerance, tremor, and tachycardia. Hyperthyroidism in older adults is most often caused by toxic multinodular goiter and Graves' disease. Thyroid hormones and thyroid-stimulating hormone assays can establish the diagnosis quickly. Antithyroid medication can be used in medically unstable older hyperthyroid patients to quickly suppress the hormones. When the patient is stable, definitive therapies such as radioactive iodine or surgery should be considered. Radioactive iodine therapy is well tolerated and effective. Surgery is indicated in patients who fail to respond to radioactive iodine therapy and patients with multinodular goiter.

Key words: thyrotoxicosis, older adults, hyperthyroidism, Graves' disease, T3 toxicosis

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1).^{15,16} There are many causes of thyrotoxicosis (excessive concentrations of thyroid hormones) in older adults (Table 1). The most common cause of hyperthyroidism in older individuals is toxic multinodular goiter^{17–24} followed by Graves' disease.^{2,3} Subacute thyroiditis may cause transient hyperthyroidism, but it is rarely a problem in older adults, and the incidence is very low in this patient population. Iodine excess or drugs that contain iodine may also lead to thyroid dysfunction among older adults.²⁵ Increased iodine uptake from drugs such as mucolytics or contrast media may cause iodine-induced hyperthyroidism (Jod-Basedow disease).

Introduction

Hyperthyroidism is common among older adults.¹ Hyperthyroidism is a highly treatable condition but can cause life-threatening complications in older individuals if not treated in a timely manner.^{2,3} Individuals over the age of 60 constitute 10–15% of those affected by hyperthyroidism.^{4,5} The prevalence of hyperthyroidism ranges from 0.5–6%.^{6–14} The thyroid gland releases two thyroid hormones, thyroxine (T4) and triiodothyronine (T3), in a molar ratio of 14:1. All of the T4 in the body is made within the thyroid gland, whereas 80% of T3 is derived in the peripheral tissues. The synthesis and release of thyroid hormone are controlled by pituitary-derived thyroid-stimulating hormone (TSH), under the influence of thyrotropin-releasing hormone from the hypothalamus.

Clinical presentation of thyroid hyperfunction differs among older adults as compared to a younger cohort (Figure

Table 1: Causes of Hyperthyroidism in Older Adults

Toxic multinodular goiter	43 %
Graves' disease	21 %
Iatrogenic thyrotoxicosis	16 %
Toxic adenoma	12 %
Iodine-induced thyrotoxicosis	1 %
Subacute thyroiditis	1 %
TSH-secreting pituitary adenoma	0.6%
Painless thyroiditis	0.3%
Factitious thyrotoxicosis	0.3%

Source: Modified from references 17–24.

Polypharmacy is common in older adults, and Table 2 lists drugs that can cause thyrotoxicosis. Amiodarone, an antiarrhythmic commonly used among older adults for atrial fibrillation, can cause hyperthyroidism in 5% of treated patients or hypothyroidism in 7% of treated patients. Amiodarone delivers 7.4 mg of free iodine load per 200 mg tablet.²⁶

Clinical Features

Among younger adults, the classic symptoms of thyroid dysfunction (tachycardia, palpitations, heat intolerance, tremors, and sweating) are usually present and make the diagnosis easier. Among older adults, the diagnosis is more often overlooked or misdiagnosed as many patients are asymptomatic or present with atypical symptoms.^{9,27} Recognition of hyperthyroidism in this patient population depends upon a high index of suspicion on the part of the clinician and willingness to seek confirmation by appropriate laboratory testing.

Hyperthyroidism may be overlooked as some symptoms such as difficulty in concentrating or weight loss may be attributed to normal aging.²⁸ At times the symptoms may be confused with commonly present coexisting illnesses in older patients.²⁹ For example, the presence of fatigue or worsening heart failure symptoms in a patient with congestive heart failure can easily be attributed to worsening heart failure. Furthermore, treatment for coexisting diseases may mask the symptoms of hyperthyroidism in older adults. Tachycardia and tremulousness caused by hyperthyroidism may be masked in a patient receiving beta-blocker for the treatment of hypertension or angina. Tremors are a classic manifestation of hyperthyroidism in younger patients, but older patients with hyperthyroidism may not have tremors: when they do have tremors, they are often coarse rather than fine, as compared to younger patients.²

Hyperthyroidism is variably expressed in different patient populations. It often causes weight loss despite increased appetite in younger adults. In contrast, older adults usually present with weight loss with anorexia. Apathetic thyrotoxicosis, a syndrome of weight loss, difficulty sleeping, and fatigue, can easily be mistaken for cancer or depression.^{30,31} Cardiac complications of hyperthyroidism in older adults usually manifest as atrial arrhythmias, usually atrial fibrillation with slow ventricular rates as compared to higher rates seen in younger patients. Congestive heart failure caused by hyperthyroidism in older individuals is usually high-output heart failure. Pre-existing angina pectoris can be

worsened by hyperthyroidism. Diarrhea is a common symptom in young hyperthyroid patients while older adults may complain of a slight increase in the frequency of bowel movements but no change in the consistency or volume; or, they may notice a correction of pre-existing constipation but usually do not have loose stools.

Some older patients may present with only one symptom of hyperthyroidism, referred as monosymptomatic hyperthyroidism.³² Thyroid myopathy is one example where muscle weakness is the predominant complaint.³³ Decreased mobility is another feature common in older adults in contrast to a younger cohort, among whom a usual complaint is hyperactivity. Fatigue, weakness, lethargy, agitation, confusion, and dementia are also common symptoms of thyroid illness in older adults.³⁴⁻³⁷ Older adults with Graves' disease may not have goiter, exophthalmos, or other ophthalmopathy. Untreated hyperthyroidism can be the cause of osteoporosis and fractures in older individuals. Clinicians need to have a low threshold for requesting thyroid function tests upon detecting any clinical change in a previously stable older patient in the setting of vague or nonlocalizing symptoms.

The monitoring of thyroid replacement therapy for older adults with hypothyroidism is challenging as well. In older individuals the metabolism of thyroid hormones slows and the half-life increases. It may take six to eight weeks after the dose initiation or change to reach a steady state in those patients who are in their seventies or older.³⁸ Sudden increases in thyroid hormone replacement therapy may result in iatrogenic thyrotoxicosis.

Physical examination of the thyroid gland in older adults may not be helpful. The gland shrinks with age in some individuals. Previous thyroiditis may have caused atrophy, and fibrosis may make palpation difficult. Additionally, the gland may be substernal in many older people due to the presence of kyphosis or kyphoscoliosis.²⁷⁻²⁹ If there is a palpable gland present, then a diffusely enlarged gland would be consistent with Graves' disease. Presence of nodules would suggest hyperfunctioning multinodular thyroid disease.³² Other causes of thyroid enlargement (goiter) causing a hyperthyroid clinical picture are listed in Table 3. Thyroid levels can change during acute illness and hospitalization. This is known as sick euthyroid syndrome (also noted in Table 4). Sick euthyroid does not cause hyperthyroidism but should be considered in the differential diagnosis of elevated TSH. Patients with this syndrome have no signs of hyperthyroidism. Their T4 and T3 usually are depressed, but occasionally the levels might be elevated.

Investigations

Measurements of thyroid function (T4, T3, and TSH) are the best way to diagnose thyroid dysfunction. Measuring free T4 and T3 is preferable instead of total T4 or total T3 to avoid the confounding effects of thyroid-binding proteins. A low TSH level with elevated T4 and/or T3 confirms the diagnosis of

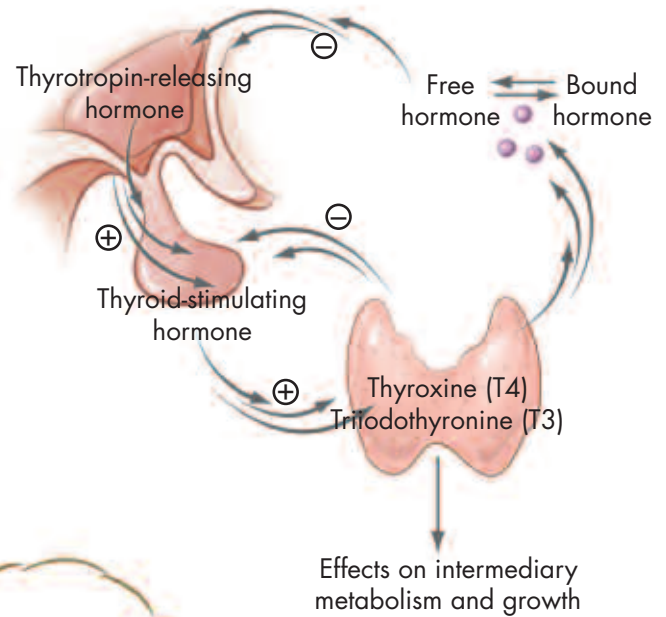
Table 2: Drugs Causing Hyperthyroidism

1. Amiodarone (due to its iodine contents)
2. Iodine ingestion
3. Radiographic contrast media
4. Interferon alfa

Figure 1:
Hyperthyroidism in the Older Adult Patient

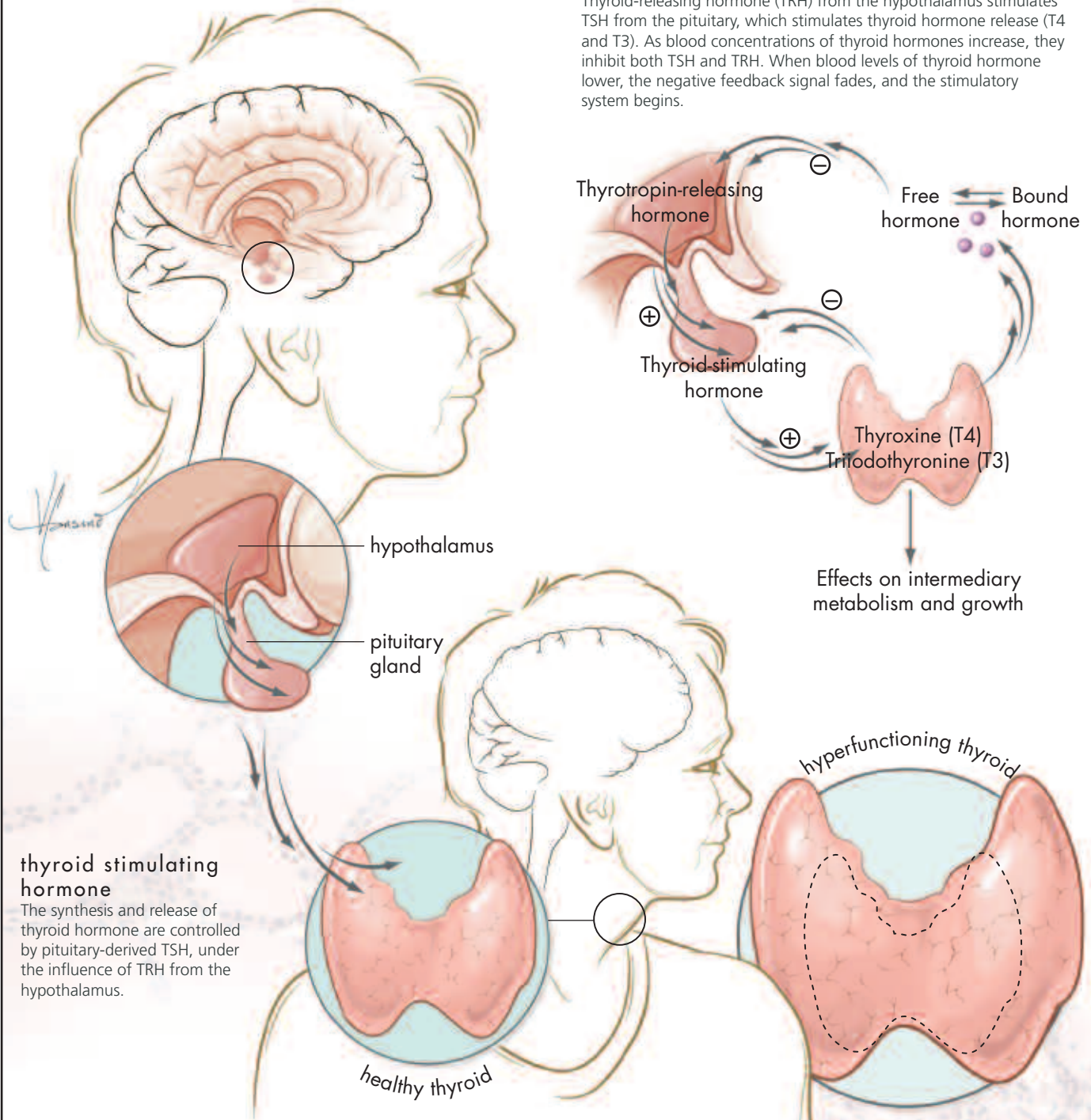
control of thyroid-stimulating hormone

Thyroid-releasing hormone (TRH) from the hypothalamus stimulates TSH from the pituitary, which stimulates thyroid hormone release (T₄ and T₃). As blood concentrations of thyroid hormones increase, they inhibit both TSH and TRH. When blood levels of thyroid hormone lower, the negative feedback signal fades, and the stimulatory system begins.



thyroid stimulating hormone

The synthesis and release of thyroid hormone are controlled by pituitary-derived TSH, under the influence of TRH from the hypothalamus.



thyrotoxicosis

There are many causes of thyrotoxicosis among older adults. The most common cause of hyperthyroidism in older adults is toxic multinodular goiter followed by Graves' disease.

Table 3: Types of Hyperthyroid Goiters

Diffuse Goiter	Nodular Goiter
Graves' disease	Solitary nodule or hyperfunctioning "hot" nodule
Autoimmune thyroiditis e.g., Hashimoto's thyroiditis*	Multinodular goiter
Iodine-containing medications	Thyroid cancer (very rarely)
Lithium	
Iodides (Jod-Basedow Disease)	
Goitrogens	
I-5-vinyl-2-thio-oxazolidone (present in cabbage, turnips, and soybeans)	
Cassava and millet contain goitrogenic substances	
Herbs like kelp and sea weed (high iodine content)	

*Hashimoto's thyroiditis causes transient hyperthyroidism in the early stage of the disease. Patients will ultimately develop hypothyroidism due to the thyroid gland's destruction and atrophy.

primary hyperthyroidism. T3 and T4 should always be ordered together. Most clinicians order just TSH, though, and if the results are abnormal, then the recommended step is to conduct further hormonal testing. In a minority of older adults T4 may be normal or low with low TSH level. In these cases the serum T3 should be measured to rule out T3 toxicosis (further described below). There are many causes of low TSH (Table 4);¹⁴ the most common causes are nodular thyrotoxicosis and Graves' disease. Medications such as corticosteroids and nonthyroidal illness could also cause low TSH. Presence of thyroid autoantibodies (anti-TSH receptor antibodies, thyroid-stimulating immunoglobulin) suggests Graves' disease while antithyroid peroxidase and antithyroglobulin antibodies indicate Hashimoto's thyroiditis.

A thyroid scan and radioactive iodine uptake measurement can generally distinguish the major causes of hyperthyroidism. A normal gland has a 10–30% uptake in 24 hours. Higher uptakes are indicative of Graves' and thyroid nodular disease. In certain hyperthyroid conditions the iodine uptake of the gland may be normal or absent as the case in transient hyperthyroidism due to autoimmune or radiation thyroiditis (Table 5).

T3 Toxicosis

Ten percent of older adults with hyperthyroid may present with the isolated finding of excessive amounts of circulating

Table 4: Causes of Low Thyroid-Stimulating Hormone

1. Hyperthyroid state
A. Both T3 and T4 elevated
1. Toxic Multinodular Goiter
2. Graves' disease
3. Toxic solitary adenoma
B. Only T3 elevated with normal T4
1. T3 toxicosis
2. Exogenous T3 ingestion (Cytomel)
Hypothyroid state
Pituitary or hypothalamic disease (both T4 and T3 low)
3. Euthyroid State
Sick euthyroid (both T3, T4 low, rT3* elevated)
Drugs like corticosteroids, dopamine, octreotide and amiodarone
{*rT3—Reverse T3 (Triiodothyronine)}
Source: Reprinted with permission from Rehman SU et al., 2005.

serum T3 with T4 remaining normal. This condition is called T3 toxicosis, an entity almost exclusively noted among older adults.² In this condition a thyroid nodule exclusively produces excessive amounts of T3. The excessive T3 suppresses the TSH and T4 levels in a negative feedback mechanism.^{32,39} The clinical presentation is the same as discussed above

Table 5: 24-Hour Radioactive Iodine Uptake (RAI) in the Diagnosis of Hyperthyroidism

Increased RAI uptake
Diffuse pattern
Graves' disease
Irregular pattern
Hot nodule/Toxic adenoma
Toxic multinodular (TMN) goiter
TSH producing pituitary adenoma
Decreased or absent RAI uptake
Silent lymphocytic thyroiditis (Hashimoto's)
Painful thyroiditis (subacute granulomatous De-Quervain's)
Factitious (exogenous) hyperthyroidism
Radiation thyroiditis

including presentation with atypical symptoms. Some patients are erroneously diagnosed with hypothyroidism due to low T4 and TSH levels.

Management

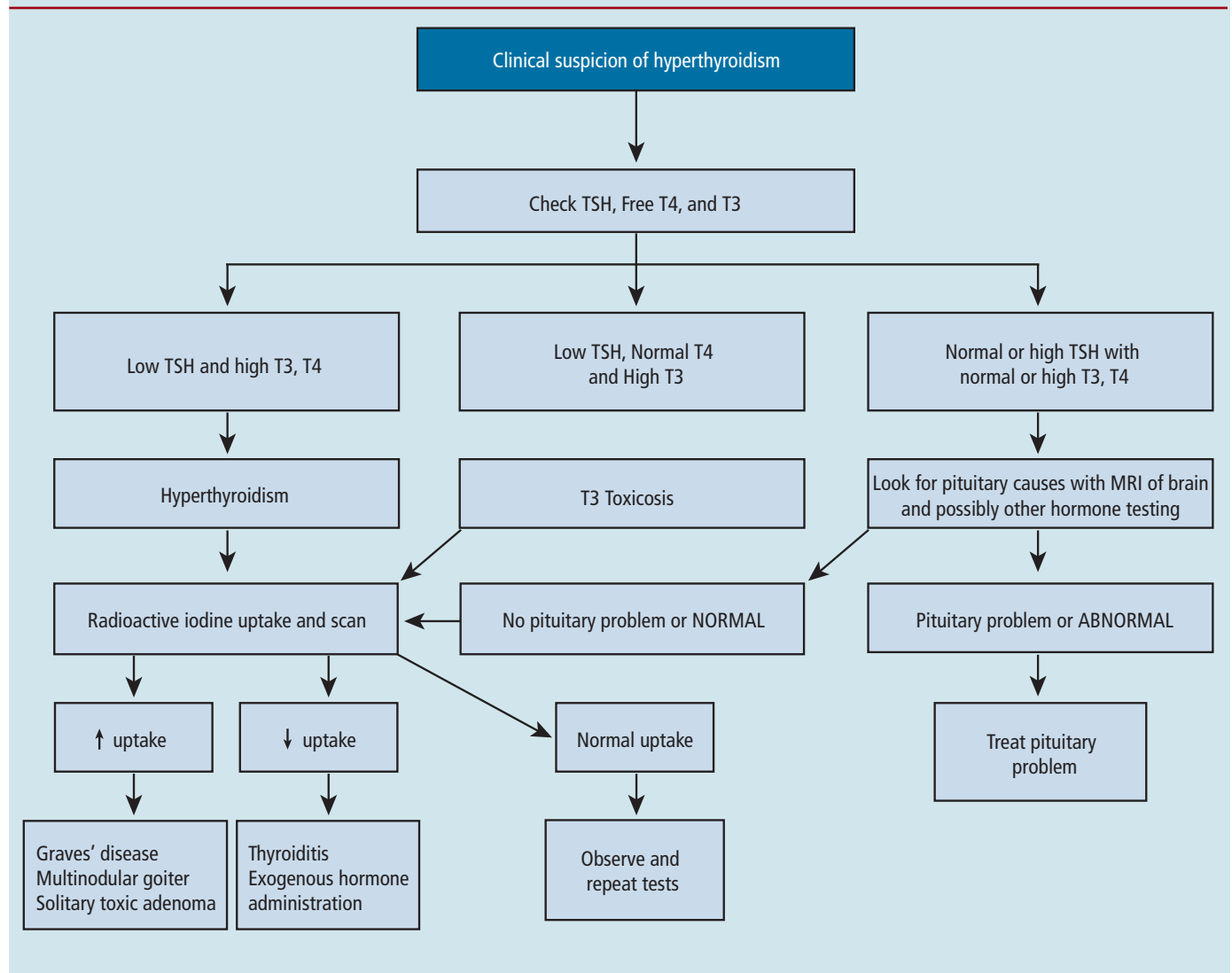
Treatment is effective and is indicated in patients with symptoms as well as in patients who are asymptomatic but with TSH values lower than normal limits. Patients with low TSH (whether from an endogenous or exogenous cause) are at increased risk of cardiac complications,^{40,41} osteoporosis and fracture,⁴² dementia,⁴³ and death.⁴⁴ The treatment of hyperthyroidism depends on the underlying cause of the disease (Figure 2). There are three main treatment modalities available for older adults with hyperthyroid: radioactive iodine (RAI), surgery, and medication. Referral to an endocrinologist should be considered when RAI is considered for the treatment. Similarly, surgical referral will be required if removal of the gland is desired.

Medication for Hyperthyroidism

Antithyroid drug therapy is very effective in reducing the symptoms of hyperthyroidism; however, these therapies are not the treatment of choice in older individuals with hyperthyroidism due to their potential side effects and the high failure rate to achieve remission. Supportive therapy is indicated in patients with thyroiditis as the process is transient and self-limiting. Beta-blockers can treat hyperadrenergic symptoms, and nonsteroidal anti-inflammatory drugs (NSAIDs) would alleviate the inflammatory symptoms and pain. Occasionally corticosteroid therapy is needed for patients with thyroiditis whose pain is not relieved with NSAID therapy.

The antithyroid drugs methimazole and propylthiouracil block production of thyroid hormone and conversion of T4 to T3. Since these medicines act quickly, they can be used in older adults whose unstable comorbid disease warrants a rapid suppression of the hyperthyroid state. Once the individual is euthyroid and stable, a decision should be made

Figure 2: Evaluation of Patients with Hyperthyroidism



about the definitive treatment. Propylthiouracil can be given 100 mg q.i.d., and for methimazole the usual dose is 10 mg q.i.d. Patients with severe hyperthyroidism may need higher doses. Propylthiouracil can be used in doses as high as 600 mg/day and methimazole can be used up to 40 mg/day. Antithyroid drugs have common side effects including rash, arthralgia, and myalgia. These agents can also cause rare but potentially life-threatening adverse effects such as agranulocytosis and hepatic damage. Agranulocytosis usually is reversible upon discontinuation of the therapy. Baseline leukocyte count should be checked before starting the therapy, and repeat testing may be done serially or with the onset of sore throat, fever, or other signs of infection.

Beta-blockers can be used for symptomatic improvement, and to control tachycardia and tremors, but do not alter the natural history of the disease. Another advantage of beta-blockers is that these agents do not interfere with thyroid uptake and scanning. If beta-blockers are contraindicated, nondihydropyridine calcium channel-blockers such as diltiazem can be used. Individuals with atrial fibrillation will need anticoagulation as usual. The warfarin dose may need to be lower for hyperthyroid patients.³⁴

Radioactive Iodine

Radioactive iodine (RAI) is the preferred therapy for patients with thyroid nodular and Graves' disease. RAI destroys thyroid tissue effectively and safely. Hyperthyroidism is gradually reversed over weeks to months. Many older adults take multiple drugs for comorbid diseases, and the addition of antithyroid medications could cause adverse interactions if given for long periods to control hyperthyroidism symptoms. An appropriate dose of RAI is calculated from the previous thyroid uptake scan. The major side effect of RAI is hypothyroidism requiring lifelong thyroid hormone replacement. RAI administration may be associated with an increase in thyroid hormone levels due to the destruction of thyroid cells with transient release of active thyroid hormone in circulation. Some individuals may exhibit the signs and symptoms of thyrotoxicosis and in rare cases may develop life-threatening thyroid storm. To avoid these complications, antithyroid medications can be prescribed to older adults with severe hyperthyroidism and/or with significant cardiopulmonary disease. Treatment with antithyroid drugs should be stopped a week before RAI therapy. There is controversy as to whether Graves' ophthalmopathy may worsen after RAI therapy. It is recommended to treat patients with ophthalmopathy with a two- to three-month course of corticosteroids to avoid worsening of Graves' ophthalmopathy. Serial TSH and T4 testing is the test of choice to determine the development of hypothyroidism among patients who have undergone RAI treatment. On occasion, a second course of therapy is needed to suppress hyperthyroidism.

Surgical Treatment of Hyperthyroidism

Surgery is also effective for treatment of thyroid nodular and Graves' diseases, but it may be contraindicated due to other coexisting conditions such as cardiac problems, which increase perioperative risk. However, some older adults with nodular thyroid disease may not respond to RAI, and for these individuals surgical removal is warranted. Surgery is the treatment of choice for any goiter causing obstructive symptoms such as dysphagia or tracheal compression. Surgery is necessary for those individuals with substernal goiters whether or not obstructive symptoms are present.^{14,45-49} If there is a suspicion of malignant disease, surgical intervention should be considered. Surgical candidates are usually pretreated with β -blockers, antithyroid drugs, and iodine to make patients euthyroid before the surgery. Indications for surgery are summarized in Table 6.

Thyrotoxic Crisis or Thyroid Storm

Hyperthyroid storm is potentially life-threatening if not recognized and treated in a timely manner.⁴⁹ The presenting symptoms of hyperthyroid storm are fever, delirium, tachycardia, hypotension, vomiting, diarrhea, jaundice, and abnormal liver function tests. Surgery, anesthesia induction, and systemic infections can precipitate the storm in those with pre-existing hyperthyroidism. Older adults with hyperthyroid storm should be admitted to an intensive care unit with close monitoring and treated with antithyroid drugs, iodine (to inhibit thyroid hormone release), glucocorticoids, beta-blockers, and occasionally iopanoic acid (to inhibit T4 to T3 conversion).⁵⁰

Conclusion

Hyperthyroidism in older adults does not present classically and hence can be easily missed. Hyperthyroidism should be considered in the differential diagnosis of weight loss, generalized weakness, frequent falling, depression, or dementia in older individuals. Examination of the thyroid gland may not be helpful in older adults due to age-related atrophy or neck abnormalities associated with conditions such as kyphoscoliosis, which may result in the thyroid becoming retrosternal.

Treatment of thyroid disorders is associated with improvement in quality of life. RAI therapy with close

Table 6: Indications for Surgery

Hyperthyroidism not controlled by drugs or radioiodine
Compressive symptoms
Retrosternal extension
Multinodular goiter
Malignancy or suspicion of malignancy

Key Points

Thyroid disorders are common among older individuals.

The most common causes of hyperthyroidism in older adults are multinodular goiter followed by Graves' disease.

Classic symptoms of hyperthyroidism are often absent in older adults.

Atypical symptoms of hyperthyroid patients are often erroneously attributed to normal aging or comorbid conditions commonly present in older adults.

Physical examination of the thyroid gland may not be helpful, as the gland often is not markedly enlarged, shrunk, or sub-sternal and difficult to palpate.

Thyroid hormones—thyroxine (T4), triiodothyronine (T3) and pituitary-derived thyroid stimulating hormone (TSH)—assays can quickly determine the diagnosis.

The three main treatment options available for individuals with hyperthyroidism are radioactive iodine therapy (RAI), surgery, and antithyroid therapy (carbimazole or propylthiouracil).

RAI therapy is most effective and a well-tolerated treatment for most individuals with hyperthyroidism.

Most older adults with multinodular goiter respond well to surgery.

follow-up is safe, effective, and preferred for most older patients. Surgery may be needed for those individuals that fail to respond to RAI therapy and in patients with multinodular goiter. Obstructive symptoms such as dysphagia or tracheal compression associated with nodular goiter and retrosternal goiter should be sent for surgery. Antithyroid medication may help relieve the symptoms and can be considered if RAI or surgery could not be used.



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