Should we screen women for hypothyroidism?

EVIDENCE-BASED ANSWER

Though evidence is insufficient to recommend screening all women for hypothyroidism, women aged >50 years are at increased risk. Screening is most likely to detect subclinical hypothyroidism. Studies evaluating treatment of subclinical hypothyroidism in women aged >50 years offer a mix of potential benefits and harms but without long-term outcome information. No studies address asymptomatic women aged <50.

Testing for thyroid-stimulating hormone (TSH) finds more cases of unrecognized hypothyroidism than history and physical examination (strength of recommendation [SOR]: **A**, based on cohort studies). Women with an initial screening TSH >10 mU/L are more likely to develop complications of hypothyroidism and to benefit from treatment (SOR: **A**, based on prospective cohort studies).

Treating women who have asymptomatic hypothyroidism and a screening TSH >10 mU/L prevents progression to symptomatic overt disease (SOR: **A**, based on prospective cohort studies) and reduces serum lipid levels (SOR: **A**, based on randomized controlled trials).

Treating women who have subclinical hypothyroidism found by screening does not reduce symptoms (SOR: **A**, small randomized controlled trials), and its effect on cardiac disease remains controversial. Treatment may increase bone loss in premenopausal women (SOR: **A**, based on randomized controlled trials and controlled cross-sectional studies), and it may cause symptoms in certain individuals (SOR: **C**, based on observational studies).

EVIDENCE SUMMARY

Screening for hypothyroidism is more likely to detect the elevated TSH and normal free thyroxine level (FT4) of subclinical hypothyroidism than it is to detect overt hypothyroidism with a high TSH and a low FT4. We reviewed the accuracy of detection, natural history, and benefits and harms of treating subclinical hypothyroidism.

Detection. Subclinical hypothyroidism is found in 7% to 26% of women (with increasing prevalence as women reach age 60 and 70 years); overt hypothyroidism occurs in approximately 5%.[1–4] Two studies assessed the ability of the history and physical to detect hypothyroidism.

The first study evaluated 1154 women (aged 50–72) in a primary care setting using both history and physical and TSH testing. TSH testing found 3 women with overt hypothyroidism not identified by history and physical. History and physical identified 286 women with indications for TSH testing, 2 of whom had mild hypothyroidism and 1 with mild hyperthyroidism.[5]

In the second study, 2000 adults from a primary care population underwent history and physical and TSH testing. The TSH screen identified 19 cases of hypothyroidism not found by history and physical, while the history and physical prompted evaluation of 35 patients without abnormal TSH.[6]

Natural history of subclinical hypothyroidism. Among 1210 primary care patients (700 women) aged >60 years, 73 women with subclinical hypothyroidism were identified and followed for 12 months. Of these, 13 (18%) progressed to overt disease.[7] Another prospective study of 30 patients (6 women) with subclinical hypothyroidism found 16 (3 women) who progressed to overt disease within 24 months. The remaining patients maintained normal FT4 levels for at least 15 years despite persistently elevated TSH.[8] A third study followed 2779 adults (1494 women) with all types of thyroid disease for 20 years and found that 55% of women with TSH >6 and a positive antibody test developed overt hypothyroidism. Ninety percent of patients with an initial TSH >10 eventually progressed to overt disease.[2]

Serum lipid reduction. A retrospective study of 709 women referred to an endocrine clinic for evaluation of abnormal lipoprotein levels identified 34 (4.8%) with undiagnosed hypothyroidism.

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Thyroid hormone treatment reduced total and LDL cholesterol in patients with an initial TSH greater than 10

Thyroid hormone treatment significantly reduced total cholesterol and low-density lipoprotein (LDL) cholesterol in patients with initial TSH >10, but not in those with a TSH <10.[9]

A randomized trial involving 42 women with subclinical hypothyroidism measured lipid levels before and after 6 months of levothyroxine treatment. Levothyroxine reduced total cholesterol and LDL significantly compared with placebo. Additionally, the subclinical hypothyroidism patients had higher baseline lipid levels when compared with 27 euthyroid controls.[10]

A meta-analysis combined 13 studies, involving 247 patients with subclinical hypothyroidism, all of whom were given thyroid replacement. All studies reported a decrease in total cholesterol (mean –7.9 mg/dL), and 9 reported a decrease in LDL (mean –10 mg/dL).[11] A second meta-analysis with 278 hypothyroid patients given thyroid replacement also found a reduction of total cholesterol (mean –15 mg/dL). LDL effects were not reported.[12] The clinical significance of lipid changes in these circumstances is unknown.

Symptom relief. Four small randomized controlled trials used symptom-rating scales to measure symptom relief with treatment of subclinical hypothyroidism. One study involved patients found by screening; the other 3 did not indicate means of diagnosis. Three studies found no significant improvement.[13–15] The most recent, involving 33 unblinded patients, found that those taking thyroid replacement had lower symptom scores (number needed to treat [NNT]=3.5).[16]

Cardiac manifestations. Subclinical hypothyroidism may be associated with ventricular dysfunction, myocardial infarction, and atherosclerosis.[18–20] A randomized controlled trial of 20 people with subclinical hypothyroidism found significantly improved left ventricular function assessed by echocardiography after 6 months of treatment with levothyroxine vs placebo.[18] Whether treatment prevents myocardial infarction and atherosclerosis is unknown.[19,20] A cohort study, involving 2779 adults studied aged >20 years, did not find an association between subclinical hypothyroidism and ischemic heart disease.[2]

Risks of replacement. A meta-analysis of 41 controlled, cross-sectional studies involving 1250 women treated with thyroid replacement for all causes (ie, not specifically subclinical hypothyroidism) found that replacement therapy (mean duration of treatment, 7 to 9 years) was associated with bone loss in premenopausal women, but not in postmenopausal women.[17]

A randomized trial of 37 patients over 55 with subclinical hypothyroidism (28 of whom were women), found that thyroid hormone reduced bone mineral density, as assessed by dual-energy x-ray absorptiometry (DEXA) scans over a 10-month period.[14] In several trials, patients withdrew due to adverse effects. Two of 37 patients receiving L-thyroxine in 1 study withdrew because of new atrial fibrillation and worsened angina, and 2 of 20 patients in another study withdrew because of nervousness and palpitations.[13,14]

RECOMMENDATIONS FROM OTHERS

The US Preventive Services Task Force concluded the evidence is insufficient to recommend for or against routine screening for thyroid disease in adults. The yield of screening is greater in high-risk groups such as postpartum women, people with Down syndrome, and the elderly; however, there is poor evidence that screening these groups leads to clinically important benefits.[21]

The American Thyroid Association recommends screening men and women beginning at age 35 and every 5 years thereafter.[22] The American Academy of Family Physicians recommends screening for men and women over age 60.[23] The American College of Physicians states screening may be indicated in women over age 50.[24]

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CLINICAL COMMENTARY:

Consider screening all female patients, particularly those over age 50

In my practice, there recently seems to be increased pressure from patients to screen for hypothyroidism, perhaps based on media or Internet information. I have used an individual "risk factor" approach when patients ask me for testing, based on their age, family history, and current symptoms. Based on the data, using the history and physical examination to tailor screening is an ineffective method of detecting hypothyroidism.

Until we have more evidence, I believe a reasonable approach is to offer screening to all of our female patients, particularly those over age 50, along with a careful acknowledgment of the lack of data for or against screening.

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Based on the data, using history and physical exam to tailor screening is ineffective for detecting hypothyroidism

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