

Review: Sensitive thyrotropin testing in unselected inpatients has low diagnostic accuracy

Attia J, Margetts P, Guyatt G. Diagnosis of thyroid disease in hospitalized patients. A systematic review. *Arch Intern Med.* 1999 Apr 12;159:658-65.

QUESTIONS

In hospitalized patients with nonthyroidal illness (NTI), are clinical signs and symptoms useful for predicting overt thyroid disease? Is the sensitive thyrotropin (thyroid-stimulating hormone [sTSH]) assay useful for detecting thyroid disease?

DATA SOURCES

Studies were identified by searching MEDLINE with the following 2 groups of terms: thyroid diseases, cohort studies, and signs or symptoms; and thyrotropin, hospitalized or medical or inpatient, and sensitivity or specificity. Bibliographies of relevant articles were scanned. Searches were done by 2 different researchers.

STUDY SELECTION

English-language studies were selected if they enrolled > 50 patients. Studies on signs or symptoms were included if they reported sufficient information to allow positive likelihood ratios (+LRs) to be calculated. Studies on sTSH assays were selected if they included patients who were acutely ill or hospitalized with an NTI and if they used second- or third-generation sTSH assays and follow-up after resolution of NTI as reference standards.

DATA EXTRACTION

2 reviewers independently extracted data on patients, study type, diagnostic standard, follow-up, and number of signs and symptoms. +LRs were calculated. The quality of study methods was assessed by using 3 criteria: follow-up of patients with normal and abnormal results; follow-up after resolution of NTI in > 60% of patients with abnormal results; and explicit, clear criteria for diagnosis of thyroid disease.

MAIN RESULTS

Signs and symptoms: No studies were found for signs and symptoms of thyroid disease in hospitalized patients. 8 studies on outpatients met the inclusion criteria. Individual signs and symptoms were examined in 6 studies, 4 of which were unblinded. The other 2 studies ($n = 1017$ and 1193) used patient self-reports for clinical signs and symptoms of hypothyroid disease and showed +LRs of 2 for decreased appetite, 2 for hoarse voice, 2.2 for fuller face, 2.2 for dry skin, and 2.3 for personal history of thyroid disease. 2 studies examined the total number of signs and symptoms. In the 1 blinded study ($n = 135$, 7% thyroid dysfunction), +LRs for thyroid disease were 6.75, 1.14, and

0.20 for ≥ 5 , 2 to 4, and 0 to 1 signs and symptoms, respectively.

sTSH assay: 2 of 8 studies provided adequate data to calculate +LRs in hospitalized patients. +LRs were 7.7 for hyperthyroid disease (cut point < 0.1 $\mu\text{IU/mL}$, $n = 272$, 4% hyperthyroid) and 11.1 for hypothyroid disease (cut point > 20 $\mu\text{IU/mL}$, $n = 157$, 8% hypothyroid).

CONCLUSIONS

No studies examined the usefulness of signs and symptoms of thyroid disease in hospitalized patients, and few studies on outpatients are blinded. The positive likelihood ratios for signs and symptoms are modest. An sTSH assay cut point of < 0.1 $\mu\text{IU/mL}$ results in a positive likelihood ratio of 7.7 for hyperthyroid disease, and a cut point of > 20 $\mu\text{IU/mL}$ results in a positive likelihood ratio of 11.1 for hypothyroid disease.

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COMMENTARY

Clinicians often order thyroid function tests with little thought about diagnostic utility or the likelihood of false-positive results. Attia and colleagues provide a useful summary of existing data on the laboratory assessment of thyroid function in hospitalized patients. Their rigorous review is laudable for several reasons: They do an exhaustive search of the published literature, use accepted criteria for the evaluation of studies about diagnostic tests (1), and conclude with pragmatic clinical recommendations based on their findings.

The major shortcoming of this analysis, and one that plagues much of the current literature about thyroid testing, is the conundrum of subclinical thyroid dysfunction, which is defined as an abnormal sTSH result with normal thyroid hormone levels. Most patients with this condition are asymptomatic, but increasing evidence shows that subclinical thyroid dysfunction is associated with adverse cardiac (2) and skeletal (3) outcomes, particularly in the elderly. Many of the studies cited by Attia and colleagues do not address the diagnostic complexity of subclinical thyroid dysfunction.

Further, the increasing use of 3rd- and 4th-generation TSH assays may reduce the number of false-positive results (4) in hospitalized patients.

This analysis nicely quantifies what most clinicians vaguely appreciate: Overt thyroid disease is relatively rare in hospitalized patients, signs and symptoms are often unhelpful, and the sTSH is a good but not perfect test. Further studies of the importance and treatment of subclinical thyroid dysfunction are needed.

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