

Thyroid Function Testing in Outpatients: Are Both Sensitive Thyrotropin (sTSH) and Free Thyroxine (FT4) Necessary?

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Background and Objectives: Despite improved thyroid function testing assays, appropriate use of these commonly ordered tests to detect thyroid dysfunction remains controversial. This study determined if a normal sensitive thyroid stimulating hormone (sTSH) test alone is sufficient to rule out thyroid dysfunction in outpatients. **Methods:** This was a retrospective analysis of initial sTSH and free thyroxine index (FT4) tests ordered during a 26-month period. Test results were classified as concordant if both the sTSH and FT4 indicated the same findings (ie, euthyroid, hyperthyroid, or hypothyroid). The results were classified as discordant if the sTSH and FT4 did not indicate the same findings. **Results:** There were 1,392 paired sTSH and FT4 results. Of 1,340 results classified as concordant (96.2%), 1,187 specimens were consistent with euthyroidism, 41 with hyperthyroidism, and 112 with hypothyroidism. Of the remaining 52 (3.8%) discordant results, 47 met the definition of subclinical thyroid dysfunction. Excluding these 47 results yielded a concordance rate of 99.6%. Of the 1,192 normal sTSH results, FT4 was low in two and high in three. If FT4 tests had not been ordered on the 1,192 specimens with normal sTSH levels, the savings over the study period would have been more than \$3,360. **Conclusions:** If the sTSH is normal, the likelihood of an abnormal FT4 is very small. sTSH alone is adequate to screen outpatients for thyroid dysfunction. Limiting FT4 tests to those with abnormal sTSH results will result in cost savings.

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Thyroid function tests (TFTs) are among the most common laboratory tests ordered in outpatient settings. A study in 1992 concluded that TFTs represent 8% of laboratory charges.¹ Methods for testing the serum concentration of thyrotropin, more commonly known as thyroid stimulating hormone (TSH), have been improved such that much lower concentrations can be detected than in the past. Despite the implementation of these sensitive and "ultra-sensitive" TSH tests and improved methods for detecting non-protein-bound, or free, thyroid hormone (FT4), the appropriate use of these tests to detect thyroid dysfunction remains controversial.

While the American Thyroid Association since 1990 recommended the use of both sensitive TSH (sTSH) and FT4 to test thyroid function,² others recommend sTSH alone,⁴⁻⁷ and a few even have recommended FT4 alone.¹ Bauer and Brown published a retrospective study in 1996 that concluded if the sTSH result is normal, the likelihood of a normal FT4 result is extremely high.^{2,3}

To explore this matter further, I performed a retrospective study of TFTs ordered during a continuous 26-month period from a family practice clinic in a military teaching hospital. The study determined (1) how often sTSH and FT4 were ordered simultaneously, (2) how often they were discordant (ie, only one of the two tests indicated thyroid dysfunction), (3) under what circumstances, if any, would a single thyroid test be adequate, and (4) the financial savings if only a single test were routinely used.

Methods

Setting

The Family Practice Clinic at Naval Hospital Jacksonville serves the family members of active duty military personnel, retirees, and active duty members. The clinic is staffed by family practice residents in various stages of training, board-certified family physicians, and family nurse practitioners. Laboratory tests are ordered by entering the order for the test into the centralized hospital computer system. Specifically, the thyroid function tests can be ordered as a pair (sTSH and FT4) by requesting "TFT." One can also order sTSH alone by entering "TSH" or FT4 alone by entering "FT4."

Test Performance

The Naval Hospital Jacksonville laboratory uses Abbott Laboratories' AxSYM System[®] Ultrasensitive hTSH II microparticle enzyme immunoassay to measure the concentration of TSH in laboratory specimens. The reference (normal) range is given as .32–5.0 uIU/mL. The reagents and raw materials cost for a single sTSH test is \$2.74. To measure the concentration of FT4, a direct two-step immunoassay from Abbott Laboratories is used. The reference (normal) range is given as .71–1.85 ng/dL. Reagents and materials for a single FT4 test cost \$2.82. These costs are the actual costs charged from Abbott Laboratories to the Naval Hospital Jacksonville Laboratory Department. These costs do not include the costs of labor and other non-consumables.

Data Collection

All the sTSH and FT4 tests ordered by clinicians at the Family Practice Clinic at Naval Hospital Jacksonville during the 26-month period between January 1995 and March 1997 were obtained from our hospital's centralized computer system. Data obtained included the patients' social security numbers (for identification purposes), the test ordered (sTSH, FT4, or both), the date of the test, and the result of the test.

Data Analysis

If an individual had more than one sTSH or FT4 test performed during the study period, only the first result was included in the study. Paired test results, ie, sTSH and FT4 ordered simultaneously, were classified as concordant or discordant. Concordant results were classified as euthyroid if both sTSH and FT4 were normal, hypothyroid if FT4 was low and sTSH was high, and hyperthyroid if FT4 was high and sTSH was low. If the test results did not fit into any of these combinations, the result was classified as discordant. Individual medical records were reviewed for cases in which the sTSH was normal and the FT4 was not.

Results

Thyroid Test Ordering

A total of 2,932 sTSH tests and 2,861 FT4 tests were ordered by clinicians in the Family Practice Clinic during the study period. All 2,861 of the FT4 tests were ordered with a simultaneous sTSH, and 71 sTSH levels were ordered alone. Thus, sTSH and FT4 tests were ordered together 98% of the time, and FT4 was never ordered alone.

To derive the final study sample, 1,469 duplicate tests from individuals with previous test results were subtracted from the total 2,861 paired tests, thereby counting only the first pair of tests ordered on each patient. The final study sample then consisted of 1,392 paired sTSH and FT4 results.

Concordance and Discordant Test Results

As shown in Table 1, of the 1,192 samples with normal sTSH results, 1,187 had concordant (ie, normal) results on the accompanying FT4 tests. The results were low in only two (.2%, 95% confidence interval [CI]=.02%–.6%) of the accompanying FT4 tests, and they were high in three (.25%, 95% CI=.05%–.7%). There were 47 specimens with normal FT4 and abnormal sTSH results (3%), and five specimens with normal sTSH and abnormal FT4 results (.3%).

Table 2 shows the concordant and discordant results. Of the concordant results, 1,187 specimens were euthyroid (normal sTSH and normal FT4), 41 specimens were hyperthyroid (high FT4 with low sTSH), and 112 specimens were hypothyroid (low FT4 with high sTSH). The remaining 52 results were classified as discordant. Combining the concordant results yields a total of 1,340 out of 1,392 for a concordance rate of more than 96% and a discordance rate of 3.8%.

Evaluation of Discordant Results

Analysis of the 52 discordant results shows that 47 of these (90%) meet the definition of subclinical thyroid dysfunction, ie, normal FT4 with low or high sTSH. Removing the 47 results that were consistent with subclinical thyroid dysfunction from the final analysis yields a concordance rate of 99.6%.

Chart review was performed for the remaining five discordant results. Of the two individuals with normal sTSH and low FT4, both the sTSH values were at the upper limit of normal, and these patients were being treated for hypothyroidism. Of the three individuals with normal sTSH and high FT4, two were being treated for hypothyroidism, and one patient's FT4 was only slightly above the upper limit of normal and did not result in treatment.

Table 1

Summary of Data

Sample size	1,392	Abnormal sTSH	200 (14%)
Normal sTSH	1,192	Abnormal FT4	158 (11%)
Normal FT4	1,234	Normal FT4 with low or high sTSH	47 (3%)
		Normal sTSH with low or high FT4	5 (.3%)

sTSH—sensitive thyroid stimulating hormone
FT4—free thyroid hormone

Table 2

Test Results

	Low sTSH	Normal sTSH	High sTSH
Low FT4	0	2	112
Normal FT4	19	1,187	28
High FT4	41	3	0

sTSH—sensitive thyroid stimulating hormone
FT4—free thyroid hormone

Concordant results are shown in *italics*.

Cost data obtained from laboratory.

Laboratory charges obtained from laboratory.

Cost Analysis

The total reagent and material costs of the thyroid function tests ordered during the study period was \$7,739 (\$3,814 for sTSH tests and \$3,925 for FT4 tests). If FT4 tests had not been ordered on the 1,192 specimens with normal sTSH results, the actual material cost savings over the 26-month study period would have been more than \$3,360. Based on laboratory charges of \$60 per FT4 test, this would result in a savings to the hospital of \$71,220 over the 26 months of the study and a projected savings of \$328,708 over 10 years from the family practice department alone.

Discussion

Based on the ordering of the thyroid function tests from our family practice clinic during the study period, sTSH and FT4 are ordered together 98% of the time. Our results indicate that in most cases, however, simultaneous measurement of both sTSH and FT4 is unnecessary. Indeed, if one excludes cases for which results indicated subclinical thyroid dysfunction, the results of this study indicate that in a routine outpatient population, if the sTSH result is normal, the likelihood of an abnormal FT4 result is less than 1%. Based on the simple cost analysis described earlier, significant cost savings will result if FT4 tests are only performed when sTSH results are abnormal.

Limitations

The most important limitation of this study is its retrospective design. This prevents analysis of why the

thyroid tests were ordered, results of previous tests at other facilities, or the presence of conditions that may have influenced test ordering. Many of the patients on whom thyroid tests were ordered undoubtedly had thyroid disorders that might have influenced the indication for testing and the testing results.

Conclusions

Based on the less-than-1% discordance rate between sTSH and FT4 results in this study, an sTSH level alone is adequate to screen outpatients for thyroid dysfunction. Ordering the sTSH alone initially, followed by FT4 in only those cases of abnormal sTSH, will significantly decrease unnecessary testing and expense. To obviate the inconvenience of having a patient with an abnormal sTSH return for repeat testing, an automated test-ordering cascade that obtains the FT4 on the same specimen could be implemented.

Finally, as with all of medicine, clinical judgment still dictates in those rare instances when testing both sTSH and FT4 or FT4 alone is appropriate. This would occur, for example, when pituitary or hypothalamic disease is suspected or known.

Note: In 2000, 3 years after data collection for this study, the American Thyroid Association (ATA) published updated guidelines on screening adults for thyroid dysfunction.⁸ In these guidelines, the ATA recommended screening with sTSH only.

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Editor's Note: This paper received a second-place award at the American Academy of Family Physicians 2002 Annual Scientific Assembly for research by a family practice resident. Dr Viera was a resident when he conducted this research.