Commentary

FT4 Should Replace TSH in Diagnosing Abnormal Thyroid Function

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Thyroid stimulating hormone (TSH) is produced by the pituitary gland. When the pituitary is functioning properly, it releases more TSH when additional thyroid hormone is needed in the blood, and less when less is needed. Thus, levels of TSH can be used to indirectly test thyroid function. Free thyroxine (FT4) is a test that directly measures the amount of available, unbound thyroid hormone in the blood and provides a more accurate way to determine thyroid function. We argue that the serum free thyroxine (FT4) assay should replace TSH as the gold standard for the diagnosis of abnormal thyroid function.

Currently, TSH assays are considered to be the gold standard for diagnosing abnormal thyroid function (1). TSH controls the amount of FT4 released from the thyroid; as TSH increases, FT4 increases and vice versa. If the pituitary recognizes low thyroid hormone levels, more TSH will be produced to subsequently signal the thyroid to make more thyroid hormone. The opposite is also true: high thyroid hormone levels in the blood signal the pituitary to stop its production of TSH. Thus, an elevated TSH suggests hypothyroidism, while a suppressed TSH suggests hyperthyroidism. Both of these potential diagnoses must be confirmed by measuring the serum FT4 level.

While TSH has been referred to as the single best screening test for evaluating thyroid function (2), in the current commentary we question this claim. It is well known that not all cases of hypothyroidism present with an elevated TSH, nor do all cases of hyperthyroidism present with suppressed levels (3). Since normal TSH results alone prove to be a “poor indicator of the body’s overall thyroid status” (4) and do not rule out either low or high levels of thyroid hormone in the blood, additional testing is required to properly diagnose the patient. Thus, testing TSH is an

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unnecessary step because abnormal thyroid function can be diagnosed on the basis of a serum FT4 alone.

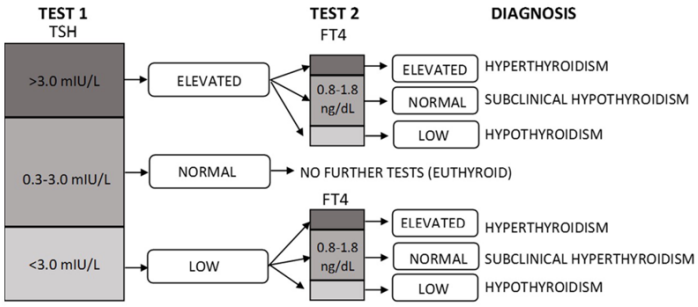

Figure 1. "TSH First" Approach Algorithm for Diagnosing Hypothyroidism. Adapted froman algorithm for the initial assessment of thyroid function, based on initial assay of serum TSH (6).

Using TSH as a screening test for hypo- and hyperthyroidism (Figure 1) can result in under-diagnosis of the condition. If the TSH level is within the normal range, and there is no follow up testing, hypo- or hyperthyroidism may be missed. This will not happen with measurement of serum FT4, since it is a direct measure of the thyroid function. Over-diagnosis with TSH screening is also a possibility, as TSH screening creates the unnecessary diagnostic categories of subclinical hypo- and hyperthyroidism (5). These conditions are defined as a normal FT4 and an abnormal TSH in an asymptomatic patient. Because the FT4 level is normal in these conditions, the patient is clinically euthyroid, making the diagnostic categories of subclinical hypo- and hyperthyroidism unnecessary. Per the "FT4 first" approach that we here suggest, these categories would be eliminated: a patient with subclinical hypo- or hyperthyroidism on the TSH approach would simply count as "euthyroid" on ours. Thus, the potential for both under-and over-diagnosis of abnormal thyroid function is reduced with the "FT4 first" approach (Figure 2).

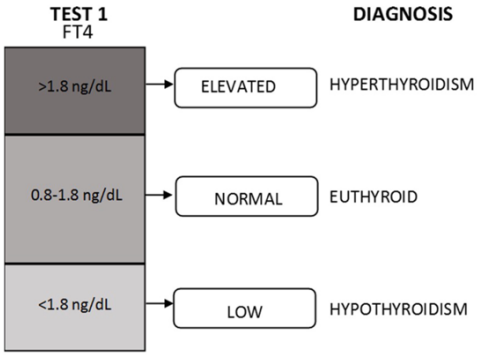

Figure 2. "FT4 First" Approach Algorithm for Diagnosing Hypothyroidism. Adapted from an algorithm for the initial assessment of thyroid function, based on initial assay of serum TSH (6).

Further, if FT4 is used as the initial screening test for abnormal thyroid function, the unnecessary costs of performing two tests (TSH and FT4) is avoided. When TSH is used as the screening test, follow up testing with the FT4 test is required for abnormal values. Thus, although the FT4 test is currently 68% more expensive than the TSH test (7), its routine usage as a screening test would be more cost-effective in the long-term since only one test is necessary for the diagnosis of abnormal thyroid function (8). Thus the current diagnostic procedure for the determination of abnormal thyroid function should be updated by replacing TSH with FT4 as the screening test for these conditions. This would allow for more accurate diagnosis by reducing the likelihood of both under- and over-diagnosis of hypo- and hyperthyroidism, while reducing screening costs over time.

References

1. USPSTF [Internet]. [place unknown]: AAFP; 2004 May 15 [cited 2017 July 12]. Available from http://www.aafp.org/afp/2004/0515/p2415.html#
2. Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the american association of clinical endocrinologists and the american thyroid association. AACE. 2012; 18(6): 989-990
3. Skugor M. Hypothyroidism and hyperthyroidism [Internet]. Lyndhurst: Cleveland Clinic Foundation Center for Continuing Education; 2014 [cited 2017 July 15]. Available from: http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/endocrinology/hypothyroidism-and-hyperthyroidism/#cetextbox3
4. Holtorf K. How accurate is TSH testing? NAH [Internet]. 2012 January 27 [cited 2016 September 13]. Available from: https://www.nahypothyroidism.org/how-accurate-is-tsh-testing/
5. Stockigt J. Clinical strategies in the testing of thyroid function. Endotext [Internet]. 2011 June 1 [cited 2016 September 13]; Available from NCBI: https://www.ncbi.nlm.nih.gov/books/NBK285558/
6. Stockigt J, NCBI. [image on the Internet]. 2011 June 1 [cited 2016 September 13]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK285558/
7. Health Testing Centers [Internet]. [place unknown]: [publisher unknown]; 2016 [cited 2016 September 13]. Available from: http://www.healthtestingcenters.com/thyroid-testing.aspx
8. de los Santos ET, Starich GH, Mazzaferri EL. Sensitivity, specificity, and cost-effectiveness of the sensitive thyrotropin assay in the diagnosis of thyroid disease in ambulatory patients. JAMA [Internet]. 1989 March [cited 2016 September 13]; 149(3):526-32. Available from PubMed: https://www.ncbi.nlm.nih.gov/pubmed/2493228