Monitoring Patients for Thyroid Cancer Recurrence

Measurement of serum thyroglobulin (Tg) is primarily used in the postoperative management and long-term surveillance of patients with differentiated thyroid cancer (DTC).1 Several studies have also suggested that the quantitative thyroglobulin antibody (TgAb) concentration can serve as a surrogate tumor marker for DTC recurrence and monitoring changes in tumor mass in certain patients.1,2

Current guidelines from the National Academy of Clinical Biochemistry recommend that TgAb concentration be measured in all specimens prior to Tg analysis.1,3 Those guidelines recommend the use of a sensitive thyroglobulin antibody assay to assist in the detection of low antibody concentrations that can interfere with Tg measurement.1 The LabCorp TgAb method is sensitive to a level of 1 IU/mL, because even low antibody concentrations can interfere with Tg measurements by immunometric assay (IMA). TgAb is detected in approximately 10% of the general population and an estimated 25% of patients with DTC.2

The most common method available for thyroglobulin measurement in the clinical laboratory is Tg-IMA. Since Tg-IMA assays often have superior sensitivity in TgAb-negative patients, their use in measuring Tg may be preferred for those patients.1 The LabCorp Tg-IMA method is sensitive to a level of 0.1 ng/mL. However, the IMA method is more prone to interference by TgAb.1,4 For DTC patients who test positive for TgAb, use of either the Tg-radioimmunoassay (RIA) or Tg-liquid chromatography/tandem mass spectrometry (LC/MS-MS) is a reflex testing option. Additional assay performance information regarding the Tg-LC/MS-MS method is available on request. A challenge with all immunological methods is that for patients with positive TgAb, there is an associated risk of interference with Tg measurement that can lead to overestimation or underestimation of Tg, a circumstance that may disguise the presence of recurrent disease.1,3

Thyroglobulin by radioimmunoassay (Tg-RIA) has been used for TgAb-positive patients because it is considered less prone to antibody interference. The published data support the use of this methodology for TgAb-positive patients.1 The Tg-RIA assay is less sensitive than the Tg-IMA assay, so it is generally most beneficial only in TgAb-positive patients.1 The Tg-RIA assay is sensitive to a level of 2.0 ng/mL.

Thyroglobulin by liquid chromatography/tandem mass spectrometry (Tg-LC/MS-MS) has been recently introduced as a new methodology to measure Tg for TgAb-positive patients. The Tg-LC/MS-MS method is sensitive to a level of 0.2 ng/mL. This new method utilizing Tg-LC/MS-MS provides physicians with an additional option for managing thyroid cancer recurrence in their TgAb-positive patients.

The reflex to Tg-IMA allows for a faster turnaround time for those patients who are TgAb-negative. The Tg-IMA assay is sensitive to a level of 0.1 ng/mL.

It has been suggested that serial Tg and/or TgAb testing on an individual patient be performed by the same method for reliable interpretation.1,2 When a change in method is necessary, it is recommended that clinicians re-establish baseline levels that can be used to interpret change over time.6

In patients with lymph node metastatic lesions or localized neck recurrence of DTC, the combination of fine needle aspirate (FNA) biopsy cytologic analysis and measurement of thyroglobulin in the needle washout (with 1 mL of saline solution) can be useful. The sensitivity and specificity of combined FNA biopsy cytology results with the thyroglobulin aspirate washout results have been shown to be nearly 100% in these patients.3

Interpreting Thyroglobulin Results in Thyroid Cancer Patients

Any changes in serum Tg concentrations should be interpreted in light of the total clinical presentation of the patient, including clinical history, data from additional testing, imaging studies, and other relevant information. The clinical significance of Tg levels close to the limit of detection is unclear, especially if Tg is only detected following TSH stimulation. The trend in Tg levels over time may be of greater clinical significance; therefore, it may be useful to compare serial Tg measurements to the postoperative baseline Tg result, if possible.

Routine preoperative Tg measurement is not recommended.2 However, because some thyroid tumors fail to secrete a detectable Tg concentration or secrete abnormal Tg isoforms not detected by certain assays,2 measurement of preoperative Tg levels may be of value when evaluating patients for absence of thyroglobulin secretion, decreased thyroglobulin immunoreactivity, or heterophilic antibodies.1,3

Reference ranges established by testing normal, euthyroid subjects have little relevance when interpreting serum Tg concentrations in DTC patients after thyroidectomy. Tg reference intervals for DTC patients depend on the residual mass of thyroid tissue left after surgery. The National Academy of Clinical Biochemistry guidelines suggest that 1 gram of normal thyroid tissue produces approximately 1 ng/mL of Tg in serum for patients with normal TSH levels, and 1 gram of normal thyroid tissue produces approximately 0.5 ng/mL of Tg in serum for patients with suppressed TSH levels (<0.1 mU/mL).1 In addition, a typical TSH stimulation of normal thyroid remnants or a well-differentiated tumor should result in at least a threefold or higher increase in serum Tg above basal (TSH-suppressed) levels for TgAb-negative patients.1 Current guidelines from the American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association also recommend using a given assay’s functional sensitivity as the minimum detection limit for distinguishing biochemically negative patients from those with residual Tg-producing tissue.3 Pediatric thyroid cancer guidelines from the American Thyroid Association recommend a stimulated Tg level of greater than 10 ng/mL as threshold for further evaluation.1
LabCorp’s Thyroglobulin Test Options

LabCorp has several test options available for measuring thyroglobulin levels.

LabCorp’s new profile, Thyroglobulin Antibody and Thyroglobulin, IMA or LC/MS-MS (042045) uses a dual-assay strategy for Tg in an effort to minimize the potential effect of TgAb interference on thyroglobulin analysis. All specimens are tested for TgAb using a sensitive immunometric assay (IMA). Specimens with TgAb concentrations below the detectable limit are then tested for Tg by a sensitive second-generation immunometric assay. Specimens with any measurable levels of TgAb are tested by a sensitive liquid chromatography/tandem mass spectrometry (LC/MS-MS) method that is less prone to interference by TgAb. When evaluating results from LabCorp’s Thyroglobulin Antibody and Thyroglobulin, IMA or LC/MS-MS, clinicians should be aware of the sensitivity of each assay as noted in Figure 1.

LabCorp also offers Thyroglobulin Antibody and Thyroglobulin, IMA or RIA (042060). This test uses the same sensitive TgAb IMA assay, and specimens with TgAb concentrations below the detectable limit are then tested for Tg by a sensitive second-generation IMA. Specimens with any measurable levels to TgAb are tested by an RIA method that is less prone to interference by TgAb. When evaluating results from LabCorp’s Thyroglobulin Antibody and Thyroglobulin, IMA or RIA, clinicians should be aware of the sensitivity of each assay as noted in Figure 2.

LabCorp also offers a thyroglobulin lymph node aspirate assay.

References

Visit the online Test Menu at www.LabCorp.com/TestMenu for full test information, including CPT codes and specimen requirements.