An Interferent No More: Measuring Thyroglobulin in the Presence of Anti-Thyroglobulin Autoantibodies

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Outline:

• Why measure thyroglobulin (Tg)?
• What measurement issues exist?
• How can we avoid these issues?
• When is MS testing for Tg most cost-effective?
Thyroglobulin (Tg): Background

- Secreted by the thyroid gland
  - Thyroid hormone precursor
  - T3 and T4

- Large protein
  - Dimer, 660 kDa
  - 19 different epitopes
Thyroglobulin (Tg): Background

• Why measure?
  – Thyroid cancer
    • Most common endocrine cancer
      – Rapidly increasing; < 55yo, F > M
    • Treatable
      – Full/partial thyroid resection
  – Biomarker for cancer recurrence
    • Monitor, every 6 to 12 months\(^1\)
    • Concentrations >2 ng/mL may indicate disease\(^1\)

\(^1\)ATA Guidelines, Thyroid (2009);19:1
Thyroglobulin (Tg): Interference

- Autoantibodies against Tg (TgAb)
  - Approximately 25% of thyroid cancer patients\(^1\)
  - 10% of general population\(^1\)
- TgAb interfere with Tg immunoassays
  - Falsely low Tg

\(^1\)JCEM 1998;83:1121-7
Thyroglobulin (Tg): Interference

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A New Way: Tg by LC-MS/MS

Measurement of Thyroglobulin by Liquid Chromatography–Tandem Mass Spectrometry in Serum and Plasma in the Presence of Antithyroglobulin Autoantibodies

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A New Way: Tg by LC-MS/MS
Tg by LC-MS/MS: Comparison to Immunoassay

MS vs. Immunoassay (IA): TgAb negative samples

\[ y = 0.99x - 3.1 \quad r = 0.980 \]

\[ y = 0.94x - 3.7 \quad r = 0.946 \]
Tg by LC-MS/MS: Comparison to Immunoassay

MS vs. Immunoassay (IA): TgAb positive samples

- 23% (16/71) of samples negative for Tg by IA had values ≥ 0.5 ng/mL by MS

\[ y = 0.53x - 0.10 \]
\[ r = 0.586 \]
Tg by LC-MS/MS: How should we use this test?

- Focus on utilization
  - LC-MS/MS preferred measurement for TgAb positive patients
  - LC-MS/MS = IA in TgAb negative patients
  - Reflex testing algorithm:
Tg by LC-MS/MS: How should we use this test?

- Analysis of Tg testing patterns (> 100,000 orders)
  - 89% utilized reflex testing
    - 89% were TgAb negative
      - Reflex to IA vs. MS directly saved > $3 million*
    - If ordered separately (TgAb + Tg by LC-MS/MS)
      - Reflex would save almost $9 million*
  - 11% ordered TgAb and Tg by LC-MS/MS separately
    - 90% were TgAb negative
      - Reflex (to IA) would have saved almost $250,000*

* Cost analysis based on average list price from 3 laboratories
Powers, Strathmann, Straseski; Poster Abstract A-068, 2015 AACC Annual Meeting
A New Way: Tg by LC-MS/MS

**MS allows for accurate measurement of Tg in the presence of interfering TgAb.**

**Utilizing MS assays when most appropriate leads to economical use of health care resources.**
Summary:

• Tg has utility in the diagnosis and monitoring of thyroid cancer recurrence.

• LC-MS/MS technology allows for the measurement of Tg in the presence of interfering autoantibodies.

• Proper test utilization in TgAb positive and TgAb negative populations can lead to substantial cost savings.
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