THYROID
Volume 21, Number 7, 2011

DOI: 10.1089/thy.2011.0158

The Roche Elecsys and Siemens-Centaur Thyroglobulin Autoantibody Assays Show Comparable Clinical Performance to the Recently Unavailable Beckman-Coulter Access Thyroglobulin Autoantibody Assay in Identifying Samples with Potentially False-Low Thyroglobulin Measurements Due to Thyroglobulin Autoantibody Interference

Alicia Algeciras-Schimnich, Michael A. Lasho, Karl M. Ness, Lynn A. Cheryk, and Stefan K.G. Grebe

Dear Editor:

Approximately 25% of thyroid cancer patients have circulating antithyroglobulin autoantibodies (anti-TgAB), which can cause false-low interference in Tg assays (1). It is therefore recommended that all Tg measurements are accompanied by TgAB testing (1).

The Beckman-Coulter Access Tg- and TgAB assays have become perhaps the most widely used assay combination for thyroid cancer follow-up in the United States, because they run on the same automated instrument and they are more sensitive than most alternative Tg/TgAB assays. Unfortunately, Beckman-Coulter has recently indicated that their TgAB assay will be unavailable for the foreseeable future, necessitating a switch to other TgAB assays to accompany Tg testing.

Such a change has a high risk of interfering with patient management. Different TgAB assays show at best a moderate numerical agreement with each other, have different detection sensitivities, and have different cutoffs for TgAB positivity (2–4). We have therefore performed a comparison study of the Beckman-Coulter TgAB assay with three other automated TgAB assays: Roche Elecsys TgAB, Siemens-Centaur TgAB, and Siemens-Immulite TgAB. As these assays are primarily marketed for the diagnosis of autoimmune thyroid disease, the manufacturer-provided diagnostic cutoffs are not optimized for the detection of interference in Tg assays. Therefore, we first determined optimal cutoffs for these assays by comparing them with the Beckman-Coulter assay in 100 archival patient samples. Next, we performed a clinical validation of these cutoffs in 130 samples from 113 Mayo Clinic patients. These samples were selected to include patients with (43 patients with 51 samples) and without (70 patients with 79 samples) definitive persistent/recurrent disease (clinical or imaging proven) (see Supplementary Methods; Supplementary Data are available online at www.liebertonline.com/thy).

We found poor numerical agreement between the Beckman-Coulter assay and the other TgAB assays, but receiver-operating characteristics (ROC) curve analysis, using the Beckman-Coulter TgAB results as the "gold standard" (negative: <4 IU/mL, $N=32$; positive: ≥ 4 IU/mL, $N=68$), showed comparable areas under the curves (see Supplementary Fig. S1): Siemens-Centaur 0.88 (95% confidence interval [CI]: 0.79–0.97), Siemens-Immulite 0.86 (95% CI: 0.81–0.92), and Roche 0.87 (95% CI: 0.77–0.95). At their respective ROC curve–derived cutoffs, the Siemens-Centaur (44 IU/mL) and Roche (22 IU/mL) missed only 1 and 3 samples, respectively, which had been positive with the Beckman-Coulter assay, whereas the Siemens-Immulite (20 IU/mL) missed 18.

The Roche assay showed the best agreement with the Beckman-Coulter assay in the clinical validation sample set with verified disease status (see Supplementary Table S1), with a negative and positive agreement of 96% and 95%, respectively. The Siemens-Immulite assay showed the worst agreement (negative and positive agreement of 79% and 78%). The Siemens-Centaur assay's performance fell in between these two with 92% negative agreement and 94% positive agreement. All 16 samples from 15 patients with clinical recurrent/persistent disease, who had undetectable serum Tg levels (<0.1 ng/mL), were positive for TgAB in all four assays, using the respective cutoffs. However, of 31 samples from 26 patients with clinical recurrence and a Tg of <2 ng/mL, a total of 3 samples from 3 patients (1 per patient) had a negative TgAB result in the Beckman-Coulter, Roche, and Siemens-Centaur TgAB assays, whereas 6 samples from 5 patients (1 patient with 2 samples) had a negative TgAB result by the Siemens-Immulite assay.

We conclude that the automated Roche Elecsys (cutoff: 22 IU/mL) and Siemens-Centaur (cutoff: 44 IU/mL) TgAB

Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.

assays show comparable clinical performance to the Beckman-Coulter Access TgAB assay (cutoff: 4 IU/mL). The Siemens-Immulite assay (cutoff: 20 IU/mL) had lesser TgAB detection sensitivity than the other assays. Incidentally, all these cutoffs are much lower than those listed in the respective package inserts, which are targeted at diagnosis of autoimmune thyroid disease. These manufacturer-stated cutoffs would miss many cases of clinically relevant TgAB levels that could cause interferences in Tg measurements.

The satisfactory performance of the Roche and Siemens-Centaur TgAB assays in identifying samples with TgAB levels that might interfere with Tg measurements does not solve all problems related to the sudden unavailability of the Beckman-Coulter TgAB assay. In particular, it remains important for laboratorians and clinicians to be mindful of the poor numerical agreement between the Beckman-Coulter assay and the other TgAB assays, when analyzing patient samples. Practitioners, who have used serial TgAB measurements with the Beckman-Coulter assay as a semiquantitative follow-up marker in TgAB-positive patients, need to re-baseline these patients with one of the alternative assays and should ensure that subsequent samples are measured using the same assay.

Disclosure Statement

The authors declare that no competing financial interests exist.

References

1. Grebe SKG 2009 Diagnosis and management of thyroid carcinoma: a focus on serum thyroglobulin. Expert Rev Endocrinol Metab **4:**25–43.
2. Spencer CA, Bergoglio LM, Kazarosyan M, Fatemi S, LoPresti JS 2005 Clinical impact of thyroglobulin (Tg) and Tg autoantibody method differences on the management of patients with differentiated thyroid carcinomas. J Clin Endocrinol Metab **90:**5566–5575.
3. La'ulu SL, Slev PR, Roberts WL 2007 Performance characteristics of 5 automated thyroglobulin autoantibody and thyroid peroxidase autoantibody assays. Clin Chimica Acta **376:**88–95.
4. Spencer C, Petrovic I, Fatemi S 2011 Current thyroglobulin autoantibody (TgAb) assays often fail to detect interfering TgAb that can result in the reporting of falsely low/undetectable serum Tg IMA values for patients with differentiated thyroid cancer. J Clin Endocrinol Metab **96:**1283–1291.

Address correspondence to:
Stefan K.G. Grebe, M.D.
Department of Laboratory Medicine and Pathology
Mayo Clinic
200 1st St. SW
Rochester, MN 55902

E-mail: grebe.stefan@mayo.edu