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Short communication

Thyroglobulin as a tumor marker: The importance of method comparison in patients with differentiated thyroid carcinoma

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Introduction

Differentiated thyroid cancer (DTC) is the most frequent thyroid malignancy (Deza et al., 2023). Even though it has a good prognosis, postoperative monitoring is a necessity for assessing the treatment effectiveness in patients who have undergone total or near-total thyroidectomy and radio-ablation iodine treatment.

Measurement of serum thyroglobulin (Tg) is an important modality to monitor patients for residual or recurrent disease. The basal serum levels of Tg in healthy individuals should range from 3-40 µg/L. Contrary, in thyroidectomized patients who respond excellently to therapies, Tg values should be below 0.2 µg/L (Monza et al., 2025).

Based on the serum Tg concentrations during follow up period, the American Thyroid Association (ATA) guidelines classify the patient responses to treatment in three categories: excellent, intermediate, and incomplete (Deza et al., 2023).

Therefore, Tg measurements should be standardized and analytically robust to support reliable interpretation during follow-up. This comparability study was conducted to evaluate the concordance between two methods performed at different platforms: current Maglumi 2000 and Atellica IM 1300 auto analyzers.

Materials and methods:

This comparability study included 60 residual serum samples obtained from subjects with and without thyroid pathology. All samples were analyzed within one day of blood collection. Only subjects with Tg-Abs negative concentrations were included for analysis.

Laboratory measurement

Tg measurements were performed using two chemiluminescent immunoassays (CLIAs). Maglumi 2000 (Snibe Diagnostics, China) is currently used in our laboratory for routine monitoring of patients with DTC. Atellica IM 1300 (Siemens Healthcare Diagnostics, USA) was used as a novel, candidate method. (Tg-M and Tg-A immunoassays, respectively). According to the manufacturers, the detection limit for Maglumi is 0.04 µg/L, with a functional sensitivity of 0.1 µg/L and 0.05 µg/L for Atellica IM 1300. The reportable interval is 0.1-500 µg/L for Maglumi and 0.05-150 µg/L for Atellica IM 1300.

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Method comparison and statistical analysis

Serum Tg-M and Tg-A measurements were evaluated across three concentration ranges: < 2 µg/L, 2-50 µg/L, and > 50 µg/L. Statistical analysis included Passing-Bablok regression, concordance correlation analysis, and Bland-Altman analysis, performed using MedCalc software.

Results and discussion

Correlation analysis of the overall study population showed a concordance correlation coefficient of 0.915 between the assays, indicating moderate agreement. However, Pearson correlation demonstrated strong precision (ρ = 0.991), and a satisfactory bias correction factor (C_b = 0.923). These findings indicate that method-comparison studies should go beyond correlation and analytical bias to evaluate their potential impact on clinical decision-making. To support reliable clinical interpretation of Tg as a tumor marker during follow-up, we separately assessed concordance across three concentration ranges: the critical range (0–2 µg/L), the reference range (2–50 µg/L), and values above the cut-off (>50 µg/L) (Civita et al., 2025).

Within the critical range, the concordance coefficient between Tg-M and Tg-A was 0.592, with ρ = 0.700 and C_b = 0.845. These coefficients indicate poor agreement between methods, with moderate precision and average accuracy meaning a noticeable constant bias is present. In contrast, substantial agreement was observed in the reference range, with a concordance coefficient of 0.963. Also, the precision and accuracy were almost perfect ρ=0.988 and C_b =0.975, indicating no significant difference in obtained results. Concentrations above the cut-off also showed very poor agreement, with a concordance coefficient of 0.464. Although precision remained strong in this range (ρ = 0.934), the accuracy was poor (C_b = 0.497), mainly because of scale shift.

The Passing-Bablok regression for the first level showed a slope of 1.389 (95% CI: 0.995-3.917) and an intercept of 0.022 (95% CI: -0.028 to 0.031). In the reference range, it rendered a slope of 0.946 (95% CI: 0.833-1.183) and an intercept of -1.075 (95% CI: -2.821 to -0.224). For concentrations above 50 µg/L, the slope was 0.512 (95% CI: -0.062-1.058) and the intercept 18.564 (95% CI: -36.829 to 71.866), indicating presence of systematic and proportional biases.

Bland Altman analysis give mean bias of -0.17 µg/L (95%CI: -1.00 – 0.65) for the critical range, mean bias of 1.9 µg/L (95% CI: -1.8 to 5.7) for the reference range and very high bias for concentrations above 50 µg/L, 30.6 µg/L (95% CI: -1.9 to 63.2). Only critical range showed good agreement with minimal bias and narrow limit of agreement.

Conclusion

Our comparative study showed the strongest agreement in the reference range, whereas differences became more apparent as thyroglobulin concentrations increased. The methods agree for low concentrations but not as magnitude of measurement increases. This study presented that the interchangeability between these two methods is very delicate and the results for Tg are not transferable within the whole reporting concentration interval.

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