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ORIGINAL ARTICLE

The Current Status of CA15-3 Measurement Based on a Commutable External Quality Assessment Program

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ABSTRACT

Background: **The goal was to evaluate the external quality assessment (EQA) performance of breast cancer-related tumor marker CA15-3.**
Methods: **CA15-3 EQA materials were distributed to each participating laboratory by cold chain transportation each round, and the laboratories returned results through the official website. The participating hospitals were grouped according to the testing reagents and methods. The median was taken as the target value. Evaluation criterion, 20.83%, was based on desirable specification derived from intra- and inter-individual biological variation. The robust CV was used to evaluate the variation trend between laboratories. The choice of high, medium, and low concentration levels was used to compare the differences between detection systems, and the pass rate was used to evaluate the test quality of the laboratory.**
Results: **In the five CA15-3 EQA from 2023 to 2025, the number of participating laboratories was 504 - 817. There was a significant difference in the composition ratio of hospitals at different levels between the rounds. In the classification of reagents, the range of robust CV was 6.48 to 7.63, and the robust CV of the first EQA of CA15-3 in 2025 was lower than that of the second EQA in 2024; the pass rates of the two quality assessments in 2024 were both higher than that of the second EQA in 2023. Of a total of 63 pairwise comparisons, the vast majority showed statistically significant differences. There was no statistical difference in the results between the three reagents of brand f, brand c and others at low and medium levels. In the classification of methods, there was no statistically significant difference in the robust CV and pass rate of CA15-3 among the five inter-laboratory quality assessments from 2023 to 2025. At low and medium levels, there was no significant difference between the results of some methods. At high levels, there were significant differences between any two groups except D - C and A - B.**
Conclusions: **The pass rate of CA15-3 was increasing, and the robust coefficient of variation was decreasing. There are differences among different detection reagents and methods, so different reference intervals and treatment cut-off values should be used to provide more accurate clinical service.**
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KEYWORDS

CA 15-3, external quality assessment (EQA), median, robust CV

INTRODUCTION

Breast cancer is one of the most common malignant tumors in women. According to statistics from the World Health Organization (WHO), approximately 2.3 million new cases of breast cancer were diagnosed globally in 2020, accounting for 24.5% of all female cancers and ranking first in cancer incidence among women [1,2]. The development of breast cancer is closely linked to genetic factors [3], hormone levels [4], and environmental influences [5], making early screening and diagnosis critical to improving cure rates. CA15-3 is an important tumor-associated glycoprotein antigen, which belongs to the mucin 1 (MUC1) family. It is composed of a soluble fragment of a transmembrane glycoprotein encoded by the MUC1 gene that is released into the blood after enzymatic digestion [6]. As one of the most widely used serum tumor markers in clinical practice, CA15-3 can be used for monitoring treatment response [7], early warning of recurrence and metastasis and prognosis evaluation of breast cancer [8]. In addition, CA15-3 can also be used for the monitoring and evaluation of malignant tumors such as ovarian cancer, pancreatic cancer, primary liver cancer and colorectal cancer [9].

The detection of CA15-3 is mainly based on immunoassay technology, and the core principle is "double antibody sandwich method". The signal detection mainly includes enzyme-linked immunosorbent assay (ELISA), chemiluminescence assay (CLIA), electrochemiluminescence assay (ECLIA), fluorescence immunoassay (FIA), etc. There are some differences in labeling technology, automation degree, throughput and sensitivity, and anti-interference ability among the detection systems of different manufacturers in the market. Studies have shown that the harmonization status of CA15-3 was outside the minimum bias criterion, with systematic differences identified. A pilot harmonization investigation for CA15-3 would be desirable [10].

External quality assessment (EQA) refers to the external quality assessment activity in which multiple laboratories use the same sample for testing, and the results are collected and evaluated by authoritative institutions to objectively evaluate the accuracy and consistency of laboratory testing [11]. Its core role is to monitor the testing capacity of laboratories, identify potential errors and systematic deviations, and promote the comparability of results between laboratories. The fundamental significance is to promote standardized operation and improve the reliability of test results through continuous quality improvement, and ultimately ensure the quality of clinical diagnosis, disease monitoring and scientific research data, so as to provide a credible basis for patient diagnosis and treatment and public health decision-making.

The data of CA15-3 in the five times of EQA from 2023 to 2025 by Beijing Center for Clinical Laboratories were analyzed, and the current status measurement of CA15-3 in the region was described. Here, we provide important reference information for the clinical application of CA15-3.

MATERIALS AND METHODS

Preparation of EQA quality control materials

The EQA of tumor markers was carried out twice a year (only the first data of 2025 was analyzed), and the quality assessment materials used in each time were 5 concentrations of the sample. The quality assessment samples were stored at 2 - 8℃. The samples were prepared based on mixed fresh human serum. After the sample was left at room temperature for 30 minutes, the test agent bottle was gently mixed. This study was approved by the Ethics Committee of Beijing Chaoyang Hospital, Capital Medical University (Approval No. 2018-ke-127).

Implementation of EQA

After receiving the samples, the laboratory tested them within the specified time, and each batch of samples was tested once. The test results and related information were then returned through the network. The relevant information includes method principle, instrument, reagent, and calibrator. Data must be reported on the day of the experiment.

Criteria for grouping

The test results were divided into groups according to the reagents and methods used. If there were more than 17 laboratories (ISO 13528-2022) for the five quality assessments, they were divided into one group, otherwise they were included in other groups. According to the reagents, they were divided into seven groups: brand a, brand b, brand c, brand d, brand e, brand f and others. According to the methods, they were divided into 6 groups. A: acridine esterification chemiluminescence method, B: magnetic particle chemiluminescence method, C: electrochemiluminescence method, D: luminol/isoluminol labeled chemiluminescence method, E: 3-(2-helixadamantane)-4-methoxy-4-(3-phosphoroyl)-phenyl-1, 2-dioxocyclic ethane disodium salt labeled microparticles chemiluminescence method, and F: others.

Evaluation of participating laboratories performance

The quality assessment materials were distributed to each participating laboratory by centralized distribution method twice a year, and 5 lots were measured each time. After grouping according to the above two methods, for each of the 5 EQA samples from each participating laboratory in the group, the deviation between

the test result and the target value of CA15-3 was calculated. Then, the satisfaction of the test results was evaluated based on whether the deviation was within the acceptable range (± 20.83%). In this study, the median of the results returned for each lot number was used as the target value. The choice of high, medium and low concentration levels was used to compare the differences between detection systems. Referring to the statistical methods in ISO13528, Robust CV = 0.7413 x (Q3-Q1)/Median value x 100% [12].

Statistical analysis

Excel 2016 and SPSS 27.0 software were used for statistical processing and analysis. Kruskal-Wallis test was used for comparison between groups and $p < 0.05$ was considered statistically significant. Significance was adjusted for multiple tests with the use of Bonferroni correction.

RESULTS

From 2023 to 2025, the number of participating hospitals in CA15-3 EQA showed a significant fluctuation. The number of laboratories decreased from 592 to 538 in the second half of 2023, surged to 817 in the first half of 2024, then plunged to 504 in the second half of 2024, and rose slightly to 522 in the first half of 2025. In the level classification, secondary and tertiary hospitals account for the vast majority, with tertiary hospitals accounting for 25.40% to 51.86%, and secondary hospitals accounting for 34.8% to 44.42%. In the first EQA of 2023, the proportion of tertiary hospitals reached the highest level of 51.86%, with 45.41% in the first EQA of 2024. There was a statistically significant difference in the proportion of tertiary hospitals between these two rounds and the others (Table 1).

The sample with a low concentration level (about 10 U/mL) was the sample with a second test in 2024 sample 1, a medium concentration level sample (about 20 U/mL) was the sample with a first test in 2025 sample 1, and the sample with a high concentration level (about 30 U/mL) was the sample with a first test in 2023 sample 1. When classified by reagent, 21 comparisons were made for each concentration level, and a total of 63 comparisons were made for the three concentration levels, of which a total of 50 comparisons were statistically different. The lowest detected values of the three concentration levels were all in brand a, and the differences between brand a and brand c, d, e, f and others were statistically significant. The highest detection values of the three concentration levels were all in brand e, and the differences between brand e and brand a, b, c, d, f and others were statistically significant (Table 2).

When classified by methods, 15 comparisons were made for each concentration level, and a total of 45 comparisons were made for the three concentration levels, of which a total of 31 comparisons were statistically different. The lowest detection values of the three concentration levels were all in group E, and there were significant differences between group E and A, B, C, D, and F except for the detection values of method D at low concentration levels. The highest detection values of the three concentration levels were all in method C group, and the differences between the three concentration levels and methods E, F, and A were statistically significant. There was no significant difference in D - F, D - A and F - A between the low and medium levels, but there was a significant difference in the high level ($p < 0.05$). There was no significant difference in A - B at three levels (Table 3).

The results of reagent classification showed that the median robust CV of CA15-3 decreased from 7.63 in the second EQA in 2024 to 6.84 in the first EQA in 2025, and the difference between the two was statistically significant ($p < 0.05$). The median pass rates of the first and second quality assessment in 2024 were 98.33% and 98.48%, respectively, which were both greater than those of the second quality assessment in 2023 (92.86%), and the difference was statistically significant ($p < 0.05$). According to the statistical results of the assay method, the median robust CV and median pass rate of CA15-3 EQA were not statistically different between 2023 and 2025 ($p > 0.05$) (Figure 1 and Table 4).

DISCUSSION

This is the first large-scale evaluation of the detection status of CA15-3 in the region. The five CA15-3 EQA data from 2023 to 2025 were systematically analyzed. The results showed that although the overall pass rate was increasing and the inter-laboratory variation was decreasing, there were still common and significant differences among different detection systems and reagents, highlighting the urgency and complexity of achieving the standardization of CA15-3 testing.

Our study found that reagents were one of the main factors contributing to the differences in detection. In a total of 63 pairwise comparisons between reagents, up to 79% of combinations showed statistically significant differences at different concentration levels ($p < 0.05$). This finding is highly consistent with the conclusion of the feasibility study by van Rossum HH et al. [10], based on global EQA data, that the harmonization status of CA15-3 is far from reaching the minimum bias standard and there are systematic differences. Of particular note, brand e yielded significant positive deviations at all concentration levels, with consistently higher median detection values than all other brands. This high value deviation strongly suggests that the calibrator traceability or antibody specificity of this kit may be fundamentally different from other systems, and the laboratory must conduct strict comparison and verification when selecting or replacing such reagents, otherwise it may seriously affect the clinical judgment of treatment response and disease progression.

This study revealed that the heterogeneity of testing

Table 1. Classification of hospitals participating in CA15-3 EQA from 2023 to 2025.

Period	Assay	Number of laboratories	Hospital level			
			Tertiary Number/Percentage	Secondary Number/Percentage	Primary Number/Percentage	Others Number/Percentage
2023	1st	592	307 $_{a}$ (51.86%)	206 $_{a}$ (34.80%)	6 $_{a}$ (1.01%)	73 $_{a}$ (12.33%)
	2nd	538	143 $_{b}$ (26.59%)	239 $_{b}$ (44.42%)	28 $_{b}$ (5.20%)	128 $_{b, c}$ (23.79%)
2024	1st	817	371 $_{a}$ (45.41%)	315 $_{a, b}$ (38.56%)	9 $_{a}$ (1.10%)	122 $_{a, d}$ (14.93%)
	2nd	504	128 $_{b}$ (25.40%)	193 $_{a, b}$ (38.29%)	27 $_{b}$ (5.40%)	156 $_{c}$ (30.91%)
2025	1st	522	191 $_{c}$ (36.59%)	211 $_{a, b}$ (40.92%)	19 $_{b}$ (3.64%)	101 $_{b, d}$ (19.35%)

In the hospital level classification, "Others" includes third-party medical laboratories, community hospitals, physical examination centers, etc. If a, b, c, and d are different, it indicates that the composition ratios of hospital levels across the five rounds are statistically significantly different. If marked with the same letter, it indicates no statistically significant difference in the composition ratios of hospital levels.

Table 2. The detection results of different concentration samples in different reagents were compared.

Reagents	Low level			Medium level			High level		
	N	Median	p-value	N	Median	p-value	N	Median	p-value
a - b	21 - 82	9.30 - 10.40	0.259	19 - 100	15.10 - 17.72	1.000	43 - 72	20.00 - 21.70	1.000
a - f	21 - 73	9.30 - 10.80	0.001 ***	19 - 77	15.10 - 21.90	0.000 ***	43 - 49	20.00 - 35.10	0.000 ***
a - g	21 - 134	9.30 - 11.16	0.000 ***	19 - 99	15.10 - 21.85	0.000 ***	43 - 66	20.00 - 28.05	0.000 ***
a - c	21 - 22	9.30 - 11.50	0.000 ***	19 - 27	15.10 - 21.73	0.000 ***	43 - 47	20.00 - 30.30	0.000 ***
a - d	21 - 132	9.30 - 12.16	0.000 ***	19 - 147	15.10 - 23.60	0.000 ***	43 - 281	20.00 - 34.20	0.000 ***
a - e	21 - 40	9.30 - 14.68	0.000 ***	19 - 53	15.10 - 24.98	0.000 ***	43 - 34	20.00 - 39.00	0.000 ***
b - f	82 - 73	10.40 - 10.80	0.383	100 - 77	17.72 - 21.90	0.000 ***	72 - 49	21.70 - 35.10	0.000 ***
b - Others	82 - 134	10.40 - 11.16	0.001 ***	100 - 99	17.72 - 21.85	0.000 ***	72 - 66	21.70 - 28.05	0.001 ***
b - c	82 - 22	10.40 - 11.50	0.022 *	100 - 27	17.72 - 21.73	0.000 ***	72 - 47	21.70 - 30.30	0.000 ***
b - d	82 - 132	10.40 - 12.16	0.000 ***	100 - 147	17.72 - 23.60	0.000 ***	72 - 281	21.70 - 34.20	0.000 ***
b - e	82 - 40	10.40 - 14.68	0.000 ***	100 - 53	17.72 - 24.98	0.000 ***	72 - 34	21.70 - 39.00	0.000 ***
f - Others	73 - 134	10.80 - 11.16	1.000	77 - 99	21.90 - 21.85	1.000	49 - 66	35.10 - 28.05	0.000 ***
f - c	73 - 22	10.80 - 11.50	1.000	77 - 27	21.90 - 21.73	1.000	49 - 47	35.10 - 30.30	0.000 ***
f - d	73 - 132	10.80 - 12.16	0.000 ***	77 - 147	21.90 - 23.60	0.000 ***	49 - 281	35.10 - 34.20	1.000
f - e	73 - 40	10.80 - 14.68	0.000 ***	77 - 53	21.90 - 24.98	0.000 ***	49 - 34	35.10 - 39.00	0.016 *
Others - c	134 - 22	11.16 - 11.50	1.000	99 - 27	21.85 - 21.73	1.000	66 - 47	28.05 - 30.30	1.000
Others - d	134 - 132	11.16 - 12.16	0.000 ***	99 - 147	21.85 - 23.60	0.000 ***	66 - 281	28.05 - 34.20	0.000 ***
Others - e	134 - 40	11.16 - 14.68	0.000 ***	99 - 53	21.85 - 24.98	0.000 ***	66 - 34	28.05 - 39.00	0.000 ***
c - d	22 - 132	11.50 - 12.16	0.925	27 - 147	21.73 - 23.60	0.021 *	47 - 281	30.30 - 34.20	0.000 ***
c - e	22 - 40	11.50 - 14.68	0.000 ***	27 - 53	21.73 - 24.98	0.000 ***	47 - 34	30.30 - 39.00	0.000 ***
d - e	132 - 40	12.16 - 14.68	0.000 ***	147 - 53	23.60 - 24.98	0.009 **	281 - 34	34.20 - 39.00	0.000 ***

a - f represents different brands.
Low level: 2024 - 2nd, sample 1, Medium level: 2025 - 1st, sample 1, High level: 2023-1st, sample 1.
*** significant difference ($p < 0.05$), ** very significant difference ($p < 0.01$), *** extremely significant difference ($p < 0.001$).**

methodology has an important impact on the comparability of results. Methodology group analysis showed that method E (3- (2-helix adamantane) -4-methoxy-4 - (3-phosphoryloxy) -phenyl-1, 2-dioxycycloethane disodium salt labeled particle chemiluminescence method) was significantly different from all other methods at all

Table 3. The detection results of samples with different concentrations in different detection methods were compared.

Methods	Low level			Medium level			High level		
	N	Median	p-value	N	Median	p-value	N	Median	p-value
E - D	51 - 67	9.90 - 10.80	0.176	54 - 19	17.10 - 22.20	0.003 **	55 - 46	20.10 - 34.60	0.000 ***
E - F	51 - 71	9.90 - 10.80	0.011 *	54 - 50	17.10 - 21.90	0.000 ***	55 - 88	20.10 - 31.20	0.000 ***
E - A	51 - 77	9.90 - 11.20	0.002 **	54 - 74	17.10 - 21.63	0.000 ***	55 - 54	20.10 - 28.60	0.003 **
E - B	51 - 93	9.90 - 11.41	0.000 ***	54 - 172	17.10 - 21.53	0.000 ***	55 - 60	20.10 - 22.25	0.000 ***
E - C	51 - 145	9.90 - 12.05	0.000 ***	54 - 153	17.10 - 23.60	0.000 ***	55 - 289	20.10 - 34.10	0.000 ***
D - F	67 - 71	10.80 - 10.80	1.000	19 - 50	22.20 - 21.90	1.000	46 - 88	34.60 - 31.20	0.010 **
D - A	67 - 77	10.80 - 11.20	1.000	19 - 74	22.20 - 21.63	1.000	46 - 54	34.60 - 28.60	0.000 ***
D - B	67 - 93	10.80 - 11.41	0.001 ***	19 - 172	22.20 - 21.53	1.000	46 - 60	34.60 - 22.25	0.000 ***
D - C	67 - 145	10.80 - 12.05	0.000 ***	19 - 153	22.20 - 23.60	0.015 *	46 - 289	34.60 - 34.10	1.000
F - A	71 - 77	10.80 - 11.20	1.000	50 - 74	21.90 - 21.63	1.000	88 - 54	31.20 - 28.60	0.003 **
F - B	71 - 93	10.80 - 11.41	0.034 *	50 - 172	21.90 - 21.53	1.000	88 - 60	31.20 - 22.25	0.036 *
F - C	71 - 145	10.80 - 12.05	0.000 ***	50 - 153	21.90 - 23.60	0.000 ***	88 - 289	31.20 - 34.10	0.004 **
A - B	77 - 93	11.20 - 11.41	0.134	74 - 172	21.63 - 21.53	1.000	54 - 60	28.60 - 22.25	1.000
A - C	77 - 145	11.20 - 12.05	0.000 ***	74 - 153	21.63 - 23.60	0.000 ***	54 - 289	28.60 - 34.10	0.000 ***
B - C	93 - 145	11.41 - 12.05	1.000	172 - 153	21.53 - 23.60	0.000 ***	60 - 289	22.25 - 34.10	0.000 ***

A: acridine esterification chemiluminescence method, B: magnetic particle chemiluminescence method, C: electrochemiluminescence method, D: luminol/isoluminol labeled chemiluminescence method, E: 3- (2-helix adamantane) -4-methoxy-4 - (3-phosphoroyl) -phenyl-1, 2-dioxocyclic ethane disodium salt labeled microparticles chemiluminescence method and F: Others (methods used except A - E)
Low level: 2024 - 2nd, sample 1, Medium level: 2025 - 1st, sample 1, High level: 2023 - 1st, sample 1.
*** significant difference ($p < 0.05$), ** very significant difference ($p < 0.01$), *** extremely significant difference ($p < 0.001$).**

Table 4. Analysis of CA15-3 external quality assessment.

Evaluation indicators	Classification Criteria	Numerical value	2023-1st	2023-2nd	2024-1st	2024-2nd	2025-1st
Robust CV (%)	reagents classification	maximum	24.11	23.37	19.69	18.17	15.57
		minimum	4.87	5.06	4.96	5.58	3.64
		median	6.53	7.21	6.85	7.63	6.48
	methods classification	maximum	40.31	53.33	38.71	41.44	21.63
		minimum	5.49	4.68	5.81	6.08	5.05
		median	11.98	13.38	9.54	13.52	11.53
Pass Rate (%)	reagents classification	maximum	100.00	100.00	100.00	100.00	100.00
		minimum	54.55	66.99	76.15	69.40	75.76
		median	97.15	92.86	98.33	98.48	96.30
	methods classification	maximum	100.00	100.00	99.09	100.00	100.00
		minimum	56.82	52.22	46.32	51.61	71.51
		median	88.09	83.18	90.19	83.40	86.09

concentration levels, indicating that there may be problems in its detection performance. It is not recommended to use interchangeably with other methods without adequate validation. More noteworthy, the result of method B is concentration-dependent (magnetic particle chemiluminescence): it is consistent with the results of mainstream methods such as D, F, and A at low and medium concentration levels, but shows a significant negative deviation at high concentration levels. This phenomenon may be due to its "Hook effect" or insuf-

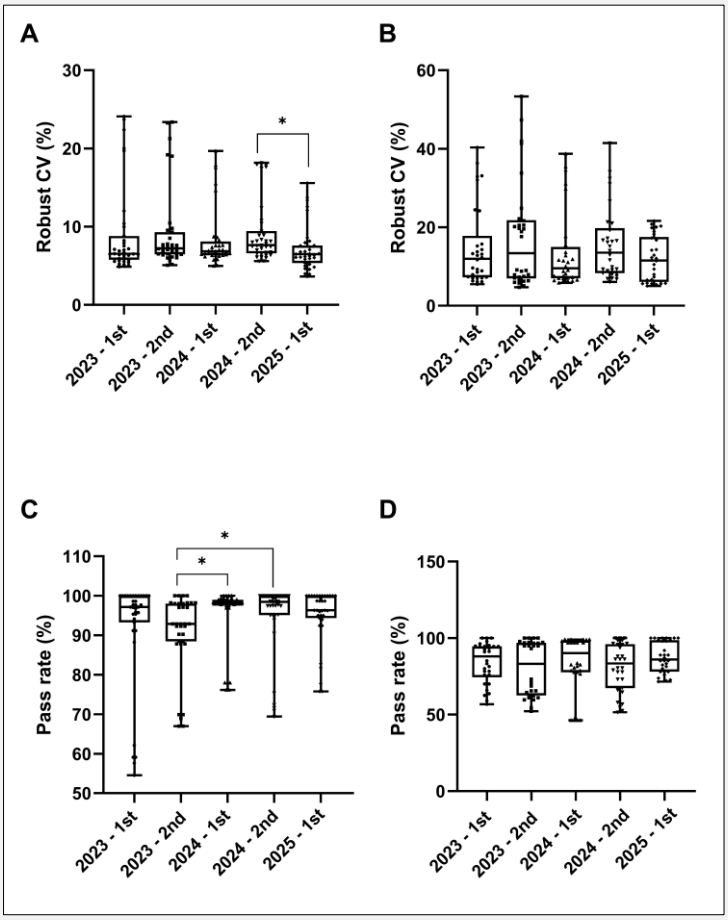

Figure 1. External quality assessment of CA15-3.

A: Robust CV analysis according to assay reagent category, B: Robust CV analysis according to test method, C: Pass rate according to assay reagent category, D: Pass rate according to test method.

ficient linear range in the region of high values, which would pose an extremely high risk for monitoring samples with high concentrations (such as patients with advanced or metastatic breast cancer), possibly leading to underestimation of results and clinical misjudgment. In contrast, methods D (luminol/isoluminol labeled chemiluminescence), F (other methods) and A (acridine esterification chemiluminescence) showed good agreement at low and medium concentration levels, suggesting that these methods may be currently more comparable and interchangeable choices.

The concentration level is a key variable affecting the inter-method agreement. This study clearly showed that most of the reagents and methods showed good consistency in low concentration samples (for example, brand f, brand c, others reagent groups showed no differences in low and medium levels; D, F, A, B methods showed no differences in low and medium levels). However, with higher concentrations, the differences become common and complex. This is consistent with the characteristic that CA15-3 itself often involves a wide concentration range in monitoring. Therefore, EQA programs or in-laboratory validation cannot rely on samples with only a single concentration, and must cover the entire range of clinically relevant low, medium, and high concentrations to fully assess the performance of the assay system.

Despite these differences, this study also offers positive signals: the median robust CV for reagent-based groups showed a downward trend from 2023 to 2025, and the median rate of qualified EQA was significantly higher in 2024 than in the second EQA in 2023, even though the tertiary hospitals accounted for the highest proportion in the first EQA of 2023. Although the proportion

of tertiary hospitals does not rise year on year, the performance was getting better. This reflects that testing quality is gradually improving in laboratories within the region and interlaboratory precision is improving through continued EQA participation and feedback. The core value of EQA is precisely to promote the comparability of laboratory results by identifying problems and promoting improvement.

In this study, the median value was used as the target value, which met the requirements of ISO 13528-2022 and ensured robustness to non-Gaussian distributed data. This approach minimizes the influence of common extreme outliers in multi-laboratory data sets. Robust statistics were used to deal with skewed distribution data, which reduced the interference of outliers compared with the mean. The iterative weighting algorithm was used to calculate the robust CV, which reduced the evaluation error for the highly skewed data group. The limit of deviation (CA15-3: $\leq \pm$ 20.83%) was derived from the Westgard biological variation database, which ensured a performance threshold of clinical relevance. The laboratories participating in EQA were divided into seven reagent groups (a - g) and six method groups (A - F) according to the reagents and methods. This method can separate the technical specific bias, optimize the equipment parameters, and provide reference for accurately locating the blind area of quality control.

The main use of tumor markers is in the long-term monitoring of cancer patients. If results come from laboratories that use different methods or if laboratories have to switch tests, this may affect the clinical interpretation of changes in trends. The differences in results may hinder the adoption of regional uniform judgment critical value and make its implementation difficult [13]. The study by Van Rossum HH et al. showed that the coordination state of CA15-3 can be significantly improved by recalibration of a limited number of measurement procedures [14]. In addition, the concordance status of CA125, CA15-3, and CA19-9 was found to be outside the minimum bias criterion and significantly different between testing systems by testing the EQA samples provided by six countries [10]. Xiao Y et al. analyzed the 8-year EQA results of six common tumor markers from 2006 to 2013, and showed that the robustness of CA125 and CA15-3 showed a downward trend, and the percentage difference was gradually decreasing, but the standardization and consistency among the test systems still needed to be improved [15]. This is consistent with our trend of 5 tests of CA15-3 from 2023 to 2025.

Although the samples in this study covered five concentration levels, the lack of extremely high or low clinical range concentrations and the failure to establish a reasonable concentration gradient may have underestimated the hook effect or sensitivity issues. Small sample sizes for some methods or reagents complicated longitudinal comparisons. Meanwhile, the EQA samples used in this study were mixed clinical samples, and their commutability was not validated. Additionally, the detailed calibration and quality control procedures of all participating laboratories were not obtained, and these factors might also contribute to the differences in the results.

For future EQA work, the following improvements are recommended: A correction and tracking system should be established for laboratories with low acceptance rates and precision. This system should facilitate the development of on-site audit and reagent recalibration programs and establish a real-time feedback loop.

Declaration of Generative AI in Scientific Writing:
This study was conducted without any AI help.

Declaration of Interest:
The authors declare that they have no conflicts of interests.

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