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Evaluation of the analytical performance of the Sysmex CS-2500 automated blood coagulation system

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Abstract

The aim of this study was to evaluate the analytical performance of the two new CS-2500 automated systems recently acquired by the laboratory. These are Sysmex automated systems that perform multiparametric haemostasis tests based on coagulometric, chromogenic and immunological principles with an optical detection system. The aim of this study was to evaluate their performance for prothrombin time (PT) and activated partial thromboplastin time (APTT) tests. Comparability results with the CS-2100 department's previous automated system showed high agreement between the systems, with high correlation coefficients (R ≥ 0.993). Intra-series and inter-series repeatability was less than 5%, demonstrating excellent measurement stability. The search for inter-sample contamination was negative. The automated systems showed excellent linearity over a wide range of values. All the results obtained during this evaluation point to very good analytical performance, making the CS-2500 suitable for medium- to high-activity haemostasis laboratories.

Keywords: Automatic Coagulation Analyzer; Performance; Sysmex CS-2100 - CS-2500.

1. Introduction

In medical biology laboratories, it is essential to evaluate the analytical performance of any automated device before its routine use, to guarantee the reliability of the results. This study focuses on the evaluation of the automated hemostasis systems, Sysmex® CS-2500, capable of performing routine hemostasis tests as well as platelet aggregometry analyses. The comparison was made with the previous model, the CS-2100, which has been in service for several years within the laboratory. Our evaluation focuses on two key parameters: prothrombin time (PT) and activated partial thromboplastin time (aPTT). These first-line tests are essential for the exploration of coagulation, evaluating the extrinsic and intrinsic pathways of the coagulation cascade, respectively. This study aims to ensure that the introduction of the CS-2500 maintains the quality and reliability of analytical results while ensuring a smooth transition in our laboratory practices.

Objective of the Study

The main objective of this study is to evaluate the performance of the two new Sysmex CS-2500 analysers for haemostasis testing, focusing on the two parameters used as first-line coagulation tests: prothrombin time (PT) and activated partial thromboplastin time (APTT). This assessment includes tests of comparability, repeatability, accuracy and bias analysis, as well as linearity and inter-sample contamination. By applying standardised evaluation protocols in accordance with the recommendations of the Clinical and Laboratory Standards Institute (CLSI) [3]. We will examine these parameters to assess the efficiency, reproducibility and linearity limits of the systems.

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2. Materials and Methods

2.1. Principle of tests

The measurement principle is based on the optical method with turbidimetric detection of clot formation for the coagulometric technique, the use of a fluorochrome for the chromogenic technique and finally, for the immunological technique on the turbidimetric detection of the formation of antigen-antibody complexes.

2.2. Population studied

Blood samples were collected from patients hospitalized at the Mohammed VI University Hospital in Marrakech for coagulation assessments, in Plus blood collection tubes (BD Vacutainer, 9NC; BD, Plymouth, UK) containing sodium citrate 0.109 mol/l in a ratio of 9/1: blood/citrate, by international recommendations [4]. Blood samples were centrifuged at 3000 × g for 15 min. Lipemic, icteric and hemolyzed samples were excluded. Samples were analyzed within 4 hours of collection. The comparability study covered a total of 40 samples for each parameter. A total of 10 samples were used for the repeatability study.

2.3. Experimental procedures

The Analyses were performed using the Sysmex CS-2500 and CS-2100 analysers for the comparability study under the following conditions:

2.3.1. Prothrombin time (PT):

- Method: Coagulometric.
- Reagents: Innovin®.
- Protocol: Measurement of the time required for clot formation after addition of thromboplastin and calcium to citrated plasma at 37°.
- Quality control: Normal and pathological control plasmas.

2.3.2. Activated partial thromboplastin time (aPTT):

- Method: Coagulometric.
- Reagents: Actin FS® and Actin FSL® (used to research the anticoagulant lupus), the two TCA reagents FS and FSL are used to decide between normal and pathological.
- Protocol: Measurement of the time necessary for clot formation after activation of the intrinsic pathway with cephalin and an activator at 37°.
- Quality control: Normal and pathological control plasmas.

2.4. Evaluation criteria

The following tests were carried out for each of the two CS2500 systems to be evaluated:

- Comparability: The comparability of measurements is assessed by calculating the correlation coefficients (R) between the results obtained with each of the CS-2500 analyzers and the CS2100 for each coagulation parameter. Bland-Altman plots are also used to visualize the differences between measurements of the two systems and quantify the agreement between them.
- Repeatability: Assay repeatability is assessed by measuring intra-assay coefficients of variation (CV%) according to the Clinical and Laboratory Standards Institute (CLSI) guidelines [3]. Ten replicates of each sample are analyzed 10 times in succession to determine intra-assay variability.
- Accuracy and Bias: Precision biases are assessed by comparing results obtained with CS-2500 analyzers to established reference methods [1.5].
- Linearity: Linearity is assessed by analyzing samples with increasing concentrations of coagulation parameters. Samples are diluted gradually to cover a wide range of values. The correlation coefficients (R^2) are calculated for each test to confirm this linearity.
- Contamination study: Inter-sample contamination was evaluated by analyzing the following sequence 6 times: 3 successive measurements of pathological plasma followed by 3 successive measurements of normal plasma for each parameter.

2.5. Statistical Analysis

The data obtained is statistically analyzed to evaluate the performance of the CS-2500 analyzers. IBM SPSS Statistics is used to compare test score averages between the two systems. Linear regression tests are applied to assess the correlation and linearity of measurements using Bland-Altman difference plots.

3. Results

3.1. Prothrombin time (PT)

3.1.1. Comparability

Correlation between PT Measurements (Prothrombin Time):

The correlation between Prothrombin Time (PT) measurements in seconds obtained with the CS-2500 and CS-2100 analyzers is very high, with a correlation coefficient of 0.997. In addition, the correlation between the TP measurements expressed as a percentage (%), carried out with the two machines, is also solid, with a coefficient of 0.962. Finally, the correlation of the INR (International Normalized Ratio) values between the machines CS-2500 and CS-2100 is equally high, with a coefficient of 0.997. This demonstrates excellent agreement between the two systems for the evaluation of these parameters.

Bland-Altman diagrams

Bland-Altman diagrams were used to visualize the differences between the measurements of the two automata (Figure 1): For the prothrombin time (PT) in seconds, the majority of points are located near the mean line, with few dispersions, which indicates good agreement between the measurements of the two systems. Concerning the TP expressed as a percentage, although most of the points are also close to the mean line, a slight dispersion is observable. However, the differences remain within acceptable limits. Finally, for the INR, the majority of points are again close to the mean line, with low dispersion, confirming good agreement between the measurements of the two machines for this parameter.

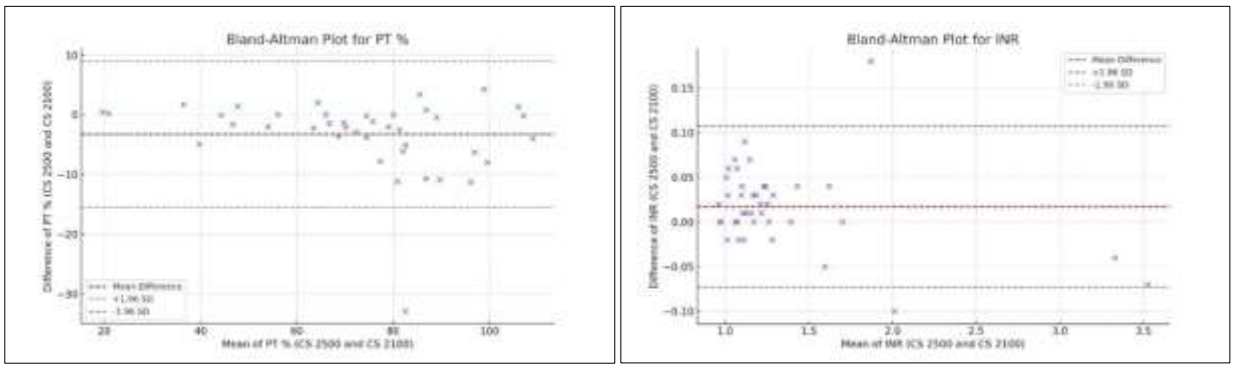

Figure 1 Bland-Altman plots of comparisons of prothrombin time and INR measurements.

3.1.2. Repeatability

Table 1 Measurement of coefficients of variation (CV%)

Type	Average TP (Sec)	PT Standard Deviation (Sec)	CV% PT (Sec)	Average PT (%)	Average PT (%)	CV% PT (%)	Average INR	INR standard deviation	CV% INR
Normal	13.69	0.088	0.64%	82.02	0.68	0.83%	1.18	0.03	2.54%
Pathological	36.24	0.16	0.44%	22.41	0.12	0.52%	3.49	0.06	1.72%

The results show very good repeatability of the two machines for normal and pathological measurements, with low coefficients of variation for both types of measurements (Table 1).

3.1.3. Measurement accuracy

To assess the accuracy of the CS-2500 measurements, we compared the results obtained by the CS-2500 with the reference values available in the CS-2400/2500 system application guide [6]. The percentage differences from the target mean were calculated using the formula:

$$\text{Percentage difference} = \frac{\text{measured result - target mean}}{\text{Target mean}} \times 100$$

The mean of the results obtained was calculated to assess total effect and bias. The Clinical Laboratory Improvement Amendments (CLIA) [7] has determined an acceptable accuracy percentage of less than 15%. The CS-2500 machines show good accuracy for PT measurements. Biases are small and most differences are within the 95% confidence limits, indicating that both systems provide reliable and consistent results.

3.1.4. Linearity study

To assess the linearity of the CS-2500 measurements, regression analyses were carried out for the parameters PT SEC, PT % and INR. The coefficients of determination (R^2) were calculated to assess the linearity of the measurements.

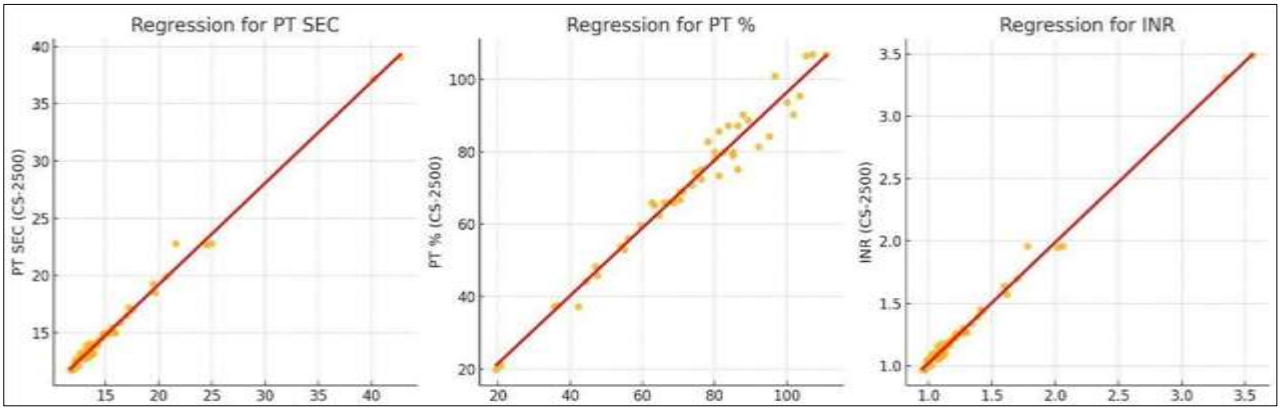

Figure 2 Regression plots of comparisons of prothrombin time and INR measurements.

The regression analyses carried out for the prothrombin time in seconds (PT SEC) showed a high correlation (R^2 = 0.999), and for the percentage of PT (PT %), the regression graph revealed an equally high correlation (R^2 = 0.998). Finally, the regression analysis for INR also showed an excellent correlation (R^2 = 0.997). These results confirm that both automata produce linear and reliable measurements over a wide range of values (Figure 2).

3.1.5. Contamination

The contamination study was carried out to evaluate the ability of the CS-2500 automated systems to avoid cross-contamination between samples. Pathological samples were measured followed by normal samples to detect any contamination.

No contamination between samples was observed. The contamination index C% was calculated at 0.11% (limit: 2%).

3.2. Activated partial thromboplastin time (aPTT)

3.2.1. Comparability

Correlation between APTT (activated partial thromboplastin time) measurements

The correlation between activated partial thromboplastin time (aPTT) measurements obtained with the CS-2500 and CS-2100 automated systems revealed the following results: for the parameter APTT SEC, the correlation is R=0.993, while for APTT FS-R, it reaches R=0.994. These high correlations indicate a strong agreement between the measurements of the two automata for the TCA parameter.

Bland-Altman diagrams: were used to visualize the differences between the measurements of the two machines (Figure 3):

APTT SEC: The majority of points are close to the mean line with low dispersion. The red lines representing the 95% confidence limits show that most of the differences fall within this interval, indicating good agreement between the measurements from the two automata.

APTT FS-R: Likewise, the majority of points for APTT FS-R are close to the mean line with little dispersion. The 95% confidence limits also show that most of the differences are in this interval, confirming good agreement between the measurements of the two automata.

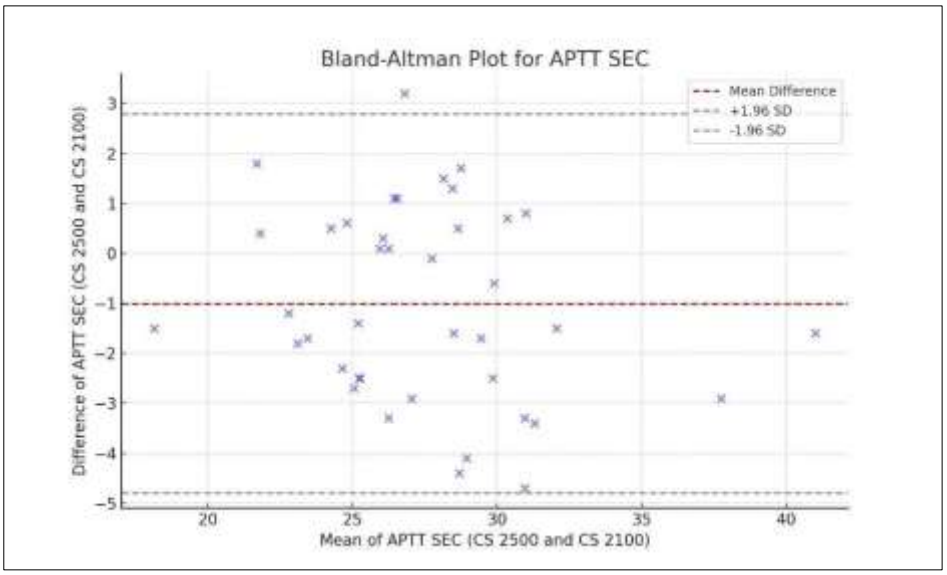

Figure 3 Bland-Altman plots of TCA time measurement comparisons**.**

3.2.2. Repeatability

Repeatability analysis was performed on CS-2500 analyzers using normal and pathological samples for APTT SEC and APTT FSR parameters. The results show very good repeatability, indicated by low coefficients of variation (CV%) (Table 2).

Table 2 Measurement of coefficients of variation (CV%)

Type of Measurement	Average APTT SEC	CV% APTT SEC	Average APTT FSR	CV% APTT FSR
Normal	29.00	0.26%	1.09	0.41%
Pathological	39.03	0.46%	1.46	0.76%

3.2.3. Measurement accuracy

To assess the accuracy of the CS-2500 automata, we compared the results obtained with the reference values of the CS-2400/2500 system application guide [6]. The average of the results obtained was calculated to assess the total effect and bias., the results are follows:

APTT SEC: Average of 28.6 seconds, standard deviation of 0.5, bias of -1.4.

APTT FSR: Mean of 1.17, standard deviation of 0.1, bias of 0.07.

The CS-2500 automatons show good accuracy for TCA measurements, with low biases.

3.2.4. Linearity study

To investigate linearity, linear regression curves were plotted, and correlation coefficients were calculated for the APTT SEC and APTT FSR parameters (Figure 4).

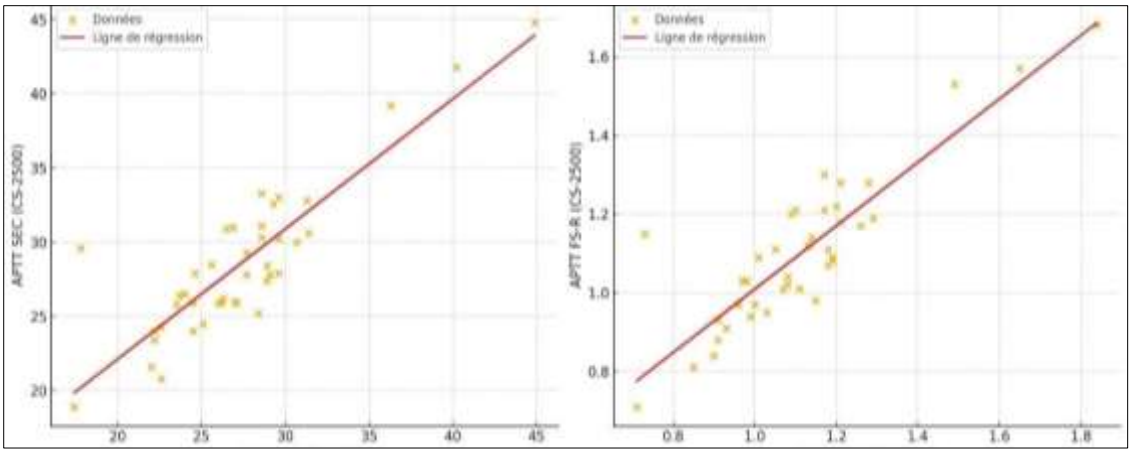

Figure 4 Regression plots of TCA measurement comparisons.

The CS-2500 analyzers demonstrate excellent linearity for TCA measurements, with high correlation coefficients indicating a strong linear relationship between actual concentrations and measured values. These results confirm the ability of the two automatons to provide precise and reliable measurements over a wide range of concentrations.

3.2.5. Contamination

No contamination between samples was observed. The contamination index C% was calculated at 0.11% (limit: 2%).

4. Discussion

The results of this comparative study show a strong agreement between the measurements obtained with the Sysmex CS-2100 and CS-2500 automated systems for the parameters of prothrombin time (PT) and partial thromboplastin time with activator (aPTT). The high correlation coefficients ($R \geq 0.993$) indicate that the two machines produce very similar results for these coagulation tests. The Bland-Altman plots confirm this good agreement by showing that the majority of differences between measurements are within the 95% confidence limits, which is consistent with expectations for high-precision laboratory systems.

Repeatability analysis revealed very low coefficients of variation (CV%) for normal and pathological measurements with both machines. This indicates excellent stability and reliability of the measurements made by the CS-2500. For example, for prothrombin time (PT), the CV% are 0.83% and 0.52% for normal and pathological samples, respectively. These results demonstrate that both systems provide satisfactory intra-assay and inter-assay precision, essential for routine clinical use.

Accuracy evaluation showed that the CS-2500 controllers provide reliable and consistent results compared to established reference values. Precision biases are small and most differences are within the 95% confidence limits. For example, for the TQ, the automatons show minimal biases compared to the target values, thus confirming their ability to produce precise measurements. These results are in line with the performance criteria defined by the Clinical Laboratory Improvement Amendments (CLIA) [7], which require an acceptable precision percentage of less than 15%.

The linearity study showed very high coefficients of determination (R^2) for the parameters analyzed, including PT SEC, PT%, INR, APTT SEC and APTT FSR. These results indicate an excellent linear relationship between the actual concentrations and the values measured by the two automata. For example, the correlation coefficient for PT SEC is 0.999, confirming an accurate linear response over a wide range of concentrations. This linearity is crucial to ensure that the analyzers can provide accurate and reliable measurements, even at varying concentrations of coagulation parameters.

The study of inter-sample contamination showed that there was no contamination detected between pathological and normal samples. The contamination index (C%) was calculated at 0.11%, well below the acceptable limit of 2%. This indicates that the CS-2500 controllers are effective in preventing cross-contamination, ensuring the integrity of measurement results.

The results of this study are comparable to those found in the literature. A study conducted by Martin-Toutain et al. [1] showed that the Sysmex system exhibits intra-assay and inter-assay coefficients of variation below 5% for most parameters. Similarly, a performance evaluation of the CS-2500 revealed coefficients of variation below 3.5% for the TP-INR and APTT tests [8].

5. Conclusion

The usage modalities of the CS-2500 automated system during this study were straightforward, and the overall assessment of the laboratory was very positive. The results obtained suggest that the CS-2500 analyzers are suitable for medium to high-activity hemostasis laboratories. However, certain improvements, particularly in terms of reagent and sample management, could further optimize their daily use. These systems demonstrate significant potential for broader adoption, especially with updates to integrate missing features and enhance waste management.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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