Evaluation of the Roche CoaguChek XS Handheld Coagulation Analyzer in a Cardiac Outpatient Clinic

Myung-Hyun Nam,¹ Kyoung Ho Roh,¹ Hui-Nam Pak,² Chang Kyu Lee,¹ Young-Hoon Kim,² Kap No Lee,¹ and Yunjung Cho¹
Departments of ¹Laboratory Medicine and ²Internal Medicine, College of Medicine, Korea University, Seoul, Korea

Abstract. This study evaluated the performance of a handheld coagulation analyzer for measurements of capillary blood specimens of 93 outpatient cardiology patients with atrial fibrillation who were receiving oral anti-coagulant therapy. The international normalized ratio (INR) results of the CoaguChek XS system (Roche Diagnostics) were compared with those obtained in the central laboratory with citrated venous blood specimens using the ACL9000 coagulation analyzer (Instrumentation Laboratory). The INR results for prothrombin time by the CoaguChek XS analyzer were closely correlated with the central laboratory’s results in the INR range of 0.96~8.53 (r = 0.964). A statistically significant difference was noted between 2 lots of test strips, but the difference was miniscule (mean ± 95% confidence interval: 0.04±0.02). The CV of 8 replicate assays with the CoaguChek XS for a blood specimen with high INR value (INR=3.9) was 1.4%; for a blood specimen with medium INR value (INR=1.3), the CV of 8 replicate assays was <0.1%. This study shows that the CoaguChek XS analyzer is precise and reliable for assessment of INR results at clinically significant ranges in cardiac outpatients.

Keywords: coagulation analyzer, point-of-care testing, prothrombin time, INR

Introduction

Point-of-care (POC) measurement of capillary blood prothrombin time (PT) and the international normalized ratio (INR) for patients receiving oral anti-coagulation therapy was introduced in the early 1990s. Since then, many POC devices for INR assays have been introduced. Measuring the INR with POC devices has several advantages over measurements in the laboratory. POC devices do not require a venipuncture, thus increasing convenience and safety. Because the INR result is displayed immediately, the POC device facilitates communication between the physician and patient. These features enable physicians to monitor the INR frequently and adjust the warfarin dose.

The CoaguChek XS system (Roche Diagnostics, Mannheim, Germany) is a recently introduced POC system for INR measurement, which has improved features compared with previous CoaguChek systems. The aim of this study was to evaluate the analytical performance of this system in a cardiac outpatient clinic.

Materials and Methods

Patients. This study was performed at the cardiac outpatient clinic of Korea University Anam Hospital. Patients with atrial fibrillation who were taking warfarin for oral anti-coagulation therapy were enrolled in this study. The protocol was approved by the Institutional Review Board and the participants all signed informed consent before beginning the study. Ninety-three patients (65 men, 28 women) participated in the study and no patients were drawn more than once. The patients' mean age was 62 yr (range 43-83 yr).

Coagulation analyzer. The CoaguChek XS system consists of a hand-held meter, test strips, a code chip containing
calibration information, and a lancing device. Measurement begins by inserting a test strip into the meter and placing a small drop of capillary blood, obtained by finger prick, on the strip. Each finger prick of capillary blood was collected just before venipuncture for central laboratory analysis. All finger prick procedures were performed by a skilled technician. After about 1 min, the result is displayed as INR, %Quick, or PT ratio. In the present study, only the INR values were used for analysis.

**Reference method.** The INR results of the CoaguChek XS were compared with the INR results obtained in our central laboratory with citrated venous blood samples, using an ACL 9000 coagulation analyzer (Instrumentation Laboratory, Lexington, MA, USA). The thromboplastin reagent was PT-Fibrinogen HS (Instrumentation Laboratory), which had an ISI of 1.39.

**Lot-to-lot variation.** Three lots of test strips for the CoaguChek XS analyzer were used to evaluate lot-to-lot variation. The lot numbers tested were: 20149531 (lot a), 20149334 (lot b), and 20149131 (lot c).

During venipunctures to obtain citrated blood for INR analysis in the central laboratory, 42 additional venous blood specimens were drawn into plain tubes without anticoagulant. With a pipette, 15 µl of each whole blood specimen was immediately applied to a test strip from each lot and the INR results were obtained with 3 different CoaguChek XS analyzers.

**Analytical precision.** Venous whole blood specimens from 2 patients with high and medium INR values were selected for a study of analytical precision. Immediately after being

![Fig. 1. Scatter plot of the relationship between INR results by the CoaguChek XS and the central laboratory (ACL 9000) assay (n = 93, r = 0.964, y = 1.010x + 0.088).](image1)

![Fig. 2. Bland-Altman bias plot for INR results by the CoaguChek XS and central laboratory (ACL9000) INR assays. The graph shows the agreement between the paired results as a function of increasing INR.](image2)

![Fig. 3. Mean differences between the INR results with 3 different lots of test strips for the CoaguChek XS. The error bars and values in parentheses are the 95% confidence intervals. Each lot of test strips is designated by a letter; eg, a - b represents the mean difference between INR results obtained with lots a and b.](image3)
drawn, each sample was applied to 8 test strips and measured simultaneously with 8 different CoaguChek XS analyzers.

**Statistical methods.** The differences of INR values between 3 different test strip lots were analyzed by repeated measures ANOVA. The INR results obtained by the CoaguChek and the central laboratory were compared by linear regression. A Bland–Altman plot was used to assess the magnitude of disagreement between the CoaguChek XS and the central laboratory INRs [1]. The statistical analyses were performed using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA) and p values <0.05 were considered significant.

**Results**

**Comparison of CoaguChek XS and central laboratory INR results.** The mean INR values (with ranges in parentheses) for the central laboratory and CoaguChek XS were 2.08 (0.96 – 8.53) and 2.02 (0.9 – 6.9), respectively. Based on linear regression analysis of these data, the CoaguChek XS INR values were closely correlated with the central laboratory INR values (r = 0.964, y = 1.010x + 0.088, Fig. 1). The Bland–Altman difference plot of the data is shown in Fig. 2. The mean difference of INR results (CoaguChek XS minus central laboratory) was -0.07.

**Lot-to-lot variation of test strips.** Forty-two venous blood specimens were used to determine lot-to-lot variation of INR assays using 3 different lots of test strips. As shown in Fig. 3, the mean differences (with 95% confidence intervals in parentheses) were -0.01 (-0.03 ~ 0.01) between lots a and b, 0.04 (0.02 ~ 0.06) between lots b and c, and -0.03 (-0.06 ~ -0.01) between lots c and a, respectively. Based on repeated measures ANOVA, a significant difference was observed (p = 0.003) among the INR values obtained with the 3 lots of test strips. Paired comparisons of these data (Fig. 3), showed that only the miniscule mean difference (0.04) between the INR values for lots b and c was statistically significant (p = 0.01).

**Precision.** Based on simultaneous replicate assays with 8 different CoaguChek analyzers, a blood sample with high INR value (mean INR = 3.9) yielded a CV of 1.4%. A blood sample with a medium INR value (mean INR = 1.3) yielded a CV of <0.1%.

**Discussion**

Warfarin is a widely used anti-thrombotic agent for thromboembolic prophylaxis. However, the narrow therapeutic window and the substantial inter-individual and intra-individual variation in the biological effect of such vitamin K antagonists require frequent INR monitoring. For this reason, many POC devices have been developed for INR monitoring of warfarin therapy. The CoaguChek XS system is a newly introduced point-of-care (POC) coagulation analyzer. This system detects the activity of thrombin, instead of detecting a clot by mechanical or optical methods. The test strip contains reagents such as human recombinant tissue factor and a peptide substrate (Electrocyme TH), which reacts with thrombin to generate an electrical signal. The human recombinant tissue factor used in the CoaguChek test strip has low international sensitivity index (ISI) standards.

This study evaluated the performance of the CoaguChek XS in an outpatient clinical setting. The agreement of INR results of the CoaguChek XS with INR results in the central laboratory was excellent; the correlation coefficient of this study (r = 0.964) was higher than in other recently published articles that evaluated the CoaguChek XS system (r = 0.91 and 0.835, respectively) [2,3]. This may be due to the relatively small number of samples tested and a lower set of INR values in the present study, compared with the previous studies. We enrolled patients with only a single disease entity, while the previous groups included assorted patients receiving long-term oral anti-coagulant therapy.

Several criteria have been proposed to determine whether two INR values will result in the same warfarin dosing decision [4]. These criteria rely primarily upon the numerical distance of the INR values from one another and whether the INRs are within the target therapeutic range. The suggested maximum numerical distances between two INR values that result in the same warfarin dosing varied from 0.2 to 0.9. In our study, the mean INR difference between the CoaguChek XS value and the central laboratory value was 0.14, which is lower than the suggested criteria. There were 5 cases where the INR differences exceeded 0.5 units. In one case, the INR result of the CoaguChek XS
assay was less than that of the ACL9000 assay (6.9 vs 8.5). In 3 cases, results of the CoaguChek XS exceeded those of ACL9000 (5.2-5.5 vs 4.1-4.4). In the fifth case, the INR result was 1.5 for the CoaguChek assay vs 2.3 INR for the ACL9000 assay. In this instance, the warfarin dosing decision might be different for each result because the INR result for the POC assay was below the therapeutic range and that for the central laboratory assay was within the reference range.

In our study, the ISI value of the thromboplastin reagent for the ACL9000 assay was 1.39, which is higher than in a previous study [2]. Because the INR result depends on the ISI value, our correlation might have been even better if the reference method used thromboplastin reagent with a lower ISI.

The INR determination in the central laboratory involves liquid quality control materials. The CoaguChek XS system uses integrated quality control with an “on board single channel strip control” (OS2C). Calibration information is stored in the code chip, which is provided for each lot of test strips. There is a risk of inconsistency between lots of test strips. Variations were evident between lots of the strips used in the previous CoaguChek S system [5,6]. In our evaluation of 3 lots of test strips for the CoaguChek XS system, a statistically significant difference was noted among the INR results. The INR results with lot b averaged 0.04 units higher than with lot c, but this difference was much less than the criteria for clinically significant differences mentioned above [4].

Since no available stable quality control material was available for the CoaguChek XS system, we used fresh blood samples from two patients for the evaluation of precision, and we measured each sample 8 times. The CV (1.4%) of the high INR value sample in our study was less than that reported (5.5%) in another study evaluating the CoaguChek XS system [3]. Our CV was also significantly lower than reported CV values for the CoaguChek S system (3.3-5.5%) [7-10].

In conclusion, the new CoaguChek XS system provides precise and reliable results for INR assays to monitor patients treated with an oral anticoagulant in an outpatient setting.

Acknowledgement

We thank Roche Diagnostics Korea for providing the CoaguChek XS analyzers and test strips.

References