



Letter to the Editors-in-Chief

Evaluation of the analytical and clinical performance of the Micropoint qLabs INR point-of-care system



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1. Introduction

The anticoagulation status of patients receiving vitamin K antagonists (VKA) should be monitored and INR values should be within a pre-defined therapeutic range to prevent both thrombotic and bleeding complications. Point-of-care (POC) INR meters are widely used for self-monitoring and self-management. The qLabs POC INR meter is an interesting new meter since it has Bluetooth function and lower costs for both the meter and strips as compared to the commonly used POC CoaguChek-XS meter.

Previous studies [1,2] on patients using oral anticoagulants showed variable performance of the qLabs meter and only one of these studies mentioned an aspect of the user-friendliness. Additionally there are no data comparing the qLabs meter with laboratory methods that use Innovin or HemosIL RecombiPlasTin. Therefore the aim of this study was to evaluate the analytical and clinical performance and the user-friendliness of the qLabs POC meter as compared to two central laboratory methods using Innovin, HemosIL RecombiPlasTin and the CoaguChek-XS.

2. Material and methods

2.1. Study population and sample collection

80 self-monitoring patients receiving VKA were included after informed consent. From each patient two venous blood samples were obtained for two central laboratory INR measurements: CS5100 (Sysmex) with Dade Innovin reagent (Siemens, lot 539270) at Meander Medical Center, Amersfoort, and ACL-TOP 300 (Werfen) with HemosIL RecombiPlasTin 2G reagent (Werfen, lot N1143467) at the thrombosis unit 'het Gooi', Hilversum, the Netherlands. The venous samples were followed by 2 alternating capillary blood droplets for the POC CoaguChek-XS (Roche Diagnostics, Mannheim, Germany, strip lot 206195-12) and the POC qLabs INR meter (Micropoint Biotechnologies, Inc., Shenzhen, China, strip lot 3050G0905). The study was performed on 5 separate days. On day 3, a second qLabs meter (qLabs2, strip lot 3050G0305) was added to the study. qLabs1 and qLabs2 meters are similar (same model), except qLabs2 is slightly modified by a minor software enhancement (i.e. longer heating time).

The same investigator obtained all venous and capillary samples. Since the qLabs meter was a new POC device the investigator was trained and qualified by the manufacturer. The investigator was trained to work with the CoaguChek-XS by an experienced employee according to the manufacturer instructions. The study protocol was approved by the local scientific committee. The strips used were all certified by the Dutch Coagulation Reference Lab, dept. of Clinical Chemistry and Laboratory Medicine of Leiden University Medical Centre, and were compliant with the WHO standard rTF09. The INR devices meet the requirements for the ISO-17593 verification.

2.2. Analytical performance

Accuracy was evaluated by correlation, (Deming) regression and Bland-Altman plots [3]. Mean difference and standard deviation (SD) was calculated and compared with student's paired *t*-test (two-tailed) using Graphpad Prism. A mean INR difference of ± 0.2 INR compared to the laboratory method is defined as accurate [4].

Two results from qLabs1 were defined as outlier due to extreme values compared to the laboratory INR (CS5100 INR 5.4 vs qLabs1 INR 9.1 and CS5100 INR 3.8 vs qLabs1 INR 0.9). For qLabs2, 1 result was defined as outlier (CS5100 INR 4.1 vs qLabs2 INR 1.6). No explanation was found for these outliers, the meters reported no error codes. One tube for ACL-TOP laboratory INR measurement was lost.

2.3. Clinical performance

INR results were determined to be clinically different when the paired POC and laboratory INR differed $\geq 15\%$ [5]. In addition we used 2 models to assess whether differences between POC and laboratory INR would result in different VKA dosing. The first model is based on the clinical agreement criteria based on the method of Anderson [6] and Douketis et al. [7]. Paired INR results are in agreement when meeting one of the following criteria: a) both INR measurements are within the patient's therapeutic range b) both are above therapeutic range and these pairs are within 0.8 INR units, c) both are below therapeutic range and these pairs are within 0.4 INR units, or d) one is within therapeutic range and the pair is within 0.5 INR units.

Secondly, INR results were analyzed according to the guidelines of

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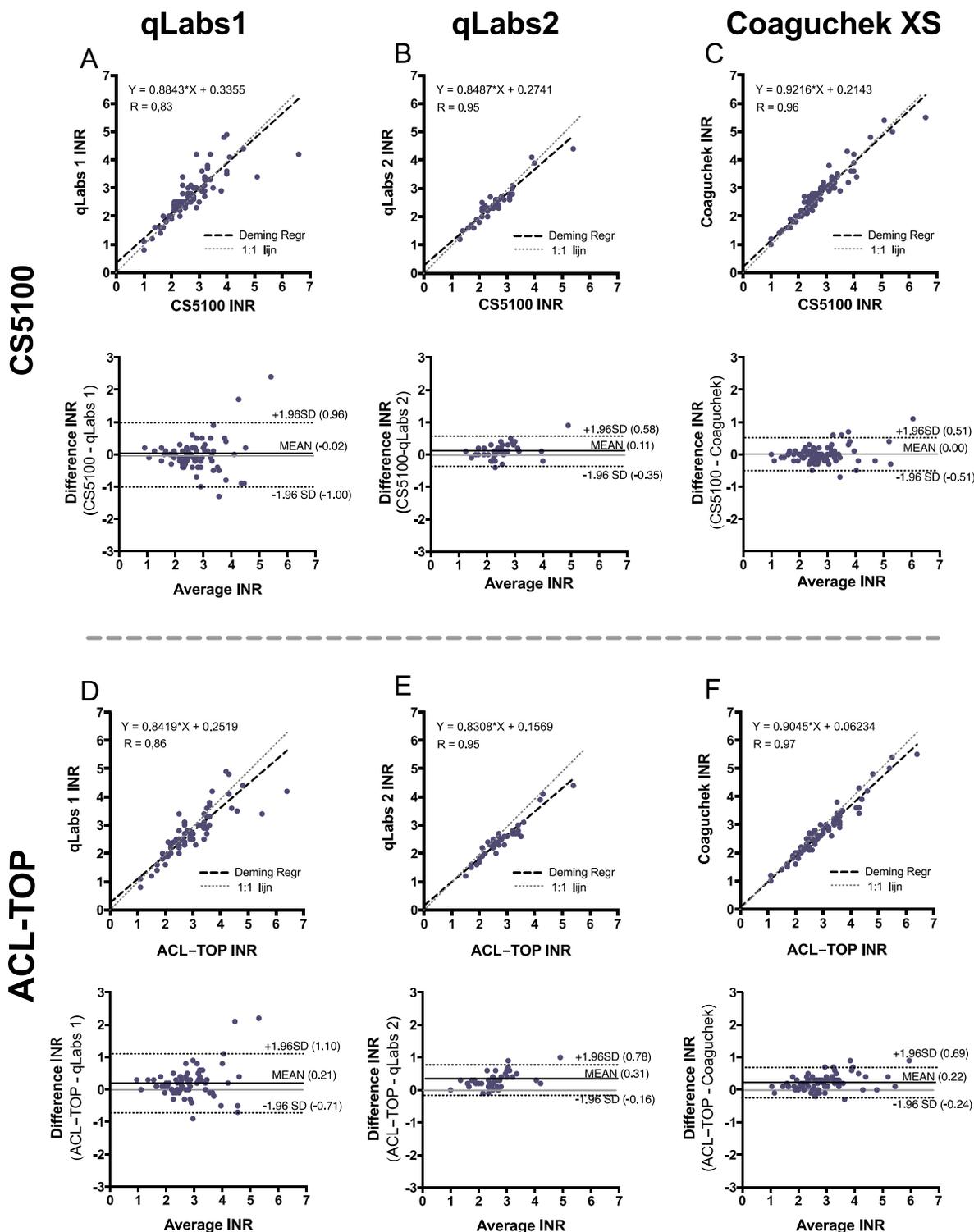


Fig. 1. A, B, C: Correlation (upper graphs) and Bland-Altman difference plots (lower graphs) of venous INR determined on the Sysmex CS5100 with Dade Innovin (Siemens) reagent plotted against the different POC-INR coagulometers A) qLabs1, B) qLabs2 and C) CoaguChek-XS. D,E,F: Correlation (upper graphs) and Bland-Altman difference plots (lower graphs) of venous INR determined on the Werfen ACL-TOP with HemosIL recombiplastin (I.L) reagent plotted against the different POC-INR coagulometers D) qLabs1, E) qLabs2 and F) CoaguChek-XS. In the Bland-Altman plots, the continuous gray line represents the zero line. The black line represents the mean difference (bias) and the dotted lines 95% limits of agreement.

the Dutch Federation of Anticoagulation Clinics, which uses INR range: 2.0–3.0 for the low intensity group and 2.5–3.5 for the high intensity group [8]. The INR results were interpreted according to the patients' own therapeutic range and were categorized as being below, within or above their therapeutic range.

3. Results

3.1. Analytical performance

Correlation of qLabs1 INR with both laboratory methods was modest (R 0.83–0.86), this was confirmed by the wider limits of

Table 1

Effects on vitamin K antagonist dosing. A) Percentage of clinical agreement between POC and laboratory INR according to clinically relevant agreement criteria. B) Percentage (and absolute number) of INR results below, within or above the patient's own therapeutic range.

A				
	qLabs2	CoaguChek-XS	ACL-TOP/CS5100	
Agreement with CS5100	98%	98%	100%	
Agreement with ACL-TOP	93%	95%	100%	
B				
	Laboratory INR		POC INR	
Therapeutic range	CS5100 (N = 80)	ACL-TOP (N = 79)	qLabs2 (N = 42)	CoaguChek-XS (N = 80)
Below range	17% (14)	10% (9)	22% (9)	15% (12)
Within range	64% (51)	60% (47)	71% (29)	66% (53)
Above range	19% (15)	30% (23)	7% (3)	19% (15)

agreement in the Bland-Altman plots (Fig. 1). The investigator was trained more extensively after day 2 and subanalysis of qLabs1 measurements on day 3 to 5 showed a good correlation with both laboratory methods (R 0.92, data not shown). This suggests that the results from qLabs1 during the first 2 days were due to inappropriate use of the meter. Both qLabs2 and CoaguChek-XS had a $R > 0.95$ with both laboratory methods. With respect to the bias, qLabs2 measured slightly but significantly lower than the CS5100 (-0.11 INR \pm 0.24, $P < 0.01$). The bias of qLabs2 with ACL-TOP was larger (-0.31 \pm 0.23, $P < 0.001$). This is due to the bias between both laboratory methods; the ACL-TOP measured on average 0.22 INR \pm 0.16 SD ($P < 0.001$) higher than the CS5100 (data not shown).

3.2. Clinical performance

Given the practical problems qLabs1 was excluded from further evaluation. Between qLabs2 and CS5100 and also between CoaguChek-XS and CS5100, only a few INR results (7%, 3/42 and 8% (6/80) respectively) were clinically different. However, between qLabs2 and ACL-TOP a much larger number of results (24%, 10/41) were clinically different, which is due to the more pronounced bias between ACL-TOP and qLabs2.

According to the clinical agreement criteria, the bias of qLabs2 with the two laboratory methods, does not lead to pronounced dosing differences, since the clinical agreement of qLabs2 with CS5100 and ACL-TOP was good (98% and 93% respectively) and was comparable with the CoaguChek-XS (Table 1A). On the contrary, when analyzing the results according to the guidelines of the Dutch Federation of Anticoagulation Clinics, qLabs2 shows more INRs below range and less above the therapeutic range (Table 1B).

3.3. User-friendliness

The main difficulty of the qLabs meter is that it should be placed on a stable surface. Therefore, the patients' finger should be moved to the meter. Additionally, the investigator reported difficulties with changing batteries and a longer time for the meter to report the result compared to the CoaguChek-XS. The qLabs strips were packed separately, which is an advantage, since it provides better protection from moisture and dirt.

4. Discussion and conclusion

In this study we evaluated the analytical and clinical performance and the user-friendliness of the qLabs POC INR meter. qLabs2 shows good correlation with two laboratory methods (Sysmex, Innovin and ACL-TOP, HemosIL RecombiPlasTin). However a slight but significant bias is observed. This bias is most pronounced when the qLabs meter is compared to the ACL-TOP laboratory method and exceeds > 0.2 INR over the whole range. This results in a substantial amount of INRs that are clinically different. However this bias does not affect the VKA dosing according the clinical agreement criteria of Anderson [6] and Douketis et al. [7]. According to the guidelines of the Dutch Federation of Anticoagulation Clinics, qLabs2 shows substantial differences, i.e. more INRs below the therapeutic range and less above compared to the other methods. Also other studies [9] showed that small INR differences can result in dosing differences. This suggests that with qLabs2 more patients would receive a VKA dose increase. Importantly, there is no absolutely true INR and whether the differences in dosing would lead to more long-term bleeding complications or to less thrombotic complications should be investigated in future studies.

The differences between our study and previous studies [1,2] may be due to improved quality of the strips, the quality of the meter or the appropriate use of the meter. The strips used in our study are compliant with the WHO standard, which is a requirement for introduction in the Netherlands. Given the extra training and the strict way of using the meter to obtain accurate results, this may have played a role in the better analytical and clinical performance results in this study, as compared to Dillinger et al. [1].

It is important to realize that judgment of the performance of a POC-INR meter depends on the laboratory instrument it is compared to. Since a bias between methods may have clinical consequences, it is essential to, in addition to the analytical performance, investigate the effect on VKA dosing. Preferably by the dosing method used within its own institute.

In conclusion, the qLabs meter in this prospective observational study shows good correlation with the two laboratory methods used. The meter measured significantly lower than the two laboratory methods. The extend of this bias and the effect on VKA dosing is dependent on which laboratory method it is compared with. Extensive training was necessary to obtain good analytical results and the overall user-friendliness of this meter can be improved.

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Conflict of interest

Micropoint Biotechnologies, Inc., Shenzhen, China has provided the qLabs1 and qLabs2 POC-INR meters and corresponding strips.

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