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Letter to the Editors-in-Chief

Precision and accuracy of the new XPrecia Stride mobile coagulometer

1. Introduction

Oral anticoagulation therapy (OAT) with coumarins (vitamin K antagonists) is generally used for both prophylactic and therapeutic use in patients at increased risk of thromboembolism [1]. In this contest, prothrombin time (PT) International Normalized Ratio (INR) monitoring is fundamental to adjust OAT dosage in order to prevent bleeding complications or thrombotic events [1]. In the last years, INR point-of-care testing (POCT) has evolved from both primary healthcare providers and patients, for receiving laboratory results more rapidly and especially for reducing the amount of required sample volume. Although POC devices have shown acceptable accuracy and reliability for clinical setting, several limitations in comparison with the standard plasma-based methodologies have been reported in various conditions, such as increased INR level [2,3]. Here are presented the first results obtained by the new Xprecia Stride Coagulation Analyzer (Siemens Healthcare Diagnostics) in comparison to those determined by the traditional cs 2100i Sysmex Siemens in order to evaluate the possible inclusion of the Xprecia Stride in the routinely clinical practice.

2. Material and methods

2.1. Study population and sample preparation

This pilot study was conducted at the Clinical Laboratory and Molecular Diagnostics of the National Institute of Research and Care of Aging, INRCA-IRCSS, Ancona, Italy. The sample consisted of 163 patients, 67 men and 96 women (mean age = 77.4 years old (yo); from 50 yo to 92 yo) all under Warfarin OAT (inclusion criteria) for whom the INR was assessed. The power of the study was set as 95% (more details on Supplemental Material). Patient written inform consents were obtained to collect fingerstick and venous specimens. The study protocol complied with the Helsinki II declaration and was approved by the local scientific committee.

Subjects provided two separate whole blood samples: a) venous blood by venepuncture for PT/INR determination by the traditional cs 2100i Sysmex (Siemens Heathcare) and b) capillary blood via finger puncture for immediate PT/INR testing by the Xprecia Stride Coagulation Analyzer. The samples were processed and analysed immediately after collection, according to the routine procedures of the laboratory.

A complete description of the Xprecia Stride coagulation analyzer can be found at the Siemens website [4].

Abbreviations: OAT, oral anticoagulation therapy; PT, prothrombin time; INR, International Normalizes Ratio; POCT, point-of-care testing; CV, Coefficient of Variation; SD, standard deviation; CHAID, Chi-squared Automatic Interaction Detector; CI, confidence interval; LQC, Liquid Quality Control.

2.2. Determination of precision, accuracy and overall agreement

Precision of XPrecia Stride coagulation analyzer was evaluated both on Liquid Quality Control (LQC PT 1 and LQC PT 2, Siemens Healthcare) and on human samples (more details on Supplemental Material). Two INR ranges were considered: a) $1.0 < INR < 2.0$; b) $2.0 < INR < 3.0$. Data, expressed as Coefficient of Variation (CV %) and mean of standard deviations, were obtained after five repeated measures for each sample.

Analytical accuracy was evaluated by calculating the mean difference from the value measured by the traditional method and the mean percentage absolute relative deviation (MRD).

The agreement between the two INR measurements was evaluated through the Cohen's kappa coefficient, the Bland-Altman proportional bias and the Lin's concordance correlation coefficient.

The diagnostic accuracy was evaluated according to the definition by Poller et al. [5] where a deviation of ≥15% was defined as clinically important.

2.3. Statistical analysis

SPSS Version 22.0 was used for analysis. Statistical tests were based on One-way ANOVA ($p < 0.05$) considering: a) 3 groups based on INR levels: group 1 ($n = 41$) with $1 < INR < 2$, group 2 ($n = 103$) with $2 < INR < 3$ and group 3 ($n = 19$) with $3 < INR < 4$, and b) 4 groups based on age: group 1 ($n = 10$) with age < 65 yo, group 2 ($n = 41$) with 65 < age < 75 yo, group 3 ($n = 89$) with 75 < age < 85 yo and group 4 ($n = 23$) with age > 85 yo. More details on Supplemental Material.

3. Results and discussion

In this pilot study, the new Xprecia Stride mobile Coagulometer showed a mean INR value slightly lower ($n = 163$; mean difference = -0.16 ± 0.23; $p < 0.05$) than that one obtained by the traditional cs 2100i Sysmex Siemens (Table 1). Considering also the MRD = 6.78%, the analytical accuracy was in line with other known devices (2, 6). Precision was evaluated in both LQC (PT 1 and PT 2) and in human samples. In the latter resulted excellent both in INR range 1.0–2.0 ($n = 5$; mean CV = 0.64%; SD mean = 0.006 INR units) and in INR range 2.0–3.0 ($n = 5$; mean CV = 0.37%; SD mean = 0.010 INR units). Also LQC samples showed acceptable precision both in INR range 1.0–2.0 (LQC PT 1: mean CV = 2.8%) and in INR range 2.0–3.0 (LQC PT 2: mean CV = 3.0%).

Agreement between the two measures showed also good results in comparison to those obtained from other devices [2,6]. In fact, while Lin's Concordance resulted substantial (0.962) and the Cohen's Kappa coefficient showed results "from fair to good" (Kappa = 0.646; 95% CI, 0.547–0.748), the Bland-Altman Proportional Bias showed almost the same mean difference between the two measures in all the three INR

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Table 1
Comparison between INR Lab and INR POCT within Age groups in each INR group.

INR group	Age group	Stat	N	INR Lab mean (SD)	INR POCT mean (SD)	p^*
Overall	77.4 (7.9)		163	2.31 (0.55)	2.15 (0.59)	$p < 0.05$
1 < INR < 2	65 < age < 75	b	7	1.61 (0.30)	1.57 (0.37)	ns
	75 < age < 85	c	25	1.64 (0.24)	1.48 (0.27)	$p < 0.05$
	age > 85	d	9	1.79 (0.17)	1.68 (0.16)	ns
2 < INR < 3	age < 65	a	9	2.34 (0.26)	2.22 (0.44)	ns
	65 < age < 75	b	29	2.35 (0.25)	2.23 (0.41)	ns
	75 < age < 85	c	55	2.37 (0.28)	2.19 (0.37)	$p < 0.01$
	age > 85	d	10	2.40 (0.31)	2.15 (0.20)	$p < 0.05$
3 < INR < 4	age < 65	a	1	3.20	3.40	–
	65 < age < 75	b	5	3.44 (0.24)	3.28 (0.33)	ns
	75 < age < 85	c	9	3.45 (0.25)[a]	3.26 (0.37)	ns
	age > 85	d	4	3.21 (0.08)	3.12 (0.49)	ns

p^*: comparison analysis between INR Lab and INR POC by one-way ANOVA.
INR: International Normalized Ratio; SD: standard deviation.
[a] $p < 0.05$; statistically significant different with respect to the value of the Age group 4 (age > 85) of the same INR group.

ranges (Fig. 1). In the overall population, for differences with 95% limits of agreement, INR POCT differed from the INR Lab from −0.3 INR to 0.6 INR (Fig. 1a). The mean difference of the INR measurements was 0.13 (±1.96 SD, −0.22, 0.48) in the lower range (1.0–2.0 INR, Fig. 1b), 0.17 (±1.96 SD, −0.3, 0.64) in the medium range (2.0–3.0 INR) and 0.14 (±1.96 SD, −0.37, 0.65) in the higher range (3.0–4.0), respectively (Fig.1 b-d). Considering all the population, only the 5% was outside the CI. In the ranges 1.0–2.0, 2.0–3.0, 3.0–4.0, the patients outside the CI were 2.4%, 4.2% and 10%, respectively. An explication to the consistent INR difference in the whole INR range could be addressed to the same Dade® Innovin® reagent that was used by both Xprecia™ and Sysmex. This feature indeed exclude any possible bias due to the coagulation reagent.

In order to understand whether the statistical difference between the two measures was dependent on sex and/or on the age of the population, a generalised linear model was developed. The test of model effect showed that INR values are strictly related to gender ($p < 0.001$) and age ($p < 0.001$) (Supplemental Table 3). However, although the difference between the two measures were not gender dependent (Supplemental Tables 1 and 3), patients with age above 75 yo showed the highest difference in almost all INR ranges (Table 1 and Supplemental Table 4).

Concerning sensitivity, the table of agreement displayed the best results in the INR range 1.0–2.0 which count 95.1% of patients within the same INR group obtained by the traditional system (Supplemental Table 5). Concerning specificity, the best result was found in INR range 2.0–3.0 which count 92.7% of the measures within the same group obtained by the traditional system (Supplemental Table 5).

Regarding clinical accuracy, XPrecia Stride showed values > 15% than those obtained from Sysmex in 20% of the population study. Considering that other devices, considered clinically acceptable, overstep this limit

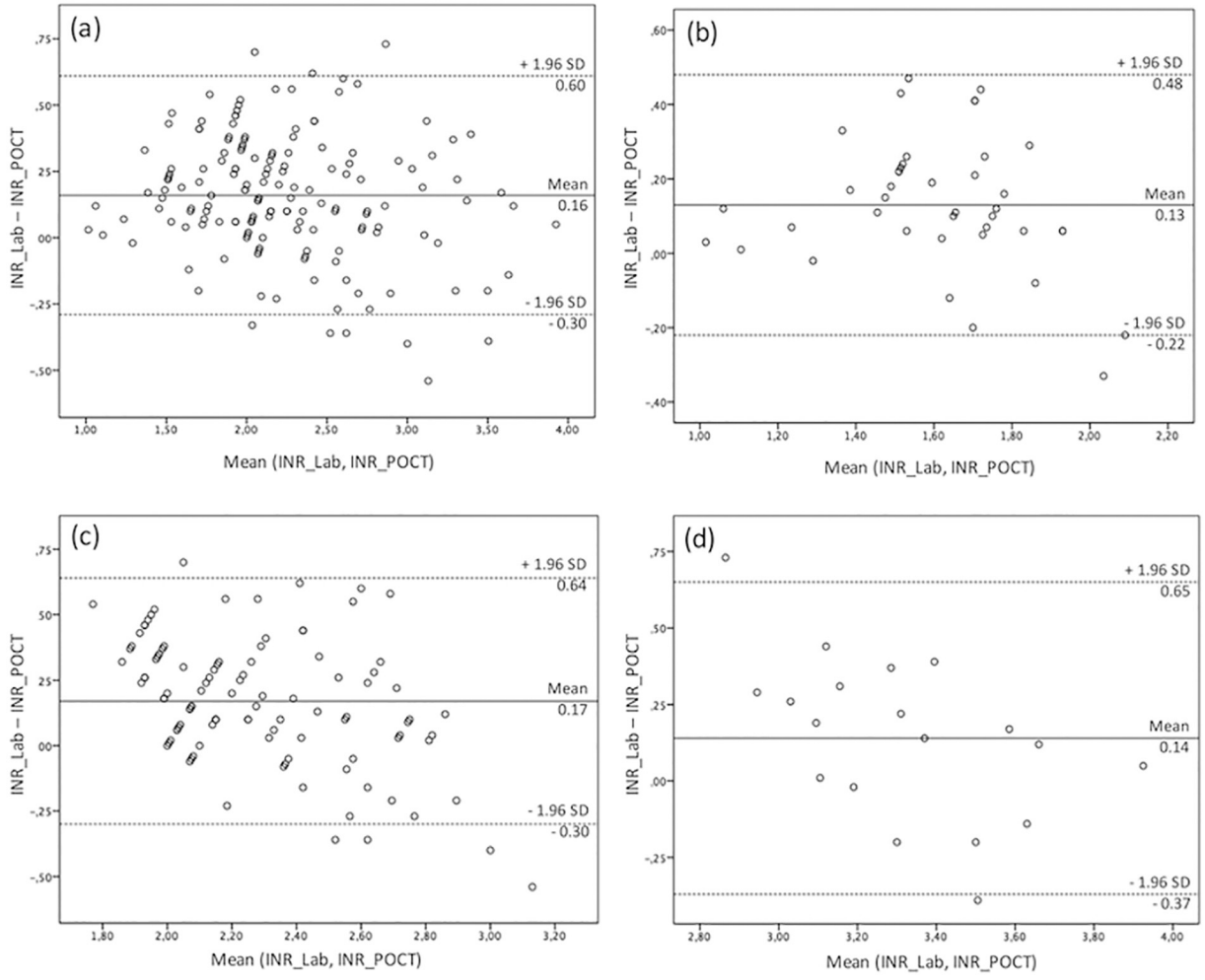

Fig. 1. Bland Altman plot. In the overall population, the mean difference between INR Lab and INR POCT is 0.16 with 95% limits of agreement from −0.3 INR to 0.6 INR (Fig. 1a). The mean difference of the INR measurements is 0.13 (±1.96 SD, −0.22, 0.48) in the lower range (1.0–2.0 INR, panel b), 0.17 (±1.96 SD, −0.3, 0.64) in the medium range (2.0–3.0 INR) and 0.14 (±1.96 SD, −0.37, 0.65) in the higher range (3.0–4.0), respectively (panels b–d). Considering all the population, 5% of subjects are outside the CI (panel a). In the ranges 1.0–2.0, 2.0–3.0, 3.0–4.0, subjects outside the CI are 2.4%, 4.2% and 10%, respectively (panels b–d).

in 40% of cases [7], this pilot study places the new XPrecia Stride at least at the same level of the most used commercially devices. In this study, most of cases which deviation from the Sysmex value was above 15%, had an INR (Sysmex) between 2.0 and 3.0 (15% of the overall population) whereas only 4% had an INR between 1.0 and 2.0 (Supplemental Fig. 2). Considering that no "under-estimated" cases were present above 3.0 INR and no "over-estimated" cases were present below 1.5 INR (the higher risk conditions for bleeding and thromboembolism, respectively), we can conclude that this mobile coagulometer has positive perspectives for the implementation in a clinical setting.

4. Conclusions

This first experimental study with the new Xprecia Stride mobile coagulometer (Siemens) clearly demonstrates excellent precision, acceptable accuracy and overall good agreement of this POC device in comparison both with the traditional laboratory instruments (i.e. Sysmex) and with the well-known mobile coagulometers (i.e. CoaguChek). Whether analytical and clinical results need to be improved through a larger trial in order to obtain firm conclusions on the reliability and the limits of this device, the XPrecia showed deep outcomes in terms of daily practice in clinical setting, safety and the possibility to be implemented for self-tests and self-management. The onscreen tutorials, the auto-calibration and the test strip eject button represent concrete advantages for both patients (especially elderlies) and clinicians. Concerning the future of mobile coagulometers in a contest where NOACs are the way for treatment of atrial fibrillation (AF) and venous thromboembolic disease, probably NOACs limits showed in some pathological conditions such chronic kidney disease (from moderate to severe), will keep warfarin still mainly prescribed from most of clinicians. In this contest, an improvement of both analytical and clinical accuracy of mobile coagulometers is mandatory.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.thromres.2017.05.032.

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Conflict of interest

None.

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Francesco Piacenza
Translational Research Centre of Nutrition and Aging, Scientific and Technological Pole, National Institute of Health and Science on Aging, INRCA-IRCCS, Ancona, Italy
Corresponding author at: Translational Research Centre of Nutrition and Aging, National Institute of Health and Science on Aging, IRCCS-INRCA, Via Birarelli 8, 60121 Ancona, Italy.
E-mail address: f.piacenza@inrca.it.

Roberta Galeazzi
Clinical Laboratory and Molecular Diagnostics, INRCA-IRCCS, Ancona, Italy

Maurizio Cardelli
Advanced Technology Center for Aging Research, Scientific and Technological Pole, National Institute of Health and Science on Aging, INRCA-IRCCS, Ancona, Italy

Fausto Moroni
Clinical Laboratory and Molecular Diagnostics, INRCA-IRCCS, Ancona, Italy

Mauro Provinciali
Elisa Pierpaoli
Advanced Technology Center for Aging Research, Scientific and Technological Pole, National Institute of Health and Science on Aging, INRCA-IRCCS, Ancona, Italy

Simona Giovagnetti
Stefania Appolloni
Francesca Marchegiani
Clinical Laboratory and Molecular Diagnostics, INRCA-IRCCS, Ancona, Italy

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