ORIGINAL ARTICLE

Accuracy and clinical utility of the CoaguChek XS portable international normalised ratio monitor in a pilot study of warfarin home-monitoring

Luke R Bereznicki, Shane L Jackson, Gregory M Peterson, Ella C Jeffrey, Katherine A Marsden, David M Jupe

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See end of article for authors' affiliations

Correspondence to: Mr L R Bereznicki, Unit for Medication Outcomes Research and Education, Tasmanian School of Pharmacy, Private Bag 83 Hobart, Hobart Tasmania, Hobart 7001, Australia; Luke.Bereznicki@utas.edu.au

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Aim: To evaluate the accuracy of the CoaguChek XS international normalised ratio (INR) monitor compared with the laboratory method.
Methods: The accuracy and ease of use of the recently marketed CoaguChek XS portable INR monitor was evaluated in 17 patients involved in a trial of warfarin home monitoring. INR results from the monitor were compared with those from the laboratory method. Clinical applicability was measured by discrepant INR values, defined in the literature by expanded and narrow agreement criteria, and by the proportion of INR values differing by >15% and by >20% from those derived by the laboratory method.
Results: Participants provided 59 comparison INR measurements for analysis. The paired results were highly correlated (r = 0.91). Expanded and narrow agreement between paired INR values occurred 100% of the time. Only three CoaguChek XS (5.1%) results differed by >15% compared with the laboratory method; no results differed by >20% or were discrepant by >0.5 INR units.
Conclusions: In the hands of patients the CoaguChek XS showed good correlation with laboratory determination of INR and compared well with expanded and narrow clinical agreement criteria. Both patients and doctors were highly satisfied with the accuracy and ease of use of the CoaguChek XS.

The effectiveness and safety of warfarin is maximised by the maintenance of a target international normalised ratio (INR) range, below which effectiveness is lost, and above which the bleeding risk is unacceptably high.[1] The key objective of point-of-care testing is to provide a fast, accurate result so that appropriate treatment can be started or treatment modified, leading to an improved clinical state or economic benefits.[2] In a previous study, we found that general practitioners suggested that the availability of portable INR monitors would assist in the management of their patients with atrial fibrillation and would perhaps increase their prescribing of warfarin for atrial fibrillation.[3]

The CoaguChek XS portable INR moniter (Roche Diagnostics, Basel, Switzerland) was released in October 2005 and, although the results of the master lot calibration have been published,[4] its accuracy has not been assessed in clinical practice to date, particularly through comparison with the laboratory method when used by patients. The objective of this study was to assess the accuracy and clinical utility of the CoaguChek XS monitor, when used by patients to perform weekly self-testing in a pilot study involving communication to and from the general practitioner via the Internet.

MATERIALS AND METHODS

Participants and point-of-care procedure

This evaluation was undertaken as a component of a warfarin home-monitoring pilot study. The pilot study involved 22 patients recruited from southern Tasmania, Australia who were both interested in home monitoring of anticoagulation and had access to the Internet at their home. In all, 17 of these patients received two training sessions to enable self-monitoring; the first involved theoretical aspects of anticoagulation treatment and a practical demonstration of the CoaguChek XS, and the second involved revision and practical testing to ensure that the INR monitoring technique was adequate. In the time between the first and second sessions (usually 1 week), patients completed at least two comparison tests consisting of a home test with the CoaguChek XS and a laboratory INR test at the patient's usual laboratory within 4 h of each other. These results were documented by the research team and if the CoaguChek XS INR differed by >15% compared with the laboratory INR, the patient was asked to conduct another comparison test. If further tests were >15% discrepant, the patient was excluded from the trial.

Once two comparison tests were completed and were within 15% of the corresponding laboratory values, the patient entered the pilot study and completed home monitoring once weekly. External quality control was completed every second month via the laboratory method while the patient was enrolled in the study, or at the discretion of the patient's general practitioner. Patients enrolled in the pilot study spent up to 3 months self-monitoring. The pilot study was granted ethics approval by the Tasmanian Human Research Ethics Committee Network, and all patients and doctors provided written consent.

The CoaguChek XS is a portable coagulometer that measures the INR using whole blood obtained by fingerprick. It has been designed specifically for use by non-health professionals. The procedure involves insertion of a test strip into the monitor and application of a drop of blood onto the test strip. The monitor uses an amperometric (electrochemical) method to determine the prothrombin time after activation of coagulation with thromboplastin within the test strip. The prothrombin time is then converted to an INR using the international sensitivity index (ISI), determined for the batch of test strips, found on the control chip. The CoaguChek XS uses a recombinant human thromboplastin with an ISI value close to 1. An INR result is provided within 1 min of application of the blood sample to the

Abbreviations: INR, international normalised ratio; ISI, international sensitivity index

Table 1 Comparison of CoaguChek XS and laboratory international normalised ratio results

Parameter*	CoaguChek XS	Laboratory	p Value
INR, mean (SD)	2.31 (0.52)	2.38 (0.46)	0.01
Mean difference (SD)	−0.07 (0.06)		df=58
			t=−2.56
Percentage within 0.5 INR units	100		
INR value, n (%)	59 (100)	59 (100)	
⩽1.9	19 (32.2)	10 (16.9)	
Mean INR (SD)	1.79 (0.15)	1.95 (0.19)	p<0.01
Mean difference (SD)	−0.16 (0.08)		df=19
			t=−4.29
Percentage within 0.5 INR units	100		
2.0–3.5	39 (66)	48 (81.4)	
Mean INR (SD)	2.38 (0.45)	2.46 (0.39)	p<0.01
Mean difference (SD)	−0.08 (0.06)		df=48
			t=−2.71
Percentage within 0.5 INR units	100		
⩾3.6†	1 (1.7)	1 (1.7)	

INR, international normalised ratio.
*Mean differences are between the paired INR values that may or may not have been in the same INR subgroup.
†Statistical analysis not completed, given only one value.

test strip. An INR result is not displayed if internal quality control conditions are not met. The new model offers several improvements over the previous model (CoaguChek S), including improved ease of use, reduced size, the use of a recombinant human thromboplastin with a lower ISI and internal quality control included on the test strip.

Laboratory procedure

Patients used their normal pathology collection centre or general practitioner for venepuncture for comparison INRs, which were sent to a central pathology laboratory. Thus, the CoaguChek XS method was compared with the patient's usual testing method. The laboratory method consisted of phlebotomist nurses drawing venous samples of blood into 0.138 M sodium citrate tubes at several pathology collection sites. Centrifuged samples were then analysed in a centralised laboratory with CA1500 (Sysmex, Kobe, Japan, distributed by Dade Behring in Australia). The thromboplastin used by the laboratory was Thromborel S (Dade International, Miami, Florida, USA), which had an ISI of 1.08.

Comparison of techniques

Clinical agreement was measured by discrepant INR values that could have resulted in a different clinical decision. Discrepancy was defined as the percentage of INR results from the CoaguChek XS that was different from the laboratory in the categorisation of the individual patient's INR value. The INR categories were nominated as 1–1.9, 2–3, 3.1–3.9 and 4–4.9.

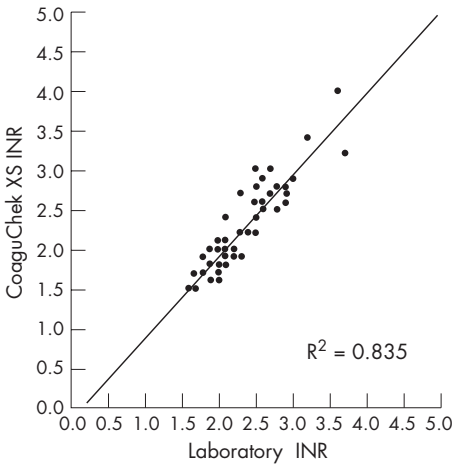

Figure 1 Relationship between CoaguChek XS and laboratory INR values.

Published criteria for clinical agreement (expanded and narrow)[5] were also assessed. Expanded agreement was achieved if both the CoaguChek XS and the laboratory INR were within, above or below the target range, or the difference between the CoaguChek XS and the laboratory INR when one of the pair was within the targeted range was no more than 0.5 units. Narrow agreement was achieved if both the CoaguChek XS and the laboratory INR were within the patient's targeted range, both the CoaguChek XS and the laboratory INR were above the targeted range and the values were within 0.8 units, both the CoaguChek XS and the laboratory INR were below the therapeutic range and the values were within 0.4 units, or the difference between the CoaguChek XS and the laboratory INR was no more than 0.5 units when only one of the pair was within the targeted range.

The attitudes of patients who used the CoaguChek XS and their doctors were assessed using a questionnaire featuring visual analogue scales to quantify the answers.

Statistical methods

Accuracy of the CoaguChek XS was determined by comparing the INRs from the monitor and the laboratory by linear regression analysis. A Bland–Altman plot[6] was used to assess the magnitude of disagreement between the monitor and the laboratory INRs. A paired t test ($p<0.05$ considered significant) was used to compare the INR values from the CoaguChek XS and laboratory methods. A χ^2 test was used to compare categories of INR results obtained by both methods ($p<0.05$ considered significant).

RESULTS

In all, 17 of the initial 22 patients entered the pilot study and successfully completed training requirements. Five patients did not attend training sessions and did not go on to use the CoaguChek XS. A total of 59 comparison INRs (CoaguChek XS and laboratory INR within 4 h of each other) were completed either on entry into or during the trial by the participants (median age 73 years; 12 male and 5 female). Table 1 shows the mean INR values for the CoaguChek XS and laboratory methods, and the status of anticoagulation. The CoaguChek XS INR values were significantly correlated with the laboratory

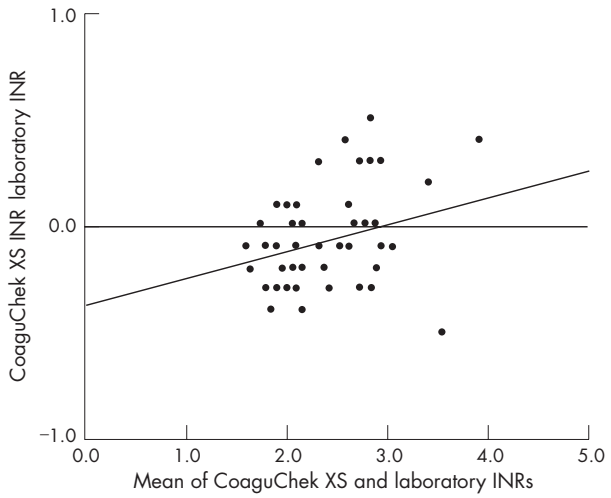

Figure 2 Bland–Altman style bias plot for CoaguChek XS and laboratory INR values.

INR values ($r = 0.91$, $p = 0.01$; fig 1). The mean (standard deviation (SD)) difference in INR values (laboratory minus CoaguChek XS) was 0.07 (0.06) ($t = 2.56$, $df = 58$, $p = 0.01$). The CoaguChek XS method was more likely to underestimate the INR, relative to the laboratory, particularly at INR values of <3. In all, 3 of 59 (5.1%) CoaguChek XS tests differed by >15% compared with the corresponding laboratory INR. No CoaguChek XS INRs differed from their corresponding laboratory INRs by >20%. Similarly, no paired INR tests differed by >0.5 INR units. Figure 2 shows the Bland–Altman style plot.

Table 2 shows the categorisation of laboratory and CoaguChek XS INRs. There was a significant relationship between the two methods ($\chi^2 = 77.0$, $df = 6$, $p<0.001$). Discrepant categorisation of the INR value between the laboratory and CoaguChek XS methods occurred in 20.3% (12/59) of cases—that is, 79.7% (47/59) of CoaguChek XS values were placed in the same nominal category as the laboratory INR. Most of the discrepant values were falsely low (10/12, 16.9% of all values), whereas 2 of 12 (3.4% overall) results overestimated the laboratory INR. Expanded and narrow agreement criteria were met for all paired values.

Patients gave a median score of 7.5/10 when asked how easy they found the CoaguChek XS to use, and a median score of 9/10 when asked how confident they were with the accuracy of the CoaguChek XS compared with the laboratory method ($n = 15$). Doctors responded with a median score of 8.2/10 when asked how confident they were with the accuracy of the CoaguChek XS ($n = 16$).

DISCUSSION

In a study designed to test the accuracy of CoaguChek XS INR determination compared with laboratory-determined INR, we found the CoaguChek XS to be 100% accurate against expanded and narrow agreement criteria.[5] This compares favourably with data from other previously published studies by the authors, where the CoaguChek S model was found to be between 90% and 93% accurate against expanded agreement criteria, and between 88% and 90% accurate against narrow agreement criteria.[7 8] Previous studies by the investigators with the CoaguChek S model found that INRs were categorised in the same nominal range on 69%[7] and 85%[9] of occasions. This study found that 80% of dual INR results were in the same category.

The correlation ($r = 0.91$) between INR results determined by the CoaguChek XS and those by the laboratory method was similar to that seen in prior studies of earlier models of the CoaguChek ($r = 0.89$–0.97).[7–10] Regression analysis is only a measure of correlation, not accuracy; a far superior measure is the Bland–Altman analysis.[6] This plot provides a more accurate representation of disagreement for a given mean INR by both methods. Both of these analyses indicated a general underestimation of the INR, which needs to be considered in the interpretation of INR results provided by the CoaguChek XS monitor. This was also shown in prior evaluations of the CoaguChek S device.[7–9] All dual measurements were within 0.5 INR units in this study, which compares well with figures of 83%,[7] 85%[9] and 88%[8] reported by the investigators in previous evaluations of the CoaguChek S. As with prior evaluations, the CoaguChek XS was more accurate when within the bounds of the therapeutic INR range. This finding has also been observed with other portable INR monitors.[11–13]

The accuracy data for the CoaguChek XS in this study are particularly impressive in light of a number of potential variables. The users of the CoaguChek XS were not researchers or even health professionals, but were patients who were generally elderly and had received two training sessions regarding the use of the monitor. Additionally, a number of pathology collection sites were used. From these results, it could be extrapolated that if the CoaguChek XS was implemented in community practice, and if appropriate training was provided to patients interested in self-monitoring, the CoaguChek XS would provide accurate and dependable results.

This accuracy comparison is limited by a small number of comparison results and patients. However, given the diversity of the users of the CoaguChek XS in this study, the monitor performed extremely well and is probably a testament to the ease of use of the device. The previous model, CoaguChek S, performed similarly well when used by a variety of users in general practice and community pharmacy.[8 9]

The CoaguChek XS performed admirably in this pilot study. In addition to being highly accurate, participants found it simple to use, and both doctors and patients were highly satisfied with its performance. Despite the disadvantage of having been used by 17 different patients, and blood having been drawn at different pathology collection centres, the CoaguChek XS was highly accurate compared with the laboratory method. Thus, the CoaguChek XS has the potential to become a part of everyday practice for doctors as well as

Table 2 Comparison of international normalised ratio categories for CoaguChek XS and laboratory results (values given as percentage of laboratory readings)

		CoaguChek XS				
	INR range	**1–1.9**	**2–3**	**3.1–3.9**	**4–4.9**	**Total**
Laboratory	1–1.9	90 (9)	10 (1)	—	—	100 (10)
	2–3	22 (10)	78 (36)	—	—	100 (46)
	3.1–3.9	—	—	67 (2)	33 (1)	100 (3)

INR, international normalised ratio.

Take-home messages

- The CoaguChek XS is a new portable coagulometer that has not been previously evaluated in clinical practice.
- The CoaguChek XS is accurate compared with the pathological method.
- Trained patients are able to use the CoaguChek XS in their home to provide a fast and reliable international normalized ratio (INR) result.
- General practitioners and patients are highly satisfied with the accuracy of the device in clinical practice.
- Further evaluation is required to determine the accuracy and precision of the device for INR results outside standard INR target ranges.

patients who are willing to self-monitor or manage their warfarin treatment.

Authors' affiliations
Luke R Bereznicki, Shane L Jackson, Gregory M Peterson, Ella C Jeffrey, Unit for Medication Outcomes Research and Education, School of Pharmacy, University of Tasmania, Hobart, Australia
Katherine A Marsden, David M Jupe, Department of Haematology, Royal Hobart Hospital, Hobart, Australia

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