

Precision and accuracy of CoaguChek S and XS monitors: The need for external quality assessment

Leon Poller

European Action on Anticoagulation (EAA), Central Facility, The University of Manchester, Faculty of Life Sciences, Manchester, UK

Greater recognition of the value of oral anticoagulation in a widening range of clinical disorders including atrial fibrillation (AF), has led to increasingly heavy demands for oral anticoagulant control worldwide, putting a great strain on the existing facilities in hospitals and community clinics. Anticoagulation to be safe and effective must conform to defined therapeutic intervals expressed as international normalised ratios (INR). INR less than 2.0 are generally ineffective in prevention of thrombosis whereas INR greater than 4.5 dramatically increase the risk of bleeding.

To meet demands and ease the burden on existing facilities, a range of elegant, hand-held, easy to use, prothrombin time monitors designed for patient self-testing and to lesser extent patient self-management has been developed. By far the most popular and widely used is the CoaguChek monitor. Several hundred thousand are reported to be in use with finger-prick specimens in Germany alone, by patients engaged in self-monitoring. The CoaguChek is also stated to be employed by 150,000 patients in self-testing/self-dosage (1). It is important therefore that the CoaguChek instruments provide accurate INR results. The earlier models, CoaguChek and CoaguChek S, which have been in widespread clinical use and employed in clinical trials of patients' self-testing/self-management for a number of years, are now being replaced by the CoaguChek XS.

A United Kingdom Health Technology Assessment (2) in 2007 reported that in 16 selected randomised and eight non-randomised trials, patient self-monitoring of oral anticoagulation therapy was more effective than poor-quality usual care provided by family doctors and as effective as good-quality specialised anticoagulation clinics in maintaining the quality of anticoagulation therapy. There was, however, no significant reduction of major bleeding events between patient self-monitoring and usual care controls. Pooled analyses of results found that compared with primary care or anticoagulation control clinics, self-monitoring was associated with significantly fewer thromboembolic events. The conclusion was that for selected and successfully trained patients, self-monitoring is effective and safe for long-

term oral anticoagulation. In general, although patient self-management is unlikely to be more cost-effective than the current specialised anticoagulation clinics in the UK, more self-monitoring may enhance the quality of life for some patients who are frequently away from home, in employment or education, or who find it difficult to travel to clinics.

One of the important advantages of patient self-management is that anticoagulation control can be more frequent when tested by self-monitoring (every 1–2 weeks) than by usual care provided by family doctors or hospital clinics (every 2–4 weeks). Longer intervals up to 10 weeks are regular practice in some hospital clinics. The recent American College of Chest Physicians (ACCP) Guidelines (3) recommend a maximum four week interval between tests but this is frequently exceeded in routine practice. More frequent testing is easier with CoaguChek self-testing than with other control methods and generally improves the percentage of time in target INR range.

Results from controlled trials were summarised in the UK Assessment by stating that patient self-management is better than poor-quality anticoagulation control provided by family doctors, particularly in the prevention of inadequate anticoagulation (proportion of time INR spent below the target therapeutic range). This was on average 19% in patients using self-monitoring compared with 33% in patients managed by family doctors. Overall CoaguChek patient self-management was as effective as the usual care of specialised anticoagulant clinics. Patient self-management is unlikely, however, to be more cost-effective than the current high-quality care provided by specialised anticoagulation clinics.

In the current issue of *Thrombosis and Haemostasis* a team of Danish investigators, Christensen and colleagues, report a prospective study evaluating the accuracy and precision of a single CoaguChek S instrument and a single instrument of the newly introduced CoaguChek XS type, both tested in a group of patients on warfarin together with the local laboratory prothrombin time method (4). A total of 564 venous blood samples was obtained from 24 patients and tested weekly in parallel over a

Correspondence to:
Professor L. Poller
EAA Project Leader
European Action on Anticoagulation
Central Facility, The University of Manchester, Faculty of Life Sciences
3.614 Stopford Building, Oxford Road, Manchester, M13 9PT, UK
Tel.: +44 161 275 5316/5424, Fax: +44 161 275 5316
E-mail: ecaa@manchester.ac.uk / leon.poller@manchester.ac.uk

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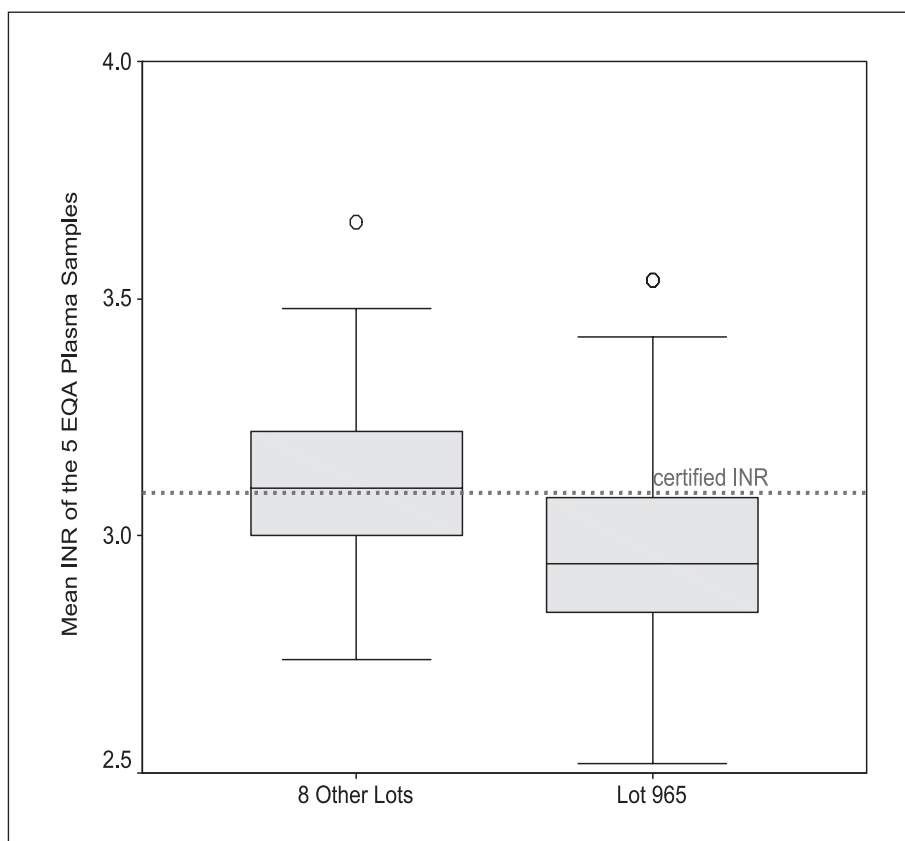


Figure 1: Distribution of international normalised ratio (INR) values using CoaguChek strip lot 965 (n=289) compared with eight other lots combined (n=234). Dotted line, certified INR; solid line in box, median INR; box, interquartile range; circles, outliers. EQA = external quality assessment.

42-day period on the two different types of monitor as well as with the authors' conventional hospital prothrombin time method. The latter employed a low ISI rabbit thromboplastin (ISI 0.98 – 1.0) and a Stago coagulometer. The target INR was 2.0–3.0.

In agreement with other recent reports (5–9) precision was better with the new CoaguChek XS monitor compared with the CoaguChek S but only the new instrument was regarded as giving satisfactory precision, although this was less than with the routine hospital method. Christensen et al. state, however, that the INR results recorded on both types of CoaguChek instrument were considerably lower than with the hospital method (0.33 and 0.42 INR respectively for the CoaguChek S and CoaguChek XS) (4). No ISI calibration of the local laboratory method was performed but it was stated to have been certified according to ISTH Guidelines on use of certified calibration plasmas.

The observations of the authors on accuracy are most important and their results are similar to those of the joint European Action on Anticoagulation (EAA)/European Concerted Action on Thrombosis (ECAT) study (10) where CoaguChek and CoaguChek S monitor results deviated in over 20% of tests by more than 15% INR from certified INR values on the same set of plasmas. They concluded that external quality assessment (EQA) and perhaps calibration of CoaguChek monitors seems mandatory.

The EAA/ECAT study (10) to which they refer was a combined internal and EQA survey involving a total of 523 CoaguChek monitors. These were brought by their patient users to nine

Netherlands Thrombosis Centre Clinics for checking by trained personnel using a set of five ECAA lyophilised EQA test plasmas. Their INR had been certified by expert centres in a multi-centre exercise using WHO international reference preparations for thromboplastin (human and rabbit). Twenty percent of the CoaguChek monitors in this study gave unacceptable deviation (15% or more) with at least one of the test plasmas. Results varied with different numbered lots of manufacturer's CoaguChek test strips. Indeed, one lot of the test strips which was tested on 289 of the 523 monitors gave significantly lower INR across all five QA samples compared with eight other numbered lots of CoaguChek strips (Fig. 1). Furthermore, a second ECAA/ECAT report (11) showed that the 15% deviation from the certified INR obtained with the set of five CoaguChek test plasmas by the 20% of participants' monitors was comparable to a 15% deviation from the median INR, the conventional method for interpretation of results in UK external quality assessment surveys.

The current report from the Danish team and the previous ECAA/ECAT study therefore provide similar conclusions, although they were different in content and design. Both agree on the absolute need for EQA of this important widely-used home testing monitor. To derive adequate information for the users on the reliability of the performance of their individual CoaguChek monitors by conventional centrally originally organised EQA would entail large-scale participation by other CoaguChek users in such an EQA program to derive satisfactory central analysis. None of the current EQA programs provide sufficient lyophilised test EQA plasmas (at least five certified plasmas are required

on a single occasion) to assess the performance of an individual CoaguChek monitor. National EQA as organised at present, with one or two test samples to be tested by the home monitors in a survey, would require several sequential exercises and central analysis to provide reliable EQA assessment, whilst taking months or even years to complete. On the other hand, the simpler alternative from EAA/ECAT, i.e. the provision of a set of five INR certified EQA plasmas to be used on a single occasion on an individual monitor, gives an immediate on-site EQA result. Hitherto there has been no reliable and suitable method for EQA of the CoaguChek similar to the conventional prothrombin time.

The evidence therefore from the present Danish study and the previous EAA/ECAT findings clearly agree that EQA of the CoaguChek instruments, independent of the manufacturer, is mandatory. This is now possible with the general availability of the test kits from ECAT. Results from these monitors can then be used with greater confidence by medical staff and patients, particularly those involved in self-management and self-dosage. CoaguChek monitors will in this way provide a practical and perhaps safer alternative to routine hospital/community control, particularly as testing can be performed more frequently by those engaged in self-testing.

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