was effective in preventing recurrences in patients with SLE and in patients with other causes of thrombophilia. However, since information for combined thrombophilic states is lacking in the most recent communications,[3-5] further investigation is needed to assess whether combined thrombophilia requires different management.

A recent consensus meeting suggested that a target INR of 2.5 may not be enough to prevent recurrences in patients with stroke.[6] In our experience, arterial thrombosis did not behave differently from venous thrombosis. Moreover, patients with both arterial and venous thrombosis also remained free from recurrences during the follow-up despite being older. Our study, which included ambispective data and a long follow-up, adds to the observations by Crowther[3,5] and Finazzi[4] that standard anticoagulation is efficacious and safe, even in patients with concomitant prothrombotic conditions. Finally, we identified possible clinical predisposing factors for recurrence, having observed recurrent PE in a patient with two previous episodes and an IVCF. The number of previous events and the rheologic disturbance due to the filter are prognostic factors for recurrence. Patients with predisposing factors may need to be managed by setting a higher target INR.

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Patient-specific errors in agreement between International Normalized Ratios measured by a whole blood coagulometer and by a routine plasma-based method

We applied a new statistical method[1] to improve comparisons between systems measuring prothrombin time (PT) by splitting disagreement into systematic errors, which can be eliminated, and random errors, which can not. We found that the disagreement between International Normalized Ratio (INR) measurements based on plasma and whole blood was significantly patient–dependent.

A number of studies have sought to investigate the accuracy[2] of whole blood coagulometers by comparison with plasma-based methods. Usually, however, only the systematic component of trueness (the mean difference) is evaluated whereas the other component, the random variation between patients, is neglected.

In cases in which the two PT systems to be compared are alike (e.g. if both are automatic and based on analysis of plasma with plain thromboplastin preparations) the random component may be small.

However, in other situations, as demonstrated in a recent study,[1] the random component may be large, indicating that the test system is unable to produce measurements that agree with the reference system across patients, even after appropriate calibration.

Our study included 64 consecutive patients on stable oral anticoagulation (OAT) who were seen for routine laboratory control of INR at Skejby Sygehus, Aarhus University Hospital. They had their INR measured by two types of portable whole blood coagulometers (CoaguChek (CC) and CoaguChek S (CCS), Roche Diagnostics, Mannheim, Germany) described elsewhere,[3] and a plasma based method routinely used in our central laboratory (LAB). The thromboplastin preparation used in the LAB was Nycotest (rabbit, combined, ISI approximately 1, manufactured by Axis-Shield PoC AS, Oslo, Norway) and the LAB PT system was calibrated on site by means of two plasma calibrators with assigned INR, provided by the Danish Institute of External Quality Control in Hospital Laboratories. Four CC devices were randomly selected and four CCS devices were supplied by the manufacturer. Each of the 32 combinations of CC, CCS, and order of device type was run in 2 patients, such that the total number of runs, randomized over patients, was 64 and the total number of CC and CCS measurements was 128. The same lot (no. 169) of test strips was used for all measurements on both the CC and CCS devices.

Figure 1 contains scatterplots of logarithmic INR values for CC, CCS and LAB. Ten patients had a LAB INR less than 1.1 and were excluded from further analysis. We found a systematic difference of 6.7% (95% confidence limits 4.6%,

Table 1. Estimates of slopes, intercepts, and standard deviations of linear errors, with 95% confidence intervals in brackets, of log(INR) for each pair of PT systems.

y-axis	x-axis	Slope	Intercept	Standard deviation of linear error
LAB	CC	1.015 (0.923, 1.108)	0.167 (0.098, 0.236)	0.106 (0.076, 0.129)
LAB	CCS	0.895 (0.805, 0.985)	0.193 (0.119, 0.267)	0.120 (0.090, 0.144)
CC	CCS	0.911 (0.882, 0.939)	0.002 (-0.020, 0.024)	0.000 (0.000, 0.027)

8.9%) between CCS and CC. The CV of INR levels between portable coagulometers (adjusted for type) was 1.4%. The CV within devices was 4.1%, assuming the same CV within each type. The latter CV may be considered a measure of precision under conditions of repeatability, whereas the total CV of devices, $(0.014^2 + 0.041^2)^{1/2}$=4.3%, may be interpreted as the imprecision under reproducibility conditions, when measurements are performed by a trained laboratory technician. The biological CV of *true* INR levels between patients was 32%. In the analysis of linear errors there were no signs of non-normality or non-linearity. For the measurement errors the estimated CV of 4.3% (with 47 degrees of freedom) was assumed for both CoaguChek systems. For the LAB measurements a CV of 3.6% (with 500 degrees of freedom), based on within-day measurements of plasma controls (*data not shown*), was assumed. The resulting estimates of slopes, intercepts, and standard deviations of linear errors, with 95% confidence intervals in brackets, are shown in Table 1. None of the pairs was perfectly calibrated, since for each pair either the slope or the intercept was significantly different from one or zero, respectively. Moreover, the pairs involving LAB and one of the CoaguChek systems had significant linear errors such that for an INR determined without error on the CoaguChek S system, the CV of the corresponding INR, excluding measurement error, determined by our routine hospital laboratory was at least 10%. Thus, for example, if a number of patients had an INR of 3.0 measured without error on CoaguChek, then the 95% prediction interval of the INR for these patients measured without error on the LAB would be 3.0±1.96*10%, i.e. 2.4 to 3.6 INR. Adding the usual measurement errors results in clinically important deviations between the two methods. Therefore, we recommend that a new standard based on whole blood determinations of INR should be considered. Moreover, as long as INR target recommendations are based on plasma-based methods of INR determination, the whole blood target INR should be corrected for patient-specific differences so that the patient obtains the recommended plasma-based INR.

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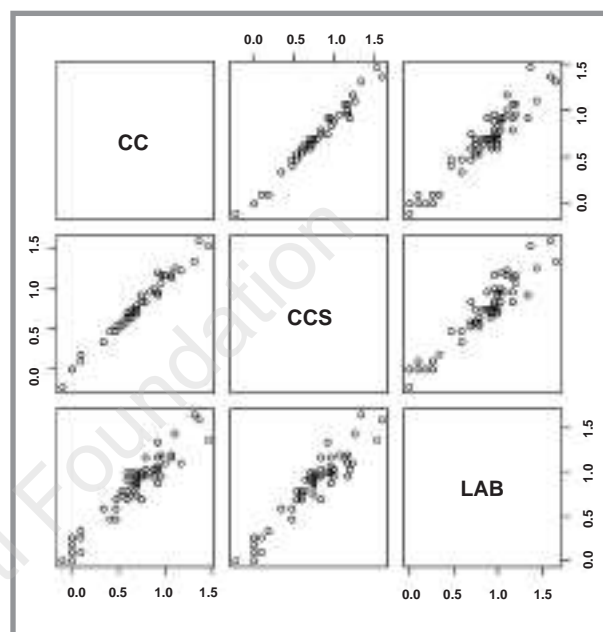
Figure 1. Scatterplots of logarithmic INR values for CoaguChek, CoaguChek S and routine hospital laboratory. Six patients with a LAB INR less than 0.8 were excluded.

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