

Validation of the Use of a Point-of-Care Device in Monitoring the International Normalised Ratio in Postoperative Cardiac Patients

Dear Editor,

Warfarin is prescribed for various conditions including mechanical heart valves, atrial fibrillation and venous thromboembolism. Prevention of bleeding and thromboembolic complications require maintenance in a tight therapeutic range. The use of patient self-testing has been well documented in the United Kingdom and Europe in prospective and retrospective studies.¹⁻⁵

CoaguChek[®] XS (Roche Diagnostics, Basel, Switzerland) prothrombin coagulation monitoring system^{6,7} provides point-of-care (POC) monitoring with a measurement range of 0.8 to 8.0 international normalised ratio (INR) and consists of a CoaguChek[®] XS monitor and test strips.

To date, validation studies have been limited to stable outpatient anticoagulation clinic cohorts,⁷ with studies done in cardiac patients perioperatively.⁸⁻¹⁰ However, these used arterial or whole blood samples and evaluated patients in the immediate perioperative period. Therefore, there is a void of data in the validity of such devices using capillary blood samples in cardiac patients during the recuperative in-hospital phase.

The study aimed to validate the POC testing (POCT) device with capillary samples in an Asian cohort during the postoperative phase. By introducing the concept and validity of POC self-testing in patients, it would help to empower the patient to participate in his or her care, laying ground for developing an outpatient self-testing programme. The authors believe that this period is a window of opportunity for the implementation of self-POCT as patients are under closer supervision and more motivated.

Materials and Methods

Study Population

Consecutive adult patients, between the age of 21 and 80, who had undergone open heart surgery at the National Heart Centre Singapore (NHCS) from February 2014 to May 2014 and initiated on warfarin therapy were recruited (Table 1). Patients on additional heparin coagulation were not excluded to reflect real-life situations.

Patients with anti-phospholipid antibodies,¹¹ haematocrit outside the range of 25% to 55%, triglyceride level of more than 7 mmol/L, absence of previous unhaemolysed renal

Table 1. Demographic and Clinical Characteristics of Patients Participating in the Study

| Patient characteristics | |
|---|------------|
| Male | 33 (35.3%) |
| Female | 18 (64%) |
| Mean age (years) | 58 |
| Indication for anticoagulation | |
| Valve replacement | 20 (39.2%) |
| Valve repair | 14 (27.5%) |
| Atrial fibrillation | 11 (21.6%) |
| Valve repair and atrial fibrillation | 3(5.9%) |
| Valve replacement and atrial fibrillation | 2 (3.9%) |
| Left ventricular assist device | 1 (2.0%) |
| Concurrent anticoagulation | |
| IV heparin | 4 (7.8%) |
| Subcutaneous enoxaparin | 1 (2%) |
| None | 46 (90.2) |

IV: Intravenous

panel assay or serum bilirubin of more than 513 mmol/L were excluded, as recommended by the manufacturer in accordance with their device insert.¹²

For validation tests, venous blood samples were drawn in 3.5 mL sodium citrate tubes and prothrombin time (PT) was obtained by Diagnostica Stago's STart[®] 4 analyser using the Neoplastine C1 Plus 5 thromboplastin. The international sensitivity index (ISI) for the batch used was 1.26. For the POCT, capillary blood is obtained by lancing the side of the patient's fingertip. A drop of blood was expressed onto the test strip within 15 seconds. The meter performed a quality control test on the test strip before displaying the result on the screen of the device.

CoaguChek[®] XS

This device uses a human recombinant thromboplastin with an ISI value of 1.0 to activate the coagulation cascade in the blood. Thrombin⁷ cleaves peptide substrate on the test strip to generate an electrochemical signal. The time elapsed from sample application to signal generation is used to calculate the INR value. INR results are obtained within 1 minute. The test strips also include an internal quality control system. This has been validated in multiple reports.¹³

Recruited patients were initiated on warfarin postoperatively as per managing clinician’s discretion. A randomisation list was created by a statistician. Patients were randomised to receive POCT testing from day 1 to 8 of commencement of warfarin in order to capture a range of INR readings. On the randomised day, both venous and capillary INR readings were within a median of 5.4 hours of each other by a physician.

Ethical approval was granted by Centralised Institutional Review board (CIRB) and patients were recruited from the NHCS Department of Cardiothoracic Surgery and gave informed consent (CIRB protocol number 2013/758/C).

Statistical Analysis

All statistical data analysis was performed using SPSS version 21.0 (IBM Corp 2012). Baseline demographic and clinical characteristics of the study population were expressed as an average with standard deviation. Statistical significance was defined as $P < 0.05$. The linear regression and correlation of the 2 methods of assay were analysed, and a scatter diagram and regression line of the 2 were plotted. The Bland-Altman analysis was used to plot a scatter diagram with the deviation and mean INR measured obtained with the 2 methods of assay.

Results

A total of 84 patients underwent open heart surgery from February 2014 to May 2014. Two patients declined to participate, 11 patients had a haematocrit $< 25\%$. Twenty-one patients were discharged before their scheduled POCT and were excluded (Fig. 1). The remaining 51 patients with their baseline characteristics as shown in Table 1 underwent venous and capillary INR testing.

Indications for anticoagulation included valve repair, valve replacement, atrial fibrillation postoperatively and left ventricular assist device implantation (Table 1).

Comparison of Venous laboratory and CoaguChek® XS INR

Venous and CoaguChek® XS INR were obtained from 51 patients (Table 1).

A significant regression equation was found ($F [1,49] = 711.082$). There is good correlation between the measured INR values obtained through both assays with an R^2 of 0.93 ($P < 0.05$) (Fig 2). The degree of bias can be observed in the Bland-Altman plot of CoaguChek® XS INR and venous INR (Fig. 2). The gap between the measured value from the CoaguChek® XS INR and the venous INR is 0.168 ± 0.176 , proving good consistency between the 2 groups.

Discussion

This is the first prospective cohort study looking at the reliability of the CoaguChek® XS device in an Asian cohort during the recuperative hospital phase of cardiac surgery, using capillary blood.

This study shows that the capillary INR obtained through the CoaguChek® XS device is reliable. Though the cost between the 2 methods is similar,¹⁴ the availability of a POCT device with a result that is instantaneous allows

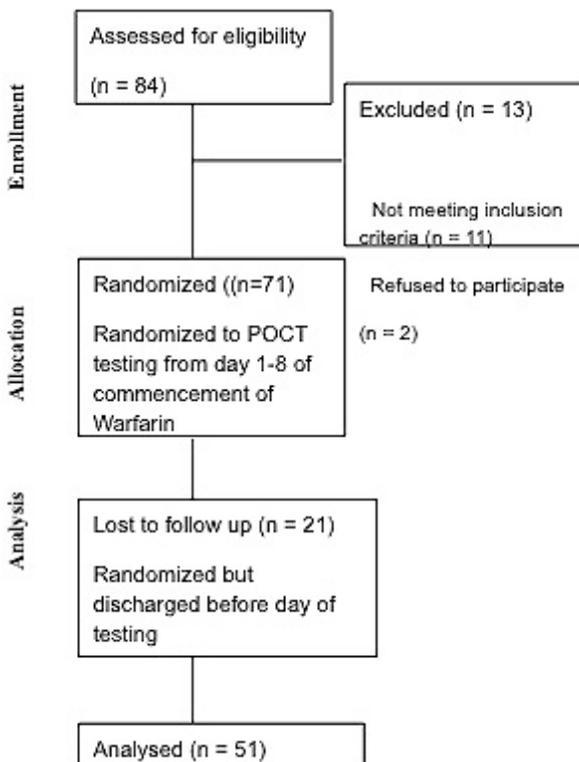


Fig. 1. Participant flow diagram.

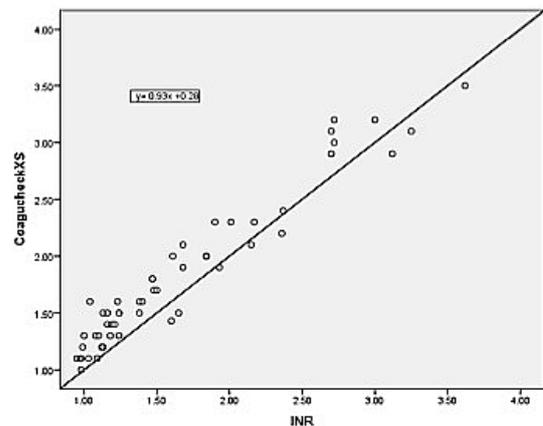


Fig. 2. Bland-Altman plot of CoaguChek® XS INR and venous laboratory INR. INR: International normalised ratio

doctors to prescribe the appropriate dose of warfarin during morning rounds in a timely manner, without having to wait for laboratory results. There have been situations where the time to target INR, and hence hospitalisation stay, has been delayed as a result of omitting warfarin while awaiting the results of laboratory samples.

Patients can be trained to use a POCT device. With purchase or home loan services, and the setup of a physician infrastructure to follow up postdischarge, the number of visits to the anticoagulation clinic can be reduced. This empowers patient to be proactive in their own care and can also translate to cost and time saving and freeing up of slots within the anticoagulation clinic in addition to increased safety.

Study Limitations

The results of this POCT device are limited to venous INR up to 3.5. However, the range of INR depicted parallels real life where the risk of bleeding due to an raised INR, is a real concern.

While there was significant time delay between venous and capillary INR monitoring (Table 3), results still showed a strong correlation between both readings despite the time difference. The difference between the 2 INRs has a mean of 0.168 which we feel while being statistically significant, is not significant clinically.

Conclusion

The strong correlation coefficient between laboratory-obtained INR values and CoaguChek® XS values suggests that CoaguChek® XS is suitable for use in the recuperative in-hospital phase. This will help in initiating patients to self-testing programmes during this period.

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Disclosure

Roche Diagnostics provided the CoaguChek® XS coagulometer as well as the test strips used in the study. The conception, design and implementation of the study as well as the preparation of the manuscript and conclusions were independent of industry support.

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