Original Research

Efficacy of Point-of-Care for INR Testing Compared to Standard Laboratory Methods at a Tertiary Care Hospital in Saudi Arabia

Manzoor Bhat,[1] Yacoub Abuzied,[2] Zahra Fagih,[1] Tariq Wani,[3] Ismael Gawan,[4] El Mae Andalay,[4] Mohammed AlSheef[5]

[1]Point of Care Testing Department, Pathology and Clinical Laboratory Medicine, King Fahad Medical City, Riyadh, Saudi Arabia
[2]Nursing Department, Rehabilitation Hospital, King Fahad Medical City, Riyadh, Saudi Arabia
[3]Research Center, King Fahad Medical City, Riyadh, Saudi Arabia
[4]Nursing Department, Outpatient Administration, King Fahad Medical City, Riyadh, Saudi Arabia
[5]Medical Specialties Department, Main Hospital, King Fahad Medical City, Riyadh, Saudi Arabia

Address correspondence to Yacoub Abuzied (yabuzied@kfmc.med.sa)

Source of Support: None. Conflict of Interest: None.

Received: November 30, 2019; Accepted: March 09, 2020.

Bhat M, Abuzied Y, Fagih Z, Wani T, Gawan I, Andalay EM, AlSheef M. Efficacy of point-of-care for INR testing compared to standard laboratory methods at a tertiary care hospital in Saudi Arabia. *Glob J Qual Saf Healthc*. 2020; 3:98–104. DOI: 10.36401/JQSH-19-36.

© Innovative Healthcare Institute

ABSTRACT

Introduction: Regular testing of the international normalized ratio (INR) is essential for people taking vitamin K antagonists as part of anticoagulation therapy. This study was undertaken to ascertain the efficacy of point-of-care testing (POCT)-INR versus conventional core laboratory testing in terms of result adequacy, waiting-time reduction, and patient satisfaction enhancement at the thrombosis clinic of the outpatient Medical Specialties Department in King Fahad Medical City, Saudi Arabia. **Methods:** The study was conducted prospectively for 6 months (from June 2017 to December 2017) on 182 eligible participants out of 250 entitled patients who were attending the thrombosis clinic for warfarin dose adjustment and who fulfilled all the prerequisites for performing dual testing by fingerstick at the clinic and venipuncture by the core laboratory. The data-capturing template created on Microsoft Excel recorded turnaround times (TATs), clinical concordance of INR result variables by POCT, and laboratory methods. Individual patient experience was recorded to gauge satisfaction rate, and all the data were analyzed statistically. **Results:** Of 182 patients included in the study, overall good concord was observed between POCT whole blood and laboratory plasma INR results with median bias of 0.07 and 92.3% agreement using acceptability criteria for clinical concordance of Clinical Laboratory Standards Institute (CLSI) 14-A and International Standards Organization (ISO) 17593-2007, respectively. Marked improvement in terms of patient's time spent at the clinic was noted, with substantial reduction from 180 to ~30 minutes ($p < 0.001$). Survey questionnaire responses indicated that POCT of INR was highly convenient and enhanced patient experience in terms of shorter wait time, minimal invasive procedures, and immediate result availability ($p < 0.001$). Predominantly, participants (75.4%) endorsed and expressed a strong preference for the POCT procedure over conventional laboratory testing. **Conclusions:** Whole blood INR testing for warfarin dose adjustment with validated POCT devices is adequately comparable to the core laboratory results. It also simplifies workflow steps at the thrombosis clinic, enhancing patient experience and convenience via the immediate availability of results, a less invasive procedure, and a marked reduction in waiting time. However, caution is needed with regard to higher INR results (≥4.7), which call for core laboratory confirmation.

Keywords: thrombosis, international normalized ratio, turnaround time, anticoagulation therapy, point-of-care device

INTRODUCTION

Warfarin, a vitamin K antagonist, is used to prevent and treat blood clots as in venous thromboembolism (VTE). It also helps in reducing the risk of heart attack or stroke and conditions that increase the risk of developing blood clots. Inadequate warfarin anticoagulation predisposes patients to recurrent VTE and stroke, while

an excess may cause intracranial hemorrhage and massive gastrointestinal bleeding.[1]

The risk of bleeding while on warfarin is highest in patients previously not exposed to it and in the first 3 months of treatment.[2] Therefore, close monitoring is essential in patients taking warfarin.

Prothrombin time (PT) and the associated international normalized ratio (INR) are assays evaluating the extrinsic pathway of coagulation to assess the risk of bleeding or thrombosis. This also helps in monitoring patient response to anticoagulant therapy.[3]

International normalized ratio testing is a well-established integral part of warfarin treatment. It plays a critical role in maintaining the drug response within a therapeutic range and providing anticoagulation benefits while avoiding the risks of hemorrhage.[3]

Today's health care faces a pressing need for faster laboratory turnaround time (TAT) and the development of newer and innovative testing devices. Traditionally at a hospital thrombosis clinic, patients upon arrival have to go through certain procedural steps from registration to required vital signs, obtaining a test order from the physician, and then queuing at phlebotomy for blood draw by invasive venipuncture followed by waiting for laboratory results afterward, and queuing again for physician consultation. At times, a patient is required to visit the clinic more than once to get appropriate warfarin dosing prescribed. The entire process is cumbersome and uncomfortable, especially for those residing far away from the health care facility.

Point-of-care testing (POCT) devices offer rapid results with very little blood and are portable. This helps in making faster management decisions and ensures better clinical outcomes and patient satisfaction.[4] Studies[5.6] have singled out POCT-INR for anticoagulation management as a reliable and rapid alternative, enhancing patient satisfaction with significant improvement in waiting time. This allows the clinician to prescribe and adjust appropriate and safe warfarin dosage in a timely manner, and facilitates data proximity to caregivers for time in therapeutic range calculations to assess anticoagulation control over the period.[5.6]

The Hemochron Signature Elite whole blood microcoagulation system by International Technidyne Corporation (ITC) is a battery-operated, handheld instrument that performs individual point-of-care coagulation tests on fresh or citrated whole blood. The device includes a patented clot detection system, a data storage module, interfaces for a laboratory computer and/or printer, a streamlined user-interface panel, and an integrated barcode scanner.[7] The Food and Drug Administration approved and cleared the product for marketing in 2005.[8]

The present study was designed keeping in view the seriousness of the problem that could be addressed by introduction and implementation of robust POCT technology, benefitting both patients and physician practices. The aim of the study was to ascertain the efficacy of POCT of INR versus conventional core laboratory testing in terms of result adequacy, waiting-time reduction, and patient and physician satisfaction enhancement at the thrombosis clinic, King Fahad Medical City (KFMC), Saudi Arabia.

METHODS

Study Design

This prospective cohort study was conducted at KFMC, Riyadh on 250 patients attending the thrombosis clinic for warfarin dose adjustment from June 2017 to December 2017. The participants were included after meeting the criteria and consenting to be a part of dual testing, first by fingerstick using POCT and then core laboratory testing by venipuncture, and also to participate in the satisfaction survey.

Participants and Recruitment

The participating patients with clinical indications such as VTE were attending the thrombosis clinic for warfarin dose adjustment and/or prophylaxis against stroke and systemic embolism in atrial fibrillation or mechanical heart valve conditions.

During the study period, 487 patients attending the thrombosis clinic were screened for eligibility as potential participants. Initially 250 patients were considered for participation as the remaining 237 could not qualify due to other comorbidities. Finally, 68 patients had to be removed from the analysis for not fulfilling the prerequisites for participating in the patient satisfaction survey, or for not appearing at the phlebotomy suite on the same day to get venous blood extraction done for laboratory comparison. Eventually 182 patients were selected for the study as those remaining did not meet the inclusion criteria.

Ethical Considerations

The participation of patients was entirely voluntary and written consent was obtained. Personal identities were kept confidential. In addition, permission was obtained from the Institutional Ethics Committee, and the participants were informed about their right to withdraw at any given time during the study.

Intervention

Point-of-care testing-INR was done by the Hemochron Signature Elite device at the thrombosis clinic by trained staff using capillary blood by fingerstick while venipuncture was carried out at the phlebotomy suite and samples were sent to the core laboratory for analysis on the ACL-TOP 550 (Instrumentation Laboratory) for comparison and clinical concordance.

Data Collection Procedure

The selected nursing staff at the thrombosis clinic were trained to operate the Hemochron Signature Elite and collect data for the study. Standard operating procedures

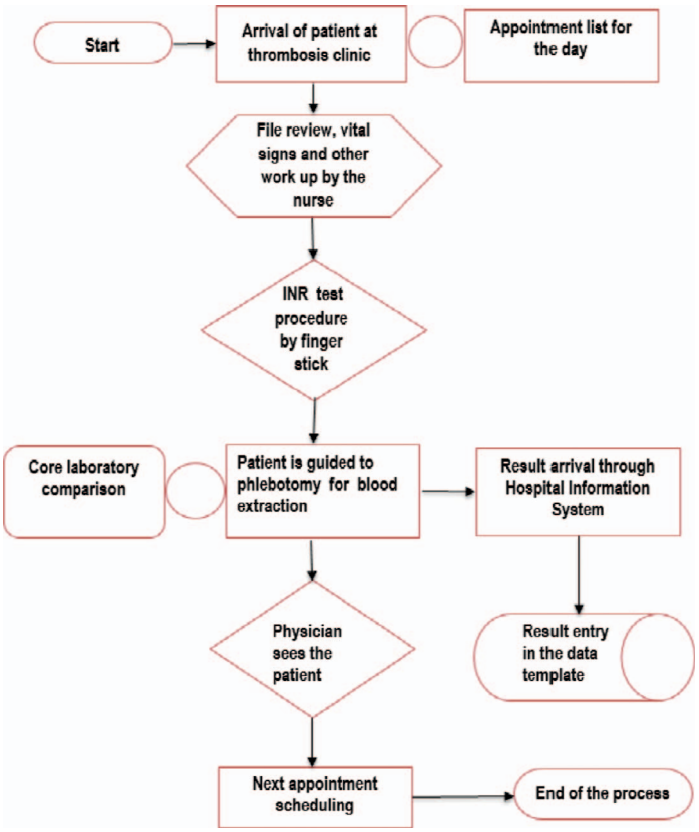

Figure 1.—Flowchart showing process of care during the study period for international normalized ratio (INR) testing at the thrombosis clinic. Circle indicates "connected to."

were formulated with a step-by-step procedure for a quick reference on how to operate and to generate and interpret the results. The system measured whole blood clotting times using Hemochron Jr. disposable single-use cuvettes. Each cuvette contained all the reagents necessary for a specified test.

Data capturing and variable measurements were done on a defined Microsoft Excel (Redmond, WA) template.

Point-of-care testing TAT was defined as the time recorded from patient arrival through vital signs, POCT procedure, waiting time for physician encounter, and subsequent prescription.

Laboratory TAT was defined as time recorded from patient arrival through vital signs, waiting time at the phlebotomy suite, laboratory processes, and result entry time in the Hospital Information System (CorTTex), waiting time for physician encounter, and prescription.

A tailored workflow during the study period for dual INR testing was adopted to smoothly facilitate the logistics (Fig. 1).

Individual patient experience was captured in a questionnaire with six survey questions provided in Appendix I and in local Arabic language in Appendix II (available as online supplements). A flowchart of participant entitlement and exclusion criteria with screening methodology is depicted in Appendix III (available as an online supplement).

Table 1.—Age and sex distribution of the studied subjects

Age, Years	Female	Male	Total
<18	2 (1.3%)	2 (6.3%)	4 (2.2%)
18–45	116 (77.3%)	21 (65.6%)	137 (75.3%)
46–65	25 (16.7%)	7 (21.9%)	32 (17.6%)
>65	7 (4.7%)	2 (6.3%)	9 (4.9%)
Total	150 (82.4%)	32 (17.6%)	182 (100.0%)
Mean ± SD	39.4 ± 12.4	38.1 ± 13.8	39.2 ± 12.6
(min, max)	(13, 80)	(12, 67)	(12, 80)

Data are presented as *n* (%) unless otherwise stated.

Statistical Analysis

Categorical data were described as frequency percent and the scale measurement data as mean ± SD. Pearson correlation was applied for determining the association between POCT and conventional INR parameters, and linear regression was fitted. Average discrepancy was evaluated by paired *t*-test, and the Bland-Altman method was used to analyze agreement between the two systems. All the inferences were drawn at 95% CI. Data analysis was done with SPSS Statistics 25.0 (IBM) and Microsoft Excel software.

RESULTS

Of 182 participants, 150 (82.4%) were females and the rest ($n = 32$; 17.6%) were males. One hundred thirty-seven ($n = 137$; 75.3%) were in the age range of 18 to 45 years followed by 32 (17.6%) patients from 46 to 65 years. There were nine (4.9%) patients who were >65 years and four (2.2%) patients of age below 18 years (Table 1).

Comparison/Correlation Variable

Clinical Laboratory Standards Institute (CLSI) 14-A agreement limits

There was overall good agreement between POCT and laboratory plasma INR results within a median bias of 0.12 (1.0–2.5 INR range), –0.03 (2.6–3.5 INR range), and –0.50 (3.6–5.0 and above INR range) using CLSI 14-A agreement limits ±0.4 (INR 1.0–2.5), ±0.7 (INR 2.6–3.5), and ±0.9 (INF 3.6–5.0) (Table 2).

International Standards Organization (ISO) 17593-2007 on acceptability criteria

In totality, 92.3% of the results of the two INR categories fell into the acceptability criteria (90.1% in the < 2 INR category and 93.7% in the 2.01–4.5 INR category), achieving agreement with ISO 17593-2007; that is, 90% of all results with allowable difference of ±0.5 in the less than 2.0 INR range and ±30% in the 2.01 to 4.5 INR range (Table 3).

Average discrepancy between POCT INR (2.466 ± 0.951) and LAB INR (2.401 ± 0.997) was evaluated by paired *t*-test; the difference was not significant. Furthermore, Bland-Altman analysis depicted limits of agreement in 95.5% of the observations, and bias rate of less

Table 2.—CLSI 14-A agreement limits for INR testing by point-of-care testing device

INR Range	*N*	Mean Bias	Median Bias	CLSI POCT 14-A Agreement Limits	Outcome
1.0–2.5	120	0.15	0.12	± 0.4	SE < AE
2.6–3.5	49	0.01	−0.03	± 0.7	SE < AE
3.6–5.0 and above	13	−0.51	−0.50	± 0.9	SE < AE

AE: allowable error (agreement limits); CLSI: Clinical Laboratory Standards Institute; INR: international normalized ratio; *N*: number of samples in the range; POCT: point-of-care testing; SE: system error.

than 5% within the established threshold of tolerance limits, implying that the POCT-INR device results are compatible with the reference LAB-INR (Fig. 2).

Although a significant relationship of the two methods was noted on the Pearson correlation graph, POCT-INR results demonstrated drifting away from the laboratory reference when INR was greater than or equal to 4.7 (Fig. 3).

Waiting-Time Reduction Variable

Marked improvement was achieved with a substantial reduction of patient's waiting time, less than 30 minutes with POCT intervention against 180 minutes with the conventional laboratory procedure. The POCT-INR test procedure was performed in an estimated 7 minutes followed by 15 minutes of waiting in the lounge for the physician encounter. The LAB-INR result TAT comprised an average 15 minutes for queuing at the phlebotomy suite for blood draw, 150 median minutes in the lounge to wait for the results, and then another 15 minutes to line up for physician consultation (Fig. 4).

Patient Experience Variable

The satisfaction survey was completed by 182 qualified patients; 137 (75.4%) revealed that POCT device INR testing was a preferred choice over venipuncture; 45 (24.6%) gave no explanation and were assumed to be equivocal (Fig. 5).

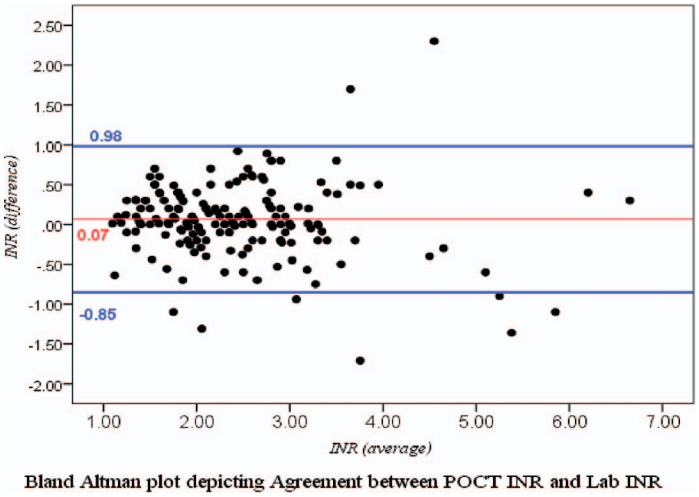

Figure 2.—Bland-Altman plot of agreement and bias rate determining compatibility of point-of-care testing (POCT) device. INR: international normalized ratio; LAB: core laboratory.

As to other queries in the survey, a 74.6% response indicated that POCT-INR was a convenient process; there was a substantial reduction in waiting time with immediate availability of results (75.7%). Respondents indicated that the fingerstick capillary blood drawing technique was less invasive (69.9%), applying a small volume of blood (72.7%). Nevertheless, 91.1% of participants expressed contentment with the courtesy shown by the staff during the process at the anticoagulation clinic (Fig. 6).

DISCUSSION

Long waiting time can lead to increased patient dissatisfaction especially in elderly patients with multiple comorbidities. In order to achieve timely results alongside ensuring patient convenience and satisfaction, robust technology could be considered after meticulous cost-benefit analysis. A study by Curtis et al.[5] reported improved patient quality of care with the application of POCT. It enabled prompt clinical decisions supported by a quick therapeutic TAT. Similarly, in the present study,

Table 3.—INR testing acceptability criteria using ISO 17593-2007 standard, reviewed in 2011 on in vitro monitoring systems

Allowable Difference†	INR in Less Than or Equal to 2.0 Range	INR in 2.01 to 4.5 and Above Range	Total
Results within criteria limits	64 (90.1%)	104 (93.7%)	168 (92.3%)*
Results not within criteria limits	7 (9.9%)	7 (6.3%)	14 (7.7%)
Total	71 (39.0%)	111 (61.0%)	182 (100.0%)

INR: international normalized ratio; ISO: International Standards Organization.
INR range: no criteria set above greater than or equal to 4.5 INR; ISO 17593-2007 criteria of allowable difference within 90% of all results, that is, ±0.5 in less than or equal to 2.0 and ±30% in 2.01 to 4.5.
* In totality 92.3% results of the two INR categories fall into the acceptability criteria, that is, exceeding allowable difference within 90% of all results, achieving agreement between the two methods.
† Criteria of allowable difference within 90% of all results, that is, ± 0.5 in less than 2.0; and ± 30% in 2.01 to 4.5 INR range. No criteria is set above greater than or equal to 4.5 INR.

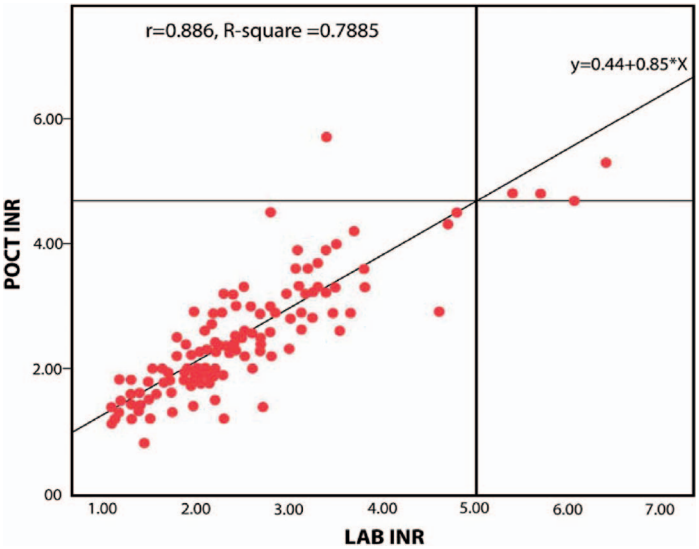

Figure 3.—Pearson correlation graph between two testing methods: point-of-care testing (POCT) versus core laboratory (LAB). INR: international normalized ratio.

POCT intervention was found to reduce the overall waiting time markedly from 180 minutes to less than 30 minutes. These findings also resonate with the findings of Kasinathan et al.[6]

On comparing and correlating the results of POCT (with a handheld device) and core laboratory analyzer, an overall good agreement between POCT and laboratory plasma INR results using CLSI 14-A agreement limits and ISO 17593-2007 acceptability criteria of allowable difference within 90% of all results was achieved; this makes the Hemochron POCT device adequate for clinical use. Although ISO 17593-2007 criteria do not pertain to in vitro measuring systems assessing vitamin K antagonist (warfarin) therapy at a health care facility, we applied it to guide individuals who could use such handheld devices to perform INR self-testing for monitoring and or managing their own warfarin therapy. There are

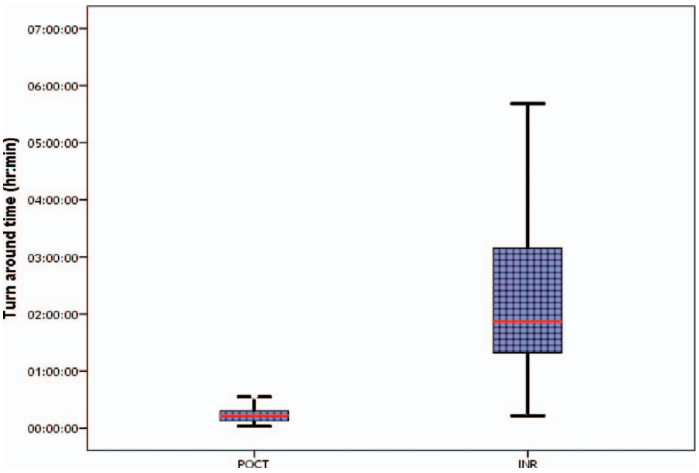

Figure 4.—Reduction in turnaround time (TAT) by two methods: point-of-care testing (POCT) versus core laboratory.

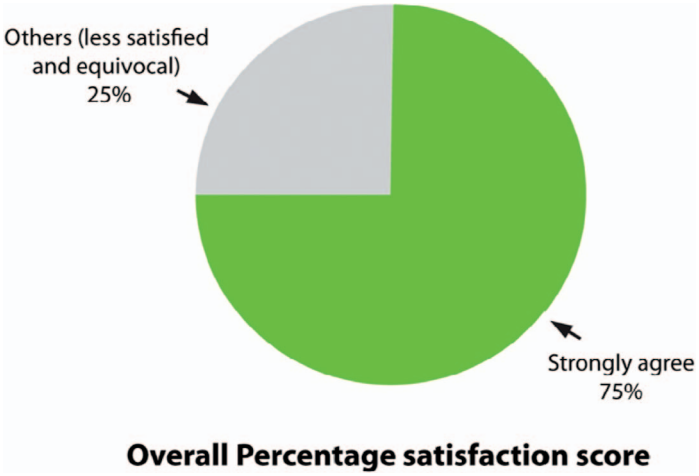

Figure 5.—Point-of-care testing (POCT) model, a preferred choice of patients through survey questionnaire. INR: international normalized ratio.

several studies published to this effect wherein the Hemochron Signature and other POCT devices have been considered a fast and reliable alternative to conventional laboratory testing.[9,10]

Nevertheless, this study noted a drift in POCT in which INR was greater than or equal to 4.7, evoking caution regarding verifying the results by the core laboratory method under such conditions. This was also pointed out in a comparative Brazilian study[11] in 2014 wherein INR values of greater than 3.5 were confirmed by laboratory method instead of the Coaguchek XS system. Also, a Turkish study reported similar results with INR greater than 5.0.[12]

Moreover, a few studies observed that INR values obtained with Hemochron Signature Elite showed only moderate agreement with laboratory values and limits of agreement were wide; hence they do not recommend its use in diagnosing coagulopathy and guiding patient treatment in acute hemorrhage.[13,14] In the present study, INR by POCT was not acceptable in smaller samples with INR greater than or equal to 4.7 and demonstrated drift on the correlation graph at this breakpoint. As the POCT gives results within a brief TAT with the patient still in the hospital, a confirmatory

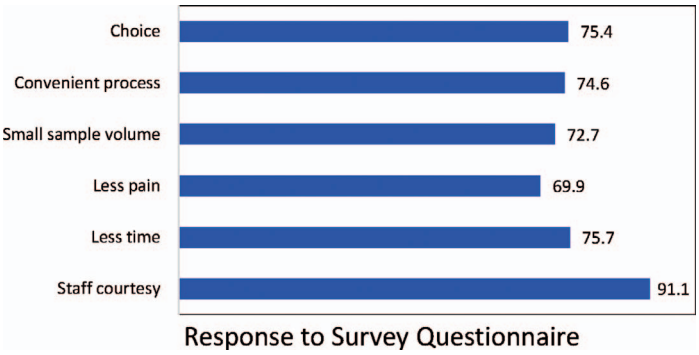

Figure 6.—Satisfaction and agreement rate on implementation of point-of-care testing model at the thrombosis clinic.

test with the core laboratory method can be performed to get better insights into the results, and thereby the correct dosage of anticoagulant therapy in these patients could be planned.

In current study, 75% of respondents indicated that on-spot POCT of INR was largely convenient and enhanced their experience in terms of reduction in waiting period, use of a less invasive procedure, and immediate result availability.

Comparable results were obtained from a survey by Thompson et al.[15] at the Medical University of South Carolina, where 95% of patients preferred the POCT device over conventional laboratory testing. Reasons for the preference included more face-to-face interaction, shorter wait time, reduced pain owing to fingerstick versus venipuncture, requirement of a smaller blood sample, and quicker results. Other studies from different regions also reported high levels of patient satisfaction and acceptability with POCT.[16,17]

Though the target of patient satisfaction and reliability was achieved at 75.4% against the projected greater than or equal to 90%, this could be attributed to patient apprehension and wariness as to the accuracy of results at the clinic and their preference for venipuncture over fingerstick.

A cost-benefit analysis with the microcosting approach was not within the scope of this study, as the focus was adequacy of results, patient convenience, and outcomes of extra-laboratory INR testing at the thrombosis clinic, although the unit cost of a POCT-INR cartridge appears to be more than at the core laboratory. However, based on our considered opinion, POCT-INR testing is a preferred option in our institutional setting when estimates combined with clinical usefulness and rapid availability of results, patient satisfaction, and streamlined workflow outcomes are taken into account for overall cost-effectiveness.

This study implies that POCT-INR levels are usually comparable to conventional core laboratory testing except for values above 4.7; in this case the recommendation is to complete a laboratory test for result confirmation before any clinical interventions.

To be regulatory compliant, laboratory guidance on device use, training and quality requirements regarding appropriate specimen collection, result management, device maintenance, and troubleshooting tips also referred to in relevant standard operating procedures should be adhered to.

Continuous education and awareness regarding the limitations of a measuring device or test system among health care providers performing testing is essential to sustain improvements.

Limitations

Key limitations of this study were poor correlation of INR values greater than or equal to 4.7 that may be attributable to differences in the methodology (e.g., mechanical versus electrochemical). An alternative scheme was put in place for elevated POC INR results, sending the patient's venous samples to the core laboratory (gold standard) for confirmatory testing.

As to potential errors emerging from the lack of expertise of health care providers performing INR testing, the gap is being closed at the onset with robust and technologically advanced POCT devices having different lockouts sustaining quality assurance and laboratory-based overall POCT supervision for quality and competency of staff.

CONCLUSIONS

Performing INR testing with the POCT device at the thrombosis clinic on whole blood samples is adequate and advantageous. It significantly enhances patient experience owing to convenience, reduced waiting time, and a painless fingerstick procedure. The key conclusions of this study are that point-of-care models for INR testing have simpler and more effective workflows than conventional care with leaner processes, as fewer steps are needed to produce the result with device portability. However, caution is needed with higher INR results ($\geq$ 4.7), which call for laboratory confirmation.

ACKNOWLEDGMENTS

We thank the healthcare workers for their support in this study. We want to acknowledge King Fahad Medical City for technical support and help in writing the manuscript through the research center as all of this was for free.

References

1. Witt DM, Clark NP, Kaatz S, Schnurr T, Ansell JE. Guidance for the practical management of warfarin therapy in the treatment of venous thromboembolism. *J Thromb Thrombolysis*. 2016;41:187–205.
2. Hylek EM, Evans-Molina C, Shea C, Henault LE, Regan S. Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. *Circulation*. 2007;115:2689–2696.
3. Tripathi MM, Egawa S, Wirth AG, Tshikudi DM, Van Cott EM, Nadkarni SK. Clinical evaluation of whole blood prothrombin time (PT) and international normalized ratio (INR) using a Laser Speckle Rheology sensor. *Sci Rep*. 2017;7:9169.
4. Medical Advisory Secretariat, Health Quality Ontario. Point of care international normalized ratio (INR) monitoring devices for patients on long term anticoagulation therapy: an evidence-based analysis. *Ont Health Technol Assess Ser*. 2009;9:1–114.
5. Curtis CM, Kost GJ, Louie RF, Sonu RJ, Ammirati EB, Sumner S. Point-of-care hematology and coagulation testing in primary, rural emergency, and disaster care scenarios. *Point Care*. 2012;11:140–145.
6. Kasinathan G, Pairan S, Rowther S, et al. Efficacy of point-of-care testing (POCT) in reducing total waiting time at warfarin clinic of a district hospital: a cohort study. *OALibJ*. 2016:3:68257. DOI: 10.4236/oalib.1102428.

7. Accriva Diagnostics. Whole blood microcoagulation system. www.accriva.com/uploads/literature/hx1101_1212.pdf. Accessed November 29, 2018.
8. International Technidyne Corporation. 510(k) submission. https://www.accessdata.fda.gov/cdrh_docs/pdf5/K050016.pdf. Accessed March 25, 2019.
9. Al-Meman A. I-stat, Coaguchek XS plus, and hemochron versus reference laboratory INRs: pharmacist-managed clinics. *Int J Pharmacy Pharm Sci*. 2015;7:284–288.
10. St John A. The evidence to support point-of-care testing. *Clin Biochem Rev*. 2010;31:111–119.
11. Araújo ACO, Domingues RB, van Bellen B. Comparison between the conventional method and a portable device for determination of INR. *J Vasc Bras*. 2014;13:88–93.
12. Kalçık M, Yesin M, Gürsoy MO, et al. Comparison of the INR values measured by CoaguChek XS coagulometer and conventional laboratory methods in patients on VKA therapy. *Clin Appl Thromb Hemost*. 2017;23:187–194.
13. Shermock KM, Streiff MB, Pinto BL, Kraus P, Pronovost PJ. Novel analysis of clinically relevant diagnostic errors in point-of-care devices. *J Thromb Haemost*. 2011;9:1769–1775.
14. Gauss T, Hamada S, Jurcisin I, et al. Limits of agreement between measures obtained from standard laboratory and the point-of-care device Hemochron Signature Elite(R) during acute hemorrhage. *Br J Anaesth*. 2014;112:514–520.
15. Thompson AN, Ragucci KR, Fermo JD, Whitley HP. Evaluation of patient perceptions and outcomes related to anticoagulation point-of-care testing in ambulatory care clinics. *Pharm Pract (Granada)*. 2009;7:213–217.
16. Chaudhry R, Scheitel SM, Stroebel RJ, Santrach PJ, Dupras DM, Tangalos EG. Patient satisfaction with point-of-care international normalized ratio testing and counseling in a community internal medicine practice. *Manag Care Interface*. 2004;17:44–46.
17. Laurence CO, Gialamas A, Bubner T, et al.; Point of Care Testing in General Practice Trial Management Group. Patient satisfaction with point-of-care testing in general practice. *Br J Gen Pract*. 2010;60:e98–e104.