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Anticoagulant monitoring in ventricular assist device patients: a feasibility study

Ashish Joshi^{a,*}, Diane Smith^b, Mohit Arora^a, and Robert Poston^b

^aDepartment of Information Systems, University of Maryland, Baltimore County, 1000 Hilltop Circle, Baltimore, MD 21201, USA

^bDivision of Cardiac Surgery, University of Maryland, School of Medicine, Baltimore, MD, USA

Abstract

We conducted a feasibility study to monitor coagulation using a point-of-care device (proTime micro coagulation system) in ventricular assist device (VAD) patients. The aim of the study was to compare International Normalized Ratio (INR) readings using a standard laboratory method and proTime micro coagulation device in order to confirm a correlation between these two methods. The nurse's feedback about anticoagulation monitoring using portable anticoagulant monitoring devices in the hospital was also assessed. Four patients admitted in the cardiac surgery unit at University of Maryland, Baltimore were enrolled between 25 November 2006 and 17 January 2006. These patients had given consent to undergo both venous and finger-stick blood samplings to monitor their anticoagulant levels. Six hospital nurses participated in the study. Forty-one INR readings were compared using both methods. Correlation coefficients determined association between INR readings using two methods. All the patients were males and were hypertensive. Significant positive association was seen in the INR readings using two methods ($r=0.96$; $P<0.0001$). Four of the six nurses believed patients would be significantly safer if INR is monitored by VAD patients in their homes. Further research needs to be done to determine the impact of home INR monitoring and long-term health in these patients.

Keywords

Anticoagulation; Ventricular assist device; Portable device; Point-of-care; Nurses

1. Background

Heart failure affects an estimated 4.7 million Americans, with 550,000 new cases diagnosed annually and annual costs ranging from \$10 billion to \$40 billion [1]. Treatment alternatives for congestive heart failure include coronary artery bypass surgery, dynamic cardiomyoplasty, partial left ventriculectomy, implantation of ventricular assist devices (VAD), and cardiac transplantation [2]. Cardiac transplantation has become an established therapy in the treatment of end-stage heart failure [3]. On an annual basis, between 20,000 and 40,000 Americans would benefit from cardiac transplantation; the number of donor hearts available annually is only 2000.

Mechanical circulatory support has been introduced to bridge patients to cardiac transplantation. These devices are indicated following acute myocardial infarction, during post cardiac-surgical cardiogenic shock, and as a bridge to cardiac transplantation [4]. Despite

*Corresponding author. Tel.: +1-410-455-8837; fax: +1-410-455-1217. E-mail address: asjoshi@umbc.edu (A. Joshi).

considerable improvements in hemodynamic function, thromboembolism is still a feared complication during their use [5]. No definitive guidelines for anticoagulation therapy are available as mechanism of these thromboembolic events is poorly understood [6]. The main reasons are the contact between blood components and the foreign surfaces of the assist device system and altered rheologic conditions with different velocities of blood flow and blood stasis in the native heart [7]. Embolism in these patients mainly affects the brain and has shown to be clinically evident in 47% of 36 observed patients [8]. Heparin induced thrombocytopenia is a frequent complication in cardiac surgical patients especially VAD patients and, therefore, requires tight anticoagulant monitoring in these patients [9]. The anticoagulation protocols during postoperative time change according to the different implanted VADs [10]. Therapeutic-dose anticoagulation is fundamental for management, as in the VAD patient where a balance is always needed to prevent both hemorrhagic complications and thromboembolism [10]. Bleeding episodes remain a serious complication of VAD support. This cannot be explained by the individual anticoagulation regimen alone in several cases, but may be symptomatic of acquired von Willebrand disease (VWD) [11].

The concept of allowing patients to perform their own international normalized ratio (INR) as part of anticoagulation therapy is not new [12]. An earlier study has shown routine self-assessment of the INR by the patients after VAD implantation using the CoaguCheck device [13]. INR is the primary unit to monitor the clotting propensity for patients on anticoagulation therapy. Prothrombin time testing is the standard care for monitoring the extrinsic clotting pathway in patients on oral anticoagulant therapy. Oral anticoagulants have been found effective in the prevention and treatment of thromboembolism in a variety of health conditions including chronic atrial fibrillation, venous thromboembolism, coronary artery disease or a prosthetic heart valve [14].

Of the various methodologies being developed to administer oral anticoagulation, patient self-testing (PST) has perhaps the greatest untapped potential. Most of the patients travel to a blood test center for a venipuncture for their INR monitoring [12]. Currently, portable coagulo-meters are available to measure INR easily and reliably and have shown to greatly facilitate patient monitoring by decreasing waiting time and allowing for patient counseling in face-to-face interviews [14]. This enhances patient self-testing and patient self-management [14]. INR monitoring with these point-of-care devices may demonstrate variation in the INR results.

In light of these goals, we conducted a feasibility study to monitor coagulation using a point-of-care device: 'proTime micro coagulation system' in patients with ventricular assist device while they were in the hospital. The study had two main aims: (1) to compare INR readings using standard laboratory method and portable micro coagulation device in order to confirm a correlation between these two methods and (2) to measure the perception of the nurses using the portable device. The study is important as it represents the first step towards the eventual widespread use of coagulation monitoring in VAD patients.

2. Material and methods

Four cardiac assist device patients were enrolled in the study between 25 November 2006 and 20 December 2006 after providing consent to undergo both venous and finger-stick blood samplings. To be a part of this study, patients should be above 18 years, had a ventricular assist device implant and should be on warfarin. The exclusion criteria included patients with poor cognitive levels and not willing to participate in the study. Mini mental status examination (MMSE) was used to assess cognition levels in these patients. Forty-one INR readings were assessed in these four patients while they were in the hospital. Six nurses in the Division of Cardiac Surgery at the University of Maryland, Baltimore participated in this study and were the users of proTime Microcoagulation system. Two one-hour training sessions were given to

the nurses by company representatives so as to get hands-on experience in using this device. In addition to the training session, a user manual, and an interactive CD as a guide to use this proTime Microcoagulation system were provided to the nurses. Three proTime Microcoagulation devices were placed at different floors of the hospital where these patients were admitted. Device A was used in two patients, devices B and C were used in the other two patients.

2.1. Point-of-care testing

The proTime Microcoagulation system for prothrombin time testing, PT-INR testing, consists of the proTime instrument, the reagent cuvette with built-in quality control, and the Tenderlett Plus sample collection system (ITC, NJ). The proTime accepts and stores patient and/or operator ID for reduced transcription errors. Further, the off-meter sampling feature provides unparalleled safety against possible sample contamination and disease transmission. According to the manufacturer, there is no need for calibration or reagent checks and no external controls are necessary.

2.2. Study procedure

The same patient who had given consent, a finger-stick sample was performed with Tenderlett plus finger-stick device and blood sample was again placed into the blood collection cup and immediately run on the proTime analyzer. The readings from the proTime Microcoagulation system were then recorded onto the patient record near their bedside. The time when the test was done was also recorded. The nurses in the cardiac surgery unit made sure that the blood collected for the device was at the same time when the blood was collected for the standard lab assay. Nurse's perception about the use of point-of-care device for coagulation monitoring in cardiac assist device patients was assessed using an attitudinal survey. The survey consisted of 11 questions focused primarily on gathering information about the nurse's attitudes towards the use of the system.

2.3. Statistical methods

Descriptive statistics was performed using univariate analysis to describe the study population. Pearson correlation coefficients were used to compare results for individual proTime microcoagulation devices with the laboratory data as well as to compare all proTime results with the laboratory results. Analysis of variance was used to compare the various INR measurements in all the three proTime meters. Bland Altman plots were used to compare the differences between the corresponding methods (proTime and lab) plotted against the average of the two measurements to look for trends and systematic bias. Bland Altman is a statistical method that allows the clinician to compare two different measurement techniques. All analyses performed were two tailed with *P*-values of 0.05 using SAS version 9.1 (Inc NC, Cary). The study was approved by the University of Maryland IRB board.

3. Results

The average age of patients with ventricular assist device was 52 (S.D.=1.3) years and all of them were males, hypertensive and target INR for was 2.5–3.5. The average difference in INR between all proTime devices and the laboratory device was 0.11 ± 0.28 (95% CI 0.03; 0.19) and absolute mean \pm S.D. was 0.23 ± 0.19 (95% CI 0.18; 0.28).

There was a significant correlation between the portable proTime device and the laboratory readings ($r=0.96$; $P<0.0001$). In addition, significant correlation coefficients for the individual proTime devices vs. the laboratory readings were seen varying from 0.86 to 0.98 (Table 1). There were no significant differences in the INR measurements across different proTime devices ($F=0.02$; $P=0.98$).

Correlation curves for the INR values reported by the proTime vs. the hospital lab INR values have been shown using linear regression analysis (Fig. 1). There was a significant positive correlation and the adjusted R^2 for the model was 0.927. A Bland Altman plot is constructed from the differences between each of the instrument's reported value and the average value (Fig. 2). Bland Altman analysis showed a bias of 0.11 and the limits of correlation were -0.45 and 0.66. The INR obtained from the proTime INR was within 0.5 of the hospital laboratory INR for 95% of the number of INR observations.

3.1. Nurses perception of using portable micro coagulation system

Six hospital nurses at the University of Maryland Hospital participated in this pilot study. An eleven item attitudinal survey gathered nurse's perception about using a portable point-of-care device. Results show that four out of six nurses had performed 2–5 INR tests; the others had performed 6–10 and 11–15 INR tests, respectively. Half of them found themselves comfortable after performing 1–2 tests using the proTime micro coagulation system. Three out of six nurses found performing finger stick with the Tenderlett most difficult. Four out of six hospital nurses indicated that most help in learning how to perform the INR test using this device was during their observation when the test was actually done by another nurse. Four out of six nurses considered INR testing using point-of-care device as a minimal interruption with their usual nursing activities. Three out of six nurses took <5 min to perform the INR test using this device. All six nurses agreed that it would be very important for them to know the results of the patient's self-testing INR right away. Four out of six nurses perceived that patients were likely to be 'significantly safer' if INR testing was routinely available to them after hospital discharge at their homes.

4. Discussion

Because of narrow therapeutic window of warfarin during VAD support, there is a great need to have continuous access to frequent and accurate monitoring of INR. It has been shown that patients who 'self-manage' their anticoagulation and check their INR more frequently are able to maintain a greater proportion of INRs within the therapeutic range compared with those whose therapy is monitored by a physician [15]. As a result of this more aggressive monitoring, a significant reduction in thromboembolic events (odds ratio (OR) 0.45), major hemorrhagic events (OR=0.65) and all-cause mortality (OR=0.61) has been noted and suggested that one way to improve anticoagulation management is the use of home testing devices. These handheld devices have proved sufficiently reliable to allow the patient to measure INR with only a drop of whole blood required.

In this study, we used proTime as a point-of-care device to monitor the degree of oral anticoagulant in VAD patients while they were in the hospital. This monitoring was performed using two methods: portable device proTime and standard laboratory method. Significant positive correlation was seen between INR levels measured using standard laboratory and portable device methods.

The study is of great importance, as it would improve patient safety by reducing the risk of bleeding associated with anticoagulant therapy in this high-risk VAD patient population. The patients can self-test or self-adjust treatment according to their dose-schedule and advantages may include improved convenience for the patients, better treatment compliance, and more frequent monitoring. There are several limitations of the study. One of the limitations is a small sample size and also the study was all males and so the generalizability of the results is difficult. The study should also include females to see if there are any gender differences in the use of portable point-of-care micro coagulation devices. The patients' ability to use portable point-of-care micro coagulation devices at home needs to be studied. Further, the long-term impacts of this monitoring on health outcomes were not assessed.

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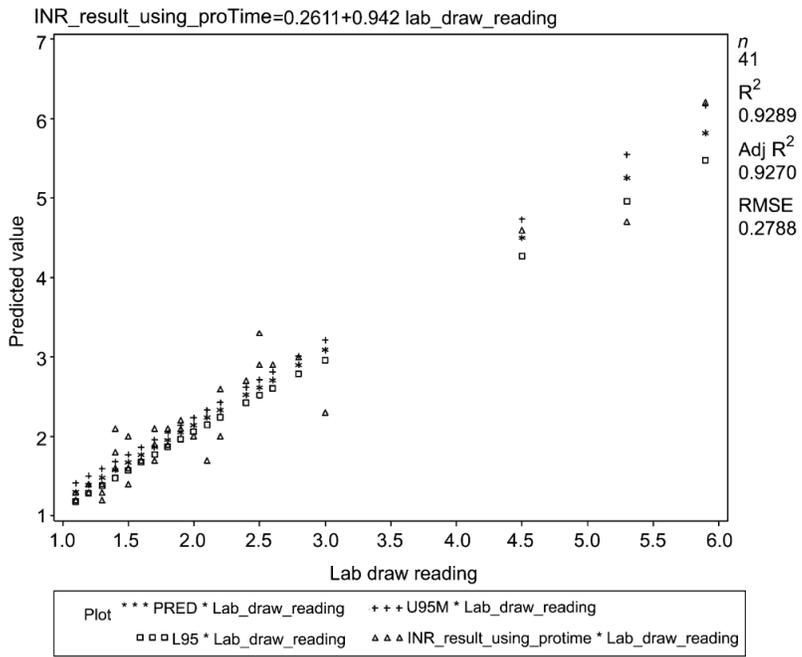


Fig. 1. Regression curves for INR measurements reported by the proTime vs. the hospital laboratory assay. Adjusted R^2 is 0.927.

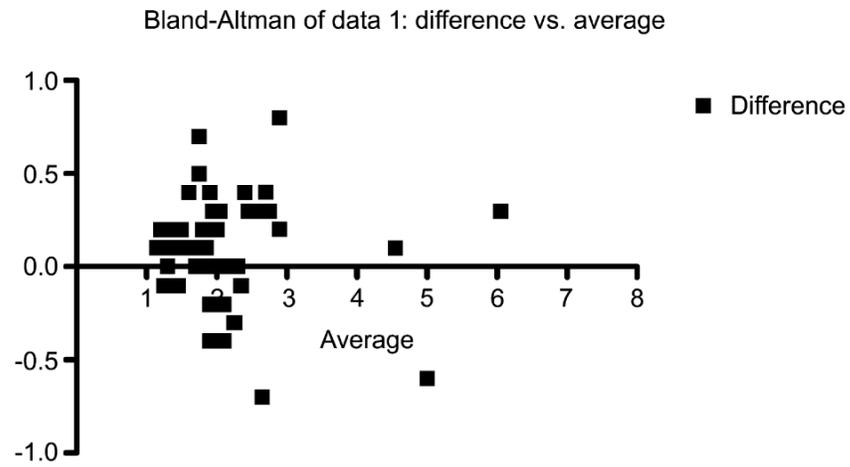


Fig. 2. Bland Altman analysis. The plot demonstrates that the majority of the international normalized ratio (INR) readings lie within a difference of 0.5.

Correlation coefficients (r) and P -values (P) of laboratory INR readings compared to overall proTime INR readings and also individual proTime microcoagulation devices

Table 1

Variable	Statistics	INR assessments using laboratory and proTime micro coagulation device	Device A $n=9$	Device B $n=3$	Device C $n=29$
INR assessments	r	Total $n=41$	0.92	0.98	0.86
	P	<0.0001	<0.0001	<0.0001	0.003