



Evaluation of a point-of-care coagulation device, the thrombolytic assessment system (TAS), for measuring prothrombin times, activated partial thromboplastin times, and high-dose heparin anticoagulation

R.C. GOSSELIN,¹ J.T. OWINGS,² M.E. POLLOCK,² E. LARKIN¹

Departments of¹Pathology and²Surgery, University of California Davis Medical Center, Sacramento, CA

ABSTRACT

The thrombolytic assessment system (TAS) is a new point-of-care analyzer that performs several coagulation assays from citrated whole blood or plasma. The purpose of this study was to determine the performance characteristics of this point-of-care analyzer vs. parent laboratory and other point-of-care methods (Coumatrak PT and Ciba-Corning 512 aPTT) on prothrombin times (PT) and activated partial thromboplastin times (aPTT). Activated clotting times (ACT) were compared with the TAS heparin management test for monitoring patients on high-dose heparin during cardiopulmonary bypass procedures. The TAS had statistically insignificant differences ($p = 0.56$) between parent lab PT using international normalized ratios. The TAS aPTT was significantly different from that of the clinical laboratory ($R^2 = 0.53$, $p < 0.05$) because of differences in reference intervals and heparin sensitivity. The TAS heparin management test was equivalent to the ACT ($R^2 = 0.68$) with better correlation to heparin levels than the ACT (R^2 for TAS = 0.49; R^2 for ACT = 0.23). *Lab Hematol* 4:217-224, 1998

KEY WORDS: Activated clotting time · Cardiopulmonary bypass · Heparin management test · International normalized ratio

INTRODUCTION

Point-of-care coagulation testing has been in use for more than 30 years. Hattersly [1] developed the activated clotting time (ACT) in 1966 as a means of monitoring heparin anticoagulation during

cardiopulmonary bypass. Since that time, other methods and mechanical detection systems have been developed for facilitating patient care by providing coagulation testing outside the laboratory. The thrombolytic assessment system (TAS) (Cardiovascular Diagnostics, Raleigh, NC) is a new point-of-care device used for performing prothrombin times (PT), activated partial thromboplastin times (aPTT), and a test equivalent to activated clotting time, the heparin management test (HMT). Several point-of-care coagulation analyzers are currently available for clinical use. They primarily use whole blood from a fingerstick, while the TAS methods require citrated whole blood or plasma. The purpose of this study was to compare the TAS with an established clinical laboratory method and other point-of-care devices used for assessing coagulation status.

METHODS

Sample Selection and Preparation

Normal donors, patients documented to be receiving oral anti-coagulation or heparin therapy, or patients with clinical events associated with coagulopathy (including disseminated intravascular coagulation, liver disease, and trauma) were selected for PT and aPTT analysis. The high-dose heparin anticoagulation of patients undergoing cardiopulmonary bypass was monitored with both ACT and HMT.

All samples to be analyzed using TAS were collected into 0.105-M buffered sodium citrate vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ) using a 21-gauge butterfly needle and syringe. For whole blood testing, a single drop of whole blood was immediately (within 15 seconds) added to the test cartridge before citrate anticoagulation. Citrated whole blood samples were first tested on the TAS system. The residual citrated sample was then centrifuged at 1500g for 15 minutes to achieve platelet-poor plasma ($<10 \times 10^9/L$) and subsequently tested using the standard clinical laboratory methods described below. Plasma samples requiring additional testing were frozen at $-70^\circ C$ until tested. Except for whole blood assays, all samples were tested within 1 hour of collection. To prevent cold activation of factor VII, all citrated samples

Address correspondence to John T. Owings, MD, University of California Davis Medical Center, 4301 X Street, Sacramento, CA 95817.

Received 29 June 1998; accepted 18 September 1998

TABLE 1. Operational features of the point-of-care devices analyzed

	TAS	Coumatrak	Ciba-Corning 512	Hemotec
Detection method	Paramagnetic iron oxide particles	Optical detection of changes in blood flow	Optical detection of changes in blood flow	Optical detection of changes in mechanical resistance
Reagent activator				
PT	Rabbit brain thromboplastin	Rabbit brain thromboplastin	Soybean phosphatides	Kaolin
aPTT	Aluminum magnesium silicate	—	Bovine brain sulfatide activator	—
HMT	Celite	—	—	—
ISI	1.62	2.04	NA	NA
Sample type	Citrated whole blood or plasma	Whole blood	Whole blood	Whole blood
Dimensions (L × W × H) (inches)	10.5 × 6 × 3.9	6.8 × 3.6 × 2.0	6.7 × 3.5 × 2.0	9.5 × 8.0 × 6.5
Weight (kg)	1.9	0.52	0.55	3.4

were maintained and processed at room temperature (22–28°C). All tests were performed according to manufacturer's instructions.

TAS

The TAS method uses a single-use test cartridge containing paramagnetic iron oxide particles [2] and a specified reagent for each analyte (Table 1). Each TAS test cartridge is lot-specific and is magnetically coded with cartridge (test) type and any appropriate calibration factors or normal reference intervals determined by the manufacturer. The TAS instrument reads this encoded information before testing. Citrated whole blood (or plasma) is added to the test cartridge once it has been inserted into the TAS device. The blood moves via capillary action and mixes with the paramagnetic iron oxide particles and reagent within the testing chamber. Simultaneously, the device creates a pulsating magnetic field that causes the iron oxide particles to move up and down. As the sample clots, the decreased movement of the particles is detected optically, and the resultant time is displayed in seconds, as well as ratios and international normalized ratios (INR) for PT. The TAS unit can be set up to use either a fixed reference mean (as determined by the manufacturer) or can be altered by the end user. Unless otherwise specified, the reference mean and international sensitivity index (ISI) are encoded on the test cartridge. For PT, the TAS uses rabbit brain thromboplastin source with an ISI of 1.62. The aPTT reagent contains rabbit

brain phospholipids, calcium chloride, buffers, and aluminum magnesium silicate as activator. The HMT uses celite as activator.

Point-of-Care PT

The Coumatrak (distributed by Boehringer Mannheim, Indianapolis, IN) is a small point-of-care coagulation device that uses whole blood for performing PT tests [3]. With the Coumatrak, whole blood is added to a single-use cartridge inserted into the device. The blood travels via capillary action into the reagent chamber and continues along a track. As the sample clots, the decrease in blood flow is optically monitored by a laser, and the resultant time displayed in seconds, with PT ratio (PT seconds/reference mean) and INR. The thromboplastin source is rabbit brain with a fixed reference mean (determined by the manufacturer) and an ISI of 2.04 encoded on each test cartridge. The usual sample type is whole blood acquired by fingerstick, but manufacturer recommendations and previous studies [4] have indicated that whole blood from phlebotomy is acceptable.

Parent Clinical Laboratory Method

Processed citrated plasma samples were tested on the MLA 1000C coagulation analyzer (Medical Laboratory Automation, Pleasantville, NY) using Dade (Miami, FL) reagents. For PT testing, a recombinant thromboplastin (Innovin) was used with an

TABLE 2. Correlation data of TAS methods vs. parent clinical laboratory and Medtronic ACT methods

	TAS vs. Innovin (INR)	TAS aPTT vs. Actin FS (INR)	TAS HMT vs. Medtronic ACT
n	62	121	326
R ²	0.953	0.53	0.68
Slope (95% CI)	1.12 (1.18 to 1.05)	1.19 (0.99 to 1.39)	2.13 (1.98 to 2.30)
Intercept (95% CI)	-0.17 (-0.29 to -0.04)	-9.36 seconds (-19.1 to -0.41)	-230.4 seconds (-290.7 to -169.4)
Standard error	0.26	10.1	155.8
Mean bias ± SD	-0.02 ± 0.33	0.50 ± 16.6	-183.4 ± 197.2
p value	0.56	<0.005	<0.005

Mean bias data was calculated by the TAS method minus the predicate device method. P values were determined using Student's paired t-test.

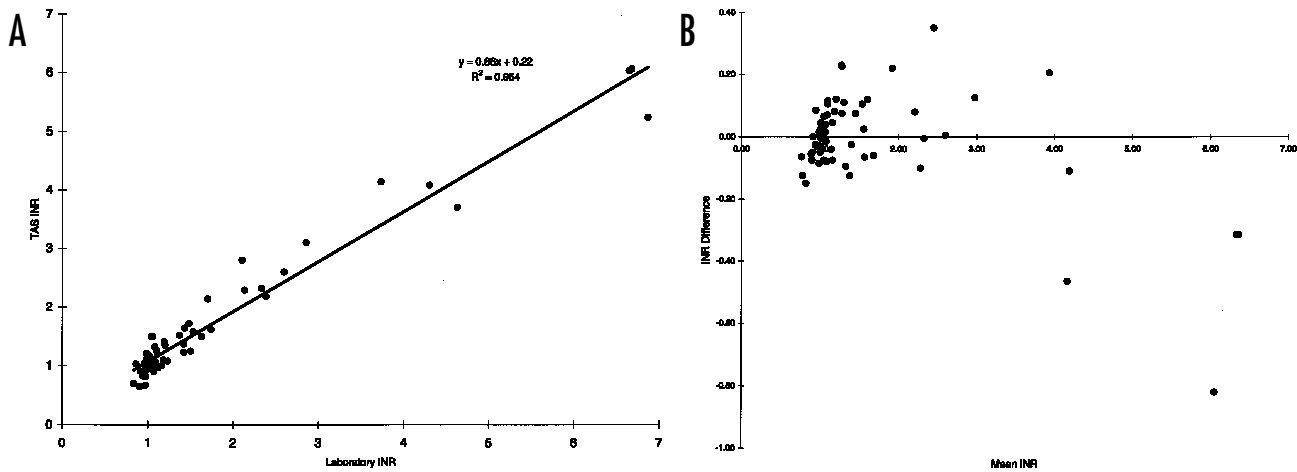


FIGURE 1. A. Regression analysis of the TAS INR to the clinical laboratory method using Innovin recombinant thromboplastin. B. Bland and Altman plots demonstrating the bias between the TAS INR and method mean. The data indicate an increasing negative bias with the TAS method with prolonged INRs of >4.5.

MLA system–specific ISI of 0.93. Reference mean was determined from 100 normal healthy donors before clinical use of Innovin. INRs were calculated by the MLA instrument. For aPTT testing, Actin FS was used, containing ellagic acid as activator, stabilizers, and buffers.

Point-of-Care aPTT

The Ciba-Corning 512 (distributed by Boehringer Mannheim) also uses a whole blood sample. The device's principle of operation is the same as the Coumatrak method, except the test cartridge contains a soybean activator and phospholipids.

ACT

Blood samples routinely drawn from patients undergoing cardiopulmonary bypass to monitor the degree of heparin anticoagulation [5] were used to compare the ACT with the TAS HMT. Samples were drawn just before anesthesia induction (baseline), immediately after heparin dosing, during hypothermic cardiopulmonary bypass, and immediately post-bypass after protamine reversal. All patients received porcine heparin (Elkin-Sinns, Cherry Hill, NC) at an initial dose of 300 U/kg; their dose was adjusted (if necessary) to

maintain ACTs of greater than 400 seconds while on bypass. All patients were given 30 mg/kg protamine at the end of bypass.

For ACT testing, whole blood was drawn and tested using the Hemotec (Medtronic Hemotec, Englewood, CO) ACT. Its method [5,6] uses a double-well reagent cartridge containing kaolin as activator. A whole blood sample is dispensed into a prewarmed (37°C) reagent cartridge inserted into the ACT instrument. When the testing cycle is initiated, plungers in the cartridge move up and down, mixing the reagent and blood together. These plungers continue to move until fibrin is formed. As fibrin strands adhere to the plunger, the reduced movement of the plunger is detected optically and the resultant time is displayed in seconds.

Heparin Levels

Heparin levels were determined on plasma from patients receiving heparin treatment and during cardiopulmonary bypass procedures. All quantitative heparin levels were determined in duplicate using a chromogenic method based on factor Xa inhibition (Stago Asserachrom Heparin, Parsippany, NY) on the MLA 900C coagulation analyzer. Cardiopulmonary bypass samples that had heparin levels beyond the assay's linear range (>0.6 U/mL) were diluted

TABLE 3. Correlation data between the TAS and other point-of-care devices

	Coumatrak	Ciba-Corning 512
n	45	59
R^2	0.86	0.56
Slope (95% CI)	1.22 (0.96 to 1.48)	0.51 (0.39 to 0.63)
Intercept (95% CI)	-5.2 seconds (-9.5 to -0.87)	19.0 seconds (12.2 to 25.9)
Standard error	2.5	8.5
Mean bias \pm SD	-1.6 \pm 2.6 seconds	-7.1 \pm 12.4 seconds
p value	0.05	<0.005

Mean bias result is the average difference (in seconds) between the TAS methods less the respective point-of-care methods. p values were determined using Student's paired t-test.

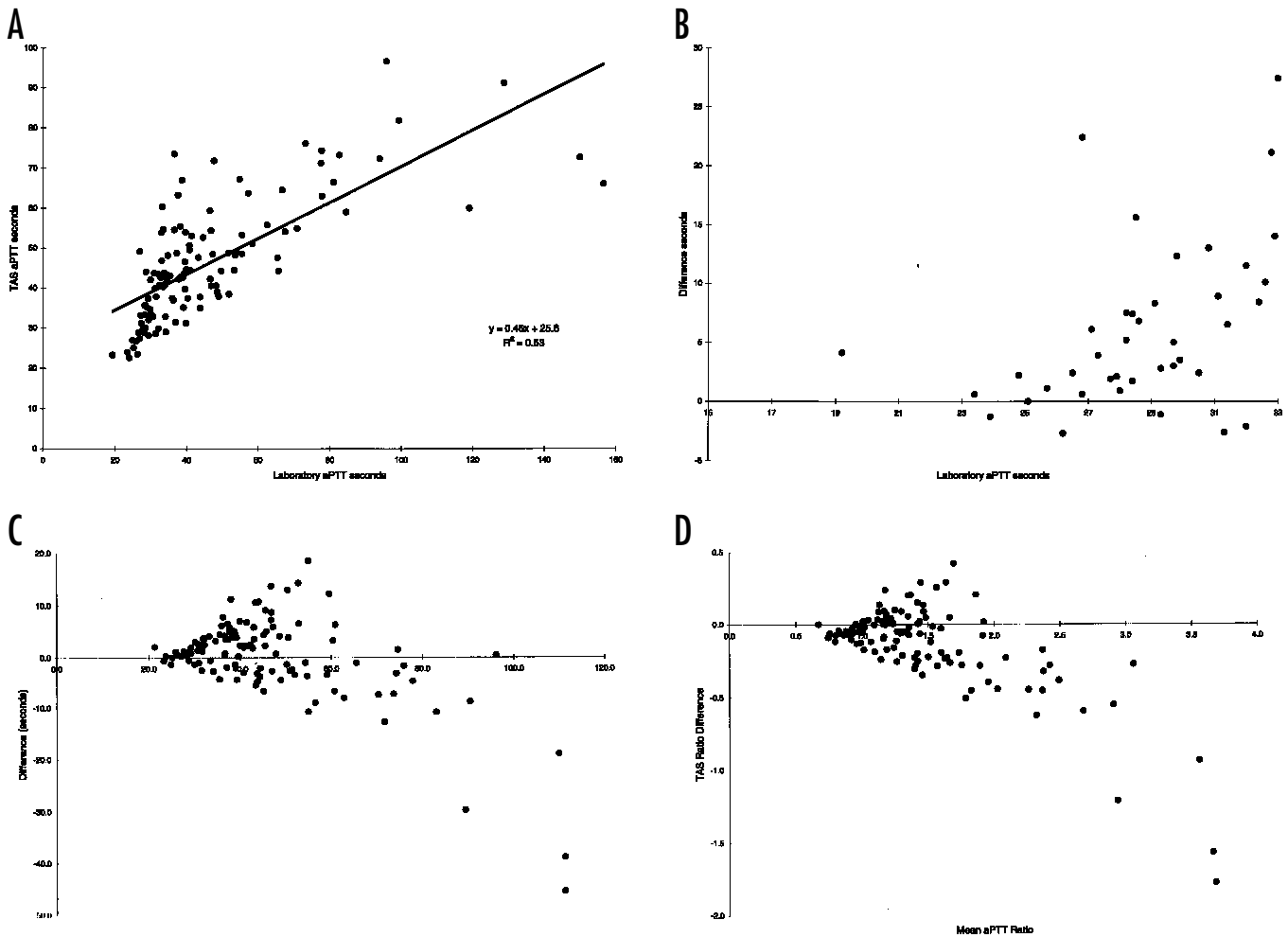


FIGURE 2. A. Regression analysis of the TAS aPTT to the clinical laboratory method using the MLA 1000C and Actin FS reagent. B. A subpopulation of the previous figure indicating the bias between the TAS and the clinical laboratory for normal samples. C. Bland and Altman plots demonstrating the bias between the TAS aPTT method and the clinical laboratory method. The data indicate a negative bias with increasing aPTTs. D. Bland and Altman plots demonstrating the bias between the TAS aPTT and the clinical laboratory method when comparing ratios.

with saline at two different dilutions and repeated, and the final results were corrected for the required dilution.

Precision Studies

Within-run and day-to-day precision studies were performed on the PT and aPTT TAS methods. Within-run analysis used a single-donor whole blood sample. Day-to-day studies were performed using reconstituted lyophilized plasma, prepared according to manufacturer's instructions, separated into aliquots, and quick-frozen at -70°C until use. The frozen plasma was thawed in a 37°C water-bath for 5 minutes and gently mixed before use.

Statistical Analysis

For all methods, correlation was established based on a regression analysis, slope, intercept (with 95% confidence intervals), and standard error. Mean bias differences were also calculated. Differences between the mean values at a given time point for different

test methods were evaluated with the Student's paired t -test. A p value of <0.05 was established as significant.

RESULTS

Statistical correlations between the TAS methods and the reference PT, aPTT, and ACT are listed in Table 2. Given the frank differences between Innovin and the TAS ISI values, the PTs were not expected to match and did not ($R^2 = 0.63$, data not shown). Only the INRs were correlated ($R^2 = 0.953$) for all samples. This correlation did not change significantly when samples from patients on oral anticoagulant therapy of ≥ 7 days were analyzed separately ($R^2 = 0.949$). The regression analysis and bias plot graphs (Fig. 1) indicate fairly even distribution, but there appears to be a negative bias between the TAS and laboratory methods at INRs of greater than 4.5. Increasing bias for PTs and INRs outside the therapeutic interval has been noted in other studies [7,8]. The TAS prothrombin

TABLE 4. Correlation data for respective systems and heparin levels based on factor Xa inhibition

	Actin FS	TAS	Ciba-Corning 512	Medtronic ACT	HMT
n	25	25	25	326	326
R ²	0.76	0.44	0.17	0.23	0.49
Slope (95% CI)	182.4 (138 to 227)	112.9 (58.1 to 167.8)	58.5 (33.2 to 83.9)	69.6 (57.2 to 82.1)	39.2 (35.2 to 43.2)
Intercept (95% CI)	7.6 seconds (-11.0 to 26.3)	29.0 seconds (5.9 to 52.1)	63.0 seconds (2.8 to 123.2)	355.3 (309.2 to 401.5)	236.8 (221.9 to 251.7)
Standard error	28.1	34.7	38.2	267.7	86.4
Mean bias ± SD	-3.2 ± 22.7	-4.0 ± 13.5	8.3 ± 24.0	NA	NA

Bias data were calculated from individual system results minus the average for all system results.

times correlated with the Coumatrak whole blood method ($R^2 = 0.86$) as well as with the INRs ($R^2 = 0.85$) (Table 3).

For aPTT testing, the correlation between the TAS and parent laboratory method was not as strong ($R^2 = 0.53$) as the INR correlation. The regression graph (Fig. 2A) and bias plots indicate positive bias with normal samples (Fig. 2B) and negative bias with prolonged aPTTs (Fig. 2C). APTT ratios were determined using the mean normal interval for each group (MLA, 28.7 ± 3.0 seconds [mean \pm SD]; TAS, 34.7 ± 8.6 seconds) as the respective denominator for each result, with negative bias for prolonged aPTTs but smaller bias within the normal or slightly prolonged aPTTs (Fig. 2D). An additional component to the poor aPTT correlation can be explained by each method's differing response to heparin (Fig. 3). All aPTT methods correlated fairly poorly with anti-Xa levels (Table 4). The therapeutic heparin range using a modified heparin response curve [9,10] would be 60–132 seconds for the Actin FS, 60–107 seconds for the TAS, and 75–102 seconds for the Ciba-Corning 512. The TAS method correlated poorly with the Ciba-Corning whole blood method ($R^2 = 0.56$), and the differences were statistically significant (Table 3).

The HMT is an ACT-equivalent test intended for monitoring high-dose heparin anticoagulation used in cardiopulmonary bypass surgery. In this study, the HMT demonstrated statistically significant differences from the Medtronic ACT. The correlation ($R^2 = 0.68$), slope, and intercept all indicate a negative bias of the HMT to the ACT. This is further demonstrated by the bias plot figure (Fig. 4A). There was also a poor correlation to heparin levels (as measured by anti-Xa activity) with both methods, although the HMT showed a stronger correlation than the ACT (Table 4). Poor correlation of the ACT to heparin levels has been documented [6,11].

The within-run and day-to-day precision for PT and aPTT are listed in Table 5. Precision studies were not performed on the other point-of-care devices, but for comparison, manufacturer-provided within-run and day-to-day precision data are listed for the Coumatrak and Ciba-Corning 512. The clinical laboratory precision is based on weekly (within-run) and monthly (day-to-day) data collection as part of the routine quality control performed in our laboratory.

DISCUSSION

Point-of-care coagulation testing has been used primarily to monitor the pharmacological effects of heparin and coumadin anticoagulation. Point-of-care measurement of prothrombin times facilitates

rapid assessment of coumadin anticoagulation in outpatient settings including anticoagulation clinics, home care, hospice programs, and patient self-testing [3,11–15]. In addition to monitoring heparin anticoagulation for thromboprophylaxis [16–19], point-of-care monitoring of heparin anticoagulation has been used in continuous venovenous hemodialysis [20–22], extracorporeal membrane oxygenation [23,24], and post-angioplasty sheath removal [25,26]. Measuring the anticoagulation effect of heparin at therapeutic and prophylactic doses can be achieved with the aPTT. Procedures that require higher heparin dosing, such as interventional radiology, would require alternative methods (such as the ACT or HMT) because the aPTT is too sensitive to the heparin dose used and will often surpass the maximum clot time allowed (therefore generating the result “no clot detected”). Higher-dose heparin anticoagulation used in cardiac catheterization and cardiopulmonary bypass has been monitored using ACT or alternative monitoring devices such as thromboelastography [5,26,27]. The poor correlation of ACT to heparin levels may be due in part to other conditions known to affect coagulation, including hypothermia, hemodilution, diminished antithrombin levels noted during bypass, decreased fibrinogen level, and the effect of concomitant drugs such as aprotinin.

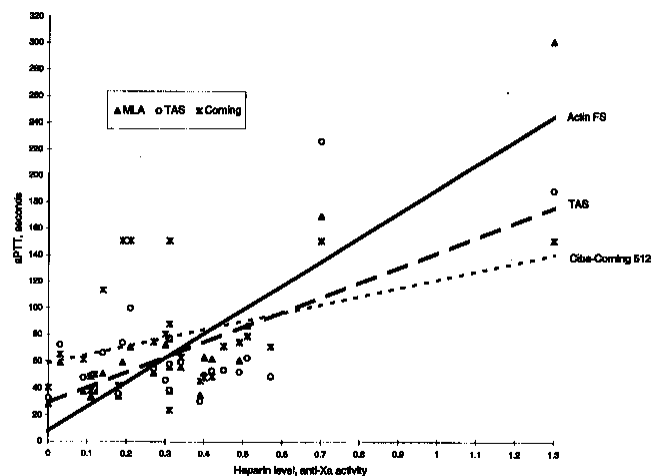


FIGURE 3. Modified heparin response curve for the laboratory (MLA), TAS, and Ciba-Corning 512 methods, comparing aPTT times with anti-Xa activity.

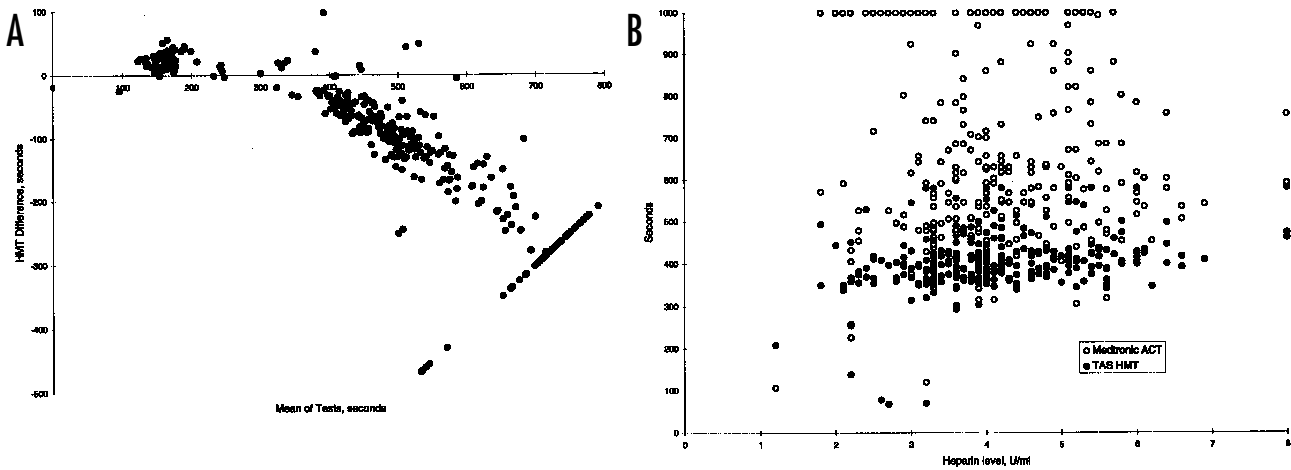


FIGURE 4. A. Bland and Altman plots for the TAS HMT method compared with the Medtronic ACT. B. Scatterplot for the HMT and ACT results with corresponding heparin levels determined by anti-Xa activity. These data include only samples tested after heparin bolusing and during cardiopulmonary bypass. Preheparinization and protamine reversal after bypass were not included in this analysis.

The TAS is capable of performing multiple coagulation assays and, unlike most other point-of-care coagulation methods, which use whole blood, it uses either citrated whole blood or plasma (we

used citrated whole blood in this study); the manufacturer has since developed a whole blood HMT. The current recommendations for thromboplastin sensitivity for prothrombin time testing

TABLE 5. Precision and accuracy studies for TAS PT and aPTT

	TAS		Coumatrak ^a		Laboratory	
	Level I	Level II	Level I	Level II	Level I	Level II
PT						
Day-to-day precision						
n	34	35	—	—	45	45
Mean (seconds)	11.6	28.2	12.2	20.1	11.2	29.8
SD (seconds)	0.8	1.70	—	—	0.2	0.8
CV (%)	6.9	6.0	3.5	2.2	1.8	2.7
Within-run reproducibility						
Mean (seconds)	—	25.1	12.3	20.0	13.8	—
SD (seconds)	—	3.55	—	—	0.1	—
CV (%)	—	8.0	4.9	2.9	0.7	—
	TAS		Ciba-Corning ^a		Laboratory	
	Level I	Level II	Level I	Level II	Level I	Level II
aPTT						
Day-to-day precision						
n	30	30	—	—	45	50
Mean (seconds)	30.0	46.5	56.2	116.8	29.7	50.0
SD (seconds)	0.6	1.3	—	—	0.5	0.7
CV (%)	2.0	2.7	5.8	3.8	1.7	1.4
Within-run reproducibility						
Mean (seconds)	—	43.5	55.7	116.1	—	38.2
SD (seconds)	—	1.54	—	—	—	0.35
CV (%)	—	6.1	4.7	4.5	—	0.9

^aThe data listed for Coumatrak and Ciba-Corning 512 are derived from product inserts. Day-to-day precision data are from analysis of control (citrate plasma) material. Within-run accuracy data are from a single abnormal citrated whole blood sample tested within 30 minutes of phlebotomy.

is an ISI of 1.0–1.2. The TAS sensitivity in our study was higher than that (ISI 1.62) but lower than that of the Coumatrak (ISI 2.04). Since the time of this study, newer TAS methods have been developed with lower ISI values (around 1.0) for both non-anticoagulated whole blood and citrated anticoagulated whole blood or plasma.

The TAS device is larger than most point-of-care coagulation devices but has additional features not found with other instruments. It has data storage capacity of approximately 2000 tests, and the data can be downloaded from an external port to a host computer or printer. The TAS unit is also equipped with a key pad to facilitate alphanumeric data entry, such as patient name and medical record number. The device can be programmed to require password access to operate the unit, preventing unauthorized use of the device by untrained personnel.

Biases are to be expected between whole blood point-of-care systems and parent clinical laboratory methods [28]. Because the TAS system uses a citrated sample, further evaluation of system biases can be facilitated (the same sample used for TAS testing can be further tested for heparin levels [anti-Xa activity] or factor activity to correlate test [PT or aPTT] sensitivity to factor deficiencies). This is not readily accomplished using whole blood samples. Unlike most other point-of-care methods, the TAS allows each site to change the reference mean for PT, which may more accurately calculate the INR.

Currently, the TAS method is approved for performing PTs, aPTTs, and HMT. Additional assays not approved for clinical use are available, including Ecarin clot time for measuring the effects of direct antithrombin drugs [29] and cartridges for measuring the effects of thrombolytic therapy, calculating lysis onset time [29,30], and detecting streptokinase antibodies.

CONCLUSIONS

In our study, the TAS system demonstrated excellent correlation with laboratory INRs in the therapeutic range. With the variations in reagent sensitivity, as expressed by the ISI, prothrombin times were statistically different between the TAS and the other PT methods, but the INR bias between the TAS and the laboratory and Coumatrak methods were not statistically significant, except for a statistically significant bias between the TAS aPTT and the laboratory method. The normal reference range for the TAS aPTT was markedly different from that of the laboratory method, but using aPTT ratios did not improve the correlation between the two systems. Part of the bias was due to heparin sensitivity, and the TAS methods correlated more strongly with heparin levels than the Ciba-Corning 512, but both methods correlated poorly. The HMT was statistically different from the ACT, but correlated more strongly with heparin levels. As a result of the bias, use of the HMT in cardiopulmonary bypass may require different monitoring targets than the recommended >400 seconds with the ACT.

REFERENCES

- HATTERSLY PG: Activated clotting time of whole blood. *JAMA* 196:436, 1966
- OSBERHARDT BJ, DERMOTT SC, TAYLOR M, ALKADI ZY, ABRUZZINI AF, GRESALFI NJ: Dry reagent technology for rapid, convenient measurement of blood coagulation and fibrinolysis. *Clin Chem* 37:520, 1991
- MCCURDY SA, WHITE RH: Accuracy and precision of a portable anticoagulation monitor in a clinical setting. *Arch Intern Med* 152:589, 1992
- GOSSELIN RC, OWINGS JT, LARKIN E, WHITE RH, HUTCHINSON R, BRACH J: Monitoring oral anticoagulation therapy with point-of-care devices: Correlations and caveats. *Clin Chem* 43:1785, 1997
- SPIESS BD: Coagulation function in the operating room. *Anesth Clin North Am* 8:481, 1990
- GRAVLEE GP, HADDON WS, ROTHBERGER HK, MILLS SA, ROGER AT, BEAN VE, BUSS DH, PROUGH DS, CORDELL AR: Heparin dosing and monitoring for cardiopulmonary bypass. A comparison of techniques with measurement of subclinical plasma coagulation. *J Thorac Cardiovasc Surg* 99:518, 1990
- BADER R, MANNUCCI PMM, TRIPODI A, HIRSH J, KELLER F, SOLLEDER EM, HAWKINS P, PENG M, PELZER H, TEJIDOR LM, RAMIREZ IE, KOLDE HJ: Multicentric evaluation of a new PT reagent based on recombinant human tissue factor and synthetic phospholipids. *Thromb Haemost* 71:292, 1994
- SCHMITZ LL, OLSON SL, SHAPIRO RS, MCCORMICK SR, KUBIC VL: Failure to generate comparable international normalized ratio values using five different thromboplastin reagents in parallel studies of patients receiving warfarin. *Clin Appl Thromb/Hemost* 1:142, 1995
- BRILL-EDWARDS P, GINSBERG JS, JOHNSTON M, HIRSH J: Establishing a therapeutic range for heparin therapy. *Ann Int Med* 119:104, 1993
- HIRSH J, RASCHKE R, WARKENTIN TE, DALEN JE, DEYKIN D, POLLER L: Heparin: Mechanism of action, pharmacokinetics, dosing concentrations, monitoring, efficacy and safety. *Chest Suppl* 108:258S, 1995
- HORKAY F, MARTIN P, RAJAH SM, WALKER DR: Response to heparinization in adults and children undergoing cardiac operations. *Ann Thorac Surg* 53:822, 1992
- WANG JS, LIN CY, HUNG WT, KARP RB: Monitoring of heparin-induced anticoagulation with kaolin activated clotting time in cardiac surgical patients treated with aprotinin. *Anesth* 77:1080, 1992
- MASSICOTTE P, MARZINOTTO V, VEGH P, ADAMS M, ANDREW M: Home monitoring of warfarin therapy in children with a whole blood prothrombin time monitor. *J Pediatr* 127:389, 1995
- YANO Y, KAMBAYASHI JI, MURATA K, SHIBA E, SAKON M, KAWASAKI T, MORI T: Bedside monitoring of warfarin therapy by a whole blood capillary coagulation monitor. *Thromb Res* 66:583, 1992
- ROSE VL, DERMOTT SC, MURRAY BF, MCIVER MM, HIGH KA, OSBERHARDT BJ: Decentralized testing for prothrombin time and activated partial thromboplastin time using a dry chemistry portable analyzer. *Arch Pathol Lab Med* 117:611, 1993
- BECKER BC, CYR J, CORRAO JM, BALL SP: Bedside coagulation monitoring in heparin-treated patients with active thromboembolic disease: A coronary care unit experience. *Am Heart J* 128:719, 1994
- DESPOTIS GJ, HOGUE CW, SANTORO SA, JOIST JH, BARNES PW, LAPPAS DG: Effect of heparin on whole blood activated partial thromboplastin time using a portable, whole blood coagulation monitor. *Crit Care Med* 23:1674, 1995
- WERNER M, GALLAGHER JV, BALLO MS, KARCHER DS: Effect of analytic uncertainty of conventional and point-of-care assays of activated partial thromboplastin time on clinical decisions in heparin therapy. *Am J Clin Pathol* 102:237, 1994
- REINER JS, COYNE KS, LUNDERGAN CF, ROSS AM: Bedside monitoring of heparin therapy: Comparison of activated clotting time to activated partial thromboplastin time. *Cath Cardiovasc Diag* 32:49, 1994
- STROHSCHNEIN BL, CARUSO DM, GREENE KA: Continuous venovenous hemodialysis. *Am J Crit Care* 3:92, 1994
- MARTIN PY, CHEVROLET JC, SUTER P, FAVRE H: Anticoagulation in patients treated by continuous venovenous hemofiltration: A retrospective

- study. *Am J Kidney Dis* 24:806, 1994
- 22 LEEUWENBERG JFM, MAT O, ABRAMOWICZ D, GASTALDELLO R, TIELMANS C, BUURMAN WA: Increased plasma levels of soluble tumor necrosis factor-receptors in uraemic patients: Effects of dialysis, type of membrane, and anticoagulation method. *Nephrol Dial Transplant* 9:1125, 1994
 - 23 MCMANUS ML, KEVY SV, BOWER LK, HICKEY PR: Coagulation factor deficiencies during initiation of extracorporeal membrane oxygenation. *J Pediatr* 126:900, 1995
 - 24 NEWBERRY J: Coagulation monitoring during extracorporeal membrane oxygenation: The role of thromboelastography. *J Extracorporeal Tech* 27:137, 1995
 - 25 PEET GI, MCGRATH MA, BRUNT JH, HILTON JD: Femoral sheath removal after PTCA: A cross-Canada study. *Can J Cardiovasc Nurs* 6:13, 1995
 - 26 BOWERS J, FERGUSON JJ: The use of activated clotting times to monitor heparin therapy during and after interventional procedures. *Clin Cardiol* 17:357, 1994
 - 27 DESPOTIS GJ, JOIST JH, HOGUE CW JR, ALSOUFIEV A, KATER K, GOOD-NOUGH LT, SANTORO SA, SPITZNAGEL E, ROSENBLUM M, LAPPAS DG: The impact of heparin concentration and activated clotting time monitoring on blood conservation. *J Thorac Cardiovasc Surg* 110:46, 1995
 - 28 MACIK BG: Designing a point-of-care program for coagulation testing. *Arch Pathol Lab Med* 119:929, 1995
 - 29 OBERHARDT BJ, MIZE PD, PRITCHARD CG: Point-of-care fibrinolytic tests: The other side of blood coagulation. *Clin Chem* 43:1697, 1997
 - 30 SANE DC, GRESALFI NJ, ENNEY-O'MARA LA, CALIFF RM, GREENBERG CS, BOVILL EG, OBERHARDT BJ: Exploration of rapid bedside monitoring of coagulation and fibrinolysis parameters during thrombolytic therapy. *Blood Coagul Fibrinol* 3:47, 1992