Factors Affecting the Activated Clotting Time

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Abstract

The activated clotting time (ACT) has become an important tool for monitoring the status of coagulation potential in patients undergoing cardiopulmonary bypass (CPB). Variability in results leads to confusion in interpretation of results. This study examined several CPB variables that may affect the ACT.

Samples from a controlled patient population were analyzed to evaluate relationships between blood gas analysis, hematocrit, total protein concentration and temperature at which ACT was performed and the ACT.

Duplicate samples were drawn for ACT determination (one in a 37°C. heat block and one at room temperature). Concurrent blood gas analysis, hematocrit and total protein measurements were made.

There were significant differences between room temperature and heat block ACT during all stages of CPB but, at most times, a strong correlation existed (r ranged between .21 and .89). A positive correlation between post heparin ACT and hematocrit was shown, r=.48, while a negative correlation between post protamine ACT and hematocrit occurred, r=-.23.

Conditions under which the ACT is measured are very important for accuracy and it may be desirable to adjust a patient's dose response based on the hematocrit.

Introduction

Accurate assessment of coagulation potential is important for successful CPB.[1] The ACT is a popular method of evaluating the patients response to heparin because of its reliability, sensitivity and simplicity.[2,3]

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Prolongation of the ACT in the heparinized patient is directly proportional to the concentration of heparin in the blood.[4] However, it has been reported that the ACT may be influenced by variables other than heparin concentration.[5] Hemodilution,[6] coagulation factor depletion[7] and hypothermia[8] have been shown to prolong the ACT. Other phenomena may also vary the ACT during CPB.

This study was designed to investigate the relationship between hematocrit, pH, pCO_2, total protein concentration and the ACT. The hypothesis to be tested is that there is no difference between these variables and the ACT.

Materials and Methods

Twenty-one adult male patients, aged 40-70 years, weighing 55-105 kilograms and undergoing CPB for coronary artery bypass graft, were selected. A Travenol modular pump[a] and either a Travenol membrane oxygenator[b] or a Shiley S-100A were utilized along with a non-filtered cardiotomy reservoir[c], arterial line filter[d], PVC tubing and monitoring accessories. Priming volume was 2500cc, consisting of 500cc 6% hydroxyethyl starch[e], 1500 units beef lung heparin[f] and 2000cc Ringers Lactate[a]. Patients requiring the addition of blood or additional heparin during CPB were eliminated from the study.

Each patient received 300 units per kilogram of beef lung heparin[f] at least five minutes prior to CPB. ACT

a Travenol Laboratories, Deerfield, IL 60015.
b Shiley, Inc., Irvine, CA 92714.
c Bentley Laboratories, Model Q220, Irvine, CA 92714.
d Pall Biomedical Products Corp., Model 3840, Glen Cove, NY 11542.
e Hespan, American Critical Care, McGraw Park, IL 60085.
f Upjohn, Kalamazoo, MI 49001.

TABLE 1
Hb ACT vs RT ACT

	Baseline	5 min post Heparin	5 min on Bypass	Hypothermia	Rewarm	20 min post Protamine
$\overline{HB}$ ACT	100±13.4	351.5±69.5	372±70.6	346±52.3	317±88.3	101±12
$\overline{RT}$ ACT	150.9±40.7	803.3±239.5	910.5±363.5	825±237.1	646±308.9	161.5±34.5
n=20	r=.71	r=.79	r=.82	r=.49	r=.87	r=.21

and blood gas samples were analyzed at the following times:

1. Baseline ACT prior to any major surgical trauma;
2. Five minutes after the heparinizing dose was administered;
3. Five minutes after CPB was initiated;
4. Upon achievement of hypothermia (24-28 °C);
5. Upon rewarming just prior to CPB termination (36-38 °C);
6. Twenty minutes after protamine administration.

The ACT's were performed using a modified Hattersley technique[5] and a Lab-Line Instruments heat block[g] (HB) at 37 °C. Total protein concentration[h], hematocrit (HCT), pCO_2[i] and pH[i]* were measured simultaneously. An ACT at room temperature (RT) was also concurrently performed. Data comparing HB ACT versus RT ACT were analyzed using the Student's T-Test. Other data were analyzed by means of linear regression and correlation coefficient

Results

Table 1 and Figure 1 present data comparing the HB ACT versus RT ACT. There are significant differences at all phases of bypass.

Though a relationship exists between ACT and HCT, the only time that is achieved significance was five minutes post heparin when a positive correlation was shown. See Table 2 and Figure 2. An inverse relationship between ACT and HCT was shown twenty minutes post protamine. See Figure 3.

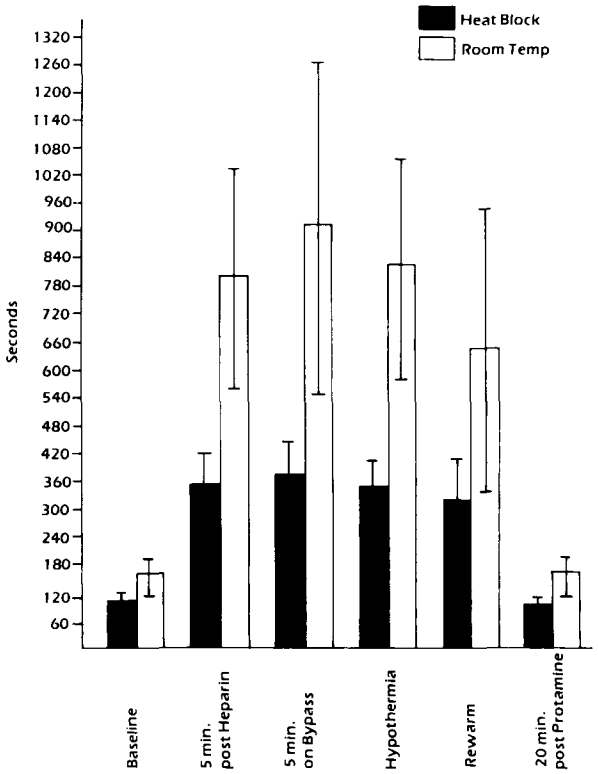

Figure 1: Heat Block ACT versus Room Temperature ACT

There were two times when hydrogen ion concentration and pCO_2 appeared to have an effect on ACT. The regression equations are presented in Table 3. There was no association between ACT and total protein concentration.

Discussion

The large differences documented in Table 1 and Figure 1, between HB and RT ACT's stress the importance of standardizing the conditions under which the test is performed. It should be noted that several of the RT samples (from the five minutes on bypass and at

g Lab-Line Instruments Inc., Module Heater No. 2090, Melrose Park, IL 60161.
h American Optical Refractometer, Buffalo, NY 14240.
i Instrumentation Laboratory Inc., Lexington, MS 02173.

* Although pH was measured, all results are reported in hydrogen ion concentration in order to calculate mean, standard deviation and develop regression coefficients.

TABLE 2

Baseline	5 min post Heparin	5 min on bypass	Hypothermia	Rewarm	20 min post Protamine
$\overline{HCT} = 36 \pm 4.1$	$\overline{HCT} = 38 \pm 4.3$	$\overline{HCT} = 26.1 \pm 3.4$	$\overline{HCT} = 26.5 \pm 2.6$	$\overline{HCT} = 24.7 \pm 2.0$	$\overline{HCT} = 26.8 \pm 2.7$
$\overline{ACT} = 100 \pm 14.8$	$\overline{ACT} = 350 \pm 67.9$	$\overline{ACT} = 371.4 \pm 68.9$	$\overline{ACT} = 349 \pm 49.1$	$\overline{ACT} = 313 \pm 88$	$\overline{ACT} = 101 \pm 12$
$Y = .26x + 90.8$	$Y = 7.6x = 62.5$	$Y = 4.8x + 244.7$	$Y = 4.4x + 233$	$Y = 3.1x + 235.8$	$Y = 1.1x + 129.6$
$r = .1$	$r = .48$	$r = .23$	$r = .24$	$r = .1$	$r = -.23$
Unable to show relationship at $\propto = .05$ or $\propto = .01$	There is a relationship at $\propto = .05$	No relationship at either $\propto = .05$ or $\propto = .01$	No relationshio at either $\propto = .05$ or $\propto = .01$	No relationship at either $\propto = .05$ or $\propto = .01$	No relationship at either $\propto = .01$

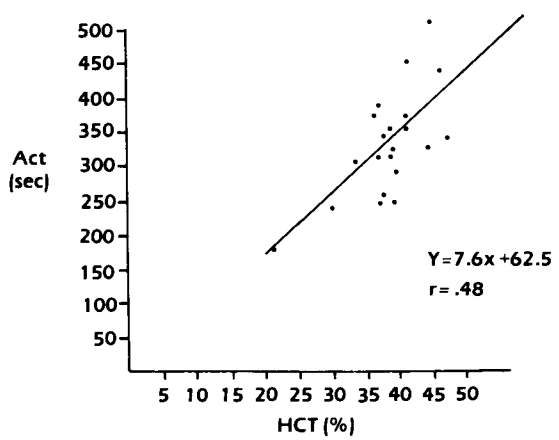

Figure 2: ACT vs HCT 5 Minutes Post Heparin

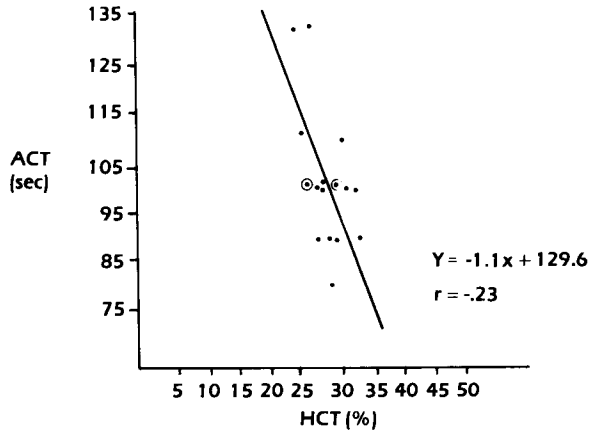

Figure 3: ACT vs HCT 20 Minutes Post Protamine

TABLE 3
ACT vs Acid Base Status
5 Minutes Post Heparin

ACT vs pH ($\{H^+\}$)	ACT vs pCO_2
$Y = -10.1x + 672$	$Y = -6.5x + 568.2$
$r = -.426$	$r = -.41$
Critical value at $\propto = .05$ is .4329	Critical value at $\propto = .05$ is .4329

hypothermic periods) showed no sign of clot at fifteen minutes so tilting was discontinued. The prolonged measurement time of the RT ACT's interferes with the prompt evaluation of adequate heparinization of the patient. We strongly recommend the use of a heat block for rapid and accurate measurement of the patient's coagulation potential at all phases of the open heart procedure.

Although a relationship exists between the ACT and HCT, the only time when it met statistical significance was five minutes post heparin. The fact that higher HCT's caused greater prolongation of the ACT is explainable if one understands that heparin is a drug which works on plasma proteins. The plasma volume will be small in a patient with a high HCT which will

result in a higher heparin concentration and a greater anticoagulant effect. This results in an extension of the ACT. This theory is supported by the inverse relationship between ACT and HCT in the post protamine data. We feel it may be valid to adjust the patient's dose response utilizing the patient's HCT.

The apparent relationship between acid-base balance and the heparinized ACT suggests that a higher hydrogen ion concentration may interfere with the strongly acidic heparin function. This will require further investigation.

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