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**Original Article*****Hemostatic Assessment of Patients Undergoing Intraaortic Balloon Pump Therapy***

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**ABSTRACT**

Patients undergoing intraaortic balloon pump (IABP) therapy are at risk for developing coagulopathies due to the adverse effects of prolonged exposure of the synthetic surface of the polyurethane balloon to blood components. Hemorrhagic risk has been attributed to a number of factors including thrombocytopenia, vascular injury, and/or platelet degranulation which increase the potential of receiving autogeneic blood transfusions. The present study is a prospective evaluation of coagulation using a viscoelastic monitor (Thrombelastograph - TEG) that measures functional aspects of clot development and stabilization in patients being treated with IABP therapy.

Following Institutional Review Board approval, six patients undergoing IABP therapy for hemodynamic instability were enrolled in this study. Blood samples were taken prior to balloon insertion, at 8, 16, 24, 48, 72, and 96 hours on IABP therapy, and 24 hours following the removal of the balloon when applicable. Samples were incubated with heparinase to degrade heparin and TEG profiles were subsequently determined in duplicate. Measured parameters on the TEG included R-time, K-time, maximum amplitude, alpha angle, and lysis at 30 and 60 minutes with calculation of the TEG index.

Mortality was 33% following IABP discontinuation. Transfusion of packed red blood cells occurred in 50% of the patients during their balloon pump therapy. Patients demonstrated a significant deviance in fibrinolytic potential from pre-IABP lysis ( $1.6\% \pm 1.8$ ) at both 24 hours ( $18.8\% \pm 22.9$ ) and 48 hours ( $21.9\% \pm 28.5$ ) of therapy ( $p < 0.05$ ) which returned to baseline shortly after balloon removal. Activation of coagulation factors appeared evident by a steadily increasing alpha angle from pre-IABP data ( $31.1 \pm 9.2$ ) throughout the duration of therapy and 24 hour recovery ( $53 \pm 14$ ;  $p < 0.005$ ), and by a steadily trending increase in the TEG index pre-IABP ( $.251 \pm 1.4$ ) to post-IABP ( $2.6 \pm 1.7$ ;  $p < 0.05$ ).

The results indicate that IABP therapy induces an increase in fibrinolytic potential at 24 to 48 hours of balloon pump therapy with a paradoxical trend toward increased coagulability, potentially predisposing the patient to hemorrhagic risk.

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## INTRODUCTION

The intraaortic balloon pump (IABP) is a device inserted most often into the descending thoracic aorta of patients in cardiogenic shock to augment coronary blood flow and decrease angina and ischemic damage (1). This is accomplished by a synchronous inflation and deflation of a polyurethane balloon timed to the patient's cardiac cycle. Inflation during diastole pushes blood back into the coronary arteries, and deflation during systole reduces afterload and thus myocardial oxygen consumption.

The first clinical use of the IABP occurred in 1967 by Kantrowitz for treatment of cardiogenic shock (2). Subramanian et al. introduced the percutaneous method of IABP insertion in 1980 (3). With the increased ease of placement due to this technique, IABP use has expanded and now includes a wide realm of indications including: unstable angina refractory to medical therapy, acute myocardial infarction, congestive heart failure or low output syndrome, cardiomyopathy, mitral valve failure, support prior to cardiac surgery or transplantation, and weaning from cardiopulmonary bypass (CPB) (1). Absolute contraindications to IABP therapy include irreversible brain damage or other end-stage organ failure, incompetent aortic valve or dissecting aortic or thoracic aneurysms. A relative contraindication may be peripheral vascular disease. Complications of IABP therapy include, most frequently, limb ischemia (1) but also hematologic destruction, aortic or iliac dissection, local bleeding, systemic infection, and balloon complications such as rupture (4,5).

Postoperative bleeding is a common citation in most forms of invasive ventricular assist (6). Blunt trauma of the blood cells by the surface of the balloon adversely affects the blood components. Transfusions due to decreased circulating platelets and red blood cells have been cited frequently (4,7,8). Bolooki et al noted that with greater than three days of balloon assist, packed red blood cell transfusions were required to maintain a 10.5 g/dL hemoglobin concentration (7). These hematological complications resolved immediately following IABP discontinuation. McCabe et al observed significant platelet transfusions throughout the duration of IABP counterpulsation due to worsening thrombocytopenia as the counterpulsation continued (8). Similarly to Bolooki's observations with red blood cells, platelet levels in McCabe's patients recovered quickly following balloon removal. Although most of McCabe's patients underwent both CPB and IABP therapy, thrombocytopenia was also observed in three patients who received only the IABP. Dunkman et al. also cited a 50% decrease in platelet count during the first sixty hours of balloon pumping (9), and Alvarez et al. reported a 26% platelet transfusion rate due to IABP-induced thrombocytopenia. In the latter study, the patients who received platelets were matched by age, gender, and CPB duration and compared to non-IABP CPB counterparts. The balloon pump patients received significantly higher quantities of transfused platelets than did the CPB only patients.

While quantitative platelet disorders with IABP therapy have been well documented, the effects on qualitative platelet dysfunction are unknown. Harker et al. reported both thrombocytopenia and platelet function disturbances in patients undergoing CPB surgery (10). Platelet aggregation resulting from collagen exposure and ADP release from damaged red blood cells or damaged platelets results in amplification of the secretion of granule contents such as platelet factor 4, fibrinogen, and factor V from alpha granules, as well as ADP, ATP, calcium, and serotonin from dense granules (11). Collagen exposure has been documented by Bick, who noted that with IABP therapy there is a marked denuding of the aortic endothelium adjacent to the balloon as a result of inflation and deflation within the vessel (12). Long term ventricular assistance with an indwelling balloon pump catheter may result in significant alterations of the hemostatic mechanism.

The purpose of this study was to evaluate the changes in coagulation status in patients undergoing IABP therapy and document the altering hemostatic mechanisms as time on the IABP increased.

## MATERIALS AND METHODS

Upon admittance to the institution, routine blood work was completed and analyzed. Tests included but were not limited to: hemoglobin, hematocrit, platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), and bleeding time. After Institutional Review Board approval and obtainment of informed consent from a family member (within 24 hours of IABP therapy), patients were enrolled in the study after balloon pump therapy was indicated by the cardiology team in the Catheterization Laboratory. All patients were placed on one of two types of Datascope IABP<sup>a</sup>, with a 9.5 French Datascope Percor Stat-DL polyurethane intraaortic balloon<sup>b</sup> (IAB) placed percutaneously. Baseline coagulation parameters were established prior to IAB insertion by the withdrawal of a 1 ml sample of blood from the patient's indwelling arterial line. The samples were analyzed on the thromboelastograph (TEG)<sup>c</sup> for baseline coagulopathies.

Following baseline hemostatic assessment, the patient was followed throughout the duration of balloon counterpulsation. One ml samples were drawn for TEG analysis pre-IABP, 8, 16, and 24 hours post-IAB insertion and every 24 hours throughout the duration of IABP therapy. An additional sample was drawn 24 hours post-IABP discontinuation. Throughout the patient's Intensive Care Unit stay, routine laboratory tests including hemoglobin and hematocrit, platelet count, and coagulation parameters of PT and aPTT were drawn at the attending physician's discretion as clinical conditions dictated. No thrombolytic medi-

a Systems 95 & 97, Datascope Corp., Fairfield, NJ

b Datascope Corp., Fairfield, NJ

c Haemoscope, Skokie, IL

cations were administered between baseline and final samples. Other observed parameters included: IABP related complications and transfusion requirements.

The TEG coagulation monitor is a kinetic device used to analyze the hemostatic state of whole blood from the time of sample acquisition through clot formation and clot lysis, allowing for global evaluation of the ex vivo coagulation process. As the TEG records the acquired information, a profile is created that measures the viscoelastic change of the sample, displaying the following parameters: Reaction time (first sign of the clot), K-time (indicator of clot firmness), Maximum Amplitude (maximum strength of the clot), alpha angle (rate of clot growth), and lysis (breakdown of the clot). The TEG index is a mathematically derived value that incorporates R-time, K-time, Maximum Amplitude (MA) and alpha angle (A) into a discriminant equation weighting the importance of each measured parameter according to its involvement in the development of clot. It is calculated using the following equation:

$$T.I. = (.1227)R + (.0092)K + (.1655)MA - (.0241)A - 5.0220$$

This value is descriptive of the patient's overall coagulation but does not include clot lysis or retraction. The fibrinolytic index is a value taken of the clot breakdown from 30 and 60 minutes after Maximum Amplitude has been reached and is derived by

dividing the amplitude at 30 and 60 minutes by the Maximum Amplitude and multiplying by 100 to express the value as a percentage (13).

Data was collected and subsequently organized on a personal computer in a spread sheet format for analysis. One-way analysis of variance (ANOVA) for intragroup comparison was utilized. Where significant f ratios were achieved, further multiple comparison tests such as least significant difference (LSD) were performed. Statistical significance rejected the null hypothesis at  $p < .05$ . All data was presented as mean +/- standard deviation of the mean.

## RESULTS

Six patients (4 male, 2 female) were given IABP therapy due to hemodynamic instability, unstable angina, or acute myocardial infarction (AMI). Average BSA was  $2.03 \pm 0.19 \text{ m}^2$ , average age was  $60.2 \pm 7.6$  years, and average ejection fraction was  $39.2 \pm 20.1\%$  (Table 1). Patients were placed on heparin prior to the initiation of the procedure. Before IABP insertion and after heparin exposure, a sample was taken for pre-IABP analysis of coagulation on the TEG. The patients were not administered any thrombolytic medications following this sample.

Average length of time on the IABP was  $52.7 \pm 35.3$  hours with an overall mortality of 33%. Thrombocytopenia was observed in all patients with smear counts decreasing in excess of 33% within three days on the IABP. Platelets were not administered to any of the patients. Transfusion of red cells, however, were indicated and administered in 50% of the patients when the hematocrit decreased to 25%. Platelet function, observed by the maximum amplitude, was increased with additional time on the IABP (Table 2), as was the calculated TEG index.

Fibrinolytic changes (Figure 1), measured by clot lysis percent after 60 minutes of clot detection on the TEG, were seen at 24 and 48 hours ( $p < .05$ ). These fibrinolytic changes were resolving at 72 hours and were back to baseline values by 24 hours post IABP therapy. The trend toward increased co-

**Table 1: Anthropomorphic Data**

Patient Number	1	2	3	4	5	6
Age (yrs.)	59	58	71	67	56	50
Gender	M	F	M	F	M	M
BSA (m <sup>2</sup> )	2.18	1.96	1.82	2.32	2.03	1.89
Hrs. on IABP	96	24	36	16	48	96
Mortality	Y	N	N	N	N	Y
PRBCs (units)	0	2	0	0	2	2
Diagnosis	AMI	AMI	AMI	CHF	AMI	CS
EF (%)	25	55	71	unknown	25	20
# diseased vessels	4	1	3	3	2	2

AMI= Acute Myocardial Infarction, BSA=Body Surface Area, CHF=Congestive Heart Failure, CS=Cardiogenic Shock, EF=Ejection Fraction

**Table 2. Thrombelastograph Data**

	Pre-IABP	8	16	24	48	72	96	Post-IABP
R	30.1±5.7	28.6±6.2	26.8±9.0	20.8±6.1	26.2±3.2	23.2±8.8	26.0±0.0	16.0±12.0
K	14.6±7.2	16.0±6.7	12.9±7.2	8.3±2.9	7.2±1.5	8.5±2.8	7.25±0	6.9±4 <sup>a</sup>
MA	57.9±6.0	58.1±2.9	64.6±5.2	61.1±12.1	70.8±3.9 <sup>b,c</sup>	70.3±12.7	70.5±0.0	65.5±5.2
A	31.1±9.2	31.8±8.4	42.6±11.1 <sup>b</sup>	47.8±5.5 <sup>b,c</sup>	52.3±5.5	50.5±3.5 <sup>b,c</sup>	52.3±0.0 <sup>b</sup>	53.0±14.3 <sup>b,c</sup>

P values: a= $p < 0.05$  vs. Hr-8, pre-IABP; b= $p < 0.05$  vs. pre-IABP; c= $p < 0.05$  vs. Hr-8; R=R-time (sec); K=K-time (seconds); MA=Maximum Amplitude (mm); Alpha=alpha angle (degrees)

Figure 1: Fibrinolysis with IABP therapy

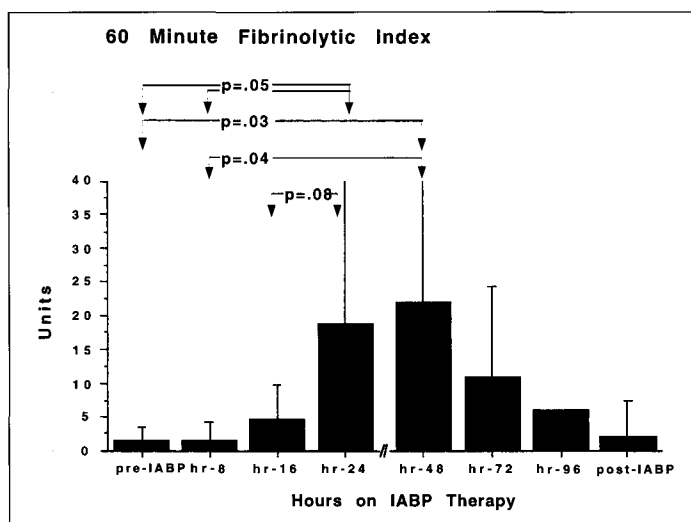
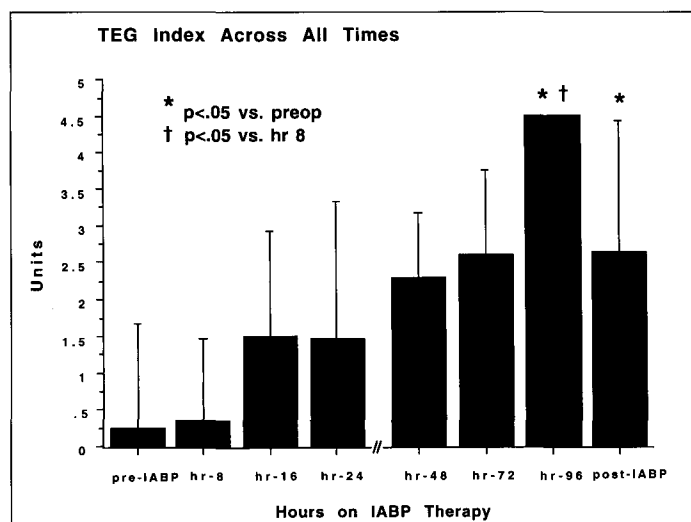


Figure 2: TEG index with IABP therapy



\*=p<0.05 vs. Pre-IABP; +=p<0.05 vs. Hr-8

agulability can be observed from the TEG indices (Figure 2). Pre-insertion TEG index was  $0.25 \pm 1.4$  and increased to  $2.61 \pm 1.1$  ( $p < 0.06$ ) at 72 hours and  $2.64 \pm 1.7$  ( $p < 0.01$ ) at 24 hours post-IAB removal (Figure 2).

The commonly observed fibrinolytic progression is best exemplified by the TEG of Patient 1, with the exception of the 24-hour post-IAB sample which could not be obtained due to mortality (Figure 3). In addition, this figure also illustrates that Maximum Amplitude did not decrease as theorized, inferring no change in platelet function status. Table 2 reveals this steady increase from  $57.9 \pm 6.0$  pre-balloon insertion to  $70.8 \pm 3.9$  ( $p < 0.05$ ) at 48 hours, after which the Maximum Amplitude values remained unchanged from their peak value.

## DISCUSSION

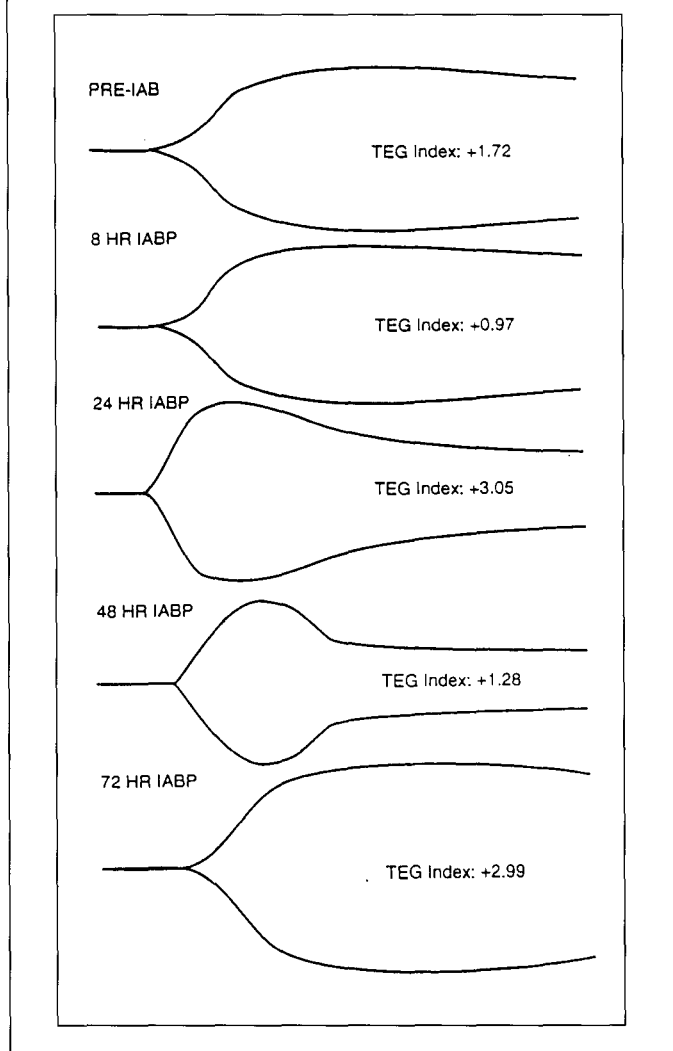
The process of platelet aggregation and activation causes platelets to become round and extend pseudopods. The entire reaction leads to the formation of glycoproteins IIb and IIIa (important for the development of platelet stickiness) and activation of the arachidonic acid pathway (14). Platelet activation in the arachidonic acid pathway results in cyclo-oxygenase conversion of arachidonate to prostaglandins  $G_2$  and  $H_2$ , followed by conversion by thromboxane synthetase to thromboxane  $A_2$ , a platelet aggregating agent (11).

Coagulopathies are frequently observed in patients undergoing IABP therapy and can be attributed to a variety of mechanisms of action. The foreign surface of the balloon may cause platelet degranulation, leading to moderate or severe thrombocytopenia, occasionally to the extent that platelet transfusions are necessary (4). In the present study, this phenomenon was also observed with platelet counts decreasing in excess of 33%. It is important to acknowledge that function is unaffected in the remaining circulating platelets as observed by TEG profiles. This information may be valuable when weighing the options of transfusion for marginal thrombocytopenia. The value of global assessment of coagulation status may be more desirable than individual assays of coagulation, which do not take into consideration *in toto* coagulation.

Fibrinolysis was a significant and prominent observation with IABP therapy in these patients and this is another potential mechanism of action for hemorrhagic complications. Fibrinolysis was stimulated at or around 24 hours of IABP therapy and continued throughout the next 24 hours before initially resolving at or about 72 hours and completely resolving by 24 hours post-IAB removal. While hemorrhage is a commonly cited complication of the IABP, this study concludes that this hemorrhage may not be a result of platelet dysfunction but may instead be a result of the combined effects of fibrinolysis and thrombocytopenia.

The results also indicate that IABP therapy results in continuous coagulation stimulation as observed by the steadily rising TEG index throughout the duration of cardiac assist; a mechanism which may predispose the patient to hypercoagulability. This continuous coagulation stimulation may potentially result from factor XII activation due to the contact of the blood components with the synthetic surface of the polyurethane balloon. Mechanical trauma may occur as a result of the pulsatile action upon the fragile plasma proteins, causing denaturation, and in turn, stimulating production of supplemental replacement factors.

The intrinsic pathway of the coagulation cascade was inhibited due to the constant infusion of heparin. The procoagulant effect that can be observed by the steadily increasing TEG in-

**Figure 3: TEG profile from Patient 1**

dex as IABP therapy continues may be attributed to platelet and protein activation or extrinsic activation due to balloon-induced aortic endothelial damage. However, there is no observed corresponding trend in clot stability. In fact, just the opposite was observed, with clot stability appearing to be decreased in spite of the coagulation stimulation. This may be explained by a stimulated plasminogen-plasmin system, or altered endothelial plasminogen activator activity induced by the surface of the balloon, resulting in primary fibrinolysis and plasmin-induced degradation of coagulation proteins similar to that seen with cardiopulmonary bypass (12).

In conclusion, the results of this study indicate that IABP therapy results in continuous coagulation stimulation, despite diminishing platelet number. A profound hyperfibrinolysis was observed between 24 and 48 hours following IABP mechanical assist that spontaneously resolved during the third day of therapy. The total contribution of both these coagulopathic states remains to be quantified, and the mechanisms of action require further evaluation.

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