Estimation of Fibrinogen Concentration During Extracorporeal Circulation in Pediatric Cardiac Surgery

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Abstract

Maintenance of adequate fibrinogen levels during cardiopulmonary bypass (CPB) is important in assuring adequate post-CPB hemostasis. Fresh frozen plasma (FFP) is used in the pediatric CPB circuit as a prime constituent as a source of coagulation factors, including fibrinogen; yet the resultant on-CPB fibrinogen concentration is related to multiple factors.

Accurate formulas for predicting post-dilutional fibrinogen levels and the minimal FFP volume to prime the extracorporeal circuit (ECC) to maintain post-dilutional fibrinogen levels greater than 100 mg/dL were developed prospectively from seventy-five infant and pediatric patients. The patients weighed less than twenty-five kilograms and underwent CPB for the correction of various congenital cardiac anomalies. Variables expected to affect fibrinogen level were: height, weight, body surface area, pre-dilutional hematocrit, pre-dilutional fibrinogen concentration, patient circulating blood volume, circuit priming volume, FFP volume added to the prime pre-CPB, pre-CPB blood loss, and volume added by anesthesia pre-CPB.

Equations to predict the post-dilutional fibrinogen value and the minimal volume of FFP to add to the ECC prime were formulated using multiple linear regression with the results shown in the tables below.

VARIABLE	REG COEF	STD ERROR	2TAIL SIG
Dependent variable: Post-dilutional fibrinoqen value			
PRIME VOL	0.06	0.02	0.001
FFP VOL	0.05	0.02	0.011
INTERCEPT	29.37	17.10	0.090
r = 0.477, p = 0.0001, std error = 24.38 mg/dL			

Dependent variable: Minimal FFP volume to add to prime			
WEIGHT	-17.19	3.38	<0.001
PRE-HCT	5.25	1.54	0.001
PRE-FIB	-1.58	0.24	<0.001
PRIME VOL	0.42	0.11	<0.001
ACTUAL FIB	1.02	0.50	0.044
INTERCEPT	36.80	111.38	0.742
r = 0.777, p < 0.001, std error = 106.04 ml			

Utilization of the formula for predicting the quantity of FFP necessary to achieve a minimum circulating fibrinogen concentration revealed no significant difference when compared to actual levels on CPB. The clinical use of formulas which accurately estimate the volume of FFP necessary to optimize the post-dilutional concentration of coagulation factors may reduce patient exposure to unnecessary homologous blood products.

Introduction

Hemorrhage following cardiac surgery is a frequent and serious complication of the post-operative period among children, especially those with congenital heart diseasel. A review of the literature revealed the most common reasons for post-operative bleeding include: thrombocytopenia[2-8], decreased levels of coagulation factors[2-9] (due to direct denaturation,[2, 10, 11] intravascular coagulation,[3, 5, 7, 8, 12] or accelerated fibrinolysis,[3, 5-11, 13]) inadequate heparin reversal,[2, 7] excess protamine,[2,8] inadequate surgical hemostasis,[2,5,7] defective clot retraction,[1,4] abnormal platelet function,[3, 5] and increased plasminogen activator activity.[14-16]

Post-dilutional maintenance of adequate levels of coagulation factors is a process that the perfusionist has control over during cardiopulmonary bypass (CPB). One important coagulation factor is Factor I: fibrinogen. Fibrinogen is a soluble protein synthesized in the parenchymal cells of the liver,[17, 18] which plays a unique role as the key component of hemostasis: it represents the readily available and mobilizable form of fibrin, the insoluble fibrous protein which participates in hemostasis in areas of vascular injury. Fibrinogen is enzymatically converted to fibrin by thrombin in the common pathway of the coagulation cascade (Figure 1). Fibrinogen, at a concentration ranging from 150-400 mg/dL, also plays an important role in the maintenance of a normal colloid osmotic pressure.[19] CPB causes fibrinogen levels to decrease by absorption, activation of the coagulation system, activation of the fibrinolytic system, and dilution. Fibrinogen is absorbed, to some extent, by foreign surfaces within the various components of the extracorporeal circuit (ECC) (such as the arterial line filter and the membrane oxygenator), causing the level of fibrinogen to drop with the initiation of bypass. Despite the anticoagulation achieved on bypass, blood has

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a tendency to clot outside its intravascular environment.[20] The intrinsic mechanism of blood coagulation is platelet-mediated and is thought to be initiated by contact of blood with foreign surfaces; the ECC is, by definition, an active stimulus to intrinsic coagulation and results in a decrease in the fibrinogen concentration on CPB.[21] Activation of coagulation by the ECC may also be achieved by the products of destroyed blood cells which results in consumption of coagulation factors in vivo and defibrination.[10,22]

Increased fibrinolysis is accepted as one of the factors which causes a drop in the fibrinogen level during CPB.[12,21] ECC is a form of physical stress, and changes in the metabolism and acid- base balance associated with the induction of hypothermia, metabolic acidosis, and defibrillation all stimulate the release of fibrinolytic activators.[16] By activation of the fibrinolytic system, ECC leads to the proteolytic digestion of fibrin, fibrinogen and other coagulation factors.[14]

The use of plasma expanders (low molecular dextran and albumin) in the priming solution decreases the concentration of fibrinogen.[14] This may be a dilutional effect caused by the movement of extravascular water into the vasculature, or by activation of the coagulation system by the plasma expanders. Fibrinogen levels are also compromised by the hemodilutional process of CPB. Hemodilutional CPB is important during hypothermia, especially when circulatory arrest is employed to correct more complex cardiac defects.[23] Hemodilution helps to alleviate sludging in the microcirculation that occurs with increased viscosity of the blood during hypothermia. Minimum priming volumes of our infant and pediatric circuits range from 700-1000 milliliters (ml) and once CPB is initiated, the priming volume may comprise 45-80% of the total circulating volume. Without blood products in the prime, the result would be a significant dilution of red blood cells, hemoglobin, plasma proteins, clotting factors and other humoral components upon the initiation of CPB.[7,16] Dilution of fibrinogen could result in fibrinogen concentrations less than optimal for hemostasis. Depending on the reference, the critical low limit for fibrinogen varies from 50 to 100 mg/dL[9,17,24,25] with most references citing 70 mg/dL. Lower values could manifest clinically as increased post-operative bleeding resulting in increased homologous blood product administration.

Unusual bleeding is known to complicate surgery in patients with cyanotic congenital heart disease.[4,26] In a large number of instances, pre-existing defects in the coagulation system can be demonstrated.[1,4,5,6,12,21,26,27] ECC introduces additional problems with regard to blood coagulation, as previously described, and may further interfere with an already faulty clotting mechanism, thereby aggravating the likelihood of hemorrhage in these patients.[26]

Compromised cyanotic patients have an increased red cell volume to compensate for their low oxygen carrying capacity.[28] This is associated with an impairment of clot retraction, alteration in the blood clotting factors, and increased fibrinolysis.[29] It has been shown that patients with cyanotic heart disease and polycythemia have significantly lower levels of the factors consumed in disseminated intravascular coagulation (DIC): platelets, fibrinogen, Factors V and VIII.[1,4,26,27] It is theorized that the sludging in the microcirculation secondary to the polycythemia triggers generalized coagulation which consumes clotting factors to the point that functional clotting is impossible.[28] Conflicting evidence has been reported as to whether there is intravascular coagulation occurring in these patients or not.[1,6,7,27,30,31] A study done in 1985 by Suarez et al revealed that definitive evidence of activation of the hemostatic system in children with cyanotic congenital heart disease was reflected by elevated levels of fibrinopeptide A (FPA).[6] These elevated levels reflect generation of thrombin resulting in fibrinogen cleavage with liberation of FPA. FPA, being one of the earliest products of fibrinogen degradation, can be elevated before there is any clinical evidence of coagulation system activation.[6] Fibrin degradation products have also been found to correlate with increased hematocrit.[27] These finding seem to support the theory of intravascular coagulation in these patients.

As well as the theory that sluggishness of the local microcirculation associated with high blood viscosity causes decreased fibrinogen values (and other coagulation factors) in cyanotic patients, it has also been proposed that deficient synthesis of the procoagulants resulting from hepatic hypoxia may be occurring.[1,12]

Young cyanotic children in whom polycythemia has not yet developed tend to have increased levels of the consumption factors. There appears to be an altered mechanism of coagulation (hypercoagulability) prior to the onset of polycythemia in these patients.[1] As coagulation occurs throughout the body, the supply of clotting factors becomes depleted. As a result, the blood becomes hypocoagulable. It appears that patients with cyanotic heart disease, both polycythemic and not polycythemic, have altered coagulation processes. During and after CPB these abnormalities may become magnified and severe enough to result in a hemorrhagic diathesis.[14]

Given the above information, the importance of predicting post-dilutional plasma fibrinogen concentrations in pediatric patients (especially those with cyanotic heart defects) prior to CPB can be appreciated. It is essential for the surgical team to understand and correct any anticipated deficiencies, thereby alleviating unnecessary post-operative bleeding complications and homologous blood product administration. At this institution, the post-dilutional fibrinogen values are routinely estimated. If required, fresh frozen plasma (FFP) is added to the ECC prime to ensure a fibrinogen concentration greater than 100 mg/dL.[32] FFP has been found suitable for correcting hemostatic deficiencies due to its content of both labile and stable non-activated coagulation factors.[9,33,34]

In an analysis of 45 infant and pediatric patients, the dilutional formula currently used was found to provide post- dilutional fibrinogen values that were statistically higher than the actual values ($p<0.05$). The current study

was undertaken in an attempt to determine: 1) a formula which includes variables that may influence post-dilutional fibrinogen values in addition to those used in the present dilutional formula and, 2) a formula to calculate the minimum volume of FFP to add to the prime to maintain post-dilutional fibrinogen values greater than 100 mg/dL. The development of a formula which accurately predicts the volume of FFP necessary to optimize the concentration of coagulation factors may decrease the incidence of post-operative bleeding due to low fibrinogen concentrations which may reduce patient exposure to unnecessary homologous blood products. An accurate formula for predicting the post-dilutional fibrinogen concentration may eliminate the need to take fibrinogen samples while on CPB which would result in a decrease in patient cost.

Materials and Methods

Seventy-five consecutive infant and pediatric patients, weighing less than 25 kilograms (kg), undergoing cardiopulmonary bypass for the correction of various congenital anomalies were studied prospectively to determine the factors that significantly effect the post-dilutional fibrinogen concentration and the volume of FFP to add to the ECC prime to maintain post-dilutional fibrinogen concentrations greater than 100 mg/dL. The following information was collected on each patient: name, date, procedure, reoperation, height, weight, body surface area (BSA), pre-operative hematocrit, pre-operative fibrinogen concentration, patient blood volume, ECC priming volume, volume of fresh frozen plasma added to the prime, pre-CPB blood loss, pre-CPB anesthesia volume, and actual post-dilutional fibrinogen value. Surgeon protocol specifies for a post-dilutional fibrinogen concentration to be drawn; therefore, no extra blood samples were drawn.[32] Pre-operative fibrinogen levels and pre-operative hematocrit values were obtained from the patients' pre-operative lab work-up. When a pre-operative fibrinogen was not obtained, a value of 200 mg/dL was assigned.[32] At this institution, if the patient is polycythemic, no fibrinogen concentration measurement is performed. A reason fibrinogen concentrations are not drawn is that polycythemic patients' blood is extremely viscous and sludges, causing the blood sample to clot before coagulation profiles can be run. Five minutes after the initiation of CPB, before a cardioplegia dose was administered, a post-dilutional fibrinogen concentration was obtained. All samples were sent to the MUSC clinical lab for routine analysis. Two milliliters of blood was added to 0.3 ml of sodium citrate. This sample was spun at 1600 rpms for 10 minutes which removed platelet poor plasma to a 12 X 75 mm plastic test tube. This sample was then analyzed using an Electra 80 Automatic Coagulation Timer.[a] A quantitative measurement of fibrinogen was obtained by comparing the clotting time with that of a standard preparation of known concentration.

All cases were performed using a standard Stockert-Shiley[b] roller pump, either a Sarns[c] Infant or Sci-Med[d] oxygenator with the respective soft-shelled venous reservoir, a William Harvey[e] filtered cardiotomy, and a Bentley[f] infant, mixed, or pediatric custom tubing pack. A Pall[g] infant or adult arterial line filter was used on all cases. The post-dilutional hematocrit was maintained between 25-30% (less than 25% if circulatory arrest is anticipated); post-dilutional fibrinogen concentration was maintained greater than 100 mg/dL; and the colloid osmotic pressure was maintained at or near -16 mmHg.[32] Packed red blood cells, fresh frozen plasma, and 25% salt-poor albumin were added to the Plasmalyte A[h] used to prime the ECC as necessary to achieve these values. All blood products were filtered with a Pall 40 micron transfusion filter upon addition to the ECC.

Dilutional formulae were used to calculate the volume of packed red blood cells, albumin or FFP to add to the prime as shown below.[17,32]

Eq. 1.0

$$POST\_FIB = \frac{(1 - PRE\_HCT/100) * (\text{Blood volume}) * (PRE\_FIB)}{(1 - POST\_HCT/100) * (\text{Blood volume} + \text{Prime volume})}$$

Where POST_FIB is the post-dilutional fibrinogen (mg/dL), PRE_HCT is the pre-dilutional hematocrit (%), PRE_FIB is the pre- dilutional fibrinogen concentration (mg/dL), and POST_HCT is the post-dilutional hematocrit (%). The blood volume is an estimate based on patient weight and is as follows: 0-10 kg, the blood volume is 85 ml/kg; 10-25 kg, the blood volume is 80 ml/kg.[17] When FFP was added to the prime to increase the post-dilutional fibrinogen value, a factor of 40,000 was added to the numerator of the above equation. This is based on 200 mg/dL of fibrinogen in a 200 ml unit of FFP.[9,32,35] Multiple linear regression and correlation using the BMDP Statistical Software[i] computer program were employed to determine the best combination of variables which predict the actual post-dilutional fibrinogen value and the amount of FFP added to the prime. Pooled t-tests were done comparing variables in the cyanotic and acyanotic groups. A $p < 0.05$ was considered significant.

Results

The defects being corrected and their occurrence in this study are as follows: Tetralogy of Fallot (13), ventricular septal defect (9), transposition of the great arteries (8), atrial septal defect (8), pulmonary artery stenosis/atresia (6),

a Medical Laboratory Automation Inc. Pleasantville, NY 10570
b Shiley, Inc. Irvine Ca 92714
c Sarns, Inc. Ann Arbor, Michigan 48103
d Sci-Med Life Systems, Inc. Minneapolis, Minnesota 55441
e Bard Cardiopulmonary Division Billerica, MA 01822
f Bentley Laboratories, Inc. Irvine CA 92714
g Pall Biomedical Products Corp. Glen Cove, NY 11542
h Baxter Healthcare Corp., Deerfield IL 60015
i BMDP Statistical Software Inc., Los Angeles CA 90025

single ventricle (5), double outlet right ventricle (4), AV canal defect (4), aortic stenosis (4), total anomalous pulmonary venous return (3), truncus arteriosus (2), hypoplastic left heart (2), Wolfe-Parkinson-White syndrome (2), interrupted aortic arch (1), mitral valve repair (1), pulmonary vein obstruction (1), abnormal origin of the left main coronary artery (1), and Ebstein's anomaly (1). Of these, 42 (56%) were cyanotic cardiac lesions and 33 (44%) were acyanotic cardiac lesions. Of the patients with cyanotic lesions, 18 (42.8%) were polycythemic (HCT > 47%). In the acyanotic lesion group, 2 (6%) patients were polycythemic. Forty-eight (64%) patients had measured pre-operative fibrinogen values. Twenty-seven (36%) patients had 200 mg/dl estimates assigned to them. Nineteen (44%) of the patients with cyanotic defects, and eight (25%) of the patients with acyanotic defects had estimated pre-operative fibrinogen concentrations.

Summary Statistics

Table 1 lists the summary descriptive statistics obtained on the data. Table 2 separates the descriptive statistics for cyanotic defects and acyanotic defects. The variables between the two groups were comparable with the exception of the pre-operative hematocrit ($p < 0.001$) and the FFP volume added to the prime ($p < 0.05$).

ON-CPB FIBRINOGEN VALUE

The combination of variables that best predicted the post-dilutional fibrinogen value were the ECC prime volume (p=0.001) and the volume of FFP added to the pump prime (p=0.011). The correlation coefficient was significant at 0.477 (p= 0.0001). Table 3 lists the regression coefficients, standard error, and the 2-tailed significance of the variables listed above. The equation is:

Eq. 2.0

ON-CPB [FIB] = PRIME VOL * (0.06) + FFP VOL * (0.05) + 29.37

FFP TO ADD TO PRIME

The combination of variables that best predicted the FFP volume to add to the pump prime were patient weight (p<0.001), pre-operative hematocrit (p=0.001), pre-operative fibrinogen concentration (p<0.01), ECC priming volume (p<0.001), and post-dilutional fibrinogen concentration desired (p=0.044). The correlation coefficient was significant at 0.777 (p< 0.001). Table 4 lists the regression coefficients, standard error, and 2-tailed significance of the variables listed above. The equation is:

Eq. 3.0

FFP VOL = WT * (-17.19) + PRE HCT * (5.25) + PRE FIB * (-1.58) + PRIME VOL * (0.42) + ACT FIB * (1.02) + 36.80

The actual fibrinogen obtained (ACT FIB) in the equation is the desired post-dilutional fibrinogen value entered by the perfusionist or medical team.

Discussion

The most important factor in the decrease in fibrinogen concentration in infant and pediatric patients is hemodilution.

The smaller the patient size, the greater the dilution upon the initiation of CPB. The perfusionist can minimize the priming volume, but without the addition of FFP, significant dilution still occurs, especially in smaller patients. Some institutions routinely add one or two units of FFP to the prime in pediatric patients without calculating the post-dilutional fibrinogen value. Not all patients need FFP added to the prime. Accurate formulas for estimating the volume of FFP to add to the prime to maintain a minimum circulating fibrinogen concentration and the post- dilutional fibrinogen value could result in a decrease in patient exposure to unnecessary homologous blood products and result in less post-operative bleeding.

In the regression equation for the post-dilutional fibrinogen value (Eq.2.0), the only two significant factors were the ECC priming volume and the volume of FFP added to the prime. As the FFP volume (and its fibrinogen concentration) added to the prime increases, the actual post-dilutional fibrinogen value increases due to less dilution of the total fibrinogen upon the initiation of CPB. As the prime volume increases, the actual post-dilutional fibrinogen value increases, due to the fact that larger priming volumes are employed in patients with larger blood volumes. Since the ratio of blood volume to priming volume is high, less hemodilution occurs upon the initiation of bypass.

In the formulated equation for the FFP volume to add to the prime (Eq.3.0), an increased patient weight results in an decreased volume of FFP necessary. This is due to the fact that larger patients have larger blood volumes; therefore, upon the initiation of CPB, the effects of hemodilution are not as dramatic when compared to smaller patients who have smaller blood volumes. As the pre-operative hematocrit increases, the volume of FFP needed also increases. The direct relationship between pre-operative hematocrit and FFP added to the prime seems to be consistent with the theory that most polycythemic patients have lower pre-operative fibrinogen values. The data collected in this study do not appear to support this theory. The pre-operative fibrinogen concentrations were not significantly different between the polycythemic patients and the non-polycythemic patients in the cyanotic group ($p > 0.05$). The dilutional formula used to calculate the volume of FFP to add to the prime (Eq. 1.0) was dependent upon the dilution of the plasma volumes. Patients with increased hematocrits have smaller plasma volumes; therefore, the estimated post-dilutional fibrinogen concentration is lower, resulting in more FFP necessary to maintain desired fibrinogen levels on CPB. If patients start out with lower pre-operative fibrinogen concentrations, more fibrinogen must be added to the prime to maintain 100 mg/dL after hemodilution has occurred. As the pre-operative fibrinogen value increases,

the volume of FFP needed decreases. The same dilution of a larger initial concentration results in a larger resultant concentration; therefore, less fibrinogen is necessary to maintain a critical level once hemodilution occurs. As the prime volume increases, the FFP needed increases as a result of greater dilution. The higher the desired post-dilutional fibrinogen concentration, the more FFP necessary to achieve this value.

When the equation for FFP volume to add to the prime is used (Eq.3.0), increasing the prime volume results in increased FFP required in the prime. This equation takes into account that smaller patients undergo more hemodilution resulting in greater volumes of FFP needed to counteract the hemodilution. When the equation for FFP volume is used prior to that for the actual post- dilutional fibrinogen value, the value predicted by the equation is not be significantly different from that actually achieved on CPB (P>O-05).

The mean fibrinogen concentration in the 49 patients with measured pre-operative fibrinogen values was 229+61 mg/dL (94-404 mg/dL). Rearranging the equation for FFP volume to add to the prime (Eq. 3.0) and solving for the pre-operative fibrinogen value in those patients with 200 mg/dL estimated pre-operative fibrinogen values revealed a calculated mean pre-operative fibrinogen to be 189.31 + 55.01 mg/dL (59-291 mg/dL). Figure 2 shows the estimated pre-operative fibrinogen concentration variation from the 200 mg/dL estimate. Although the mean fibrinogen concentration is not significantly different from the estimate ($p > 0.05$), it can be seen that in some patients there is a large variation from the estimate. It appears that the 200 mg/dL estimate used at this institution is a reasonable number when fibrinogen concentration is unavailable pre-operatively. However, in those patients with cyanotic heart disease, the presence or absence of polycythemia may alter this value. Fibrinogen values in cyanotic, polycythemic patients may be lower than normal. In these patients who do not have pre-operative fibrinogen values, utilization of the 200 mg/dL estimate was found adequate to determine FFP volume to add to the prime. Even with the estimating equations, it may still be necessary in some patients to analyze fibrinogen concentrations once on CPB.

Conclusion

Having an accurate estimate of the post-dilutional fibrinogen value before going on bypass allows the surgical team to precisely correct any anticipated fibrinogen deficit by adding FFP to the prime. By safely maximizing the concentration of coagulation factors with the addition of FFP to the ECC prime, we can minimize the possibility of post-operative bleeding due to decreased coagulation factor concentrations. Dilution of clotting factors is one variable for which we have control. Perfusionists should not, however, routinely add FFP to all pediatric patient priming solutions. Addition of FFP increases the risk of transmission of blood-borne diseases and other problems associated with homologous blood product administration and should be minimized.

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Questions and Comments

Steve Thompson, Baltimore, Md.

Q. I have a two part question. In one of your slides you showed several references to fibrinogen necessary for coagulation to take place. I am wondering if that is for adult patients or pediatric patients, if there is a distinction.

A. There was no distinction.

Q. And I am wondering if you were able to correlate the diluted fibrinogen levbel with any kind of postoperative outcome as far as chest tube drainage, or blood products necessary after surgery.

A. No, we didn't. We just looked at the fibrinogen concentration post dilutional. We just tried to maintain it a t greater than 100 ml, but that's all.

Al Stammers, S.C.

Q. When would you predict the most important time for having that fibrinogen level at 100 ml/dec. If you had to extrapolate from your data, would you say during bypass, immediately after bypass? Can we have anesthesia calculate your values and have anesthesia hang this volume so it's not hemodiluted in the pump and perhaps get a higher fibrinogen? What are your feelings as to when to add the FFP.

A. Well, th efresh frozen plasma does not only contain the fibrinogen, but also all the plasma proteins and we find that adding it to the pump prime helps maintain our colloid pressure so we don't have to add as much albumin to help maintain it.

Q. Excellent presentation. I just wanted to add that we use a formula called functional hemodilution which we take into consideration how much the fibrinogen levels would hemodilute and use a factor between 40-50 percent activity level during bypass, sort of correlates to what you are doing there. That way we are establishing what patients are able to utilize FFP administration those that that would nor require it and seems to be very paramount right now at our institute. I want t thank you for your study.

TABLE 1
DESCRIPTIVE STATISTICS
n = 75

VARIABLE	MEAN + S.D.	SMALLEST	LARGEST
HEIGHT (cm)	78.61+ 19.89	42	134.00
WEIGHT (kg)	10.11+ 5.22	2.21	24.20
BSA (m2)	0.45+ 0.18	0.15	0.97
PRE-HCT (%)	41.14+ 8.12	22	64.50
PRE-FIB (mg%)	220.63+ 53.23	94	404
BLD VOL (ml)	817.08+400.29	188	1936
PRIME VOL (ml)	964.15+164.89	745	1575
BLD LOSS (ml)	35.93+ 77.17	0	550
PRE-FLUID (ml)	230.24+168.81	16	975
ACTUAL FIB (mg%)	100.39+ 27.36	63	194
FFP ADDED (ml)	240.45+162.70	0	605

SD, +l standard deviation; BSA, body surface area; PRE-HCT, pre-operative patient hematocrit; PRE-FIB, pre-operative patient fibrinogen concentration; BLD VOL, patient estimated blood volume; PRIME VOL, extracorporeal circuit priming volume; BLD LOSS, patient blood loss in the operating room prior to cardiopulmonary bypass initiation; PRE-FLUID, crystalloid and colloid administration by anesthesia in the operating room prior to cardiopulmonary bypass initiation; ACTUAL FIB, actual post-dilutional fibrinogen concentration; FFP ADDED, fresh frozen plasma volume added to the prime .

TABLE 2
COMPARISON OF CYANOTIC AND ACYANOTIC DEFECTS
SELECT DESCRIPTIVE STATISTICS

VARIABLE	CYANOTIC	ACYANOTIC	p VALUES
HEIGHT	76.02+ 16.44	82.09+ 23.22	NS
WEIGHT	9.65+ 4.00	10.85+ 6.40	NS
PRE-HCT	44.75+ 7.86	36.58+ 5 .79	p<0.001
PRE-FIB	234.54+ 69.96	234.04+ 60.93	NS
PRIME VOL	945.95+146.01	988.94+184.00	NS
ACTUAL FIB	100.23+ 26.73	100.64+ 28.16	NS
FFP ADDED	275.23+170.47	187.85+142.82	p<0.05

Results are expressed as mean + 1 standard deviation. P value relates to significance of difference between cyanotic and acyanotic patient variables. HEIGHT (cm); WEIGHT (kg); PRE-HCT (%), pre-operative patient hematocrit; PRE-FIB (mg/dL), pre- operative patient fibrinogen concentration (does not include those patients with estimated pre-operative fibrinogen concentrations); PRIME VOL (ml), extracorporeal circuit priming volume; ACTUAL FIB (mg/dL), actual post-dilutional fibrinogen concentration; FFP ADDED (ml).

TABLE 3
DEPENDENT VARIABLE: ACTUAL FIBRINOGEN

VARIABLE	REG COEF	STD ERROR	SIG
PRIME VOL	0.06	0.02	0.001
FFP	0.05	0.02	0.011
INTERCEPT	29.37	17.10	0.090

r = 0.477, p = 0.001, std error = 24.38 mg/dL

Results of multiple linear regression analysis using the post- dilutional fibrinogen concentration as the dependent variable. P value relates to the significance of the correlation value. REG COEF, regression coefficient; STD ERROR, standard error; SIG, two- tailed significance of each independent variables; r, correlation coefficient.

TABLE 4
DEPENDENT VARIABLE: FFP VOLUME

VARIABLE	REG COEF	STD ERROR	SIG
WEIGHT	-17.19	3.38	<0.001
PRE-HCT	5.25	1.54	0.001
PRE-FIB	-1.58	0.24	<0.001
PRIME VOL	0.42	0.11	<0.001
ACTUAL FIB	1.02	0.50	0.044
INTERCEPT	36.80	111.38	0.742

r = 0.777, p = 0.001, std error = 106.04 ml

Results of multiple linear regression analysis using the FFP volume as the dependent variable. P value relates to the significance of the correlation value. REG COEF, regression coefficient; STD ERROR, standard error; SIG, two-tailed significance of each independent variable; r, correlation coefficient.

Figure 1
Illustration of the coagulation cascade. Xa, activated factor X (Stuart Factor).

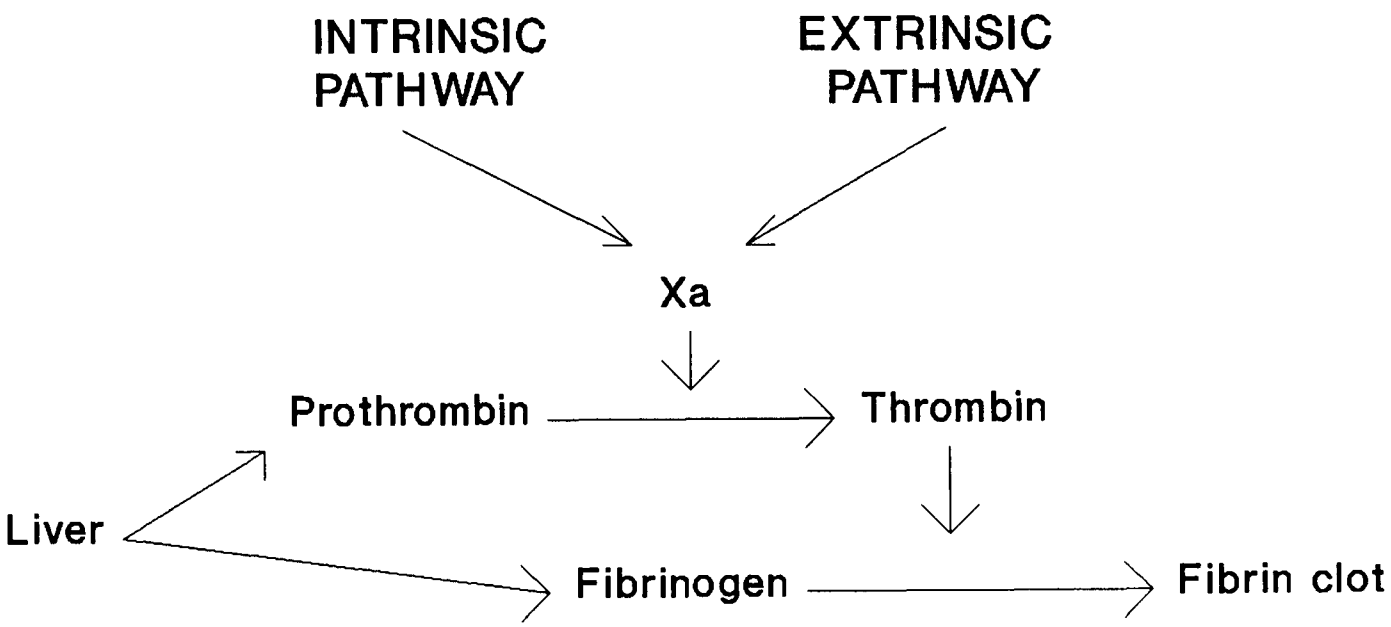

Figure 2
Variability of the calculated pre-operative fibrinogen concentration
(derived from rearranging E~uation 3.0) from the 200 mg/dL estimate currently used. Fibrinogen concentration expressed as mean + 1 standard deviation. Mean value not significantly different from the estimate (*p > 0.05).