TITLE: THE ACTIVATED COAGULATION TIME INDEPENDENTLY DETERMINES ADEQUATE ANTICOAGULATION DURING HYPOTHERMIC CARDIOPULMONARY BYPASS

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Introduction. Monitoring anticoagulation during cardiopulmonary bypass (CPB) with the activated coagulation time (ACT) has become accepted practice, but hypothermia and hemodilution distort the expected linear relationship between ACT and blood heparin levels, prolonging the ACT while heparin levels decrease (1). Since these factors do not affect protamine titration heparin assays, one could argue that heparin levels should be monitored during CPB. We investigated the adequacy of the ACT as an independent anticoagulation monitor during hypothermic CPB.

Methods. After obtaining informed consent, we investigated 10 patients requiring CPB. Exclusion criteria included coagulation disturbances, recent anticoagulant therapy, and the absence of CPB hypothermia below 30°C. Each patient received heparin pre-CPB to produce an ACT greater than 400 seconds (300 IU/kg in 7 patients, 250 IU/kg in 3 patients). Additional heparin was given during CPB only if the ACT decreased below 400 seconds. Every 30 minutes, an ACT (Hemochron method) and heparin level (Hepcon® protamine titration method) were measured. Subclinical coagulation was determined by I-125 radioimmunoassay (Malinkrodt) for fibrinopeptide A (FPA), the N-terminal peptide cleaved from fibrinogen by thrombin. Pre-CPB FPA samples were drawn before anesthetic induction, after sternotomy, and 3 minutes after heparin administration. During CPB, FPA was sampled at the nadir of the temperature curve, any time the ACT decreased below 400 seconds (before and after heparin administration), and after rewarming to 37°C. Post-CPB, FPA was determined after giving protamine. All samples were withdrawn from a radial artery catheter. A prothrombin time (PT), partial thromboplastin time (PTT), and fibrinogen level were obtained preoperatively and immediately following protamine, and fibrin degradation products (FDP) were measured following protamine. Post-operative blood loss was measured at 8 and 24 hours. FPA levels during CPB were compared with post-sternotomy levels using the paired t-test.

Results. Seven patients underwent coronary artery bypass grafting and 3 had valve replacements. Mean age was 62±13 years. Total heparin dose was 352±97 IU/Kg, with 3 patients not requiring redosing despite a mean CPB time of 107±48 minutes. Lowest temperature during CPB was 27.4±2.1°C. ACT is listed with FPA and heparin levels in Table 1. FPA decreased during CPB ($p<0.05$) and rose to exceed post-sternotomy values after protamine ($p<0.05$). No patient demonstrated a CPB FPA level exceeding the post-sternotomy value as long as the ACT remained greater than 400 seconds. The mean post-operative platelet count was 145,000±42,000 per ml. Table 2 lists additional coagulation studies. Four patients had clearly abnormal post-CPB bleeding studies (3 PTT, 1 FDP), none of whom bled excessively. Post-operative blood loss at 8 and 24 hours was 413±206 and 671±270 ml, respectively.

Discussion. Young showed that marginal CPB anticoagulation (ACT <400) subclinically depletes coagulation factors, setting the stage for post-CPB coagulopathy (2). FPA levels that would produce clotting factor consumption have not been established, so we assume that CPB FPA levels below those produced by surgical incision alone reflect adequate CPB anticoagulation. The absence of excessive post-CPB bleeding supports this assumption. Post-CPB coagulation tests compare favorably with usual results (3). Hemodilution alone comparably decreases fibrinogen and platelet count (4). Despite blood heparin levels that would have produced sustained ACT values below 400 seconds without hemodilution and hypothermia, CPB FPA levels did not exceed post-sternotomy values. We conclude that ACT values above 400 seconds adequately protect against subclinical coagulation whether prolonged by heparin alone or by a combination of heparin, hypothermia, and hemodilution. Consequently we see no need to measure blood heparin levels during CPB other than to determine the protamine dose needed for post-CPB heparin neutralization.

References

1. Culliford AT: Ann Surg 193(1):105, 1981.
2. Young JA: Ann Thorac Surg 26(3):231, 1978.
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Table 1. Anticoagulation Studies (Mean ± SD)

TIME	ACT sec	Heparin IU/ml	FPA ng/ml
Preinduction	139±15	0	9.4± 4.7
p-Sternotomy	---	0	20.7± 7.3
Post-heparin	523±130	4.2± 0.8	22.9±11.4
Hypothermia	752±273	3.5± 0.5	11.4± 7.1
37°C	511±96	3.4± 0.8	14.7± 6.9
p-Protamine	127±20	0.04±0.12	37.1±17.4

Table 2. Coagulation Studies (Mean ± SD)

TIME	FIBRINOGEN ng/ml	PT sec	PTT sec
Preinduction	310±84	12.0±0.32	24.8±1.9
p-Protamine	168±36	15.1±1.02	33.5±6.5