Perturbations in Laboratory Values After Coronary Artery Bypass Graft Surgery With Cardiopulmonary Bypass

Patrick Möhnle, MD,* Nanette M. Schwann, MD,† William K. Vaughn, PhD,‡ Michael C. Snabes, MD, PhD,§ Winnie Lau, BS,§ Jack Levin, MD,‖ and Nancy A. Nussmeier, MD¶

Objective: **The purpose of this study was to describe the sequential changes in commonly obtained laboratory values after coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB).**

Methods: **The authors examined laboratory data from 375 patients who underwent uncomplicated CABG with CPB in a multicenter clinical trial of a medication for postoperative pain. Data were obtained preoperatively, at the time of postoperative extubation, and at 4 subsequent intervals ending 14 days after extubation. Data obtained before study drug administration are reported for all patients; thereafter, only data from placebo patients without perioperative complications (n = 123) are reported.**

Results: **Mean postoperative coagulation values remained within their reference ranges at the time of extubation. However, platelet counts increased to a peak value well above the reference range by the end of the study. Postoperative white blood cell counts rose above the reference range, mainly because of increased neutrophils. Serum chemistries were also altered; most patients showed a persistent postoperative hyperglycemia. Creatine kinase levels rose to nearly 4 times the upper limit of the reference range in the early postoperative period. Lactate dehydrogenase, serum aspartate aminotransferase, and alanine aminotransferase levels also increased above the reference range. Total protein and albumin values were below the reference range throughout the postoperative period.**

Conclusions: **Laboratory values for hematology, blood coagulation, and serum chemistry change substantially after uncomplicated CABG with CPB. Recognition of these changes will facilitate the conduct of clinical research and may prevent inappropriate treatment based on abnormal laboratory findings that have no clinical significance.**

KEY WORDS: coronary artery bypass graft surgery, cardiopulmonary bypass, standard laboratory tests, hematologic tests, clinical chemistry tests, blood coagulation tests

EXTRACORPOREAL CIRCULATION causes perturbations of clinical chemistry, hematologic, and blood coagulation measurements.[1-3] Specifically, changes in laboratory values may be caused by hemodilution, hypothermia, nonphysiologic flow states, anticoagulation, acid-base status, decreased levels of platelets and coagulation factors, and activation of platelets, endothelium, and leukocytes caused by the "inflammatory response to cardiopulmonary bypass (CPB)."[3,4] These values are often outside the reported reference ranges, yet many of these laboratory "abnormalities" are not necessarily associated with adverse clinical outcomes.

Although laboratory data are obtained routinely in clinical investigations, the ubiquitous changes in these values caused by CPB have not been reported in more than 20 years.[1] The primary objective of this investigation was to define the expected changes in commonly obtained biochemical, hematologic, and blood coagulation laboratory values after coronary artery bypass graft (CABG) surgery with CPB without intraoperative or perioperative complications. Recognition of common changes would facilitate conduct of clinical research that includes laboratory measurements and may prevent inappropriate clinical treatment of "abnormalities."

METHODS

Patients

After institutional approval and informed consent were obtained, 462 patients undergoing elective, isolated primary CABG via median sternotomy were enrolled in a multicenter, double-blind, controlled clinical trial comparing a study medication for postoperative pain therapy (parecoxib/valdecoxib) to a placebo. Both groups also received standard care. Patients from 58 institutions in the United States (n = 170), Canada (n = 124), Germany (n = 124), and the United Kingdom (n = 44) were randomized in a 2:1 ratio to the treatment and standard-care groups, respectively, within each center between January and May 2000 (Table 1). The primary findings are reported elsewhere.[5]

Preoperative inclusion criteria were age ≤77 years, body mass index ≤40 kg/m^2, weight >55 kg, left ventricular ejection fraction ≥35%, and New York Heart Association Class I to III. Patients were excluded if they underwent emergency surgery or had a recent (ie, in the previous 48 hours) myocardial infarction, had insulin-dependent or uncontrolled diabetes (fasting blood sugar >350 mg/dL), had increased concentrations of liver enzymes (aspartate aminotransferase [AST, previously SGOT] or alanine transferase [ALT, previously SGPT] >1.5 times the upper limit of normal), had creatinine levels >1.5 mg/dL, or had any laboratory result suggesting abnormal blood coagulation. Also excluded were patients with stroke or transient ischemic attack within the previous 6 months, current substance abuse (opioids, any other analgesics, or alcohol), allergy to nonsteroidal anti-inflammatory agents, or a history of gastric or duodenal ulcer.

Intraoperative exclusion criteria included a CPB time >3 hours or insertion of an intra-aortic balloon pump. Also, patients were excluded if they had an intraoperative complication that, in the opinion of the primary investigator, significantly increased the patient's postoperative risk. In the postoperative period and before randomization, patients

*From the *Clinic for Anesthesiology, Ludwig-Maximilians-Universität, München, Germany; †Drexel University College of Medicine, Philadelphia, PA; ‡Department of Biostatistics and Epidemiology, Texas Heart Institute, Houston, TX; §Pharmacia Corporation, Skokie, IL; ‖Department of Laboratory Medicine, University of California School of Medicine, San Francisco, CA; the ¶Department of Cardiovascular Anesthesiology, Texas Heart Institute at Saint Luke's Episcopal Hospital, Houston, TX; and from the Multicenter Study of Perioperative Ischemia (McSPI) Research Group and the Ischemia Research and Education Foundation (IREF) Investigators, San Francisco, CA.*

Supported by an unrestricted educational grant from Gentiae Clinical Research, Inc (a subsidiary of the Ischemia Research & Education Foundation), San Francisco, CA.

Address reprint requests to Nancy A. Nussmeier, MD, c/o Editorial Office, Ischemia Research and Education Foundation, 250 Executive Park Blvd., Suite 3400, San Francisco, CA 94134. E-mail: nnussmeier@heart.thi.tmc.edu

1053-0770/05/1901-0004$30.00/0
doi:10.1053/j.jvca.2004.11.004

Table 1. Number of Patients (n = 462) Enrolled by Each Institution (n = 58)

Number of Patients Enrolled (Range)	Number of Institutions Enrolling This Range
<5	23
5-10	24
11-15	6
>15	5

were excluded from the study if they were receiving 3 or more inotropic infusions; had developed a symptomatic arrhythmia or new Q-wave myocardial infarction; had a cardiac index <1.5 L/min, chest tube output >500 mL in a 2-hour period, urine output <50 mL/h, hemoglobin <8 g/dL, creatinine >1.2 mg/dL or 30% above baseline; or temperature <36°C or >38°C at the time of initial study drug administration. Tracheal extubation was mandated (per protocol) within 15 hours of surgery.

Three hundred eleven patients received the study medication, and 151 received placebo. For the purposes of the present study, a total of 37 patients were excluded because of postoperative mortality (n = 4) and/or serious postoperative adverse events (n = 33), including myocardial infarction, cardiac failure, cerebrovascular disorder, pneumonia, and renal dysfunction.[5] An additional 50 patients were excluded because surgery was performed "off-pump" without CPB, including 21 patients in the placebo group. Thus, the analyzed data were derived from 375 low-risk patients who underwent CABG surgery with CPB without complications. Patients who received transfusions of fresh frozen plasma (n = 5) or platelets (n = 2) were excluded from further analyses of related laboratory values (eg, prothrombin time [PT], activated partial thromboplastin time [aPTT], and platelet count).

Laboratory Testing

Laboratory data were collected preoperatively and at 5 postoperative time points: just before extubation (within 15 hours of surgery), the day after extubation (day 1), the third or fourth day after extubation (day 3 or 4), the day of hospital discharge, and at the end of the study (on day 14, or sooner if premature termination occurred). Analyses of laboratory values obtained preoperatively and in the postoperative period prior to extubation (before study drug administration) included all 375 patients. Analyses for all remaining time periods (after active study drug administration) included only the 123 placebo patients.

All blood samples from all centers were analyzed by a central laboratory (Covance Central Laboratory Services, Inc, Princeton, NJ). Laboratory tests consisted of hematologic, blood coagulation, hepatic, renal, electrolyte, and enzymatic profiles. (Normal ranges for these tests are presented in Table 2.) Hemoglobin and hematocrit were not analyzed because many patients received perioperative packed red blood cell transfusions that were not documented in the study database.

Anesthetic and Surgical Techniques and Postoperative Care

Anesthesia was induced with fentanyl and/or midazolam, isoflurane, and a muscle relaxant for tracheal intubation. Anesthesia was maintained with isoflurane and/or propofol, fentanyl, midazolam, and pancuronium at all institutions. CPB with membrane oxygenators and hemodilution was used in all patients included in this analysis by using the technique of hemodilution. Although the conduct of the anesthesia and surgical intervention was similar among the institutions, no attempts were made to further standardize technique.

After admission to the intensive care unit, initial management allowed the administration of propofol, morphine, or midazolam at the clinician's discretion. Each patient received 80 to 325 mg of aspirin per day. Shortly after tracheal extubation, patients meeting the inclusion criteria were randomized to receive the study drug or placebo. Standard care was allowed, including administration of any clinically necessary medications except for nonsteroidal anti-inflammatory drugs. No information was collected regarding intraoperative administration of drugs such as calcium chloride or potassium chloride. Only descriptive statistics (means ± SD) were computed for this study.

Table 2. Reference Ranges

Laboratory Parameter	Reference Range
Platelet count ($\times 10^3/\mu L$)	130-394
PT (s)	10.5-14.9
aPTT (s)	23.0-37.0
WBC ($\times 10^3/\mu L$)	3.8-10.7
Neutrophils (%)	40.5-75.0
Bands (%)	0-3.0
Lymphocytes (%)	15.4-48.5
Monocytes (%)	2.6-10.1
Eosinophils (%)	0-6.8
Basophils (%)	0-2.0
Total bilirubin (mg/dL)	0.2-1.2
Alkaline phosphatase (U/L)	
20-58 years	31-110
≥59 years	35-115
AST (SGOT) (U/L)	
Female	9-34
Male	11-36
ALT (SGPT) (U/L)	
Female 0-68 years	6-34
Female ≥69 years	6-32
Male 0-68 years	6-43
Male ≥69 years	6-35
LDH (U/L)	53-234
Total protein (g/dL)	
4-58 years	6.1-8.4
≥59 years	6.0-8.0
Albumin (g/L)	
<69 years	3.3-4.9
≥69 years	3.5-4.6
BUN (mg/dL)	4.0-24.0
Creatinine (mg/dL)	
Female	0.4-1.1
Male	0.5-1.2
Sodium (mEq/L)	
0-58 years	132-147
≥59 years	135-145
Potassium (mEq/L)	3.4-5.4
Chloride (mEq/L)	94-112
Bicarbonate (mEq/L)	17.0-30.6
Calcium (mg/dL)	8.4-10.3
Inorganic phosphorus (mg/dL)	2.2-5.1
Creatine kinase (CK) (U/L)	
Female	21-169
Male	22-198
Glucose (mg/dL)	
0-58 years	70-115
≥59 years	70-120

NOTE. Unless otherwise indicated, normal values are identical for adult men and women.

Abbreviations: PT, prothrombin time; aPTT, activated partial thromboplastin time; WBC, white blood cell count; AST, aspartate aminotransferase; SGOT, serum glutamic oxoacetic transaminase; ALT, alanine aminotransferase; SGPT, serum glutamic pyruvic transaminase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen.

Table 3. Initial Postoperative* Changes in Laboratory Values in Coronary Artery Bypass Graft Patients (n = 375)

Laboratory Parameter	Preoperative				Postoperative				Change in Mean
	Mean ± SD	Range	25th %	75th %	Mean ± SD	Range	25th %	75th %	
Platelet count (×10³/μL)	230 ± 60	98-491	186	261	166 ± 52	69-433	127	195	−63
PT (s)	12.7 ± 2.8	10.1-60.0	12	12.9	14.4 ± 1.8	11.4-39.7	13.6	14.9	1.7
aPTT (s)	26.8 ± 6.7	17.9-60.0	23.0	28.1	30.0 ± 8.5	19.4-97.1	24.6	33.2	3.2
WBC (×10³/μL)	7.3 ± 2.0	3.2-14.3	5.9	8.6	**12.6 ± 4.7**	3.7-29	9.0	15.8	5.3
Neutrophils (%)	62.0 ± 8.2	34-80	57	62	**81.9 ± 6.5**	54-94	78	87	20.0
Bands (%)	0.0 ± 0.0	0-0	0	0	0.4 ± 1.7	0-1.4	0	0	0.4
Lymphocytes (%)	28.9 ± 7.5	13-57	24	34	**11.9 ± 6.6**	1-42	7	15	−17.0
Monocytes (%)	6.1 ± 1.9	2-16	5	7	4.7 ± 2.2	0-14	3	6	−1.3
Eosinophils (%)	2.5 ± 1.3	0-8	2	3	0.9 ± 0.9	0-4	0	1	−1.6
Basophils (%)	0.8 ± 0.5	0-3	1	1	0.1 ± 0.4	0-2	0	0	−0.7
Bilirubin (mg/dL)	0.5 ± 0.3	0.2-1.9	0.3	0.6	0.7 ± 0.5	0.2-4.8	0.4	0.9	0.2
Alkaline phosphatase (U/L)	69 ± 21	27-119	55	81	45 ± 16	18-131	34	53	−24
AST (SGOT) (U/L)	24 ± 12	11-117	17	26	**45 ± 38**	15-594	29	50	21
ALT (SGPT) (U/L)	30 ± 20	3-176	18	34	24 ± 21	6-302	15	27	−6
LDH (U/L)	154 ± 44	74-464	130	168	**258 ± 84**	96-684	203	300	104
Total protein (g/dL)	6.8 ± 0.7	3.5-8.7	64	73	**4.5 ± 0.7**	2.5-6.5	4.0	5.0	−2.3
Albumin (g/dL)	3.8 ± 0.5	2.0-4.8	3.5	4.2	**2.6 ± 0.5**	1.4-4.1	2.3	2.9	−1.2
BUN (mg/dL)	16.5 ± 4.5	7.0-33.6	13.7	19.0	14.8 ± 3.9	7.0-30.0	12.0	17.1	−1.7
Creatinine (mg/dL)	0.9 ± 0.2	0.4-2.0	0.8	1.0	0.8 ± 0.2	0.4-1.5	0.7	0.9	−0.1
Sodium (mEq/L)	140 ± 3	132-148	139	142	141 ± 3.4	130-152	139	143	0.3
Potassium (mEq/L)	4.2 ± 0.4	2.7-5.9	4.0	4.5	4.5 ± 0.6	2.3-5.8	4.1	4.8	0.3
Chloride (mEq/L)	105 ± 3	91-115	103	107	111 ± 4	99-122	108	114	6
Bicarbonate (mEq/L)	25.1 ± 3.2	14-38	23	27	21.3 ± 2.8	12-39	20	23	−3.8
Calcium (mg/dL)	8.7 ± 0.8	5.4-10.5	8.4	9.2	**7.5 ± 0.7**	5.1-10.0	7.1	8.0	−1.2
Inorganic phosphorus (mg/dL)	3.7 ± 0.9	2.0-12.4	3.3	4.0	3.2 ± 1.2	0.7-12.1	2.5	3.7	−0.5
Creatine kinase (CK) (U/L)	87 ± 57	18-599	52	106	**517 ± 366**	98-323	297	635	430
Glucose (mg/dL)	**121 ± 44**	65-360	95	129	**178 ± 55**	85-378	142	205	56

NOTE. Values outside the reference range are in bold print. (Reference ranges provided in Table 2.)

Abbreviations: aPTT, activated partial thromboplastin time; WBC, white blood cell count; AST, aspartate aminotransferase; SGOT, serum glutamic oxoacetic transaminase; ALT, alanine aminotransferase; SGPT, serum glutamic pyruvic transaminase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen.

*Immediately before extubation (within 15 hours of surgery).

RESULTS

Initial Postoperative Changes in Patients Having CABG With CPB

Abnormalities in laboratory tests were common in both treatment groups but similar between groups.[5] Initial postoperative laboratory values obtained just before extubation (mean 7.6 ± 4.1 hours after the end of surgery) tended to deviate considerably from preoperative values (Table 3). Preoperatively, only the mean value for serum glucose was above normal. After CABG with CPB, PT and aPTT increased but remained within the reference range. The platelet count decreased considerably but also remained within normal range. The white blood cell count (WBC) rose above the normal range, whereas the percentage of neutrophils increased and the percentage of lymphocytes decreased to values outside the reference range.

Serum chemistries were also altered after CABG with CPB. AST (SGOT) and lactate dehydrogenase (LDH) levels rose above their normal ranges. A marked postoperative hyperglycemia developed in many patients; the mean glucose level was 178 ± 55 mg/dL at the time of tracheal extubation. Postoperative mean creatine kinase (CK) activity showed an almost 6-fold increase to values far above the reference range. Total protein, albumin, and calcium decreased to values below their reference ranges. Total bilirubin rose above preoperative levels but remained within the reference range. Also remaining in the reference range were the postoperative values for alkaline phosphatase, ALT (SGPT), BUN, and creatinine, although each of these decreased below preoperative levels.

Changes From Postoperative Day 1 to 14

Analysis of hematologic, coagulation (Table 4), and serum chemistry laboratory values (Tables 5 and 6) collected during the rest of the study period was restricted to the 123 patients who received placebo and did not experience serious adverse events. In these patients, the mean platelet count decreased but remained within the reference range on postoperative day 1, but it subsequently increased to a peak value well above the reference range by the end of the study. Mean PT values remained within the reference range at all time points. Mean aPTT values decreased immediately after surgery; thereafter, aPTT remained low but within the reference range. On day 3 or 4, the total WBC count, percentage of neutrophils, and percentage of lymphocytes returned to their reference ranges, but these measures had not fully returned to their preoperative values by the

Table 4. Postoperative Changes in Laboratory Values in Coronary Artery Bypass Graft Patients (n = 123) (Placebo Patients Only): Hematology and Coagulation

Laboratory Parameter	Preop				Day 1				Day 3 or 4				Hospital Discharge				2 Weeks Postop			
	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %
Platelet count ($\times 10^3/\mu L$)*	216 ± 50	126-392	182	246	157 ± 41	76-288	125	185	206 ± 55	113-349	165	232	308 ± 92	109-546	229	364	**499 ± 132**	228-1079	416	572
PT (s)†	12.5 ± 0.7	10.7-14.8	12	13.1	13.5 ± 1.4	10.4-24.7	12.9	13.9	13.1 ± 2.6	10.9-35	12.3	13.3	13.0 ± 1.2	10.9-20.8	12.3	13.4	12.9 ± 1.2	11.2-22.3	12.4	13.2
aPTT (s)†	26.6 ± 6.3	18.8-55.7	23.3	27.4	26.4 ± 4.7	18.1-60	23.7	25.9	24.8 ± 6.6	18.8-67	22	25.3	23.4 ± 2.6	17.6-29.4	21.4	24.9	24.5 ± 3.5	18.4-39.9	22.4	25.8
WBC ($\times 10^3/\mu L$)	7.2 ± 2.0	3.3-14.3	6	8.2	**12.8 ± 3.5**	5.5-24.3	10.8	14.6	9.5 ± 2.6	4.3-19.8	7.6	10.7	9.6 ± 2.5	5.3-16.2	7.9	10.9	8.9 ± 2.2	5.1-18	7.3	10.2
Neutrophils (%)	61.7 ± 8.5	34-80	56	68	**81.9 ± 5.5**	60-93	78	85	74.2 ± 7.0	53-89	71	78	70.1 ± 5.6	57-83	67	73	68.9 ± 6.8	49-85	65	74
Bands (%)	0.0	0-0	0	0	0.1 ± 0.5	0-5	0	0	0.0 ± −	0	0	0	0.1 ± 0.5	0-0.3	0	0	0.0 ± 0.3	0-0.3	0	0
Lymphocytes (%)	29.1 ± 7.9	13-57	25	34	**11.4 ± 4.9**	3-34	8	14	17.6 ± 6.0	7-40	14	21	19.7 ± 5.5	6-36	17	22	21.6 ± 5.6	7-42	18	25
Monocytes (%)	6.1 ± 2.1	3-16	5	7	5.6 ± 2.4	2-17	4	7	5.5 ± 2.3	1-15	4	6	6.3 ± 2.4	2-19	5	7	5.8 ± 2.4	3-23	5	6
Eosinophils (%)	2.4 ± 1.4	0-8	1	3	0.9 ± 0.9	0-5	0	1	2.4 ± 1.4	0-9	1	3	3.4 ± 1.9	0-10	2	4	3.1 ± 2.4	0-14	2	4
Basophils (%)	0.9 ± 0.5	0-2	1	1	0.2 ± 0.4	0-1	0	0	0.4 ± 0.6	0-4	0	1	0.7 ± 0.6	0-3	0	1	0.8 ± 0.4	0-2	1	1

NOTE. Values outside reference range are in bold print. (Reference ranges provided in Table 2.)
Abbreviations: PT, prothrombin time; aPTT, activated partial thromboplastin time; WBC, white blood cell count.
*Patients with platelet transfusion (n = 2) excluded from platelet count analyses.
†Patients with fresh frozen plasma transfusion (n = 5) excluded from PT and aPTT analyses.

Table 5. Postoperative Changes in Laboratory Values in Coronary Artery Bypass Graft Patients (n = 123) (Placebo Patients Only): Clinical Chemistries (Renal and Hepatic)

Laboratory Parameter	Preop				Day 1				Day 3 or 4				Hospital Discharge				2 Weeks Postop			
	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %
Total bilirubin (mg/dL)	0.5 ± 0.3	0.2-1.9	0.3	0.6	0.7 ± 0.4	0.2-2.4	0.4	0.8	0.7 ± 0.4	0.2-2.0	0.4	0.8	0.6 ± 0.3	0.2-1.7	0.4	0.7	0.4 ± 0.2	0.2-1.0	0.3	0.5
Alkaline phosphatase (U/L)	68 ± 18	27-121	55	79	49 ± 15	24-123	38	55	74 ± 41	33-291	51	80	103 ± 80	43-542	63	114	106-37	54-256	84	114
AST (SGOT) (U/L)	24 ± 13	11-116	18	26	**39 ± 19**	16-114	26	46	**40 ± 64**	6-528	19	36	**38 ± 31**	11-200	20	43	22 ± 11	10-69	15	26
ALT (SGPT) (U/L)	30 ± 21	7-176	18	34	23 ± 16	6-155	15	25	**49 ± 133**	8-988	17	35	**63 ± 107**	11-734	23	51	33 ± 22	9-130	20	39
LDH (U/L)	155 ± 40	77-339	131	166	**242 ± 54**	120-419	212	266	222 ± 70	130-676	183	241	227 ± 65	132-616	191	260	182 ± 37	84-306	161	203
Total protein (g/dL)	6.9 ± 0.6	4.8-8.2	6.5	7.3	**5.3 ± 0.6**	3.8-7.4	4.9	5.6	**5.7 ± 0.6**	4.4-7.7	5.2	6.1	6.3 ± 0.6	4.9-8.3	5.8	6.6	6.9 ± 0.6	5.5-8.6	6.6	7.2
Albumin (g/dL)	3.9 ± 0.4	2.6-4.8	3.6	4.2	**2.8 ± 0.4**	1.8-4.4	2.5	3.1	**2.8 ± 0.4**	1.9-3.6	2.5	2.9	**3.0 ± 0.3**	2.2-3.8	2.8	3.2	3.4 ± 0.3	2.5-4.2	3.2	3.7
BUN (mg/dL)	16.8 ± 4.5	8.1-33.6	14	19	18.7 ± 5.7	7-33	14	22	20.0 ± 7.0	8.1-41.2	15.1	22.4	19.0 ± 6.8	7.3-44.0	16.0	21.0	18.7 ± 6.8	8.4-52.7	15.1	21.3
Creatinine (mg/dL)	1.0 ± 0.2	0.5-1.4	0.8	1.1	1.0 ± 0.2	0.5-1.7	0.8	1.1	0.9 ± 0.2	0.5-1.5	0.8	1.0	0.9 ± 0.2	0.5-2.0	0.8	1.0	1.0 ± 0.3	0.6-2.3	0.8	1.1

NOTE. Values outside reference range are in bold print. (Reference ranges provided in Table 2.)
Abbreviations: BUN, blood urea nitrogen; AST, aspartate aminotransferase; SGOT, serum glutamic oxoacetic transaminase; ALT, alanine aminotransferase; SGPT, serum glutamic pyruvic transaminase; LDH, lactate dehydrogenase.

Table 6. Postoperative Changes in Laboratory Values in Coronary Artery Bypass Graft Patients (n = 123) (Placebo Patients Only): Other Clinical Chemistries

	Preop			Day 1			Day 3 or 4			Hospital Discharge			2 Weeks Postop		
Laboratory Parameter	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %	Mean	Range	25th %	75th %
Sodium (mEq/L)	141 ± 2	132-146	139	142	139 ± 4	130-151	136	141	138 ± 6	104-150	137	141	139 ± 3	134-146	137	140	139 ± 3	133-145	138	141
Potassium (mEq/L)	4.2 ± 0.4	3.1-5.2	4	4.5	4.4 ± 0.4	3.6-5.5	4.1	4.7	4.1 ± 0.5	2.9-5.6	3.7	4.3	4.3 ± 0.5	2.8-5.6	4.1	4.6	4.6 ± 0.4	3.5-5.5	4.3	4.9
Chloride (mEq/L)	105 ± 3	98-112	104	107	105 ± 5	94-123	102	108	102 ± 6	74-115	99	105	102 ± 3	93-111	100	105	103 ± 3	95-109	102	106
Bicarbonate (mEq/L)	25.0 ± 3.0	17-38	23	27	25.4 ± 3.3	19-35	23	28	26.5 ± 3.1	18-34	25	29	26.1 ± 3.2	16-33	24	28	25.5 ± 2.9	16-33	24	27
Calcium (mg/dL)	8.8 ± 0.6	6.3-10.1	8.5	9.2	**7.8 ± 0.5**	6.3-9	7.6	8.1	**8.0 ± 0.5**	6-9.3	7.7	8.4	8.4 ± 0.5	7.4-9.7	8.1	8.7	8.9 ± 0.4	8-10.2	8.6	9.2
Inorganic phosphorus (mg/dL)	3.7 ± 1.1	2.4-12.4	3.3	4.0	3.3 ± 1.8	1.5-19.4	2.4	3.7	2.8 ± 0.8	1.0-5.2	2.3	3.3	3.7 ± 0.8	1.0-6.0	3.2	4.3	4.1 ± 0.6	2.7-5.5	3.7	4.5
Creatinine kinase (CK) (U/L)	89 ± 68	18-599	56	105	**731 ± 546**	125-3736	370	885	**267 ± 213**	35-1122	120	366	106 ± 75	18-456	52	146	48 ± 46	18-430	29	57
Glucose (mg/dL)	**125 ± 48**	76-320	95	129	**162 ± 49**	85-388	131	180	**144 ± 44**	83-321	110	165	**144 ± 50**	77-333	108	160	**124 ± 46**	65-322	95	142

NOTE. Values outside reference range are in bold print. (Reference ranges provided in Table 2.)

Table 7. Laboratory Values Outside the Reference Range

Time Point	Laboratory Parameter
Preop*	Glucose(↑)
Time of extubation*	WBC(↑), neutrophils(↑), lymphocytes(↓), AST(↑), LDH(↑), total protein(↓), albumin(↓), calcium(↓), CK(↑), glucose(↑)
Postop day 1†	WBC(↑), neutrophils(↑), lymphocytes(↓), AST(↑), LDH(↑), total protein(↓), albumin(↓), calcium(↓), CK(↑), glucose(↑)
Postop day 3 or 4†	AST(↑), ALT(↑), total protein(↓), albumin(↓), calcium(↓), CK(↑), glucose(↑)
Day of hospital discharge†	AST(↑), ALT(↑), albumin(↓), glucose(↑)
End of study (day 14)†	Platelet count(↑), glucose(↑)

NOTE. (↑) indicates values above, and (↓) indicates values below the reference range. (Reference ranges provided in Table 2.)

Abbreviations: WBC, white blood cell count; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; CK, creatine kinase; ALT, alanine aminotransferase.

*Laboratory values shown for all 375 patients.

†Laboratory values shown for 123 placebo patients.

end of the study period. The WBC count obtained 2 weeks postoperatively was within the reference range.

By the end of the study period, all serum chemistry measurements were within the reference range with the exception of serum glucose, which had returned to preoperative levels but was still above normal (Tables 4 and 5). However, AST (SGOT) values were above the reference range on day 1 and remained elevated through hospital discharge and then returned to normal during the 2 weeks after surgery. ALT (SGPT) measurements were above the reference range on day 3 or 4 and at hospital discharge. Total protein and serum albumin values were below the reference range on day 1 and on day 3 or 4, but they returned to normal by the time of hospital discharge. Serum LDH was very slightly elevated on postoperative day 1. CK levels were above the reference range at extubation and peaked at day 1; they remained above the reference range at day 3 or 4 but returned to the reference range by the day of hospital discharge and decreased below preoperative levels (but remained within the reference range) by the end of the study. Calcium measurements were below the reference range in the early postoperative period. Table 7 summarizes all laboratory results that were outside the reference range.

DISCUSSION

The present results show that CABG with CPB initiates a consistent pattern of substantial hematologic, coagulation, and serum chemistry changes, resulting in laboratory values that are often outside the reference range. However, these laboratory abnormalities do not necessarily indicate adverse outcomes, as shown in this group of low-risk patients who underwent CABG without complications.

Hematology and Blood Coagulation

It is of interest that no clinically significant abnormalities in platelet count, PT, or aPTT were observed at extubation even though disturbances in blood coagulation are known to be caused by CPB-related hypothermia,[6-8] high-dose heparin administration,[9] sequestration and destruction of platelets,[2,10,11] qualitative platelet abnormalities,[10,11] and decreased serum coagulation factors as a consequence of exposure of blood to the perfusion circuit.[6] However, patients with excessive postoperative bleeding were excluded from this study. Therefore, the laboratory values analyzed were obtained from those patients who were most likely to have near-normal coagulation. Nonetheless, 2 weeks after surgery, the mean platelet count rose to more than double the preoperative mean. This finding is consistent with previous observations that thrombocytosis commonly occurs after surgical procedures[12,13] and that coagulation tests may be abnormal for at least 2 months postoperatively.[14]

The immediate postoperative increase in white blood cell count after CABG may be because of a nonspecific inflammatory response to the trauma and bleeding caused by major surgery.[4] Similarly, the increase in the percentage of neutrophils is likely to be an expression of this nonspecific response.[4,15] The failure of the mean total WBC count and percentage of neutrophils to return to their preoperative values by the end of the study may also indicate a lingering nonspecific inflammatory response.

Serum Chemistries

Several serum chemistry measurements were outside the reference range after surgery. Postsurgical decreases in total protein persisted until day 3 or 4, and decreased albumin levels persisted until hospital discharge. These observations are consistent with the intraoperative administration of large volumes of crystalloid and its consequent dilutional effects. However, interpretation of postoperative albumin values may be impaired by variations in practice with respect to albumin administration during the intraoperative and/or postoperative periods. A dilutional mechanism may also explain the early postoperative hypocalcemia observed in these patients, although calcium levels must be interpreted with caution in the presence of hypoalbuminemia. Hemodilution in the immediate postoperative period may also explain other serum chemistry changes observed in these patients; ALT (SGPT), alkaline phosphatase, BUN, and creatinine levels all decreased postoperatively, although they remained within the reference range.

The CABG patients displayed an increase in LDH to levels slightly above normal and a smaller increase in serum bilirubin, which remained within the normal range. These changes may be explained by hemolysis caused by the shear forces associated with the use of cardiotomy suction and CPB pumps.[16] Additionally, the nonphysiologic flow pattern of extracorporeal circulation may have impaired microcirculatory perfusion, causing minor hepatic tissue damage that contributed to the postoperative increase in serum LDH and AST.[17] An interesting finding in this study was that the mean ALT (SGPT) value was above the normal range on day 3 or 4 and at hospital discharge, possibly because hepatic perfusion, microcirculation, and/or metabolism were affected by CPB or hypotension. In fact, a moderate loss of hepatocellular integrity has been described in patients undergoing prolonged CPB.[18] However, given that none of the patients in the current study had any adverse events, the observed chemical changes probably reflect a subclinical phenomenon rather than significant pathophysiologic change. Furthermore, BUN and creatinine values remained within the reference range throughout the postoperative period, suggesting that renal function was preserved.

The mean preoperative serum glucose level was above normal, and marked postoperative hyperglycemia was observed. Although the authors cannot exclude the possibility that intravenous dextrose was administered in the perioperative period, it is likely that postoperative hyperglycemia was caused primarily by the stress response to surgical trauma and extracorporeal circulation.[19,20] Serum glucose levels remained outside the reference range 2 weeks after CABG.

Potential Limitations

The potential limitations of this study include the relatively small number of placebo patients without serious adverse events who were available for the entire postoperative study period (n = 123). However, laboratory values were obtained at several time points over a 2-week period for each patient, increasing the descriptive value of the study. Additionally, the inclusion of only those patients with an absolutely uncomplicated postoperative course is a strength, in that the laboratory values in this group describe the perturbations to be expected in patients without any morbid event or complication.

Although the timing of the first set of postoperative laboratory tests to extubation (mean 7.6 ± 4.1 hours after surgery) was mandated by the study protocol, a more ideal timing would have been 8 or 12 hours after the end of CPB. Furthermore, it could be argued that the sample of patients in this study was overly heterogenous, in that the patients were treated at many different centers and only the sickest patients were excluded. However, this diversity makes the sample more representative of the CABG population as a whole. Unfortunately, there were too few patients undergoing "off-pump" CABG to allow useful comparisons between patients with and without CPB. Finally, the effect of CPB on qualitative platelet function was not assessed in this study.

CONCLUSIONS

In conclusion, it is clear that there are substantial fluctuations in standard laboratory values after cardiac surgery with CPB. In many instances, values rose above or dropped below the reference range. However, because all patients with serious morbidity were excluded from this study, these changes in laboratory values did not indicate any morbid outcome and therefore were not clinically significant. Instead, the consistent pattern of changes in laboratory values shown in this study may be a useful reference for the objective evaluation of cardiac surgical patients enrolled in clinical trials. Furthermore, in patients having routine cardiac surgery, knowledge of expected perturbations in laboratory values may prevent unnecessary treatment based on "abnormal" laboratory findings, with subsequent inappropriate resource utilization and possible iatrogenic complications.

ACKNOWLEDGMENT

The authors are indebted to Stephen N. Palmer, PhD, for his invaluable contributions to the writing of this article.

REFERENCES

1. Milam JD, Austin SF, Martin RF, et al: Alteration of coagulation and selected clinical chemistry parameters in patients undergoing open heart surgery without transfusion. Am J Clin Pathol 76:155-162, 1981

2. Gelb A, Roth RI, Levin J, et al: Changes in blood coagulation during and following cardiopulmonary bypass: Lack of correlation with clinical bleeding. Am J Clin Pathol 106:87-99, 1996

3. Ascione R, Lloyd CT, Underwood MJ, et al: Inflammatory response after coronary revascularization with or without cardiopulmonary bypass. Ann Thorac Surg 69:1198-1204, 2000

4. Herskowitz A, Mangano DT: Inflammatory cascade: A final common pathway for perioperative injury? Anesthesiology 85:957-960, 1996

5. Ott E, Nussmeier NA, Duke PC, et al: Efficacy and safety of the cyclooxygenase 2 inhibitors parecoxib and valdecoxib in patients undergoing coronary artery bypass surgery. J Thorac Cardiovasc Surg 125:1481-1492, 2003

6. Westaby S: Coagulation disturbance in profound hypothermia: The influence of anti-fibrinolytic therapy. Semin Thorac Cardiovasc Surg 9:246-256, 1997

7. Boldt J, Knothe C, Welters I, et al: Normothermic versus hypothermic cardiopulmonary bypass: Do changes in coagulation differ? Ann Thorac Surg 62:130-135, 1996

8. Rohrer MJ, Natale AM: Effect of hypothermia on the coagulation cascade. Crit Care Med 20:1402-1405, 1992

9. Horne MK III, Chao ES: Heparin binding to resting and activated platelets. Blood 74:238-243, 1989

10. Hyde JA, Chinn JA, Graham TR: Platelets and cardiopulmonary bypass. Perfusion 13:389-407, 1998

11. Holloway D, Summaria L, Sandersara J, et al: Decreased platelet number and function and increased fibrinolysis contribute to postoperative bleeding in cardiopulmonary bypass patients. Thromb Haemost 59:62-67, 1988

12. Santhosh-Kumar CR, Yohannan MD, Higgy KE, et al: Thrombocytosis in adults: Analysis of 777 patients. J Intern Med 229:493-495, 1991

13. Buss DH, Cashell AW, O'Connor ML, et al: Occurrence, etiology, and clinical significance of extreme thrombocytosis: A study of 280 cases. Am J Med 96:247-253, 1994

14. Parolari A, Colli S, Mussoni L, et al: Coagulation and fibrinolytic markers in a two-month follow-up of coronary bypass surgery. J Thorac Cardiovasc Surg 125:336-343, 2003

15. Edmunds LH Jr: Inflammatory response to cardiopulmonary bypass. Ann Thorac Surg 66:S12-16, 1998

16. Hansbro SD, Sharpe DA, Cathpole R, et al: Haemolysis during cardiopulmonary bypass: an in vivo comparison of standard roller pumps, nonocclusive roller pumps and centrifugal pumps. Perfusion 14:3-10, 1999

17. Chew MS, Brandslund I, Brix-Christensen V, et al: Tissue injury and the inflammatory response to pediatric cardiac surgery with cardiopulmonary bypass: A descriptive study. Anesthesiology 94:745-753, 2001

18. Kumle B, Boldt J, Suttner SW, et al: Influence of prolonged cardiopulmonary bypass times on splanchnic perfusion and markers of splanchnic organ function. Ann Thorac Surg 75:1558-1564, 2003

19. Loef BG, Epema AH, Navis G, et al: Off-pump coronary revascularization attenuates transient renal damage compared with on-pump coronary revascularization. Chest 121:1190-1194, 2002

20. Lehot JJ, Piriz H, Villard J, et al: Glucose homeostasis: comparison between hypothermic and normothermic cardiopulmonary bypass. Chest 102:106-111, 1992