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

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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

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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.