

# Adverse Gastrointestinal Complications After Cardiopulmonary Bypass: Can Outcome Be Predicted from Preoperative Risk Factors?

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Adverse gastrointestinal (GI) outcome after cardiac surgery is an infrequent event but is a clinically important health care problem because of associated increased morbidity and mortality. The ability to identify patients at greatest risk before surgery may be helpful in planning appropriate perioperative management strategies. We examined the pre- and intraoperative characteristics of 2417 patients from 24 diverse United States medical centers enrolled in the Multicenter Study of Perioperative Ischemia Study who were undergoing cardiac surgery using cardiopulmonary bypass as predictors for adverse GI outcome. Resource utilization was evaluated for patients with and without adverse GI outcomes. Adverse GI outcomes occurred in 5.5% of patients (133 of 2417), increased in-hospital mortality 6.5-fold, prolonged the mean intensive care unit length

of stay by 1 wk, and more than doubled the mean postoperative hospital stay ( $P < 0.0001$ ). Predictors of adverse GI outcome included decreased left ventricular function, hyperbilirubinemia, thrombocytopenia, prolonged partial thromboplastin time, prior cardiovascular surgery, combined coronary artery bypass graft surgery and intracardiac or proximal aortic surgery, pharmacological cardiovascular support, and intraoperative transfusion. The literature suggests that adverse GI outcome after cardiac surgery is secondary to poor splanchnic perfusion, which many of these risk factors may predict. Therefore, patients deemed to be at risk before surgery may benefit from tightly controlled hemodynamic management and other strategies that optimize perioperative organ perfusion.

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**G**astrointestinal (GI) complications after cardiopulmonary bypass (CPB) are relatively infrequent events (0.58%–3.7%) but may result in significantly increased adverse outcome. Of the estimated 1 million patients who undergo cardiac surgery annually throughout the world, those who sustain a GI complication have a disproportionately frequent mortality rate (14.8%–67%) (1–13). Diagnosis of a GI complication is often difficult because of the complexity and variety of clinical presentations. It is proposed, therefore, that the preoperative identification of

patients at increased risk for developing GI complications may allow heightened vigilance during the perioperative period and earlier diagnosis and intervention, possibly improving outcome.

Most previous studies examining risk factors for GI complications after cardiac surgery have focused on intraoperative and postoperative predictors (2,4,7,8,10,11,13). Only a few retrospective studies have included preoperative risk factors in their analyses (1,6,7,12). No large prospective multicenter study has examined preoperative risk factors for GI complications after CPB. This study identifies preoperative risk factors for the development of GI complications after CPB. Because intraoperative events have been shown to influence adverse GI outcome, preoperative risk factors were also analyzed in the context of these events. The effect of adverse GI outcome on morbidity, mortality, and hospital resource utilization was also examined.

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**Table 1.** Summary of Adverse GI Outcomes

Adverse GI outcome	No. Patients	% Patients with GI event (n = 133)	% Total patients (n = 2417)
Hyperbilirubinemia—total <sup>a</sup> (mg/dL)	90	67.7	3.7
3.1–5.0	54	40.6	2.2
5.1–9.0	19	14.2	0.8
>9.0	17	12.8	0.7
GI bleeding	28	21.0	1.2
Pancreatitis	19	14.3	0.8
Cholecystitis	7	5.3	0.3
Bowel perforation	2	1.5	0.1
Bowel infarction	2	1.5	0.1

GI = gastrointestinal.

<sup>a</sup> Hyperbilirubinemia was defined as maximum total bilirubin after surgery >3.0 mg/dL.

## Methods

The Multicenter Study of Perioperative Ischemia Research Group Cardiac Surgery Epidemiological Study (EPI-I) is a prospective observational study of 2417 patients undergoing coronary artery bypass graft (CABG) surgery (with or without concurrent intracardiac or other procedures) using CPB. Patients were enrolled from 24 United States medical institutions (Appendix 1) from September 1991 to September 1993. After IRB approval and informed consent, approximately 100 patients were prospectively enrolled at each center, according to a systematic random sampling scheme based on the CABG surgery caseload at that institution. Perioperative demographic, clinical, and laboratory data were collected by using standardized case report forms that included approximately 1500 data fields per patient addressing the period from hospital entry to discharge. Demographic data, perioperative clinical information, 12-lead electrocardiograms, and laboratory data were collected prospectively and recorded on the standardized case reports by a site investigator who had undergone specific training and used a study operation manual. Additional autopsy data for cause of death classification were also collected.

Adverse GI outcome was defined as postoperative GI bleeding, pancreatitis, bowel infarction or perforation, acute cholecystitis, or a maximum postoperative bilirubin of >3.0 mg/dL (11,12). Potential predictors of GI outcome were categorized as preoperative or intraoperative (Appendix 2). Mortality was noted from the records, and, when possible, cause of death was examined. Associations with other morbidities or adverse outcomes were also examined, e.g., myocardial infarction, renal failure (postoperative serum creatinine >2.0 mg/dL) (14), and stroke. Resource utilization was assessed on the basis of postoperative length of stay in the intensive care unit and hospital.

Univariate associations between potential preoperative and intraoperative predictors (Appendix 2) and adverse GI outcome were assessed with either Fisher's exact test or  $\chi^2$  tests, as appropriate. Patients with

missing data for potential predictors were analyzed as described previously for the risk of adverse GI outcome. They were then included in the group for that predictor with a similar risk category after the robustness of this approach was ensured (18). Then stepwise logistic regression was performed for adverse GI outcome (separately for preoperative and intraoperative predictors) and included all potential predictors associated with a  $P < 0.1$  from the univariate analysis. Our final model for the 2 separate time periods included only those predictors associated with adverse GI outcomes at a significance level of  $P < 0.05$ . Finally, the independent predictors of adverse GI outcome for the two separate time periods were merged, and stepwise logistic regression was performed. This combined model included only those predictors associated with adverse GI outcomes at a significance level of  $P < 0.05$ . Results for the multivariate models are reported as odds ratios with associated 95% confidence intervals. Morbidity, mortality, and resource utilization data were analyzed by Fisher's exact,  $\chi^2$ , or two-sample Student's  $t$ -tests, as appropriate, with  $P < 0.05$  considered to be significant.

## Results

One hundred thirty-three (5.5%) of the 2417 patients developed 1 or more new postoperative adverse GI outcomes (Table 1). The most common adverse outcome was hyperbilirubinemia (maximum postoperative total bilirubin >3.0 mg/dL), which occurred in 3.7% (90 patients), followed by GI bleeding (1.2%; 28 patients) and pancreatitis (0.8%; 19 patients) (Table 1). A total of 148 GI complications occurred in 133 patients. The most commonly coinciding postoperative GI adverse outcomes were hyperbilirubinemia and GI bleeding (seven patients), followed by hyperbilirubinemia and cholecystitis (four patients) and hyperbilirubinemia and pancreatitis (another four patients). Only one patient incurred three postoperative GI

**Table 2.** Selected Preoperative Characteristics of the Study Patients: Incidence of Adverse GI Outcome

Characteristic	Incidence of adverse GI outcomes			P value
	Incidence of characteristic in all patients (n = 2417) (%)	Patients with characteristic (%)	Patients without characteristic (%)	
Age >75 yr	14.4	8.79	4.94	0.0045
Female	23.7	5.93	5.37	0.6045
Obesity	38.1	4.90	6.02	0.2506
Morbid obesity	6.1	6.25	5.55	0.7234
History of diabetes	25.6	5.17	5.62	0.6735
History of renal dysfunction	5.3	9.45	5.25	0.043
Preoperative CHF	31.1	7.46	4.62	0.0047
History of smoking	66.6	5.60	5.40	0.8412
History of liver disease	4.2	5.88	5.43	0.8447
Heavy alcohol use	13.7	5.40	5.05	0.7952
Hepatic medications	43.7	6.44	4.78	0.0753
Antithrombotics	76.6	5.51	5.48	0.9756
Regular aspirin use	56.8	5.10	5.62	0.5822
Contraceptives/estrogen use	3.6	3.45	5.58	0.3921
Ejection fraction <0.4	21.4	9.05	4.94	0.0019
Increased preoperative total bilirubin (>1.2 mg/dL)	4.3	17.28	5.03	<0.0001
Platelets			NA	<0.0001
<100,000/ $\mu$ L	0.7	5.6		
100-130,000/ $\mu$ L	2.0	20.83		
>130,000/ $\mu$ L	97.2	5.05		
Prolonged PT (>14.9 s)	2.5	8.47	5.25	0.2767
PTT (s)			NA	0.0045
$\leq$ 37	76.0	4.68		
>37 to <45	4.2	4.12		
$\geq$ 45	19.8	8.52		
Decreased albumin (<3.3 g/dL)	10.4	8.82	5.26	0.0564
Increased SGOT/AST (>36 U/mL)	16.3	7.09	5.19	0.1307
Increased SGPT/ALT (>43 U/mL)	16.3	4.59	4.46	0.9327
Transfusion	2.5	4.92	5.52	0.8393
Prior cardiovascular surgery	14.0	12.09	4.43	<0.0001
History of major peripheral vascular or abdominal surgery	27.7	6.12	5.27	0.04103
Combined cardiac procedures	11.3	14.34	4.38	<0.0001
Emergency surgery	5.2	8.80	5.32	0.0969

GI = gastrointestinal; SGOT = serum glutamic oxalacetic transaminase; AST = aspartate aminotransferase; SGPT = serum glutamic pyruvate transaminase; ALT = alanine aminotransferase; PT = prothrombin time; PTT = partial thromboplastin time; NA = not applicable (because all patients fell into one of the platelet or PTT variable categories); CHF = congestive heart failure.

events (hyperbilirubinemia, GI bleeding, and cholecystitis) during the hospitalization. By using predictors identified by univariate analysis of adverse GI outcome ( $P < 0.1$  in Tables 2 and 3), logistic regression identified 7 principal preoperative and 4 principal intraoperative predictors of adverse GI outcome (Table 4). The preoperative independent risk factors related to advanced age, preexisting increased total bilirubin, decreased cardiac function, and indicators predisposing to hemorrhage or more difficult surgical procedures. The intraoperative independent predictors were related to prolonged or more difficult surgical procedures, transfusion of packed red blood cells, or hypoperfusion. In the final model that combined pre- and intraoperative predictors (Table 4), the 6 preoperative and 2 intraoperative variables that retained significance related to preexisting GI/hepatic

dysfunction, bleeding, more complicated or prolonged surgical procedures, and hypoperfusion.

Patients with adverse GI outcomes were 6.5 times more likely to die during hospitalization than those without adverse GI outcomes (Table 5). Patients with an adverse GI outcome were also more likely to experience myocardial infarction, renal failure, and stroke. The mean duration of postoperative stay in the intensive care unit was increased by more than 1 wk and the median stay increased more than threefold for those with adverse GI outcomes compared with patients without an adverse GI outcome. Likewise, adverse GI outcome more than doubled the mean post-surgical hospital stay to 3.5 wk and also doubled the median hospital length of stay.

Of the adverse GI outcomes examined in this study (Table 6), GI bleeding was associated with the highest

**Table 3.** Selected Intraoperative Characteristics of the Study Patients

Characteristic	Incidence of adverse GI outcome			P value
	Incidence of characteristic in all patients (n = 2417) (%)	In patients with characteristic (%)	In patients without characteristic (%)	
CPB time >100 min	53.2	7.0	3.8	0.0006
Aortic cross-clamp time >55 min	54.1	6.96	3.78	0.0006
Hypotension	11.9	11.11	4.75	<0.0001
Circulatory failure	14.3	12.46	4.34	<0.0001
Hypoxemia	2.2	5.66	5.44	0.9448
Embolic risk	23.5	7.38	4.92	0.0246
Pharmacologic cardiovascular support	52.7	7.69	3.06	<0.0001
Dysrhythmia	11.0	8.4	5.21	0.0336
Systemic temperature (°C)			NA	0.3578
≤26	22.0	6.99		
>26 to ≤30	46.7	5.33		
>30 to ≤34	22.5	4.99		
>34	8.8	4.25		
Transfusion of PRBCs (U)			NA	<0.0001
0	51.4	2.98		
1-3	33.7	5.04		
4-5	10.6	10.2		
>5	4.4	27.36		
Intraoperative TEE	30.5	7.32	4.71	0.0095

GI = gastrointestinal; NA = not applicable (because all patients fell into one of the temperature or transfusion variable categories); PRBCs = packed red blood cells; TEE = transesophageal echocardiography; CPB = cardiopulmonary bypass.

**Table 4.** Risk Factors Associated with Adverse Gastrointestinal (GI) Outcome

Variable	Models for adverse GI outcome (n = 133): odds ratio (95% CI)		
	Preoperative model	Intraoperative model	Both models
Increased preoperative total bilirubin >1.2 mg/dL <sup>a</sup>	2.4 (1.2-4.9)		2.5 (1.2-5.0)
Combined cardiac procedures	2.9 (1.8-4.5)		2.0 (1.3-3.2)
Preoperative platelets ≤130,000/μL	2.9 (1.3-6.4)		2.8 (1.3-6.2)
Prior cardiovascular surgery	3.0 (1.9-4.7)		2.2 (1.4-3.4)
Preoperative EF <0.4 <sup>a</sup>	1.9 (1.2-3.0)		1.7 (1.1-2.6)
Age >75 yr	1.8 (1.1-2.9)		
Preoperative PTT >37 s	2.0 (1.3-3.1)		1.7 (1.1-2.5)
Pharmacologic cardiovascular support		1.9 (1.3-2.9)	2.0 (1.3-3.2)
Intraoperative transfusion of PRBCs		1.9 (1.6-2.3)	1.7 (1.4-2.1)
Intraoperative circulatory failure		1.7 (1.1-2.6)	
Aortic cross-clamp time		1.5 (1.0-2.3)	

CI = confidence interval; EF = ejection fraction; PTT = partial thromboplastin time; PRBCs = packed red blood cells.

<sup>a</sup> Missing data were included as low risk on justification.

risk of in-hospital mortality, renal failure, and stroke, whereas postoperative hyperbilirubinemia was more highly correlated with myocardial infarction.

## Discussion

This prospective, multicenter observational study examined the incidence of adverse GI outcome in 2417 patients undergoing coronary revascularization with or without other intracardiac procedures or proximal aortic

surgery. Five and a half percent of our patients experienced a postoperative adverse GI outcome. This incidence is more than the 0.58%-3.7% incidence of adverse GI outcome noted in previous studies (1-13). Similar to these previous studies, adverse GI outcome resulted in significantly increased morbidity, mortality, and postoperative resource utilization. The determination of preoperative risk factors for adverse GI outcome and the preoperative identification of those patients at risk for adverse GI outcome is extremely

**Table 5.** Morbidity, Mortality, and Hospital Resource Utilization in Patients with Adverse Gastrointestinal Outcome

Variable	GI outcome, % (n) <sup>a</sup>	No GI outcome, % (n) <sup>b</sup>	P value
Mortality in hospital	19.6 (26)	2.80 (64)	<0.0001
Myocardial infarct	22.6 (30)	8.27 (189)	<0.0001
Renal failure	12.8 (17)	1.23 (28)	<0.0001
Stroke	7.52 (10)	3.50 (80)	0.017
LOS in ICU (d)			
Mean (SD)	11.5 (15.4)	3.0 (4.4)	<0.0001
Median (range)	6.4 (0.8–103.6)	2.0 (0–82.6)	
LOS in hospital (d)			
Mean (SD)	24.6 (24.9)	10.6 (13.9)	<0.0001
Median (range)	16.3 (1.5–125.2)	8.1 (0.1–372.1)	

LOS = length of stay; ICU = intensive care unit; GI = gastrointestinal.

<sup>a</sup> n = 133.

<sup>b</sup> n = 2284.

**Table 6.** Odds Ratio Comparison of Morbidity, Mortality, and Resource Utilization for Adverse GI Outcome and Individual Adverse GI Outcome Compared with No Adverse GI Outcome

Postoperative morbidity and mortality	All adverse GI outcomes (n = 133)	Bilirubin >3.0 mg/dL (n = 90)	GI bleed (n = 28)	Pancreatitis (n = 19)
Death				
Odds ratio	8.43	6.58	9.26	4.98
95% CI	5.14–13.8	3.66–11.85	3.83–22.39	1.42–17.41
P value	0.0001	0.0001	0.0001	0.005
Renal failure				
Odds ratio	11.8	13.64	16.43	10.52
95% CI	6.28–22.2	6.97–26.69	6.31–42.77	2.95–37.46
P value	0.0001	0.0001	0.0001	0.0001
Stroke				
Odds ratio	2.24	2.28	3.18	1.44
95% CI	1.13–4.43	1.02–5.08	0.94–10.72	0.19–10.92
P value	0.017	0.039	0.049	0.722
Myocardial infarct				
Odds ratio	3.23	4.23	1.69	1.18
95% CI	2.09–4.98	2.61–6.86	0.58–4.90	0.27–5.15
P value	0.0001	0.0001	0.333	0.823

GI = gastrointestinal; CI = confidence interval.

important and clinically relevant because it may direct perioperative management and also influence the overall decision regarding fitness for surgery.

In this study, previous revascularization, combined cardiac procedures (CABG plus an intracardiac or proximal aortic procedure), ejection fraction (EF) <0.4, preoperative total bilirubin level >1.2 mg/dL, low platelet count, and prolonged partial thromboplastin time (PTT) were independent preoperative predictors of adverse GI outcome in the combined preoperative and intraoperative multivariate model (*P* < 0.05). The transfusion of bank blood and the use of pharmacologic cardiovascular support were identified as independent intraoperative risk factors.

Previous studies suggest that a significant reduction of splanchnic blood flow occurs during CPB (15,16). Factors that contribute to splanchnic hypoperfusion are therefore thought to predispose to an adverse GI outcome, and, consistent with this theory, hypotension and the

duration of CPB have been implicated as the strongest predictors of an adverse GI outcome (1,6). In a large retrospective study of cardiac surgical patients, 18.4% of patients with a documented low cardiac output state developed hepatic failure, and 11.1% developed GI bleeding (17). Similarly, poor preoperative left ventricular performance, hemodynamic instability, and emergency surgery have also been identified as risk factors (6).

In our study, with the exception of patients with pre-existing evidence of liver dysfunction (increased serum bilirubin), our preoperative predictors were poor cardiac performance (a low EF or previous revascularization) and a predisposition to perioperative bleeding due to thrombocytopenia or a deranged coagulation profile (prolonged PTT). Both poor cardiac performance and an increased bleeding risk may contribute to reduced splanchnic perfusion. Intraoperative predictors of adverse GI outcome—pharmacological cardiovascular

support and intraoperative transfusion—are also markers of a possible hypoperfusion state. The preoperative identification of patients at risk for postoperative GI events therefore appears to also identify patients who may develop splanchnic hypoperfusion. Therefore, appropriate management in the preoperative and intraoperative period with tighter hemodynamic controls and intervention to enhance splanchnic perfusion may avoid a GI event and improve overall outcome.

There are a number of limitations to this investigation. EPI-I was an observational study not specifically designed to investigate GI outcome. Laboratory analyses were not standardized in terms of tests performed or times of testing but were collected according to the routine clinical protocol at the individual institution. Therefore, a number of patients have missing data for some of the predictors. Five-hundred-forty-six patients had no preoperative total bilirubin recorded. These patients were analyzed separately and had a risk for GI outcome similar to that of patients with normal bilirubin concentrations. Therefore, they were included in the same low-risk category. Similarly, the risk of GI outcome in the 1235 patients without preoperative EF data was comparable to that of patients with a preoperative EF  $>0.4$ . These patients were included in the same lower-risk category for EF. The justification for including these data in the lower-risk category is that the data are not missing at random and that the test was not ordered by the physician because, in the physician's judgment, it was not needed. The term used to describe missing data of this nature is *nonignorable*. This method of analysis for missing data was used after a sensitivity analysis was performed by using a model with listwise deletion (dropping missing data from the analysis) and by excluding the variable from the model altogether (18). When patients with missing total bilirubin and/or EF data were excluded from analysis, the results were consistent, but the association of GI outcome with EF was weakened. Exclusion of total bilirubin and/or EF from multiple logistic regression analysis did not change the association of GI outcome with the other risk factors remaining in the model.

Data on the use of perioperative drugs that are active at the gastric mucosa (e.g.,  $H_2$  blockers and proton pump inhibitors) were not collected in this database. Therefore, it is unknown whether the use of such drugs may have influenced the number of patients who developed GI hemorrhage. Limiting the scope of this study to pre- and intraoperative risk factors may have also ignored some potentially important postoperative predictors of adverse GI outcome. However, because this was a purely observational study without specified laboratory investigations or timing of these investigations, it is not possible to comment on the temporal relationship between an adverse GI outcome and any other adverse event.

This study may not be fully representative of current clinical practice. However, over the past 10 years, there have been only a few changes in the technology of CPB and the practice of anesthesia for cases involving CPB. In our study, intraoperative transesophageal echocardiography (TEE) was used in less than a third of patients (738 of 2417). Of interest, the incidence of GI complications in the patients who had intraoperative TEE was 7.3%, compared with a 5.5% incidence of GI complications in our overall study population. The use of TEE itself was evaluated as a possible risk factor for the development of GI complications and was not an independent predictor in multivariate analysis. Although there has been some discussion about the risk of GI bleeding associated with intraoperative TEE (19,20), there was no evidence of increased risk in our study. It is likely that TEE was used more often for patients who were already at an increased risk for GI complications (such as those with impaired ventricular function or those who had combined CABG/valve surgery).

The recent increase in the use of antifibrinolytic drugs may prevent perioperative blood loss and hypotension (21). Therefore, with these improved perioperative management strategies, the frequency of an adverse GI outcome may be less than that found in this study. However, with the increasing age and acuteness of the patient population presenting for cardiac surgery, with more advanced cardiac disease and with a more frequent incidence of comorbidities, it is probable that the current cardiac surgical population exhibits many of the risk factors identified as independent predictors of adverse GI outcome in this study. Preoperative identification of these patients and increased vigilance in their care may result in improved outcome.

Finally, this study does not address the question of adverse GI outcome after off-pump revascularization (OPCAB) procedures, because the EPI-I study includes only patients undergoing surgery using CPB. Although large randomized studies of conventional CABG surgery using CPB versus OPCAB have not yet been reported, there is some evidence to suggest that there is no difference in mortality, major morbidity (22), or inflammatory responses (23) between the two techniques. However, the need for blood products, an independent intraoperative predictor in our study, was significantly more in the conventional CPB group, indicating the possibility of a better GI outcome in high-risk patients with an OPCAB procedure.

In conclusion, we identified a number of independent preoperative predictors of adverse GI outcome after myocardial revascularization. In the combined preoperative and intraoperative model, increased bilirubin, thrombocytopenia, increased PTT, combined cardiac procedures, prior revascularization, and decreased left ventricular EF retained significance as preoperative risk factors. Adverse GI outcomes are significantly associated with increased postoperative

morbidity, in-hospital mortality, and resource utilization. The preoperative identification of patients at risk for adverse GI outcomes may allow for increased vigilance and early recognition of potential problems and may suggest changes in anesthetic, surgical, or perioperative care for this population at risk.

## Appendix 1

The following institutions and persons coordinated the Multicenter Study of Perioperative Ischemia Research Group Cardiac Surgery Epidemiological Study (McSPI EPI-I) **Study Chairman**—D. Mangano; **Coordinating Center: Ischemia Research and Education Foundation**—C. Dietzel, V. Katseva, E. Kwan, A. Herskowitz, C. Ley, and L. Ngo; **Outcome Validation Committee**—S. Graham, C. Mora Mangano, N. Nussmeier, G. Ozanne, G. Roach, and R. Wolman; **Biostatistics**—P. Hsu, D. Kardatzke, and S. Wang; **Editorial/Administrative Group**—D. Beatty and B. Xavier.

The following institutions and persons participated in the McSPI EPI-I study. **University of Alabama at Birmingham**—W. Lell; **Baylor College of Medicine**—S. Shenaq and R. Clark; **Cedars-Sinai Medical Center**—A. Friedman; **University of Chicago**—M. Frankina and W. Ruo; **Cleveland Clinic Foundation**—C. Koch and N. Starr; **Cornell University**—O. Patafio and R. Fine; **Duke University**—T. Stanley and M. Newman; **Emory University**—C. Mora Mangano and J. Ramsay; **Harvard University: Beth Israel Hospital**—M. Comunale; **Brigham and Women's Hospital**—S. Body and R. Maddi; **Massachusetts General Hospital**—M. D'Ambra; **University of Iowa**—A. Ross; **Kaiser-Permanente Medical Center, San Francisco**—G. Roach and W. Bellows; **University of Michigan**—J. Wahr; **New York University**—M. Kanchuger and K. Marschall; **University of Pennsylvania**—J. Savino; **Rush Presbyterian, St. Luke's Medical Center**—K. Tuman; **Stanford University**—E. Stover and L. Siegel; **Texas Heart Institute**—S. Slogoff and M. Goldstein; **Milwaukee Veterans Administration Medical Center**—A. Aggarwal; **San Francisco Veterans Administration Medical Center**—G. Ozanne and D. Mangano; **Medical College of Virginia**—J. Fabian and R. Wolman; **University of Washington**—B. Spiess; **Yale University**—J. Mathew.

## Appendix 2

### *Preoperative Variables*

1. Age in years as a continuous or discrete variable (advanced age defined as age >75 yr).
2. Gender.

3. Obesity, defined as body mass index = (weight in kg)/(height in meters)<sup>2</sup> >28.
4. Morbid obesity, defined as body mass index >35 kg/m<sup>2</sup>.
5. History of diabetes, defined by history or the preadmission or preoperative use of insulin or oral hypoglycemic drugs.
6. History of renal dysfunction (creatinine >2 mg/dL (14) or dialysis before admission).
7. Preoperative congestive heart failure (CHF) by history or any two positive findings on physical examination (jugular venous distention, rales, or S3 gallop).
8. History of smoking.
9. History of liver disease.
10. Heavy alcohol use, defined as a history of alcohol abuse (heavy drinking, hospitalization, withdrawal, or more than two drinks per day).
11. Hepatic medications, defined as preadmission and preoperative medications with hepatic effects (phenytoin, hydralazine, methyl dopa, antihyperlipidemia drugs).
12. Antithrombotics, defined as the preadmission and preoperative use of antithrombotic medications.
13. Regular aspirin use, defined as a history of recent or continuing aspirin use.
14. Contraceptive/estrogen use, defined as the preoperative use of oral contraceptive drugs or estrogen-containing compounds.
15. Ejection fraction <0.4, defined as preoperative left ventricular ejection fraction <0.4 (40%) as the highest recorded on ventriculography, radionuclide studies, or echocardiography.
16. Increased preoperative total bilirubin, defined as >1.2 mg/dL.
17. Low preoperative platelets, defined as ≤130,000/μL.
18. Prolonged preoperative prothrombin time, defined as a prothrombin time >14.9 s.
19. Prolonged preoperative partial thromboplastin time, defined as a partial thromboplastin time of >37 s.
20. Decreased preoperative serum albumin, defined as <3.3 g/dL.
21. Elevated preoperative serum glutamic oxalacetic transaminase/aspartate aminotransferase, defined as >36 U/mL.
22. Elevated preoperative serum glutamic oxalacetic transaminase/aspartate aminotransferase, defined as >43 U/mL.
23. Transfusion, defined as the preoperative transfusion of packed red blood cells.
24. Prior cardiovascular (or redo) surgery, defined as prior coronary artery bypass graft (CABG), valvular, or aortic surgery involving the ascending aorta or aortic arch only (previous sternotomy).

25. History of major peripheral vascular or abdominal surgery, defined as other prior surgery, including descending, thoracoabdominal renal, and abdominal aortic surgery and other abdominal surgery.
26. Combined cardiac procedures or surgery, defined as CABG plus valve, other intracardiac, or proximal aortic surgery.
27. Emergency surgery, defined as emergency surgery due to unstable angina or ischemia, myocardial infarction, failed angioplasty, ventricular failure, or dysrhythmia; emergency support therapies including cardiopulmonary resuscitation, intraaortic balloon pump placement, or other mechanical assist devices; or other reasons unable to be determined.

### *Intraoperative Variables*

1. Cardiopulmonary bypass (CPB) time in minutes.
2. Aortic cross-clamp time in minutes.
3. Hypotension, defined as a systolic blood pressure <80 mm Hg for >10 min during induction or before or after CPB or mean arterial blood pressure <40 mm Hg during CPB for >10 min.
4. Circulatory failure, defined as a cardiac index <1.5 l · min<sup>-1</sup> · m<sup>-2</sup> before or after CPB or a return to CPB (for all reasons except hemorrhage) or requiring an assist device.
5. Hypoxemia, defined as arterial oxygen saturation <90% at any time for more than two consecutive minutes.
6. Embolic risk, defined as lack of the use of an arterial filter or use of a bubble oxygenator rather than membrane oxygenator, or the presence of moderate or severe proximal aortic atherosclerosis, or presence of an atrial or ventricular thrombus, or difficult aortic cannulation, or presence of an air embolism, or use of an intermittent aortic cross-clamping technique.
7. Pharmacologic cardiovascular support, defined as the intraoperative use of inotropes and/or vasoconstrictors other than those routinely used at the reporting institution.
8. Dysrhythmia, defined as the occurrence of moderate or severe dysrhythmias requiring treatment during induction and before, during, or after CPB.
9. Systemic temperature.
10. Transfusion of PRBCs.
11. Intraoperative TEE.

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