JACC Vol. 28, No. 5
November 1, 1996:1147–53

A Model That Predicts Morbidity and Mortality After Coronary Artery Bypass Graft Surgery

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Objectives. **This study was performed to develop a method for identifying patients at increased risk for morbidity or mortality after coronary artery bypass graft surgery.**

Background. **Postoperative morbidity is more common than mortality and is important because of its relation to cost.**

Methods. **Univariate and forward stepwise logistic regression analysis was used to retrospectively analyze a group of 1,567 consecutive patients who underwent bypass surgery between July 1991 and December 1992. We developed a model that predicted postoperative morbidity or mortality, or both, which was then prospectively validated in a group of 1,235 consecutive patients operated on between January 1993 and April 1994. A clinical risk score was derived from the model to simplify utilization of the data.**

Results. **The following factors, listed in decreasing order of significance, were found to be significant independent predictors: cardiogenic shock, emergency operation, catheterization-induced coronary artery closure, severe left ventricular dysfunction, increasing age, cardiomegaly, peripheral vascular disease, chronic renal insufficiency, diabetes mellitus, low body mass index, female gender, reoperation, anemia, cerebrovascular disease, chronic obstructive pulmonary disease, renal dysfunction, low albumin, elevated blood urea nitrogen, congestive heart failure and atrial arrhythmias. Observed morbidity and mortality for the validation group fell within the 95% confidence interval of that predicted by the model. Costs were closely related to the incidence of postoperative morbidity.**

Conclusions. **Analysis of preoperative patient variables can predict patients at increased risk for morbidity or mortality, or both, after bypass surgery. Increased morbidity results in higher costs. Different strategies for high and low risk patients should be used in cost reduction efforts.**

(J Am Coll Cardiol 1996;28:1147–53)

Coronary artery bypass graft surgery (CABG) is now the most commonly performed major operation in the United States (1). Operative mortality has been the primary criterion for judging the quality of surgical results, and several models have been developed to predict mortality based on preoperative data (2–5). However, death after CABG is an uncommon event, with an incidence <4% (6). The ability to predict operative mortality is important to patients, families and physicians, but it is an incomplete method for determining surgical outcome. Major morbidity is more common than mortality after CABG and has greater economic importance because it results in a prolonged hospital stay and greater utilization of resources. A few statistical models that predict morbidity or cost, or both, have been developed, but the results have not been extensively verified or proven clinically useful (7–13). This study presents a clinical risk score (CRS) based entirely on preoperative data and that reliably predicts morbidity and mortality for patients undergoing CABG.

Methods

This study was derived from the Allegheny General Hospital's cardiothoracic surgery data base. The data base was implemented in July 1991, with prospective data collection on all patients undergoing cardiac surgery. This computerized system now contains detailed data on >6,000 patients. Daily prospective data collection is performed by research staff, and the validity of the entered data is checked by reabstracting 15% of the patient entries and by randomly reentering 10% of the patient records. This data base contains 170 preoperative variables pertaining to the severity of the patient's primary condition and comorbid diseases before the operation. Another 50 variables document procedural and intraoperative events, and another 100 variables are specific for postoperative outcome and discharge status. Standardized criteria and defi-

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Manuscript received December 18, 1995; revised manuscript received May 17, 1996, accepted June 26, 1996.

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0735-1097/96/$15.00
PII S0735-1097(96)00310-5

Abbreviations and Acronyms
CABG = coronary artery bypass graft surgery
CRS = clinical risk score
ROC = receiver operating characteristic

nitions for variables are listed in Appendix 1. Data are retrieved from the data base by a procedural query language, and computations are performed using SPSS, BMDP and EPI INFO statistical programs.

Hospital charge data were obtained from a computerized system that records all resources consumed and services provided during a patient's hospital stay. Total hospital charges are imperfect reflections of actual cost, but are often used as a proxy for cost (14). Because charges do not precisely reflect actual costs, we chose to compare the relative charges for various groups of patients rather than analyzing actual costs in absolute amounts. In this scheme, the cost for the least expensive group was given a value of one, and the costs for the more expensive groups were expressed as multiples of the low cost group.

Study design. All patients who had CABG only during the study period were analyzed and those who had concomitant procedures were excluded. Data were prospectively collected on 1,567 consecutive CABG patients between July 1, 1991 and December 31, 1992. Univariate and forward stepwise multivariate logistic regression analysis was then performed retrospectively on these 1,567 patients (test group) to develop a model to predict morbidity and mortality. The clinical predictive model was validated on 1,235 consecutive patients undergoing CABG between January 1, 1993 and April 30, 1994. Table 1 lists the clinical and demographic information for the test and validation groups. No significant differences were noted between the two study groups.

Statistical analysis. The association of 125 preoperative variables with postoperative morbidity or mortality was determined by univariate analysis. For the purpose of analysis, *morbidity* was defined as an unexpected postoperative complication, major or minor, which resulted in the increased consumption of hospital resources owing to the required treatment. The definitions of major and minor complications are given in Appendix 2. *Mortality* was defined as death at any time during the hospital stay. Morbidity and mortality were handled as separate end points. Categoric variables were tested for association with morbidity and mortality using the chi-square test or the Fisher exact test, as appropriate. Dichotomous variables were converted to numerical values—0 = absent and 1 = present. If dichotomous variables could not be verified, they were considered to be missing. In the univariate contingency tables, relative risk was used to assess the association between the independent variable and the end point. Continuous data were assessed for association with the end points using the Student *t* test and one-way analysis of variance. With the exception of age, left ventricular function and creatinine, continuous data were reduced to dichotomous variables by identification of thresholds. The data were ranked from highest to lowest, and the observed end point rates were computed for each data increment. Intervals with similar rates of end point incidence were combined, and the interval with the best end point association was selected as the cutoff point. For regression analysis, indicator variables were created for age, left ventricular ejection fraction and serum creatinine. If >5% of any variable was missing, the variable was excluded from the analysis. Missing variable patterns were tested for evidence of nonrandomization by subdividing the data into two subgroups and testing the distribution of the other variables in the analysis between the two groups. Variables that reflected treatment processes or practice preferences instead of disease diagnosis were excluded from consideration as independent variables. Variables were tested for significant interactions by univariate analysis of variable distribution in subgroups and by analysis of the correlation matrix and the computation of variable tolerance values. Multivariate correlates of morbidity or mortality were determined by stepwise forward regression analysis using the computer program BMDP-LR. The Hosmer-Lemeshow statistic was used to evaluate the goodness of fit of the regression modules, and the predictive accuracy of the models was tested by computing the area under the receiver operating characteristic (ROC) curve.

Development of the risk prediction model. To create a calibrated clinical risk prediction model that could accurately predict risk for an individual patient according to his or her specific characteristics, univariate variables with $p < 0.15$ were entered into two separate forward stepwise logistic regression modules. Module 1 comprised those variables relevant to operative morbidity and module 2 comprised variables associated with operative mortality. Mortality was censored in module 1. Statistically significant independent variables ($p < 0.05$) from modules 1 and 2 were entered into a final model in which operative morbidity and mortality were combined as one dependent variable. The goodness of fit for all three models was verified using the Hosmer-Lemeshow chi-square test. To assess the ability of the independent variables to predict the end point, their odds ratio, which is related to the coefficient in stepwise logistic regression analysis, was calculated—the odds ratio being the ratio of the odds of achieving an end point in a group, divided by the odds of achieving the end point in the reference group.

Clinical risk score. A CRS was developed from the logistic regression analysis to simplify utilization of the data. Signifi-

Table 1. Study Groups

	Test Group (n = 1,567)	Validation Group (n = 1,235)
Mean (±SD) age (yr)	65 ± 9	65 ± 10
Male/female (%)	70/30	72/28
Emergency or urgent operation (%)	16	13
Reoperation (CABG) (%)	9	8

CABG = coronary artery bypass graft surgery.

Table 2. Risk Factors for Morbidity and Mortality

Variable	Clinical Risk Score	Odds Ratio	Coefficient	Incidence (%)
Cardiogenic shock	7	29.9	5.311	2
Emergency operation	5	7.14	2.76	5
Urgent operation	4	3.5	1.945	8
Catheterization-induced coronary closure	4	3.68	1.874	3
Severe left ventricular dysfunction (ejection fraction <30%)	4	2.89	1.906	7
Age ≥75 yr	3	2.93	1.845	16
Cardiomegaly	2	3.3	2.4	7
Peripheral vascular disease	2	1.7	2.177	17
Chronic renal insufficiency (creatinine >1.9 mg/dl)	2	2.6	1.613	5
Age 70–74 yr	2	1.45	1.14	19
Insulin-dependent diabetes mellitus	2	2.5	1.121	9
Non–insulin-dependent diabetes mellitus	1	1.49	0.3384	14
Low body mass index	1	1.45	0.3158	23
Female gender	1	1.48	0.3777	30
Reoperation	1	1.39	0.2115	9
Age 65–69 yr	1	1.35	0.3024	21
Anemia	1	1.8	0.3321	15
Cerebrovascular disease	1	1.62	0.5855	7
Chronic obstructive pulmonary disease	1	1.39	0.7076	15
Albumin <4.0 mg/dl	1	1.23	0.2103	48
Renal dysfunction (creatinine 1.5–1.9 mg/dl)	1	1.8	0.8435	5
Elevated blood urea nitrogen (>29 mg/dl)	1	1.74	0.5522	8
Congestive heart failure	1	2.3	0.8262	11
Atrial arrhythmia	1	1.4	0.5812	7

cant independent predictors of morbidity and mortality from the logistic regression model were assigned points to reflect their predictive power. The points for the scoring system were derived from the variables' logistic regression coefficient, odds ratio and relative risk. The risk points were assigned to the predictive factors by taking the average of the coefficients for each variable from the modules and then adding increments of points based on the variables' average odds ratio, relative risk and improvement in the area under the ROC curve. Variables with coefficients <1 were assigned one point and were not eligible for additive weight. The predictive power of the CRS was evaluated by scoring the risk of morbidity or mortality for each patient in the test and validation groups. The patients were then stratified according to their predicted risk from lowest to highest. The predicted and observed rates for each interval were compared using contingency tables. Patients with similar risk scores were combined to create calibrated risk intervals. The relation between the CRS and end point rates was compared using linear regression. Ninety-five percent confidence intervals were calculated for the predicted results to see if the validation observed rates fell within those limits. Receiver operating characteristic curves were used to verify the predictive accuracy of the CRS in the validation group.

Results

Risk prediction model. Forward stepwise logistic regression analysis identified 20 independent predictors of morbidity or mortality, or both. The risk factors, beta coefficients, odds ratios and weighted scores are listed in Table 2. The most powerful predictors were those associated with emergency operation and depressed cardiac function. Other factors reflect comorbid disease processes, such as chronic obstructive pulmonary disease, renal insufficiency, peripheral vascular disease, diabetes, low serum albumin and anemia. Finally, age, gender and low body mass were also significant predictors. Obesity was not a predictor of morbidity or mortality.

The scoring is shown in Table 2. The total number of points is 50, but the maximal score for a patient is 37 because some factors such as age, serum creatinine and surgical priority are listed more than one time depending on severity, but can only be scored once per patient. It is rare for a patient's score to exceed 20. Predicted operative mortality was divided into five categories of increasing risk, and predicted morbidity was divided into four categories by increasing incidence, as defined by a patient's total CRS. These categories are presented in Table 3.

Validation of the risk prediction model. The operative mortality rate in the test group was 3.8% (59 of 1,567). Major and minor morbidity occurred in 16% and 36% of the patients, respectively, whereas 48% of the patients had no major or minor postoperative morbidity. The results in the validation group were very similar. Operative mortality was 3%, the major morbidity rate was 12% and the incidence of minor morbidity was 40%. Forty-eight percent of the patients in the validation group had no morbidity.

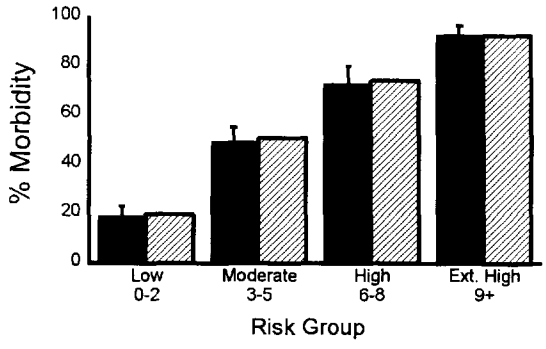
Table 3. Coronary Artery Bypass Graft Surgery Risk Groups

	Points	% Predicted
Mortality		
Low	0–4	0.2
Average	5–8	2
Moderate	9–11	6
High	12–18	30
Extremely high	19+	95
Morbidity		
Low	0–2	20
Moderate	3–5	50
High	6–8	74
Extremely high	9+	93

The predicted versus observed morbidity and mortality by CRS category for the validation group are shown in Figures 1 and 2, respectively. The observed morbidity and mortality fell within the 95% confidence interval of the predicted rate for each category. The correlation coefficient between the CRS and the incidence of morbidity was 0.98, and that between the CRS and death was 0.97. The area under the ROC curve was analyzed to determine the capacity of the model to correctly measure the occurrence of predicted morbidity and mortality. The predictive power for morbidity was 0.82, and for mortality it was 0.86.

Morbidity groups and cost. To examine the relation between cost and morbidity, the patients were divided into three groups based on the incidence and severity of postoperative complications. Group 1 had no complications; group 2 had one or more minor complications but no major complications; and group 3 had one or more major complications with or without minor complications or death, or both. Group 1 was the low cost group and was assigned a relative cost of one. Costs for group 2 were 1.7 times higher than costs for group 1. Costs for group 3 were 3.4 times higher than costs for group 1. In terms of overall costs, group 1 constituted 48% of the patients but only 32% of the total costs, whereas group 3 constituted only 12% of the patients but accounted for 27% of the total costs (Fig. 3).

Figure 1. Bar graph showing the predicted (**solid bars**) and observed (**hatched bars**) incidence of morbidity by increasing risk category. Ext. = extremely.



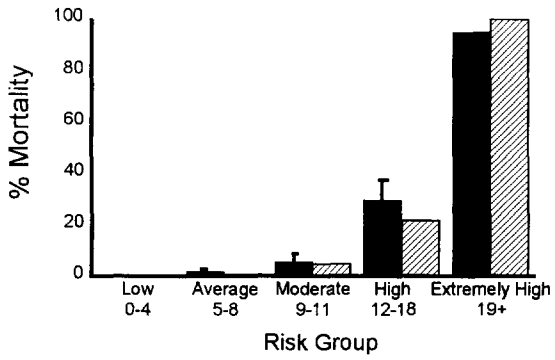


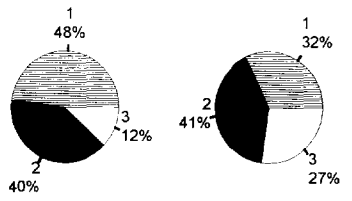
Figure 2. Bar graph showing the predicted and observed incidence of mortality by increasing risk category. Symbols as in Figure 1.

Discussion

Published reports. The capacity to predict the outcome of CABG before undertaking the operation has always been of interest to physicians and their patients. Recently, this subject has become of greater general interest because CABG accounts for a significant portion of the total health care expenditure in the United States. However, it is difficult to compare the results of one surgeon or institution with those of another because the acuity of patient illness and the incidence of comorbid diseases are not necessarily equal. A validated scoring system based on readily available preoperative information that correlates with morbidity and mortality provides a framework for developing meaningful outcome analysis in CABG.

Several recent reports have addressed the issue of predicting outcome in CABG using multivariate regression analysis. Parsonnet et al. (2) published a prospectively validated CRS system based on readily available patient data. The analysis included all types of cardiac surgery, including CABG, valve replacements, combined CABG and valve replacement and other less common procedures. In addition, the study modeled operative mortality but not morbidity. Subsequent studies by several investigators have analyzed factors that predict increased length of hospital stay, major complications and morbidity (7–13). Other reports have combined data from multiple institutions to predict mortality (3,4,13). Higgins et al. (5) published a CRS system that predicted both morbidity and mortality in patients undergoing CABG or CABG with con-

Figure 3. Pie graphs illustrating (**left**) number of patients in each morbidity group and (**right**) percentage of total costs generated by each morbidity group. 1 = no morbidity; 2 = minor morbidity; 3 = major morbidity.



comitant procedures, but a discussion of cost was not included. This study builds on the body of earlier work but differs in that we have focused primarily on morbidity. In addition, this study examined only patients having isolated CABG, whereas several previous studies looked at all patients having cardiac surgery or included patients having concomitant procedures in addition to CABG.

In the past 5 years, the states of New York and Pennsylvania have published reports on operative mortality for CABG by institution and by surgeon (15,16). The reports have attempted to stratify patients by expected risk, but the risk analysis is not as detailed as the one presented in this paper or in the publication by Higgins et al. (5). The assumption common to these efforts is that patient outcome is predominantly a function of surgical skill and institutional care. Some data exist to support this assumption. O'Connor et al. (3) reported that differences in operative mortality between different centers and surgeons could not be accounted for solely by differences in case mix. Other reports have demonstrated lower operative mortality for surgeons and institutions having a higher volume of operations (17). This finding is confirmed by the data from Pennsylvania: Allegheny General Hospital has had the highest volume of CABG procedures in the state for several years and has had lower than expected mortality in each of the years that the data have been published (16). However, surgeon-specific factors are not the major determinants of patient outcome. A recent analysis of "report cards on cardiac surgeons" found that combined surgeon-specific and institution-specific factors explained <10% of the variance in observed mortality (18).

This report emphasizes the importance of patient-related factors in determining postoperative outcome. We have identified multiple factors that are associated with increased morbidity, which are consistent with previously identified risk factors. In general, the predictors of an adverse outcome can be divided into several categories: 1) unstable patient condition leading to an urgent or emergency operation for cardiogenic shock, failed angioplasty, unstable angina or acute myocardial infarction; 2) impaired cardiac function as evidenced by cardiogenic shock, low ejection fraction, congestive heart failure or cardiomegaly; 3) comorbid diseases, especially peripheral vascular disease, cerebrovascular disease, diabetes, renal insufficiency and chronic obstructive pulmonary disease; 4) physical factors, such as advanced age, female gender and small stature; and 5) nonspecific laboratory abnormalities, such as anemia, low albumin and elevated creatinine. Categories of risk factors associated with the largest increase in morbidity and mortality are emergency operation and impaired cardiac function.

Clinical significance. This analysis has practical significance for improvements in clinical practice. To date, most efforts in this area have focused on reducing costs by decreasing length of hospital stay. This strategy will be the most effective in patients who have low or average risk for morbidity. Early extubation, short intensive care stay and early discharge can be reliably accomplished in these patients and tracked by means of critical pathways. In contrast, patients who suffer major complications such as stroke or respiratory failure cannot be "fast-tracked" for early discharge. This model identifies these high risk patients prospectively with an accuracy of ~82%.

A logical question is whether anything can be done to reduce complications in high risk patients. Patients with poor ventricular function and unstable symptoms are at high risk but also derive the largest benefit from the operation (19). Some patients who are at high risk because of comorbid diseases and conditions may be better served with medical therapy or catheter-based interventions, but the majority of high risk patients will need to have an operation. In this situation the challenge becomes how to reduce or prevent complications, which can be facilitated by identifying the patients at high risk before surgery. This allows the development of protocols to reduce specific complications in selected patients, without the necessity of changing the approach to all patients, many of whom are not at risk for the specific problem. For example, a recent study has shown a large reduction in postoperative stroke rates in high risk patients by maintaining a high blood pressure during cardiopulmonary bypass (20). Protocols could also be developed to manage elderly patients undergoing CABG, especially those who present with depressed left ventricular function and unstable angina.

Study limitations. The major limitation of this study is in the area of cost analysis. Reliable data on the actual cost for each patient are difficult to determine. Hospital charges have therefore been used as a surrogate for cost, which has been done in most studies on this subject. Another problem is that hospital charges for CABG vary widely by region and individual hospital, which makes analysis of charges at one institution difficult to generalize to other institutions. In addition, hospital charges for CABG are decreasing rapidly, which makes retrospective data obsolete within a year or two. To avoid these methodologic problems, we have chosen to greatly simplify the issue by making an analysis of relative cost for low, medium and high cost groups, which uses the low cost group as a benchmark. This is a superficial approach to cost analysis, but this is all that is warranted given the limitations of the data.

This model identifies patients at high risk for postoperative morbidity and mortality but does not directly predict cost. Nonetheless, we have demonstrated that hospital charges are closely related to the occurrence and severity of postoperative complications, which means that the model will prospectively identify patients who are at risk for morbidity and excess cost. The model was developed from the experience of one institution. It has been validated at the Allegheny General Hospital, but not at other institutions. This will need to be done before the model can be used to compare the results between different cardiac surgery centers.

Conclusions. This study presents a model that prospectively predicts postoperative morbidity and mortality using data that are readily available to the clinician before surgery. Patients who develop minor and major complications after the operation have excess cost in comparison to patients who have no complications. Cost reduction in clinical practice should use

different strategies for patients depending on the risk level. The potential for cost reduction is greatest in high risk patients, but this requires a reduction of postoperative morbidity.

Appendix 1

Standardized Criteria and Definitions of Variables

Cardiogenic shock: Systolic blood pressure <90 mm Hg or mean systemic blood pressure <50 mm Hg and a cardiac index <2.0 liters/min per m^2 and evidence of peripheral hypoperfusion

Emergency operation: Operation performed immediately to prevent death. The patient is having an acute event that is refractory to all other appropriate forms of therapy and is hemodynamically unstable.

Urgent operation: Operation performed to reverse or stabilize a deteriorating clinical condition. These patients are already receiving support with an intraaortic balloon pump, inotropic medications, nitroglycerin or heparin, or a combination of these. These operations are done 24 to 48 h from the onset of the acute event precipitating the symptoms.

Catheterization-induced coronary occlusion: Iatrogenic coronary occlusion or dissection secondary to a diagnostic catheterization or angioplasty, or both, that requires heart surgery within 24 h

Severe left ventricular dysfunction: Left ventricular ejection fraction <30%

Cardiomegaly: Enlarged heart as determined by chest radiography or echocardiography

Peripheral vascular disease: Claudication, ischemic rest pain, prior peripheral vascular surgery, absent lower extremity pulses, inability to insert an intraaortic balloon pump from the groin and/or a noninvasive vascular test showing >50% obstruction of the lower extremity vasculature

Chronic renal insufficiency: History of chronic renal disease or serum creatinine ≥1.9 mg/dl, or both

Insulin-dependent diabetes mellitus: Diabetes that has been treated with insulin before the surgical procedure

Non-insulin-dependent diabetes: Diabetes that has been treated with oral hypoglycemic agents before the surgical procedure

Low body mass index: ≤24 kg/m^2

Reoperation: Any prior cardiac surgery

Anemia: Hemoglobin ≤12.5 g/dl and ≤11 g/dl for males and females, respectively, or the need for preoperative blood transfusion

Cerebrovascular disease: History of a transient ischemic attack, embolic stroke or nonembolic stroke and/or angiographic evidence of internal carotid stenosis >50%

Chronic obstructive pulmonary disease: Pulmonary disease that results in functional disability or requires bronchodilator therapy and/or results in abnormal spirometry, as defined by a forced expiratory volume in 1 s, <75% of that predicted

Low serum albumin: <4.0 mg/dl

Renal dysfunction: Serum creatinine 1.5 to 1.9 mg/dl

Elevated blood urea nitrogen: Blood urea nitrogen >29 mg/dl

Congestive heart failure: Documented history of or treatment for heart failure and/or clinical evidence of heart failure, as defined by an S_3 gallop, jugular venous distention, pleural effusion, pulmonary edema, peripheral edema or radiographic evidence of interstitial edema (flash pulmonary edema excluded)

Atrial arrhythmias: Prior admission or outpatient treatment for atrial fibrillation, flutter or tachycardia

Appendix 2

Definitions of Major and Minor Complications

Major Complications

Cardiovascular failure: Intraoperative or postoperative acute myocardial infarction, intraaortic balloon pump, ventricular assist device, arrest with resuscitation and/or inotropic cardiac support requiring two or more drugs for >24 h

Respiratory failure: Postoperative ventilatory support for >48 h or tracheostomy, or both

Acute renal failure: New onset of oliguria or increasing serum creatinine resulting in dialysis or worsening of prior renal insufficiency requiring initiation of dialysis

Permanent cerebral deficit: Focal brain injury documented by scan with a permanent functional deficit

Major wound infection: Any surgical wound site manifesting clinical evidence of sepsis requiring additional hospital stay or surgical treatment, or both, for resolution

Pulmonary embolus: Documented by V̇/Q scan

Surgical intervention after coronary artery bypass grafting: Any surgical procedure performed during the postoperative period necessary to treat an adverse event that occurs secondary to bypass surgery

Minor Complications

Temporary central nervous system deficit: Documentation of a focal event by scan without a permanent deficit

Acute renal insufficiency: Oliguria or increasing serum creatinine requiring treatment with renal dose dopamine, diuretics or other pharmacologic means, but not resulting in dialysis

Atrial arrhythmias: Atrial fibrillation, flutter or tachycardia that is sustained long enough to be documented, produces patient symptoms and requires treatment with pacing, electrical cardioversion or drugs

Ventricular arrhythmias: Sustained ventricular fibrillation, tachycardia or premature contractions that require treatment with drugs, defibrillation, pacing and/or result in consultation with an electrophysiologist

Heart block: Complete heart block that is sustained, causes symptoms and requires treatment with drugs or pacing, or both

Superficial wound infection: A wound site with clinical evidence of infection, but that only requires treatment with antibiotics and topical medications

Respiratory insufficiency: Postextubation oxygen desaturation, hypercapnia or labored respirations, or all of these, leading to prolonged oxygen therapy

Pleural effusion: An effusion that requires thoracentesis or other therapy for resolution

Pneumothorax: A pneumothorax that requires placement of chest tube for resolution

Systemic sepsis: Culture-proven respiratory, urinary or blood infection that requires additional drug therapy and causes a delay in discharge

Gastrointestinal bleeding: Gastrointestinal hemorrhage documented by positive heme-stool tests

Postoperative mediastinal bleeding: Postoperative chest tube drainage of >1,500 ml or reexploration for bleeding, or both

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