Determinants of Hospital Mortality After Coronary Artery Bypass Grafting*

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Objectives: To examine causes of death and to find predictors of hospital mortality after elective coronary artery bypass graft (CABG) surgery.

Design: Case-control study.

Setting: Tertiary teaching hospital.

Methods: We prospectively collected various preoperative, operative, and immediate postoperative variables in a cohort of patients undergoing elective CABG surgery.

Results: Of the 2,014 consecutive patients (mean [± SD] age of 61.3 ± 6.7 years old) undergoing elective CABG over a 2-year period, 27 patients (1.3%) died during their hospitalization. The main causes of death (either isolated or in combination) were cardiogenic shock (n = 13), brain death or stroke (n = 7), septic shock (n = 4), ARDS (n = 2), and pulmonary embolism (n = 1). A univariate statistical analysis revealed factors that significantly correlate with outcome: patient age, preoperative left ventricular ejection fraction, bypass time, aortic cross-clamp time, number of blood units transfused, number of inotropic agents administered in the operating room during the first postoperative day (POD), history of arterial hypertension, intra-aortic balloon pump usage, and perioperative development of shock. A logistic regression analysis showed that the combination of the number of inotropes and the number of blood units administered in the operating room during POD 1 was the most important determinant of outcome, with an overall positive predictive value of 91.7%.

Conclusions: We conclude that the analysis of simple variables enhances our ability to accurately predict hospital mortality in patients undergoing elective CABG surgery. The number of inotropic agents and blood transfusions administered during the immediate postoperative period is the most important independent predictor of hospital mortality.

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Key words: cardiovascular surgery; coronary artery bypass; heart; risk of mortality

Abbreviations: APACHE = acute physiology and chronic health evaluation; CABG = coronary artery bypass graft; IABP = intra-aortic balloon pump; LCOS = low cardiac output syndrome; LVEF = left ventricular ejection fraction; POD = postoperative day

Coronary artery bypass graft (CABG) surgery has become a common surgical procedure worldwide. Over the last decade, an increasingly larger proportion of high-risk patients have been undergoing CABG, resulting in greater morbidity, a longer ICU stay, and a greater burden on available resources.1,2 The ability to accurately predict patient outcome after cardiac surgery may be particularly useful when determining a rational allocation of resources in a given institution.

The scoring systems used to predict patient outcome in general ICUs are not reliable when considering postoperative cardiac surgery patients.3 Attempts have been made to develop predictive models of outcome for this particular group of patients; however, the majority of the reported models are complex and of modest predictive ability.4,5 These shortcomings, at least in part, may be due to the fact that the majority of these studies analyzed preoperative variables and ignored variables related to the operation itself or to early postoperative care.6

The objectives of this study were to examine causes of death and to find predictors of hospital mortality (death occurring after the first postoperative day [POD] in the cardiothoracic ICU) for patients undergoing elective CABG surgery. We analyzed preoperative and immediate postoperative variables in order to develop a simple but accurate
predictive index for patient outcome in the ICU. An analysis of immediate postoperative variables has the theoretical advantage of being able to identify certain aspects of medical care that are amenable to therapy.\(^7\)

**Materials and Methods**

This is a case-control study of patients undergoing elective CABG surgery over a 2-year period (from July 1993 to June 1995) at the Onassis Cardiac Surgery Center, in Athens, Greece. During this period, a total of 2,014 consecutive adult patients (1,792 men and 222 women) with a mean age of 61.3 \(\pm\) 6.7 years old (range, 22 to 83 years old) were admitted to the cardiothoracic ICU. Of these 2,014 patients, 27 patients died (the case group); a sample of 708 patients who were successfully discharged from the hospital served as the control group. Of the 735 total patients enrolled in the study, 646 patients (87.9%) were men and 89 patients (12.1%) were women. The majority of these patients, 646 patients (87.9%) were men and 89 patients (12.1%) were women. The majority of these patients (\(n = 523;\) 71.2%) were smokers. The preoperative left ventricular ejection fraction (LVEF) was grade 1 (\(>50\%\)) in 209 patients, grade 2 (35 to 50%) in 406 patients, grade 3 (20 to 34%) in 112 patients, and grade 4 (\(<20\%\)) in 8 patients. All patients undergoing repeat, urgent, or emergency CABG surgery during this period were excluded from the study.

The operations were performed by five surgeons. Myocardial protection was achieved using combined antegrade and retrograde cold blood cardioplegia or antegrade cold crystalloid cardioplegia. Anesthetic management was provided by three teams according to a standard protocol. Ethical approval was obtained from the Ethics and Research Committee of the Onassis Cardiac Surgery Center.

The data collected on each patient included demographics, medical history, and several preoperative, perioperative, and immediate postoperative variables that were thought to influence outcome. Also considered were all complications that occurred during the ICU stay, the length of the ICU stay, the outcome (death or discharge), and the cause of death. The variables consisted of age, gender, preoperative LVEF assessed by angiography (grade 1, \(>50\%\); grade 2, 35 to 50%; grade 3, 20 to 34%; and grade 4, \(<20\%\)), and New York Heart Association class. Other variables were bypass time, aortic cross-clamp time, number of grafts, type of cardioplegia used, number of inotropic agents administered during POD 1 (for at least 6 consecutive hours) in the ICU, use of an intra-aortic balloon pump (IABP), and number of blood units transfused in the operating room and during POD 1 in the ICU. A blood transfusion was given when the patient’s packed cell volume was \(<27\%\).

All patients had one or two central venous catheters. A Swan-Ganz catheter was used in patients with \(<35\%\) preoperative LVEF, as well as in patients with postoperative low cardiac output syndrome (LCOS) and/or sepsis. Inotropic drugs were administered to treat LCOS, defined as a cardiac index of \(<2\) L/min/m\(^2\), despite optimal filling pressures (wedge pressure, 12 mm Hg). The inotropes were included only if they were given in this situation consisted of dobutamine, epinephrine, or dopamine (not arenal dose) up to the maximum dosages (epinephrine, 2 \(\mu\)g/kg/min; dobutamine, 20 \(\mu\)g/kg/min; or dopamine, 20 \(\mu\)g/kg/min). If there was a need for additional inotropic support within this critical period (for persistence of the condition), milrinone, 1 \(\mu\)g/kg/min, or norepinephrine, 0.3 \(\mu\)g/kg/min, was then added.\(^8\)

**Definitions**

All definitions were used as stated in the study protocol. Cardiogenic shock was defined as the failure of the cardiac pump to maintain a systemic blood flow sufficient to fulfill the patient’s metabolic requirements.\(^9\) Perioperative acute myocardial infarction was defined as the appearance of a new and persistent Q wave on ECG and/or the elevation of the creatinine phosphokinase/myocardial band enzyme to \(>40\) U total or a persistent elevation of \(>10\%\) for \(>24\) h.

The patients were defined as having severe sepsis if they manifested the following: (1) at least two of the following criteria: (a) body temperature \(>38\)°C or \(<36\)°C, (b) WBC counts \(>12 \times 10^9/\mu\)L or \(<4 \times 10^9/\mu\)L or immature neutrophils \(>10\%\), (c) heart rate \(>90\) beats/min, and (d) respiratory rate \(>20\) breaths/min or Pa\(_{CO_2}\) \(\leq 32\) mm Hg; (2) a documented infection; and (3) a systemic manifestation of peripheral hypoperfusion, such as lactic acidosis, oliguria (daily urine output \(<400\) mL), or acute alteration of mental status.\(^10\) Septic shock was defined as the combination of hypotension (a systolic BP \(<90\) mm Hg or a decline of \(>40\) mm Hg from baseline in the absence of other causes for hypotension) not responding to \(\geq500\) mL of IV fluid challenge and signs of tissue hypoperfusion in a patient with severe sepsis.\(^11\)

The diagnostic criteria for ARDS included (1) a history of a precipitating condition, (2) refractory hypoxemia (Pa\(_{O_2}\) \(<60\) mm Hg and fraction of inspired oxygen \(<0.6\) ), (3) radiologic evidence of bilateral pulmonary infiltrates suggesting pulmonary edema, (4) pulmonary artery occlusion pressure \(\leq 15\) to 18 mm Hg, and (5) total thoracic compliance \(\leq30\) mL/cm H\(_{2}\)O.\(^12\) The mortality rate refers to death occurring in the hospital following open heart surgery after POD 1.

**Statistical Analysis**

The data were analyzed using the appropriate software (SAS, version 6.03; SAS Institute; Cary, NC\(^{13}\); and Stata, version 4.0; Stata Corporation; College Station, TX).\(^14\) The differences were calculated using Fisher’s Exact Test for dichotomous or categorical variables and the two-sample Wilcoxon test for continuous variables. A backward stepwise regression analysis was used to identify the set of independent variables that contributed significantly to the fit of the model (removing criterion, \(p > 0.20\)). When a multilevel categorical variable was found to be significant, tests were conducted to determine whether some levels could be combined. Gender and cardioplegia were binary determinants; LVEF, aortic cross-clamp time, bypass time, number of grafts, units of blood transfused, and numbers of inotropic drugs administered were interval-scaled determinants. The dependent variable was binary, with 1 denoting death and 0 denoting a live discharge from the hospital. The predictability of the final logistic regression model regarding patient mortality was assessed by comparing the expected and actual number of deaths. The fit of the model was assessed by the Hosmer-Lemeshow goodness-of-fit statistic.\(^15\) All reported \(p\) values are two-sided.

**Results**

Of the 27 patients who died, 25 were men (92.6%) and 2 were women (7.4%), with a mean (\(\pm\) SD) age of \(67.2 \pm 7.2\) years old. The patients who died had a mean (\(\pm\) SD) preoperative LVEF of 0.35 \(\pm\) 0.1. The overall mortality rate was 1.3%. All deaths occurred in the ICU. The causes of death were cardiogenic
shock in 13 patients (48.1%), stroke or brain death in 7 patients (25.9%), septic shock in 4 patients (14.8%), ARDS in 2 patients (7.4%), and pulmonary embolism in 1 patient (3.7%). The patient characteristics and several perioperative variables of surviving and nonsurviving patients are shown in Table 1.

Among the determinants of outcome, an age > 65 years old was associated with an odds ratio of 4.3 (p < 0.001); perioperative shock necessitating IABP usage significantly increased the risk of death (odds ratio, 21.9; p < 0.001). A bypass time > 95 min similarly increased the risk of death in the ICU (odds ratio, 15.3; p < 0.001). However, the most significant determinant of death was the administration of more than one inotrope in the operating room and/or the ICU during POD 1 (odds ratio, 71.8; p < 0.001), as well as the transfusion of > 6 blood units during the same period (odds ratio, 30.3; p < 0.001).

A multivariate logistic regression analysis was used to identify the determinants of death. Thirteen potential determinants were entered into the initial model: age, gender, history of diabetes mellitus, history of arterial hypertension, preoperative LVEF, bypass time, aortic cross-clamp time, type of cardioplegia, number of grafts, LCOS, number of inotropes used, IABP usage, and number of blood transfusions. The backward selection procedure led to a final model including only age (p < 0.001), number of inotropes used, IABP usage, and number of blood transfusions. The levels of inotropes observed are presented in Table 2. In the group of patients receiving less than two inotropes, only two patients (0.3%) died. On the contrary, in the group of patients who died, 25 patients (92.6%) received at least two inotropes.

Table 3 shows the number of patients in the outcome groups as a function of blood transfusions. Patients who were given < 7 blood units during POD 1 had a mortality rate of 0.5%, and patients receiving ≥ 7 blood units had a mortality rate of 14% (p < 0.001).

Using inotropes as a binary predictor (with values of 0 and 1 indicating a good outcome and values of ≥ 2 indicating death) in combination with blood units transfused (with values of < 7 indicating a good outcome and values of ≥ 7 indicating death), the overall positive predictive value was 91.7% and the overall negative predictive value was 99.3% (Table 4).

In nonsurviving patients, the mean (± SD) for both mechanical ventilatory support and length of ICU stay was 20.3 ± 16.1 days (range, 1 to 62 days). The nonsurviving patients were more likely to have prolonged ventilatory support (> 1 day) than the control group, respectively: 100% vs 5.8% (p = 0.001). The nonsurviving patients were also more likely to have a longer ICU stay (> 2 days), respectively: 85.2% vs 10.2% (p = 0.001).

**Discussion**

Our study included both preoperative and immediate postoperative variables into a logistic regression model and developed an index to predict outcome after elective CABG surgery. Of all the parameters that were analyzed, we found that the number of inotropic drugs and the number of blood transfusions that were administered in the immediate postoperative period were the best reliable predictors of poor outcome in this group of patients.

Predicting outcome in postoperative cardiac surgery patients has proved to be an extremely difficult task. The severity-of-illness scoring systems that are commonly used in medical ICUs have not been very effective in this group of patients.

#### Table 1—Demographics, Preoperative, and Immediate Postoperative Variables in Surviving and Nonsurviving CABG Patients*

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Survivors</th>
<th>Nonsurvivors</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>708</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>621 (87.7)</td>
<td>25 (92.6)</td>
<td>&lt; 0.76</td>
</tr>
<tr>
<td>Female</td>
<td>87 (12.3)</td>
<td>2 (7.4)</td>
<td>&lt; 0.76</td>
</tr>
<tr>
<td>Age, yr</td>
<td>60.5 ± 10.5</td>
<td>67.2 ± 7.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Smokers</td>
<td>503 (71.0)</td>
<td>20 (74.1)</td>
<td>&lt; 0.5</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>0.43 ± 0.1</td>
<td>0.35 ± 0.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Grade 3 or 4 (&lt; 34%)</td>
<td>108 (15.2)</td>
<td>12 (44.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>223 (31.5)</td>
<td>9 (33.3)</td>
<td>&lt; 0.54</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>278 (39.3)</td>
<td>18 (66.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cardioplegia</td>
<td>58 ± 17</td>
<td>89 ± 61</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD or No. (%).

#### Table 2—Outcome Groups as a Function of Number of Inotropes Used*

<table>
<thead>
<tr>
<th>Outcome Group</th>
<th>Inotropes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–1</td>
</tr>
<tr>
<td>Good outcome</td>
<td>603 (99.7)</td>
</tr>
<tr>
<td>Death</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>Total</td>
<td>605 (100)</td>
</tr>
</tbody>
</table>

*Data are presented as No. of patients (%).
useful in predicting death in these patients, as high scores are often not associated with poor outcome. Our ability to normalize physiology by means of pharmacologic and/or mechanical support may in part account for this limited use of physiology-based scoring systems.5 Indeed, the most recent simplified acute physiology score II, mortality probability model II, and APACHE (acute physiology and chronic health evaluation) III scoring systems have excluded cardiac surgery patients.16–18

Over the last two decades, several studies have attempted to predict outcome by using preoperative risk factors in CABG surgery patients, but their success rate usually has likewise been limited.1,6 In some of these studies, outcome prediction involved a large number of preoperative variables19 or exponential equations20 that made their application impractical. A common characteristic of these studies is that they have focused exclusively on preoperative variables and, in general, have not taken into account events (ie, surgical complications) that can affect patient outcome during the operative or immediate postoperative period. Because cardiac surgery now involves a greater proportion of high-risk patients (eg, more repeat operations), operative complications occur more frequently now than a decade ago2 and they are unlikely to be predicted by any preoperative variable.

In a recent study, Turner et al21 took into account the intraoperative course and the complications that occurred during the first 24 h in the ICU, and attempted to develop a predictive model for CABG surgery patients. In this study,21 APACHE II and III criteria were not associated with mortality or survival, and the Parsonnet score overestimated hospital mortality (particularly in the lower ranges), just as it did in another study.22 This led the authors to conclude that cardiac surgery remains a difficult area for outcome prediction, although the inclusion of intraoperative and postoperative variables can improve predictive ability.

The number of inotropes administered during the immediate postoperative period (a gross index of myocardial function) has also been found by previous investigators21,23 to be an independent determinant of outcome in these patients. Unlike preoperative LVEF, this index is more likely to include patients with intraoperative complications (eg, myocardial ischemia or infarction), inadequate revascularization, LCOS related to systemic inflammatory response syndrome, stunned myocardium, or inadequate myocardial protection during bypass. Apparently, none of these conditions can be accurately predicted using any preoperative variable. Furthermore, in some high-risk cases (eg, low LVEF), there may be a great improvement in the left ventricular function postoperatively as a result of successful revascularization.24

It follows that, although low preoperative LVEF is a known predictor of poor immediate postoperative outcome following cardiac surgery, not all patients with low preoperative LVEF require inotropic support.24

According to our study, in the presence of perioperative parameters (eg, blood units and inotropes), the preoperative LVEF proved to be a nonsignificant determinant of outcome. In this respect, our data are in agreement with those of Turner et al21 and Thompson et al,23 who similarly showed that when both preoperative and postoperative variables are analyzed, the preoperative variables usually have little or no contribution to the final predictive model.

The independent association of blood transfusions with poor outcome deserves special comment. In our study, the transfusion requirements were relatively high, even for the control group. This was due to the fact that blood conservation techniques were not used during the study period and also to our excessive zeal to correct low hematocrit values in the ICU. Nevertheless, this finding raises the possibility that blood transfusions may indeed lead to increased mortality, presumably by their immunosuppressive effects.25 The relation of transfusion-induced immunosuppression and increased mortality rates in surgical patients has been highly debated over the last decade.26 There is still a controversy as to whether a cause-and-effect relationship exists between transfusion-induced immunosuppression and increased mortality or if excessive blood transfusions are simply a marker of disease severity.27 In postoperative cardiac surgery patients, recent studies showed that excessive blood transfusion was an important independent risk factor for sternal wound infection,28 early bloodstream infection,29 severe sepsis,30 or increased morbidity and mortality.31

This study illustrates the importance of preventing the development of LCOS by providing adequate myocardial protection during cardiopulmonary bypass. In addition, any strategy targeting the avoid-

### Table 3—Outcome Groups as a Function of Blood Unit Groups

<table>
<thead>
<tr>
<th>Outcome Group</th>
<th>&lt; 7</th>
<th>≥ 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good outcome</td>
<td>560 (99.5)</td>
<td>148 (86.0)</td>
</tr>
<tr>
<td>Death</td>
<td>3 (0.5)</td>
<td>24 (14.0)</td>
</tr>
<tr>
<td>Total</td>
<td>563 (100)</td>
<td>172 (100)</td>
</tr>
</tbody>
</table>

*Data are presented as No. of patients (%).
ance of allogenic transfusion may significantly reduce the possibility of an unfavorable outcome after CABG surgery.

The limitations of the present study should be pointed out. First, the index was derived from data obtained following an ICU stay of about 24 h; therefore, these data cannot be used as a preoperative indicator of outcome. Nevertheless, despite this delay in predicting outcome, we believe that there is still considerable value in predicting outcome during the early postoperative period. In comparison with previous studies\textsuperscript{22,32} using only preoperative variables, the accuracy of our prediction is much higher. Second, the surgery was performed by one group of surgeons; therefore, one may argue that the results of the present study are institution-specific and not pertinent to all patient groups. Thus, our predictive index of outcome requires validation in a different setting.

In conclusion, we found that the inclusion of certain postoperative variables into the analysis of risk factors significantly increases our ability to predict hospital mortality in postoperative CABG surgery patients. Of all the variables analyzed, the combination of inotropic drug therapy and excessive blood transfusions is significantly associated with hospital death following CABG.

REFERENCES

14 Stata Statistical Software: release 4.0. College Station, TX: Stata Corporation, 1995
16 Le Gall FR, Lemeshow S, Saulnier F. A new simplified acute physiology score (SAPS) based on a European/North American multicenter study. JAMA 1993; 270:2957–2963
19 Magyverna JA, Sakert T, Magyverna GJ, et al. A model that

### Table 4—Outcome Prediction Based on the Logistic Regression Model (Death if Predictive Probability ≥ 0.5)*

<table>
<thead>
<tr>
<th>Variables</th>
<th>&lt; 2</th>
<th>&lt; 2</th>
<th>≥ 2</th>
<th>≥ 2</th>
<th>Total Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>473</td>
<td>132</td>
<td>40</td>
<td>90</td>
<td>735</td>
</tr>
<tr>
<td>Deaths, No.</td>
<td>0</td>
<td>2</td>
<td>22</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Predictive probability, mean</td>
<td>0.0001</td>
<td>0.01</td>
<td>0.51</td>
<td>0.06</td>
<td>0.04</td>
</tr>
<tr>
<td>SD</td>
<td>0.0003</td>
<td>0.00</td>
<td>0.42</td>
<td>0.15</td>
<td>0.16</td>
</tr>
<tr>
<td>Model sensitivity, %</td>
<td>—</td>
<td>50</td>
<td>86.4</td>
<td>66.7</td>
<td>81.5</td>
</tr>
<tr>
<td>Model specificity, %</td>
<td>100</td>
<td>100</td>
<td>88.9</td>
<td>100</td>
<td>99.7</td>
</tr>
<tr>
<td>Positive predictive value, %</td>
<td>—</td>
<td>100</td>
<td>90.5</td>
<td>100</td>
<td>91.7</td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>100</td>
<td>99.20</td>
<td>84.2</td>
<td>98.9</td>
<td>99.3</td>
</tr>
</tbody>
</table>

*Categories are determined by the number of inotropes administered and blood units transfused.


