Intraoperative and Postoperative Risk Factors for Respiratory Failure After Coronary Bypass

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Background. Unlike preoperative events, the influence of intraoperative or postoperative events on respiratory failure after coronary artery bypass grafting (CABG) remains unclear. The purpose of this study was to identify intraoperative and postoperative risk factors that predispose respiratory impairment after CABG.

Methods. A single institutional database combined with a mandatory report submitted to the Cardiac Surgery Registry of the New York State Department of Health was used. A total of 8,802 consecutive patients who underwent primary CABG with or without a concomitant cardiac operation from January 1993 through December 2000 were included. Respiratory failure was defined as the need for postoperative mechanical ventilatory support longer than 72 hours. Univariate and multivariate logistic regression model was used in the analysis.

Results. Of 8,802 consecutive patients (6,234 males and 2,568 females) who underwent CABG with or without a concomitant operation, 491 patients (5.6%) suffered from postoperative respiratory failure. Although univariate analysis identified 39 statistically significant preoperative risk factors for post-CABG respiratory failure, only six preoperative risk factors were statistically significant by multivariate analysis ($p < 0.001$). CPB time (in 30 minutes increments) was the only validated intraoperative variable that increased the risk of postrespiratory failure (odds ratio [OR], 1.2; p less than 0.0001). Postoperative events contributing significantly to an increased risk of post-CABG respiratory failure were (1) sepsis and endocarditis (OR, 90.4; $p < 0.0001$), (2) gastrointestinal bleeding with or without infarction and perforation (OR, 38.8; $p < 0.0001$), (3) renal failure (OR, 30.7; $p < 0.0001$), (4) deep sternal wound infection (OR, 11.3; $p < 0.0001$), (5) new stroke, intraoperative at 24 hours (OR, 9.3; $p < 0.0001$), and (6) bleeding that required reoperation (OR, 5.5; $p < 0.0001$). All perioperative variables together accounted for only 28.6% (R^2) of the variation.

Conclusions. Respiratory function after CABG is readily influenced by postoperative occurrence of extracardiac organ or system complications.

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Respiratory failure is common after coronary artery bypass grafting (CABG) and continues to be a major cause of potentially fatal morbidity after CABG [1–3]. Recent advances in anesthesia, myocardial protection, and surgical techniques have led to fast-track CABG, in which patients have been extubated within a few hours and discharged within 3 to 5 days of operation [4]. At the same time, because of the increasing age and comorbidity of the CABG population, a subset of these patients will require prolonged ventilation in the postoperative period [5, 6].

Most cardiac surgical patients, presenting for either elective or emergent operations, have adequate pulmonary function. For other types of operations, patients would not require prolonged mechanical ventilation; a general rule of thumb is that if a patient was not intubated preoperatively, the need for prolonged postoperative mechanical ventilatory support is unlikely [7]. Importantly, patients undergoing emergent cardiac operation typically do not behave differently when compared with elective postoperative patients. Those patients who require prolonged intensive care unit stay with mechanical ventilatory support are similar to those who might require such support in other operative settings [8].

Since the widespread use of CABG for the treatment of ischemic heart disease, several investigators have attempted to define preoperative characteristics that predict postoperative survival, but the reliability of their predictive value has been controversial [9]. It is possible that an individual with adequate pulmonary function before CABG may have severe respiratory failure develop postoperatively secondary to other organ dysfunction or failure. Therefore our aim in this study was to identify intraoperative and postoperative risk factors that predispose pulmonary impairment after CABG.

Patients and Methods

All patient variables and perioperative events were obtained from the Cardiac Surgery Registry of the New York State Department of Health combined with our institutional perfusion database. A total of 8,802 consecutive patients (6,234 males and 2,568 females) who un-

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derwent CABG with or without a concomitant cardiac operation from January 1993 through December 2000 at Albany Medical Center (Albany, NY) were included in the analysis to determine their impact on postoperative respiratory failure.

Respiratory failure was defined as pulmonary insufficiency requiring intubation and ventilation for a period of 72 hours or more at any time during the postoperative stay. For patients who were placed on and taken off ventilation several times, the total of these episodes were 72 hours or more. Chronic obstructive pulmonary disease (COPD) was assumed in patients who require chronic (more then 3 months) bronchodilator therapy to avoid disability from obstructive airway disease, or have a forced expiratory volume in one second of less than 75% of the predicted value or less than 1.25 L, or have a room air P_{O_2} less than 60 or P_{CO_2} more than 50 mm Hg. In analysis, COPD was not included unless the patient's record contained documented evidence of the criteria previously described regardless of how much the patient may have smoked. In the database, smoking history was separately recorded if the patient has smoked any tobacco products or used chewing tobacco within the past 2 weeks or within the past year.

A complete list of the preoperative variables in the database is shown in the Appendix and in Table 1. Intraoperative variables within the database were type of operation, aortic cross-clamp time, cardiopulmonary bypass (CPB) time, type of cardioplegia (cold or warm crystalloid or blood), delivery method of cardioplegia (antegrade, retrograde, or both), use of blood products, need for inotropic agents, vasodilators, phosphodiesterase inhibitors, or antiarrhythmic agents. Postoperative variables were return to operating room for hemodynamic decompensation, stroke, transmural or nontransmural myocardial infarction, bleeding required reoperation, deep sternal wound infection, use of insertion of intraaortic balloon pump during and after operation, gastrointestinal (GI) bleeding with or without infarction and perforation, renal failure, implantation of permanent pacemaker caused by heart block, malignant ventricular tachycardia, and septic endocarditis.

Data were entered by a dedicated cardiac surgical registrar, a full-time employee of the hospital, with no association to the surgeon who performed the operation. Random strict audit was periodically performed by the New York State Department of Health to ensure accuracy of the data.

Statistical Analysis

Statistical analysis was done by using the software StatView version 5.0.1 (SAS Institute Inc, San Francisco, CA). Preoperative, intraoperative, and postoperative variables were analyzed separately by applying univariate logistic regression (Tables 1, 2, 3, and 4). A multivariable logistic regression analysis was used to validate the risk factors for respiratory failure after CABG (Table 5). Survival was calculated as either early (30-day) or hospital discharge. A p value less than 0.05 was considered statistically significant.

Table 1. Univariate Logistic Regression Analysis of Preoperative Risk Profile

	Risk of Respiratory Failure	
Variables	Odds Ratio	p Value
Myocardial rupture	20.3	<0.0001
Shock	12.7	<0.0001
Active endocarditis	9.5	<0.0001
Surgical priority, emergency	5.8	<0.0001
Requirement of intraaortic balloon pump insertion	5.2	<0.0001
Emergency transfer to operating room after diagnostic catheterization	4.4	0.0002
MI < 6 hrs	4.4	0.0002
MI 6 to 23 hrs	4.2	0.0016
CHF at current admission	4.1	<0.0001
Unstable hemodynamics	4.0	<0.0001
Renal failure (creatinine > 2.5 mg/dL)	3.9	<0.0001
Renal failure requiring dialysis	3.3	<0.0001
Extensively calcified asscending aorta	2.7	<0.0001
Surgical priority, urgent	2.4	<0.0001
Cardiomegaly	2.4	0.0003
CHF before current admission	2.2	<0.0001
Malignant ventricular arrhythmia	2.1	0.0151
Thrombolysis within 7 days	2.1	0.0004
Age > 70 years	2.0	<0.0001
IV nitroglycerin within 24 hours	2.0	<0.0001
Femoro-popliteal arterial disease	1.9	<0.0001
Stroke	1.9	<0.0001
Aorto-iliac disease	1.9	<0.0001
Chronic obstructive pulmonary disease	1.9	<0.0001
Left ventricular hypertrophy on electrocardiogram	1.6	<0.0001
Previous 1 operation	1.6	0.0033
Body mass index > 30 kg/M^2	1.6	<0.0001
Carotid/cerebrovascular disease	1.6	0.0001
Diabetes on medication	1.4	<0.0001
> 1 MI	1.4	0.0036
Age in 10-year increments	1.4	<0.0001
Hypertension	1.3	0.0032
LVEF in 10% increments	0.7	<0.0001
Male gender	0.6	<0.0001
LVEF 20% to 40%	0.6	0.0300
Preoperative cardiopulmonary bypass hematocrit > 30%	0.3	<0.0001
LVEF > 20%	0.3	<0.0001
LVEF > 40%	0.3	<0.0001

CHF = congestive heart failure; IV = intravenous; LVEF = left ventricular ejection fraction; MI = myocardial infarction.

Results

Of 8,802 patients undergoing CABG with or without a concomitant cardiac operation, 491 (5.6%) suffered from postoperative respiratory failure. These 491 patients with postoperative respiratory failure had 30-day survival of 75.7%, whereas the remaining patients with any one or more postoperative complication other than respiratory failure had early survival of 90.0% ($p < 0.05$).

Table 2. Univariate Logistic Regression Analysis of Intraoperative Risk Profile

	Risk of Respiratory Failure	
Variables	Odds Ratio	p Value
CABG concomitant with		
Ventricular septal defect repair	25.1	< 0.0001
Mitral valvuloplasty	5.3	< 0.0001
Double valve replacement/ double valvuloplasty	4.5	< 0.0001
Mitral valve replacement	4.2	< 0.0001
Nonuse of arterial conduit	3.3	< 0.0001
CABG concomitant with		
Aortic valve replacement/ aortic valvuloplasty	2.2	< 0.0001
Carotid endarterectomy	1.9	0.0024
Total ischemic time (30-min increments)	1.4	< 0.0001
Cardiopulmonary bypass time (30-min increments)	1.4	< 0.0001
Arterial conduit > 1	0.6	0.0034

CABG = coronary artery bypass grafting.

Table 1 shows univariate analysis of preoperative patient variables with their relationship to respiratory failure after CABG. The influence of any other operation combined with CABG on the risk of developing respiratory dysfunction is depicted in Table 2. The effects of commonly used vasoactive or antiarrhythmic agents on post-CABG respiratory complications is shown on Table 3. The association between postoperative respiratory impairment and other postoperative events are displayed in Table 4.

Cardiopulmonary bypass time significantly increased the risk of respiratory failure. Patients undergoing a concomitant procedure with CABG also had significant risk of respiratory failure. Nonuse of arterial conduit was also a strong predictor of respiratory failure. However none of these variables had been validated by multivariate analysis. Use of vasopressin, norepinephrine, nitroglycerin, phenylephrine, and sodium nitroprusside in the postoperative intensive care unit were strongly associated with development of respiratory failure. Nonuse of antiarrhythmics was inversely related to respiratory failure. However none of them was identified as a risk factor for respiratory failure by multivariate analysis.

Table 3. Univariate Logistic Regression Analysis of the Relationship Between the Use of Pressors, Inotropes, Vasodilators, Antiarrhythmics after Coronary Artery Bypass Grafting and the Risk of Respiratory Failure

	Risk of Respiratory Failure	
Variables	Odds Ratio	p Value
Vasopressin	22.1	< 0.0001
Norepinephrine	8.7	< 0.0001
Nitroglycerin	5.1	< 0.0001
Phenylephrine	2.8	< 0.0001
Sodium nitroprusside	2.2	0.0194
No antiarrhythmics	0	< 0.0001

Table 4. Univariate Logistic Regression Analysis of Postoperative Risk Profile

	Risk of Respiratory Failure	
Variables	Odds Ratio	p Value
Septic endocarditis	90.4	< 0.0001
Gastrointestinal bleeding with or without infarction and perforation	38.8	< 0.0001
Renal failure	30.7	< 0.0001
Deep sternal wound infection	11.3	< 0.0001
New stroke (intraoperative, 24 hrs)	9.3	< 0.0001
Bleeding requiring reoperation	5.5	< 0.0001
Transmural myocardial infarction, new Q wave	3.7	0.0082

Table 5 lists the multivariate analysis of preoperative, intraoperative, and postoperative variables. In decreasing order of importance, factors validated by multivariate analysis that contributed significantly to an increased risk of post-CABG respiratory failure were (1) postoperative septic endocarditis; (2) postoperative gastrointestinal bleeding with or without infarction and perforation; (3) postoperative renal failure; (4) postoperative new stroke (intraoperative, 24 hours); (5) postoperative deep sternal wound infection; (6) bleeding requiring reoperation; (7) preoperative insertion of intraaortic balloon pump; (8)

Table 5. Multiple Logistic Regression Analysis of Perioperative Risk Profile

	Risk of Respiratory Failure	
Variables	Odds Ratio	p Value
Postoperative septic endocarditis	34.9	< 0.0001
Postoperative gastrointestinal bleeding with or without infarction and perforation	20.7	< 0.0001
Postoperative renal failure	12.8	< 0.0001
New stroke (intraoperative, 24 hrs)	9.2	< 0.0001
Deep sternal wound infection	7.4	< 0.0001
Bleeding requiring reoperation	4.7	< 0.0001
Preoperative intraaortic balloon pump insertion	4.6	< 0.0001
CHF at current admission	1.9	< 0.0001
CHF before current admission	1.5	0.0024
Chronic obstructive pulmonary disease	1.4	0.0124
Age (10-year increments)	1.3	< 0.0001
Cardiopulmonary bypass (30-minute increments)	1.2	< 0.0001
Left ventricular ejection fraction (10% increments)	0.8	0.0014

CHF = congestive heart failure.

congestive heart failure at current admission; (9) COPD; (10) age in 10-year increments; and (11) CPB time in 30-minute increments. All perioperative variables together accounted for only 28.6% (R^2) of the variation.

Comment

Prolonged ventilatory support after cardiac operation occurs in 5% to 22% of patients [3]. Postoperative respiratory failure had been documented in 5.6% of our patients who underwent CABG with or without a concomitant cardiac operation. The preoperative risk factors associated with prolonged ventilation after CABG have been addressed in a number of studies. These studies have shown left ventricular dysfunction, COPD, reoperation, unstable angina, age, peripheral vascular disease, impaired renal function, and associated valvular disease as risk factors for respiratory dysfunction [3, 5, 6].

With the number of CABG surgical procedures approaching 600,000 per year in the United States, a complication such as respiratory failure can significantly increase hospital costs and diminish overall quality of life [10]. Postoperative incidence of respiratory failure (17.1%) is common in septuagenarians [11]. As in our study, it is not surprising that the risk of postoperative respiratory failure increases with increasing age, because these patients generally have more preoperative comorbid conditions and less physiologic reserve [10, 12–14]. Increased operative risk in women has been noted before [9, 15]. Although we did not find the impact of female gender as an independent risk factor of respiratory failure, male gender in our patient population had a significantly less chance of respiratory failure after CABG (Table 1).

Although patients with COPD (irrespective of age) stay in the intensive care unit and in the hospital longer after coronary artery bypass grafting [16], hospital mortality in most patients with mild-to-moderate COPD undergoing CABG is similar to those without COPD [17]. Postoperative cardiac function and the occurrence of complications are more significant than preoperative pulmonary function in determining the duration of endotracheal intubation after cardiac operation. Routine spirometry is probably unnecessary for most adult cardiac patients [18]. It is interesting to note that among our patients the risk of postoperative respiratory failure was only modestly increased by the presence of COPD; nevertheless, multivariate analysis identified COPD as a significant independent predictor of respiratory failure. Although univariate analysis showed slightly increased risk of respiratory failure in diabetic patients, multivariate analysis failed to show any significant relationship between diabetes and postoperative respiratory failure.

A well-recognized risk factor for operative morbidity and mortality is the history of previous cardiac operation [11, 12]. Reoperation seemed to have mild increased risk of respiratory failure only on univariate analysis in our study. Coronary artery bypass grafting is technically a more difficult procedure in the setting of prior cardiac operation, given the areas of scarring that must be crossed, the limited options for graft vessels, and the generally more advanced stage of coronary disease found in such patients. Patients undergoing CABG emergently or urgently had a significant and independent elevation in risk for postoperative respiratory failure by univariate analysis.

Intraaortic balloon pumps are effective both prophylactically and intraoperatively in patients who would not otherwise survive cardiac operations. The use of preoperative intraaortic balloon pump in high-risk patients lowers hospital mortality and shortens the stay in intensive care unit due to improved cardiac performance. Although the procedure is cost-beneficial, intraaortic balloon pump does not significantly affect the outcome in terms of postoperative morbidity or hospital mortality [19]. In our patients, preoperative intraaortic balloon pump was a strong independent predictor of respiratory failure, as it was identified by both univariate and multivariate analyses.

It has been suggested that pulmonary diagnosis, lung mechanics, and blood gas values do not offer the clinician definite rules in predicting postoperative respiratory outcome, and these should not be used as exclusion criteria for CABG operations [20]. It has been postulated that myocardial revascularization with or without CPB causes a similar degree of pulmonary dysfunction, and the deterioration in pulmonary gas exchange associated with cardiac operation conceivably is due to factors other than the use of CPB [1].

We do not document the specific reasons for development of respiratory failure in each patient, but note that, in addition to causes of isolated respiratory failure, many patients had multiple organ system involvement. However, recent research would demonstrate that even very sick, high-risk patients may derive significant survival benefit from CABG [21–26]. Although we comment on increased risk associated with these factors, we make no suggestion that CABG should be withheld from any particular patient, but rather that these conditions should be addressed before operation when possible.

In summary, our study has identified intraoperative and postoperative risk factors in addition to preoperative ones predicting post-CABG respiratory failure. The major limitation of this study is that it includes a large set of variables into one multiple logistic regression analysis which is somewhat overwhelming. However, the novel aspect of this work is primarily the evaluation of intraoperative and immediate postoperative events as risk factors for post-CABG respiratory failure. In addition, having a large number of patients in the analysis is consistent with ensuring reliable results at a single institution. These data lend support to further emphasizing the practice of preoperative optimization of acute and chronic extracardiac problems before CABG to minimize the risk of postoperative respiratory failure.

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Appendix

Other Variables in the Database

Age, gender, body mass index (kg/m^2), left ventricular ejection fraction, preoperative myocardial infarction, use of intravenous nitroglycerin, stroke, previous cardiac operation, diabetes, hypertension, renal failure (serum creatinine $>$ 2.5 mg/dL), renal failure requiring dialysis, current congestive heart failure, congestive heart failure before current admission, COPD, intraaortic balloon pump, arrhythmia, prior percutaneous transluminal coronary angioplasty more than 6 months ago, percutaneous transluminal coronary angioplasty before admission, use of thrombolytics, coronary artery stent thrombosis, angina (Canadian Cardiovascular Society, CCS class), different degree of stenosis of coronary arteries, pathology of heart valves, active endocarditis, carotid and cerebrovascular disease, calcified ascending aorta, aorto-iliac disease, femoropopliteal disease diagnosed during cardiac catheterization, urgency of operation, and smoking history.

INVITED COMMENTARY

Among numerous risk factors, perioperative infection is identified as a major risk factor associated with prolonged ventilation after coronary artery bypass grafting (CABG). Aiming to reduce postoperative duration of mechanical ventilation, several questions have to be raised based on the presented results. (1) Is appropriate attention paid to local and systemic infection during the pre-, intra-, and postoperative period in day to day clinical routine? (2) Can prophylactic measures reduce the incidence of infection and prolonged mechanical ventilation? (3) Does clinical and basic research associated with CABG focus on perioperative infection and prolonged mechanical ventilation to an adequate extent?

Perioperative use of antibiotic prophylaxis is clinical routine for CABG and has substantially reduced morbidity and mortality. However, the antibiotic regimens show

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