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Research Paper

Risk Factors for Ventilator Dependency Following Coronary Artery Bypass Grafting

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Abstract

Background: Ventilator dependency following coronary artery bypass grafting (CABG) is often associated with significant morbidity and mortality. However, few reports have focused on the independent risk factors for ventilator dependency following CABG. This study aimed to evaluate the independent risk factors for ventilator dependency following coronary artery bypass grafting (CABG). **Methods:** The relevant pre-, intra- and post-operative data of patients without a history of chronic obstructive pulmonary disease undergoing isolated CABG from January 2003 to December 2008 in our center were retrospectively analyzed. Elapsed time between CABG and extubation of more than 48 hours was defined as postoperative ventilator dependency (PVD). **Results:** The incidence of PVD was 13.8% (81/588). The in-hospital mortality in the PVD group was significantly higher than that in the non-PVD group (8.6% versus 2.4%, p=0.0092). Besides the length of ICU and hospital stay, PVD correlated with negative respiratory outcomes. The independent risk factors for PVD were preoperative congestive heart failure (OR=2.456, 95%CI 1.426-6.879), preoperative hypoalbuminemia (OR=1.353, 95%CI 1.125-3.232), preoperative arterial oxygen partial pressure (PO_2) (OR=0.462, 95%CI 0.235-0.783) and postoperative anaemia (OR=1.541, 95%CI 1.231-3.783). **Conclusions:** Preoperative congestive heart failure, preoperative hypoalbuminemia, low preoperative PO_2 and postoperative anaemia were identified as four independent risk factors for ventilator dependency following CABG.

Key words: Coronary artery bypass grafting; ventilator dependency; risk factor.

Introduction

Ventilator dependency following coronary artery bypass grafting (CABG) is often associated with significant morbidity and mortality [1, 2]. Previous studies have reviewed the concept that ventilator dependency following heart surgery results from a combination of risk factors, partly due to the nature of the patient population and partly to the process of patient care [1, 2]. However, few reports have focused on the independent risk factors for ventilator dependency following CABG. The purpose of this study was to evaluate the independent risk factors for postoperative ventilator dependency (PVD), in order to prevent and treat ventilator dependency following CABG.

Materials and methods

Patients

From January 2003 and December 2008, 588 consecutive patients (471 males and 117 females, with a mean age of 66.3 ± 6.9 years) suffering from coronary artery disease without a history of chronic obstructive pulmonary disease underwent isolated CABG. Coronary artery angiography revealed double vessel disease in 34 patients and triple vessel disease in 554 patients. All patients underwent fast-track anesthesia (anesthesia was induced with midazolam (2-3mg), fentanyl (0.2mg), propofol (0.5-1.5mg/kg) and vecuronium and maintained with isoflurane and continuous infusion of propofol (2 to 5mg/kg/h); 0.1-0.2mg fentanyl was intravenously administered before skin incision, sternotomy, aortic cannulation and initiation of cardiopulmonary bypass, respectively; total amount of fentanyl was less than 15μg/kg during operation). 66.3% (n=390) of patients received CABG without cardiopulmonary bypass (CPB). The remaining patients (n=198) received cardioplegic arrest CABG. The number of bypass conduit ranged from 2 to 5 (mean 3.2 per patient). Left internal mammary artery was used as a bypass conduit in 548 (93.2%) patients, radial artery in 386 (65.6%) patients and great saphenous vein graft in 534 (90.8%) patients. This study protocol was approved by the ethics committee of Tongji University and was consistent with the spirit of the *Declaration of Helsinki*.

Criteria for extubation and definition of postoperative ventilator dependency

Criteria for extubation [3] included an alert and hemodynamically stable patient with no excessive bleeding, ability of the patient to breathe through a T tube for at least 30 minutes with a fraction of inspired oxygen of less than 0.40 and a respiratory rate less than 25 breaths/min, an arterial blood PO_2 greater than 70mmHg, a PCO_2 less than 40mmHg and a pH greater than 7.35, with no metabolic acidosis. Other criteria included a tidal volume of 6ml/kg, a peak negative inspiratory pressure of less than -20cmH_2O and a mandatory chest radiograph before extubation to rule out pneumothorax, pleural effusion and atelectasis.

With reference to previous reports where 48 hours was taken as a cut off point to discriminate whether PVD or not [1, 2], we used the same criterion in this study to describe PVD, that is elapsed time between CABG and extubation of more than 48 hours was defined as ventilator dependency following CABG.

Methods

From January 2003 to December 2008, the charts of all patients without a history of chronic obstructive pulmonary disease undergoing isolated CABG in our medical center were reviewed. The relevant pre-, intra- and post-operative data of all selected patients were investigated and retrospectively analyzed. Preoperative data included age, gender, body mass index (BMI), recent smoking (within 4 weeks of surgery), diabetes mellitus (the need for oral medication or insulin prior to CABG), hypertension, renal dysfunction (creatinine more than 2.5mg/dl or requiring dialysis), prior cerebro-vascular accident, recent myocardial infarction (MI) (evidence of MI within the last 30 days before surgery), preoperative congestive heart failure (New York Heart Association (NYHA) class III and IV), prior heart operation, extent of coronary artery disease, left main trunk disease, left ventricular aneurysm, left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), PO_2 and hypoalbuminemia (serum albumin less than 30g/L). Intraoperative data included emergent operation, type of procedure (CABG with or without CPB), CPB time, aortic cross clamping (ACC) time, number of grafts and operation time. Postoperative information included hypoxemia, pulmonary hypertension (mean pulmonary arterial pressure exceeding 30mmHg), low cardiac output syndrome, acute myocardial infarction (AMI) (new Q-wave infarction within 48h after surgery), requirement of intra-aortic balloon pump (IABP), atrial fibrillation, ventricular fibrillation, acute renal failure (creatinine more than 2.5 mg/dl over 7 days or requiring dialysis), stroke (new permanent neurological event), bleeding requiring re-exploration (re-operation to control bleeding within 36h following initial surgery) and postoperative anaemia (haematocrit less than 34%) [3-6].

Hemodynamic parameters were monitored intra- and post-operatively by Swan-Ganz catheter (Arrow International, Inc. USA). Arterial oxygen partial pressure (PaO_2) was measured pre-, intra- and post-operatively by blood gas analyzer (I-STAT Corporation, USA). Left ventricular ejection fraction and left ventricular end-diastolic diameter were measured preoperatively by Doppler-Ultrasound (GE VIVID 7, USA).

Statistical analysis

Statistical analysis was performed using the SPSS13.0 statistical software package. All p values <0.05 were considered to be statistically significant. Univariate analysis, using the unpaired t-test or t'-test according to homogeneity test for variance to compare measurement data and chi-square or *Fisher's* exact test to compare enumeration data, was performed to assess statistically significant variables, and those with p<0.10 were then entered into a logistic regression analysis to identify the independent risk factors for postoperative ventilator dependency. The

Hosmer-Lemeshow goodness of fit coefficient was computed for the regression model.

Results

Five hundred and eighty-eight consecutive patients without a history of chronic obstructive pulmonary disease who underwent isolated CABG were entered into this study. Overall mean Euro-SCORE (European system for cardiac operative risk evaluation [7]) was 4.7±1.6. The mean intubation time was 16.1 ± 4.9 hours. Among them, 81 patients accounting for 13.8% of the total population were extubated beyond 48 hours after CABG and were included in the PVD group.

Complications after extubation, the length of ICU and hospital stay and in-hospital mortality are shown in Table 1. There were no significant differences in the incidence of most complications, except for pneumonia and pulmonary atelectasis. Patients in the PVD group had longer length of ICU and hospital stay and higher in-hospital mortality.

Results of the univariate analysis are shown in Table 2. It can be observed that preoperative hypertension, preoperative congestive heart failure, preoperative LVEF, preoperative PO_2, preoperative hypoalbuminemia, duration of CPB, postoperative hypoxemia, postoperative pulmonary hypertension, postoperative low cardiac output syndrome, postoperative IABP requirement, postoperative atrial fibrillation, postoperative ARF and postoperative anaemia were relative risk factors for ventilator dependency following CABG.

Table 1. Comparison of morbidities and mortality between the two groups.

	PVD (n=81)	Non-PVD (n=507)	p value
Re-intubation or tracheotomy	3(3.7%)	5(1.0%)	0.0843
Pneumonia	15(18.5%)	38(7.5%)	0.0030
Pulmonary atelectasis	9(11.1%)	12(2.4%)	0.0008
LCOS	6(7.4%)	16(3.2%)	0.1040
Atrial fibrillation	15(18.5%)	58(11.4%)	0.0999
Ventricular fibrillation	1(1.2%)	1(0.2%)	0.2567
AMI	1(1.2%)	0	0.1378
ARF	1(1.2%)	3(0.6%)	0.4482
Stroke	3(3.7%)	5(1.0%)	0.0843
ICU stay (days)	4.56±0.85	2.85±0.53	<0.0001
Hospital stay (days)	13.28±3.14	8.13±1.58	<0.0001
In-hospital mortality	7(8.6%)	12(2.4%)	0.0092

PVD: postoperative ventilator dependency; LCOS: low cardiac output syndrome; AMI: acute myocardial infarction; ARF: acute renal failure; ICU: intensive care unit.

Table 2. Comparison of pre-, intra- and post-operative data between the two groups.

Factors	PVD (n=81)	Non-PVD (n=507)	p value
Preoperation			
Age (years)	66.9±8.6	66.2±6.6	0.40
Age over 65 years old	54(66.7%)	312(61.5%)	0.39
Female	19(23.5%)	98(19.3%)	0.37
BMI (kg/m^2)	26.2±2.6	25.8±1.7	0.07
Recent smoking	40(49.4%)	198(39.1%)	0.09
Diabetes mellitus	20(24.7%)	118(23.3%)	0.67
Hypertension	39(48.1%)	165(32.5%)	0.01
Renal dysfunction	7(8.6%)	20(3.9%)	0.08
Cerebrovascular disease	25(30.9%)	132(26.0%)	0.42
Recent MI	10(12.3%)	48(9.5%)	0.42
Prior heart operation	3(3.7%)	7(1.4%)	0.15
Congestive heart failure	52(64.2%)	223(44.0%)	0.0008
Triple vessel disease	78(96.3%)	476(93.9%)	0.61
Left main trunk disease	25(30.9%)	118(23.3%)	0.16
Left ventricular aneurysm	10(12.3%)	48(9.5%)	0.42
LVEF	0.51±0.10	0.54±0.06	0.0002
Preoperative LVEDD (mm)	52.9±7.6	52.3±4.2	0.30
Preoperative PO_2 (mmHg)	74.4±8.3	77.8±6.2	<0.0001
Hypoalbuminemia	18(22.2%)	41(8.1%)	0.0004
Intra-operation			
Emergency surgery	6(7.4%)	21(4.1%)	0.25
Use of CPB	32(39.5%)	178(15.4%)	0.46
CPB (min)	113.8±19.2	106.8±15.3	0.02
ACC (min)	70.2±12.4	67.1±9.2	0.10
Mean number of grafts	3.2±0.8	3.2±0.6	1.00
Operation time (min)	268.1±68.6	256.5±47.6	0.06
Post-operation (before extubation)			
Hypoxemia	36(44.4%)	135(26.6%)	0.0015
Pulmonary hypertension	38(46.9%)	97(19.1%)	<0.0001
LCOS	24(29.6%)	31(6.1%)	<0.0001
AMI	1(1.2%)	2(0.4%)	0.36
IABP requirement	31(38.3%)	46(9.1%)	<0.0001
Atrial fibrillation	38(46.9%)	167(32.9%)	0.02
Ventricular fibrillation	1(1.2%)	3(0.6%)	0.45
ARF	10(12.3%)	29(5.7%)	0.05
Stroke	5(6.2%)	17(3.4%)	0.21
Re-operation for bleeding	6(7.4%)	28(5.5%)	0.45
Anaemia	48(59.3%)	187(36.9%)	0.0002

PVD: postoperative ventilator dependency; BMI: body mass index; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; PO_2: arterial partial pressure of oxygen; CPB: cardiopulmonary bypass; ACC: aortic cross clamping; LCOS: low cardiac output syndrome; AMI: acute myocardial infarction; IABP: intra-aortic balloon bump; ARF: acute renal failure.

Those variables with p<0.10 obtained through the univariate analysis were then entered into multivariate logistic regression analysis (PVD or not as independent variable, variables with p<0.10 obtained through univariate analysis as dependent variables). As shown in Table 3, independent risk factors for ventilator dependency following CABG included preoperative PO_2 (OR=0.462, 95%CI 0.235-0.783), preoperative congestive heart failure (OR=2.456, 95%CI 1.426-6.879), preoperative hypoalbuminemia (OR=1.353, 95%CI 1.125-3.232) and postoperative anaemia (OR=1.541, 95%CI 1.231-3.783). The Hosmer-Lemeshow goodness of fit coefficient of this model was 0. 916.

Table 3. Independent risk factors for PVD through multivariate logistic regression analysis.

Predictors	OR	95%CI	p value
Preoperative PO_2	0.462	0.235-0.783	0.001
Preoperative congestive heart failure	2.456	1.426-6.879	0.003
Postoperative anaemia	1.541	1.231-3.783	0.012
Preoperative hypoalbuminemia	1.353	1.125-3.232	0.025

The *Hosmer-Lemeshow* goodness of fit coefficient of this model was 0. 916. PVD: postoperative ventilator dependency; OR: odds ratio; CI: confidence interval; PO_2: arterial partial pressure of oxygen.

Discussion

Besides the length of ICU and hospital stay, PVD correlated with negative respiratory outcomes in this study. Although there were no significant differences in the incidence of re-intubation or tracheotomy between the two groups, ventilator dependency following CABG led to a higher incidence of pneumonia and pulmonary atelectasis. The fact that there was no significant difference in the incidence of re-intubation or tracheotomy between the two groups could be related to the small 'absolute value' (3 in the PVD group versus 5 in the non-PVD group); the latter probably resulted from the limited sample size. In addition, in-hospital mortality in the PVD group was significantly higher than that in the non-PVD group, which indicated that longer ventilation support was associated with significant respiratory morbidity and mortality.

Improvement in cardiopulmonary performance, shorter ICU and hospital stay as well as reduction in costs could be achieved when cardiac surgical patients were weaned from mechanical ventilator at the appropriate time [8-12].On the contrary, prolonged ventilation support could have contributed to increased morbidity, mortality and cost [13-14]. In this study, 81 patients out of 588 patients were extubated beyond 48 hours after CABG, with an incidence of 13.8%. The in-hospital mortality in the PVD group was more than three times that in the non-PVD group (8.6% versus 2.4%, p=0.0092). So, it became crucial for clinicians to evaluate the independent risk factors for ventilator dependency following CABG. In this study, the independent risk factors for ventilator dependency following CABG were identified as preoperative congestive heart failure, preoperative hypoalbuminemia, low preoperative PO_2 and postoperative anaemia. The *Hosmer-Lemeshow* goodness of fit of the statistical model established in this study was 0. 916, indicating that the model matches the data very well, therefore the results are statistically very reliable.

Preoperative congestive heart failure was an important risk factor for ventilator dependency following CABG. Patients suffering from preoperative congestive heart failure often had left atrial hypertension and pulmonary interstitial edema, which in turn could have resulted in a change in the pulmonary ventilation/blood flow ratio, thus resulting in postoperative hypoxemia and prolonged ventilation support [15-16]. Preoperative congestive heart failure caused the lymph back to obstacle, pulmonary alveolar edema occurred then, which in turn could have resulted in a change in the pulmonary compliance, thus further aggravating respiratory dysfunction. So, patients suffering from preoperative congestive heart failure were prone to postoperative hypoxemia even postoperative acute respiratory distress syndrome. In addition, respiratory muscle weakness commonly occurred in patients with congestive heart failure and was an independent predictor of mortality [17]. Thus, proper preoperative management of congestive heart failure in CABG patients might contribute to reduce the incidence of postoperative ventilator dependency.

Serum albumin concentration can be of use in predicting metabolism and nutritional status [18]. It was reported that serum albumin concentration was one of key reference index in the incidence of morbidities and mortality [19]. In this study, preoperative hypoalbuminemia seemed to be an important risk factor for ventilator dependency following CABG. Hypoalbuminemia could have damaged the respiratory function, decreased the thickness, the strength and the endurance of respiratory muscles and impaired the immune system. In addition, hypoalbuminemia reduced the colloid osmotic pressure, resulting in high incidences of pulmonary edema and hemodynamic instability. So, postoperative ventilator dependency could have been possible.

Low preoperative PO_2 often suggested poor cardiopulmonary function or severe chronic obstructive pulmonary disease in patients. After CABG, further depression in cardiopulmonary function was expected in these patients who consequently were more prone to low cardiac output and postoperative respiratory failure, thus requiring longer ventilation support. Therefore, proper perioperative management of cardiopulmonary dysfunction in CABG patients might contribute to shorten postoperative ventilation support, and reduce the incidence of postoperative ventilator dependency.

Postoperative anaemia seemed to be also an independent risk factor for ventilator dependency following CABG. Low postoperative hemoglobin level could have been related to poor oxygen transport. The lower the level of hemoglobin after operation, the higher the need for blood transfusion, which in turn could result in a change in the pulmonary ventilation/blood flow ratio and induction of pulmonary capillary embolism, thus further affecting respiratory functions. Consequently, postoperative ventilator dependency could have been possible. Thus, meticulous intraoperative hemostasis is recommended.

Many studies have shown that older age was an independent risk factor for postoperative ventilator dependency. However, there was no significant difference in the mean age between the PVD group and non-PVD group (66.9±8.6 years versus 66.2±6.6 years, $p=0.40$) in this study, and nearly similar proportion of elderly patients to total population between the PVD group and the non-PVD group (66.7% versus 61.5%, $p=0.39$) was shown in this study. This may be relative with more elderly patients included in this study.

The retrospective nature and small sample size were the main limitations of this study. Another limitation of this study was the lack of detailed respiratory function data. PO_2 was measured preoperatively, but forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) were not routinely measured before CABG in our center.

In conclusion, preoperative congestive heart failure, preoperative hypoalbuminemia, low preoperative PO_2 and postoperative anaemia were four independent risk factors for ventilator dependency following CABG. Postoperative ventilator dependency may be avoided by reducing intra- and post-operative hemorrhage thus maintaining a reasonable postoperative hemoglobin level. The proper perioperative management of cardiopulmonary dysfunction and hypoalbuminemia may contribute towards reducing postoperative ventilator dependency and facilitate early extubation.

Competing Interests

The authors have declared that no competing interest exists.

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