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Does Baseline Pao2/Fio2 Affect the In-Hospital Outcome in Patients Undergoing Coronary Artery Bypass Grafting?

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Ultramini Abstract

There exists a potential link between baseline PaO_2/FiO_2 ratio and postoperative outcome in the group of patients undergoing elective coronary artery bypass grafting.

Abstract

Background: Oxygen saturation and the PaO_2 are the direct risk factors for post -operative respiratory outcome in patients undergoing prolonged surgery under general anaesthesia. However the effect of preoperative PaO_2 and PaO_2/FiO_2 ratio on the postoperative course of the patient undergoing coronary artery bypass grafting is not known.

Hypothesis: Pre-operative PaO_2 and PaO_2/FiO_2 ratio have a significant effect on the postoperative outcome among the patients undergoing coronary artery bypass grafting.

Study design: Prospective clinical study

Setting: Tertiary health care centre

Materials and Methods: One hundred and fifty eight consecutive patients with a EURO Score of <6 undergoing routine first time coronary artery bypass grafting were selected for this study. Patients with ventricular dysfunction, Chronic Obstructive Pulmonary Disease (COPD), renal or hepatic dysfunction, patients on mechanical ventilation, on preoperative Intra Aortic Ballon Pump (IABP) and those who had to undergo emergency surgery were excluded from the study. All patients were managed by the same anaesthesia and surgical team and the anaesthesia management protocol was similar for all the patients.

The pre-operative PaO_2/FiO_2 ratio (base line) for all patients was noted before anaesthesia induction in room air. The primary outcome measures were duration of mechanical ventilation, ICU stay and hospital stay. The secondary outcome measures were requirement of inotropes, arrhythmias, requirement of IABP, cardiogenic shock, perioperative myocardial infarction, sepsis, respiratory failure , any other organ dysfunction and death .The total duration of follow up period was one month.

Statistical analysis: Seventeen subjects were subsequently dropped because of incomplete data. Consequently, the data for 141 subjects were used for the analysis. The various methods used were Student T test, Spearman's coefficient correlation, bi-variate and univariate logistic regression analysis. In each case a p value of <0.05 was considered to be significant.

Results: There exists a positive correlation between preoperative PaO_2/FiO_2 ratio and duration of intubation (r = -0.5607, p = 0.001) as well as Intensive Care Unit (ICU) stay (r = -0.2564, p = 0.002). PaO_2/FiO_2 ratio also has a positive correlation with the use of inotropes (p=0.03) and frequency of death (p=0.014) in the patients undergoing CABG .

Conclusion: Low pre-operative PaO_2/FiO_2 ratio has a direct impact on the in-hospital outcome among the patients undergoing coronary arterybypass grafting.

Keywords: Coronary artery disease; PaO_2/FiO_2; In-hospital outcome

Introduction

Coronary Artery Bypass Grafting Surgery (CABG) contributes to a major proportion of cardiac surgery. Different determinants of postoperative morbidity and mortality had been studied widely [1]. Altered pulmonary function is one among the components that significantly contributes to the thirty days mortality. However the feasibility of pulmonary function test is a concern when patient load is maximum. It has been shown that oxygen saturation and the PaO_2 are the direct risk factors for the post-operative respiratory outcome in high risk patients undergoing prolonged surgery under general anaesthesi [2, 3]. PaO_2/FiO_2 ratio has been considered as an indicator of pulmonary gas exchange. As pulmonary function test is a relatively invasive preoperative screening procedure we thought of taking PaO_2/FiO_2 ratio as a screening test to determine adverse postoperative outcome in patients undergoing CABG under Cardiopulmonary Bypass (CPB).

Hypothesis

Pre-operative PaO_2 and PaO_2/FiO_2 ratio have a significant effect on the postoperative outcome among the patients undergoing CABG under CPB.

Materials and Methods

After hospital ethic committee approval and written informed consent from the patients, 158 patients with a Euro score of >6 who underwent first time CABG procedure at our institution between June 2010 and October 2014 were included in the study. Patients with ventricular dysfunction, COPD, renal/hepatic dysfunction, on mechanical ventilation, preoperative IABP and those who had to undergo emergency/redo surgery were excluded from the study. Seventeen subjects were subsequently dropped because of incomplete data. Consequently, the data for 141 subjects were used for the analysis.

The patients were premedicated with oral diazepam 10mg at night before and 5 mg in the morning on the day of surgery. In addition they received injection morphine $0.1mg^{-1}kg$ and injection phenergan $0.5mg^{-1}kg$ intramuscularly one hour before being shifted to the operation theatre. Arterial blood gas was taken with room air during the preoperative visit and before administration of any sedative agents. Anaesthesia was induced with intravenous thiopentone sodium $5mgkg^{-1}$, fentanyl $5\mu gm^{-1}$ kg and 1 mg kg^{-1} rocuronium bromide was used for muscle relaxation. Anaesthesia was maintained with midazolam, fentanyl and vecuronium bromide. All the patients were mechanically ventilated with 50% air-oxygen mixture with a tidal volume of 7-8 ml kg^{-1}. The plateau airway pressure was kept below 30cm of H_2O and end tidal carbon dioxide was maintained between 35-40 mmHg.

The surgery was performed by the same group of surgeons and anaesthesiologist. Patients underwent a median sternotomy, with harvesting of saphenous veins and internal mammary arteries as conduits. Myocardial protection was obtained with crystalloid and cold blood cardioplegia via the antegrade route, and moderate hypothermia (33°C). Haematocrit was maintained between 20% and 25%, and Cardiopulmonary Bypass (CPB) flow was maintained between 2.0 and 2.5 l^{-1} min^{-1} m^2. The mean perfusion pressure was kept at 70-90 mmHg by adjusting the pump flow, hematocrit, nitroglycerin or phenylephrine infusion.

After arriving at the ICU patients were ventilated mechanically with pressure regulated volume control mode. Systolic blood pressure was maintained between 100-130 mmHg and mean arterial pressure > 60 mmHg. Weaning was started as soon as the awake and alert with cerebral function adequate for cooperation. The criteria for weaning from mechanical ventilation were as follows: spontaneous tidal volume $>6mlkg^{-1}$, no significant vasoactive infusions, chest tube drainage $<100mlhr^{-1}$, stable hemodynamic without any evidence of low cardiac output syndrome, haemoglobin > 10mg dl^{-1}, endotracheal suctioning < once hr^{-1}, PO_2 of > 150 mmHg with an FiO_2 of <0.5 and $PaCO_2$ between 35-45 mmHg, SaO_2 > 95% and absence of life threatening arrhythmias, IABP or open chest. Throughout the weaning process and after extubation, arterial blood gas analysis and pulse oximetry were monitored closely. All the patients were monitored for the primary outcome measures that included the duration of mechanical ventilation, ICU stay and hospital stay as well as the secondary outcome measures like, requirement of inotropes, arrhythmias, requirement of IABP, cardiogenic shock, perioperative myocardial infarction, sepsis, respiratory failure , and death.

Statistical Analysis

Before analyzing the association between different perioperative variables which could affect postoperative outcome, we divided the patients into two groups on the basis of PaO_2/FiO_2 ratio. As the normal PaO_2/FiO_2 ratio ranges between 300-500, we have taken the lower limit as the cut-off point to divide the groups (Group I, PaO_2/FiO_2 ratio < 300 and Group II, PaO_2/FiO_2 ratio ≥ 300.Difference between two groups were assessed by t-test for continuous or ordinary variables and by the Chi-square test for dichotomous variables. A univariate analysis was performed to demonstrate the association between the perioperative predictors for adverse postoperative outcome in between the groups. The relationship between the PaO_2/FiO_2 ratio and period of intubation and length of ICU stay was determined by plotting a scatter plot and the calculation of Spearman's correlation coefficient. In each setting a p value of <0.05 was considered to be significant.

Results

The summary statistics of the patients are provided in Table 1 and 2. For further analysis of the primary and secondary outcome measures, patients were divided in two groups based on the PaO_2/FiO_2 ratio [Group 1, n=34(24.11%) and Group II, n=107(n=75.89%)].Both the groups were comparable in demographics and preoperative clinical parameters (Table 3). No difference was observed for the duration of surgery, CPB time and aortic cross clamp time (Table 4).

The characteristics of 141 CABG patients are shown in Table 1. Patients were divided into two groups. Group1: PaO_2/FiO_2 ratio<300, Group 2:PaO_2/FiO_2 ratio >300.Group 1 constituted of 34 patients and Group 2 constituted of 107 patients. A significant positive correlation was found between PaO_2/FiO_2 ratio and intubation period (r = -0.5607, p = 0.001) (Figure 1, Table 4) and ICU stay period (r = -0.2564, p = 0.002) , (Figure 2, Table 4) .Furthermore, the PaO_2/FiO_2 ratio also correlated with the use of inotropes (dopamine and noradrenaline) and the frequency of death in patients undergoing CABG (Table 3 and Table 4).

Discussion

Pulmonary dysfunction after CPB may be the result of multiple insults [4]. These include extra-CPB factors (ie, general anesthesia, sternotomy, and breach of pleura) and intra-CPB factors (ie, blood contact with artificial material, administration of heparin-protamine, hypothermia, cardiopulmonary ischemia, and ventilatory arrest) [5, 6]. There are various factors responsible for decreased postoperative pulmonary oxygen transfer after CABG. It has been shown that preoperative pulmonary function tests do not predict the outcome of the patient after CABG [7]. Arterial blood gas analysis is used in most institutions for management of patients undergoing cardiac surgery. Aim of this study was to find out the relationship between the PaO_2/FiO_2 ratio and perioperative outcomes of the patients undergoing CABG as the PaO_2 / FiO_2 ratio is easier to calculate, and may be more valuable in clinical situations.

In 1983, Covelli, et al demonstrated that oxygen tension-based indices, including both (a/A) PO2, and PaO_2 /FiO_2, were highly reliable, even in critically ill patients [8]. In a recent study to determine the effects of diabetes on pulmonary gas exchange in patients undergoing CABG, Seki, et al [5,9] concluded that the PaO_2 / FiO_2 ratio was a reliable predictor of the (a / A) PO_2 ratio during early postoperative management. In the present study, the PaO_2 / FiO_2 ratio was well correlated with intubation period and length of ICU stay.

Table 1: Summary Statistics Demographics and clinical profile

	Variables	Mean	SD
Demographic attributes	Age (yrs)	58.3	8.2
	Sex (M/F)	125/16	122.3/118.1
	Weight (kg)	73.6	11.9
Clinical Profile	Haemoglobin(gm/ dl)	12.5	1.9
	DOE	81(57.4%)	
	AOE	88(62.4%)	
	Chest pain	41(29.1%)	
	Diabetes	64(45.4%)	
	Hypertension	79(56.0%)	
	Hypothyroidism	3(2.1%)	
	Hyperlipedemia	35(24.8%)	
	Positive family history	38(26.9%)	
	Smoking	52(36.9%)	
	alcohol	11(7.8%)	
	β−λοχκερ	118(83.7%)	
	Anticholestrol drugs	111(78.7%)	
	ACE-I	40(28.4%)	
	CCB	27(19.1%)	
	Digoxin	9(6.4%)	
	Diuretic	19(13.5%)	
	Antioxidant	94(66.7%)	
	No of disease coronary branches :		
	Three:	15(10.63%)	
	Four:	110(78.01%)	
	Five	16 (11.34%)	

Data expressed as mean ± SD or number %
DOE: Dyspnoea on Exertion; **AOE** : Angina on Exertion; **ACE-I** : Angiotensin Converting Enzyme Inhibitor; **CCB**: Calcium Channel Blocker
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Table 2: Summary statistics: Perioperative factors

	Factors	Mean	SD
Perioperative Factors	CPB duration(mins)	84.1	22.5
	AOx CL(mins)	50.8	15.6
	ACT (secs)	152.1	44.9
	$EtCO_2$	79.1	
	PaO_2/FiO_2 ratio	412.7	121.4
	Intubation period(hrs)	21.8	6.85
	Pacing	14(9.9%)	
	ICU stay (hrs)	50.4	19.6
	Dopamine	52(36.8%)	
	Dobutamine	3(2.1%)	
	Adrenaline	17(12.1%)	
	Noradrenaline	7(4.9%)	
	Nitroglycerine	42(65.3%)	
	Sodium nitroprusside	8(5.7%)	
	Amiodarone	14(10%)	
	IABP use	5(3.5%)	
	Post op drainage (ml)	673.3	20.4
	Blood and blood products(ml)	1061	584.2
	Reexploration	1(0.7%)	
	Hospital stay (days)	9.3	4.45
	Death	3(2.1%)	

Data expressed as mean ± SD or number %
CPB: Cardio Pulmonary Bypass; **AOxCL**: Cross Clamp Time; **ACT**: Activated Clotting Time; **EtCO2**: End Tidal Carbondioxide; **IABP**: Intra Aortic Ballon Pump

Postoperative ventilation of patients undergoing cardiac surgery is justified because the incidence of respiratory insufficiency or low cardiac output after cardiac surgery is relatively high. However, there are many adverse effects of mechanical ventilation. Prolonged mechanical ventilation increases hospital costs, nursing dependency, airway and lung trauma, as well as stress and discomfort of endotracheal suctioning and weaning from ventilation [10]. More recently, a combination of modified anesthetia techniques, and advances in surgical procedures including myocardial protection and postoperative management has resulted in a marked decrease in postoperative intubation period [11-13]. Higgins and colleagues demonstrated that early extubation could be performed safely and did not increase perioperative morbidity [13].

The PaO_2/FiO_2 ratio has been recognized as a good index for predicting mortality and the need for endotracheal intubation in patients suffering from trauma [14]. It has also been suggested to be a reliable predictor of the arterial/alveolar oxygen tension ratio and of pulmonary dysfunction in patients undergoing CABG [15]. In addition, arterial blood gas analysis is routinely performed just after returning to the ICU in most hospitals and the PaO_2/FiO_2 ratio is the simplest of the oxygen tension-based indices to calculate. The normal range of PaO_2/FiO_2 ratio is 350–500. In the

Table 3: Univariate analysis of Preoperative, Perioperative, and Postoperative Predictors in Patients with PaO_2/FiO_2 Ratio<300 and with a PaO_2/FiO_2 ratio>300

	Factor	PaO_2/ FiO_2<300 (n=34)	PaO_2/ FiO_2>300 (n=107)	P value
Preoperative Factors	Age (yrs)	57 ± 7.7	58.6 8.3	0.39
	Weight (kg)	71.2±14.2	74.3±11.0	0.20
	Haemoglobin(gm/dl)	12.2±2.5	12.5±1.6	0.47
	hypothyroidism	2 (5.7%)	1(0.9%)	0.152
	DOE	21(60%)	60(56.6%)	0.725
	AOE	18(51.4%)	70(66.0%)	0.122
	Chest pain	10(28.6%)	31(29.2%)	0.939
	Diabetes	20(57.1%)	44(41.5%)	0.107
	Hypertension	21(60%)	58(54.7%)	0.585
	Hyperlipedemia	9(25.7%)	26(24.5%)	0.888
	Smoking	17(48.6%)	35(33.0%)	0.09
	Alcohol	4(11.4%)	7(6.6%)	0.46
	β-blocker	28(80%)	90(84.9%)	0.49
	Anticholestrol drugs	26(74.3%)	85(80.2%)	0.45
	CCB	8(22.8%)	19(17.9%)	0.52
	ACE-I	10(28.6%)	30(28.3%)	0.98
	Digoxin	1(2.9%)	8(7.5%)	0.45
	Diuretic	6(17.1%)	13(12.3%)	0.46
	Antioxidant	26(74.3%)	68(64.2%)	0.27
Perioperative Factors	CPB Time (mins)	83.424.5	84.4±21.7	0.32
	ACC time (mins)	49.9 ±21.7	51.3±15.1	0.20
	No of disease coronary branches : Three: Four: Five	4 (11.74%) 27 (79.57%) 3 (8.82%)	11(10.28%) 83(77.57%) 13(12.14%)	0.81 0.8 0.59
	Number of grafts Three Four Five	4(11.74%) 25(73.52%) 1(2.94%)	11(10.28%) 79(73.83%) 5(4.67%)	0.81 0.97 0.66
	Complete revascularization	89.88±7.5	86.63±13.52	0.18
	Duration of intubation (hrs)	28±7.7	18.99±4.0	0.001
	Dopamine	16(55.7%)	36(33.9%)	0.03
	Dobutamine	1(2.9%)	2(1.9%)	1.00
	adrenaline	6(17.1%)	11(10.4%)	0.28
	Noradrenaline	4(11.4%)	3(2.8%)	0.042
	NTG	21(60%)	71(66.9%)	0.45
	SNP	2(5.7%)	6(5.7%)	1.00
	Arrhythmia requiring treatment	6(17.1%)	8(7.6%)	0.10
	Amiodarone	6(17.1%)	8(7.6%)	0.10
	IABP use	2(5.7%)	3(2.8%)	0.59
	Pacing	3(8.6%)	11(10.4%)	0.75
	ICU stay (hrs)	60.9±24.9	45.6±14.5	0.002
	Reexploration	1(2.9%)	0	0.24
	Cardiogenic shock	3(8.6%)	0	0.014
	Respiratory failure	0	0	
	Death	3(8.6%)	0	0.014

DOE: Dyspnea on Exertion; **AOE**: Angina On Exertion; **ACE-I**: Angiotensin Converting Enzyme Inhibitor; **CCB**: Calcium Channel Blocker; **CPB**: Cardio Pulmonary Bypass; **AOxCL**: Aortic Cross Clamp Time; **ACT**: Activated Clotting Time; **$EtCO_2$** :End Tidal Carbondioxide; **NTG**: Nitroglycerine; **SNP**: Sodium Nitroprusside; **IABP**: Intra Aortic Ballon Pump

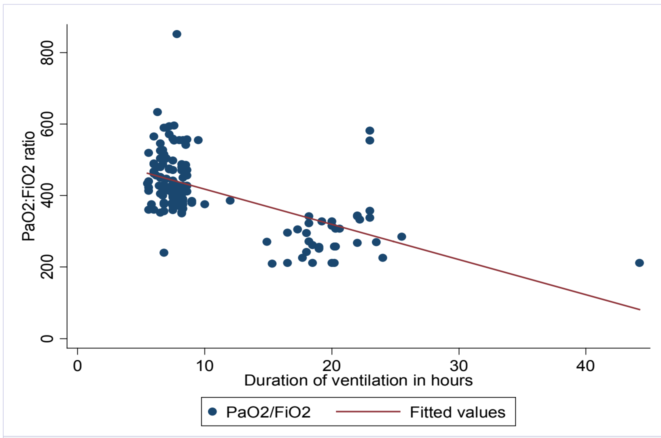

Figure 1: The relationship between PaO_2/FiO_2 Ratio and duration of mechanical ventilation

Table 4: Spearman Correlation between PaO_2/FiO_2 ratio and various factors

	Factor	Correlation
Demographic factors	Age (yrs)	0.15
	Weight (kgs)	0.02
	Haemoglobin (gm/dl)	-0.02
	CPB(min)	-0.34
	AOxCL (min)	-0.02
	ACT(sec)	0.01
	$vEtCO_2$	-0.55
	Intubation period(hrs)	-0.56
	ICU stay (hrs)	-0.25
	Postop drainage (ml)	0.09
	Blood and blood products used (ml)	0.14

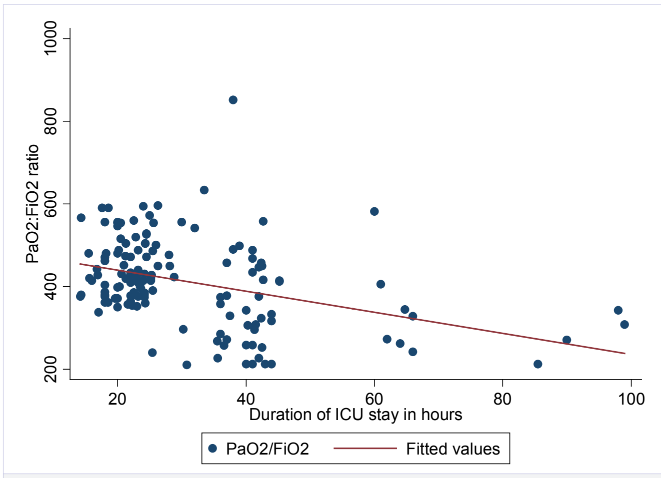

Figure 2: The relationship between PaO_2/FiO_2 Ratio and duration of ICU stay

patients in our study who had a prolonged intubation period and ICU stay the PaO_2/FiO_2 ratio was <350 .This result suggests that the PaO_2/FiO_2 ratio may be a good postoperative predictor of early extubation. Suematsu et al, demonstrated that PaO_2/

FiO_2 ratio as one of the main risk factors for pulmonary oxygen transfer in patients undergoing coronary artery bypass grafting [4]. The result of the present study also proves that there exists a significant relationship between the duration of ventilation, ICU stay and the PaO_2/FiO_2 ratio. The patients with $PaO_2/FiO_2 < 350$ needed significantly longer duration of intubation and ICU stay. The effect of PaO_2 on the control and regulation of mitochondrial as well as cellular respiration has been well described by several authors [16, 17]. In an cell culture model of pediatric cardiac myocyte, Merante F et al observed that chronically hypoxic cells exhibited significantly reduced activities of pyruvate dehydrogenase, cytochrome C oxidase and other enzymes involved in mitochondrial metabolism. This transcriptional down regulation of the key mitochondrial enzyme system leads to insufficient aerobic metabolism,production of lactic acidosis and high incidence of myocardial failure[18]. This may indirectly explain the high use of inotrope as well as percentage of death due to myocardial failure in our group I patients.

The number of inotropes administered during the immediate postoperative period (a gross index of myocardial function) has also been found by previous investigators [19-21] to be an independent determinant of outcome in patients undergoing CABG. According to Michalopoulos and colleague the combination of inotropic drug therapy and excessive blood transfusions is significantly associated with hospital death following CABG[18]. Results of our present study also suggest that the incidence of death was higher in the group with PaO_2/FiO_2 ratio < 350 which also had a higher requirement of inotropes.

Conclusion

Based on our findings, we conclude that patients with low preoperative PaO_2/FiO_2 ratio may need more careful perioperative management as these patients may have increased risk of perioperative complications.

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