

## EFFECTS OF CONTINUOUS VENTILATION DURING CARDIOPULMONARY BYPASS IN PREVENTING POST-OPERATIVE PULMONARY COMPLICATIONS IN OPEN HEART SURGERY

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### ABSTRACT

**Objective:** To compare continuous lung ventilation at low minute volume and non-ventilation during Cardiopulmonary bypass (CPB) in preventing post-operative pulmonary complications in open heart surgeries.

**Study Design:** A randomized control trial

**Place and duration of study:** Armed Forces Institute of Cardiology and National Institute of Heart Disease from December 2015- February 2016

**Material and Method:** A prospective, randomized study was carried out. The study was approved by the Institutions Ethics and Review Board and written informed consent was obtained from every patient. In total, 100 patients undergoing elective CABG were enrolled in this prospective, randomized clinical trial. On the day of surgery, the patients were selected randomly selected using non probability purposive sampling method into continuous ventilation [CV] group (n = 54) and open lung [OL] group (n = 46). PaO<sub>2</sub> was routinely measured after the induction of anesthesia and endotracheal intubation, before CPB, just after termination of CPB, just before extubation in the ICU and then at regular intervals of 4 hours till discharge to HDU. PaO<sub>2</sub>/ FiO<sub>2</sub> was calculated from the obtained values to compare the both groups. Any PPCs like development of pleural effusion, atelectatic lung on Chest X-Ray, lobar lung collapse or requirement of NIV every 4-6 hourly during the first 48 hours were also noted. CICU LOS was also recorded.

**Results:** Both the groups had no statistically significant difference. There was no major difference in PaO<sub>2</sub>/ FiO<sub>2</sub> ratios at termination of CPB, extubation, 6 hours after extubation and at 24 hours after extubation. There was statistically significant reduction in incidence of atelectasis (p value = 0.08) and requirement of NIV (0.07) in CV group as compared to OL group. However, the incidence of pleural effusion, pneumonia, and lobar lung collapse were found to be equivocal.

**Conclusion:** We conclude that low tidal volume low respiratory rate ventilation during CPB is effective in reducing atelectatic pulmonary complications in open heart surgeries.

**Keywords:** Cardiopulmonary bypass, Continuous ventilation; coronary artery bypass grafting, Postoperative pulmonary dysfunctions.

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### INTRODUCTION

The post-operative pulmonary dysfunction after cardiopulmonary bypass is practically common and connected with significant mortality and morbidity<sup>1-2</sup>. This results in increased time on mechanical ventilator, increased cardiac intensive care unit (CICU) length of stay (LOS), delayed hospital discharge and escalating treatment costs<sup>3-5</sup>. The etiology of pulmonary dysfunction after open heart surgery is thought to be multi factorial, occurring as a result of the combined effects of

anaesthesia, CPB, and surgical trauma. During cardiac surgery cardiopulmonary bypass (CPB) serves four basic functions: respiration, circulation, temperature management and provision of a blood less field. CPB in particular is known to activate the inflammatory process, resulting in increased pulmonary capillary permeability and damage to lung parenchyma<sup>6</sup>. This non-physiological condition ultimately culminates to an array of problems in early postoperative period and pulmonary dysfunction was one of the earliest recognized complications of cardiac surgery using CPB<sup>6</sup>.

Even after uncomplicated cardiac surgery, a midline sternotomy causes significant

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reductions in lung volumes and capacities which may result in postoperative atelectasis and more frequently mild hypoxemia<sup>7</sup>. Atelectasis has been the main cause of intrapulmonary shunt and poor arterial oxygenation in the post-bypass period<sup>8</sup>. Postoperative pulmonary dysfunction after CPB may include simple atelectasis, pleural effusions, pneumonia, cardiogenic pulmonary edema, pulmonary embolism, and various degrees of acute lung injury ranging from the mild to the most severe (i.e., acute respiratory distress syndrome [ARDS]). A wide range of ventilatory strategies while on CPB have been attempted; they include continuous positive airway pressure (CPAP) with pressures of 5–15 cmH<sub>2</sub>O, high frequency low tidal volume ventilation (100 breaths/min), inspired oxygen concentrations from 21% to 100%, and bilateral extracorporeal circulation using the lungs to oxygenate the blood while on bypass<sup>9</sup>.

The objective of this study was to evaluate the effects of low tidal volume low respiratory rate continuous ventilation during CPB to prevent post-operative pulmonary complications versus open lung technique during coronary artery bypass grafting (CABG).

## **MATERIAL AND METHODS**

The study was conducted after approval by the institutional Ethics and review Board subsequent to satisfying their concerns about patient privacy and consent. Informed written consent was obtained by all the participating patients. In total, 100 patients undergoing elective CABG were enrolled in this prospective, randomized clinical trial. On the day of surgery, the two patients were selected and randomized using non probability purposive sampling method into continuous ventilation [CV] group (n = 54) and open lung [OL] group (n = 46). All elective CABG surgery patients were included in the study except any patient who was American society of anesthesiologists (ASA) class > III, age > 70 years, poor left ventricular function (left ventricular ejection fraction < 40%), valvular heart disease (any disease process involving one or more of the valves of the heart), any patient requiring a reoperation, renal

impairment (elevated serum creatinine >2.4 mg/dl), and significant pulmonary disease as defined by preoperative FEV1 or forced vital capacity (FVC) values < 50% of the predicted value, re-ventilated, required IABP, having BMI >35, COPD or the patient who developed delirium/ confusion.

Arterial and central venous cannulation was conducted for all the patients, who also received a standard anesthetic technique as per protocol of our institute, using premedication with intramuscular nalbuphine (0.10 mg/kg) and promethazine (0.3 mg/kg) 2 hours before the induction of anesthesia. After preoxygenation for at least 3 minutes, anesthesia was induced by using Fentanyl (2mcg/kg), and Rocuronium (0.5 – 0.8 mg/kg), followed by manual ventilation with 100% Oxygen and 3-4% Sevoflurane for an till adequate muscle relaxation was achieved. After tracheal intubation, mechanical ventilation was started with volume control ventilation at the following setting: tidal volume (TV) = 7-8 ml/kg (lean body mass), positive end expiratory pressure (PEEP) = 0 cmH<sub>2</sub>O, inspiratory/expiratory (I/E) ratio = 1:2, FIO<sub>2</sub> = 0.45, and Respiratory Rate (RR) = 12/min. Anesthesia was maintained using 1-1.4% Isoflurane in air-O<sub>2</sub> mixture alongwith a constant infusion of fentanyl and atracurium before and after the CPB while it was maintained by a constant infusion of fentanyl, propofol, and atracurium during CPB. CABG was performed via a median sternotomy. During CPB, the patients in CV group (n = 50) underwent low tidal volume ventilation (TV = 3 ml/kg [lean body mass], RR = 6-8 / min, FIO<sub>2</sub> = 0.6, PEEP = 0 cmH<sub>2</sub>O, and I/E ratio = 1:2), and the patients in OP group (n = 50) lungs open to the atmosphere. In both groups, a standard CABG procedure was performed using the roller pump (Stockert, USA) and cold crystalloid cardioplegia (Medtronic, USA) for myocardial protection. During bypass Cobe (Apex) Sorin™ oxygenator and Euroset™ arterial line filter were used. The prime consisted of: 1.5 l Hartman's solution, 0.1l 10% mannitol and 500 mg Solumedrol. Bypass flows were maintained at 2.4 l/min<sup>2</sup> body surface area. After surgery, all the patients were

transferred to the ICU and were managed and monitored according to usual routine requirements. The postoperative care and criteria for extubation were standardized and identical for each patient. In the ICU, the lungs were ventilated using the synchronized intermittent mandatory ventilation (SIMV) ventilation mode. The initial setting was: FIO<sub>2</sub> = 0.45, RR = 12, TV = 7-8 ml/kg (lean body mass), and PEEP = 5 cmH<sub>2</sub>O. Respiratory rate and FIO<sub>2</sub> were then adapted to obtain an arterial PaCO<sub>2</sub> = 35–40 and PaO<sub>2</sub> > 90 mmHg. The decision for extubation was made according to

lung collapse or requirement of Non-invasive Ventilation (NIV) every 4-6 hourly during the first 48 hours were also noted. CICU LOS was also recorded. Data collection was performed by the nursing staff and data collection team of Research and Development Department of this institute, who were blinded to the study groups.

The data were analyzed with IBM® SPSS version 21.0. The values are expressed as mean and standard deviation. Independent sample T test was applied to compare the means in both the groups, and p values < 0.05 were considered

**Table-1: Comparison of different demographic and clinical variables between CV group and OL group.**

Variable	CV Group	OL group	p-value
No of patients	54 (54%)	46 (46%)	0.454
Gender			
Male (n)	44 (81%)	34 (74%)	0.543
Female (n)	10 (18.5)	12 (26%)	
Mean Age (years)	51.7±11.8	58.5±12.1	0.606
Weight (Kg) (mean ± SD)	69.9±12.3	71.5±12.5	0.531
Cross Clamp Time (minutes) (mean ± SD)	57.8±21.3	59.4±20.3	0.716
CPB time (minutes) (mean ± SD)	98.5±23.3	96.6±28.0	0.714
Extubation Time (hours) (mean ± SD)	4.7±3.2	7.3±6.6	0.053
CICU LOS (hours) (mean ± SD)	35.3±21.3	35.4±25.9	0.993
Requirement of Re-ventilated	1(2%)	2(4%)	0.432

**Table-2: Adverse Respiratory Events in 48 hours.**

Adverse Respiratory Events	CV Group	OL Group	p value
Pleural Effusion	2	4	0.21
Atelectasis	2	5	0.08
Pneumonia	1	2	0.50
Lobar Lung Collapse	1	3	0.15
Requirement of NIV	4	15	0.07

the protocol such as adequate gas exchange (PaO<sub>2</sub> > 70 mmHg, FIO<sub>2</sub> < 0.4, PaCO<sub>2</sub> = 35–40 mmHg, and spontaneous RR < 25), hemodynamic stability (i.e. adequate cardiac output, controlled arrhythmias, and no pulmonary edema), correction of any acid-base abnormality and absence of bleeding.

PaO<sub>2</sub> was routinely measured after the induction of anesthesia and endotracheal intubation, before CPB, just after termination of CPB, just before extubation in the ICU and then at regular intervals of 4 hours till discharge to high dependency unit. PaO<sub>2</sub>/ FiO<sub>2</sub> was calculated from the obtained values to compare the both groups. Any PPCs like development of pleural effusion, atelectatic lung on CXR, lobar

statistically significant.

## RESULTS

Demographically both the groups were statistically same (table-1). Major clinical parameters like cross clamp, CPB, Extubation times as well as CICU LOS and requirement of re-ventilation also showed statistically insignificant results (table-1). There was no major difference in PaO<sub>2</sub>/ FiO<sub>2</sub> ratios at termination of CPB, extubation, 6 hours after extubation and at 24 hours after extubation (graph-1).

The incidence was of adverse respiratory events are shown in table-2. There was statistically significant reduction in incidence of atelectasis (p value = 0.08) and requirement of

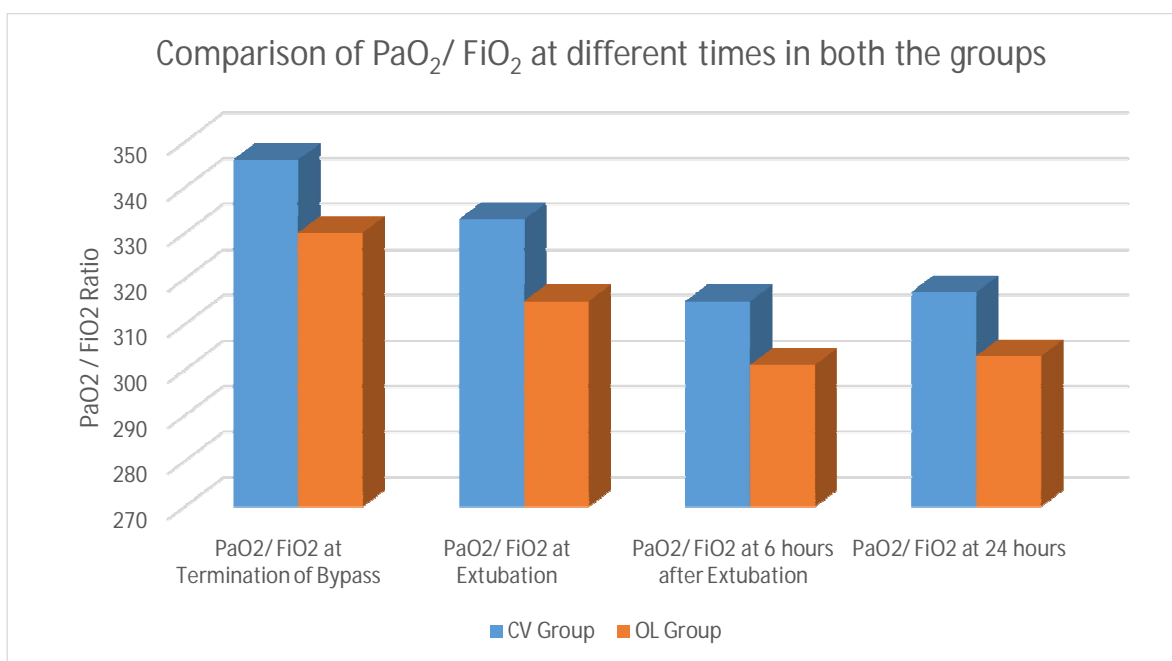
NIV ( $p$  value = 0.07) in CV group as compared to OL group. However, the incidence of pleural effusion, pneumonia, and lobar lung collapse were found to be equivocal (table-2).

## DISCUSSION

We designed this study to evaluate the influence of continued low tidal volume low respiratory rate ventilation during CPB on post-bypass lung function and oxygenation. Open heart surgery on CPB is associated with generalized inflammatory response. This response affects all organs. Lungs are usually opened to the atmosphere while on CPB to provide motionless field for the surgery; therefore, it is hypothesized that cessation of

operative pulmonary dysfunction after cardiopulmonary bypass results in increased time on mechanical ventilator, increased length of CICU stay, delayed hospital discharge and escalating treatment costs. The etiology of pulmonary dysfunction after open heart surgery is thought to be multi factorial, occurring as a result of the combined effects of anesthesia, CPB, and surgical trauma. CPB in particular is known to activate the inflammatory process, resulting in increased pulmonary capillary permeability and damage to lung parenchyma<sup>23</sup>.

We have used the simplest measurement of PaO<sub>2</sub> / FiO<sub>2</sub> ratio at different times during



**Graph-1: Shows no significant difference between the PaO<sub>2</sub>/ FiO<sub>2</sub> ratio at different times between both the groups. The maximum difference in values was less than 25 mmHg. CV = Continuous ventilation, OL = Open lung.**

normal inflation and deflation will result in accumulation of certain inflammatory mediators which can have adverse effect the respiratory membrane function. Many studies in the late 1990s and early 2000s have evaluated the continuous pressure as well as low tidal volume ventilation in open heart patients but most of those came out with equivocal results<sup>10-16</sup>. Now again there is some developing interest in this intervention and a few studies have come out with favourable results<sup>17-22</sup>. The post-

and after the surgery for evaluating the lung function. PaO<sub>2</sub> / FiO<sub>2</sub> ratio was used as it was the least expensive predictor of postoperative lung function. PaO<sub>2</sub> / FiO<sub>2</sub> ratio at different times in our study do not show remarkable difference between the two groups, as was in a study by conducted by Gagnon J et al, who have studied other parameters along with PaO<sub>2</sub> / FiO<sub>2</sub> ratio; and have come out with equivocal results<sup>24</sup>. Lindsay and Ervine have suggested the repetitive inflation and deflation of lungs at

physiological intra alveolar pressure is necessary for normal bronchial arterial flow secondary to the cyclical compression and relaxation of the vessels. In that case, cessation of ventilation during bypass would reduce the bronchial flow and predispose the patient to ischemic lung injury<sup>25</sup>. We have found continuous ventilation during CPB has some promise because there was significantly less incidence of atelectatic lung complications ( $p$  value  $<0.05$ ) and decreased need of NIV in CV group patients ( $P$  value  $< 0.05$ ) as compared to OL group.

Our results are also in conformity with some very recent clinical trials. A study by Ferrando C et al have concluded that lung-protective mechanical ventilation, inhalation anesthesia, and high FiO<sub>2</sub> have the potential to reduce postoperative complications in patients undergoing CPB<sup>21</sup>. Chaney MA et al have established that protective ventilation may be helpful to attenuate the postoperative pulmonary dysfunction commonly seen in patients after exposure to cardiopulmonary bypass<sup>26</sup>.

A John and Ervine in an elaborate study have assessed the following parameters: extravascular lung water, static and dynamic compliance, ratio of left atrial/right atrial white blood count, alveolar arterial oxygen gradient and the respiratory index together with clinical end points. They conclude that continued ventilation during bypass may reduce lung injury<sup>27</sup>.

### Limitations

Our study is limited in the sense that we did not measure any specific markers of pulmonary inflammation, or did not use the parameters like pulmonary capillary wedge pressure (PCWP), total lung water etc. These measurements of these parameters require more intervention and expenditure. Our sample size was small as well. We recommend a collaborated large multicentre study to devise local guidelines to evaluate the benefits of continuous ventilation during CPB.

### CONCLUSION

We conclude that low tidal volume low respiratory rate ventilation during CPB is effective in reducing atelectatic pulmonary complications in open heart surgeries. There is less requirement of post operative NIV in first 48 hours. These two potential benefits may result in decreased CICU LOS and reduction in hospital costs. We could not find out any significant difference in PaO<sub>2</sub> / FiO<sub>2</sub> ratios and incidence of any other pulmonary complications.

### CONFLICT OF INTEREST

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; or other equity interest), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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### AUTHORS CONTRIBUTION

Syed Muzaffar Hassan, study design and manuscript writing, Imran Bashi, manuscript writing; Kaleem Ahmad– data collection and result interpretation; Rehan Masroor – study design and manuscript writing, Safdar Ali Khan, literature review, Rehana Javaid, data analysis, Safdar Abbas and overall supervision.

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