IJTMGH International Journal of Travel Medicine and Global Health

Int J Travel Med Glob Health. 2023 Dec;11(4):423-429 doi 10.30491/IJTMGH.2023.415329.1380
http://ijtmgh.com

Original Article Open Access

An assessment effect of low tidal volume ventilation in on-pump Coronary artery bypass graft surgery on postoperative pulmonary complications: A double-blind, randomized clinical trial

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Received 2023-09-07; **Accepted** 2023-11-09; **Online Published** 2023-12-01

Abstract

Introduction: This double blind randomized clinical trial aimed to assess effect of low tidal volume ventilation in on-pump Coronary Artery Bypass Graft (CABG) surgery on postoperative pulmonary complications.

Methods: This study was conducted in Baqiyatallah Hospital from June 2021 to June 2022. 60 patients ASA class 1 and 2 CABG candidates were randomly divided into two intervention and control groups. Patients in the intervention group receive ventilation with a tidal volume (3-4 ml/kg) and several 6-8 breaths/minute. The control group doesn't receive any ventilation per the hospital routine after undergoing Cardiopulmonary Bypass (CPB). Renal and hepatic parameters are recorded before and on the first, second, and third days after surgery. Vital signs, duration of mechanical ventilation in ICU-OH, and duration of hospitalization in Intensive Care Unit (ICU) were recorded.

Results: The average age of the patients was 57.43 ± 9.82 years. Thirty-nine patients (65.0%) were male. The average Hb, two days after the operation in the first group was lower than the second group (P=0.019) .The average Cr, three days after the operation in the first group, was higher than the second group (P=0.037) .The average SGPT, three days after the operation in the first group was higher than the second group (P=0.031) .The average SGOT after surgery in the first group was higher than in the second group. The average ALK, two days and three days after surgery in the first group was higher than in the second group. The average CRP, three days after the operation in the first group was lower than the second group (P=0.001).

Conclusion: This research showed no significant difference in the two groups' average operation duration, ultrafiltration volume, X Clamp duration, ICU hospitalization duration, mechanical ventilation duration, and CPB duration. Management of ventilation during cardiovascular surgery is challenging.

Keywords: Ventilation, on-pump Coronary artery bypass graft surgery, pulmonary complications.

Citation: Latifi-Pour M, Amouzegar Zavareh S-M. An assessment effect of low tidal volume ventilation in on-pump Coronary artery bypass graft surgery on postoperative pulmonary complications: A double-blind, randomized clinical trial. Int J Travel Med Glob Health. 2023;11(4):423-429. Doi: 10.30491/IJTMGH.2023.415329.1380.

Introduction

CPB, which allows operation on a still and bloodless heart, is used in most heart surgery procedures. Recovery after cardiac surgery using CPB is generally good, with a 30-day survival rate of 98.4% [1]. However, the harmful effects of CPB on pulmonary function persist despite advances in anesthesia techniques [2]. CPB is associated with severe systemic inflammation and tissue damage with a mortality rate of 1.5%, with varying degrees of postoperative lung dysfunction in 30% of patients [3]. The underlying mechanisms that cause inflammation following CPB have not yet been fully elucidated, and currently, there is no strategy to prevent it [4] effectively.

Postoperative pulmonary complications (PPC) constitute a large part of the complications of cardiac surgery, which itself includes several events, some of them infectious (ventilator-acquired or hospital-acquired pneumonia) and some mechanical (atelectasis that requires respiratory support). Its severity ranges from

mild atelectasis to acute lung injury (ALI) or respiratory failure requiring long-term postoperative ventilation [5] or adult respiratory distress syndrome (ARDS) (6-8). PPC may be associated with increased hospital stay length and mortality at worst. Several factors, such as pulmonary collapse during cardiopulmonary bypass (CPB), bronchial arterial blood flow reduction, and systemic inflammatory response syndrome caused by CPB, have been proposed for PPC [9-15].

CPB is associated with significant physiological changes and lung damage. Ventilation is generally stopped in CBP, and the lungs are deflated to reduce mediastinal movements. Venous return is directed towards the right heart, so the pulmonary artery flow is significantly reduced. In addition, bronchial blood flow is reduced due to hemodynamic and pulsatility changes during bypass and changes in vascular resistance. These atelectatic and ischemic changes may cause tissue hypoxia, oxidative stress, and lung cell damage [16-19]. At the end of CPB, full ventilation is resumed, and pulmonary blood flow is restored with potential harms of reperfusion, including oxidative stress [20, 21] and inflammatory cell infiltration [22]. Oxidative stress can be caused by free iron-catalyzed reactions from heme released due to hemolysis when blood passes through the bypass circuit [23, 24]. Inflammatory activity and cytokine release are related to the outcome after cardiac surgery [25]. Pulmonary function 24 hours after CPB is associated with increased plasma levels of inflammatory cytokines and decreased levels of anti-inflammatory cytokines. The inflammatory response of the lung during CPB and mechanical ventilation originates in the alveolar membrane due to collapse, ischemia, reperfusion injury, and mechanical stress [26-28].

In recent years, several preventive strategies to protect the lung have been investigated and proposed [8, 29]: ultrafiltration to remove neutrophils [30], controlled hemodilution (with a hematocrit higher than 23%), steroids [31], and regulation Mechanical ventilation settings during CPB, such as applying positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) 5-15 cmH2O, high-frequency low-flow ventilation (100 acts/min), applying 100% inspiratory oxygen (FiO2) and bilateral CPB, which includes using the lungs to oxygenate the blood [32]. It has been suggested that low-frequency ventilation (LFV) during CPB may reduce hypoxia and ischemia, thereby helping to reduce inflammation [33].

This double blind randomized clinical trial aimed to assess effect of low tidal volume ventilation in on-pump Coronary artery bypass graft surgery on postoperative pulmonary complications

Methods

Overall, 60 ASA class 1 and 2 CABG candidates were randomly divided into two intervention and control groups. This study was conducted in Baqiyatallah Hospital from June 2021 to June 2022 with the code of ethics IR.BMSU.BAQ.REC.1401.046 and by obtaining informed consent from the patients. Also, IRCT registration cod was IRCT20220102053598N1. Patients who were candidates for emergency surgery who had a history of open heart surgery, suffered from liver, kidney, and lung diseases, had bleeding after surgery, or needed re-surgery for any reason were excluded in this study.

60 ASA class 1 and 2 CABG candidates were randomly divided into two intervention and control groups. This study was conducted in Baqiyatallah Hospital from June 2021 to June 2022. After obtaining informed consent from ASA class 1 and 2 CABG candidates, 60 patients were randomly divided into two intervention and control groups of 30. After establishing standard monitoring and IBP and CVP, induction of anesthesia was done with the same method in patients of both groups. After placing the patient under CPB, patients in the intervention group receive ventilation with a tidal volume (3-4 ml/kg) and a number of 6-8 breaths/minute. The control group doesn't receive any ventilation according to the hospital routine after undergoing CPB. Renal and hepatic parameters are recorded before surgery and on the first, second, and third days after surgery. Vital signs, duration of mechanical ventilation in ICU-OH, and duration of hospitalization in ICU were recorded.

Patients' Demographic information, including age, gender, smoking, and BMI, were recorded. After standard monitoring and IBP and CVP were established, anesthesia was induced with the same method in both groups of patients. The surgical team was also the same for both groups to avoid operator effects in this study. After placing the patient under CPB, the patients in the intervention group received ventilation with a tidal volume (3-4 ml/kg) and several 6-8 breaths per minute. At the same time, the patients of the control group did not receive any ventilation according to the hospital routine after undergoing CPB.

Kidney (BUN, Cr) and liver (SGOT, SGPT, ALKP) parameters were recorded before and on the first, second, and third days after surgery. In addition to laboratory parameters, vital signs, and mortality rate, the duration of mechanical ventilation in ICU-OH and the duration of hospitalization in ICU were recorded by a person who did not know the exposure status of the patients, and a comparison was made between the two groups .

After obtaining informed consent from ASA class 1 and 2 CABG candidates, 60 patients were randomly

divided into two intervention and control groups of 30. After establishing standard monitoring and IBP and CVP, induction of anesthesia will be done with the same method in patients of both groups. After placing the patient under CPB, patients in the intervention group receive ventilation with a tidal volume (3-4 ml/kg) and a number of 6 to 8 breaths per minute. Patients in the control group do not receive any ventilation according to the hospital routine after undergoing CPB. Kidney (BUN, Cr) and liver (SGOT, SGPT, ALKP) parameters are recorded before surgery and on the first, second, and third days after surgery. In addition to laboratory parameters, vital signs, duration of mechanical ventilation in ICU-OH, and duration of hospitalization in ICU are recorded by a person who does not know the exposure status of patients. After collecting the data, the data were analyzed using SPSS statistical software.

Results

The average age of the patients was 57.43 ± 9.82 years. Thirty-nine patients (65.0%) were male, and 21 (65.0%) were female.There was no significant difference in the distribution of age and gender in the two groups (Table 1). There was no significant difference in the distribution of diabetes, HTN, kidney disease, kidney disease, smoking, drug use, and hyperlipidemia in the two groups (Table 1).

Table 1: Comparison of age, sex, diabetes, HTN, kidney disease, kidney disease, smoking, drug use, hyperlipidemia, stroke and liver disease.

Items		I	II	P-value
age		59.46±11.67	55.40±7.17	0.110
Sex	Male	(%70) 21	(%60) 18	0.417
	Female	(%30) 9	(%40) 12	
Diabetic		% 56.7	% 66.7	0.426
HTN		% 63.3	% 60	0.791
Lung disease		% 6.7	% 0	0.492
kidney disease		% 10.0	% 0	0.237
Smoking		% 43.3	% 43.3	0.99
Drug use		% 30.0	% 13.3	0.209
Hyperlipidemia		% 16.7	% 0	0.052
Stroke		% 0	% 0	0.99
Liver disease		% 0	% 0	0.99

There was no significant difference in the mean operation time, ultrafiltration volume, X Clamp duration, ICU hospitalization duration, mechanical ventilation duration, and CPB duration in the two groups (Table 2).

Table 2: Comparison of operation duration, ultrafiltration volume, X Clamp duration, ICU hospitalization duration, mechanical ventilation duration, and CPB duration

Items	I	II	P-Value
Time of surgery	264.66±62.44	248.50±37.85	0.447
ultrafiltration volume	2483.33±419.42	3620.00±499.93	0.305
X Clamp duration	45.03±17.65	41.66±11.14	0.683
ICU hospitalization duration	3.43±0.72	3.50±0.73	0.699
mechanical ventilation duration	551.33±315.20	546.00±211.01	0.534
CPB duration	69.43±24.27	67.80±14.03	0.964

Table 3 shows the mean Hb, BUN, Cr, SGPT, SGOT, ALK, CRP, Troponin, and ESR before operation, one day, two days, and three days after operation in two groups.
The average age of the patients was 57.43 ± 9.82 years. Thirty-nine patients (65.0%) were male. The average Hb, two days after the operation in the first group was lower than the second group (P=0.019) .The average Cr, three days after the operation in the first group, was higher than the second group (P=0.037) .The average SGPT, three days after the operation in the first group was higher than the second group (P=0.031) .The average SGOT after surgery in the first group was higher than in the second group (Table 3) .The average ALK, two days and three days after surgery in the first group was higher than in the second group (Table 3) .The average CRP, three days after the operation in the first group was lower than the second group (P=0.001) .There was no significant difference between the two groups in Troponin and ESR in total (Table 3).

Table 3: Comparison of Hb, BUN, Cr, SGPT, SGOT, ALK, CRP, Troponin, and ESR before the operation, one day, two days, and three days after the operation (Post-Operative (OP)) in two groups

Items		I	II	P-value
Hb	before	14.07±1.84	13.82±1.65	0.142
	One day PO	9.86±1.75	10.66±1.68	0.385
	Two days PO	9.82±1.31	10.64±1.33	0.019
	Three days PO	9.58±1.36	9.87±1.17	0.331
BUN	before	18.10±5.60	16.80±3.95	0.427
	One day PO	17.80±7.04	18.60±13.33	0.130
	Two days PO	21.03±6.79	21.73±4.09	0.203
	Three days PO	22.23±11.42	19.76±3.92	0.397
Cr	before	1.05±0.29	1.08±0.24	0.555
	One day PO	0.99±0.31	1.09±0.29	0.185
	Two days PO	1.13±0.30	1.24±0.47	0.520
	Three days PO	1.15±0.25	1.09±0.43	0.037
SGPT	before	32.00±15.88	29.10±20.65	0.050
	One day PO	35.36±25.87	29.13±16.76	0.272
	Two days PO	35.76±22.03	28.46±12.42	0.269
	Three days PO	40.10±30.25	24.93±13.44	0.031
SGOT	before	31.70±11.54	23.56±9.18	0.002
	One day PO	45.16±51.88	25.53±9.15	0.003
	Two days PO	53.76±61.31	33.93±16.93	0.035
	Three days PO	56.73±60.60	31.23±8.69	0.026
ALK	before	203.46±135.88	151.03±40.05	0.906
	One day PO	160.37±69.89	152.26±41.28	0.578
	Two days PO	164.63±65.88	136.16±29.97	0.025
	Three days PO	206.60±276.08	134.23±19.86	0.026
CRP	before	5.07±8.56	3.28±1.62	0.278
	One day PO	12.58±17.78	12.86±17.42	0.700
	Two days PO	21.23±19.22	31.50±13.05	0.091
	Three days PO	22.67±20.61	42.23±9.18	0.001
Troponin	before	0.02±0.04	0.92±2.38	0.051
	One day PO	3.06±3.46	5.02±11.89	0.040
	Two days PO	2.61±2.37	2.66±4.91	0.050
	Three days PO	1.44±1.32	0.88±0.98	0.121
ESR	before	13.93±17.23	10.76±4.68	0.935
	One day PO	21.53±14.31	26.36±20.31	0.576
	Two days PO	25.20±13.35	27.16±19.02	0.688
	Three days PO	27.52±14.00	26.06±13.73	0.789

Discussion

Every year, about 1 to 1.25 million patients worldwide undergo heart surgery, which is still increasing [1]. The goal of adjusting ventilator parameters is to bring intraoperative ventilation closer to the general state, and this management of ventilation during CPB may be beneficial for patients. However, at the same time, it has an insignificant effect on the field of practice [2]. So far, the available research results on whether ventilation during CPB can improve operative outcomes are conflicting. Clinical trials have recently investigated various techniques to preserve lung function, but there is still no consensus on the best approach and performance.

In our study, there was no significant difference in the two groups' average operation duration, ultrafiltration volume, X Clamp duration, ICU hospitalization duration, mechanical ventilation duration, and CPB duration. There are various studies to confirm our results. The study of Zhang et al. in 2019 found that the use of different percentages of inspiratory oxygen (30 and 80%) in improving complications after surgery has no statistical difference. However, patients receiving pulmonary ventilation during cardiopulmonary pump compared to patients in the control group and not receiving pulmonary ventilation, had a significant improvement in symptoms after surgery [2]. Rodrigues et al showed no difference in the incidence of complications after cardiac surgery in patients receiving mechanical ventilation compared to those not receiving mechanical ventilation [3]. In a review study in 2017 that examined the effectiveness of mechanical ventilation during the heart-lung pump, after analyzing the results of the studies conducted in this field, it showed that determining the effectiveness or not of the pulmonary ventilation during the pump in improving the complications after heart surgery can be cited. It is not; more clinical studies are needed to prove its effectiveness. Only 5 trials showed the incidence of PPCs and 7 trials referred to the length of hospital stay [4]. Therefore, we cannot conclude whether intraoperative CPB ventilation affects the long-term prognosis of cardiac surgery patients.

Santini et al. showed in a study that perfusion flows of 7 ml/kg per minute of the continuous pulmonary artery in coronary artery bypass had no significant clinical advantage [5]. However, some other studies show different results from the findings of our study. The results of two meta-analyses show how protective ventilation strategies during general anesthesia can help reduce PPC and length of hospital stay [6, 7]. Suzuki et al. reported a significantly shorter duration of postoperative mechanical ventilation and improved alveolar function in infants undergoing CPB [8].

Beer et al.'s study showed that continuous mechanical ventilation improves postoperative oxygenation and can prevent the exacerbation of lung injury after CPB [9]. An observational cohort study on 1091 patients showed a lower incidence of acute lung injury and atelectasis before and after implementing the protective ventilation protocol, a reduction in the admission rate of patients in the intensive care unit, and a shorter length of hospital stay [10]. Using ventilators with low volume compared to traditional values, without increasing the number of breaths, leads to less pulmonary stress and less damage due to volume or pressure [11, 12]. The cause of this phenomenon is related to the increase of hypoxic pulmonary vasoconstriction. Protective ventilation should always be considered in pulmonary disease, prolonged anesthesia, or surgical patients at high risk of postoperative complications. Although this strategy can benefit the lungs, it can affect the cardiovascular system by reducing venous return and cardiac output, which requires fluids and vasopressors[13].

In this study, we investigated the renal parameters and liver enzymes of patients in both groups, before and after the operation, to determine the kidney and liver complications after the operation. Our results showed no significant difference between the two groups in Troponin and ESR, but significant differences were found in the rest of the parameters. Therefore, we suggest that future researchers consider these factors in their studies and compare their results with the results of our study.

Conclusion

This research showed no significant difference in the two groups' average operation duration, ultrafiltration volume, X Clamp duration, ICU hospitalization duration, mechanical ventilation duration, and CPB duration. Management of ventilation during cardiovascular surgery is challenging.

Highlights

What Is Already Known?

CPB, which permits procedure on a still and bloodless heart, is employed in most heart surgery techniques. It has been suggested that LFV during CPB may decrease hypoxia and ischemia, thereby reducing inflammation.

What Does This Study Add?

There was no significant difference in the patients with ventilation with a tidal volume (3-4 ml/kg) and several 6-8 breaths/minute and the control group in average operation duration, ultrafiltration volume, X Clamp duration, ICU hospitalization duration, mechanical ventilation duration, and CPB duration.

Ethical consideration
This study was conducted with the code of ethics IR.BMSU.BAQ.REC.1401.046 and by obtaining informed consent from the patients. Also, IRCT registration cod was IRCT20220102053598N1.

Authors' Contributions
Concept, design, data gathering, and preparing the manuscript: Masoud Latifi-Pour and Seyed Mohammadreza Amouzegar

Acknowledgements
None.

Conflicts of Interest Disclosures
We declare there is no conflict of interest.

Consent For Publication
We declare consent for publication.

Funding/Support
None.

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