



## Effects of Continuous Positive Airway Pressure (CPAP) Ventilation During Cardiopulmonary Bypass on Postoperative Outcomes

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### Research Article

#### History

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#### ABSTRACT

**Objective:** In this study, the relationship between the duration of intensive care unit stay, hospital stay, and intubation period between nonventilated and continuously ventilated groups of patients who underwent surgery with a cardiopulmonary bypass (CPB) device was investigated.

**Methods:** In the study, we divided patients into two groups. Continuously ventilated during CPB group and non-ventilated group. In the continuously ventilated group, respiratory rate was 6 per minute, tidal volume was 6 ml/kg and FiO<sub>2</sub> was 50%. In the non-ventilated group, the lungs were completely removed from the ventilator after the cross-clamp was placed.

**Results:** Although the duration of intensive care unit stays, length of hospital stay, and intubation times were relatively short in the continuously ventilated group, there was no statistically significant difference between the two groups.

**Conclusion:** There is a need for studies with a larger number of patients and subgroups regarding the maintenance of continuous ventilation during cardiopulmonary bypass.

**Keywords:** Ventilation, cardiopulmonary by-pass, open heart surgery, postoperative outcome

## Kardiyopulmoner Baypas (KPB) Sırasında Sürekli Pozitif Havayolu Basıncı (CPAP) Ventilasyonunun Postoperatif Sonuçlar Üzerine Etkileri

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#### Öz

**Amaç:** Bu çalışmada kardiyopulmoner by-pass cihazı kullanılarak ameliyat edilen hastaların ventile edilen ve edilmeyen gruplar arasında yoğun bakım kalış süreleri, hatanede kalış süreleri ve entübasyon süreleri arasındaki ilişkiyi inceledik.

**Metod:** Çalışmada hastalar kardiyopulmoner by-pass süresince ventile edilen grup ve ventile edilmeyen grup olarak iki gruba ayrıldı. Ventile edilen grup pompa süresince dakikada 6 kez, 6ml/kg tidal volüm ve % 50 FiO<sub>2</sub> ile solutuldu. Ventile edilmeyen grup ise kros klemp konduğu andan itibaren solunum cihazından ayrılarak takip edildi.

**Sonuç:** Hastanede kalış süreleri, yoğun bakım kalış süreleri entübasyon periyodu solutulan grupta solutulmayan gruba nazaran kısa olsa da gruplar arasında istatistiksel olarak anlamlı farklılık yoktu.

**Tartışma:** Kardiyopulmoner by-pass sırasında solutulmanın sürdürülmesi ile ilgili daha geniş hasta sayısı ve alt grupları içeren çalışmalara ihtiyaç vardır.

**Anahtar sözcükler:** Ventilasyon, kardiyopulmoner baypas, açık kalp ameliyatı, ameliyat sonrası sonuç

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## Background

Except for certain studies, after patients are connected to the CPB device in routine cardiac surgery, the lungs leave the ventilator and come into direct contact with the atmospheric air. As it is known, the protection of general physiology is the main principle in all kinds of medical approaches. The participation of the lungs in respiration during the surgery, even through the ventilator, has attracted the attention of some researchers. Different results have been obtained in the limited number of studies on this subject. While some studies reported that postoperative extubation is earlier in the ventilated group, some studies reported no difference between groups<sup>1, 2</sup>. In our study, we hypothesized that preservation of normal physiology may have positive effects on postoperative outcomes.

## Method

The local ethics committee approved this study, and all patients signed an informed consent form. A total of 65 patients were included in the study. Redo cases, emergency surgeries, previous lung surgery, chronic kidney disease requiring hemodialysis, chronic liver disease, and patients younger than 18 years of age were excluded from the study. Before the surgery for patients in the study, one of the researchers randomized patients by opening a sealed envelope to either continuous ventilation or non-ventilated groups during CPB. Except for the anesthesiologists, surgeons, anesthesia technicians, and the operating team, caring for the patients were blinded to the intraoperative ventilation strategy. Acetylsalicylic acid treatments of the patients were continued until the operation day.

All patients were premedicated with 10 mg of oral diazepam before the surgery. Anesthesia was provided with 2 mg/kg etomidate, 1 µg/kg fentanyl, 1 mg/kg vecuronium, 50% oxygen and 50% air 1 MAC isoflurane, 1 µg/kg remifentanyl bolus and 0.5 µg/kg/minute infusion. All patients followed with arterial monitoring via the radial artery and catheterization via the right jugular vein.

The CPB device was primed with 500 ml of isolyte-s and 5000 units of heparin. Each patient received 300 units/kg of heparin for anticoagulation. After the required ACT value (> 400) was provided, CPB started. The heart-lung machine was continued with moderate hypothermia (32-33 degrees). Median sternotomy was

performed in all patients. Cold blood cardioplegia was given to all patients before cross-clamp. Warm cardioplegia was given to all patients before the cross-clamp was removed. 1: 1 protamine was administered for heparin neutralization. All patients were taken to the intensive care unit as intubated and monitored. Analgesia and sedation were provided to all patients in the intensive care unit.

All patients were intubated as standard. After intubation, respiration was continued at a tidal volume of 8 ml/kg, respiratory rate of 12/min, and FiO<sub>2</sub> of 50%. After CPB, in the continuously ventilated patient group, the operation was continued with a tidal volume of 6 ml/kg, respiratory rate of 6 per minute, and FiO<sub>2</sub> of 50%. In the non-ventilated group, the patient left the ventilator and was directly exposed to atmospheric pressure after the cross-clamping.

SPSS 25.0 (IBM, Armonk, NY) was used to analyze the data. Categorical data were expressed as n (%) and analyzed using the  $\chi^2$  test; measurement data were expressed as mean  $\pm$  standard deviation (SD) and analyzed using the t-test. The normality of the data was assessed; a nonparametric test was used for data that did not have a normal distribution.  $P < 0.5$  indicates that the difference is statistically significant.

## Results

There was no statistically significant difference in baseline characteristics between the two groups of patients ( $P > .05$ ), as shown in Table 1. In addition, no significant difference was observed between the two groups ( $P > .05$ ) in the preoperative laboratory and echocardiographic findings (Table 3). Total CPB time and cross-clamp time were similar in both groups. Although the total intubation time and the duration of intensive care unit stay were relatively low in the continuously ventilated group, there was no significant difference between the two groups (Table 2). Considering the clinical status of the patients, it was seen that the patients with New York heart association functional classification (NYHA) class 2 and 3 were more in the continuous ventilated group (Table 4). On the other hand, it was observed that there were more patients requiring more complex surgery in the group with continuous ventilation in operation types (Table 5). In addition, postoperative in-hospital mortality was not observed in both groups.

**Table 1.** Demographic data of patients. (ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blocker)

	Nonventilation group (n=33) (%) or Mean ( $\bar{x}$ +sd)	Ventilation group (n=32) (%) or Mean ( $\bar{x}$ +sd)	P value
Age (years)	61,18 ± 14.47	60,18 ± 15.18	0,842
Sex			
Female (n)	11 (33,3%)	12 (37,5%)	-
Male (n)	22 (66,7%)	20 (62,5%)	
Tobacco use (n)	14 (42,4%)	15	0,718
Alcohol use (n)	3 (9,09%)	4	0,658
Body-mass index (kg/m <sup>2</sup> )	28,44 ± 4.14	28,18 ± 4.13	0,983
Hypertension (n)	17 (51,5%)	16	0,702
Diabetes mellitus (n)	15 (45,4%)	17	0,536
Hyperlipidemia (n)	12 (36,3%)	13	0,724
Chronic obstructive lung disease (n)	6 (18,1%)	8	0,504
Chronic renal disease	7 (21,2%)	9	0,518
Peripheral arterial disease (n)	6 (18,1%)	7	0,710
ACE inhibitör use(n)	8 (24,2%)	7	0,717
Diuretic use (n)	8 (24,2%)	10	0,528
ARB inhibitör use (n)	7 (21,2%)	9	0,518
Calcium channel blocker use (n)	6 (18,1%)	7	0,710
Beta-blocker use (n)	12 (36,3%)	12	0,924
Warfarin use (n)	3 (9,09%)	4	0,658
Clopidogrel use (n)	17 (51,5%)	17	0,897

**Table 2.** Intraoperative and intensive care unit data of patients. (CPB: Cardiopulmonary bypass)

	Nonventilation group (n=33) (%) or Mean ( $\bar{x}$ +sd)	Ventilation group (n=32)	P value
Total CPB time (minutes)	73,33 ± 16,39	74,06 ± 18.05	0,624
X clamp time (minutes)	47,93 ± 11,52	47,68 ± 11.58	1,0
Total intubation time (hours)	9,57 ± 3.08	9,37 ± 3.38	0,941
Intensive care unit time (hours)	26,03 ± 9.38	26,90 ± 10,64	0,391
Erythrocyte suspension (units)	2,45 ± 1.56	2,43 ± 1.68	0,877
Fresh frozen plasma (units)	2,27 ± 1.03	2,43 ± 1.31	0,175
Inotropes need (n)	16 (48,4%)	17 (53,1%)	0,371
Postoperative atrial fibrillation (n)	6 (18,1%)	5 (15,6%)	0,736
Total hospitalization time (days)	7,33 ± 1.38	7,31 ± 1.42	0,849

**Table 3.** Preoperative laboratory and echocardiographic data of the patients. (BUN: Blood Urea Nitrogen, MB: Myocardial Band)

	Nonventilation group (n=33) (%) or Mean ( $\bar{x}$ +sd)	Ventilation group (n=32) (%) or Mean ( $\bar{x}$ +sd)	P value
Ejection fraction (%)	51,72 ± 6.97	51,71 ± 5.95	0,459
BUN	20,30 ± 8.42	20,33 ± 8.30	0,989
Creatinine (mg/dL)	1,05 ± 0.34	1,05 ± 0.31	0,812
Total plasma protein (g/dL)	6,55 ± 0.57	6,58 ± 0.64	0,705
Albumin (g/dL)	4,11 ± 0.49	4.16 ± 0.58	0.230
Aspartate Aminotransferase (IU/L)	26,27 ± 22.17	27,09 ± 22.91	0,930
Alanine Aminotransferase (U/L)	20,60 ± 10.28	21,50 ± 11.13	0,747
Creatine Kinase (U/L)	164,96 ± 415.20	168,06 ± 421.47	0,960
Creatine Kinase-MB (IU/L)	33,15 ± 51.57	33,35 ± 48.75	0,950
Troponin-T (ng/mL)	1,52 ± 2.52	1,54 ± 2.48	0,980
White blood cell (WBC× 10 <sup>9</sup> / $\mu$ l)	9,16 ± 3.35	9,02 ± 3.09	0,866
Hemoglobin (g/dL)	13,26 ± 2.12	13,23 ± 2.06	0,870
Hematocrit (%)	39,53 ± 5.81	39,56 ± 5.82	0,993
Platelet (PLT× 10 <sup>9</sup> / $\mu$ l)	226,57 ± 72.54	224,18 ± 70.12	0,640
International normalized ratio (INR)	1,06 ± 0.86	1,06 ± 0.88	0,744

**Table 4.** Preoperative clinical classification of patients. (NYHA: New York Heart Association)

	Nonventilation group (n=33) (%)	Ventilation group (n=32) (%)
NYHA class 1	25 (75,7%)	21 (65,6%)
NYHA class 2	6 (18,1%)	7 (21,8%)
NYHA class 3	2 (6,2%)	4 (12,6%)
NYHA class 4	-	-

**Table 5.** Types of surgical procedures.

	Nonventilation group (n=33) (%)	Ventilation group (n=32) (%)
Aortocoronary bypass graft	27 (81,8%)	21 (65,6%)
Aortic valve replacement	3 (9,2%)	3 (9,3%)
Atrial septal defect repair	1 (3%)	2 (6,2%)
Mitral valve replacement + tricuspid valve repair	1 (3%)	2 (6,2%)
Myxoma excision	-	1 (3,4%)
Mitral valve replacement	1 (3%)	3 (9,3%)

## Discussion

Pulmonary dysfunction after cardiac surgery is a common and well-defined clinical condition. This condition occurs at a rate of approximately 20-25% after open heart surgery<sup>3,4</sup>. Many mechanisms have been mentioned in the pathophysiology of lung injury after open heart surgery. Factors affecting this injury; can be listed as extracorporeal circulation, anesthetic techniques, operative techniques, and hypothermia. In the mechanism related to extracorporeal circulation, the lung-ischemia hypothesis and the systemic inflammatory response syndrome hypothesis are emphasized<sup>3</sup>. In addition, transfusion-related lung damage is associated with increased mortality and morbidity<sup>5</sup>. This condition occurs in 2.4% after all open heart surgery<sup>6</sup>. The type of open heart surgery is also closely related to postoperative lung injury<sup>7</sup>.

In the literature, there are a limited number of studies on continuous ventilation of the lungs during CPB. To understand the issue and perform different or alternative CPB practices in the future, much more study is needed on this condition.

Some of the studies in the literature mention that there is no positive or negative effect of ventilation during CPB<sup>8</sup>. While some studies are reporting that ventilation during CPB has no effect on intraoperative partial oxygen pressure, there are also studies reporting that it does not reduce the inflammatory response and postoperative lung complications<sup>9,10</sup>. In our study, no significant difference was found in the postoperative intubation time, the duration of intensive care stay, and the total hospital stay. However, the patient groups used in our study were not exactly compatible in terms of surgery types and NYHA classification.

On the other hand, some studies also apply the vital capacity maneuver (VCM) and positive end-expiratory pressure (PEEP) methods in lung management during CPB or when leaving CPB. It was observed that there was no difference in postoperative outcomes and lung indicators between CPAP, PEEP, and VCM<sup>11</sup>. On the other hand, some studies are showing that CPAP application during CPB increases intraoperative

alveolar-arterial partial oxygen pressure but has no effect on postoperative results<sup>12</sup>. Many studies suggest the positive effects of ventilation during CPB. The alveolar-arterial O<sub>2</sub> gradient increase in high-frequency ventilation is one of these positive effects<sup>13</sup>. In addition, it was observed that 10 cm H<sub>2</sub>O CPAP increased partial oxygen pressure both during CPB and postoperatively<sup>14</sup>. Apart from these, there are also studies showing that postoperative extubation is faster, less lung damage is encountered and lung functions are preserved<sup>15,16</sup>. Continuation of ventilation during CPB is not only related to the duration of intubation, length of stay in intensive care, and hospital stay. Indeed, 10 cm H<sub>2</sub>O CPAP during CPB has been shown to increase pulmonary gas exchange after CPB and alleviate postoperative pulmonary complications compared to collapsed lungs<sup>17</sup>. In another study, fewer inflammatory and proteolytic responses were found in bronchoalveolar lavage samples taken from the patient group under continuous ventilation. This finding is accepted as an indicator that pulmonary functions are better protected<sup>18</sup>. On the other hand, several clinical trials related to ventilation are ongoing during CPB. The MECANO and VONTCPB trial compares 0.3 and 0.8 fractions of oxygen<sup>19,20</sup>. Many of the studies are still in progress. In the CPBVENT 2017 trial, the comparison was planned so that the patients received no mechanical ventilation, low minute volume ventilation, and continuous positive end-expiratory pressure during CPB<sup>21</sup>. Pulmonary dysfunction in cardiac surgery is not dependent on only ventilation strategy. It is multifactorial<sup>22</sup>. However, much more studies are needed to elucidate these mechanisms.

## Limitations

Our research had some limitations. Patient groups in the study were not specific. Results may differ in specific subgroups. Again, the amount of oxygen given in the study, respiratory rate, and tidal volume were given to each patient as a standard. Therefore, the amount, volume, and number to be given at different rates to different patients could change the results. In addition, the fact that all parameters of respiratory indicators were not evaluated separately in the study

limited the results of the study. Even if studies are conducted in subgroup patients, the patients will need to be well balanced in factors such as chronic obstructive pulmonary disease, heart failure stage, and the type of surgical procedures. Therefore, various factors should be taken into account in future studies. In addition, a larger sample and a broader follow-up study should be conducted to confirm our results.

## Conclusion

Although the duration of ICU stays, length of hospital stay and intubation were relatively shorter in the continuously ventilated group, there was no statistically significant difference between the two groups. It is obvious that studies with large parameters, including surgical subgroups and large patient series, are needed.

**Consent:** Written informed consent was obtained from each patient for publication of this study.

**Conflict of interest:** The authors declare no conflict of interest in preparing this article.

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