LOW TIDAL VOLUME VENTILATION IN OPEN HEART SURGERY: WHICH TIDAL VOLUME IS BETTER 8 ML/KG OR 6 ML/KG?

AÇIK KALP CERRAHİSİNDE DÜŞÜK TİDAL VOLUM VENTİLASYON: 8 ML/KG VE 6 ML/KG TİDAL VOLUMDEN HANGİSİ DAHA İYİ?

Keywords: extubation time and length of stay in the intensive care unit comparing with 6 ml/kg.

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Geliş Tarihi / Received: 12.09.2020 Kabul Tarihi / Accepted: 12.12.2020 Yayın Tarihi / Published: 05.01.2021

Abstract

Objective: To compare the outcomes of 6ml/kg vs. 8 ml/kg tidal volume in the lung protective ventilation - low tidal volume strategy in coronary artery bypass grafting operation.

Methods: Thirty-two patients enrolled in a randomized, single-center, prospective study were divided into two groups. The outcomes of 6ml/kg vs. 8 ml/kg were compared. Arterial blood pressures, heart rate, central venous pressure, expired tidal volume, respiratory frequency, the alveolar minute ventilation, the inspiratory time, static compliance, peak airway pressure, plateau pressure, driving pressure, arterial blood gas data and PaCO2- EtCO2 difference were recorded at T1 (15 min. prior to CPB), T2 (15 min. following the termination of cardio pulmonary bypass), and T3 times (at the end of the surgery). PaO2/FiO2 ratio was recorded at T3, T5 and T7 and 6th (T6) and 12th hours (T12) after extubation.

Results: In Group 6ml/kg, extubation time and length of stay in the intensive care unit were significantly longer (p<0.001, p=0.001, respectively). Discharge times were similar in both groups. In group 6ml/kg, PaCO2 was high at all times (T1, T2, T3; p=0.002, p=0.004, p=0.001, respectively), Hemodynamic changes had a similar course in both groups, in Group 6ml/kg. The PaO2/FiO2 ratio was significantly higher in Group 8ml/kg at T2 (p=0.009) and similar at other times.

Conclusion: Mechanical ventilation with a low tidal volume strategy with 8 ml/kg has more favorable outcomes by considering the shorter extubation time and length of stay in the intensive care unit comparing with 6 ml/kg.

Keywords: Open heart surgery, cardiac anestheisia, low tidal volume ventilation

Öz

Amaç: Koroner arter bypassı greftleme operasyonunda düşük tidal hacim stratejisi ile akciğer koruyucu ventilasyonda 6ml/kg ile 8 ml/kg tidal hacim sonuçlarını karşılaştırmaktayız.

Yöntem: Randomize, tek merkezli, prospektif çalışmaya alınan ardışık 32 hasta, iki eşit gruba ayrıldı. 6ml/kg ve 8ml/kg tidal volüm i

Bulgular: Grup 6ml/kg'da ekstübasyon süresi ve yoğun bakımda kalış süresi anlamlı olarak daha uzundu (srasıyla p<0.001, p=0.001). Taburculuk süreleri her iki gruba benzerdi. Grup 6ml/kg'da PaCO2 daha yüksekti (srasıyla T1, T2, T3; p=0.002, p=0.004, p=0.001). Hemodinamik değişiklikler her iki gruba da benzer seyretti. PaO2 / FiO2 oranı Grup 8 ml/kg'da T2'de anlamlı olarak daha yüksek (p=0.009) ve diğer zamanlarda benzerdi.

Sonuç: 8 ml/kg düşük tidal hacim stratejisi ile mekanik ventilasyon, 6 ml/kg ile karşılaştırıldığında daha kısa ekstübasyon süresi ve yoğun bakımda kalış süresi dikkate alınmalıdır daha olumlu sonuçlara sahiptir.

Anahtar Kelimeler: Açık kalp cerrahisi, kardiyan anestesi, düşük tidal volum ventilasyon

KOU Sig Bil Derg., 2021;7(1):59-64

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Introduction

Postoperative pulmonary dysfunction is the most important complication encountered following cardiac surgery, and the most common of these complications is atelectasis. The utilisation of cardiopulmonary bypass (CPB), increases the use of blood products, and can result with large volume shifts and acute respiratory distress syndrome (ARDS). Management of mechanical ventilation during intraoperative period is crucial to prevent the development of postoperative pulmonary dysfunction. Mechanical ventilation with low tidal volume (LTV) contributes to the development of postoperative pulmonary dysfunction by causing atelectasis and increasing atelectasis-induced lung damage, while a high tidal volume (HTV) strategy can result with postoperative pulmonary dysfunction by increasing the release of inflammatory mediators. In cardiac surgery, lung protective ventilation with LTV, a strategy which is adopted from the therapy of ARDS patients, is preferred; however, there is no clear consensus on this in practice. The amount of tidal volume meant by LTV is also not elucidated. Zochios et al. defined LTV as 6-8 ml/kg of predicted body weight (PBW). The safety of a tidal volume of 6ml/kg and its administration to all patients is investigated. Anatomically, this volume may make sense since normal physiological tidal volume (TV) for humans is approximately 6 mL/kg. Given that oxygen and carbon dioxide pressures, lung perfusion, alveolar surface area, wall thicknesses and hemoglobin level are normal, the alveolar minute ventilation (MVAlv) is equal to the difference between the TV and the dead space volume (DV) multiplied by the minute respiratory frequency (RF): MVAlv = [(VT-VD)xRF]. In a 70kg person with normal lung function MVAlv for 6ml/kg TV is calculated as MVAlv = [(6ml/kg-2ml/kg)x(10-35/min)] = 2.8-9.8 L/min. Meanwhile calculating MVAlv for 8 ml/kg for the same body weight results with 4.2-14.7L/min. According to the above mentioned formula, anemical ventilation with 6ml/kg is expected to result in higher PaCO2 levels compared to 8ml/kg, which requires higher RF to provide normcapnia. Increased RF sets the ground for auto-PEEP and, shortening the inspiration time (Ti) to prevent auto-PEEP in turn leads to the development of hypoxemia. Development of auto-PEEP may also impair hemodynamic balance, which may be harmful for patients undergoing open heart surgery. On the other hand, preventive effect of hypercapnia on lung damage should not be overlooked. Furthermore, hypercapnia enhances cardiac contractility, heart rate (HR) and cardiac output, reduces systemic vascular resistance and improves oxygen delivery to tissues by shifting the oxyhemoglobin dissociation curve to the right. We aimed to compare 6 ml/kg and 8 ml/kg TV with regard to respiratory and hemodynamic parameters in patients who had no lung disease and were scheduled for on-pump coronary artery bypass graft (CABG) surgery. We assumed that ventilation with 6ml/kg might lead to hypercapnia, respiratory acidosis, and that increased RF rates would negatively affect hemodynamics. Our primary outcomes were comparison of their effects on arterial blood gases (ABG), hemodynamic effects and respiratory mechanics. Our secondary outcomes included comparison of extubation time, length of stay in the intensive care unit (ICU), and time to discharge.

Methods

After obtaining the local ethics committee approval (KÜ GOKAEEK 2018/68, Clinical trials.gov identifier: NCT03651817) and written consent of the patients, 32 patients planned to undergo elective CABG were included in the study. Exclusion criteria were as follows: redo cases, patients with major obstructive or restrictive pulmonary disease (defined as 70% of predicted values for pulmonary function test variables of volume and flow), pulmonary hypertension (pulmonary artery pressure>35mmHg in preoperative transthoracic echocardiography), poor ventricular function (Ejection fraction<35%), renal failure (serum creatinine>1.8mg/dl) anemia (Hb<10gr/dl), morbid obesity (Body Mass Index>35kg/m²), re-exploration and smoking history up to 2 months ago. Patients were premedicated with intravenous (iv) midazolam before being transferred to the operating room. 5L/min oxygen was given via face mask, heart rate (HR) was determined by 5-channel electrocardiography, standard peripheral oxygen saturation (SpO2) and noninvasive blood pressure monitoring were performed. Radial artery cannulation was performed from the non-dominant hand following local anesthesia with lidocaine. After anesthesia induction with 0.05-0.1mg/kg midazolam, 5-10 µg/kg fentanyl, 0.1mg/kg rocuronium and 2-3mg/kg thiopental, male patients were intubated with an 8.0mm internal diameter (ID) endotracheal tube (ETT), and female patients were intubated with a 7.5mm ID ETT. A central venous pressure (CVP) catheter was placed preferably into the right internal jugular vein. Study protocol: Half of the patients recieved volume controlled mechanical ventilation with rectangular flow waveform (6-ml/kg PBW (Group 6ml/kg) and the other half with 8-ml/kg PBW (Group 8ml/kg) after intubation. Randomization was provided using the sequentially numbered opaque sealed envelope technique. Both groups were set to have an Inspiratory/Expiratory ratio of 1/2, plateau time as 20% of inspiratory time (Ti), and a PEEP of 5 cmH2O. All patients were ventilated with the same anesthesia device (Draeger, Primus, Draeger Medical AG & Co, Germany). In both groups, the respiratory rate (RR) was initially started as 10/min. RF was adjusted so that the end-tidal carbondioxide (EtCO2) values were between 30-35mmHg. Oxygen concentration was increased when SpO2 dropped below 97 percent. Anesthesia was maintained with 40% oxygen and 60% air mixture, desflurane (0.5-1.0 MAC) inhalation and remifentanil infusion (0.2-0.3µg/kg/min). Intraoperative additional analgesia was provided using iv bolus fentanyl.

CABG was performed through a median sternotomy with heparinization under CPB using aortic and two-stage atriovenous cannulation. CPB was initiated using aortic and two venous cannulas (18-20F) with BPW and utilized of cardiopulmonary bypass (CPB), increases the use of blood products, and can result with large volume shifts and acute respiratory distress syndrome (ARDS). Management of mechanical ventilation during intraoperative period is crucial to prevent the development of postoperative pulmonary dysfunction. Mechanical ventilation with low tidal volume (LTV) contributes to the development of postoperative pulmonary dysfunction by causing atelectasis and increasing atelectasis-induced lung damage, while a high tidal volume (HTV) strategy can result with postoperative pulmonary dysfunction by increasing the release of inflammatory mediators. In cardiac surgery, lung protective ventilation with LTV, a strategy which is adopted from the therapy of ARDS patients, is preferred; however, there is no clear consensus on this in practice. The amount of tidal volume meant by LTV is also not elucidated. Zochios et al. defined LTV as 6-8 ml/kg of predicted body weight (PBW). The safety of a tidal volume of 6ml/kg and its administration to all patients is investigated. Anatomically, this volume may make sense since normal physiological tidal volume (TV) for humans is approximately 6 mL/kg. Given that oxygen and carbon dioxide pressures, lung perfusion, alveolar surface area, wall thicknesses and hemoglobin level are normal, the alveolar minute ventilation (MVAlv) is equal to the difference between the TV and the dead space volume (DV) multiplied by the minute respiratory frequency (RF): MVAlv = [(VT-VD)xRF]. In a 70kg person with normal lung function MVAlv for 6ml/kg TV is calculated as MVAlv = [(6ml/kg-2ml/kg)x(10-35/min)] = 2.8-9.8 L/min. Meanwhile calculating MVAlv for 8 ml/kg for the same body weight results with 4.2-14.7L/min. According to the above mentioned formula, anemical ventilation with 6ml/kg is expected to result in higher PaCO2 levels compared to 8ml/kg, which requires higher RF to provide normcapnia. Increased RF sets the ground for auto-PEEP and, shortening the inspiration time (Ti) to prevent auto-PEEP in turn leads to the development of hypoxemia. Development of auto-PEEP may also impair hemodynamic balance, which may be harmful for patients undergoing open heart surgery. On the other hand, preventive effect of hypercapnia on lung damage should not be overlooked. Furthermore, hypercapnia enhances cardiac contractility, heart rate (HR) and cardiac output, reduces systemic vascular resistance and improves oxygen delivery to tissues by shifting the oxyhemoglobin dissociation curve to the right. We aimed to compare 6 ml/kg and 8 ml/kg TV with regard to respiratory and hemodynamic parameters in patients who had no lung disease and were scheduled for on-pump coronary artery bypass graft (CABG) surgery. We assumed that ventilation with 6ml/kg might lead to hypercapnia, respiratory acidosis, and that increased RF rates would negatively affect hemodynamics. Our primary outcomes were comparison of their effects on arterial blood gases (ABG), hemodynamic effects and respiratory mechanics. Our secondary outcomes included comparison of extubation time, length of stay in the intensive care unit (ICU), and time to discharge.
before separation from CPB. TVCM was performed by inflating the lungs to 40 cm H₂O and holding this pressure for 15 seconds immediately before termination of CPB. The same mechanical ventilation strategy was continued after CPB. Balanced electrolyte solution (Isolyte S) was preferred primarily for fluid replacement. Fluid, blood and blood product transfusion was performed according to our routine clinical practice based on vasopressor and inotropic requirements, MAP, CVP, lactate values, venous oxygen saturation, hematocrit values (Htc<24%), NIRS levels and urine output are measured. At the end of the surgery, patients were transferred to the cardiovascular surgery intensive care unit. The same ventilation protocol was continued until patients were extubated.

Hemodynamic changes [systolic, diastolic and mean arterial pressures (SAP, DAP, MAP), HR and CVP], Expiratory TV (TV-exp), RF, MV_{alv}, Ti, static compliance (C_{stat}), peak airway pressure (P_{peak}), plateau pressure (P_{plat}), driving pressure (DP), Arterial blood gas (ABG) data and PaCO₂/EtCO₂ difference were recorded 15 min prior to CPB (T₀), 15 min following the termination of CPB (T₁), and at the end of the surgery (T₂). PaO₂/FiO₂ ratio was recorded at 6th (T₆) and 12th hours (T₁₂) after extubation in addition to T₀, T₁ and T₂. DP was calculated based on the DP=PP_{plat}-PEEP formula. Extubation was performed according to mutual clinical protocols of cardiovascular surgery and cardiac anesthesiologist. Patients requiring reintubation or non-invasive mechanical ventilation support were recorded.

Statistical Analysis
In a previous study with patients undergoing open heart surgery, PaCO₂ was 35.62±3.5 mmHg before performing CPB in cases who underwent VCV with 8ml/kg PBW TV. In this study, by calculating that PaCO₂ would increase at least 10% with 6 ml/kg TVV, the number of cases was calculated as 16 for each group with 80% power. All statistical analyses were performed using IBM SPSS for Windows version 20.0 (SPSS, Chicago, IL, USA). The Shapiro-Wilk’s test was used to assess the assumption of normality. Continuous variables were presented depending on presence of normal distribution with either mean±standard deviation or (in case of no normal distribution) median (25th-75th percentile). Categorical variables were summarized as numbers (percentages). Comparisons of continuous variables between groups were carried out using the dependent samples t test/Mann-Whitney U test, whichever was appropriate. The changes in variables between time periods were analyzed by repeated measures ANOVA and Friedman’s two-way ANOVA. Association between two categorical variables was examined by the Chi-square test. All statistical analyses were carried out with 5% significance and a two-sided p-value <0.05 was considered as statistically significant.

Results
None of the 32 patients included in the study required reintubation or non-invasive mechanical ventilation after being extubated, and there were no deaths. Preoperative and demographic characteristics were similar in both groups (Table 1). Surgical and anesthetic features are demonstrated in Table 2. In Group 6ml/kg, extubation time and length of stay in the ICU were significantly longer (p<0.001, p=0.011, respectively) whereas discharge times were similar in both groups (Table 2). In group 6ml/kg, PaCO₂ was high at all times (p=0.002, p=0.004, p=0.001, respectively), pH, PaO₂, lactate, hemoglobin and hematocrit levels were similar in both groups (Table 3). Hemodynamic changes had a similar course in both groups (Table 4). When respiratory mechanics were investigated, TV_{exp} was higher, RF was less, P_{peak}, P_{plat} and DP was higher, and Ti was longer in Group 1. C_{stat} was similar in both groups (Table 5). The PaO₂/FiO₂ ratio was significantly higher in Group 8ml/kg at T₂ (p=0.009) and similar at other times (Table 6).

### Table 1. Demographics and preoperative features

|                      | Group 8ml/kg | Group 6ml/kg | p   |
|----------------------|--------------|--------------|-----|
| Age (year)           | 58(0.00,68)  | 58(55.25,74) | 0.933|
| ASA II/III(%)        | 7(4.89,9.62)| 7(4.89,9.62) | 1.000|
| Gender M/F n/(%)     | 4(25)/12(75)| 3(18.81/37.51)| 1.000|
| Weight (kg)          | 82(82.25,97) | 79(0.00,9.32) | 0.331|
| Height (cm)          | 169(169,68)| 166.93(61.62) | 0.232|
| BMI (kg/m²)          | 29(29.00,25.67-30.00) | 28.45(27.08-29.37) | 0.956|
| EF (%)               | 55(55.00,45.00-64.75) | 55.00(50.00-60.00) | 0.956|
| PBW (kg)             | 67(67.00,65.25-69.00) | 65.50(65.00-67.00) | 0.128|
| Heavy Smoking * n(%) | 9(56.30)    | 11(68.80)    | 0.715|
| Light Smoking ** n(%)| 7(43.70)    | 5(31.20)     | 0.715|

*ASA: American Society of Anesthesiologists, BMI: Body mass index, PBW: Predicted body weight, LVEF: Left ventricular ejection fraction, COPD: Chronic obstructive pulmonary disease

*p<0.05 vs 8ml/kg, **p<0.05 vs 6ml/kg

### Table 2. Comparison of intraoperative data between the groups

|                      | Group 8ml/kg | Group 6ml/kg | p   |
|----------------------|--------------|--------------|-----|
| CC time (min)        | 58(50.40,55.90-70.75) | 60(66.25,65.90-75.75) | 0.867|
| CPB time (min)       | 105.50(94.75,128.25) | 114.50(88.75,161.00) | 0.590|
| Defibrillation(n)    | 5(31.30)     | 6(37.50)     | 1.000|
| Bilateral open pleura (n) | 3(18.80) | 2(12.50)     | 1.000|
| LMA/                 | 5(31.30)     | 4(25.00)     | 1.000|
| Saphenous vein/      | 6(37.40)     | 7(43.80)     | 0.685|
| Both (n)             | 5(31.30)     | 5(31.20)     | 0.702|
| Intraoperative (n)   | 14(87.50,21,1250) | 14(87.50,21,1250) | 0.702|
| TDP                  | 3(18.80,13.81,20) | 6(37.50,166.02) | 0.433|
| TS                   | 2(12.5,14.87,50) | 2(12.50,14.87,50) | 1.000|
| Inotropic support    | 11(68.80)    | 13(81.20)    | 0.685|
| Rocuronium dose (mg) | 130,81±8,40  | 128,00±9,95  | 0.072|
| Fentanyl dose (mg)   | 850,00(800,000-900,000) | 850,00(800,000-900,000) | 0.867|
| ET_{DAS} (MAC)       | 0.80(0.80,0.90) | 0.80(0.70,0.80) | 0.196|
| Anesthesia time (min)| 275.00(243.75-326.25) | 300.00(272.50-330.00) | 0.224|
| Fluid balance (ml)   | 114.43(279,289) | 1426.87(660,24) | 0.106|
| Transfusion of ES in ICU (n) | 11(68.80) | 12(75.00)     | 1.000|
| Extubation time (h)  | 6.50(5.12-9.90) | 11.00(8.25-15.00) | 0.000|
| Length of stay ICU (h)| 4901(47.25,75.20) | 70(0.00,70.97)   | 0.991|
| Leight of Hospital Stay (day) | 8.50(7.25-10.50) | 7.50(6.25-10.50) | 0.539|

Note: CC: Cross Clamp, CPB: Cardiopulmonary Bypass, ICU: Intensive Care Unit, ES: Erythrocyt Suspension, FFP: Fresh Frozen Plasma, TS: Thrombocyte Suspension, LMA: Left internal mammarn artery, MAC: Minimum Alveolar Concentration

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Table 4. Hemodynamic data

| Parameter | Group 8ml/kg | Group 6ml/kg | p   |
|-----------|--------------|--------------|-----|
| HR (BPM)  | n=16         | n=16         |     |
| T1        | 65.00(60.00-69.50) | 65.00(60.25-80.75) | 0.809 |
| T2        | 74.80±13.02  | 75.37±16.56  | 0.916 |
| T3        | 92.80±20.32  | 96.18±17.09  | 0.615 |
| SA (mmHg) | n=16         | n=16         |     |
| T1        | 105.00(96.25-128.50) | 108.00(90.25-117.75) | 0.402 |
| T2        | 102.12±15.27 | 95.06±9.24   | 0.124 |
| T3        | 110.81±13.18 | 112.31±12.49 | 0.743 |
| DAP (mmHg)| n=16         | n=16         |     |
| T1        | 59.62±7.32   | 61.68±9.12   | 0.486 |
| T2        | 57.00(51.50-66.00) | 56.00(49.75-60.00) | 0.361 |
| T3        | 56.50±55.00-62.00 | 58.00(53.50-61.00) | 1.000 |
| MAP(mmHg) | n=16         | n=16         |     |
| T1        | 74.50±9.45   | 75.00(65.00-81.75) | 0.896 |
| T2        | 72.50(64.75-82.75) | 67.00(62.25-71.00) | 0.080 |
| T3        | 75.00(70.75-79.75) | 74.50(68.25-81.50) | 0.696 |
| CVP (mmHg)| n=16         | n=16         |     |
| T1        | 9.31±3.38    | 9.31±3.38    | 1.000 |
| T2        | 8.56±2.70    | 8.62±1.66    | 0.938 |
| T3        | 8.93±2.17    | 8.87±3.40    | 0.951 |

HR: Heart rate, SAP: Systolic arterial pressure, DAP: Diastolic arterial pressure, CVP: Central venous pressure, T1: 15 min prior to cardiopulmonary bypass, T2: 15 min following cardiopulmonary bypass, T3: End of the surgery

Table 5. Respiratory dynamics and ventilation parameters

| Parameter | Group 8ml/kg | Group 6ml/kg | p   |
|-----------|--------------|--------------|-----|
| TV (ml)   | n=16         | n=16         |     |
| T1        | 528.75±80.19 | 368.31±35.21 | 0.000 |
| T2        | 523.75±8.19  | 368.31±35.20 | 0.000 |
| T3        | 531.43±62.80 | 366.31±38.80 | 0.000 |
| RR (breath/min) | n=16 | n=16 |     |
| T1        | 12.00(12.00-12.00) | 14.00(12.00-16.00) | 0.000 |
| T2        | 12.12±1.85   | 16.25±2.72   | 0.000 |
| T3        | 13.37±1.89   | 19.25±3.25   | 0.000 |
| MV (ml/min)| n=16         | n=16         |     |
| T1        | 6.25±0.48    | 6.36±0.85    | 0.283 |
| T2        | 6.45(6.21-6.87) | 6.00(4.85-7.62) | 0.254 |
| T3        | 6.93±0.73    | 7.11±1.30    | 0.634 |
| PaCO2 (mmHg)| n=16         | n=16         |     |
| T1        | 32.00(30.25-32.75) | 32.00(30.50-35.00) | 0.160 |
| T2        | 31.50(30.00-32.00) | 31.00(30.25-34.00) | 0.867 |
| T3        | 33.00(31.25-34.00) | 32.00(31.00-34.75) | 0.696 |
| PaO2 (mmHg)| n=16         | n=16         |     |
| T1        | 35.40(33.00-53.00) | 37.00(34.50-45.00) | 0.002 |
| T2        | 34.93±2.00   | 38.14±3.57   | 0.004 |
| T3        | 35.60(34.05-37.92) | 38.90(37.17-40.42) | 0.001 |
| SaO2 (%)  | n=16         | n=16         |     |
| T1        | 98.75(97.40-99.20) | 98.60(96.67-99.00) | 0.270 |
| T2        | 98.74±0.54   | 98.45±0.62   | 0.160 |
| T3        | 98.10(96.25-98.87) | 97.90(96.25-99.05) | 0.724 |
| Lactate (mmol/L) | n=16 | n=16 |     |
| T1        | 1.47(0.80-1.75) | 1.02(0.62-1.40) | 0.149 |
| T2        | 1.20(0.92-1.50) | 0.95(0.62-1.27) | 0.073 |
| T3        | 2.70±1.34    | 2.62±1.01    | 0.860 |
| Hemoglobin (g/dl) | n=16 | n=16 |     |
| T1        | 11.93±1.50   | 12.10±1.51   | 0.754 |
| T2        | 11.93±1.75   | 12.05±1.47   | 0.216 |
| T3        | 10.20(9.72-10.67) | 9.95(9.25-10.75) | 0.669 |
| Hematocrit (%) | n=16 | n=16 |     |
| T1        | 36.76±4.51   | 37.36±4.57   | 0.714 |
| T2        | 34.72±5.22   | 37.26±4.21   | 0.140 |
| T3        | 31.55(30.07-33.05) | 30.85(28.72-33.32) | 0.669 |

Table 6. Oxygenation ratio intraoperatively and postoperatively

| Parameter | Group 8ml/kg | Group 6ml/kg | p   |
|-----------|--------------|--------------|-----|
| PaO2/FiO2 | n=16         | n=16         |     |
| T1        | 320.87±80.71 | 300.73±81.03 | 0.487 |
| T2        | 325.25±57.30 | 306.84±73.72 | 0.009 |
| T3        | 255.00(192.00-329.37) | 219.10(149.00-309.37) | 0.254 |
| T4        | 396.55±92.77 | 338.60±108.11 | 0.121 |
| T5        | 357.03±114.86 | 346.31±130.84 | 0.807 |

TV: Tidal volume, PaO2: Peak airway pressure, PaCO2: Plateau pressure, Cstatic: Static Compliancy, DP: Driving Pressure, T1: 15 min prior to cardiopulmonary bypass, T2: 15 min following cardiopulmonary bypass, T3: End of the surgery

Discussion

In this study we compared two LTV strategies with 6ml/kg and 8ml/kg in cardiac surgical patients undergoing on pump CABG. Mechanical ventilation with a LTV strategy with 8 ml/kg has more favorable outcomes by considering the shorter extubation time and length of stay in the ICU comparing with 6 ml/kg.
In the literature, the results of studies, in which LTV is used in cardiac surgery, differ. Some studies recommend \(^{19,20}\) LTV of 8 ml/kg, while others report that it has limited benefits.\(^{21}\) and some studies report no advantage of LTV.\(^{22}\) There may be several reasons for different outcomes such as what body weight was taken as a basis when calculating TV: actual, predicted or ideal body weight? Some studies do not mentioned this at all\(^{23}\) whereas some of them use ideal body weight.\(^{24}\) In lung protective ventilation strategy, it is recommended to calculate TV based on PBW.\(^{25,26}\) Another reason may be different main outcomes. In some of the studies, the main outcomes include postoperative airway pressures, lung compliance and arterial oxygenation values while in other studies, they include organ failure and length of stay in the ICU, and in some studies, main outcomes include investigating systemic and pulmonary inflammatory markers such as TNF-α, IL-1 and IL-8.\(^{19,20,22,24,25}\) On the other hand, confusion in terminology can lead to different interpretation of results. Namely, lung protective ventilation can also be applied without PEEP or recruitment maneuver (RM).\(^{26}\) Open lung ventilation (OLV) involves RM and high PEEP administration.\(^{27}\) Chaney et al.\(^{28}\) do not mention RM in their study and Lellouche et al.\(^{29}\) performed RM after weaning from CPB, Miranda et al.\(^{30}\) applied RM after induction and during the postoperative ICU stay. Therefore, in the last two studies, patients were actually ventilated with the OLV strategy.\(^{20,22}\)

The last factor that can lead to different results is the definition of LTV. According to some authors\(^{19,22,24,25}\) LTV is defined as 6 ml/kg, according to some others\(^{6}\) as 8 ml/kg, and for other researchers it is defined as TV below 10 ml/kg.

Our main aim was to compare the potential benefits of the LTV values defined as 6 or 8 ml/kg. PaCO\(_2\) value was considered as the reference in sample size calculation since no similarly designed study was found in the literature. In our study, it is expected that PaCO\(_2\) will be higher with use of 6 ml/kg TV. Despite the increase in PaCO\(_2\), pH levels remained similar. The similarity of PaO\(_2\), SaO\(_2\) and lactate levels indicates that arterial and tissue oxygenation is similarly affected by both amounts of TV. The decrease of T\(_{\text{A}}\) as a result of increasing RF at 6 ml/kg did not negatively impact oxygenation. The PaCO\(_2\)-EtCO\(_2\) value was found to be significantly different between groups in T\(_2\) and T\(_3\). Normal PaCO\(_2\)-EtCO\(_2\) difference is 2-5 mmHg.\(^{30}\) Chronic obstructive pulmonary disease, left heart failure, pulmonary embolism, the reverse Trendelenburg position, intrinsic lung disease, hypovolemia, and increased physiological dead space are among the causes for this difference. The increase in the PaCO\(_2\)-EtCO\(_2\) difference at 6 ml/kg can be explained by the increase in physiological dead space due to the inclusion of patients with intact lung function and similarity of hemodynamic data, the amount of inotropic agent used, the amount of blood and fluid replacement and the preoperative EF values in both groups. This is the result of elevated RF. Although the increase in PaCO\(_2\)-EtCO\(_2\) difference showed increased ventilation and perfusion impairment, it was not reflected in ABG.

\(\text{PaO}_2/\text{FiO}_2\) ratio was lower with 6 ml/kg at 15 minutes following weaning from CPB. This suggests that minimal atelectatic areas developing during ventilation at 6 ml/kg increase even more during CPB when ventilation ceases. Atelectatic areas caused an increase in ventilation-perfusion mismatching. The equalization of this ratio at the end of the surgery may be due to the opening of the atelectatic lung areas with the administration of RM during exit from the CPB.

Despite the elevation of arterial carbon dioxide level, increased respiratory rates and high airway pressures, similar hemodynamic responses were observed in both groups. Although \(P_{\text{peak}}\) and \(P_{\text{plateau}}\) were higher with 8 ml/kg in our study, \(P_{\text{plateau}}\) was below 30 cm H\(_2\)O recommended for lung protective ventilation.\(^{31}\) The \(P_{\text{plateau}}\) median value with 8 ml/kg TV was 19.50 cm H\(_2\)O (interquartile range: 17.25 to 21.75). Similarly, although DP is higher than the other group with 8 ml/kg, this value is lower than the upper limit value (15 cmH\(_2\)O) specified in the studies.\(^{32}\) A similar course in compliance indicates that the lungs were ventilated in the safe ventilation zone in both groups. One of the important but unforeseen results of our study was the elongation of the extubation time with 6 ml/kg. This may be due to more extensive atelectatic areas. The definitive diagnosis of this would have been possible with computed tomography of the thorax; however, this was not performed to avoid unnecessary radiation exposure. This can be considered as a limitation of our study. Although the duration of extubation and the length of stay in the ICU do not prolong time to discharge in our study, this result has a crucial importance by considering the correlation of postoperative pneumonia and intubation time.\(^{33}\) Postoperative pneumonia is more common in cardiac surgery compared to other surgeries, and constitutes a major cause of morbidity and mortality.\(^{34,35}\) Since we did not predict the results related to extubation and length of stay in the ICU when we started our study, data on postoperative pneumonia was not followed, which may be another limitation of our study.

**Conclusion**

In conclusion, 6 ml/kg and 8 ml/kg mechanical ventilation similarly affected oxygenation and hemodynamics in CABG patients who do not have any lung disease. Airway pressures were higher with 8 ml/kg, but below the recommended values for lung protective ventilation. Due to the fact that extubation time and length of stay in the ICU are shorter with 8 ml/kg mechanical ventilation, it can be preferred in patients who are at a high risk of developing postoperative pneumonia. Our results are obtained from patients with normal lung functions. Lung disease and coronary artery disease are likely to coexist due to factors such as age, smoking and obesity. The results may be different in these patients. Further comparative studies are needed regarding this topic.

**Acknowledgements**

None

**Declaration of Conflict of Interest**

None

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