Protective Ventilation Attenuates Postoperative Pulmonary Dysfunction in Patients Undergoing Cardiopulmonary Bypass

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Objective: To ascertain if protective ventilation can attenuate the damaging postoperative pulmonary effects of cardiopulmonary bypass (increases in airway pressure, decreases in lung compliance, and increases in shunt).

Design: Prospective, randomized clinical trial.

Setting: Single university hospital.

Participants: Twenty-five patients undergoing elective coronary artery bypass graft procedure and early extubation.

Interventions: Thirteen patients received conventional mechanical ventilation (CV; respiratory rate, 8 breaths/min; tidal volume, 12 mL/kg; fraction of inspired oxygen [FIO2], 1.0; positive end-expiratory pressure [PEEP], +5), and 12 patients received protective mechanical ventilation (PV; respiratory rate, 16 breaths/min; tidal volume, 6 mL/kg; FIO2, 1.0; PEEP, +5). Perioperative anesthetic and surgical management were standardized. Various pulmonary parameters were determined twice perioperatively: 10 minutes after intubation and 60 minutes after arrival in the intensive care unit.

Measurements and Main Results: The mean postoperative increase in peak airway pressure in group CV was significantly larger than the mean postoperative increase in peak airway pressure in group PV (7.1 ± 2.4 cm H2O; p < 0.001). Group CV experienced significant postoperative increases in plateau airway pressure (p = 0.007), but group PV did not (p = 0.644). The mean postoperative decrease in dynamic lung compliance in group CV was significantly larger than the mean postoperative decrease in dynamic lung compliance in group PV (14.9 ± 5.5 mL/cm H2O; p = 0.002). Group CV experienced significant postoperative decreases in static lung compliance (p = 0.014), but group PV did not (p = 0.645). Group CV experienced significant postoperative increases in shunt (15.5% to 21.4%; p = 0.021), but group PV did not (18.4% to 21.2%; p = 0.265).

Conclusions: Data indicate that protective ventilation decreases pulmonary damage caused by mechanical ventilation in normal and abnormal lungs. The results of this investigation indicate that protective ventilation may also help attenuate the postoperative pulmonary dysfunction (increases in airway pressure, decreases in lung compliance, and increases in shunt) commonly seen in patients after exposure to cardiopulmonary bypass.

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KEY WORDS: protective ventilation, pulmonary dysfunction, cardiopulmonary bypass

The relationship between ventilatory management and possible prevention of the damaging pulmonary effects of CPB has been investigated in animals and humans using a variety of endpoints.11-21 These investigations have focused only on ventilatory management of the lungs during CPB, however.11-21 To date, no investigation has examined the possible beneficial effects of protective ventilation in patients exposed to CPB. This prospective, randomized clinical study investigated the possible pulmonary benefits of protective ventilation in patients undergoing elective coronary artery bypass graft (CABG) surgery and early extubation.

METHODS

After Institutional Review Board approval and informed consent, 25 patients scheduled for elective CABG surgery and early tracheal extubation participated in the study. At this institution, all patients scheduled for elective CABG surgery are candidates for early extubation, including those undergoing reoperations and those with decreased left ventricular function (ejection fraction <40%). Patients who had undergone previous lung surgery were excluded from participation. Patients requiring preoperative intravenous inotropic or vasoactive drugs, intraaortic balloon support, supplemental oxygen, or mechanical ventilation were excluded.

Before arriving in the operating room, each patient was randomized to one of 2 groups by a random numbers table. Patients randomized to group CV (conventional ventilation) received mechanical ventilation parameters of respiratory rate, 8 breaths/min; tidal volume, 12 mL/kg; fraction of inspired oxygen (FIO2), 1.0; and positive end-expiratory pressure (PEEP) +5, after tracheal intubation; whereas group PV (protective ventilation) received mechanical ventilation parameters of respiratory rate, 16 breaths/min; tidal volume, 6 mL/kg; FIO2, 1.0; and PEEP, +5, after tracheal intubation. In both groups, the inspiratory/expiratory ratio was 1:3, and the inspiratory flow was adjusted so that the calculated tidal volume was delivered during the entire inspiratory cycle (creating the lowest peak airway pressure).
Each mode of ventilation (conventional or protective) was used during the entire intraoperative period and during the first hour after arrival in the intensive care unit (ICU). In both groups, the lungs were allowed to deflate during CPB. After 1 hour following ICU arrival (and after last data collection time), all patients received mechanical ventilation parameters of respiratory rate, 10 breaths/min; tidal volume, 8 mL/kg; FIO2, 1.0; and PEEP, +5, and were weaned from mechanical ventilation by the normal ICU protocol.

The intraoperative anesthetic technique was standardized and consisted of intravenous fentanyl, 20 μg/kg; midazolam, 150 μg/kg; and vecuronium. All of the fentanyl was administered before sternotomy. Regarding midazolam, approximately 70% of the calculated total dose was administered before sternotomy, and the balance was administered during rewarming. If required, inhaled isoflurane, intravenous nitroglycerin, or both were used for blood pressure control before initiation of CPB. Hypothermic CPB (to a lowest temperature of 26°C) with a membrane oxygenator and crystalloid prime (2.0 L of lactated Ringer’s solution, 50 mEq of sodium bicarbonate) was used in all patients. Nonpulsatile flows were maintained at 2.4 to 2.8 L/min/m², and, if needed, isoflurane was used by the perfusionist to maintain perfusion pressure at 50 to 70 mm Hg. Alpha-stat blood gas management was used in all patients. Separation from CPB was facilitated with intravenous inotropic or vasoactive drugs at the discretion of the anesthesiologist managing the case.

Peak airway pressure, plateau airway pressure, dynamic lung compliance, static lung compliance, alveolar-arterial (A-a) oxygen gradient, arterial PCO2, shunt, and deadspace were determined twice perioperatively: 10 minutes after intubation (time A) and 60 minutes after ICU arrival (time B). Derived variables were determined using standard equations (see Appendix). A pulmonary artery catheter (Swan-Ganz Thermodilution Pacer Catheter, Baxter Healthcare Corporation, Irvine, CA) was used to facilitate data collection. Perioperative fluid balance, central venous pressures, and pulmonary artery occlusive pressures were also recorded at the same times.

After completion of the CABG procedure, patients were transferred to the ICU. Postoperative care was standardized, and tracheal extubation was accomplished at the earliest clinically appropriate time. Criteria for extubation in the ICU at this institution include an appropriate sensorium, normothermia, hemodynamic stability, adequate pulmonary function (PO2 > 60 mmHg with FIO2 0.4), adequate urine output, and minimal chest tube output. If a patient developed hypertension, tachycardia, or excessive movement when tracheal extubation was not yet appropriate (for any reason), the ICU nurse administered small amounts of intravenous midazolam. In patients who were not extubated within 12 hours of arrival in the ICU, the reason for prolonged intubation (eg, hemodynamic instability, oxygenation difficulties) was ascertained. Postoperative complications and treatments were recorded daily until hospital discharge.

Pearson’s chi-square or Fisher’s exact test was applied to categorical data. The Student t-test (two-tailed) was used to compare means between the 2 groups. A P value of <0.05 was considered statistically significant. Results are expressed as mean ± 1 standard deviation unless otherwise indicated.

RESULTS

Thirteen patients were randomized to group CV, and 12 patients were randomized to group PV. Demographic and clinical characteristics and intraoperative data are presented in Tables 1 and 2. Two patients in group CV and 3 patients in group PV had previous CABG surgery.

Perioperative pulmonary data are presented in Table 3. Group CV (p < 0.001) and group PV (p = 0.031) had significant postoperative increases in peak airway pressure. The mean increase in peak airway pressure in group CV was significantly larger than the mean increase in peak airway pressure in group PV (7.1 ± 2.6 cm H2O v 2.4 ± 3.4 cm H2O; p < 0.001). Group CV experienced significant postoperative increases in plateau airway pressure (p = 0.007), but group PV did not (p = 0.644).

Peak and plateau airway pressures were similar between groups at time A but were significantly increased in group CV at time B (p < 0.001 and p = 0.020). Group CV (p = 0.001) and group PV (p = 0.018) had significant postoperative decreases in dynamic lung compliance. The mean decrease in dynamic lung compliance in group CV was significantly larger than the mean decrease in dynamic lung compliance in group PV (14.9 ± 6.7 mL/cm H2O v 5.5 ± 6.9 mL/cm H2O; p = 0.002). Group CV experienced significant postoperative decreases in static lung compliance (p = 0.014), but group PV did not (p = 0.645).

Group CV (p = 0.015) and group PV (p = 0.015) had significant postoperative increases in pulmonary function (PO2, shunt, and deadspace) at time A (p = 0.054) or time B (p = 0.162). Group CV experienced significant postoperative increases in shunt (p = 0.021), but group PV did not (p = 0.265). There was no difference between groups regarding shunt at time A (p = 0.259) or time B.
In the postoperative period, there was no difference in discharge rate between group CV and group PV (12.9 ± 3.9 days \( v \) 6.0 ± 2.5 days; \( p = 0.027 \)).

### DISCUSSION

The results of this investigation indicate that when compared with conventional mechanical ventilation, use of protective ventilation in patients undergoing elective CABG surgery attenuates postoperative increases in peak airway pressure, prevents postoperative increases in plateau airway pressure, attenuates postoperative decreases in dynamic lung compliance, prevents postoperative decreases in static lung compliance, and prevents postoperative increases in shunt. Taken together, these results indicate that protective ventilation may help attenuate the postoperative pulmonary dysfunction commonly seen in patients after undergoing CPB.

Volumes and pressures associated with conventional mechanical ventilation damage the lungs.\(^7\)–\(^10\) Animal models suggest that alveolar overdistention is more damaging than increases in alveolar pressure, and PEEP may be somewhat protective.\(^22\) Alveolar injury is thought to occur through cyclic closing and reopening of alveoli with resultant shear injury, which damages the alveolar-capillary interface, causes alterations in permeability leading to pulmonary edema, causes detrimental alterations in surfactant, and augments pulmonary inflammatory reactions.\(^7\)–\(^10\) Prior lung injury (from any cause) likely makes them more susceptible to such damage.\(^7\)–\(^10\) Protective mechanical ventilation prevents postoperative decreases in dynamic lung compliance, attenuates postoperative increases in peak airway pressure, prevents postoperative increases in plateau airway pressure, and prevents postoperative decreases in static lung compliance, resulting in reduced pulmonary edema and improved lung compliance.\(^6\)–\(^8\) These findings support the hypothesis that protective ventilation is beneficial in patients after undergoing CPB.

### Table 3. Perioperative Pulmonary Data

<table>
<thead>
<tr>
<th></th>
<th>Time A</th>
<th>Time B</th>
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</thead>
<tbody>
<tr>
<td><strong>Peak airway pressure (cm H(_2)O)</strong></td>
<td></td>
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</tr>
<tr>
<td>Group CV</td>
<td>23.5 ± 3.7</td>
<td>30.5 ± 4.6*</td>
</tr>
<tr>
<td>Group PV</td>
<td>21.3 ± 4.7</td>
<td>23.7 ± 2.9†</td>
</tr>
<tr>
<td><strong>Plateau airway pressure (cm H(_2)O)</strong></td>
<td></td>
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</tr>
<tr>
<td>Group CV</td>
<td>18.6 ± 3.5</td>
<td>21.8 ± 3.5*</td>
</tr>
<tr>
<td>Group PV</td>
<td>15.6 ± 5.2</td>
<td>17.6 ± 4.8‖</td>
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<tr>
<td><strong>Dynamic lung compliance</strong></td>
<td></td>
<td></td>
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<tr>
<td>(mL/cm H(_2)O)</td>
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<tr>
<td>Group CV</td>
<td>52.7 ± 7.5</td>
<td>37.8 ± 5.2*</td>
</tr>
<tr>
<td>Group PV</td>
<td>33.7 ± 8.8</td>
<td>28.1 ± 6.0*</td>
</tr>
<tr>
<td><strong>Static lung compliance (mL/cm H(_2)O)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group CV</td>
<td>73.4 ± 15.9</td>
<td>58.0 ± 11.4*</td>
</tr>
<tr>
<td>Group PV</td>
<td>51.9 ± 19.1</td>
<td>48.2 ± 23.0</td>
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<tr>
<td><strong>Alveolar-arterial oxygen gradient</strong> (mmHg)</td>
<td></td>
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<tr>
<td>Group CV</td>
<td>245.6 ± 68.3</td>
<td>395.1 ± 179.6*</td>
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<tr>
<td>Group PV</td>
<td>263.6 ± 119.0</td>
<td>368.6 ± 93.6*</td>
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<tr>
<td><strong>Arterial PCO(_2) (mmHg)</strong></td>
<td></td>
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<tr>
<td>Group CV</td>
<td>34.8 ± 2.5</td>
<td>42.3 ± 7.6*</td>
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<tr>
<td>Group PV</td>
<td>38.1 ± 5.0</td>
<td>46.4 ± 6.6*</td>
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<tr>
<td><strong>Shunt (%)</strong></td>
<td></td>
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<tr>
<td>Group CV</td>
<td>15.5 ± 5.0</td>
<td>21.4 ± 6.0*</td>
</tr>
<tr>
<td>Group PV</td>
<td>18.4 ± 7.0</td>
<td>21.2 ± 7.1</td>
</tr>
<tr>
<td><strong>Deadspace (%)</strong></td>
<td></td>
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<tr>
<td>Group CV</td>
<td>36.0 ± 7.2</td>
<td>37.9 ± 5.4</td>
</tr>
<tr>
<td>Group PV</td>
<td>35.8 ± 9.7</td>
<td>37.6 ± 11.1</td>
</tr>
</tbody>
</table>

*Note: Time A, 10 minutes after intubation; Time B, 60 minutes after intensive care unit arrival; Group CV, conventional mechanical ventilation; Group PV, protective mechanical ventilation.

*p < 0.05 when compared with Time A.
†p < 0.05 when compared with Group CV.
ventilation, with decreased tidal volumes and decreased airway pressures, may attenuate such damage. Two clinical investigations suggest that when compared with conventional mechanical ventilation (tidal volume approximately 12 mL/kg), use of protective mechanical ventilation (tidal volume approximately 6 mL/kg) in patients with ARDS decreases pulmonary inflammation and improves mortality. In June 1999, the National Institutes of Health/National Heart, Lung, and Blood Institute ARDS Network study comparing 6 mL/kg tidal volume with 12 mL/kg tidal volume was stopped for efficacy, with a significant survival benefit in the low tidal volume group.

CPB causes various abnormalities in the physical and functional properties of the lungs that initiate increases in pulmonary capillary endothelial permeability, decreases in lung compliance, and impaired gas exchange during the immediate postoperative period. The relationship between ventilatory management and possible prevention of these damaging pulmonary effects of CPB has been investigated in animals and humans using a variety of endpoints. These investigations have focused on ventilatory management of the lungs during CPB, however, and none has examined the possible beneficial effects of protective ventilation. To summarize these previous investigations, none of the 3 most commonly used methods of ventilatory management during CPB (passive deflation, continuous positive airway pressure, or continued ventilation) has proved superior. Some investigators have shown that passive deflation, continuous positive airway pressure, or continued ventilation may be beneficial. Conversely, some investigators have shown that passive deflation, continuous positive airway pressure, or continued ventilation may be detrimental. Other investigators have shown beneficial effects of a vital capacity maneuver performed before termination of CPB, whereas others could not determine benefits of any technique. Results from these previous investigations are difficult to interpret because of differing mechanical ventilation parameters, differing inhaled gas mixtures, differing CPB techniques, differing intravenous fluid balance protocols, and differing methods for assessing pulmonary function.

Detrimental postoperative pulmonary alterations in airway pressure, lung compliance, and shunt in patients after cardiac surgery have been documented by the authors' group and others. Such postoperative changes are likely caused by decreases in total lung capacity and functional residual capacity, atelectasis, pulmonary edema, increased inspired oxygen levels, intravenous vasodilators, and use of inhaled anesthetics, among others. This investigation reveals that protective ventilation may be useful in attenuating such postoperative pulmonary dysfunction. Patients who received protective ventilation had attenuated increases in airway pressure, attenuated decreases in lung compliance, and attenuated increases in shunt postoperatively. Although postoperative increases in A-a oxygen gradient were less in patients receiving protective ventilation, the difference did not reach statistical significance. Others have revealed that after cardiac surgery, a significant correlation \( r = 0.82 \) exists between shunt and A-a oxygen gradient.

This investigation studied a small number of low-risk patients for developing pulmonary dysfunction after undergoing CPB. Although at this institution all patients scheduled for elective CABG surgery are viewed as candidates for early extubation, all studied patients were essentially healthy and not expected to develop substantial postoperative pulmonary dysfunction that would affect extubation time, ICU time, discharge time, or mortality. Despite this situation, protective ventilation was still found to have potential beneficial effects on attenuating postoperative increases in airway pressure, decreases in lung compliance, and increases in shunt. A much larger study involving high-risk patients for developing pulmonary dysfunction after undergoing CPB is warranted. This investigation did not use optimal PEEP, which is advocated by some investigators to decrease the pulmonary damage associated with mechanical ventilation. Perhaps use of optimal PEEP with protective ventilation may further benefit patients after undergoing CPB.

In conclusion, use of protective ventilation in patients exposed to CPB attenuates postoperative increases in peak airway pressure, prevents postoperative increases in plateau airway pressure, attenuates postoperative decreases in dynamic lung compliance, prevents postoperative decreases in static lung compliance, and prevents postoperative increases in shunt. These results indicate that protective ventilation may help attenuate postoperative pulmonary dysfunction commonly observed in patients after undergoing CPB and deserves further investigation.

**APPENDIX**

**Dynamic Lung Compliance**

\[
C_d = \frac{\text{Tidal Volume}}{P_{\text{peak}} - \text{PEEP}}
\]

**Static Lung Compliance**

\[
C_s = \frac{\text{Tidal Volume}}{P_{\text{plateau}} - \text{PEEP}}
\]

**Alveolar-Arterial Oxygen Gradient**

\[
P(A-a)O_2 = P_AO_2 - PaO_2
\]

\[
P_AO_2 = \text{Alveolar PO}_2
\]

\[
\text{PaO}_2 = \text{Arterial PO}_2
\]

\[
P_AO_2 = P_tO_2 - \frac{\text{PaCO}_2}{0.8}
\]

\[
P_tO_2 = F_tO_2 \times (P_8 - 47)
\]

\[
\text{PaCO}_2 = \text{Arterial PCO}_2
\]

\[
0.8 = \text{Assumed respiratory quotient}
\]

**Shunt**

\[
\frac{Q_s}{Q_t} = \frac{CcO_2 - CaO_2}{CcO_2 - C\bar{v}O_2}
\]
\[ \dot{V}_D = \frac{1 - \dot{V}_O_2 \times 0.8 \times (P_B - 47)}{V_T \times V_E \times PaCO_2} \]

\[ V_O_2 = O_2 \text{ consumption (estimated by way of reversed Fick method)} \]

\[ P_a = \text{Barometric pressure} \]

\[ V_E = \text{Total minute ventilation} \]

\[ PaCO_2 = \text{Arterial PCO}_2 \]

\[ 0.8 = \text{Assumed respiratory quotient} \]

REFERENCES