Decompression-Triggered Positive-Pressure Ventilation During Cardiopulmonary Resuscitation Improves Pulmonary Gas Exchange and Oxygen Uptake

Axel Kleinsasser, MD; Karl H. Lindner, MD; Andreas Schaefer, MD; Alexander Loeckinger, MD

**Background**—Intermittent positive-pressure ventilation (IPPV) is the “gold standard” of ventilation during cardiopulmonary resuscitation (CPR), but continuous positive airway pressure (CPAP) is increasingly discussed as an alternative. This study investigated hemodynamics and pulmonary gas exchange applying CPAP enhanced with pressure support ventilation (CPAP\textsuperscript{PSV}) during CPR.

**Methods and Results**—Twenty-four pigs were subjected to ventricular fibrillation and CPR with CPAP\textsuperscript{PSV}, CPAP, or IPPV. Measurements were taken before (hemodynamics, blood gases, inert gas measurements) and 10 (hemodynamics, blood gases) and 20 (hemodynamics, blood gases, inert gas measurements) minutes after induction of ventricular fibrillation. Although no significant intergroup differences in hemodynamics were found, arterial partial pressure of oxygen (\(P_{\text{aO}_2}\)) was significantly higher during CPAP\textsuperscript{PSV} compared with CPAP or IPPV (98±10, 61±27, and 71±30 mm Hg, respectively, \(P<0.05\)). CPAP\textsuperscript{PSV} resulted in an alveolar-arterial partial pressure of oxygen difference of 56±17 mm Hg, whereas during CPAP, 83±21 mm Hg was detected, and during IPPV, 98±29 mm Hg was detected (\(P<0.05\)). Pulmonary blood flow to lung units with a normal \(V_\text{A}/Q_\text{O}\) ratio in percent of cardiac output was 76±17% during CPAP\textsuperscript{PSV}, 61±21% during CPAP (\(P<0.01\)), and 54±13% during IPPV (\(P<0.01\)). Oxygen uptake (\(\dot{V}_\text{O}_2\)) was significantly higher during CPAP\textsuperscript{PSV} than with the other ventilation modes (\(P<0.05\)) and comparable to the baseline value in intragroup comparison. Return of spontaneous circulation was recorded in 8 of 8 animals in the CPAP\textsuperscript{PSV} group, in 6 of 8 in the CPAP group, and in 3 of 8 in the IPPV group.

**Conclusions**—CPAP\textsuperscript{PSV} provides a straightforward and effective alternative to IPPV or CPAP during CPR that provides significantly higher \(P_{\text{aO}_2}\) and \(\dot{V}_\text{O}_2\). (Circulation. 2002;106:373-378.)

**Key Words:** heart arrest  heart cardiopulmonary resuscitation  lung  oxygen
Methods

The Austrian Federal Animal Investigational Committee approved this project, and animals were managed in accordance with the National Institutes of Health guidelines. This study was performed on 24 healthy, 16-week-old white farm pigs weighing 37 to 40 kg. Pigs were premedicated with azaperone (4 mg/kg IM) and atropine (0.01 mg/kg IM), and anesthesia was induced with propofol (2 to 4 mg/kg IV). After the trachea had been intubated, lungs were ventilated in IPPV mode (Evita 4, Dräger) at an inspiratory fraction of O₂ of 0.3 and a Vt of 10 mL/kg at 18 breaths/min. Respiratory rate was then adjusted to achieve a Paco₂ between 35 and 40 mm Hg. Anesthesia was maintained with propofol (6 to 8 mg · kg⁻¹ · h⁻¹) and remifentanil boluses (30 to 45 mg each). Ringer’s lactate solution (6 mL · kg⁻¹ · h⁻¹) and 3% gelatin solution (4 mL · kg⁻¹ · h⁻¹) were administered during the preparation phase and postresuscitation phase. A standard lead II ECG was used to monitor cardiac rhythm. Body temperature was maintained between 38°C and 39°C. Anesthesia was stopped during CPR.

Hemodynamic Measurements

A 7F catheter was advanced into a femoral artery for withdrawal of arterial blood and measurement of arterial blood pressure. A 7F pulmonary artery catheter was advanced into the pulmonary artery to measure mean pulmonary artery pressure, pulmonary arterial occlusion pressure, and cardiac output (CO) by the thermodilution technique (10 mL iced saline in triplicate) and to withdraw mixed venous blood. All catheters were filled with saline and connected to pressure transducers zeroed to ambient pressure at the level of the right atrium.

Blood Gas, Inert Gas, and Expiratory Measurements

Arterial and mixed venous blood gas variables were measured with a blood gas analyzer (Chiron), and end-tidal carbon dioxide was measured with a CO₂ analyzer (Dräger). Distributions of ventilation and perfusion were determined with the MIGET, as previously described.10 Distributions of Va and Q are presented as (1) blood flow to ventilated lung units, shunt flow (Va/Q <0.005); (2) blood flow to poorly ventilated lung units, low Va/Q (Va/Q >0.005 through 0.1); (3) blood flow to normally ventilated lung units, normal Va/Q (Va/Q >0.1 through 10); (4) ventilation of poorly perfused lung units, high Va/Q (Va/Q >10 through 100); and (5) ventilation of unperfused lung units, alveolar dead space (Va/Q >100 through infinity). The residual sum of squares was used as an indicator of fit of the data to the 50-compartment model.11

Experimental Procedure

Fifteen minutes before cardiac arrest, 5000 U heparin IV (clotting prevention) and 0.4 mg/kg piramidone were given. A 50-Hz, 60-V AC was then applied via 2 subcutaneous needle electrodes to induce ventricular fibrillation. CPR was started immediately. Animals randomly assigned to receive either IPPV, CPAP, or CPAP with PSV (CPAPPSV) were continued on the respective mode. CPAP and the pressure support in CPAPPSV were set to 12 cm H₂O. Baseline measurements (hemodynamics, inert gases, blood gases) were taken before ventricular fibrillation was induced. Repeated measurements were taken 10 minutes (hemodynamics, blood gases) and 20 minutes (hemodynamics, inert gases, blood gases) after induction of ventricular fibrillation. Closed-chest CPR was performed at a rate of 80 compressions/min with a mechanical device (Thumper, model 1016, Michigan Instruments Inc). Precordial compression force was adjusted to produce a sternal depression of 4 cm with a compression-relaxation ratio of 1:1.

The end point of the experiment was defined as hemodynamics and pulmonary gas exchange after 20 minutes of CPR without pharmacological intervention. However, we attempted to resuscitate the animals with vasopressin (0.4 U/kg) and up to 5 monophasic countershocks with an energy of 3, 4, and 6 J/kg, respectively. If asystole or pulseless electrical activity persisted after the 6-J/kg countershocks had been given, the resuscitation effort was terminated. ROSC was defined as an unassisted pulse with a systolic arterial pressure of ≥80 mm Hg, lasting for ≥5 minutes. Anesthesia was continued after ROSC and ventilation continued in IPPV mode.

Statistical Analysis

A 2-way ANOVA for repeated measures was used to determine statistical intergroup and intragroup significance. Significant results were analyzed post hoc with the Newman-Keuls and Fisher’s exact tests. Data are presented as mean±SD in the text, whereas error bars in the figures reflect SEM for reasons of space and clarity; a 2-tailed value of P<0.05 was considered significant.

Results

Before induction of cardiac arrest, there was no significant intergroup difference in any measured variable. Results described below refer to the time point after 20 minutes of CPR.
Inert Gas Measurements

Inert gas data are presented in Table 1. CPAPPSV resulted in the highest blood flow to lung units with a normal $V_{A}/Q$ ratio during CPR, whereas in animals treated with CPAP, the highest blood flow was to lung units with a low $V_{A}/Q$ ratio, and in animals treated with IPPV, the highest blood flow to lung units with a high $V_{A}/Q$ ratio was recorded. Differences in inert gas shunt were not significant. In animals treated with IPPV, higher values of the mean of the distributions of ventilation and perfusion were noted. SDs of either the distribution of ventilation (log SDV) or perfusion (log SDQ) did not undergo significant changes, indicating that the width of the distributions did not change. Alveolar dead space ventilation after 20 minutes of CPR was significantly lower in animals treated with IPPV (50±11%), than with CPAP (88±6%) or with CPAPPSV (75±17%). The adequacy of the multiple inert gas technique requires a steady-state condition. This can be evaluated by comparing thermodilution-measured cardiac output with the prediction of the inert gas algorithm, the latter being based on the Fick principle. Values were essentially identical.

Blood Gas Variables and End-Tidal Carbon Dioxide

Blood gas variables are shown in Figures 1 and 2 and in Table 2. Intergroup differences were observed in all oxygen-related variables. $P_{aO_2}$ was significantly higher in animals treated with CPAPPSV than in animals treated with CPAP ($P<0.01$) or IPPV ($P<0.05$). Mixed venous oxyhemoglobin saturation was significantly higher in animals ventilated with CPAP or IPPV than in the CPAPPSV animals, whereas CPAP animals had lower ($P<0.01$) arterial oxyhemoglobin saturations after 20 minutes of CPR. No significant intergroup difference was found in other blood gas variables. End-tidal carbon dioxide was higher in animals of the CPAPPSV group than in animals treated with CPAP or IPPV.

Alveolar-arterial oxygen pressure difference ($AaDO_2$) and oxygen uptake ($V\dot{O}_2$) at the measurement after 20 minutes of CPR are given in Figures 1 (top) and 2 (top). In an intergroup comparison with CPAPPSV, $AaDO_2$ was higher in animals treated with CPAP or IPPV. $V\dot{O}_2$ was not significantly lower during CPR when CPAPPSV was applied ($P=0.23$) compared with the baseline value. This variable was significantly higher, however, in intergroup comparison with animals treated with CPAP or IPPV at 20 minutes after CPR.

Hemodynamic and Respiratory Variables

Data are presented in Table 3 and Figure 2. No significant intergroup difference could be detected at any point in time.

Survival and Measurements Taken After Defibrillation

We attempted to resuscitate the animals after reaching the end point of the experiment. These data are presented in Tables 1 to 3 under the ROSC headings and also in Figures 1 and 2. Eight of 8 animals ventilated with CPAPPSV could be resus-
citated, whereas 6 of 8 animals treated with CPAP and 3 of 8 treated with IPPV could be successfully defibrillated. The difference between CPAPPSV and IPPV was significant ($P=0.025$).

**Discussion**

In the present study, we examined pulmonary gas exchange using 3 modes of ventilation: CPAPPSV, genuine CPAP, and IPPV during CPR. CPAPPSV triggered by the chest compressions resulted in the lowest AaDO$_2$ and thus in the highest PaO$_2$. This was based on significantly more pulmonary blood flow to lung areas with a normal V/Q ratio. A remarkable finding was that VO$_2$ during CPR with CPAPPSV was not significantly different from the pre-arrest value.

**Effect on Ventilation and Carbon Dioxide Elimination**

In CPR, IPPV is applied asynchronously to chest compressions, whereas CPAP simply provides a permanent status of inspiration that is interrupted by expirations caused by chest compression. The CPAPPSV concept for CPR improves on CPAP by adding actively triggered inspiration. In contrast to the other modes examined, in CPAPPSV both inspiration and expiration are active. Transcending the CPAP concept, in CPAPPSV, thoracic recoil and pressure support provided 2 independent factors that assisted inspiration during the period of decompression.

The breathing pattern that developed during CPAPPSV appeared to be unusually fast paced. Respiratory rate at the second time point during CPAPPSV was 73 ± 16 breaths/min; thus, >80% of the chest compressions were accompanied by a respiratory cycle. Mean Vt at this time point was 96 ± 19 mL total in a respiratory minute volume of 7.6 ± 1.9 L/min. Small Vt ventilation at high respiratory rates results in considerable dead space ventilation, which potentially impairs carbon dioxide elimination because alveolar ventilation is consequently reduced. PacO$_2$, however, was 50 ± 7 mm Hg during CPAPPSV, still within an acceptable range.

Ventilation and chest compressions are not synchronized when IPPV is used during CPR, which must result in

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**TABLE 2. Blood Gas and Expiratory Variables**

<table>
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<tr>
<th></th>
<th>Before CPR</th>
<th>10 Min CPR</th>
<th>20 Min CPR</th>
<th>ROSC+5 Min</th>
<th>ROSC+15 Min</th>
<th>ROSC+30 Min</th>
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<td>pH</td>
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<td>20±7</td>
<td>22±10*</td>
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<td>60±4</td>
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</table>

Hb indicates hemoglobin concentration; pH, arterial pH; ETCO$_2$, end-tidal partial pressure of carbon dioxide; SaO$_2$, arterial oxyhemoglobin saturation; PvO$_2$, mixed venous partial pressure of oxygen; PacO$_2$, arterial partial pressure of carbon dioxide; and PvCO$_2$, mixed venous partial pressure of carbon dioxide. Values are mean±SD.

*P<0.01 in intergroup comparison with animals treated with CPAPPSV.
interference of chest compression with inspiration. Accordingly, both CPAP and CPAPPSV resulted in significantly lower peak airway pressures (P<0.001) than IPPV. Although the hemodynamic consequences of this cannot be drawn conclusively from our data, the airway pressures observed during IPPV (39±6 mm Hg) increase the risk of barotrauma.14,15

Effect on Arterial Blood Gases

Despite significantly higher PaO₂ and a significantly lower aADo₂ in animals treated with CPAPPSV, hypercarbia (Paco₂ 50±7 mm Hg) was observed in the CPAPPSV and CPAP groups (Table 2). Increased Paco₂ caused by an increase in hydrogen ions shifts the oxygen dissociation curve to the right, thus facilitating the unloading of oxygen to the tissues (Bohr effect). In this study, CPAPPSV provided the highest PaO₂ with moderate arterial hypercarbia (Paco₂ 50±7 mm Hg). Thus, although the hemoglobin was highly saturated with oxygen (95±3%), it had a reduced affinity for oxygen. Together with a low cardiac output, this in part explains the large arterial-venous oxygen partial pressure difference of ~100 mm Hg found with CPAPPSV. In fact, VO₂ was highest in those subjects treated with CPAPPSV (see below). Also, because the carbon dioxide transport capacity of hemoglobin depends on the amplitude of peripheral oxygenation, a higher oxygen extraction ratio improves tissue carbon dioxide elimination (Haldane effect).

Effect on Efficiency of Gas Exchange

In this setting of extremely low cardiac output (Figure 2), it is crucial that most of the pulmonary blood flow be directed to lung units with a normal Vₐ/Q ratio to achieve the highest possible oxygen delivery at a given hemoglobin concentration. CPAPPSV resulted in a significantly higher percentage of blood flow to these units than did CPAP (P<0.01) or IPPV (P<0.01). When compression and inspiration occur simultaneously, intrathoracic pressure must rise, contributing to the rightward shift of the distribution of ventilation (mean of V). Blood flow to these lung units with a higher Vₐ/Q ratios was also increased with IPPV, however, resulting in a right-shifted Vₐ/Q matching that prevented further decreases in Paco₂. Conversely, such shifts produce less blood flow to lung units with lower Vₐ/Q ratios, including those units with a
normal ratio. Therefore, and because of the high $\Delta$ADo$_2$, in the IPPV group, the decrease in oxygen partial pressures from air to pulmonary end-capillary blood amounted to $\sim$138 mm Hg, a large value compared with $\sim$50 mm Hg in a healthy, spontaneously breathing subject at sea level.

It should be noted that all animals examined had excellent lung function at baseline; nevertheless, there were significant differences between groups at the measurement after 20 minutes of CPR. The question arises as to whether the magnitude of differences between the groups examined can be extrapolated to subjects with impaired gas exchange. For instance, ventilation-perfusion inequality in chronic asthma, as expressed as the second moment of the distribution of perfusion (log SDQ), was found to be 0.74 (mean of 26 subjects).\textsuperscript{16} Log SDQ in the animals in this experiment was only 0.48, consistent with previously published data collected in awake pigs\textsuperscript{13} and normal humans\textsuperscript{10} indicating healthy lungs. It is likely that differences in gas exchange and resulting PaO$_2$ between the modes examined would be more pronounced in subjects with an already existing gas exchange disorder.

**Effect on $\dot{V}$O$_2$**

$\dot{V}$O$_2$ was by far highest in the CPAP$^{PSV}$ group (Figure 2), an unanticipated finding. In animals treated with CPAP$^{PSV}$, the $\dot{V}$O$_2$ at 20 minutes of CPR was unchanged ($P=0.23$) compared with baseline. In other words, CPR did not affect $\dot{V}$O$_2$ in the CPAP$^{PSV}$ group. Which factors contributed to the differences in $\dot{V}$O$_2$? Arterial oxyhemoglobin saturation and mixed venous oxyhemoglobin saturation during CPAP$^{PSV}$ were higher or lower, respectively, compared with CPAP or IPPV, although not all differences reached significance. With regard to hemodynamics, insignificant differences in systolic, mean, and diastolic pressures may have and in cardiac output will have contributed to the higher $\dot{V}$O$_2$ in the CPAP$^{PSV}$ group. This animal model, however, cannot derive whether blood flow has been redistributed to a normal pattern and whether all organs had a better $\dot{V}$O$_2$ during CPAP$^{PSV}$.

**Resusciability**

Although it was beyond the primary end point of this experiment, defibrillation was attempted after the measurement after 20 minutes of CPR. CPAP$^{PSV}$ resulted in a significantly higher occurrence of ROSC in this animal model (CPAP$^{PSV}$, 8 of 8; CPAP, 6 of 8; and IPPV, 3 of 8) in comparison with IPPV but not with CPAP. Higher occurrence of ROSC in animals treated with CPAP$^{PSV}$ may be related to the pre-arrest range value of $\dot{V}$O$_2$ at the 20-minute measurement.

**Applicability of CPAP$^{PSV}$ and Critique of the Methods**

It should be noted that these results obtained in a porcine model cannot be fully extrapolated to resuscitation in the intensive care unit or in the field. Although CPAP$^{PSV}$ offers a number of advantages, practicability and application in the field may be limited. First, elasticity and elastic recoil of lung and thorax determine the effectiveness of CPAP$^{PSV}$ during CPR. Partly ossified rib cartilages and a consequently stiffer thorax will limit the efficacy of CPAP$^{PSV}$ in this setting. Second, accidental development of a pneumothorax, as may occur during CPR,\textsuperscript{17,18} will clearly limit the applicability of CPAP$^{PSV}$ in this setting. Third, optimal CPAP and CPAP$^{PSV}$ levels that manifest in a higher survival rate remain to be determined.

We conclude that CPAP$^{PSV}$ may be used as a simple and effective decompression-triggered mode of ventilation during CPR that provides improvements in pulmonary gas exchange and a pre-arrest range of $\dot{V}$O$_2$.

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**References**


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