Inspiratory Impedance During Active Compression-Decompression Cardiopulmonary Resuscitation
A Randomized Evaluation in Patients in Cardiac Arrest

Patrick Plaisance, MD; Keith G. Lurie, MD; Didier Payen, MD, PhD

Background—Blood pressure is severely reduced in patients in cardiac arrest receiving standard cardiopulmonary resuscitation (CPR). Although active compression-decompression (ACD) CPR improves acute hemodynamic parameters, arterial pressures remain suboptimal with this technique. We performed ACD CPR in patients with a new inspiratory threshold valve (ITV) to determine whether lowering intrathoracic pressures during the “relaxation” phase of ACD CPR would enhance venous blood return and overall CPR efficiency.

Methods and Results—This prospective, randomized, blinded trial was performed in prehospital mobile intensive care units in Paris, France. Patients in nontraumatic cardiac arrest received ACD CPR plus the ITV or ACD CPR alone for 30 minutes during advanced cardiac life support. End tidal CO₂ (ETCO₂), diastolic blood pressure (DAP) and coronary perfusion pressure, and time to return of spontaneous circulation (ROSC) were measured. Groups were similar with respect to age, gender, and initial rhythm. Mean maximal ETCO₂, coronary perfusion pressure, and DAP values, respectively (in mm Hg), were 13.1±0.9, 25.0±1.4, and 36.5±1.5 with ACD CPR alone versus 19.1±1.0, 43.3±1.6, and 56.4±1.7 with ACD plus valve (P<0.001 between groups). ROSC was observed in 2 of 10 patients with ACD CPR alone after 26.5±0.7 minutes versus 4 of 11 patients with ACD CPR plus ITV after 19.8±2.8 minutes (P<0.05 for time from intubation to ROSC).

Conclusions—Use of an inspiratory resistance valve in patients in cardiac arrest receiving ACD CPR increases the efficiency of CPR, leading to diastolic arterial pressures of >50 mm Hg. The long-term benefits of this new CPR technology are under investigation. (Circulation. 2000;101:989-994.)

Key Words: cardiopulmonary resuscitation ■ heart arrest ■ circulation ■ active compression-decompression

Active compression-decompression (ACD) cardiopulmonary resuscitation (CPR) was recently introduced as an alternative to standard manual CPR.1–4 Founded on the principle that active chest wall decompression during ACD CPR would enhance negative intrathoracic pressure during the “relaxation” phase and thereby increase venous return, this method of CPR has been reported to increase CPR efficiency in both animal models and in patients in cardiac arrest.1–7 More recently, we recognized the importance of impedance to inspiration during ACD CPR in order to further enhance the negative pressure during the decompression phase.4,8,9 On the basis of a mechanism similar to the clinical Mueller maneuver, inspiratory impedance has been demonstrated to increase vital organ blood flow by >50% using either standard or ACD CPR in a porcine model of ventricular fibrillation.8,9 Building on the results of ACD CPR in France, where hospital discharge rates were found to be significantly improved with ACD CPR compared with standard CPR,7 we evaluated the potential benefit of ACD CPR plus a new inspiratory impedance threshold valve (ITV) in patients with out-of-hospital cardiac arrest. In this prospective and blinded pilot study, subjects were randomized to receive either ACD CPR alone or ACD CPR plus the valve. Acute hemodynamic parameters were evaluated.

Methods
This study was performed in Paris France in October 1997 after receiving approval from the Consultative Council for the Protection of Persons volunteering for Biomedical Research. The prehospital emergency response chain of survival in Paris, France is 2-tiered, as recently described.7 After receiving a call for help, a basic life
support (BLS) vehicle and a mobile intensive care unit (MICU) were simultaneously dispatched to the scene. Because of a greater number of BLS vehicles covering a given region, they were frequently closer to the patient and could start BLS before the arrival of the MICU. There were at least 3 emergency medical technicians (EMTs) in each BLS vehicle together with a chief. As recommended by the Utstein style, BLS was not performed in patients with irreversible death (“decapitation, incineration, decomposition, rigor mortis, or dependent cyanosis”) or do-not-resuscitate orders.10 BLS was performed with ACD CPR according to the recommendations of the manufacturer (Ambu Inc, Glostrup, Denmark) and of Wik et al11 and Schneider et al.12 Members of the rescue team performed ACD CPR for 3 to 5 minutes and then alternated to avoid fatigue. ACD CPR was performed at a rate of 90 compressions-decompressions per minute, controlled by a metronome. Ventilation was performed with a bag-mask system with supplemental O2.

The MICU staff included 5 persons. A MICU physician (anesthesiologist or general practitioner specially trained in emergency medicine), a nurse anesthetist, a medical student, and an ambulance driver managed the patient and helped for the performance of the protocol. In addition, there was another physician (anesthesiologist) at the scene to coordinate the research protocol. According to standard guidelines governing the French EMS system, patients with known terminal illness or in whom the delay between cardiac arrest and basic CPR exceeded 30 minutes did not receive advanced life support (ALS) CPR. Patients younger than 18 years old and those with hypothermia or thoracic trauma were also excluded from the study. The BLS and ALS teams worked together under the supervision of the EMT chief and the MICU physician. The ALS team also performed ACD CPR.

Evaluation of the rhythm was made by the MICU staff. For patients in ventricular fibrillation, European Resuscitation Council as well as American Heart Association guidelines were followed.13,14 For patients in asystole and pulseless electrical activity, ACD CPR was performed continuously by the MICU staff for a minimum of 30 minutes, unless return of spontaneous circulation was achieved. No attempt was routinely made to try to pace patients who were in asystole during the resuscitation effort. Epinephrine (1 mg) was administered every 5 minutes throughout the resuscitation effort.

All patients were intubated with an endotracheal tube on arrival of the MICU team. Following intubation, patients were mechanically ventilated with a compressible ventilator bag (Ambu Spur, Ambu Inc) with 100% oxygen. Ventilation was provided with 10 L/min oxygen, at a rate of 15 breaths/min with a tidal volume of ~10 mL/kg of patient’s weight. Monitoring of tidal volume was made by a spirometer of Wright fixed just before the inspiratory part of the ventilator bag (Figure 1). This valve comprises a highly compliant silicone diaphragm, a fenestrated mount, and a safety “pop-off” valve attached to the side of the device and set to open when the intra-thoracic pressure decreases below ~22 cm H2O. The principle of the valve is to completely occlude the endotracheal tube when the pressure within the thorax is below atmospheric pressure. As such, the valve prevents inspiratory gas exchange only during the compression phase, except during the time that active ventilation is being performed by the rescuer. In practice, when the patient is actively ventilated with the ventilator bag, oxygen is passed through the fenestrated mount of the valve during insufflation directly into the endotracheal tube without any significant impedance. When active ventilation is not performed, the silicone diaphragm occludes the airway whenever the intrathoracic pressure is <0 cm of water, i.e., during the active compression phase. During exhalation and during the compression phase of CPR, respiratory gases pass in the reverse direction, pushing the silicone diaphragm out of the way without any resistance by the valve.

Using a computer-generated randomization chart, some of the valves were either enabled with the silicone diaphragm (ACD + ITV group) or disabled and the diaphragm was removed (ACD alone group). During the protocol study, it was not possible for the MICU staff to determine by visual inspection whether or not the silicone diaphragm was in place or had been removed. As such, they were blinded to the investigational device. When the diaphragm is removed, the valve does not impede inspiration, as there is a completely open conduit between the ventilator bag and the endotracheal tube. As such, gas exchange is not impaired and inhalation and exhalation are performed without any significant resistance. The randomization assignment was made before the beginning of the protocol by the hospital sterilization service. During performance of CPR and throughout the subsequent hospitalization, investigators were blinded to whether the impedance valve did or did not contain a functional diaphragm. After each use by the MICU staff, the valve was brought to this service for cleaning, and the sterile valve was then returned to the study physician in a bag with or without the diaphragm according to the randomization list.

Once patients were intubated by the MICU physician, a peripheral intravenous line was placed for drug administration. Femoral arterial (Seldicath, 5F, 12 cm, Plastimed, France) and venous cannula were placed sequentially by the study physician. A central venous cannula (2F, 60 cm, Seldiflex, Plastimed, France) introducer sheath was advanced 60 cm in the cranial direction in order to position the distal tip into the thoracic portion of the inferior vena cava. Arterial and central venous pressures were continuously monitored with heparinized fluid-flushed tubing to transducers (Sorensen Transpac III, Abbott Systems) and a monitoring system (Propac Encore, Physio-Control). Transducers were calibrated and fixed to the midaxillary line of the patient. End tidal CO2 (ETCO2) was monitored continuously after intubating the patients with a capnograph (Normocap, Datex). Data from each patient were collected and analyzed to determine the ETCO2 and the arterial and right atrial pressures. The coronary perfusion pressure was calculated as the mathematical difference between arterial and right atrial pressures at the end of the relaxation phase of CPR.9,15 Hemodynamic parameters were monitored simultaneously at both catheter sites, and measurements were made every 5 minutes, just before a new epinephrine injection. If return of spontaneous circulation was achieved, CPR was discontinued and the impedance valve was removed. Patients were then ventilated with a portable volumetric ventilator (AXR1, Airox, Datex).
TABLE 1. Baseline Characteristics of the Patients Assigned to Active Compression-Decompression (ACD) or ACD Plus an Impedance Threshold Valve (ACD+ITV) CPR

<table>
<thead>
<tr>
<th></th>
<th>ACD (n=10)</th>
<th>ACD+ITV (n=11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, %</td>
<td>80</td>
<td>63.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Mean age, y (SD)</td>
<td>52.6 (24)</td>
<td>64 (14.8)</td>
<td>0.21</td>
</tr>
<tr>
<td>Suspected cardiac etiology, %</td>
<td>40</td>
<td>63.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Initial cardiac rhythm, asystole, %</td>
<td>100</td>
<td>100</td>
<td>. .</td>
</tr>
<tr>
<td>Witnessed cardiac arrest, number (%)</td>
<td>6 (60)</td>
<td>9 (81.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Bystander CPR, number (%)</td>
<td>2 (25)</td>
<td>2 (18.2)</td>
<td>0.83</td>
</tr>
<tr>
<td>Event-to-event intervals, min (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collapse to BCLS CPR</td>
<td>5.5 (6.2)</td>
<td>7.8 (5.9)</td>
<td>0.5</td>
</tr>
<tr>
<td>Collapse to ACLS CPR</td>
<td>18.8 (7.9)</td>
<td>20.8 (8.4)</td>
<td>0.6</td>
</tr>
<tr>
<td>Total duration of ACLS CPR (SD)</td>
<td>29.3 (1.5)</td>
<td>26.3 (5.4)</td>
<td>0.1</td>
</tr>
</tbody>
</table>

ACLS indicates advanced cardiac life support; and BCLS, basic cardiac life support.

Results

Thirty-three consecutive patients in cardiac arrest were eligible for the study protocol. Three patients were excluded because they had a return of spontaneous circulation (ROSC) within the first 10 minutes after intubation (2 ACD alone patients, 1 ACD plus valve patient) and consequently, no hemodynamic measurements could be performed. The first recorded rhythm in all patients was obtained at the time of the arrival of the mobile intensive care vehicle, ~20 minutes after cardiac arrest. Five patients in asystole and 4 patients in ventricular fibrillation were also excluded because simultaneous femoral arterial and venous access could not be obtained within 10 minutes (6 in the ACD alone group, 3 in the ACD plus valve group). Twenty-one patients were prospectively enrolled in this study. Ten patients were randomized to the ACD CPR group and 11 were randomized to receive ACD CPR plus valve. As shown in Table 1, the groups were similar in terms of gender, age, suspected cardiac etiology of cardiac arrest, initial rhythm, percentages of witnessed cardiac arrests and bystander CPR, and time intervals from collapse to arrival of BLS and ALS.

As shown in Figure 2, ETCO2 levels were similar at the time of intubation (t=0), but rose more rapidly and to higher peak values in the ACD plus valve group compared with ACD CPR alone. These data include all ETCO2 measurements while patients were receiving CPR. In the ACD alone group, mean ETCO2 (mean±SEM) levels increased from 6.6±2.3 to 13±0.9 mm Hg during CPR, whereas in the ACD plus valve group, ETCO2 increased from 6.9±0.5 to 19.1±0.9 mm Hg (P<0.001 comparing maximum values). The 95% CIs for comparison of baseline ETCO2 values between groups were 1.6, 2.2 and 2.2, 9.2 for maximal values during CPR. There were fewer data points in the later time periods because some patients were resuscitated. As shown in the insert of Figure 2, in individual patients that were resuscitated, ETCO2 increased to >20 mm Hg, at which point asystole converted spontaneously to a stable blood perfusing rhythm. In these patients, sinus rhythm was restored and no additional CPR was required. This process occurred more rapidly in the impedance valve group. No patient with an ETCO2 <20 mm Hg was resuscitated during the 30-minute period of ACD CPR after intubation.

At the time the invasive monitoring was initiated (t=10 minutes), there were marked differences between groups when comparing the arterial pressures (Figure 3). There was no evidence for a compression phase gradient between the arterial
and right atrial pressures. The mean peak arterial pressures, which were observed 10 minutes after intubation in both groups, were 90±6.6 mm Hg in the ACD CPR alone group versus 108±3.1 in the valve group (P=0.05). The maximal mean diastolic arterial pressure in the ACD CPR plus valve group was 56.4±1.7 mm Hg versus 36.5±1.5 mm Hg in the ACD alone group (P<0.001; 95% CI, 14.3, 23.8). Patients who had ROSC (Figure 3 insert) had higher diastolic arterial pressures in the ACD CPR plus valve group compared with ACD CPR alone.

A comparison between the coronary perfusion pressures in patients treated with ACD plus valve CPR versus ACD CPR alone is shown in Figure 4. The maximal diastolic coronary perfusion pressure with ACD CPR plus valve was 43±1.6 mm Hg versus 25.3±1.8 mm Hg for ACD CPR alone (P<0.001; 95% CI, 12.4, 22.8). The mean coronary perfusion pressure was 70% higher in the ACD CPR plus valve group when compared with the group given ACD CPR alone. With ACD CPR plus valve, patients with a coronary perfusion pressure >40 mm Hg appeared to have a greater likelihood of ROSC.

In the present study, the first recorded rhythm for all the patients was asystole. Results related to time from intubation to ROSC, survival to 24 hour, survival after day 30, and survival to hospital discharge without neurological impairment are also shown in Table 2 for both groups of patients. There was a significant reduction in the time between intubation and ROSC in the valve group (n=4; t=19.8±2.8 minutes) versus ACD alone group (n=2; t=26.5±0.7 minutes) (P=0.03).

Discussion

This preliminary evaluation of a new inspiratory threshold valve focused on the acute hemodynamic effects of this valve...
during the performance of ACD CPR. Use of an impedance threshold valve to augment decompression phase-negative intrathoracic pressure during performance of ACD CPR resulted in a significant improvement in overall CPR efficacy. ETCO$_2$, systolic and diastolic arterial pressures, and coronary perfusion pressure were all higher when compared with ACD CPR alone. The mean diastolic blood pressures were $>50$ mm Hg in the ACD plus valve group. Results from this first demonstration of the use of an impedance valve during CPR in humans in cardiac arrest are similar to those we have previously observed in animal studies,\textsuperscript{8,9} whereas the hemodynamic values found in the ACD CPR alone group are comparable with other human studies.\textsuperscript{16} In addition to improving hemodynamics, 4 of 11 patients had a ROSC with ACD CPR with the use of ACD CPR plus the impedance valve after a significantly shorter period of total CPR time (19.8 $\pm$2.8 minutes), compared with 2 of 10 patients with ACD alone after a longer total CPR time (26.5 $\pm$0.7 minutes).

ETCO$_2$ has previously been used as a surrogate for cardiac output and blood flow through the lungs, although it is affected both by blood flow and by minute ventilation.\textsuperscript{17} The measurement of ETCO$_2$ as a surrogate for survival depends on several parameters, especially on minute ventilation. It has been previously shown that ACD CPR increased minute ventilation even during mechanical ventilation as compared with standard CPR.\textsuperscript{18,19} As such, measures of ETCO$_2$ may be underestimated with ACD CPR.\textsuperscript{20} In contrast, because the impedance valve impedes gas exchange except during active manual ventilation, measured ETCO$_2$ during ACD CPR plus the valve may be overestimated. Nonetheless, in the present study the higher ETCO$_2$ values observed in the valve group were associated with a significant improvement in hemodynamic variables, such as systolic and diastolic arterial and coronary perfusion pressures and a shorter time between intubation and ROSC.

Information related to the initial cardiac rhythm in Paris is not known until the arrival of the ALS team, about 13 minutes after initiation of BLS CPR. In the present study the first recorded rhythm was asystole in all patients. This rhythm is generally associated with the worst outcome.\textsuperscript{7,21,22} However, recent studies from Paris, France, where $>80\%$ of patients were in asystole, have demonstrated that ACD CPR results in a significant improvement in a number of clinical outcomes, including hospital discharge rates (5.5%),\textsuperscript{7,21} and 1-year survival rates (4.6%)\textsuperscript{21} when compared with standard CPR (1.9% and 1.9%,\textsuperscript{21} respectively). As such, the hemodynamic improvement achieved by optimizing the bellows-like action of the chest with ACD CPR plus the impedance valve, as observed in the present study, suggest that patients in asystole may have an even greater chance for survival than previously considered.\textsuperscript{2}

One of the limitations of the present study was that ACD CPR plus the valve could not be evaluated in patients with ventricular fibrillation, as we could not insert intravenous and arterial femoral lines in $<10$ minutes due to the multiple defibrillation attempts. Thus, although a benefit of the valve has previously been observed in animals,\textsuperscript{9} its potential value for patients in ventricular fibrillation remains unknown. A second limitation is that arterial blood gases were not measured in the present study. We have previously observed in the animal model that the partial pressure of arterial oxygen, PaO$_2$, was decreased in the ACD CPR plus valve group relative to ACD CPR alone, although PaO$_2$ values remained $>95$ mm Hg during CPR.\textsuperscript{8} Given the potential for decreased oxygenation despite active ventilation, PaO$_2$ will have to be evaluated in the future. Another limitation is that femoral arterial pressures were used to calculate the coronary perfusion pressures instead of central aortic monitoring. We used a femoral arterial catheter because it is the standard of clinical practice in intensive care units. However, femoral arterial pressure measurements in cardiac arrest have been previously reported to be comparable with aortic pressures during both compression and relaxation phases of CPR in humans.\textsuperscript{23} Finally, due to previous lack of benefit associated with pacing patients in asystole in Paris, no efforts were made to externally pace the patients. Given the elevated diastolic arterial pressures and coronary perfusion pressures achieved with ACD CPR plus valve, pacing will be tried in future studies.

It is too early to know whether use of the impedance valve will improve the chances for long-term survival. This study was designed to evaluate acute hemodynamic parameters in patients with recent cardiac arrest in a well-controlled clinical environment. Larger prehospital studies are therefore needed to evaluate the likelihood of improved long-term survival with neurological recovery with this new technique. Nonetheless, this study demonstrates that use of an inspiratory impedance valve during CPR further optimizes mechanical measures associated with ACD CPR by increasing venous return and coronary perfusion pressures. Diastolic arterial pressures and coronary perfusion pressures recorded in this study with an impedance valve are $>70\%$ higher than those achieved with ACD CPR alone. These findings further underscore the importance of lowering intrathoracic pressure during the decompression phase of CPR. On the basis of these promising findings, prospective randomized clinical trials are underway to determine potential long-term value of combining ACD CPR with an impedance threshold valve in patients with cardiac arrest.

**Acknowledgment**

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<table>
<thead>
<tr>
<th>Outcome number (%)</th>
<th>ACD (n=10)</th>
<th>ACD+ITV (n=11)</th>
<th>P</th>
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<tbody>
<tr>
<td>ROSC</td>
<td>2 (20)</td>
<td>4 (36.4)</td>
<td>0.4</td>
</tr>
<tr>
<td>H+24</td>
<td>2 (20)</td>
<td>3 (27.3)</td>
<td>0.7</td>
</tr>
<tr>
<td>Day+30</td>
<td>2 (20)</td>
<td>2 (18.2)</td>
<td>0.9</td>
</tr>
<tr>
<td>Hospital discharge</td>
<td>1 (10)</td>
<td>1 (9.1)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

H+24 indicates survival after 24 hours; Day+30, survival after 30 days; and Hospital discharge, hospital discharge without neurological impairment.
References
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